



Copper-free asymmetric allylic substitution with Grignard reagents : a new route to enantioenriched allylsilanes

Rubén Pérez Sevillano

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Sorbonne Université

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Institut Parisien de Chimie Moléculaire / Equipe ROCS

**Copper-free asymmetric allylic substitution with
Grignard reagents: a new route to enantioenriched
allylsilanes**

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Thèse de Doctorat de Chimie

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Dedicado

A mi familia

A Laura

Y a todos los que se fueron demasiado pronto

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List of Abbreviations

AAA	Asymmetric allylic alkylation
AAR	Asymmetric allylic arylation
AAS	Asymmetric allylic substitution
ACA	Asymmetric conjugate addition
CSI	Chlorosulfonyl isocyanate
DCE	Dichloroethane
DMF	<i>N,N</i> -Dimethylformamide
DEAD	Diethyl azodicarboxylate
DFT	Density functional theory
DIAD	Diisopropyl azodicarboxylate
DIBAL	Diisobutylaluminium hydride
DIPEA	<i>N,N</i> -Diisopropylamine
DMAP	4-(Dimethylamino)pyridine
DTBM	Di- <i>tert</i> -butyl-4-methoxyphenyl
EAS	Enantiomeric allylic substitution
EWG	Electron withdrawing group
GC	Gas chromatography
HMPA	Hexamethylphosphoramide
HPLC	High-performance liquid chromatography
IBS	Intramolecular bis-silylation
LA	Lewis acid
LB	Lewis base
LDA	Lithium di-isopropylamide
LDBB	Lithium di- <i>tert</i> -butylbiphenylide
LHMDS	Lithium bis(trimethylsilyl)amide
LG	Leaving group
MOP	Monophosphine
MP2	Second order Moller-Plesset perturbation
MTBE	Methyl <i>tert</i> -butyl ether
NBO	Natural bond orbital
NBS	N-Bromosuccinimide
NCS	<i>N</i> -Chlorosuccinimide
NHC	<i>N</i> -Heterocyclic carbene
NMP	<i>N</i> -Methyl-2-pyrrolidone
NMR	Nuclear magnetic resonance
PG	Protecting group
<i>rac</i> BINAP	(±)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene
RCM	Ring close metathesis
Red-Al	Sodium bis(2-methoxyethoxy)aluminum hydride

SET	Single electron transfer
TES	Triethylsilyl
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
9-BBN	9-Borabicyclo[3.3.1]nonane

General Introduction

Symmetry seems to prevail in the nature at first sight. However, if we look a little further and deeper, this is far from the truth since asymmetry rules our life. For instance, the double helix of the DNA is not symmetric, our lungs have different number of bronchi, lobes and size, even the heart is not positioned in the centre of human body.

When we come down to the molecular level, this asymmetry is exacerbated: building materials present in the tissues of living beings such as sugars and amino acids, as well as the enzymes and receptors involved in metabolic and regulatory processes are not symmetric. As consequence, geometric structural requirements are present and needed in most of the molecules, particularly to develop biological activities. Interestingly, asymmetric molecules behave differently depending on their chiral environment. Because of that, when a chiral centre is present in a bioactive molecule, one exclusive enantiomer is usually responsible for the desired physiological effect (the other can be inactive, less active or produce adverse effects).

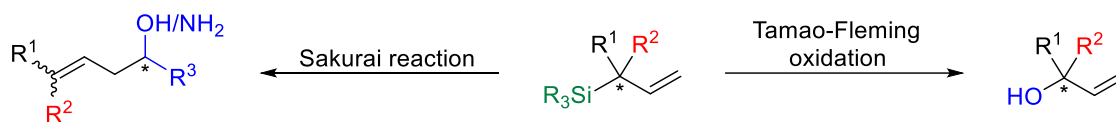
Moreover, efficient carbon-carbon, carbon-heteroatom and heteroatom-heteroatom bond formation is crucial in the synthesis of complex organic molecule such as natural products or pharmaceutical compounds. Because architectural and geometrical changes have dramatic effects on the properties of the molecules, there is a continuous ongoing development of chemical reactions to design and construct stereodefined organic scaffolds. In this context, among all the asymmetric synthesis strategies, metal-catalyzed processes are certainly the most studied and widespread methods whether in academia or in industry, highlighting those involving palladium or copper.

Although many are extremely efficient methods, the emergence of green chemistry and atom economy concepts where the environmental impact of chemistry is sought to be reduced to the minimum and the generation and use of hazardous products eliminated, asymmetric synthesis procedures where no metal are entailed have gained importance in the recent years. Furthermore, this type of strategies overcome other lifetime problems related with the sustainability and price (abundance, energy consuming processes, waste generated) of metal-based processes.

On the other side, in the last 30 years, the synthesis of asymmetric allylsilanes have raised a lot of interest. They are versatile building blocks and linchpins used for the preparation of complex molecules and molecular systems. Nowadays, they rank high as one of the most useful organic scaffolds due to the large number of transformations that can undergo through both its carbon-silicon and carbon-carbon double bond,^[1] and the large number of functional groups and reaction conditions that are tolerated. All these characteristics allow them to occupy a unique place in the armory of the organic chemist.

In view of the importance of the above-mentioned considerations, we envisioned to set up a new transition-metal free procedure to add into the extensive developed portfolio of synthesis

strategies that allow to access chiral allylsilanes. Our approach relies on the asymmetric allylic alkylation of silicon-substituted electrophiles with organomagnesium reagents in the presence of chiral NHC ligands to access enantioenriched allylsilanes. These molecules will be subsequently submitted to different type of functionalization reactions such as Tamao-Fleming oxidation or Sakurai reaction (**Scheme 1**).



Scheme 1. Functionalization of chiral allylsilane by Sakurai reaction and Tamao-Fleming oxidation.

The first part of this manuscript will be devoted to the state of the art regarding the asymmetric allylsilanes and the different synthesis strategies described in literature for their preparation. In the second part, the copper-free allylic substitution will be investigated for accessing chiral allylsilanes bearing a silyl-substituted tertiary and quaternary stereogenic centres with different silyl moieties.

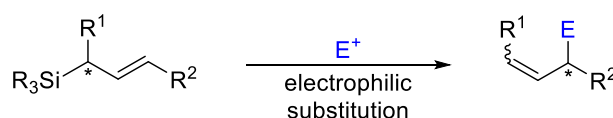
PART I:
ASYMMETRIC ALLYLSILANES
OVERVIEW

1 Asymmetric allylsilanes overview

1.1 Allylsilanes introduction

Allylsilanes have demonstrated to be particularly interesting and useful as synthons with many different applications not only in organic chemistry,^[1–4] but also in material science^[5] and medicinal chemistry.^[6] Due to their weak polarization resulting from the low electronegativity difference between both carbon and silicon atoms, the carbon-silicon bond is relatively robust, endowing these molecules with a high bench-stability and easy-handling. These features along with their low toxicity and functional group tolerance, allow allylsilanes to occupy a unique place in the armoury of the organic chemist. As a result, these molecules have attracted the interest of many scientists. In this regard, tremendous efforts and investigations, especially in the last 50 years, has been devoted to the design and development of efficient, green, direct, and simple synthetic approaches to access them. These incredible silicon-based scaffolds can undergo a great variety of silyl transformations and serve as exceptional versatile linchpins in synthetic chemistry. Depending on the nature of the process in which they are involved, allylsilanes can react regioselectively, illustrating the diverse functionalization that can be reached starting from them.^[1]

Some of these transformations include fluorodesilylation,^[7,8] ring closing and cross-metathesis reactions,^[9,10] coupling reactions (both Hiyama and Hiyama-Denmark type),^[11,12] oxidations,^[13,14] amination,^[15,16] cyclopropanations,^[17] and [2+2],^[18–20] [3+2],^[21–24] [4+2]^[25] and [4+3]^[26] annulations to access carbo- and heterocycles. Particularly interest have raised these molecules as the carbon-silicon bond can react stereoselectively in the presence of a wide variety of electrophiles (transfer of stereochemistry in these reactions when chirality lies between the silicon and the unsaturation is generally high, **Scheme 2**).^[27–30] This transformation allows the addition of allyl group,^[1–3,31] converting these molecules into convenient intermediates to perform carbon-carbon bond formation through S_E2' -mechanism. Interestingly, this reactivity represents a complementary method to the enolate based aldol reaction used in organic chemistry, depicting one of the most powerful ways to generate homoallylic alcohol derivatives.



Scheme 2. Allylsilane reaction with electrophiles.

Many of the previous-mentioned transformations, for instance the Hosomi-Sakurai reaction, can be carried out in a regiospecific and stereocontrolled manner, and as

consequence, the stereochemical outcome of the reactions depends on the configuration of the starting allylsilanes. Because of that, procedures where the nature of the silyl moiety, olefin geometry and absolute stereochemistry can be easily tuned are sought (**Figure 1**). Nevertheless, a general synthetic route that accomplishes all these requisites is not yet established and its development remains a great challenge.

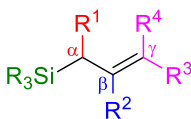


Figure 1. General allylsilane.

1.2 Preparation of asymmetric allylsilanes

The construction of molecules and molecular systems transcends many areas of science. The necessity from some fields such as agriculture, electronics, textile or medicine, to name only a few, of novel sophisticated compounds provides a huge driving force to continue developing new routes to access novel molecules. In this regard, allylsilanes are very useful and versatile organometallic-type reagents extensively used in organic synthesis (preparation of natural^[32] and non-natural molecules) and other chemistry fields, because of the large number of transformations they can undergo.^[1–3,32–35] Because of that, their synthesis has been deeply investigated and several reliable reaction protocols have been developed for their preparation. As they can undergo several stereoselective transformations, their preparation in an enantioenriched way is highly desirable and considerable studies have been made focused in finding new routes for their preparation. During these investigations, physical and theoretical studies, extrapolations from described knowledge and serendipity have helped to identify new enantioselective synthetic routes. Great efforts from the chemists have allowed to translate vague notions to specific structures and knowledge allowing them to execute multistep sequences and to develop novel routes. All these developments have increased the degree of sophistication employed to solve different problems and challenges, requiring increasing complex molecular structures. Hereafter, an overview of the different enantioselective strategies described throughout history will be provided. This section will be divided in two main parts. In one hand, we will present those strategies based on a carbon-silicon bond formation. On the other hand, the second part will be dedicated to those approaches that used silicon substituted substrates.

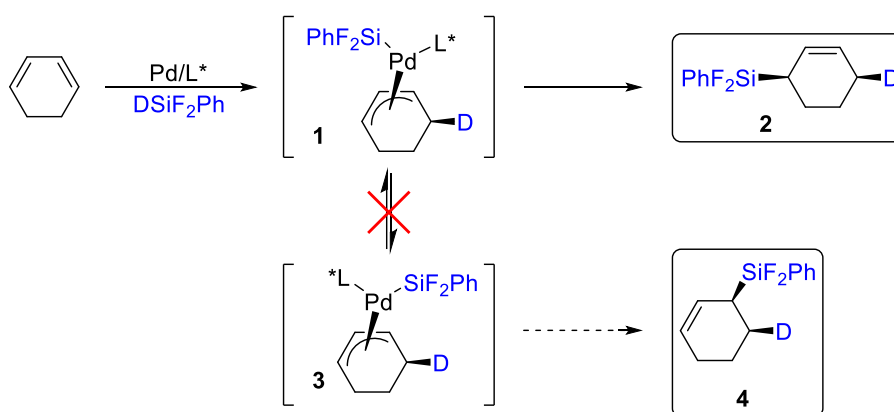
1.2.1 Stereoselective Si-C bond formation

1.2.1.1 1,4-Hydrosilylation of 1,3-dienes

The preparation of enantioenriched allylsilanes through palladium-catalyzed asymmetric hydrosilylation of 1,3-dienes is one of the most effective catalytic strategies ever developed. Since this first reports in the early 80's, where Hayashi's group unveiled the first asymmetric palladium(II)-catalyzed hydrosilylation of cyclic and acyclic 1,3-dienes,^[36,37] many efforts have been made to develop catalytic systems for the high enantioselective hydrosilylation of these unsaturated molecules.

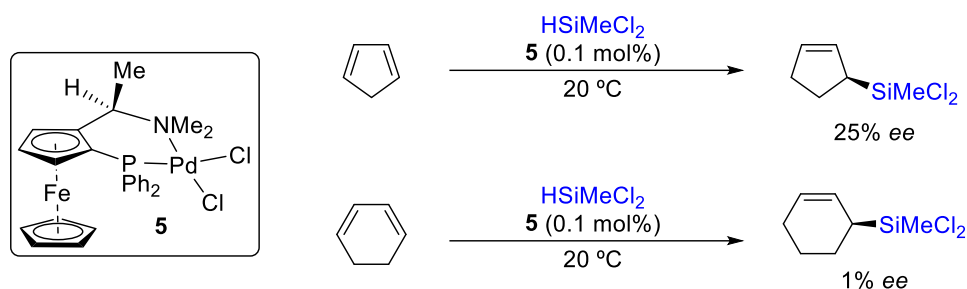
1.2.1.1.1 Cyclic 1,3-dienes

This type of hydrosilylation is thought to proceed in a 1,4-fashion to provide the targeted molecules through a single isomer as it was proved by deuterium-labelled studies over 1,3-cyclohexadiene (**Scheme 3**).^[38] The 1,4-regiochemistry and *cis*-fashion of the addition to the diene observed in allylsilane **2** may demonstrate that the allylic silanes are produced *via* (π -allyl)palladium intermediate **1** and that there is no equilibrium with **3** as no trace of allylsilane **4** was detected. By analogy, the same mechanism is considered to happen in acyclic 1,3-dienes.



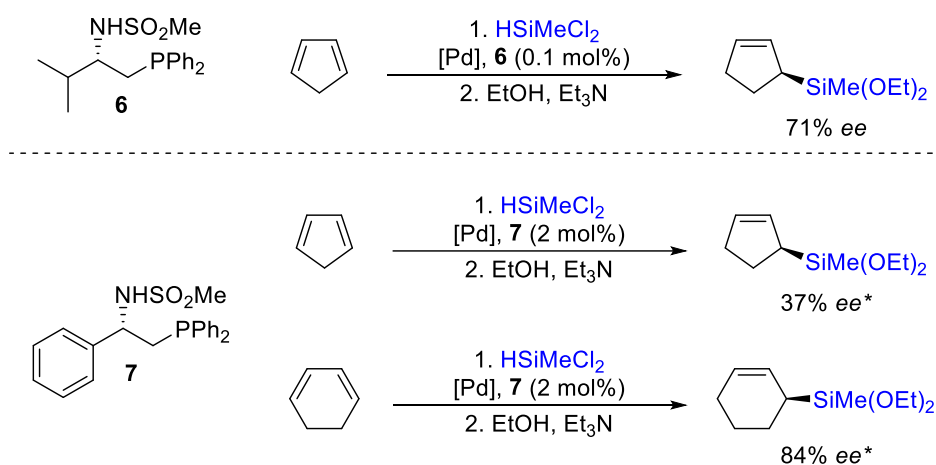
Scheme 3. 1,4-Mechanism during hydrosilylation of 1,3-dienes.

Hayashi reported the first palladium(II)-catalyzed hydrosilylation of cyclic 1,3-diene in 1983 using HSiMeCl_2 as silicon source and the ferrocenylmonophosphine ligand **5** as chiral catalyst (**Scheme 4**).^[37] It was possible to prepare optically active cyclic allylsilanes, albeit in quite poor ee (1-25%).



Scheme 4. First synthesis of cyclic chiral allylsilanes.

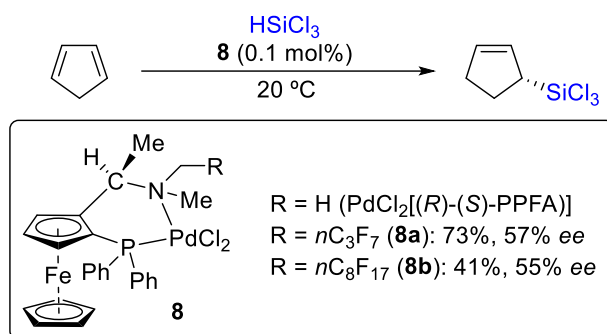
Few years later, palladium complexes of chiral (β -*N*-sulfonylaminoalkyl) phosphines were envisioned to perform the hydrosilylation of cyclopentadiene and 1,3-cyclohexadiene to give the corresponding allylsilanes in moderate enantioselectivities (37-84% ee, **Scheme 5**).^[39,40]



*Measured from the corresponding alcohols after treatment with $\text{KF}/\text{H}_2\text{O}_2$

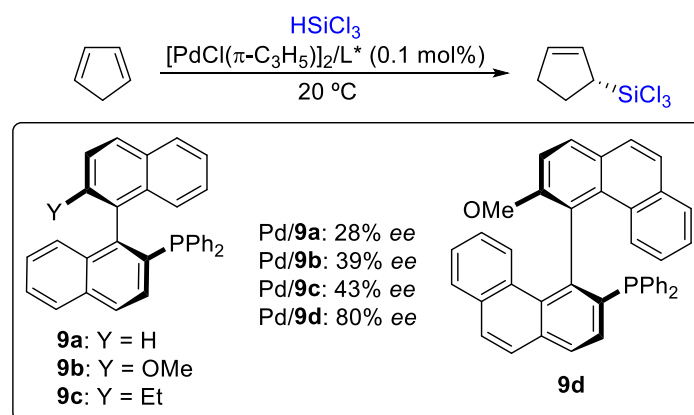
Scheme 5. Preparation of enantioenriched cyclic allylsilanes using (β -*N*-sulfonylaminoalkyl) phosphines.

Later on, the enantiomeric excesses obtained from cyclic 1,3-dienes were significantly improved by increasing the solubility of the palladium(II) catalyst in the reaction mixture via the introduction of perfluoroalkyl groups ($n\text{C}_3\text{F}_7$ and $n\text{C}_8\text{F}_{17}$) on the nitrogen atom of the phosphine ligand. With such ligands, the highly soluble palladium(II) catalyst is more active under mild conditions leading up to 57% ee with HSiCl_3 from cyclopentadiene (**Scheme 6**).^[41,42]



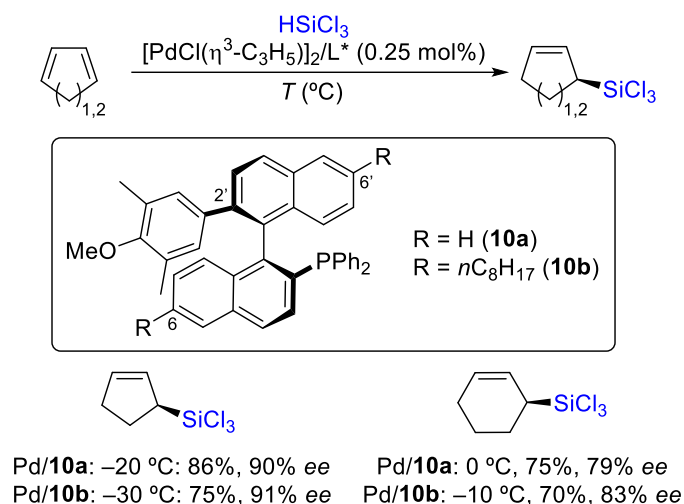
Scheme 6. Catalyzed asymmetric hydrosilylation of cyclopentadiene with HSiCl_3 in the presence of soluble palladium(II) complexes **8a** and **8b**.

Interestingly, later they were able to increase the ee using the organofluorosilanes HSiF_2Ph in the presence of 1 mol% palladium catalyst generated from $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2$ and (*R*)-(*S*)-PPF-OAc ($\text{Pd:PPF} = 1:2$) on 1,3-cyclohexadiene, to obtain the desired product with 77% ee.^[43,44] Despite increasing the ee's in the case of 1,3-cyclic dienes with HSiCl_3 , these results were still mediocre. To overcome this poor enantioselectivity, in the middle 90's, the same group reported the preparation and use of a new class of palladium(II) binaphthyl catalysts incorporating axially chiral monophosphines (MOP).^[38,45,46] The active palladium(II) complexes were *in situ* generated from $[\text{PdCl}(\pi\text{-C}_3\text{H}_5)]_2$ and MOP ligands ($\text{Pd:MOP} = 1:2$). Amongst all MOP ligands tested, the 4,4'-biphenanthryl one **9d** gave the best result since the hydrosilylation product of cyclopentadiene was obtained in 92% yield and 80% ee by the reaction with HSiCl_3 in the presence of 0.1 mol% of catalyst at 20 °C (**Scheme 7**).



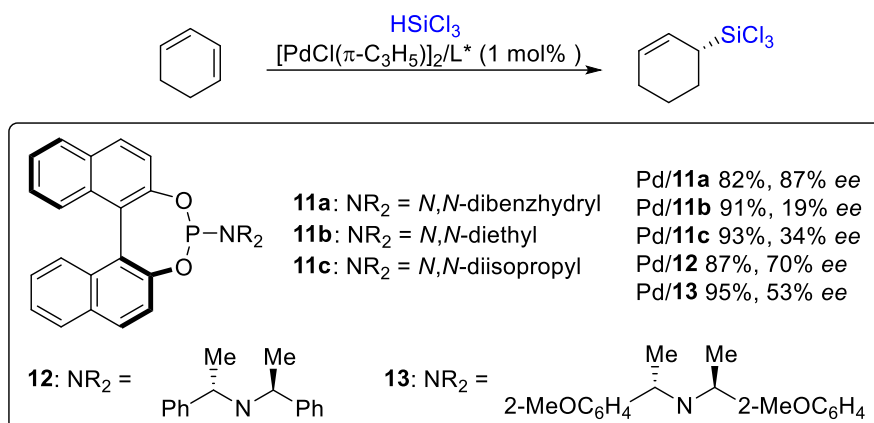
Scheme 7. Asymmetric hydrosilylation of cyclopentadiene with HSiCl_3 catalyzed by palladium(II)-MOP complexes.

Assuming that the presence of bulky groups in the MOP ligand would result in an increased enantioselectivity, various 2'-aryl-1,1'-binaphthyls were envisioned as ligands.^[47,48] In addition of the bulkiness of the aryl moiety, the study showed that an electron-donating group at the C₄-position of the aryl group led to a higher enantioselectivity. Thus, carrying out the hydrosilylation of cyclopentadiene with HSiCl_3 at $-20\text{ }^\circ\text{C}$ in the presence of 0.25 mol% of palladium(II) catalyst, *in situ* generated from $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2$ and phosphine ligand **10a** ($\text{Pd:phosphine} = 1:2$), furnished the expected allylsilane in 72% yield with 90% ee (**Scheme 8**). Under the same conditions, 1,3-cyclohexadiene was slightly less reactive at $0\text{ }^\circ\text{C}$, giving the corresponding product in 75% yield with a significantly lower 79% ee. Nevertheless, improved enantioselectivities were obtained in both cases by introducing octyl substituents on the C₆- and C_{6'}-positions of the binaphthyls. By increasing the solubility of the catalyst (generated from chiral phosphine ligand **10b** as mentioned previously), the reaction could proceed at a lower temperature resulting in a 91% and 83% ee for cyclopentadiene and 1,3-cyclohexadiene, respectively.^[48]



Scheme 8. Asymmetric hydrosilylation of cyclopentadiene and 1,3-cyclohexadiene with HSiCl_3 catalyzed by palladium(II)-phosphines **10** complexes.

Phosphoramidite ligands also provided 3-(trichlorosilyl)cyclohexene in very good 75-95% yield. The steric bulkiness of the amine substituents played a crucial role regarding the enantioselectivity of the hydrosilylation (**Scheme 9**).^[49]

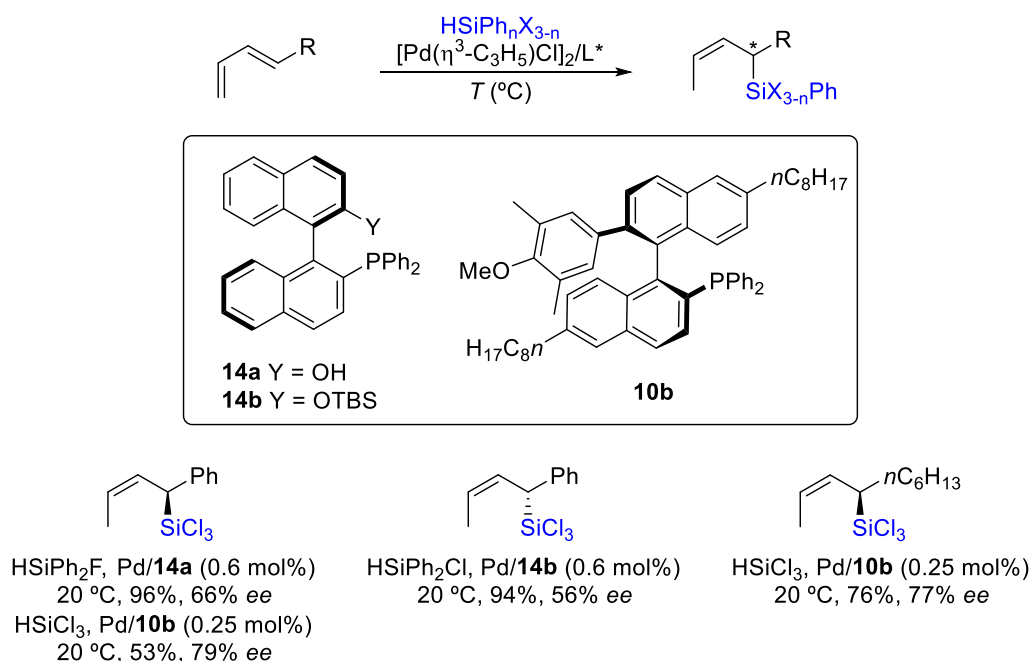


Scheme 9. Synthesis 3-(trichlorosilyl)cyclohexene with different phosphoramidite ligands.

3-(trichlorosilyl)cyclohexene with 87% ee (being the highest enantioselectivity reported in the hydrosilylation of 1,3-cyclohexadiene) and 82% yield could be obtained in the presence of 1 mol% of palladium catalyst formed *in situ* by mixing $[\text{PdCl}(\pi\text{-C}_3\text{H}_5)_2]$ and phosphoramidite N,N -dibenzhydryl ligand (Pd:ligand = 1:2), at 20 $^\circ\text{C}$ for 20 h. Yield can be improved to 97% (but not the ee) by decreasing the temperature to -10 $^\circ\text{C}$ and leaving the reaction for 84 h.

1.2.1.1.2 Acyclic 1,3-dienes

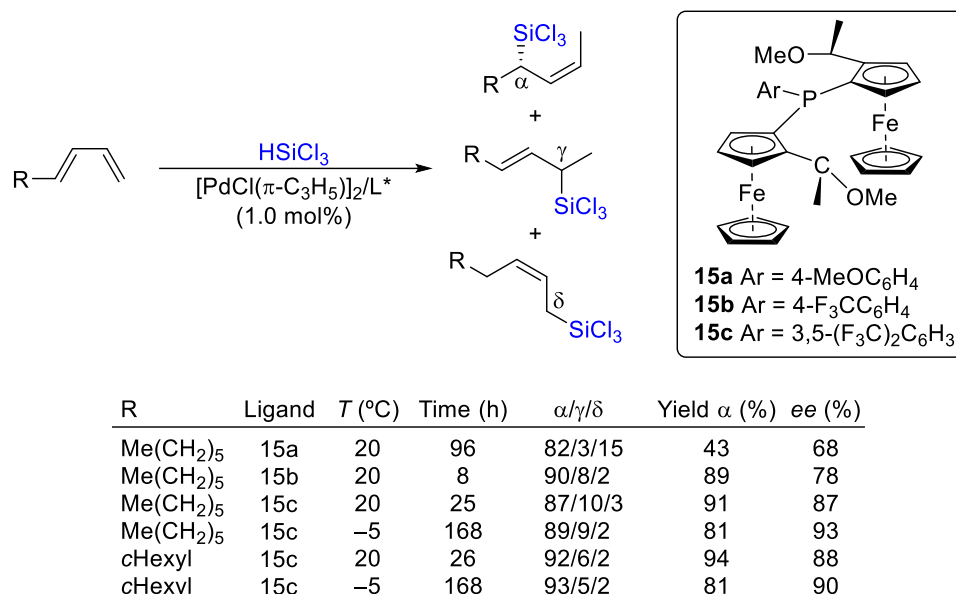
Inspired by the works of Hayashi's group on the hydrosilylation of cyclic 1,3-dienes, Hatanaka and co-workers developed new chiral catalysts for the enantioselective hydrosilylation of 1-aryl-1,3-butadienes.^[50] More particularly, performing the reaction with 1-phenyl-1,3-butadiene and phenyl(halo)silanes $\text{HSiPh}_n\text{X}_{3-n}$ (with $\text{X} = \text{Cl}$ or F and $n = 1$ or 2) in the presence of 0.6 mol% of palladium(II) catalyst *in situ* generated from $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2$ and 1,1'-binaphthyl ligands **14** ($\text{Pd}:\text{phosphine} = 1:2$), they could obtain the expected optically active allylsilanes with moderate levels of enantioselectivity ($ee \leq 66\%$) but with an excellent regioselectivity. Except for trichlorosilane HSiCl_3 (no reaction), the hydrosilylation proceeded with full control of the regioselectivity at 20 °C with the silicon group being introduced in the benzylic position and a full control of the *Z* configuration of the carbon-carbon double bond. This study also uncovered that the moderate *ee* strongly depends on the halogen in $\text{HSiPh}_n\text{X}_{3-n}$. Interestingly, under the same conditions, the enantioselectivity observed with ligand **14a** was inverse to that observed for ligand **14b**, presumably because of the coordination of the hydroxyl group of **14a** with the silane. Later, Hayashi's group developed other conditions with ligand **10b** that provided better results since 79% and 77% *ee* were obtained for 1-phenyl-1,3-butadiene and 1,3-dodecadiene, respectively (**Scheme 10**).^[48]



Scheme 10. Asymmetric hydrosilylation of acyclic 1-phenyl-1,3-butadiene and 1,3-dodecadiene.

Nevertheless, the highest *ee* were obtained by Hayashi, using chiral bis(ferrocenyl) monophosphine ligands with two planar chiral ferrocenyl moieties in the hydrosilylation of 1,3-decadiene, with the drawback that two more regioisomers were obtained.^[51] The catalytic activity as well as the enantioselectivity were dependent on the electronic effects of the substituents of the phenyl ring on the phosphorus atom. The bis(ferrocenyl) analogues with

electron-withdrawing groups, presented higher catalytic activity as well as better regio- and enantioselectivity (**Scheme 11**).

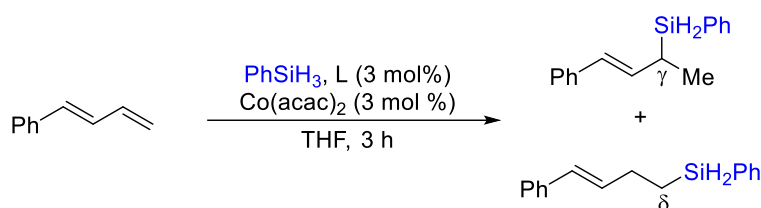


Scheme 11. Bis(ferrocenyl) catalyzed asymmetric hydrosilylation of 1,3-dienes.

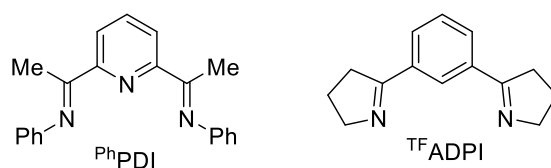
Although by reducing the temperature from 20 °C to -5 °C the hydrosilylation of 1-substituted-1,3-butadiene with HSiCl₃ in the presence of 1 mol% palladium catalyst complex **15c** requires longer reaction times to achieve full conversion (126 h vs. 25 h), a considerable increase in the ee can be observed (93% vs. 87% ee and 90% vs. 88% ee). Thus, the desired 1,4-hydrosilylated products are obtained in a 90-93% ee, with an α-regioselectivity of 89% (**Scheme 11**).

1.2.1.2 Markovnikov 1,2-hydrosilylation of 1,3-dienes

Continuing with the hydrosilylation strategy but changing the silicon and hydrogen introduction position, Markovnikov 1,2-hydrosilylation of conjugated dienes was envisioned as another interesting strategy to access α,γ-disubstituted allylsilanes. Cobalt-catalyzed regioselective and stereoconvergent 1,2-hydrosilylation was firstly reported in 2018.^[52] PhSiH₃ was added to (*E*)-1-phenyl-1,3-butadiene in the presence of the *in situ* generated Co-catalyst obtained by mixing Co(acac)₂ with different ligands in THF. When nitrogen-based ligands were utilized, a mixture of *anti*-Markovnikov/Markovnikov 1,2-hydrosilylation products was obtained in contrast with bisphosphine ligands, where α,γ-disubstituted allylsilanes were exclusively observed (**Scheme 12**). For instance, by stirring at rt for 3 h in the presence of xantphos it was possible to obtain the racemic allylsilane in 87% yield.

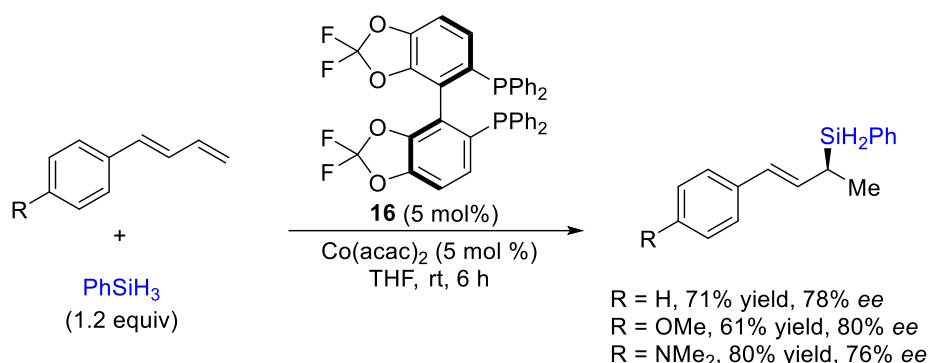


L	T (°C)	Conversion	Yield γ (%)	γ/δ
PhPDI	50	> 99	27	31/69
TFADPI	50	> 99	33	35/65
dppm	50	28	23	only γ
dppe	50	78	77	only γ
binap	50	93	76	only γ
xantphos	50	> 99	81	only γ
xantphos	rt	> 99	87	only γ



Scheme 12. Conditions evaluation for the Co-catalyzed hydrosilylation of (*E*)-1-phenyl-1,3-butadiene with PhSiH₃.

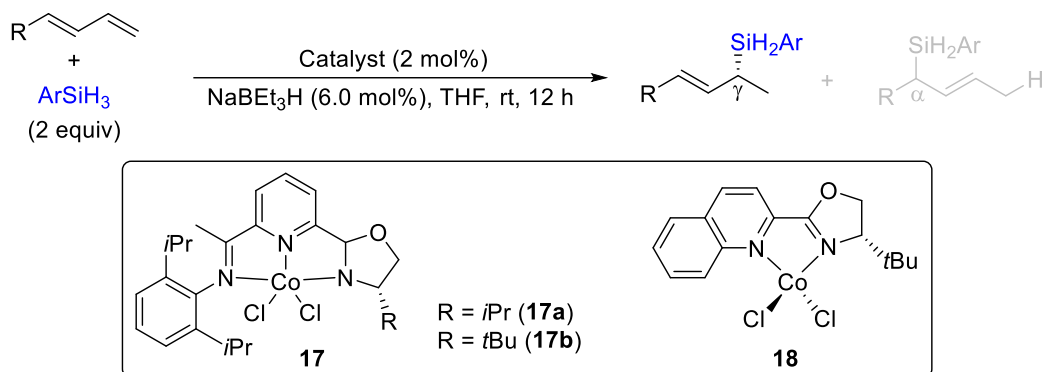
By changing the xantphos for chiral bisphosphine (*R*)-difluorophos ligand, asymmetric hydrosilylation could also be performed to obtain α -aryl- γ -methylsubstituted allylsilanes in moderate ee up to 80% (**Scheme 13**).



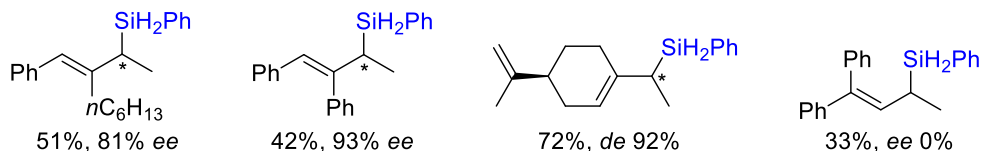
Scheme 13. Asymmetric 1,2-Markovnikov hydrosilylation.

Higher enantiomeric excesses were reached by using oxazoline ligands in the presence of CoCl₂ instead of the complex formed from mixing Co(acac)₂ and (*R*)-difluorophos. Iminopyridine-oxazoline tridentate Co complexes (**17**) in THF at 25 °C proved to give the expected molecules in good regioselectivity (up to r_γ/r_α 95/5) but low enantioselectivity (ee up to 68%, **Scheme 14**). By changing to bidentate oxazoline-containing mononuclear Co-complexes under the same conditions, higher regioselectivities were achieved (> 99/1), being the *t*Bu-substituted quinoline-oxazoline analogue **18** the one that provided the best results. In the presence of this complex, they were able to obtain the chiral allyl dihydrosilanes in high yields and enantioselectivities (up to 96% ee) within 12 h in THF at rt.^[53] The reaction can also be applied to 1,2-disubstituted dienes when augmenting the Co-complex loading to

5 mol%, albeit an erosion in the yield can be observed (> 72%) with maintenance of enantioselective levels ($ee > 81\%$). This cannot be applied over 1,1-diphenyl-1,3-butadiene, since it is too hindered to undergo the hydrosilylation and completely lose its stereochemical information (0% ee , **Scheme 14**), even when using a less hindered precatalyst ($^{Me}PyOx^{iPr}$). This strategy does neither work with 4-substituted dienes or (*Z*)-dienes, as no product was observed.

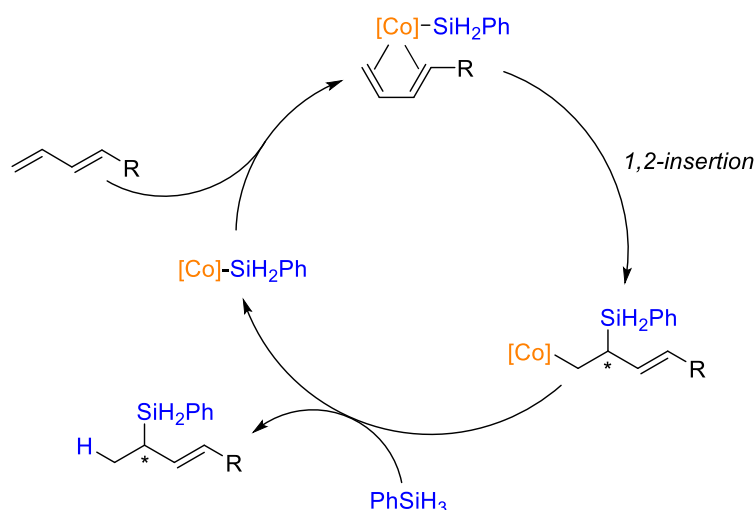


R	Ar	Catalyst	Yield (%)	ee (%)
Ph	Ph	17a	72	50
Ph	Ph	17b	88	68
Ph	Ph	18	95	93
Ph	4-MeOC ₆ H ₄	18	96	94
Ph	4-ClC ₆ H ₄	18	87	87
Ph	4-CO ₂ EtC ₆ H ₄	18	42	93
2- <i>i</i> PrC ₆ H ₄	Ph	18	86	92
4-FC ₆ H ₄	Ph	18	81	95
4-MeSC ₆ H ₄	Ph	18	87	96
<i>n</i> Hexyl	Ph	18	88	92



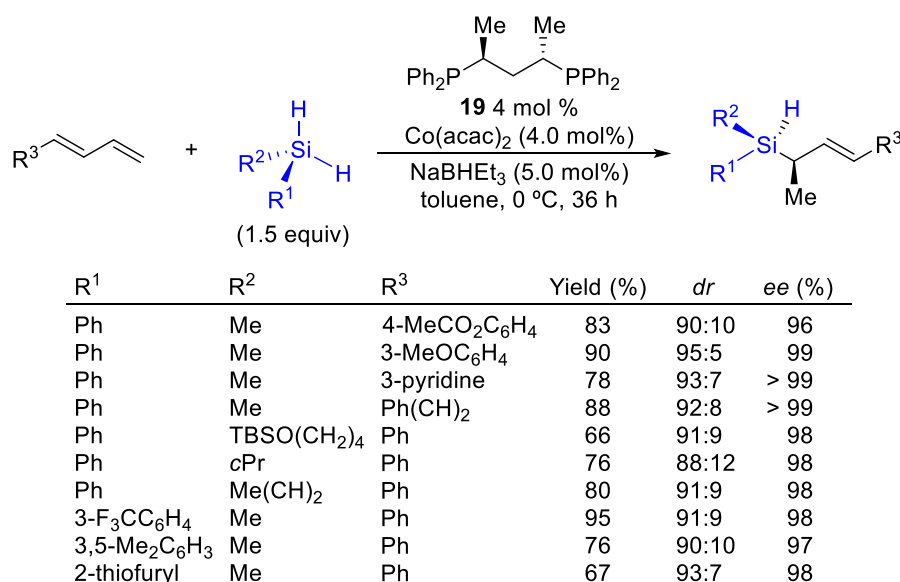
Scheme 14. Co-catalyzed asymmetric hydrosilylation of conjugated dienes with ArSiH₃.

The 1,2-insertion of the terminal double bond into the Co-Si bond, can be explained by a modified Chalk-Harrod mechanism where the formation of a π -allyl intermediate that would lead to the common 1,4-hydrosilylation is avoided (**Scheme 15**).



Scheme 15. Modified Chalk-Harrod mechanism.

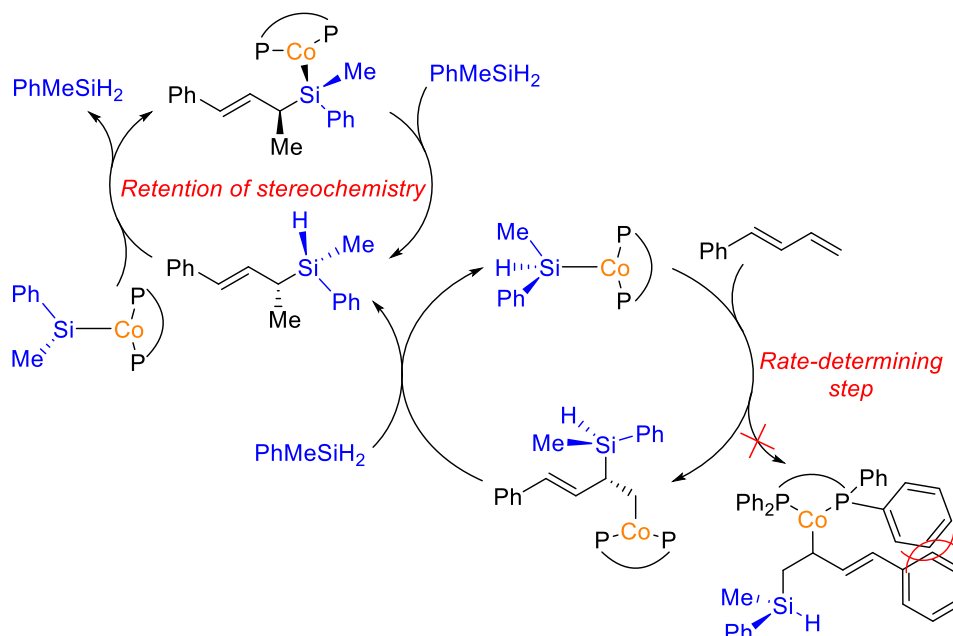
Continuing with this Markovnikov strategy, the first hydrosilylation method where simultaneous construction of carbon- and silicon-stereogenic centres in acyclic molecules *via* intermolecular transformation was unveiled (**Scheme 16**).^[54] This regio-, diastereo- and enantioselective protocol furnished optically active allylsilanes by treating 1,3-dienes and prochiral silanes with 4 mol% of Co catalyst complex (Co(acac)₂:biphosphine = 1:1) and 5 mol% of NaHBET₃ in toluene at 0 °C for 36 h. A wide range of enantioenriched allylsilanes could be accessed thanks to the high reaction tolerance on the substituted 1,3-dienes (except for 1,2-disubstituted or 1,1-disubstituted alkene moiety at the terminus) and the possibility of using prochiral silanes without the requirement of specific substituents. Nevertheless, no reaction occurred with di-arylsilanes, alkenylsilanes and halogen-substituted arylsilanes.



Scheme 16. Synthesis of optically active allylsilanes from prochiral silanes and 1,3-dienes.

The diastereo- and enantioselective outcome of the reaction was proved to be controlled by the addition of the Si-Co complex to the terminal alkene with establishment of the

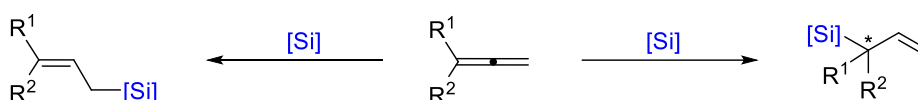
Si-stereogenic centre (**Scheme 17**). Control and kinetic experiments as well as deuterium labelling, demonstrated that σ -bond metathesis at the Si-stereogenic centre occur with complete retention of stereochemistry. Furthermore, since diastereoselectivity was dramatically influenced by the catalyst, the possibility that the first generated stereogenic centre would direct and induce the formation of the second stereogenic centre is ruled out.



Scheme 17. Catalytic cycle proposed for the hydrosilylation of dienes with chiral silanes.

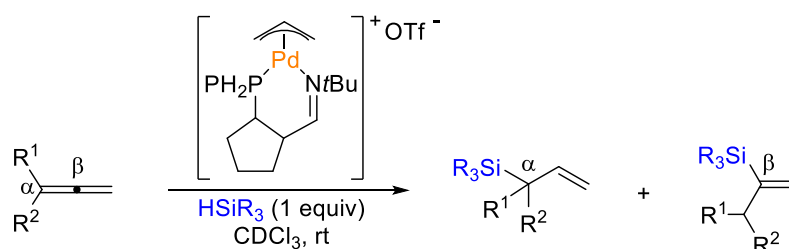
1.2.1.3 Allene hydrosilylation

Hydrosilylation strategy can also be applied to allenes, resulting in an interesting alternative methodology to access allylsilanes through internal or terminal addition (**Scheme 18**).



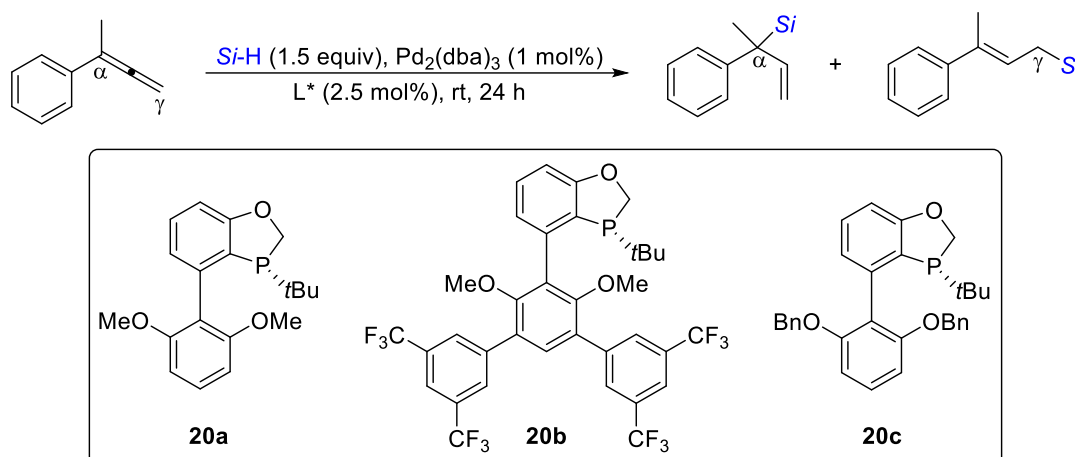
Scheme 18. Preparation of allylsilanes through allene hydrosilylation.

In this regard, chemo- and regioselectivities are strongly dependent on the nature of the transition metal ligand and the bulkiness of the hydrosilylation reagent. For instance, the first example of mono- and disubstituted hydrosilylation of allenes, was developed with R_3SiH in the presence of 1 mol% of $[(3IP)Pd(allyl)]OTf$ catalyst in $CDCl_3$ at rt, providing exclusively α -substituted silanes through internal addition on C_α and C_β (**Scheme 19**).^[55]



Scheme 19. Internal addition of silane to mono- and disubstituted allenes.

Nevertheless, it was not until several years later that the first asymmetric methodology based on this strategy was developed, carrying out the hydrosilylation with H_2SiPh_2 and 1-methyl-1-phenylallene in the presence of 2.5 mol% of chiral monophosphorus ligands and 1 mol% of $\text{Pd}_2(\text{dba})_3$.^[56] The expected α -allylsilanes (bearing a quaternary silicon-substituted stereogenic centre) were obtained with excellent regioselectivities ($\alpha/\gamma > 20/1$) but low enantioselectivity ($ee > 49\%$). Keeping the same reaction conditions employing Ph_3SiH , allows to increase the ee up to 90% but with a huge erosion on both the yield and regioselectivity (**Scheme 20**).



Si-H	Ligand	α/γ	Yield α (%)	ee (%)
Ph_2SiH_2	20a	$> 20/1$	97	49
Ph_2SiH_2	20a	$> 20/1$	98	56
Ph_3SiH	20b	1/1.3	42	73
Ph_3SiH	20c	1/1.2	45	90

Scheme 20. Asymmetric hydrosilylation of buta-2,3-dien-2-ylbenzene.

This excellent regioselectivity can be rationalized by comparing the two conformers **A** and **B**, which appears to be the species involved in the regioselective determining step (**Figure 2**). Conformer **B** that leads to the minor products is much more disfavoured than conformer **A** that gives rise to the mayor α -adducts, as the orientation required to furnish the corresponding γ -products implies some disfavoured steric interactions between the allene and the Pd-complex.

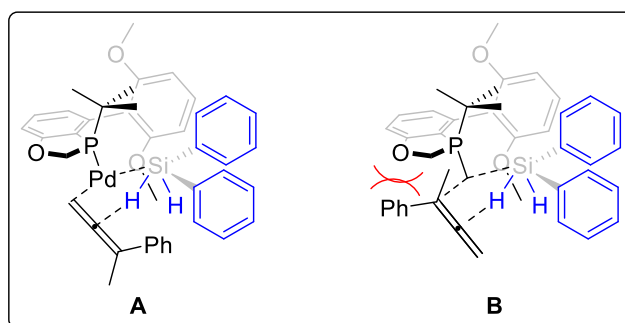
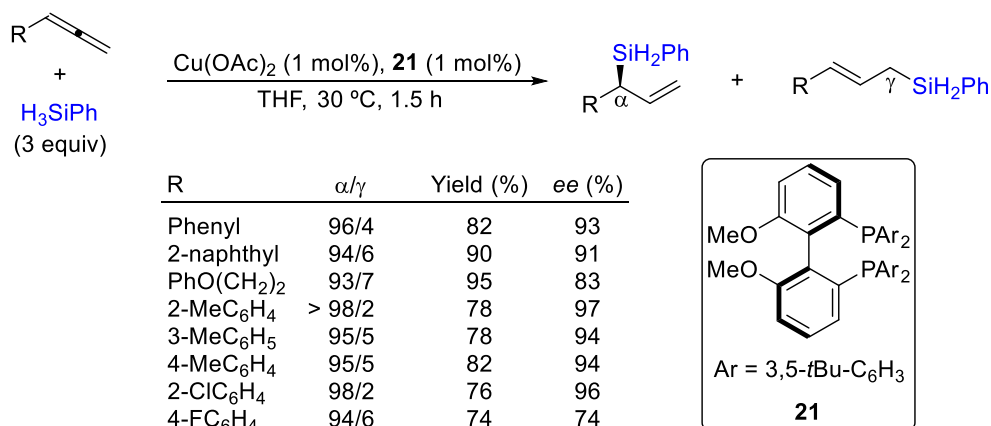


Figure 2. Possible conformers involved in the regioselective determining step.

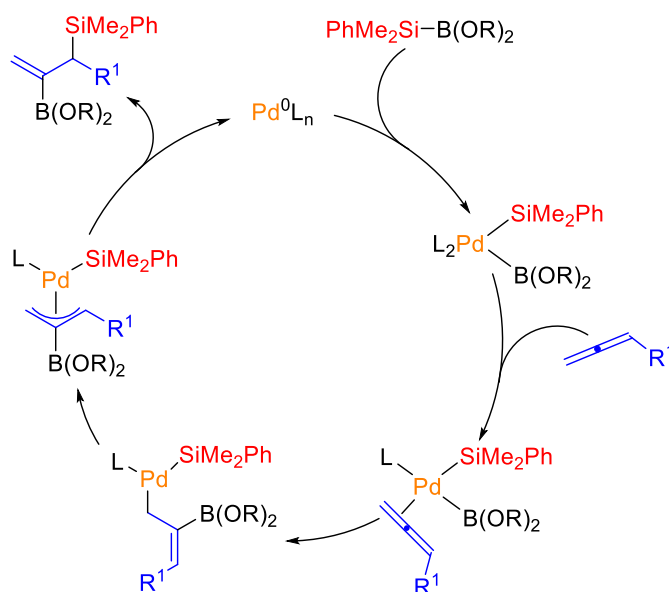
Very recently, this lack of simultaneous control of regio- and enantioselectivity was overcome by using H_3SiPh in the presence of 2 mol% of a copper complex obtained by mixing $\text{Cu}(\text{OAc})_2$ and the bisphosphorus ligand **21** in THF at 30 °C.^[57] The hydrosilylation on the monosubstituted allenes proceeded with simultaneous regio- and enantioselective control to afford the enantioenriched branched allylsilanes with high yields (74-98%), excellent regioselectivities and good enantioselectivities up to 97% ee, being the H_3SiPh the only successful silane introduced (**Scheme 21**).



Scheme 21. Copper-catalyzed regio- and enantioselective hydrosilylation of monosubstituted allenes.

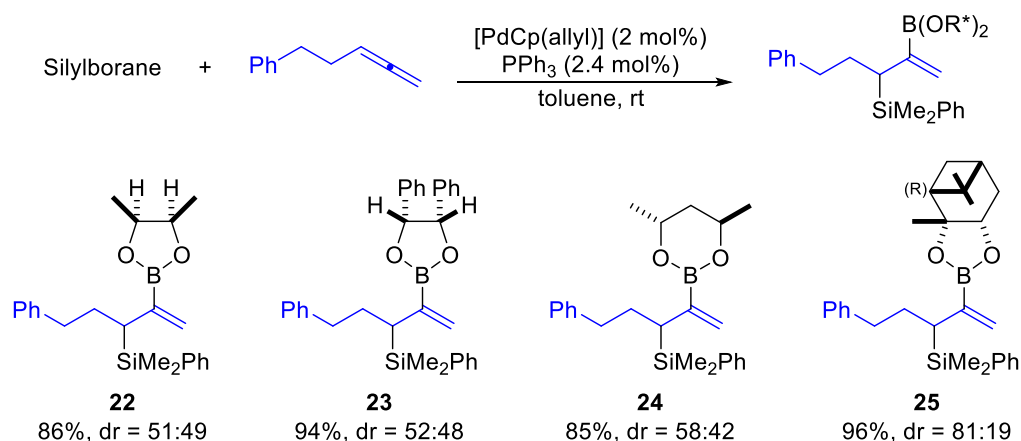
1.2.1.4 Silaboration of allenes and dienes

Parallely, allenes can also be envisioned as substrates for the preparation of enantioenriched allylsilanes through regio- and stereoselective silaboration. This strategy provides a powerful alternative to access α -substituted allylsilanes. For instance, $\text{PhMe}_2\text{SiBpin}$ is exclusively added to the internal carbon-carbon double bond of 3-substituted allenes in octane at 120 °C in the presence of Pd complex, generated *in situ* by mixing $\text{Pd}(\text{acac})_2$ and isocyanides ($\text{Pd}:\text{isocyanide} = 1:4$), in contrast to the preferred terminal addition in related Pt-catalyzed procedures.^[58,59] This regiochemistry regarding the internal addition can be explained by the preference of the silyl group for the most electron rich sp^2 carbon of the allene (**Scheme 22**).



Scheme 22. Mechanism of the internal PhMe₂SiBpin addition to allenes.

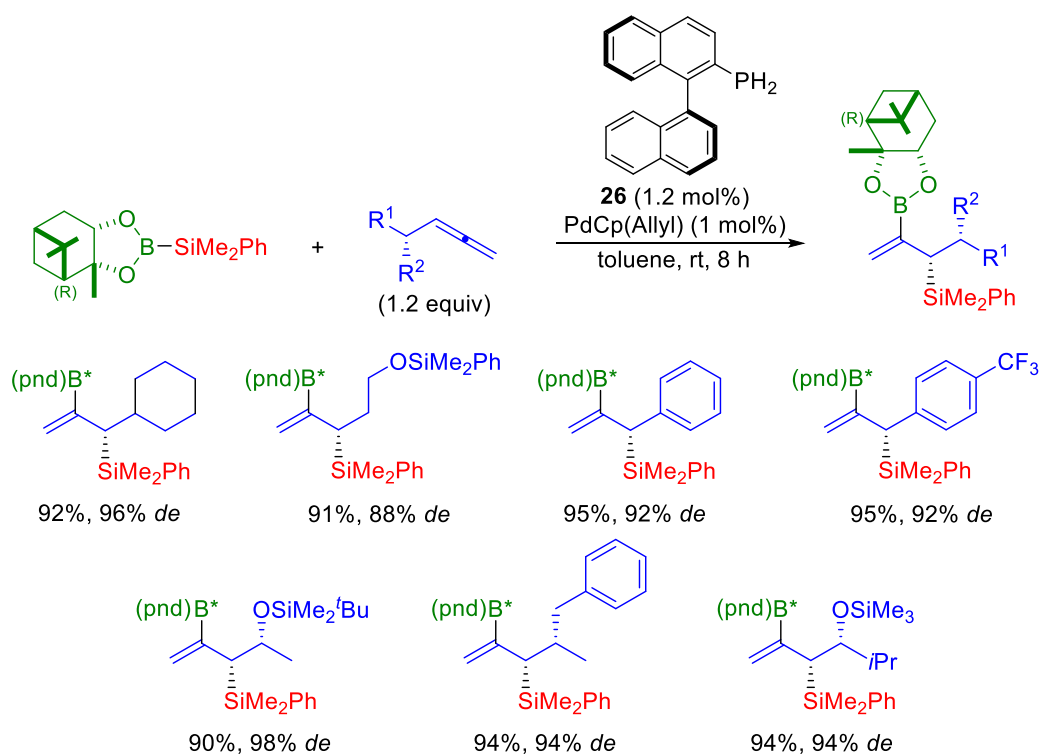
Changing Pd(acac)₂ for [PdCp(allyl)] and isocyanates for tertiary phosphines, silaboration of allenes could be performed at rt while conserving the internal regioselectivity. The first enantioenriched β -boryl allylsilane was obtained by the reaction between 3-substituted allenes and PhMe₂Si-boranes bearing diol-derivative chiral auxiliaries in the presence of 1 mol% of performed Pd-complex (Pd:Phosphine = 1:1.2) in toluene.^[60] Although perfect regioselectivity was achieved with different boryl substituents, poor diastereoselectivities were observed except for silaborane **25** that provided a dr of 81:19 (**Scheme 23**).



Scheme 23. Reaction between phenethyl allene and different silylboranes bearing chiral auxiliaries.

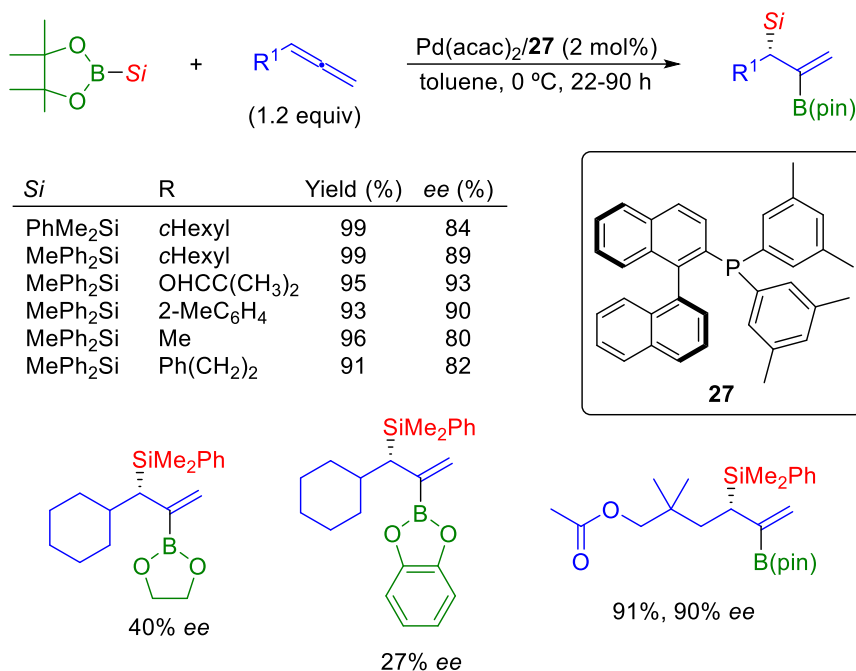
Nevertheless, this moderate dr was increased up to 94:6, under double asymmetric induction conditions utilizing the chiral monophosphine ligand **26**. This reagent system was also applied for the silaboration of α -chiral alkoxyallenes to furnish the corresponding α -alkyl- β -silyl- γ -boryl alkoxybutenes in excellent yields with good enantioface selectivities (**Scheme 24**). Higher diastereoselectivities are obtained for the products with matched effect,

ranging from 88% to 98% *de*, when compared with their mismatched analogues, from 84% to 90% *de*.^[61]



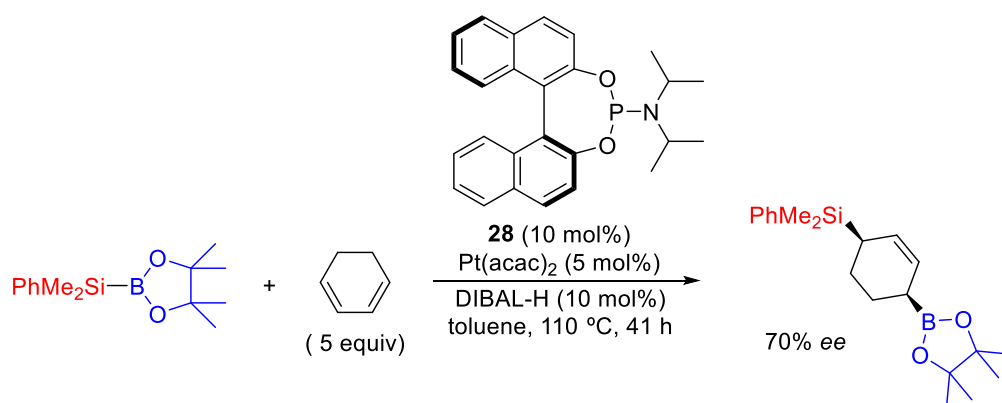
Scheme 24. Synthesis of β -borylallylsilanes.

Alternatively, the addition of MePh₂SiB(pin) to 1.2 equiv of cyclohexylallene in the presence of 2 mol% of Pd(acac)₂ and 2.4 mol% of 3,5-dimethylphenyl-diarylphosphine ligand **27** in toluene at rt, provided the corresponding borylallylsilane in 99% yield and 89% *ee*.^[62] Changing both silicon and boron moieties to less sterically hindered ones (PhMe₂Si- and ethylene glycol) resulted in a decrease of the enantiomeric excess to 84% and 40% respectively (**Scheme 25**), while more sterically demanding Ph₃Si- derivative did not react. This method allows to avoid the stoichiometric use of chiral auxiliaries (pinanedioxy groups) that were critical for obtaining high stereoselectivities in the previous strategies. Under optimized conditions, chiral α -alkyl- β -borylallylsilanes were obtained with lower enantiomeric excesses than their secondary and tertiary alkyl analogues (80-82% vs. 88-93%), proving once again the strong relation between the bulkiness of the substituents in the reaction reagents and the enantioselectivity obtained.



Scheme 25. Catalytic asymmetric synthesis of enantioenriched β -boryl allylsilanes.

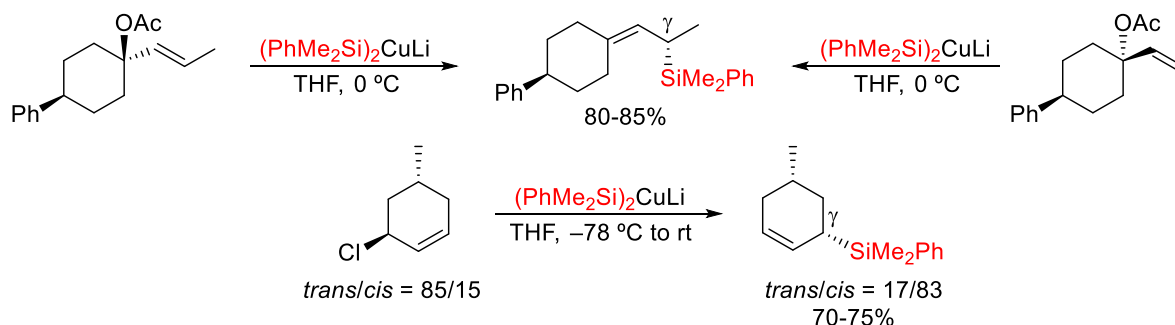
1,4-silaboration can also be performed with 1,3-dienes to obtain the corresponding chiral 4-boryl-allylsilanes. In one example, a chiral borylsilane was prepared in the presence of $\text{Pt}(\text{acac})_2$, DIBAL-H and a chiral phosphoramidite ligand **28** prepared from (*S*)-1,1'-bi-2-naphthol and diisopropylamine.^[63] By running the reaction between 1,3-cyclohexadiene and PhMe₂SiBpin in toluene at 110 °C for 41 h in the presence of Pt-complex (Ni-complex afforded racemic products while Pd-catalyst were inactive), only the *cis*-isomer was observed with a 70% ee (**Scheme 26**).



Scheme 26. Synthesis of an enantioenriched boroallylsilane.

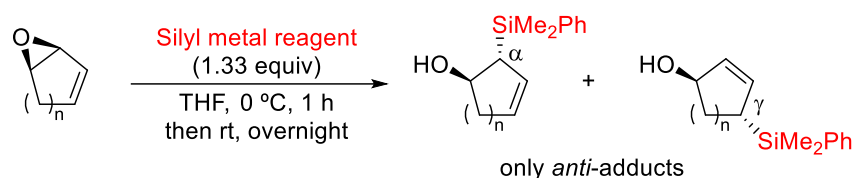
1.2.1.6 Silylation of allylic electrophiles

Since the middle 80's not only conjugated dienes were envisioned as suitable molecules to access chiral allylsilanes (reviewed before), but also allylic electrophiles. In this regard, the synthesis of allylsilanes through silylation of allylic halides, acetates, carbamates, sulfonates or phosphates, by addition of achiral silyl-metal reagents emerged as a mighty strategy.^[65–71] Me_3SiLi ^[70] and $\text{PhMe}_2\text{SiAlEt}_2$ ^[71] predominantly afforded α -products, which are obtained through a $\text{S}_{\text{N}}2$ -pathway, whereas γ -products are formed as main isomers with lithium silylcuprates from a $\text{S}_{\text{N}}2'$ -pathway.^[65,68,69] The first evidence for a regioselective stereospecific *anti*- $\text{S}_{\text{N}}2'$ process has been reported in the reaction of $(\text{PhMe}_2\text{Si})_2\text{CuLi}$ with stereodefined tertiary allylic acetates^[72] and *trans*- or *cis*-cyclohex-2-enyl chlorides^[71] giving exclusively *anti*- γ -allylsilanes (**Scheme 28**).



Scheme 28. *Anti*- $\text{S}_{\text{N}}2'$ pathway in the allylic silylation of stereodefined tertiary allylic acetates and cyclohex-2-enyl chlorides.

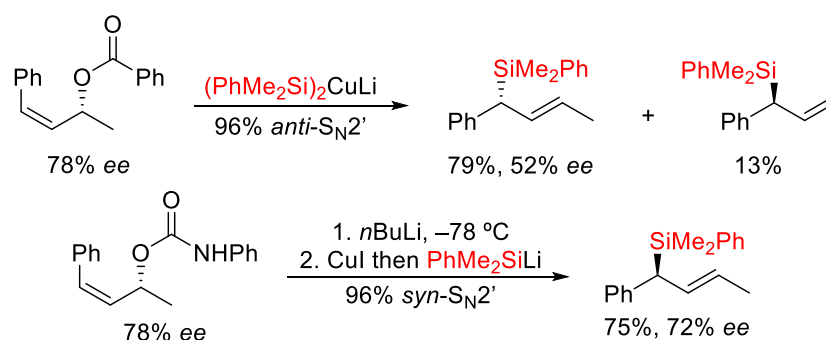
The same trend was observed in the reaction of chiral cyclic vinyloxydes with silyllithium Me_2PhSiLi or lithium cyanocuprates $(\text{PhMe}_2\text{Si})_n\text{Cu}(\text{CN})_n\text{Li}_n$ ($n = 1, 2$ or 3), which were preformed by mixing Me_2PhSiLi with variable stoichiometric amounts of CuCN . With PhMe_2SiLi , not only erratic results were obtained but also α -allylsilanes were formed, incoming from an $\text{S}_{\text{N}}2$ -pathway, as the single products in many cases. On the other hand, reproducible results were obtained with various lithium cyanocuprates, albeit the isomeric distribution of the products (i.e., the γ/α ratio) was sensitive to the $\text{PhMe}_2\text{SiLi}:\text{CuCN}$ ratio.^[73,74] Thus, a 1:1 ratio, which leads to the lithium cyanocuprate $\text{PhMe}_2\text{SiCu}(\text{CN})\text{Li}$ (1.33 equiv), gave the best results, affording *anti*- γ -allylsilanes as single regioisomers from 3,4-epoxy- cyclopentene and cyclohexene (**Scheme 29**).



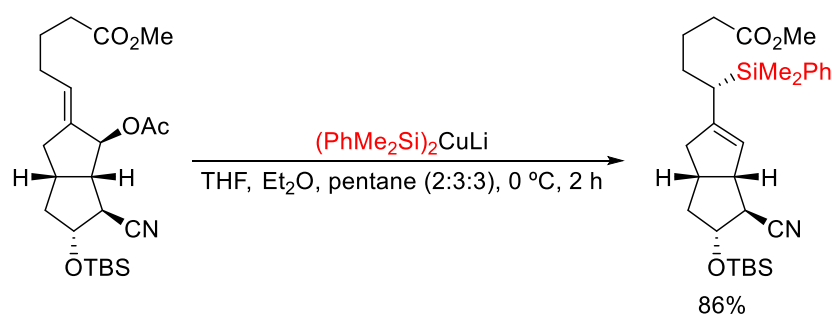
Silyl metal reagent	n	Yield (%)	γ/α
PhMe ₂ SiLi	1	27	0/100
PhMe ₂ SiLi	2	40	0/100
PhMe ₂ SiCu(CN)Li	1	72	100/0
PhMe ₂ SiCu(CN)Li	2	70	100/0
(PhMe ₂ Si) ₂ Cu(CN)Li ₂	1	79	51/49
(PhMe ₂ Si) ₂ Cu(CN)Li ₂	2	94	83/17
(PhMe ₂ Si) ₃ Cu(CN)Li ₃	1	70	60/40
(PhMe ₂ Si) ₃ Cu(CN)Li ₃	2	90	40/60

Scheme 29. Allylic silylation of chiral vinyloxyepoxides with silylmetals.

Optically active γ -allylsilanes were synthesized for the first time by the reaction of non-racemic chiral allylic carboxylates with (PhMe₂Si)₂CuLi, leading to a mixture of (*E*)- and (*Z*)- γ -isomers both resulting from an approximately 96% *anti*-stereospecific reaction (**Scheme 30**).^[75] Interestingly, a reaction with about 96% *syn*-stereospecificity operated with a carbamate moiety as leaving group through deprotonation with *n*BuLi at -78 °C and subsequent additions of CuI and PhMe₂SiLi. In this case, the stereochemical outcome differentiation is presumably due to the coordination of the silylmetal reagent to the deprotonated carbamate behaving as a directing group. The reaction with allylic acetates has been applied to the asymmetric synthesis of some natural compounds.^[76–78]

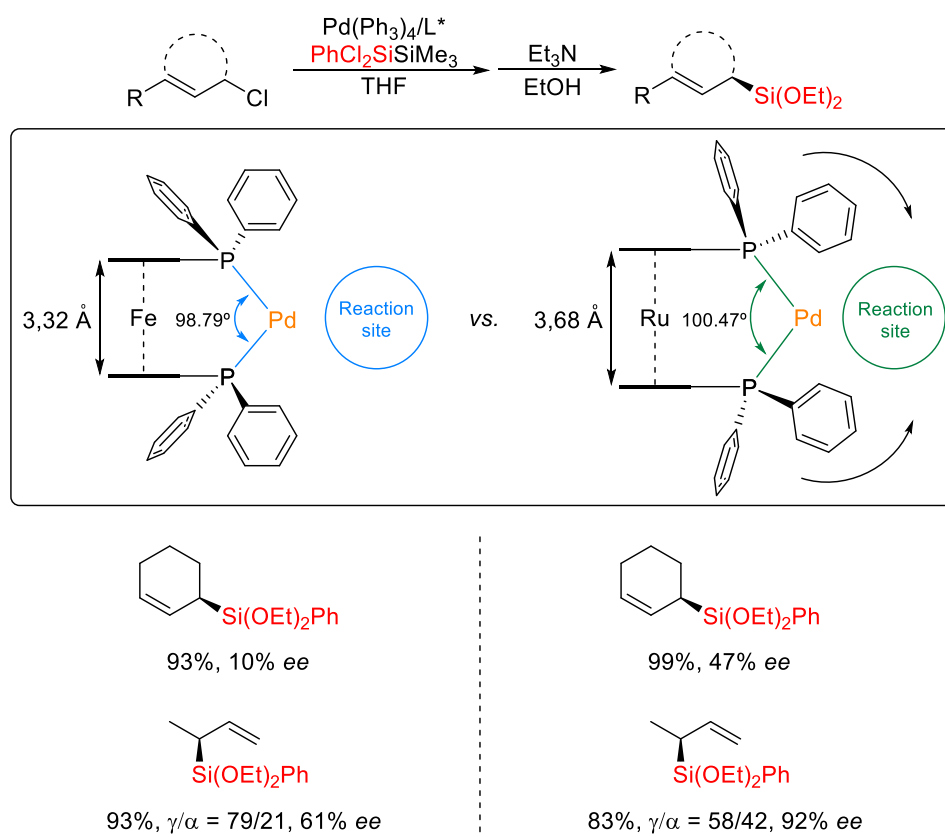


Key-step synthesis of a (\pm)-carbacyclin analogue^[77]



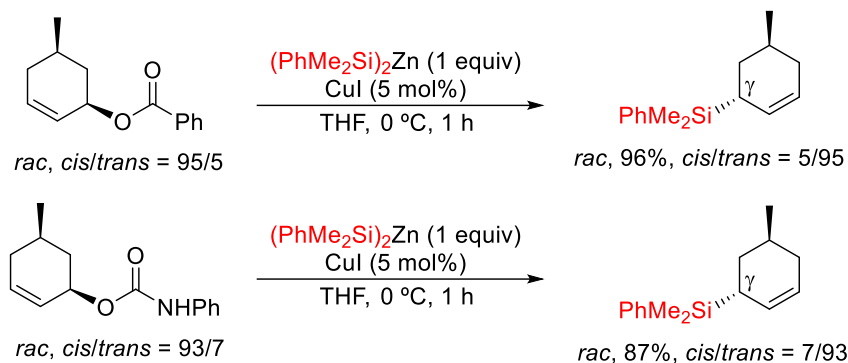
Scheme 30. S_N2' allylic silylation from chiral allylic acetates and carbamates.

Parallely to the Cu-strategies, stereospecific preparation of chiral silanes from allylic electrophiles catalyzed by palladium was unveiled at the beginning of the 80's. Reaction of non-racemic allylic acetates with $(\text{Me}_3\text{Si})_3\text{Al}$ -etherate gave α -product as the mayor stereoisomer from allylic acetates in the presence of $\text{Pd}(\text{PPh}_3)_4$, while reverse stereoselectivity was observed by using $\text{Mo}(\text{CO})_6$ toluene.^[79] Silylation of α - and γ -substituted allylic chlorides with $\text{PhCl}_2\text{SiSiMe}_3$ (subsequent treatment with triethylamine in EtOH leads to the $\text{Ph}(\text{OEt})_2\text{Si}$ -adducts) proceeded with inversion of configuration. The silylation took place in THF under the presence of 1 mol% palladium catalyst *in situ* prepared from bis(μ -chloro)bis(η^3 -allyl)dipalladium and (*R*)-(*S*)-BPPFA (Pd :ferrocenylbis-(phosphine) = 1:2.2) to yield the corresponding allylsilane in poor ee (10-61%).^[80] By changing the chiral ligand to its ruthenium analogue, enantiomeric excesses increased considerably up to 92% (**Scheme 31**).^[81] This improvement in the enantioselectivity can be explained by the wider bite angle (98.79° vs. 100.47° between the phosphorus and the palladium resulting from the greatest distance between the cyclopentadienyl rings (ferrocene 3.32 \AA vs. ruthenocene 3.68 \AA). This small change allowed to create a more effective chiral surrounding (since the phenyl rings on the phosphorus atoms come closer to the reaction site on the metal centre) that results in higher enantioface differentiation.



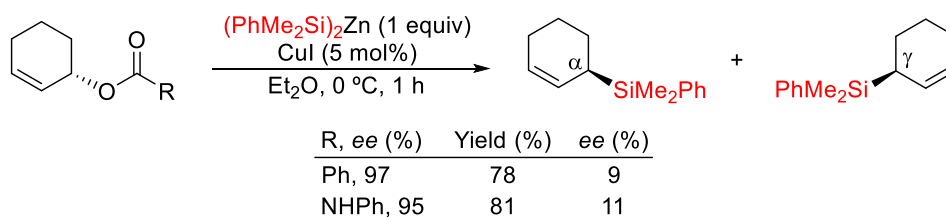
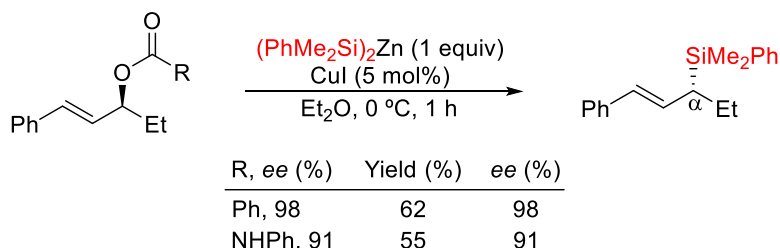
Scheme 31. Asymmetric allylsilanes and chiral surroundings of ferrocenylbis(phosphines) and ruthenobis(phosphines).

In 2005, the first copper(I)-catalyzed allylic silylation has been disclosed by the combination of bis(triorganosilylzinc) $(\text{PhMe}_2\text{Si})_2\text{Zn}$ (1 equiv) and 5 mol% of CuI.^[82] These conditions enabled the highly regio- and diastereoselective stereospecific allylic γ -silylation of racemic chiral allylic esters and carbamates giving *anti*-adducts (**Scheme 32**).

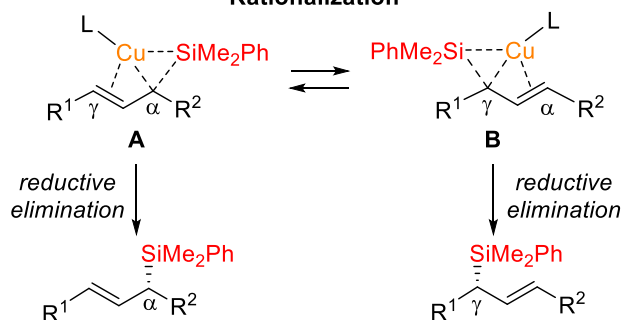


Scheme 32. Diastereoselective copper(I)-catalyzed allylic γ -silylation of allylic esters and carbamates.

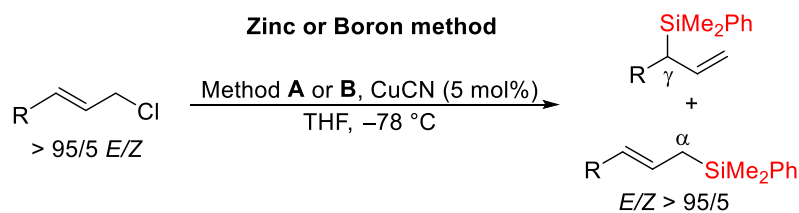
However, the reaction is poorly enantioselective since optically active secondary allylic electrophiles afford products almost as racemic mixtures, resulting from the two competitive $\text{S}_{\text{N}}2$ and *anti*- $\text{S}_{\text{N}}2'$ pathways (**Scheme 33**).^[83] Regio- and enantioselectivity have in fact been shown to be sensitive to the structure of the allylic electrophile (i.e., cyclic vs. acyclic, “symmetric” vs. “non-symmetric”). With cyclic substrates, the reaction proceeds through the two $\text{S}_{\text{N}}2$ and *anti*- $\text{S}_{\text{N}}2'$ pathways, leading to racemization. On the other hand, with acyclic and “non-symmetric” substrates, an overall inversion of configuration was observed through a $\text{S}_{\text{N}}2$ -pathway, affording the corresponding α -allylsilanes with full regio- and enantiocontrol. All these results can be explained by an equilibrium between the two $[\sigma + \pi]$ enyl transient intermediates **A** and **B** (**Scheme 33**), generated by the oxidative addition of the allylic substrate to catalytically active $\text{PhMe}_2\text{SiCu}\cdot\text{ZnX}_2$ species. This equilibrium is postulated to be fast with cyclic electrophiles, affording mixtures of compounds formed by both $\text{S}_{\text{N}}2$ and *anti*- $\text{S}_{\text{N}}2'$ addition, and slow with acyclic and “non-symmetric” ones, affording only α -adducts formed through a $\text{S}_{\text{N}}2$ -pathway.

Cyclic allylic electrophiles: racemization (S_N2 and *anti*- S_N2')Acyclic and “non-symmetric” allylic electrophiles: inversion (S_N2)

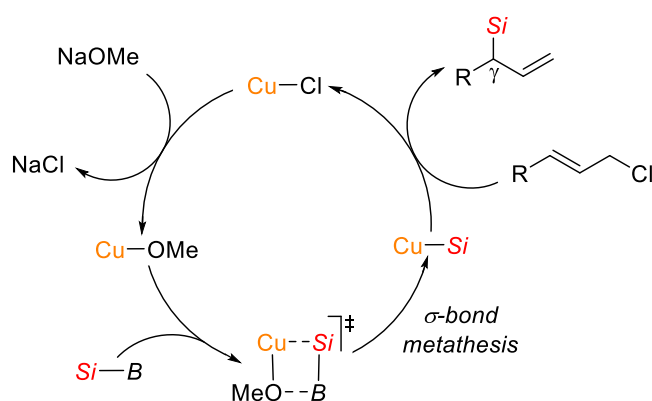
Rationalization

**Scheme 33.** Copper(I)-catalyzed allylic silylation of secondary chiral allylic esters and carbamates.

The regioselectivity of the allylic silylation of primary allylic electrophiles has been shown to depend on the leaving group.^[84,85] Thus, when allylic esters, carbamates and carbonates are reacted with the combination of $(\text{PhMe}_2\text{Si})_2\text{Zn}$ (1 equiv) and 5 mol% of CuI or CuCN in THF at $-78\text{ }^\circ\text{C}$ (zinc method), achiral α -allylsilanes (i.e., linear products) were obtained as exclusive regioisomers, through an S_N2 -pathway. In sharp contrast, allylic phosphates, chlorides and bromides gave γ -allylsilanes (i.e., branched products) as major regioisomers, through an S_N2' -pathway. More particularly, chloride revealed to be the leaving group of choice allowing to obtain γ -allylsilanes in excellent yields and with high γ -regiocontrol ($\gamma/\alpha \geq 93/7$) within 15 min at $-78\text{ }^\circ\text{C}$ (**Scheme 34**). Interestingly, better levels of γ -selectivity were achieved by the copper(I)-catalyzed activation of the silicon-boron bond of silylboronate $\text{PhMe}_2\text{SiBpin}$ (1.5 equiv) in the presence of NaOMe (1.5 equiv).^[84] It is worthy to note, that under these conditions (boron method), no reaction occurred in the presence of bulkier NaOtBu , presumably because the generated copper alkoxide CuOtBu is too sterically hindered to allow for the σ -bond metathesis to take place (**Scheme 34**).

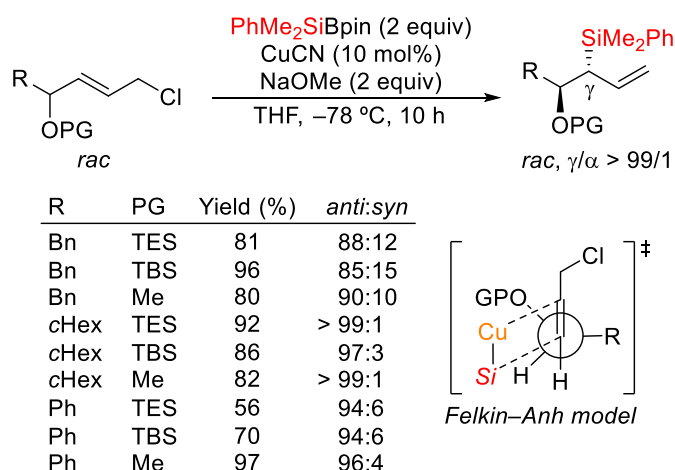


R	Method	Yield (%)	γ/α
<i>i</i> Pr	A	84	> 99/1
<i>i</i> Pr	B	86	98/2
cHex	A	81	> 99/1
cHex	B	84	> 99/1
Ph	A	88	98/2
Ph	B	85	96/4
3-MeOCH ₆ H ₄	A	94	99/1
3-MeOCH ₆ H ₄	B	82	95/5
4-MeOCH ₆ H ₄	A	77	98/2
4-MeOCH ₆ H ₄	B	69	94/6
4-BrCH ₆ H ₄	A	95	98/2
4-BrCH ₆ H ₄	B	84	96/4
4-CF ₃ CH ₆ H ₄	A	83	98/2
4-CF ₃ CH ₆ H ₄	B	91	93/7
Me ₃ Si	A	72	76/24
Me ₃ Si	B	89	76/24



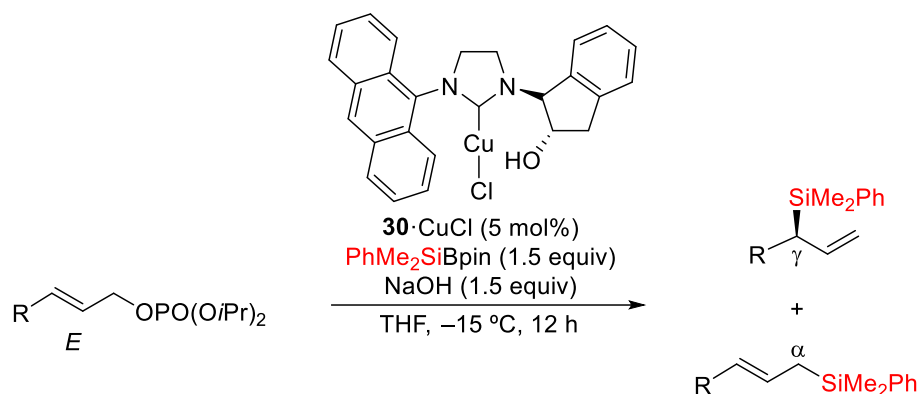
Scheme 34. Copper(I)-catalyzed synthesis of γ -allylsilanes from allylic chlorides.

The boron method can be applied to the allylic silylation of chiral protected δ -hydroxy allylchlorides (**Scheme 35**).^[86] In all cases *anti*-adducts, are obtained within 10 h at -78°C in THF in fair to high yields (56-97%) with excellent γ/α regioselectivities (> 99/1) whatever the protected group, although the best diastereoselectivity is reached with methylethers ($\text{dr} \geq 90:10$). The high *anti*-1,2-stereoselection has been rationalized by a Felkin-Anh transition state model wherein the protected alkoxy moiety OPG is “smaller” than the substituent R.



Scheme 35. Allylic silylation of protected δ -alkoxy allylchlorides.

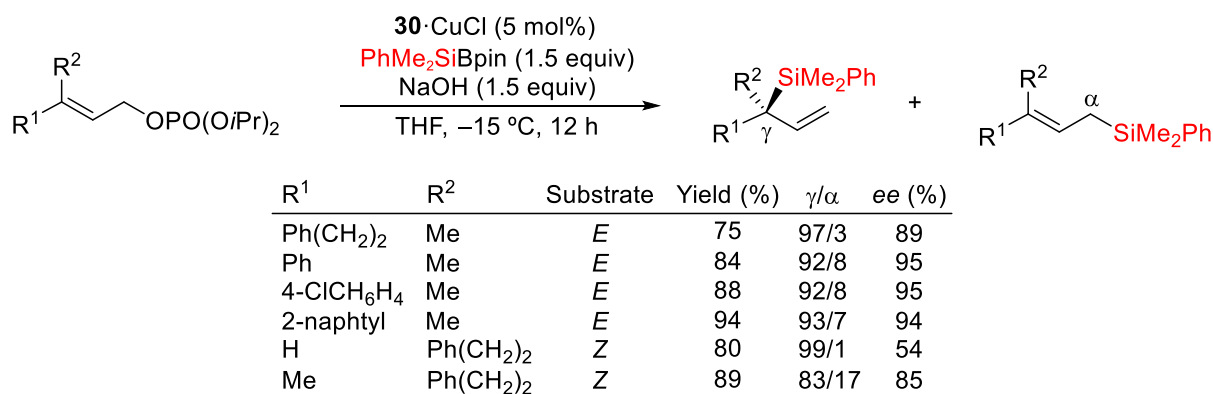
In the presence of chiral *N*-heterocyclic carbene NHC-copper(I) complex **30**·CuCl (5 mol%), which was *in situ* generated from the corresponding imidazolium salt and CuCl, the boron method gave access to enantioenriched γ -allylsilanes under copper(I)-catalysis.^[87] Both, diisopropylphosphates, instead of their diethyl congeners, and NaOH (1.5 equiv), instead of all other alkoxide sources that have been tested, realize better regio- and enantiocontrols (**Scheme 36**). Except in the case of the bulky *tert*-butyl substituent, the method gave rise to the formation of trisubstituted γ -allylsilanes in high yields ($\geq 78\%$) with high γ -regiocontrol ($\gamma/\alpha \geq 92/8$) and enantioselectivity ($ee \geq 86\%$) within 12 h in THF at $-15\text{ }^\circ\text{C}$. Under these conditions, a wide range of functional groups are well tolerated.



R	Yield (%)	γ/α	ee (%)
Me	90	95/5	86
cHex	97	98/2	91
<i>t</i> Bu	72	77/23	95
Ph(CH ₂) ₂	93	99/1	91
PhCO ₂ CH ₂	89	> 99/1	88
Ph	91	98/2	92
2-MeCH ₆ H ₄	91	> 99/1	95
2-BrCH ₆ H ₄	83	99/1	94
3-MeCH ₆ H ₄	87	99/1	91
4-MeCH ₆ H ₄	90	98/2	92
4-ClCH ₆ H ₄	87	99/1	90
1-naphtyl	78	98/2	93
2-naphtyl	96	> 99/1	90
3-thienyl	94	99/1	89

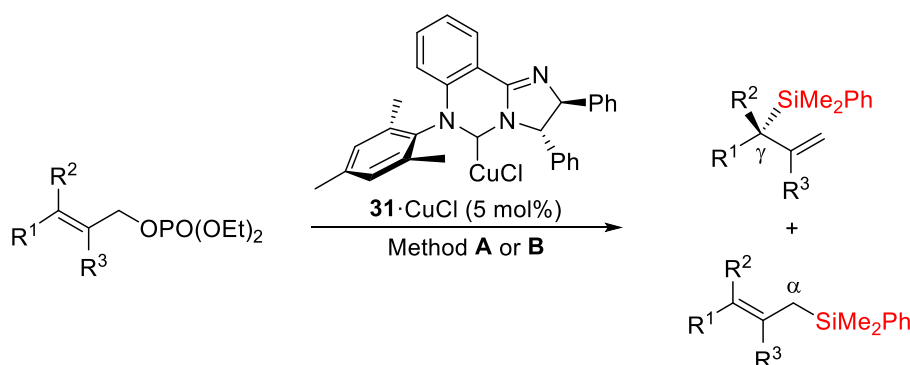
Scheme 36. Copper(I)-catalyzed formation of trisubstituted γ -allylsilanes from (*E*)-allylic phosphates.

The reaction also enables the synthesis of tetrasubstituted γ -allylsilanes with a silyl-substituted allylic quaternary centre from γ,γ -disubstituted allylic phosphates (**Scheme 37**). Similar yields ($\geq 75\%$) and enantioselectivities ($ee \geq 89\%$) but slightly lower γ -regioselectivities ($\gamma/\alpha \geq 92/8$) are obtained. The same reaction conditions afford the γ -allylsilanes with the opposite absolute configuration of the quaternary centre from (*Z*)-allylic phosphates, albeit with significantly eroded γ -regioselectivity (γ/α in the range of 83/17 to 99/1) and enantioselectivity ($ee \leq 85\%$).



Scheme 37. Copper(I)-catalyzed synthesis of tetrasubstituted γ -allylsilanes from (*E*)- and (*Z*)-allylic phosphates.

Better regio- and enantioselectivities were achieved when replacing NHC-catalyst **30**·CuCl with preformed McQuade NHC-copper(I) complex **31**·CuCl (**Scheme 38**).^[88,89] Under the best conditions, the reaction was run at 0 °C in CH₂Cl₂ with silylboronate PhMe₂SiBpin (1.5 equiv) in the presence of NaOMe (1.5 equiv) and 5 mol% of the McQuade complex (boron method). Except in the case of the bulky *tert*-butyl group in the γ -position which predominantly led to the α -product ($\gamma/\alpha = 6/94$) in modest yield (35%), all allylic phosphates afforded the γ -products as the main isomers in high yields (81-93%) with high γ -regiocontrol ($\gamma/\alpha \geq 96/4$) and enantioselectivity ($ee \geq 88\%$). The reaction could also be efficiently applied to a β -substituted substrates that gives the corresponding γ -product, albeit in very poor yield (25%) and significant loss of regio- and enantioselectivities ($\gamma/\alpha = 65/35$ and 78% ee).



Method **A** (Boron): PhMe₂SiBpin (1.5 equiv), NaOMe (1.5 equiv)

CH₂Cl₂, 3 h at 0 °C then 6 h at rt

Method **B** (Zinc): (PhMe₂Si)₂Zn·4LiCl (1.2 equiv)

Et₂O, -78 °C to 0 °C until completion by TLC

R ¹	R ²	R ³	Substrate	Method	Yield (%)	γ/α	ee (%)
<i>i</i> Pr	H	H	<i>E</i>	A	91	97/3	97
<i>i</i> Pr	H	H	<i>E</i>	B	70	97/3	94
cHex	H	H	<i>E</i>	A	88	98/2	95
cHex	H	H	<i>E</i>	B	70	> 99/1	95
<i>t</i> Bu	H	H	<i>E</i>	A	35	6/94	–
Ph(CH ₂) ₂	H	H	<i>E</i>	A	81	97/3	88
Ph(CH ₂) ₂	H	H	<i>E</i>	B	76	> 99/1	96
Ph	H	H	<i>E</i>	A	82	97/3	96
Ph	H	H	<i>E</i>	B	80	> 95/5	> 99
Ph	H	H	<i>E</i>	B	80*	> 95/5*	98*
3-MeOCH ₆ H ₄	H	H	<i>E</i>	A	92	96/4	95
3-MeOCH ₆ H ₄	H	H	<i>E</i>	B	74	> 99/1	98
4-CF ₃ CH ₆ H ₄	H	H	<i>E</i>	A	93	97/3	93
4-CF ₃ CH ₆ H ₄	H	H	<i>E</i>	B	95	95/5	> 99
H	Ph	H	<i>Z</i>	A	88	97/3	91
H	Ph	H	<i>Z</i>	B	60	88/12	64
Ph	Me	H	<i>E</i>	A	96	73/27	93
Ph	Me	H	<i>E</i>	B	75	94/6	94
Ph	H	Me	<i>E</i>	A	25	65/35	78 ^[88]
Ph	H	Me	<i>E</i>	A	56	32/68	68 ^[89]
Ph	H	Me	<i>E</i>	B	65	92/8	70

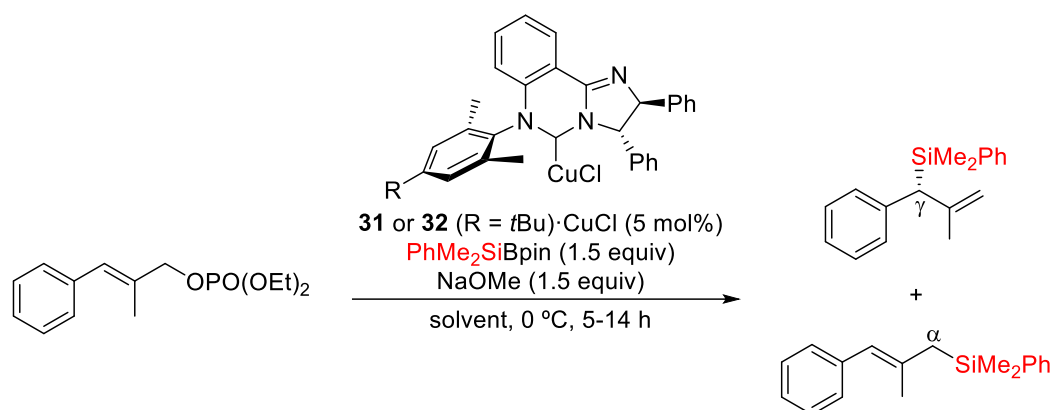
*From allylic chloride.

Scheme 38. Allylic silylation of (*E*)- and (*Z*)-allylic phosphates catalyzed by **31**·CuCl McQuade complex.

Preformed McQuade's catalyst **31**·CuCl was also applicable to a protocol that implies bis(triorganosilyl) zincs.^[90] The reaction was conducted with *in situ* prepared

(PhMe₂Si)₂Zn·4LiCl (1.2 equiv) in the presence of 5 mol% of **31**·CuCl in Et₂O from –78 °C to 0 °C. Except in the notable case of (*Z*)-allylic phosphates where enantio- and regioselectivity were significantly deteriorated, this method was superior to the previously described boron method in terms of both regio- and enantiocontrol. In addition, the zinc method could be successfully applied to allylic chlorides as substrates.

The results were nevertheless disappointing in the case of β-substituted substrates (R³ ≠ H, **Scheme 38**). Indeed, the zinc method led to only 70% ee while with the boron method regio- and enantioselectivities appear to be somewhat erratic. However, with the boron approach, the bulkier McQuade complex **32**·CuCl offered better results than **31**·CuCl both in terms of regio- and enantiocontrol. A dramatic influence of the solvent had also been pointed out. Toluene is thus the solvent of choice to achieve high γ/α ratio and enantioselectivity, whereas the α-isomer is formed as the major product in THF (**Scheme 39**).^[89]

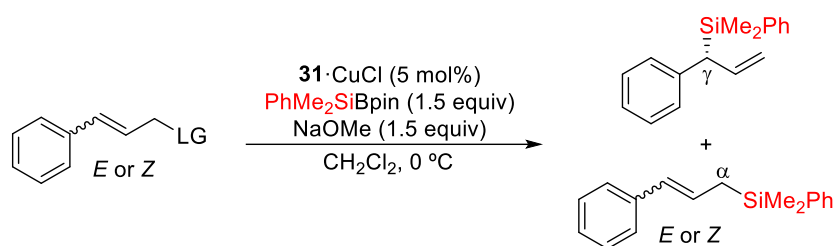


Ligand	R	Solvent	Yield (%)	γ/α	ee (%)
31	Me	CH ₂ Cl ₂	erratic results		
32	<i>t</i> Bu	CH ₂ Cl ₂	68	57/43	90
31	Me	THF	75	4/97	–
32	<i>t</i> Bu	THF	98	3/97	–
31	Me	Et ₂ O	87	51/49	49
32	<i>t</i> Bu	Et ₂ O	95	75/25	87
31	Me	toluene	92	70/30	82
32	<i>t</i> Bu	toluene*	95	73/27	85

*43% yield, γ/α = 91/9 and 93% ee at –35 °C

Scheme 39. Influence of the solvent in allylic silylation of (*E*)-allylic phosphates catalyzed by NHC·CuCl McQuade complexes.

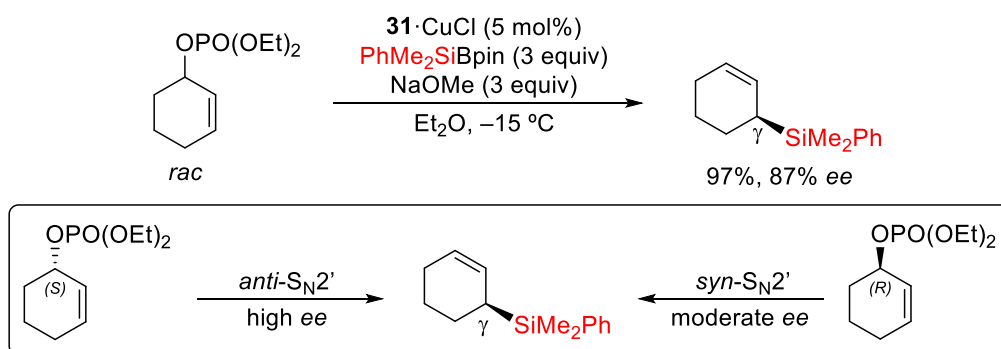
Interestingly, the boron method using McQuade complex **31**·CuCl was enantioconvergent. The same γ-allylsilane was indeed obtained in high yields (82% and 88%) and high regio- (γ/α = 97/3) and enantioselectivity (91% and 96% ee) from either (*E*)- and (*Z*)-allylic phosphates. The same trend was observed with allylic chlorides, albeit with a significant erosion of the enantioselectivity for both (*E*)- and (*Z*)-isomers (**Scheme 40**).



LG	Substrate	Yield (%)	γ/α	ee (%)
Cl	<i>E</i>	87	96/4	71
Cl	<i>Z</i>	91	98/2	31
OP(O)(OEt) ₂	<i>E</i>	82	97/3	96
OP(O)(OEt) ₂	<i>Z</i>	88	97/3	91

Scheme 40. Allylic silylation enantioconvergence of (*E*)- and (*Z*)-allylic chlorides and phosphates catalyzed by **31**·CuCl McQuade complex.

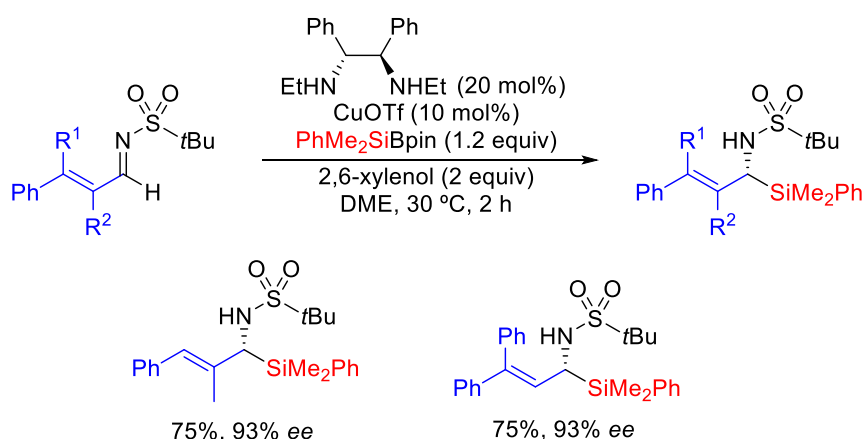
The convergent regioselective synthesis of an enantioenriched cyclic γ -allylsilane from racemic allylic electrophiles has been also reported by the employment of McQuade complex **31**·CuCl (**Scheme 41**).^[91] An allylic phosphate, rather than allylic ester, carbamate, carbonate or halide congeners, along with low temperature (−15 °C) in Et₂O were required to obtain the γ -adduct as the single regioisomer in a good 97% yield and with a high 87% ee using PhMe₂SiBpin (3 equiv) in the presence of preformed McQuade's catalyst **31**·CuCl (5 mol%) and NaOMe (3 equiv). Under these reaction conditions, a direct enantioconvergent transformation of the two enantiomers take place, to furnish the same enantioenriched γ -allylsilane by two distinctive S_N2'-pathways. The stereochemically matched γ -silylation with the (*S*)-enantiomer occurred in a highly enantioselective *anti*-S_N2'-fashion whereas the stereochemically mismatched reaction with the (*R*)-enantiomer took place in a moderate enantioselective *syn*-S_N2'-fashion.



Scheme 41. Convergent regio- and enantioselective conversion of a racemic cyclic allylic phosphate catalyzed by **31**·CuCl McQuade complex.

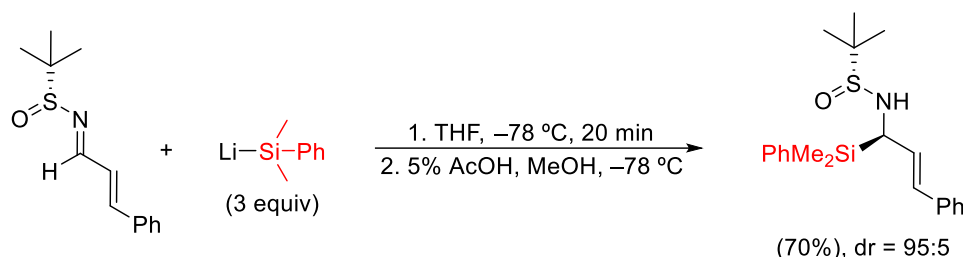
1.2.1.7 1,2-silylation of imines

Another silylation-based strategy envisioned conjugated sulfonyl imines as appropriate starting materials to access chiral allylsilanes. In this regard, two α -amino allyl silanes were described to be obtained through catalytic enantioselective silylation of *N*-*tert*-butylsulfonyl allylic imines with $\text{PhMe}_2\text{SiBpin}$.^[92] Contrary to other Cu-catalyzed carbonyl 1,2-silylations, chiral phosphine ligands led to unsatisfying yields and enantiomeric excesses. Nevertheless, Cu-secondary diamine complex, *in situ* prepared from CuOTf and *N,N*-diethyl-1,2-diphenylethylenediamine (Cu:diamine = 1:2), catalyzed the attack of bimetallic $\text{PhMe}_2\text{SiBpin}$ (1.2 equiv) to protected imines in DME at 30 °C under the presence of 2,6-xyleneol (2 equiv) to yield two different *N*-*tert*-butylsulfonyl- α -amido silanes in good ee (**Scheme 42**). The presence of 2,6-xyleneol not only plays a key role in the reaction as proton source to accelerate the regeneration of the catalyst but also in the enantioselective outcome of the reaction; in the absence of alcohol, 42% yield and 68% ee are achieved whereas 91% yield and 86% ee are obtained with 2,6-xyleneol.



Scheme 42. Synthesis of α -amino allylsilanes from *N*-*tert*-butylsulfonylimines.

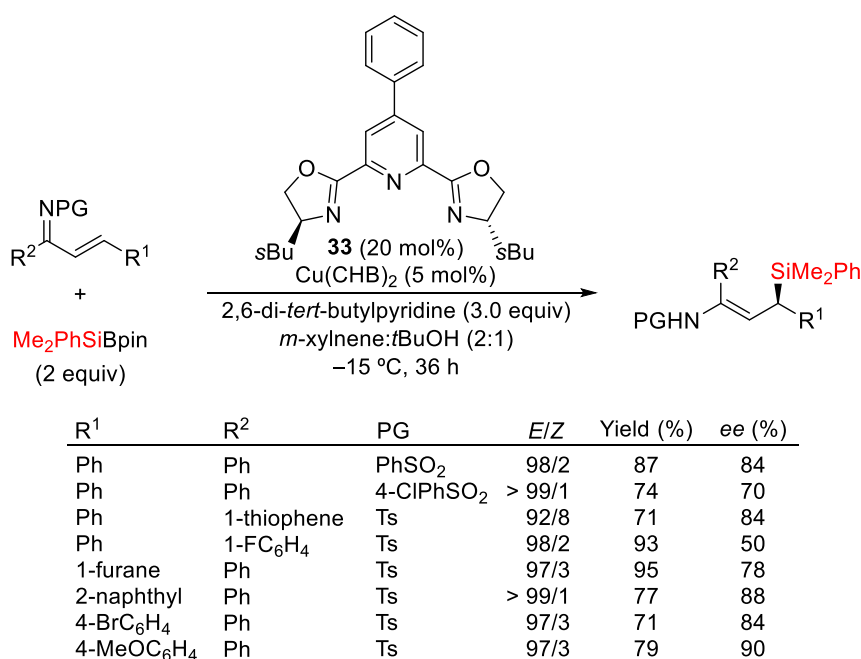
On the other hand, the same 1,2-silylation strategy can be applied in the absence of copper with non-racemic chiral *tert*-butanesulfinyl imines (**Scheme 43**).^[93] Direct addition of silyl nucleophiles (PhMe_2SiLi) on the activated carbon-nitrogen double bonds takes place at -78 °C in THF. Quenching with 5% acetic acid in methanol furnished the α -silylamine in 70% yield and dr = 95:5. The chiral *tert*-butanesulfinyl substituent is crucial not only regarding the diastereoselective levels of the reaction, but also plays a key role in the carbon centre activation as well as avoiding *aza*-Brooks rearrangements by delocalizing the nitrogen anion generated during the reaction.



Scheme 43. Preparation of allylsilanes starting from *tert*-butanesulfinyl imines.

1.2.1.8 Conjugate addition on carbonyl derivatives

Racemic γ,γ -disubstituted allylsilanes can be accessed through the Michael addition of the silicon atom to conjugated imines. Cu-catalyzed conjugate protosilylation of α,β -unsaturated ketimine with Suginome silaboronate in the presence of 5 mol% of copper bis(4-cyclohexylbutyrate), 10 mol% of 2,2'-bipyridine and 3 equiv of *N,N*-diisopropylamine (DIPEA) in a solvent mixture of *m*-xylene and *tert*-butanol (2:1), proceed at $-15\text{ }^{\circ}\text{C}$ to furnish (*E*)- α -phenyl allylsilanes in excellent stereoselectivities.^[94] An asymmetric version of this reaction was achieved by changing the base to 2,6-di-*tert*-butylpyridine and the ligand to (S,S)-4-Ph-Pybox-sBu. The phenyl substituent connected to the pyridyl ring of the Pybox ligand generate a π - π interaction with the dimethylphenylsilyl group of the borane, resulting in a higher enantioselectivity (ee up to 92%) of the (*E*)-trisubstituted allylsilanes (**Scheme 44**). Better enantioselectivities and lower reactivity were observed for electron rich substrates, which could be explained by the lower electrophilicity and stronger interaction between the Suginome silaboronate and the Cu(II)·Pybox species generated *in situ*.



Scheme 44. 1,4-Michael type addition of Bpsilane to α,β -unsaturated imines.

The high (*R*)-*E*-isomer formation of β -tosylamine-substituted allylsilanes could be explained by the favoured *Re*-face nucleophilic attack of [PhMe₂Si-Cu(II)] intermediate to the double bond. This attack is encouraged because of the minimum steric interaction between the isobutyl group of the ligand and the tosyl group of the substrate in transition state **A** (**Figure 3**) as well as π - π interaction of phenyl rings.

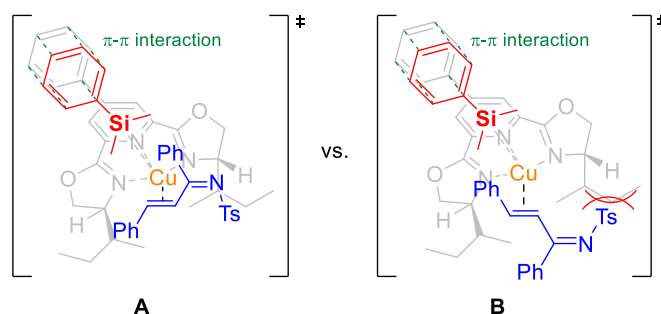
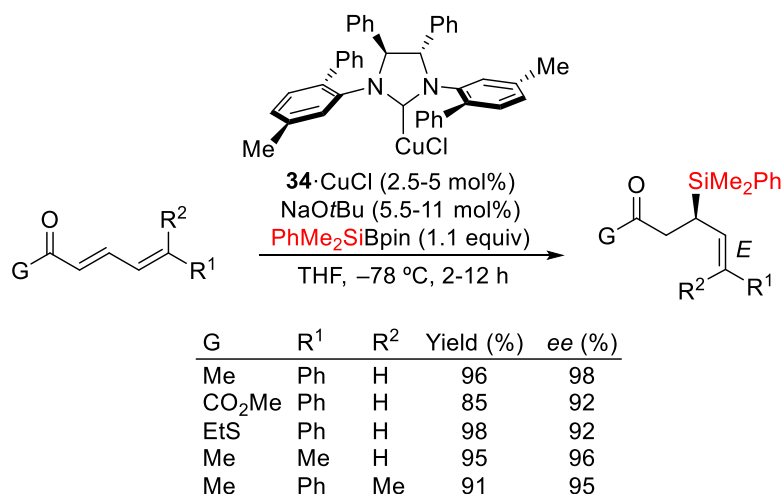


Figure 3. Comparison of the possible transition states to form (*E*)-(*R*)-allylsilanes.

1.2.1.9 Conjugate addition on dienones and dienoates

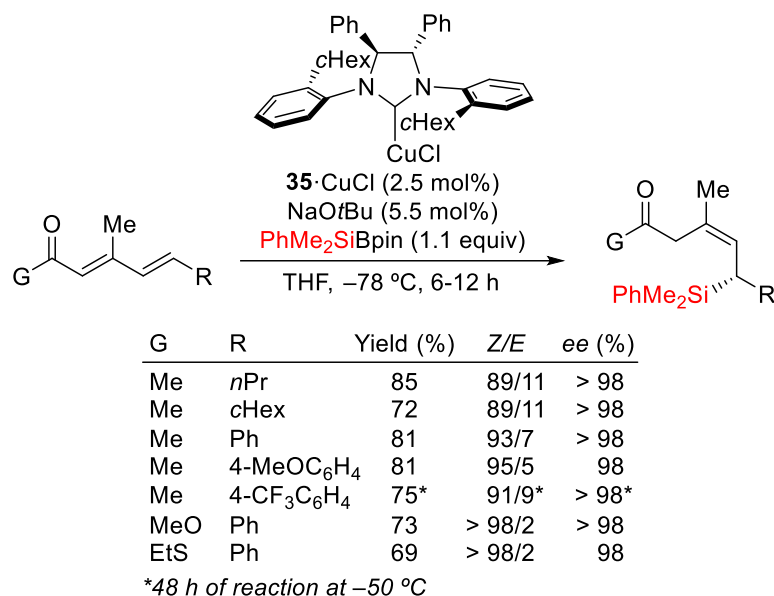
In the same vein, the copper(I)-catalyzed enantioselective conjugate silyl addition to dienones and dienoates also allows the formation of allylsilanes. The reaction was run with silylboronate PhMe₂SiBpin (1.1 equiv) in the presence of NHC-copper complexes (2-2.5 mol%), *in situ* generated from imidazolium salts and CuCl, and a catalytic amount of NaOtBu (4.4-11 mol%) in THF at -78 °C.^[95,96] With dienones and dienoates, that do not bear a substituent in the β -position (**Scheme 45**), NHC complex **34**·CuCl was the most efficient affording (*E*)-allylsilanes as single diastereomer (through a 1,4-mode addition of the silyl moiety) in excellent yields ($\geq 85\%$) and enantioselectivities ($ee \geq 92\%$).



Scheme 45. Conjugate silyl 1,4-addition on acyclic dienones and dienoates.

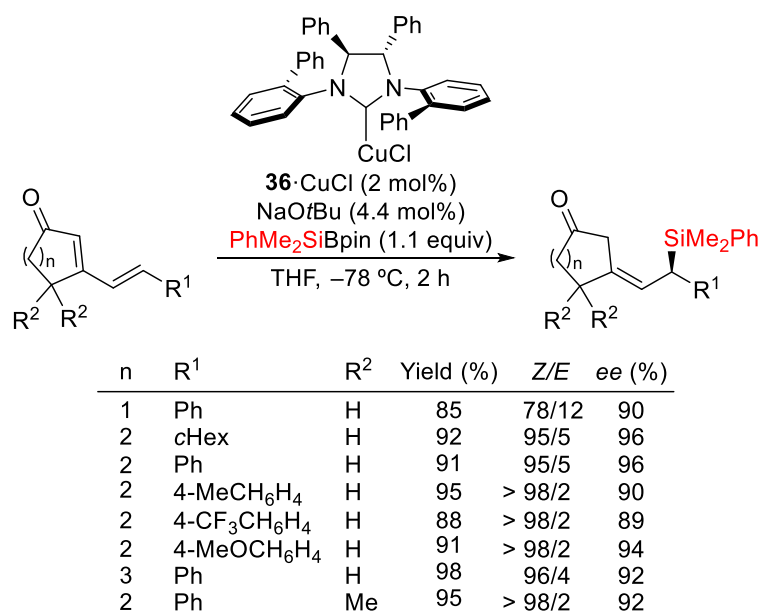
By contrast, in the presence of a β -substituent, the 1,6-mode of addition of the silyl group predominated, giving (*Z*)-allylsilanes as single isomers (**Scheme 46**). The use of NHC complex

35·CuCl was required to achieve good yields ($\geq 69\%$) and both high (*Z*)- (*Z/E* $\geq 89/11$) and enantioselectivity (*ee* $\geq 98\%$).



Scheme 46. Conjugate silyl 1,6-addition on acyclic dienones and dienates.

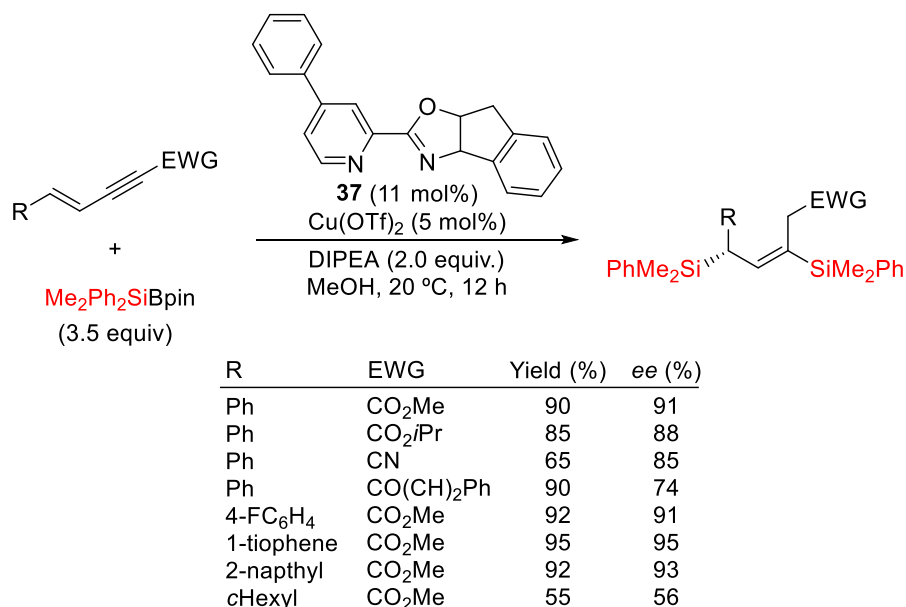
With β -cyclic dienones, the best results were obtained by employing NHC complex **36**·CuCl (**Scheme 47**) which leads to excellent yields ($\geq 85\%$) and enantioselectivities (*ee* $\geq 89\%$). Except in the peculiar case of the cyclopentenone, the *Z*-selectivity was always high (*Z/E* $\geq 95/5$).



Scheme 47. Conjugate silyl 1,6-addition on cyclic dienones.

In the same field of 1,4- and 1,6-addition, double cascade silylations of electron-deficient conjugated enynes in a one-pot manner was also developed to access 1,3-bis(silyl)propene products in a regio- and enantiodefined way.^[97] This procedure involves the 1,4-addition of

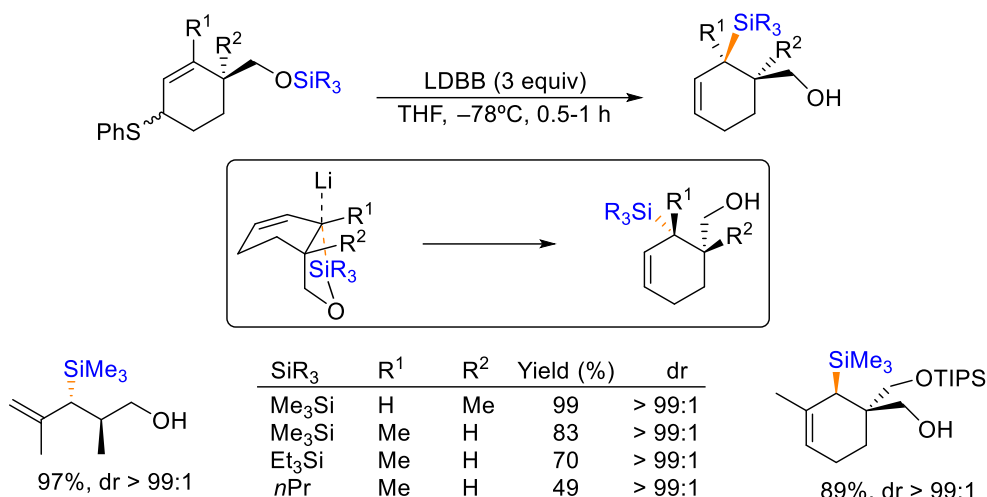
silylboronate $\text{PhMe}_2\text{SiBpin}$ (3.5 equiv) to different (*E*)-conjugated polar enynes in the presence of 5 mol% of $\text{Cu}(\text{OTf})_2$, 11 mol% of chiral C_4 -pyridine substituted oxazoline-based ligand **37** and DIPEA (2.0 equiv) in MeOH at -20°C for 12 h. Then, the conjugated dienoates undergo a 1,6-addition to furnish the expected enantioenriched allylsilanes in good yields and ee (up to 97% and 95% respectively). With the alkyl substituted cyclohexylenynoate, desired α -alkylsubstituted allylsilane was obtained but with a big erosion of both the yield and enantioselectivity. Contrarywise, this methodology was unsuccessful when applied with (*Z*)-enyne analogues, since a complex mixture of products is obtained with very low yield.



Scheme 48. Synthesis of chiral allylsilanes through double cascade protosilylation.

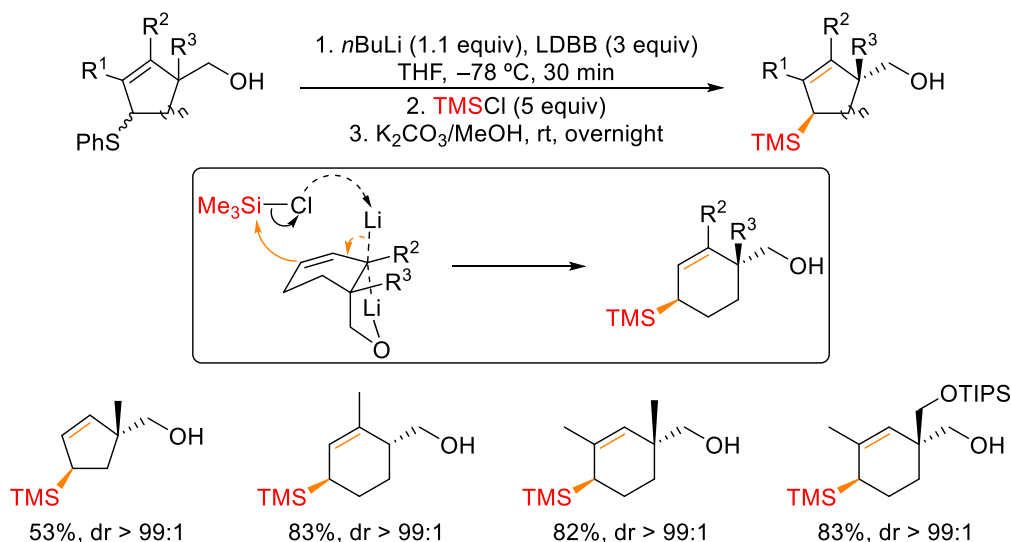
1.2.1.10 Retro-Brook rearrangement

Changing completely both the substrate and the strategy and taking advantage of the facile migratory aptitude of the silyl groups, cyclic and acyclic γ -silylated alkanols were prepared by exposing silyl ether allylsulfides to 3 equiv of lithium di-*tert*-butylbiphenylide (LDBB) in THF at -78°C for 1 h.^[98,99] Under these conditions, high regio- and stereoselective 1,4-migration of the silyl group from the oxygen to the carbanionic site occurred, yielding *anti*-acyclic and *syn*-cyclic allylsilanes as exclusive diastereoisomers (**Scheme 49**). Different silicon groups were able to perform this retro-Brook rearrangement except the $i\text{Pr}_3\text{Si}$ moiety due to its high bulkiness. The rearrangement stereochemical outcome can be explained by a sp^2 -like configuration of the allyllithium intermediates, where the axial-oriented $\text{CH}_2\text{-OSiR}_3$ deliver the silyl group in a way that *cis*-substituted α -hydroxymethyl allylsilanes are formed.



Scheme 49. Synthesis of allylsilanes through a retro-Brook rearrangement.

Surprisingly, the treatment of the free alcohol analogues with *n*BuLi (1 equiv) followed by the addition of LDBB (3 equiv) and subsequent quench of the *in situ* formed dilithiated species with ClSiMe₃ (5 equiv), furnished disilylated species that after treatment with K₂CO₃ in MeOH give the corresponding chiral allylsilanes with the other regioselectivity. Excellent diastereoselectivities (dr > 99:1) in favour of the *anti*-isomer were observed. This preferred diastereoselectivity outcome can be rationalized by the high steric hindrance around the OLi that favours a *syn*-S_E2 process to yield *trans*-substituted alcohols (**Scheme 50**).

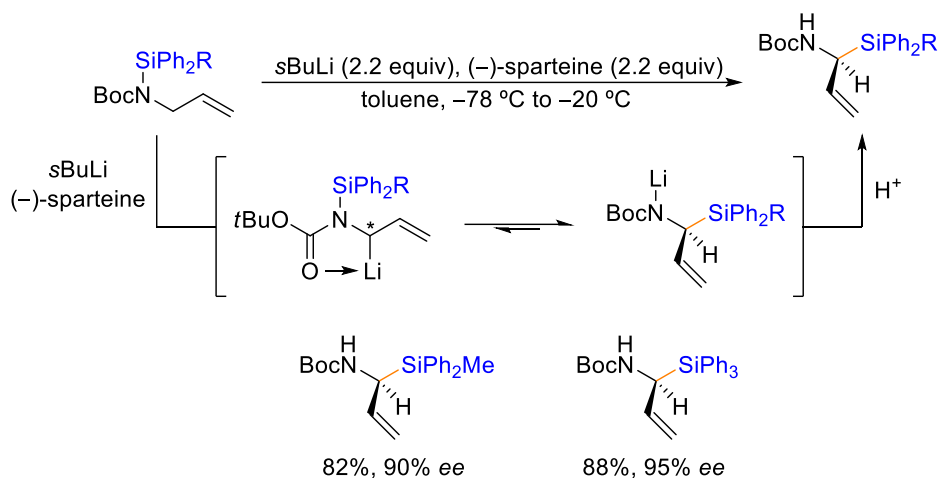


Scheme 50. Preparation of enantioenriched allylsilanes from allylsulfides alcohols.

1.2.1.11 Reverse-aza-brook rearrangement

Taking advantage of the migration ability of the silicon group, preparation of chiral α -aminoallylsilanes involving the metalation of Boc-protected *N,N'*-allylsilylamines with a (–)-sparteine *sec*-butyllithium complex in toluene was reported.^[100] Under these conditions, enantiodefined lithium species are generated that allow the subsequent controlled migration

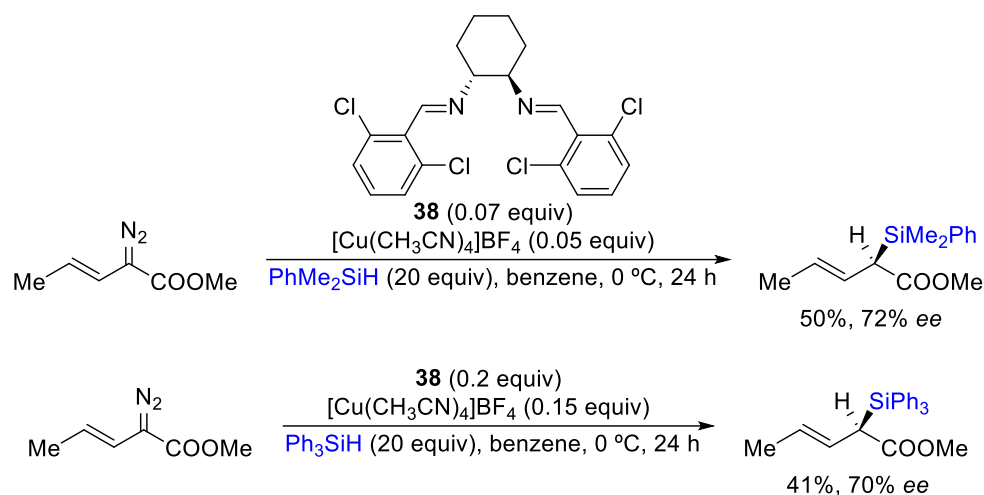
of the $\text{RPh}_2\text{Si-}$ group from the nitrogen to carbon, yielding the corresponding allylsilanes in good yields and excellent enantioselectivities (**Scheme 51**).



Scheme 51. Synthesis of α -*N*-Boc-aminoallylsilanes.

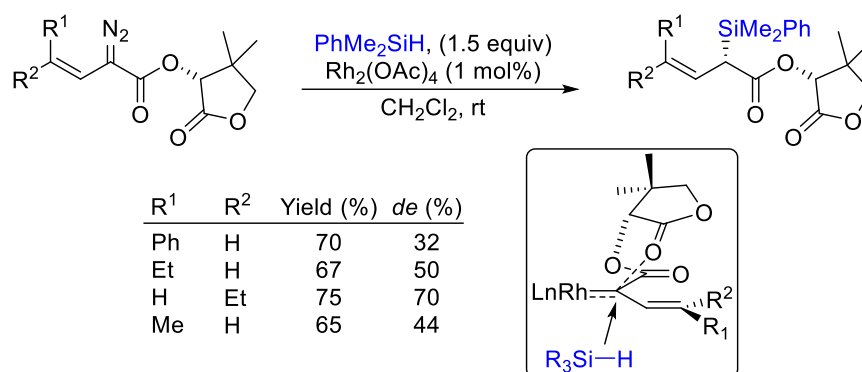
1.2.1.12 Insertion of vinylcarbenoids in Si-H bond

Another completely different approach that also relied on the formation of a carbon-silicon bond for the preparation of chiral allylsilanes, was based on a synthetic strategy developed in the mid 60's by Nozaki and co-workers. They reported the enantioselective cyclopropanation of styrene *via* decomposition of ethyl diazoacetate in the presence of a Cu(II) chiral Schiff base complex, opening the development of chiral catalysts for asymmetric reactions of metal carbenoids.^[101] Among all the transition metals, Ir, Cu and Rh complexes stand out as the best promoters for the carbene Si-H bond insertion. However, the enantioselective Si-H insertion on α -vinyl diazoesters has been almost exclusively achieved using Rh catalyst. Only one example was described where two chiral allylic silanes with carbon-centred chirality were prepared in moderate yields ($\leq 50\%$) and enantioselectivities (70-72% ee) *via* Cu-catalyzed insertion of vinylcarbenoids in Si-H bond (**Scheme 52**).^[102] In the presence of preformed Cu(I) complex **38** (dichlorodiimine ligand: $[\text{Cu}(\text{CH}_3\text{CN})_4(\text{BF}_4)] = 1:1.4$) and 5-20 equiv of Ph_3SiH or PhMe_2SiH in benzene at 0 °C, the insertion takes place to give rise to the corresponding allylsilanes.



Scheme 52. Asymmetric copper-catalyzed insertion of vinylcarbenoids in Si–H bond.

Alternatively, vinylrhodium carbenoid species could also be stereospecifically inserted into the Si–H bond of trialkylsilanes with stereoselective control of the allylic chiral centre formed. Asymmetric decomposition of α -diazo- β,γ -unsaturated esters, having (*R*)-pantolactone as chiral auxiliary, in the presence of 2 equiv of R_3SiH ($\text{R} = \text{alkyl, Ph}$) and 1 mol% of $\text{Rh}_2(\text{OAc})_4$ in CH_2Cl_2 at rt afforded the corresponding chiral α -silyl esters in moderate yields and diastereoselectivities (**Scheme 53**).^[103]

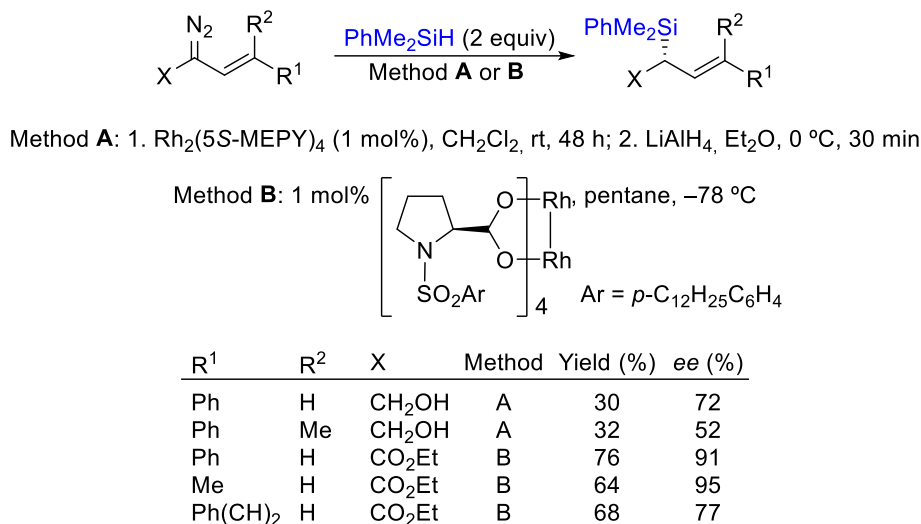


Scheme 53. Asymmetric insertion of Rh-vinylcarbenoids into Si–H bonds and proposed transition state.

Using (*R*)-pantolactone as a chiral auxiliary leads to a rigidification of the transition state resulting in a high diastereofacial preference by coordination of the carbenoid centre with the carbonyl of the pantolactone (**Scheme 53**). Improved selectivities are achieved compared to non-coordinating chiral auxiliaries such as menthol. However, reduction of the ester (to remove chiral auxiliary) occurred with partial epimerization of the stereogenic centre.

Another approach involving the insertion of achiral vinyl diazoesters into the Si–H bond in the presence of 1 mol% of $\text{Rh}_2(5\text{S-MEPY})_4$ in CH_2Cl_2 at rt yields the corresponding enantioenriched β -silylhomoallylic alcohols bearing different silicon moieties with enantiomeric excesses up to 72% but considerably lower yields (< 32%).^[104] Changing the catalyst to $\text{Rh(II)-(S)-N-[p-(dodecylphenyl)sulfonyl]prolinat}$, decomposition of vinyl-diazomethanes at

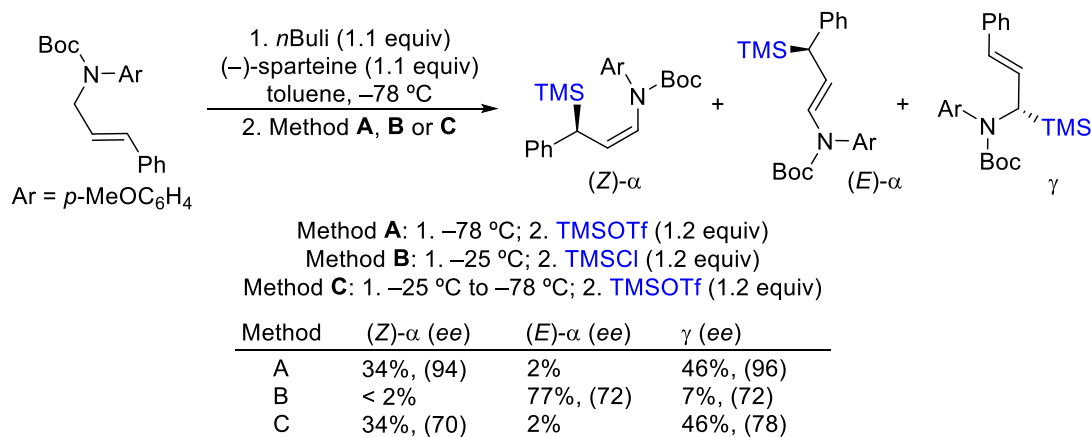
$-78\text{ }^{\circ}\text{C}$ in pentane resulted in the formation of allylsilanes in 77-95% ee and yields $\geq 64\%$ (**Scheme 54**).^[105] It is worthy to mention that vinylrhodium carbenoid insertion into silanes takes place regioselectively α to the ester group, maintaining the geometry of the starting double bond.



Scheme 54. Asymmetric Rh(II)-catalyzed decomposition of vinyl diazomethanes in the presence of PhMe_2SiH .

1.2.1.13 Silylation of allylic amines

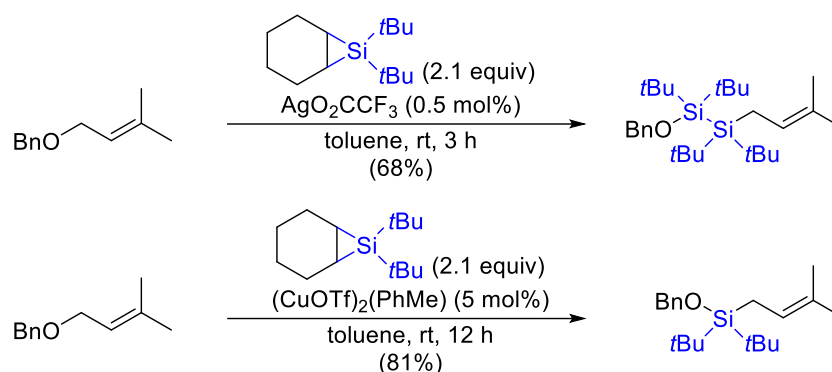
An alternative two steps procedure consisting in the (–)-sparteine mediated lithiation-silylation of tertiary amines was unveiled to furnish chiral allylsilanes as a mixture of isomers.^[106,107] (–)-sparteine mediated asymmetric deprotonation α to the nitrogen of *N*-Boc-*N*-(*p*-methoxyphenyl)-cinnamylamine with 1.1 equiv of *n*BuLi at $-78\text{ }^{\circ}\text{C}$ in toluene provides dipole-stabilized carbanions (organolithiums) that are subsequently trapped with TMS electrophiles to provide chiral allylsilanes as a mixture of (*Z,S*)- and (*E,R*)- α -isomers and (*E,S*)- γ -isomer. The stereoselectivity as well as the enantioselectivity of each isomer are dependent on both the temperature and the nature of the electrophile (**Scheme 55**).



Scheme 55. Temperature and electrophile dependent synthesis of α -amino allylsilanes as a mixture of isomers.

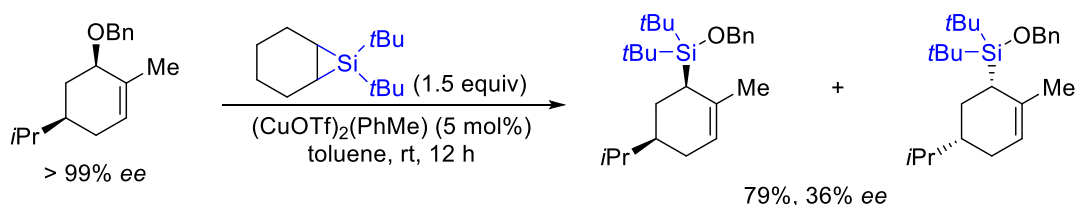
1.2.1.14 Metal-catalyzed silylene insertions

Another strategy for the preparation of allylsilanes where only one substrate was investigated consists in silane insertion into C–O bond.^[108] Silylene insertion in the allylic C–O bond can be applied to 1,2-substituted and trisubstituted alkenes but not monosubstituted ones for which the formation of silacyclopropenes is observed. By changing the metal used as catalyst, two (with AgO_2CCF_3) or one (with $(\text{CuOTf})_2(\text{PhMe})$) di-*tert*-butylsilylene groups from cyclohexene silacyclopropane are inserted in the C–O to form the corresponding allylic disilane or silane (**Scheme 56**).



Scheme 56. Metal-catalyzed synthesis of diallyl and monoallylsilanes.

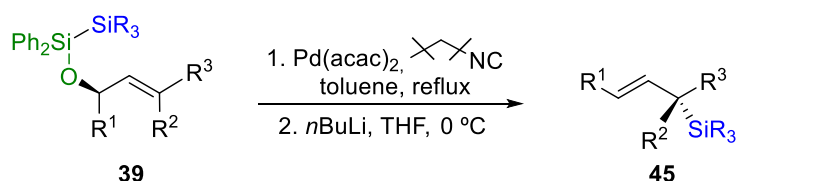
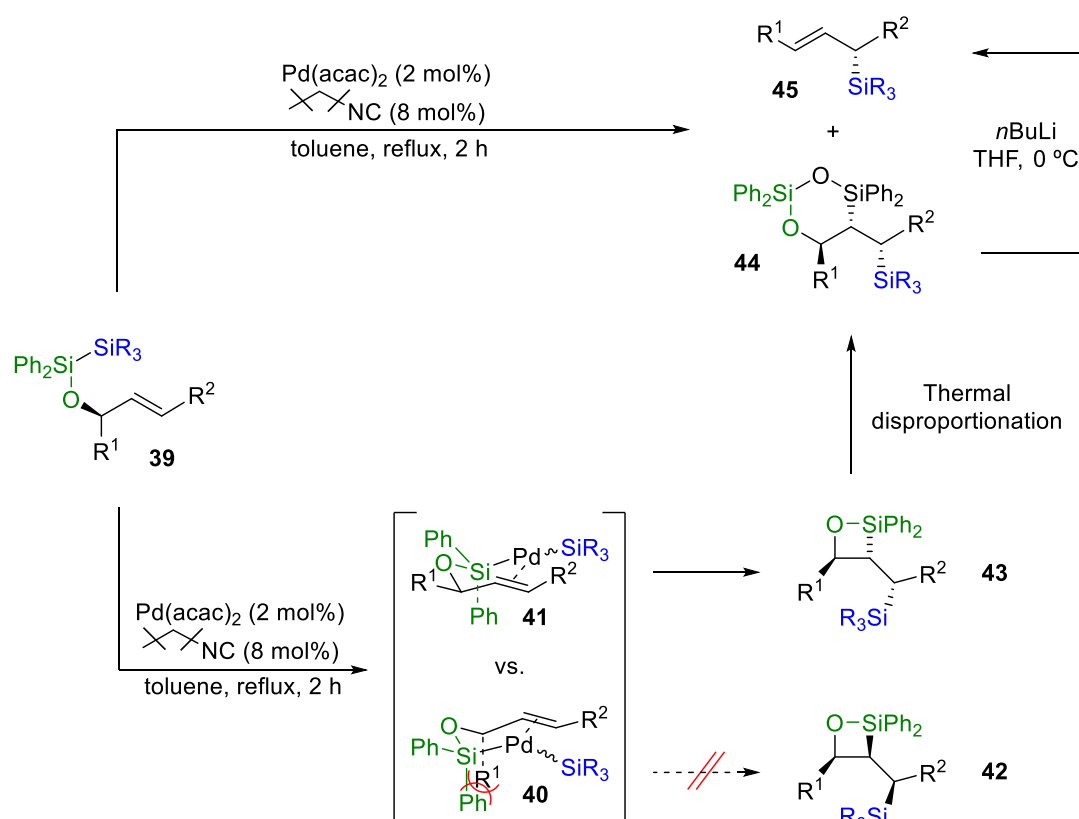
Same strategy can be applied with enantiopure trisubstituted cyclohexene in the presence of 5 mol% of $(\text{CuOTf})_2(\text{PhMe})$ in toluene at rt to furnish the corresponding *cis*-allylsilane isomer (the new carbon-silicon bond is exclusively formed on the same face of the carbon-oxygen bond that is broken) with low enantiomeric excess (**Scheme 57**).



Scheme 57. Preparation of enantioenriched allylsilanes through silylene insertions.

1.2.1.15 Intramolecular bis-silylation (IBS) of allylic alcohols.

In the vein of the chiral allylsilane synthesis through the formation of a novel carbon-silicon bond, when (*Z*)- or (*E*)-allylic alcohols react with 1-chloro-1,1-diphenyl disilanes in the presence of Et₃N and DMAP, the corresponding (*Z*)- or (*E*)-disilanyl ethers **39** are formed as exclusive isomers. Subsequently, a one pot procedure consisting in the treatment of homoallylic silylethers with 2 mol% of Pd-complex *in situ* prepared from Pd(acac)₂ and 1,1,3,3-tetramethylbutyl isocyanide (Pd:CN = 1:4) in reflux of toluene affords a mixture of the corresponding (*E*)-allylsilanes **45** ((*Z*)-disilanes provide (*E*)-isomers with opposite absolute configuration) along with the six-membered cyclic disiladioxane **44**. These cyclic molecules, formed from the reaction of *trans*-oxasiletanes **43** and Ph₂Si=O (*in situ* generated from the *syn*-elimination on **43**), can be converted to the target allylsilanes through a Peterson-type *syn*-elimination after treatment with *n*BuLi (1 equiv) in THF at 0 °C (**Scheme 58**).^[109–111] This procedure takes place with high regioselectivity and almost complete 1,3-chirality transfer from the allylic alcohols. These features can be attributed to the highly stereoselective IBS (*cis*-addition of the two silicon atoms to the carbon-carbon double bond) that exclusively produces *trans*-oxasiletanes through the bis-(silyl)palladium(II) intermediate **41** where the substituent α to the oxygen lies in the pseudoequatorial position to minimize steric interactions (**Scheme 58**). The two phenyl groups on the silicon atom on the oxygen are crucial for achieving enough reactivity for the addition on the internal carbon-carbon double bond, as well as to reach high stereoselectivity. Several different silyl groups can be utilized without eroding the chiral transfer and the yields, except for the *i*Pr₃Si analogue, where the yield decreased to 62% (**Scheme 58**).^[110]

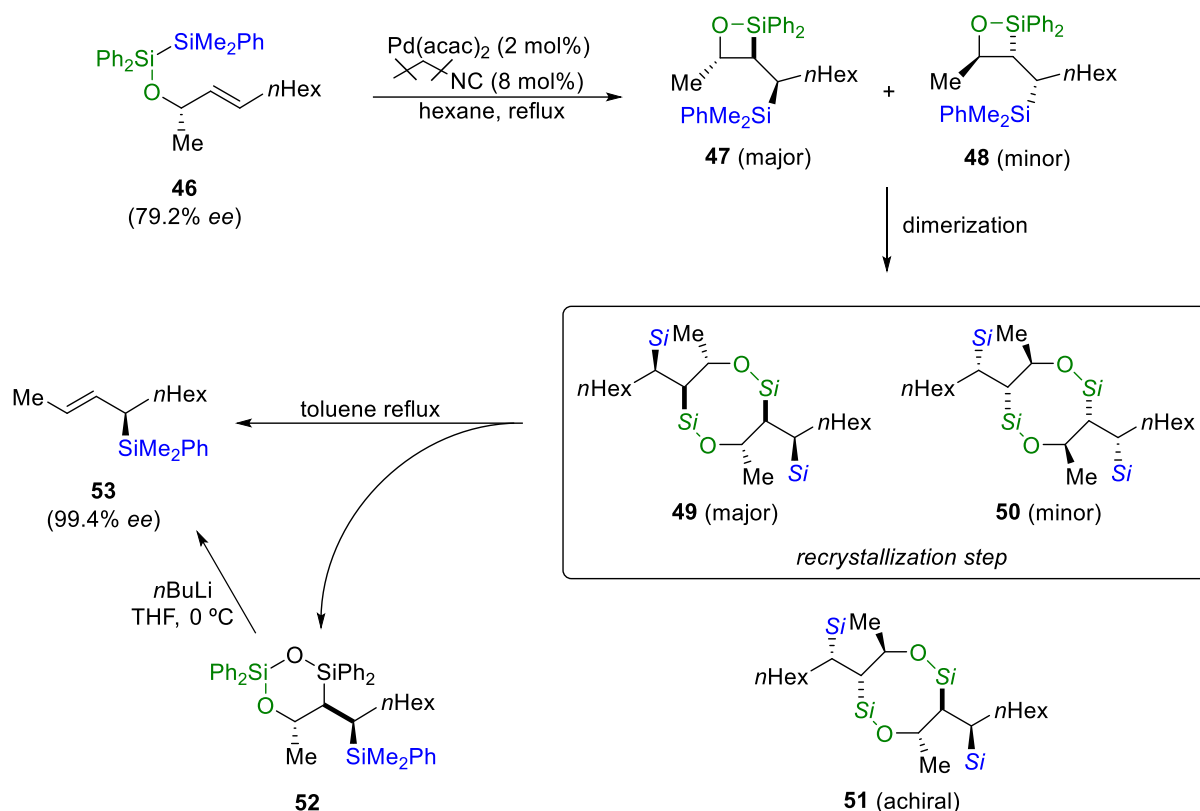


ee 39 (%)	SiR_3	R^1	R^2	R^3	Yield (%)	ee 45 (%)
99.7	PhMe_2Si	Me	H	$n\text{Hex}$	90	99.1
96.0	PhMe_2Si	Me	$n\text{Hex}$	H	84	95.4
99.6	Me_3Si	Me	H	$n\text{Hex}$	81	99.1
99.6	$t\text{BuMe}_2\text{Si}$	Me	H	$n\text{Hex}$	82	99.4
99.6	Et_3Si	Me	H	$n\text{Hex}$	94	99.2
99.6	$i\text{PrSi}$	Me	H	$n\text{Hex}$	62	98.8

Scheme 58. Synthesis of allylsilanes through IBS of disilananyl ethers derived from allylic alcohols.

Later studies enable the preparation of eight-membered cyclic structures (dioxadisilacyclooctanes) by dimerization of oxasiletanes, through a thermal disproportionation in refluxed toluene, affording the corresponding allylsilane **45** and disiloxane **44** (subsequently transformed to the corresponding allylsilane in the presence of $n\text{BuLi}$).^[111] Since during the dimerization step, isolable diastereoisomeric intermediates are formed (chiral and achiral), they envisioned the possibility of obtaining highly enantioenriched allylsilanes from optically active allylic alcohols with lower enantiopurity. This was applied in the case of **46** (79.2% ee), where highly enantioenriched allylsilanes **53** was isolated in 99.4% ee, after recrystallization

of the corresponding chiral diastereoisomers and their subsequent treatment with *n*BuLi in refluxed toluene (**Scheme 59**).



Scheme 59. Synthesis of chiral allylsilane from poor enantiopure allylic alcohols.

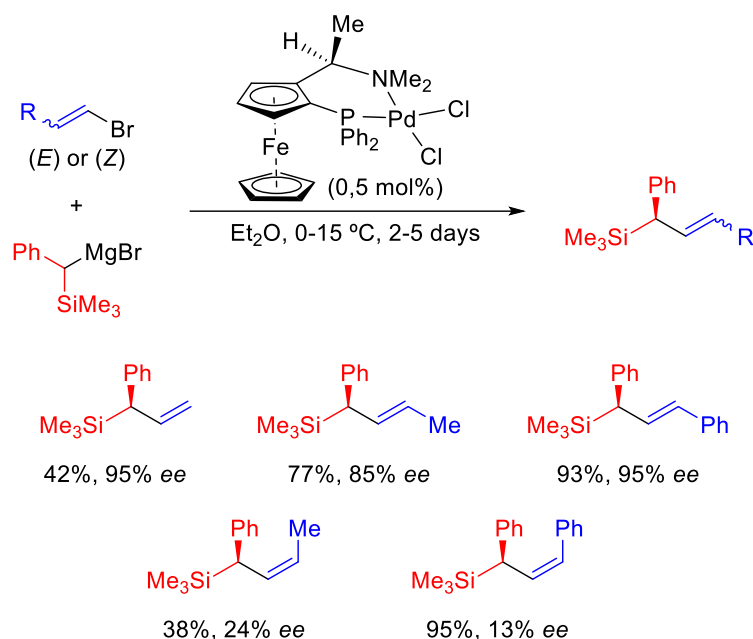
1.2.2 Stereoselective functionalization of silyl-substituted substrates

As it was mentioned before, the synthesis strategies for the preparation of asymmetric allylsilanes could be divided in two main groups depending how the silicon moiety is introduced in the desired molecule. After overhauling the methods where a carbon-silicon bond was created using many different precursors (1,3-dienes, allylic electrophiles, α,β -conjugated carbonyl derivatives...), we will now draw our attention over those methods implying silicon substituted substrates.

1.2.2.1 α -silyl-substituted Grignard reagents for Kumada-Corriu cross coupling

The first synthesis of optically active allyl silanes was developed in 1982 based on a Pd-catalyzed asymmetric cross coupling between α -(trimethylsilyl)benzyl organomagnesium reagents and 2-substituted vinyl bromides. Both (*E*)- and (*Z*) vinylbromides can be used as coupling reagents in the presence of 0,5 mol% of Pd-ferrocenylphosphine complex

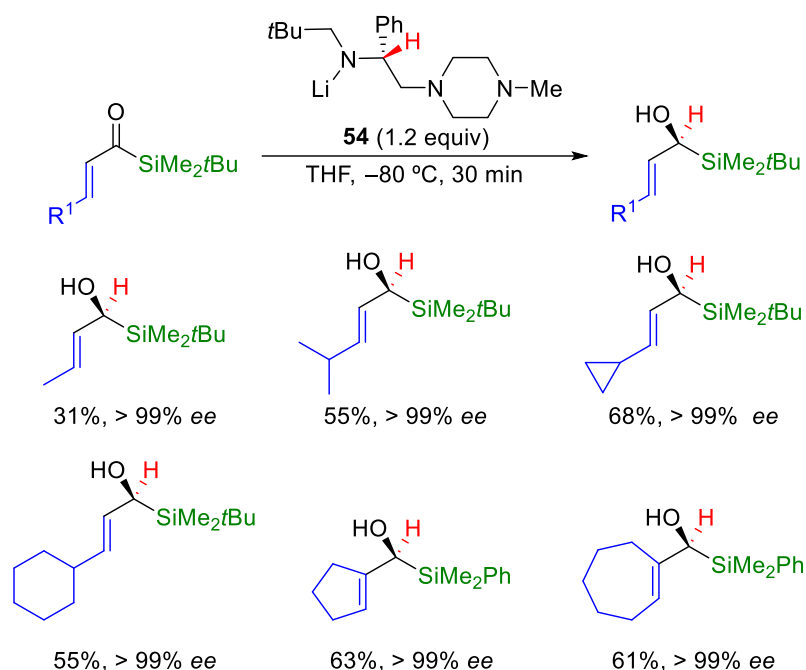
(*R*)-(*S*)-BPPFA) in Et₂O (**Scheme 60**).^[112] Nevertheless, *cis*-isomers give rise to the corresponding (*Z*)-allylsilanes with very poor ee ($\leq 24\%$).



Scheme 60. Synthesis of chiral allylsilanes by Kumada cross-coupling.

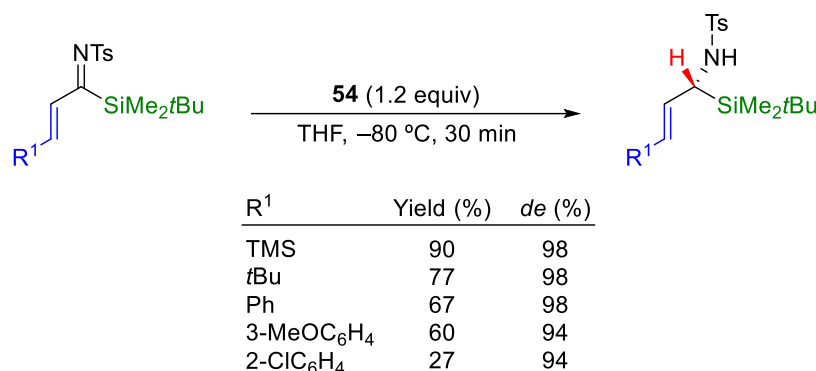
1.2.2.2 Meerwein-Ponndorf-Verley-type reduction

Enantioselective reduction of carbonyl derivatives *via* hydride transfer from chiral lithium amides is a potent strategy for the preparation of chiral alcohols. Although it was first reported in 1969 with common ketones, it was not until 1999 when it was used over acylsilanes for the preparation of chiral allylsilanes.^[113] In this regard, α,β -unsaturated acylsilanes were asymmetrically reduced in the presence of 1.2 equiv of **54** in THF at -80 °C to provide the corresponding α -silyl alcohols in low to moderate yields (31-68%, with no full conversion achieved) but ee > 99% (**Scheme 61**).



Scheme 61. Enantioselective reduction of α,β -unsaturated acylsilanes.

The same strategy can be applied with *N*-tosylsilylimines to synthesize α -silylamines in excellent enantioselectivities (ee $\geq 94\%$) but with moderate yields (27-90%, **Scheme 62**).^[114]



Scheme 62. Asymmetric reduction of α,β -unsaturated imines.

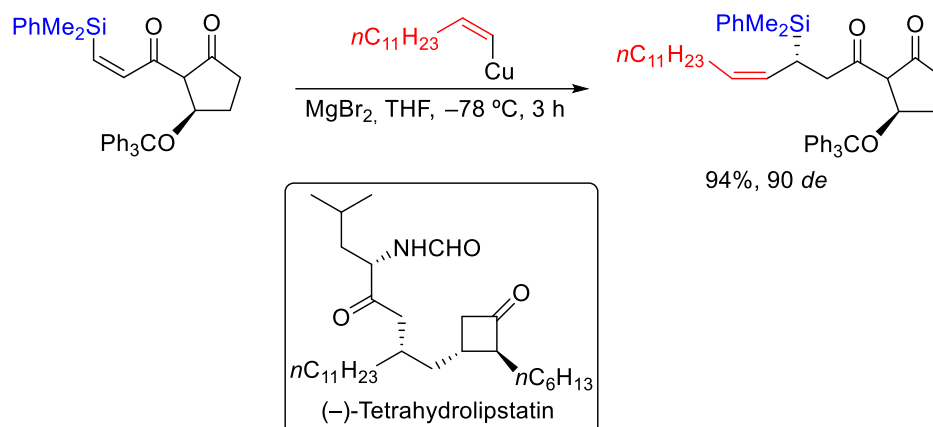
1.2.2.3 Addition on β -silyl- α,β -unsaturated carbonyl derivatives

α,β -Unsaturated carbonyl derivatives with the silicon in the β -position of the C=O double bond were also envisioned as suitable substrates to access valuable chiral allylsilanes through vinylation, alkylation and arylation.

1.2.2.3.1 Vinylation

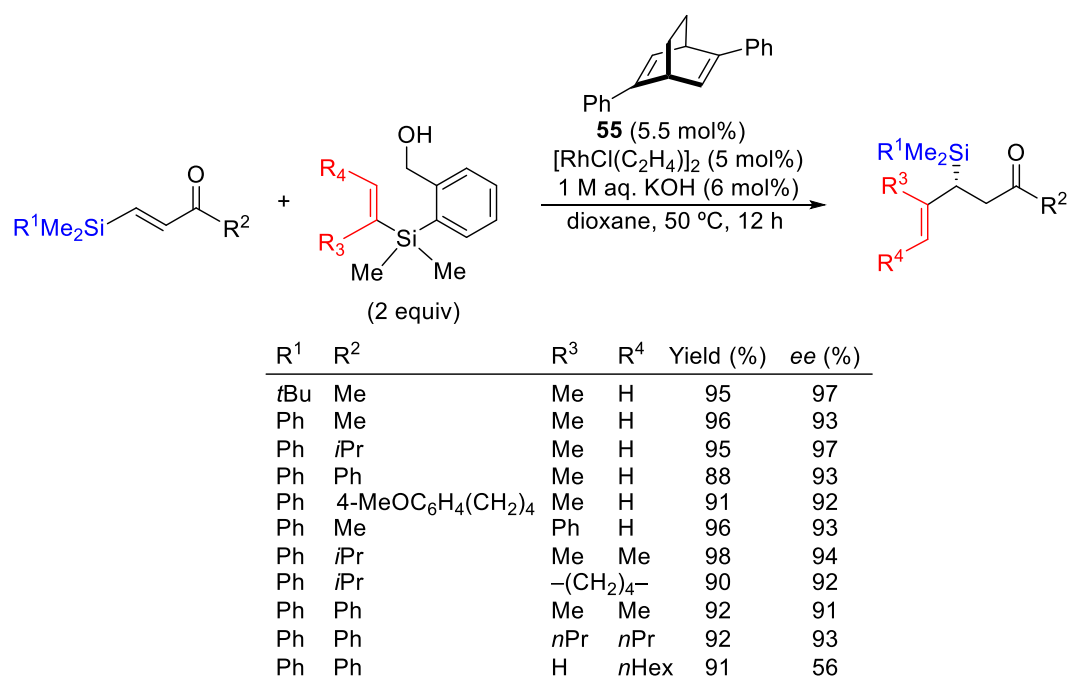
The vinylation was reported at the beginning of the 90's for the preparation of an enantioenriched allylsilane that was subsequently used for the synthesis of (–)-Tetrahydrolipstatin.^[115] This lactam was prepared in high diastereoselectivity (90% *de*) by

the conjugate addition of a vinylcuprate over a nonracemic β -silyl-substituted acryloyl lactam reagent in the presence of magnesium dibromide in THF at $-78\text{ }^{\circ}\text{C}$ (**Scheme 63**).



Scheme 63. Vinylcopper addition on a β -silyl-substituted acryloyl lactam.

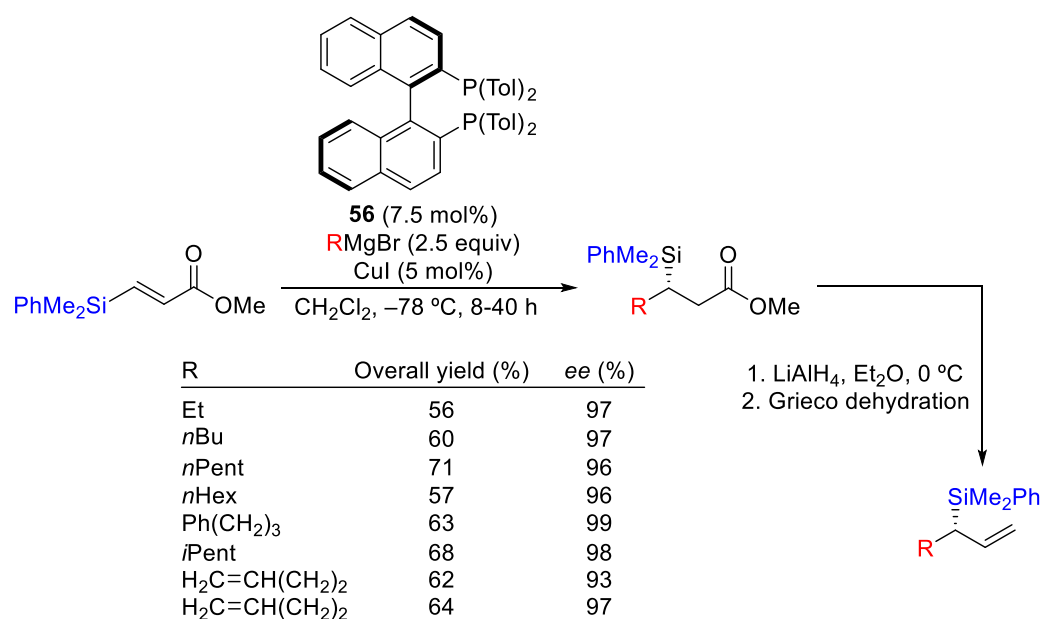
Following the same strategy, enantioenriched β -silyl- γ,δ -unsaturated ketones were prepared by the rhodium(I)-catalyzed asymmetric conjugate addition of various alkenyl nucleophiles to β -silyl- α,β -unsaturated ketones. The reaction was run with a combination of 5 mol% of $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ and 5.5 mol% of (*R,R*)-2,5-phenylbicyclo[2.2.2]octadiene **55** using alkenyl[2-(hydroxymethyl)phenyl]-dimethyl-silanes (2 equiv) in the presence of 6 mol% of aqueous KOH, within 12 h at $50\text{ }^{\circ}\text{C}$ in 1,4-dioxane (**Scheme 64**).^[116] Under these conditions, a plethora of allylsilanes was obtained in high yields (up to 98%), although the use of 1-substituted vinylsilanes were crucial to achieve high enantioselectivity (up to 97% ee, **Scheme 64**).



Scheme 64. Rhodium(I)-catalyzed allylic vinylation of β -silyl- α,β -unsaturated ketones.

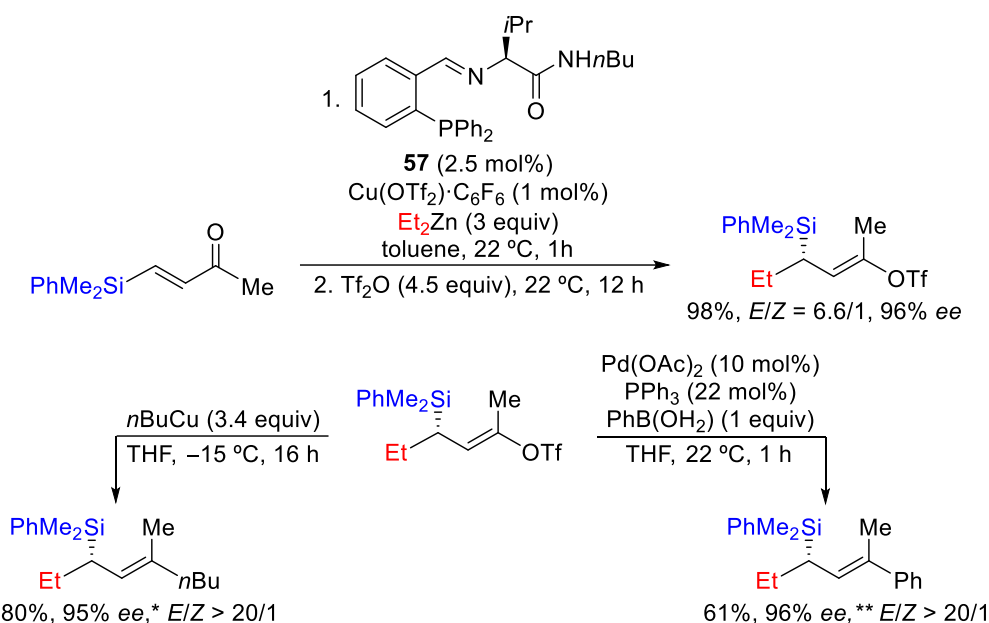
1.2.2.3.2 Alkylation

Later on, similar strategies were developed using alkyl nucleophiles. In those cases, post-functionalization of the carbonyl function was necessary to obtain the desired allylsilane. A multi-step procedure that involved an asymmetric copper(I)-catalyzed conjugate addition of alkyl Grignard reagent to 3-dimethylphenylsilyl methyl acrylate and subsequent reduction and Grieco dehydration was developed (**Scheme 65**).^[117] Under the optimal conditions, 5 mol% of CuI and 7.5 mol% of (*R*)-Tol-BINAP ligand **56** are used in CH₂Cl₂ at -78 °C. A plethora of tertiary α -alkyl-substituted allylsilanes was obtained in good overall yields (56-71%) and enantioselectivity (*ee* \geq 93%).



Scheme 65. Synthesis of allylsilanes through asymmetric copper(I)-catalyzed addition of Grignard reagents on 3-dimethylphenylsilyl methyl acrylate.

A second example involves the asymmetric conjugate addition of diethylzinc (3 equiv) to 4-dimethylphenylsilylbut-3-en-2-one in the presence of Cu(OTf)₂·C₆H₆ (1 mol%) and the chiral valine-based phosphine **57** (2.5 mol%) within 1 h in toluene at 22 °C (**Scheme 66**).^[118] Upon treatment with triflic anhydride, the resulting product afforded an enol triflate which was in turn subjected either to Suzuki cross coupling with phenylboronic acid or alkylation with *n*Butylcopper to deliver the corresponding enantioenriched (*E*)- γ,γ -disubstituted allylsilanes in fair yields (61% and 80%) with high enantio- and diastereoselectivities (*E/Z* > 20/1).

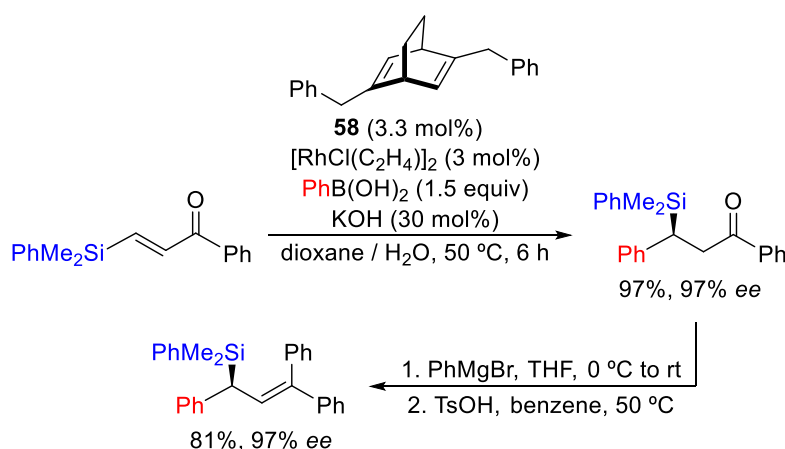


*Determined on the alcohol obtained by Hosomi-Sakurai reaction with benzaldehyde.
 **Determined on the alcohol obtained after epoxidation and fluoride mediated desilylation/epoxide cleavage.

Scheme 66. Two-step syntheses of allylsilanes via copper(I)-catalyzed addition of diethylzinc to 4-dimethylphenylsilylbut-3-en-2-one.

1.2.2.3.3 Arylation

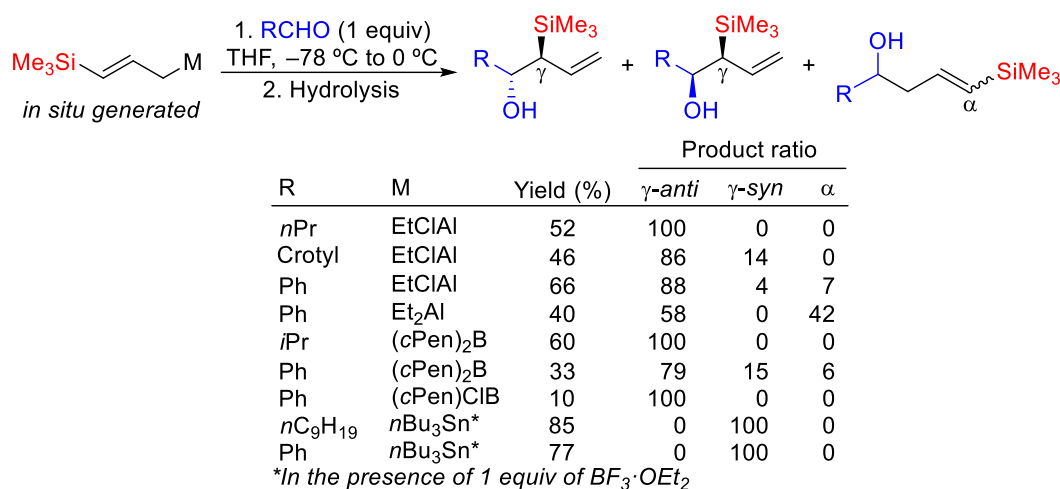
The same strategy was applied using an aromatic nucleophile for the preparation of one chiral allylsilane in excellent enantioselectivity.^[119] A related three-step procedure involving addition of phenylboronic acid (1.5 equiv) to phenyl 3-dimethylphenylsilylpropen-1-one by using 3 mol% $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ and 3.3 mol% of (*R,R*)-2,5-dibenzylbicyclo[2.2.2]octadiene **58** in the presence of 30 mol% of KOH has been disclosed (**Scheme 67**). The product obtained within 6 h at 50 °C in a 1,4-dioxane/ H_2O (10:1) mixture treated with phenylmagnesium bromide and subsequent dehydration under acidic conditions affords the corresponding allylsilane in good overall yield (76%) with high enantioselectivity (97% ee).



Scheme 67. Two-step synthesis of an allylsilane via rhodium(I)-catalyzed addition of phenylboronic acid to phenyl 3-dimethylphenylsilylpropen-1-one.

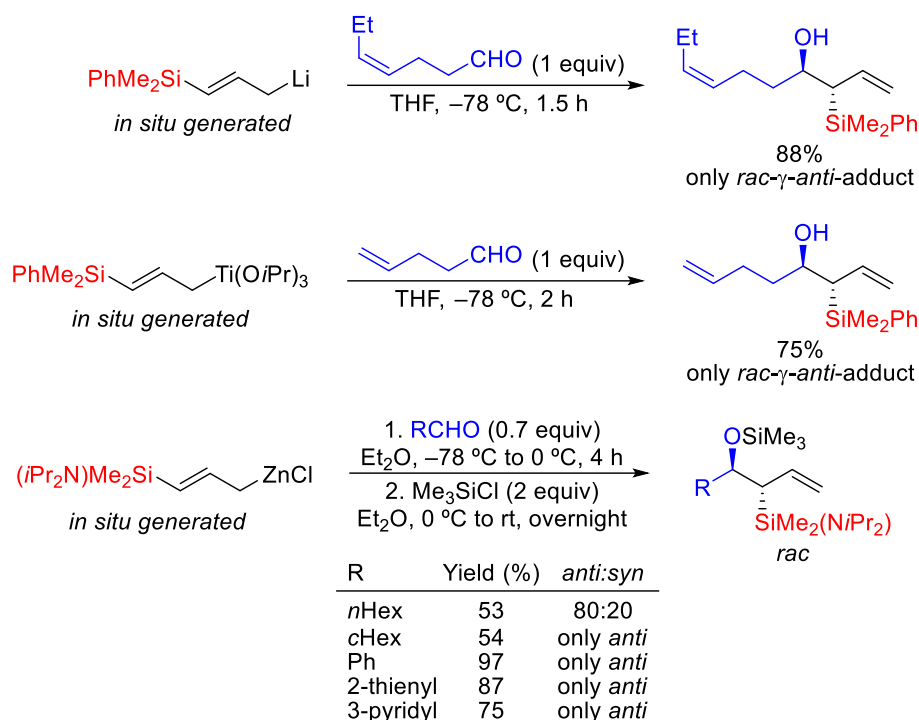
1.2.2.4 Addition of γ -silyl-substituted organometallics to carbonyl derivatives

Alternatively, silyl-substituted carbon-based nucleophiles were used with saturated carbonyl derivatives to access allylsilanes. For instance, the condensation of γ -silyl-substituted allylmetals with aldehydes is a valuable way to access β -hydroxy allylsilanes. Achiral γ -(trimethylsilyl)allylmetals condensed with aldehydes at low temperature in THF to afford predominantly, if not exclusively, γ -adducts upon aqueous work-up. Racemic γ -adducts are isolated as *syn*- or *anti*-stereoisomers depending on the nature of the metal. (**Scheme 68**).^[120–123] Generally, boron and aluminium gave the γ -*anti*-isomer predominantly, although the ratio is dependent on the nature of the aldehyde and the substituents on the metal. In contrast, tin exhibits exclusive *syn*-selectivity whatever the aldehyde.



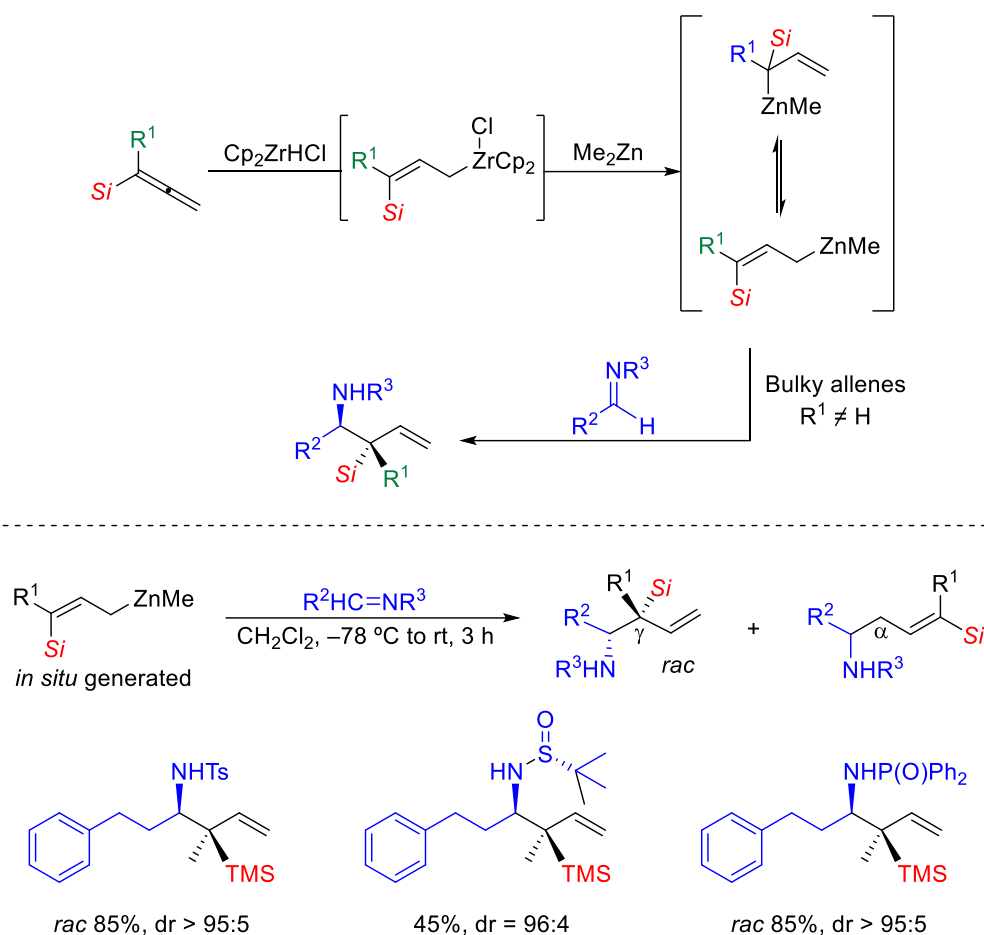
Scheme 68. Synthesis of *anti*- or *syn*- β -hydroxy allylsilanes by condensation of γ -(trimethylsilyl)allylmetals with aldehydes.

(*E*)- γ -(Dimethylphenylsilyl)allyl-lithium and triisopropoxytitanium reagents have also been described to react with aldehydes to give exclusively the corresponding racemic γ -*anti*-adducts in good yields (**Scheme 69**).^[10] Similar results have been reported for the synthesis of β -silyloxy allylsilanes through reaction of (*E*)- γ -(diisopropylaminodimethylsilyl)-allylzinc chloride with aldehydes upon quenching with trimethylsilylchloride.^[124]



Scheme 69. Synthesis of *anti*- β -alkoxy allylsilanes through condensation of γ -silyl-substituted allylmetals with aldehydes.

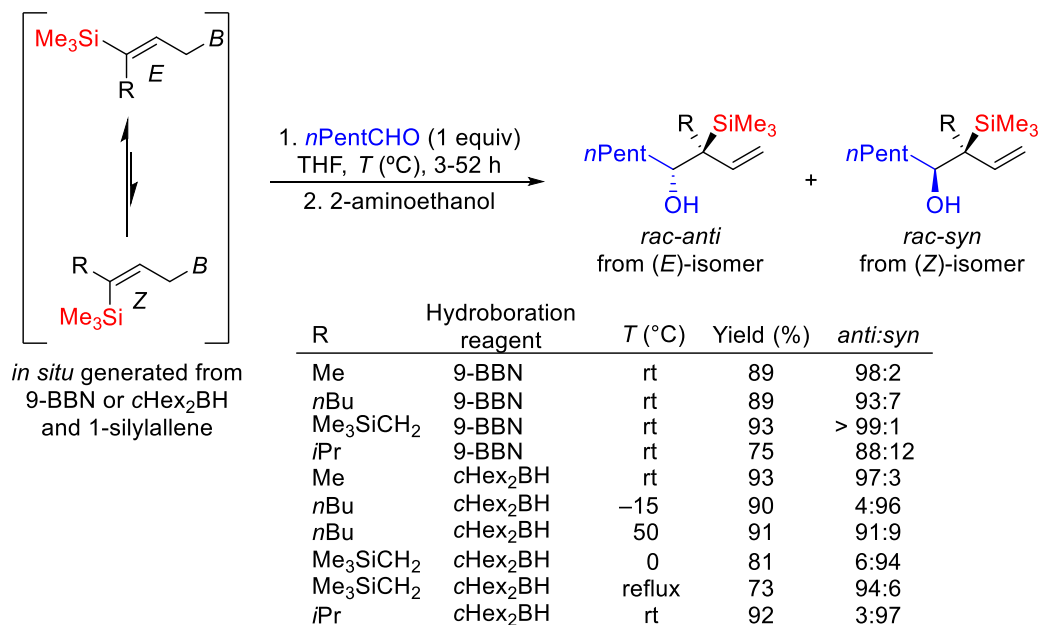
γ -Silyl-substituted organozinc reagents also allow to access quaternary β -trimethylsilyl homoallylic secondary amines from aldiimines. The two-step procedure for the *in situ* preparation of the γ -trimethylsilyl-substituted allylzinc reagents involves hydrozirconation of 1-silyl-1-substituted allenes with 1 equiv of Swartz reagent Cp_2ZrHCl in CH_2Cl_2 at -78°C and subsequently transmetalation with dimethylzinc to regioselectively generate the corresponding allylzirconocenes (**Scheme 70**).^[125] Thus, the reaction of (*E*)- γ -trimethylsilyl- γ -methyl-disubstituted allylzincs with *N*-phosphinyl- or *N*-tosyl-aldiimines in CH_2Cl_2 at room temperature within 3 h provides racemic *syn*- β -amino allylsilanes, bearing an allylic quaternary silyl-substituted stereogenic centre, in high yields (81-85%) and diastereomeric ratios (*syn*:*anti* > 95:5). With a chiral Ellman's *N*-*tert*-butylsulfinyl aldiimine, the reaction provides the expected product with a high *syn*-selectivity (*syn*:*anti* = 96:4), albeit a moderate 45% yield is obtained (**Scheme 70**).



Scheme 70. Synthesis of *syn*-β-amino allylsilanes.

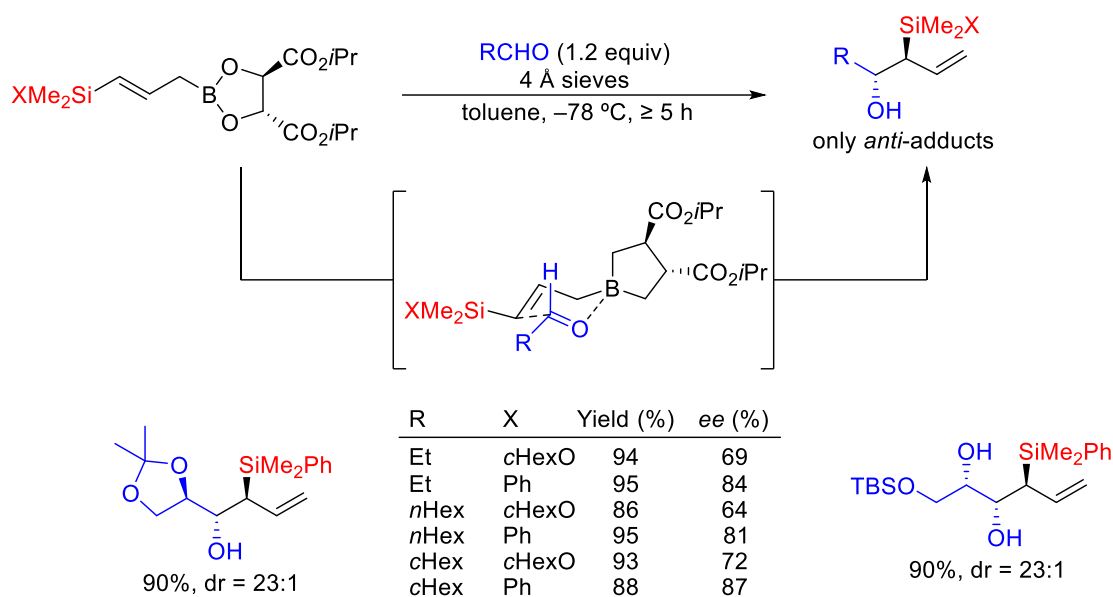
Allylic quaternary γ-silyl-substituted stereogenic centres can also be created by reaction of γ-trimethylsilyl-γ-(alkyl)allylboron reagents, obtained through hydroboration of 1-alkyl(trimethylsilyl)allenes. The reaction has been shown to stereochemically depends on the substituents on the boron atom (**Scheme 71**).^[126] The allylboron reagent obtained from hydroboration with 9-BBN reacts with hexanal in THF at room temperature to provide, upon treatment with 2-aminoethanol, racemic β-hydroxy allylsilanes with an allylic γ-silyl-substituted quaternary stereogenic centre in high yields (≥ 75%) and stereoselective levels (*anti:syn* ≥ 88:12). By contrast, the stereoselectivity strongly varies with the reaction temperature when dicyclohexylborane is used in the hydroboration step. Indeed, the *syn*-stereoisomers predominate at low temperatures (*anti:syn* ≤ 6:94) whereas higher temperatures give the *anti*-stereoisomers as major adducts (*anti:syn* ≥ 91:9), with high yields (≥ 73%) in each case. Both *syn*- and *anti*-stereoisomers are issued from Zimmerman-Traxler transition state models. The *anti*-stereoisomers result from the thermodynamic (*E*)-γ-(silyl)allylboron reagents, whereas the *syn*-stereoisomers come from the initially generated kinetic (*Z*) ones. The reversal in the selectivity observed with dicyclohexylborane is explained by the slow isomerization of the kinetic (*Z*)-γ-(silyl)allylboron reagents due to the

bulkiness of the two cyclohexyl substituents. At low temperature, the isomerization is very slow so that the (*Z*)- γ -(silyl)allylboron reagents have time to react with hexanal before they isomerize. On the other hand, at high temperatures, the isomerization is faster, making the (*E*)- γ -(silyl)allylboron reagents the reactive species.



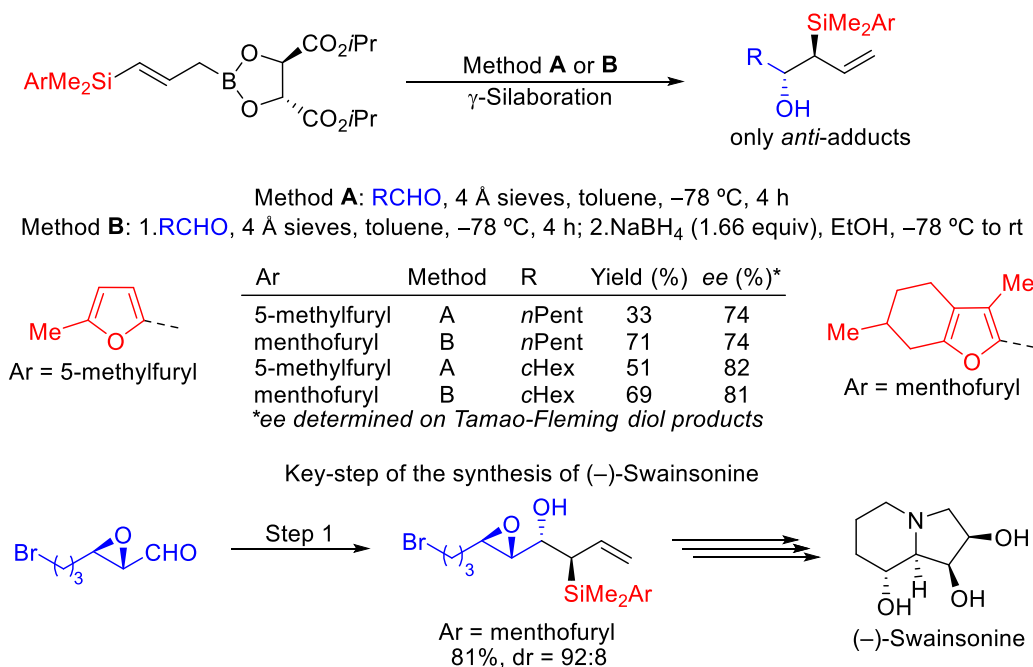
Scheme 71. Addition of γ -trimethylsilyl- γ -(alkyl)allylboron reagents to hexanal.

On the other hand, the first enantioenriched β -hydroxy allylsilanes were obtained in the early 90's by the reaction performed between chiral non-racemic diisopropyl tartrate (*E*)- γ -(silyl)allylboronates and aldehydes in toluene at -78°C in the presence of 4 \AA molecular sieves (**Scheme 72**).^[127–129] Under these conditions, with (*E*)- γ -(cyclohexyloxydimethylsilyl)-substituted allylboronates the reaction proceeded with full *anti*-diastereoselectivity in high yields ($\geq 86\%$) but with moderate enantioselectivities (up to 72% ee). Moreover, the replacement of cyclohexyloxy substituent on the silicon for a phenyl gave rise to a significant increase in the enantioselectivity (from 64-72 to 81-87% ee), while the yields remained excellent ($\geq 88\%$). In both cases, the stereochemical outcome has been rationalized by a Zimmerman-Traxler transition state model wherein the boron reagent approaches from the *Si*-face of the aldehyde. This methodology has been applied in double asymmetric reactions with chiral aldehydes, achieving outstanding stereoselectivity (up to dr = 23:1) in the matched cases.



Scheme 72. Addition of (*E*)- γ -(silyl)allylboronates to aldehydes.

Despite the high enantioselectivity level obtained with the (*E*)- γ -(dimethylphenylsilyl)allylboronates, the resulting *anti*- β -hydroxy allylsilanes cannot be oxidized to the corresponding allylic 1,2-diols by the Tamao-Fleming oxidation. The oxidation is however efficient by replacing the dimethylphenylsilyl group with the 5-methyl- or menthofuryldimethylsilyl groups (**Scheme 73**).^[130]

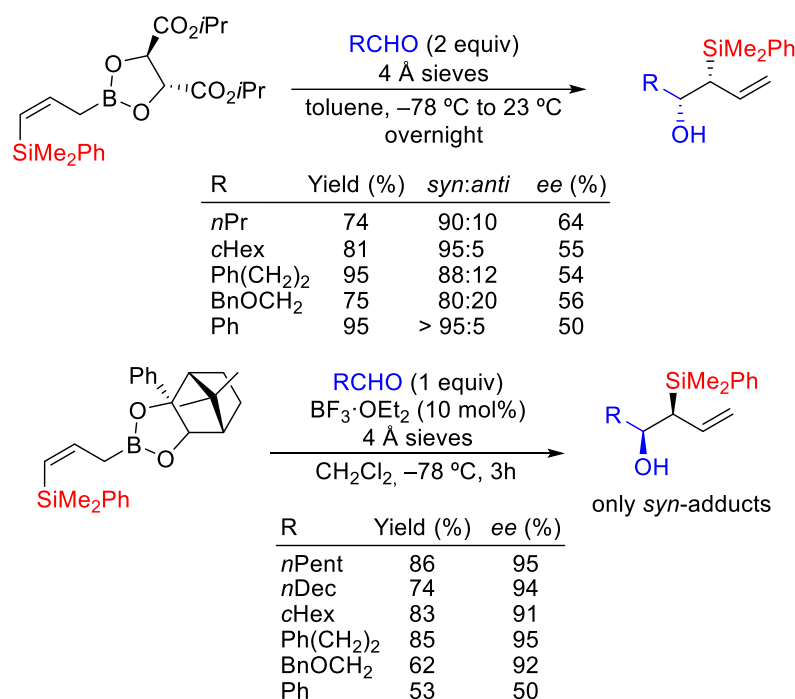


Scheme 73. Addition of (*E*)- γ -5-methyl- and menthofuryldimethylsilyl-substituted allylboronates to aldehydes.

These two new (*E*)- γ -(silyl)allylboronates disclosed a novel two-step strategy for the preparation of *anti*-1,2-diols with high enantioselectivity (up to 82% ee). The procedure was

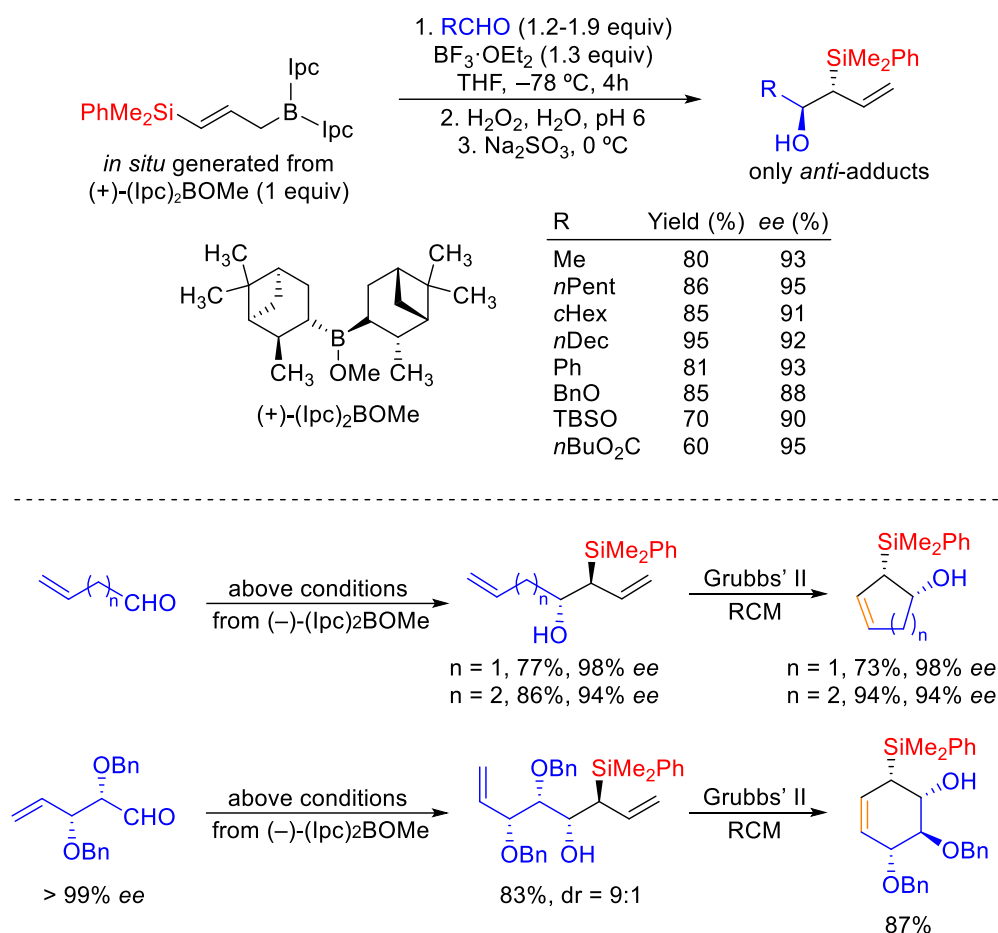
also applied to the asymmetric synthesis of (–)-Swainsonine through the reaction with a chiral epoxy aldehyde (**Scheme 73**).

On the other hand, non-racemic *syn*- β -hydroxy allylsilanes were obtained using chiral (*Z*)- γ -silylallylboronates (**Scheme 74**). Reaction of aliphatic and aromatic aldehydes with readily available modified diisopropyl tartrate (*Z*)- γ -(silyl)allylboronate in toluene at –78 °C and in the presence of 4 Å molecular sieves, gave γ -adducts in high yields ($\geq 74\%$) and *syn*-diastereoselectivity (*syn:anti* $\geq 88:12$), but with low to moderate enantiomeric excess (up to 64% *ee*).^[86] By contrast, the use of modified α -pinanediol-derivative (*Z*)- γ -(silyl)allylboronate analogue in CH₂Cl₂ at –78 °C for 3 h in the presence of both 4 Å molecular sieves and catalytic BF₃·OEt₂ (10 mol%), led to an improvement in both diastereo- and enantioselectivity levels with aliphatic aldehydes (*ee* $\geq 91\%$), although a low enantioselectivity still remains in the case of benzaldehyde (**Scheme 74**).^[131]



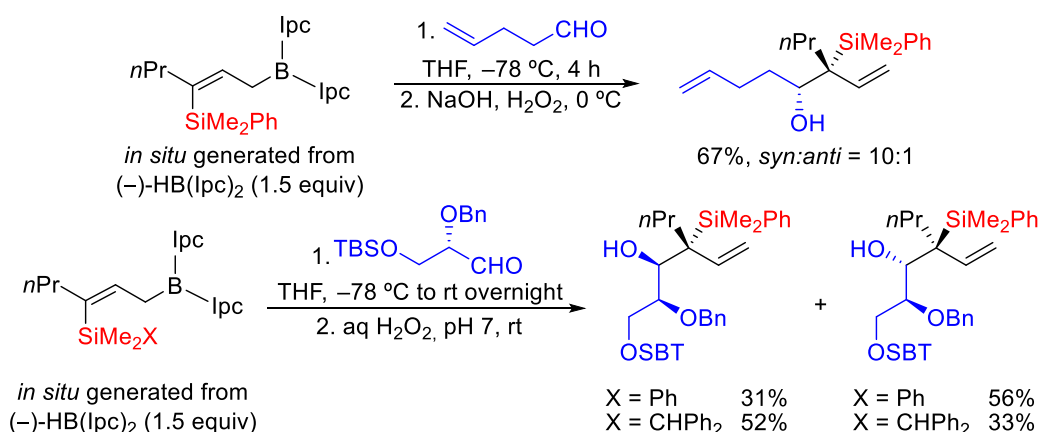
Scheme 74. Addition of (*E*)- γ -silyl, γ -propyl-disubstituted allyl diisopinocampheyl boranes to aldehydes.

Significantly better levels of enantioselectivity (up to 95% *ee*) than those obtained with diisopropyl tartrate (*E*)- γ -(silyl)allylboronates were achieved using the (diisopinocampheyl)-allylborane analogue within 4 h at –78 °C in THF (**Scheme 75**).^[132] The method was also used with success for the synthesis of cyclic β -hydroxy allylsilanes, by γ -silylboration of β,γ - or γ,δ -unsaturated aldehydes and subsequent ring-closing metathesis reaction.^[133] The same strategy was applied in the total asymmetric synthesis of conduritols and inositols involving the diastereoselective reaction with a chiral aldehyde (**Scheme 75**).^[134,135]



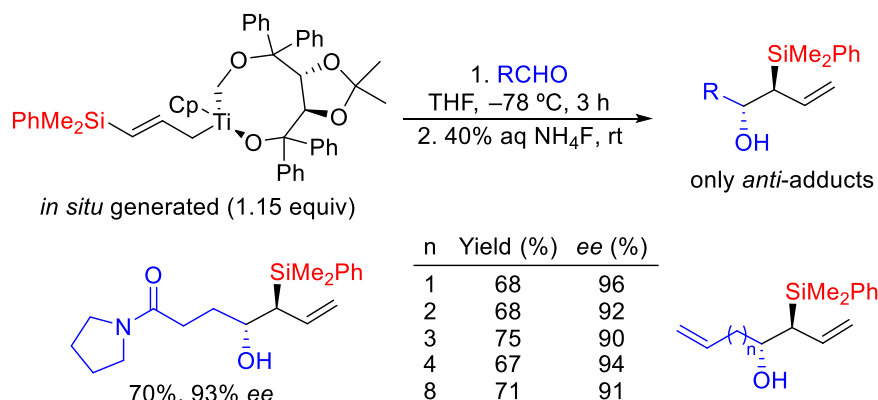
Scheme 75. Addition of *(E)*- γ -dimethylphenylsilyl(diisopinocampheyl)allyl borane to aldehydes.

(Z)- γ -silyl- γ -propyl-disubstituted (diisopinocampheyl)allylboranes also condensed with aldehydes to furnish enantioenriched β -hydroxy allylsilanes that bear an allylic γ -silyl-substituted quaternary stereogenic centre (**Scheme 76**).^[133] For instance, the γ -silylallylboration of pent-4-enal, carried out in THF at -78 °C, affords a mixture of two diastereoisomers, with the *syn*- β -hydroxy allylsilane predominating (*syn:anti* = 10:1), albeit no information about the enantioselectivity has been given. Worthy of note, low temperature was necessary to prevent the isomerization of the kinetic *(Z)*- γ -silyl- γ -propyl-disubstituted allylborane and to achieve high level of *syn*-stereoselectivity. Unexpectedly, in the stereochemically mismatched reaction with chiral aldehydes that bear a stereogenic centre in the α -position, the replacement of the phenyl group on the silicon atom with the benzhydryl group led to the reversal in stereoselectivity.^[136]



Scheme 76. Addition of (*E*)- γ -silyl- γ -propyl-disubstituted (diisopinocampheyl)allyl boranes to aldehydes.

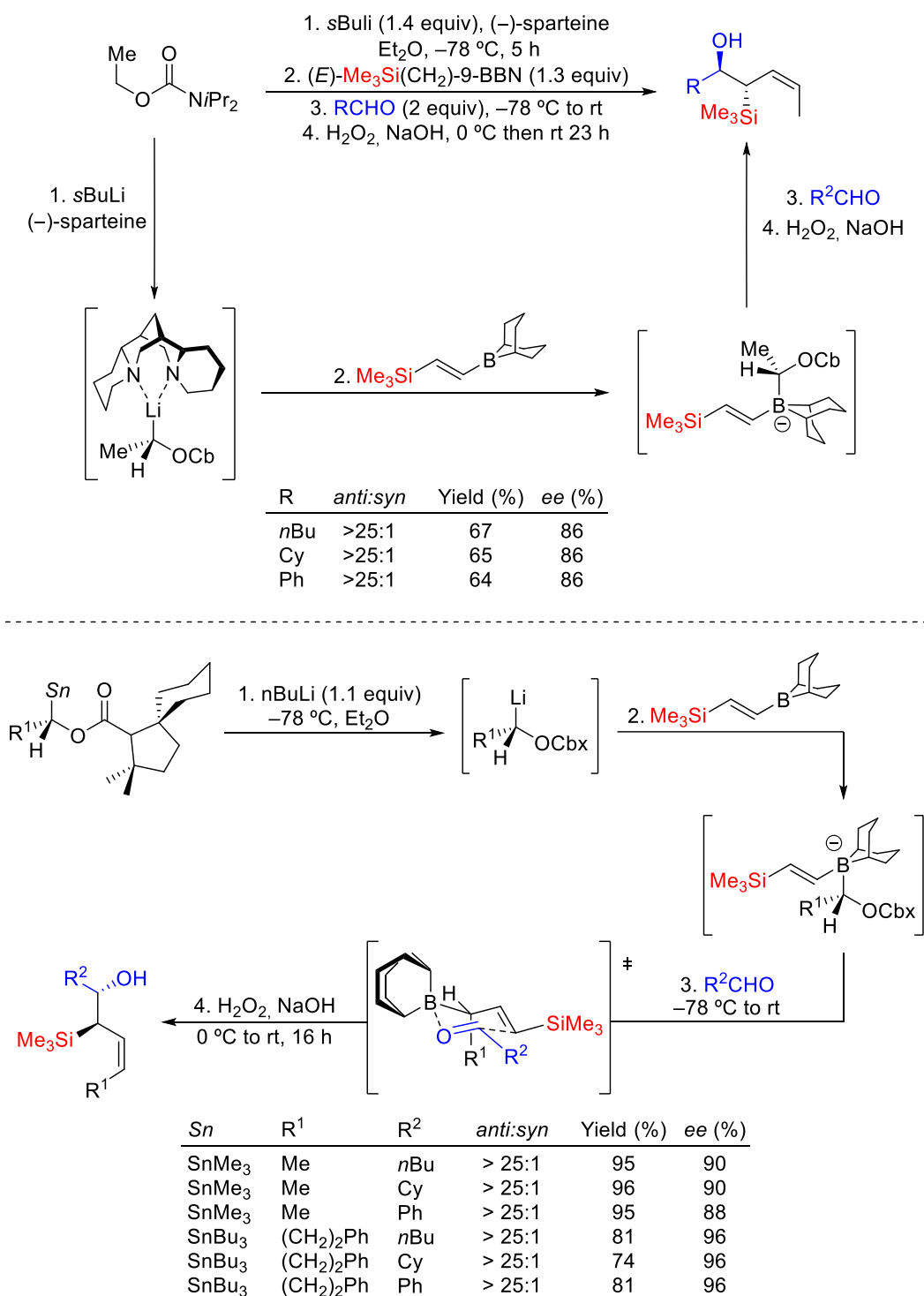
Alternatively, chiral (*E*)- γ -dimethylphenylsilyl-substituted TADDOL-derivative, prepared *in situ* from (cyclopentadienyl)allyltitanium through deprotonation of (dimethylphenyl)allylsilane by *n*BuLi followed by transmetalation with chiral titanium (*R,R*)-Cl-TiCpTADDOL, was added to aldehydes in THF within 3 h at -78°C to provide exclusively *anti*- β -hydroxy allylsilanes in good yields ($\geq 67\%$) and high enantiomeric excesses ($ee \geq 90\%$, **Scheme 77**).^[137]



Scheme 77. Addition of (*E*)- γ -dimethylphenylsilyl-substituted TADDOL-derivative to aldehydes.

More recently, a one pot three step procedure for the stereocontrolled synthesis of β -hydroxy (*Z*)-allylsilanes was unveiled. A plethora of allylsilanes was synthesized with excellent double bond stereocontrol ($Z/E > 25/1$), as well as high diastereo- (*anti:syn* > 25:1) and enantioselectivities ($ee > 86\%$) by trapping chiral boranes with aldehydes (**Scheme 78**).^[138] Stereodefined lithiated carbamates prepared from mixing primary carbamates with 1.3 equiv of *s*BuLi in the presence of (–)-sparteine, react with 1.3 equiv of β -silyl vinyl borane in Et_2O at -78°C to form allylboranes intermediates through a $\text{S}_{\text{N}}1$ process with inversion of lithium carbamate configuration, that reacted with 2 equiv of aldehyde to give the corresponding *anti*-(*Z*)-hydroxyallylsilanes after oxidation. Alternatively, the other set of *anti*-enantiomers could be prepared from stannane carbamates where the tin-lithium exchange occurred with retention of configuration in the absence of diamine (**Scheme 78**). Various

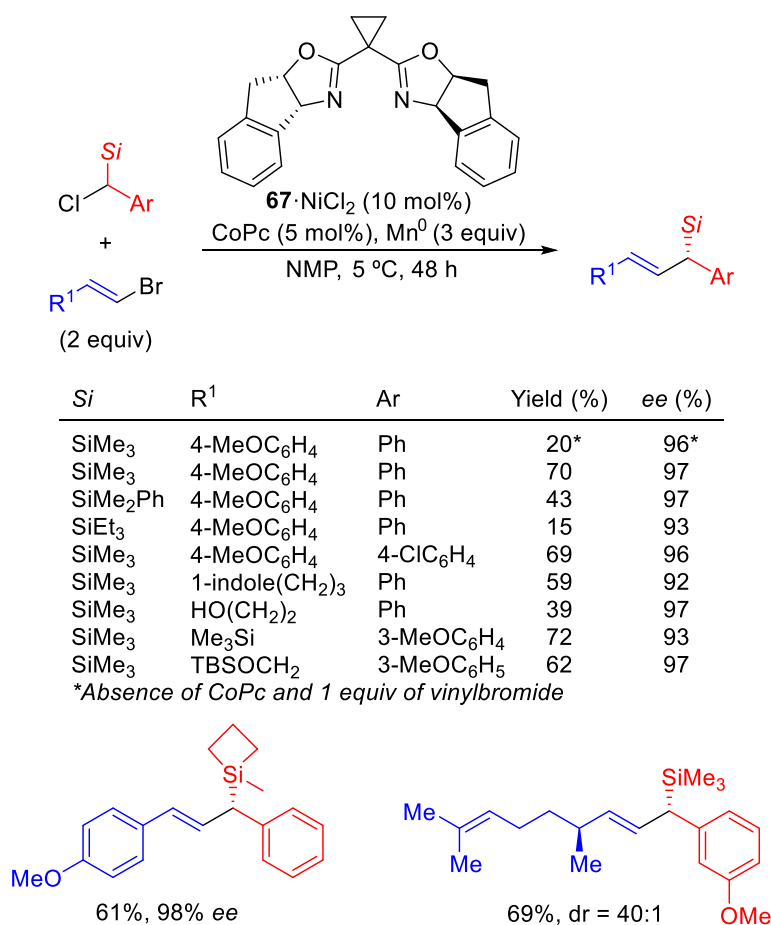
aldehydes are well tolerated, with condensation proceeding through a chair like transition state where the alkyl substituent of the allyborane lies in axial position to reduce the repulsions with 9-BBN.



Scheme 78. Preparation of β -hydroxyallylsilanes.

1.2.2.5 Ni-catalyzed reductive cross coupling with vinyl bromide

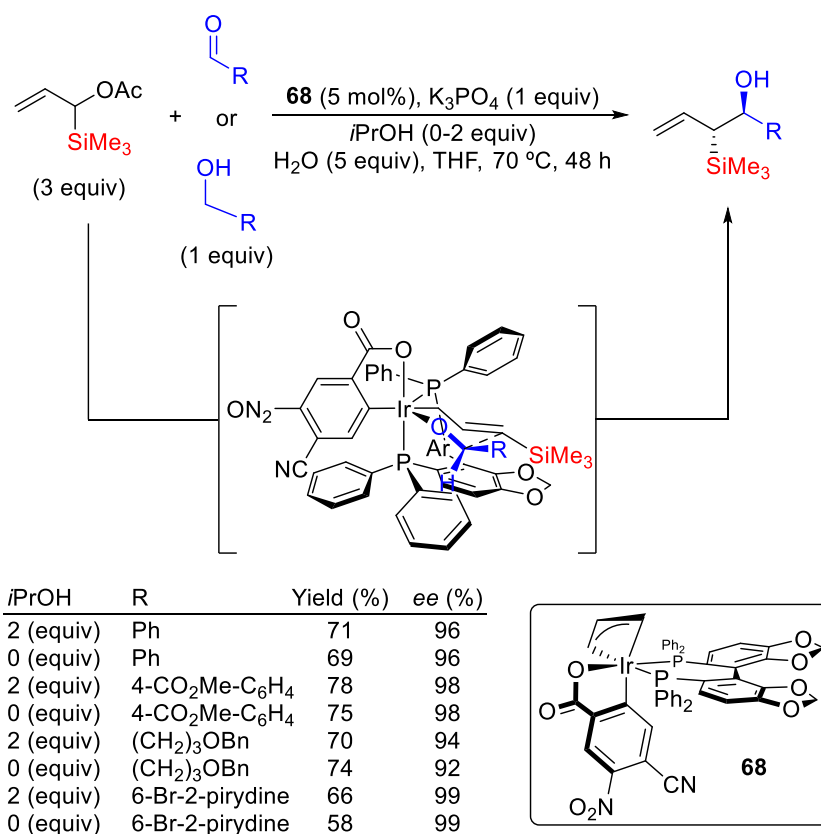
Another powerful direct procedure for the preparation of non-racemic allylsilanes consisting in the asymmetric reductive alkenylation of (chlorobenzyl)silanes was described.^[139] A reaction with excellent control of regioselectivity operated when chlorobenzylsilane and 2 equiv of vinylbromide were set in *N*-methyl-2-pyrrolidone (NMP) at 5 °C in the presence of chiral bis(oxazoline) ligand **69** (11 mol%), 10 mol% of NiCl₂(dme) and 3 equiv of Mn⁰. The desired allylsilane was obtained with an ee of 96% but a very low yield (20%). By adding cobalt(II) phthalocyanine as co-catalyst to favour the alkyl radical generation, significant better yield was observed (70%). No side product arising from the homocoupling of the silanes was observed as it occurred when performing the reaction with non-silyl substituted benzyl electrophiles.^[140] Under the optimal mild conditions, a wide array of chlorobenzyl silanes as well as a diverse set of functionalized alkenyl bromides were well tolerated to hand the desired chiral allylsilanes in moderate yields but excellent ee > 92% (**Scheme 79**). On the other hand, no reaction was observed with (*Z*)-alkenes and tri- or tetra-substituted alkenyl bromides, in the same way that neither aldehyde nor nitrile derivatives are tolerated.



Scheme 79. Synthesis of (*E*)-allylsilanes from Ni-catalyzed reductive cross coupling.

1.2.2.6 Silylation of carbonyl derivatives

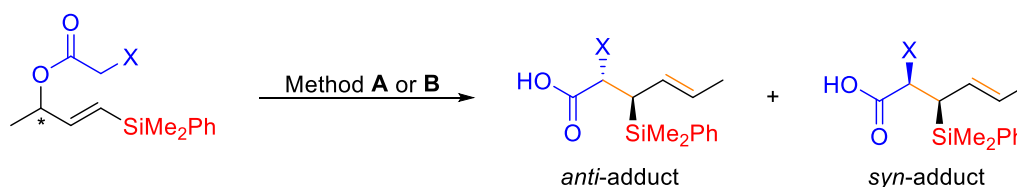
Another highly enantioselective silylation of carbonyl derivatives was described using one *ortho*-cyclometalated iridium-complex as catalyst. Allylsilane transfer from α -(trimethylsilyl)allyl acetate to aldehydes is mediated by isopropanol in the presence of preformed 5 mol% of π -allyl iridium, K_3PO_4 (1 equiv) and H_2O (5 equiv) in DMF at 70 °C to furnish the corresponding homoallylic alcohols in good yields (58-78%), with excellent levels of enantio- and diastereoselectivity (**Scheme 80**).^[141] In this regard, isopropanol plays a key role in the reaction allowing the regeneration of *ortho*-cyclometallated complex **68** through hydrogen transfer. The exclusive formation of *anti*-diastereoisomers suggests a chairlike transition state involving the (*E*)- σ -allyl vinylsilane isomer during the carbonyl addition (**Scheme 80**). The same conditions but in the absence of 2-propanol also allows the iridium-catalyzed coupling to occur directly from the corresponding alcohols to provide an identical set of adducts with a negligible erosion in the yield and enantioselectivity.



Scheme 80. Enantioselective α -(trimethylsilyl)allylation with alcohols and aldehydes.

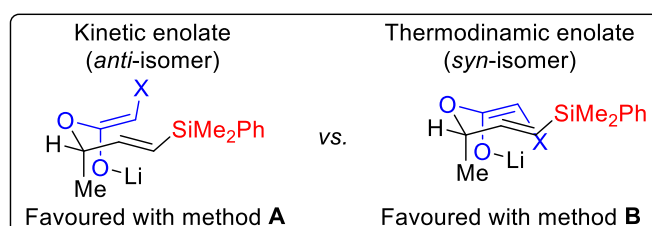
1.2.2.7 [3, 3]-sigmatropic rearrangement

Along history, a wide range of different rearrangements have been developed allowing to access complex molecules and scaffolds. In this regard, the potential of this kind of reactions was also exploited in order to develop several methods to access chiral allylsilanes. One of these methodologies relies in a Claisen rearrangement from vinyl silane derivatives. This strategy provided access to highly substituted well defined allylsilanes. With this approach, two contiguous stereogenic centres are created during the transformation. The diastereoselectivity could be controlled by the configuration of the intermediate enolate that leads either to the *syn*- or the *anti*-diastereoisomer. First evidence was reported regarding the preparation of α -substituted- β -silyl hexenoic acids from γ -acycloxy (*E*)-vinylsilanes.^[142] In the presence of lithium amide base in THF and using TMSCl, simple propionate esters lead to (*E,E*)-silyl ketene acetals, obtained from kinetic enolate, that rearranged in the corresponding *anti*-isomers with good levels of diastereoselectivity *anti:syn* 12:1 (entry 1, **Scheme 81**). This preferred *anti*-selectivity could be reversed to 1:16 *anti:syn* ratio (entry 2, **Scheme 81**) in the presence of HMPA, employing *t*BuMe₂SiCl and by heating at reflux. By contrast, in the case of α -heteroatom-substituted esters, the strong chelating ability of the glycolate oxygen promoted the formation of the thermodynamic enolate leading to the *syn* adduct after rearrangement whatever the conditions were (entry 3-4, **Scheme 81**).



Method **A**: LDA (1.7 equiv), TMSCl (10.8 equiv), pyridine (11.9 equiv), THF -78°C to 0°C

Method **B**: LHMDs (2.0 equiv), TBSCl (2 equiv), HMPA (2 equiv), THF, -78°C to reflux

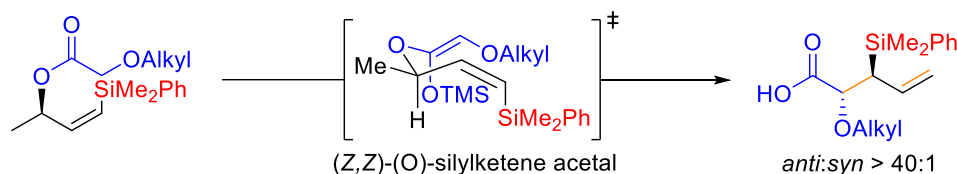


Entry	Method	Stereo	X	Yield (%)	<i>anti:syn</i>
1	A	S	CH ₃	81	12:1
2	B	S	CH ₃	69	1:16
3	A	S	OCH ₃	55	1:22
4	B	S	OCH ₃	51	1:23
5	A	<i>rac</i>	OSiMe ₂ <i>t</i> Bu	65	2.2:1
6	B	<i>rac</i>	OSiMe ₂ <i>t</i> Bu	75	3.6:1

Scheme 81. Synthesis of (*Z*)- and (*E*)-crotylsilanes.

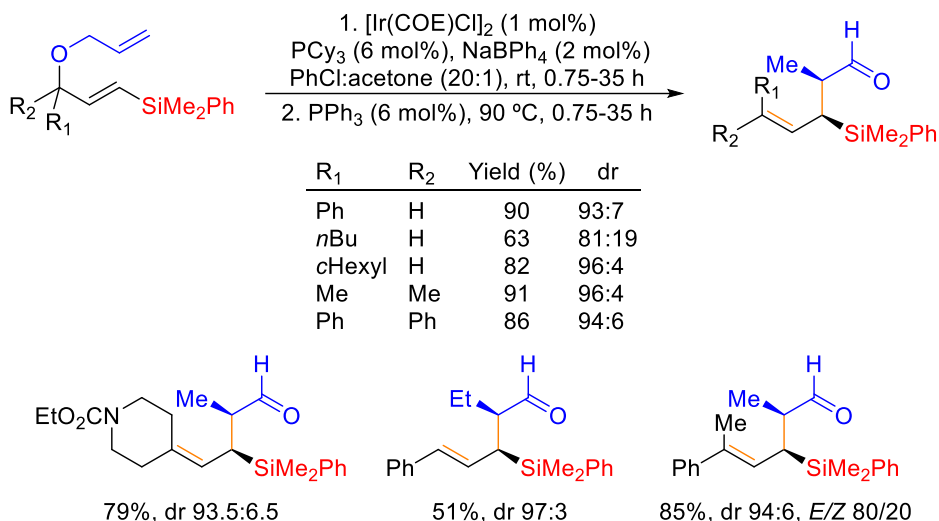
On the other hand, *anti*-isomer was favoured (entry 5-6, **Scheme 81**) when bulky protecting groups such as *t*BuMe₂Si were employed on the glycolate oxygen, although with

poor levels of diastereoselectivity. In this way, the chelating capacity of the oxygen atom is disfavoured, decreasing the formation of the thermodynamic enolate. Using (*Z*)-vinylsilanes could however allow the formation of *anti*-adducts as the main products from α -heteroatom-substituted esters (alkyl = Me, CH₂Ph, CH₂OMe, 4-MeOC₆H₄CH₂). In this way, (*Z,Z*)-O-silyl ketene acetals are formed during the enolization step in THF in the presence of LiN(TMS)₂ (**Scheme 82**), leading to the corresponding *anti*-(*E*)-crotylsilanes in good yields and diastereomeric ratios (*anti:syn* \geq 40:1).^[143]



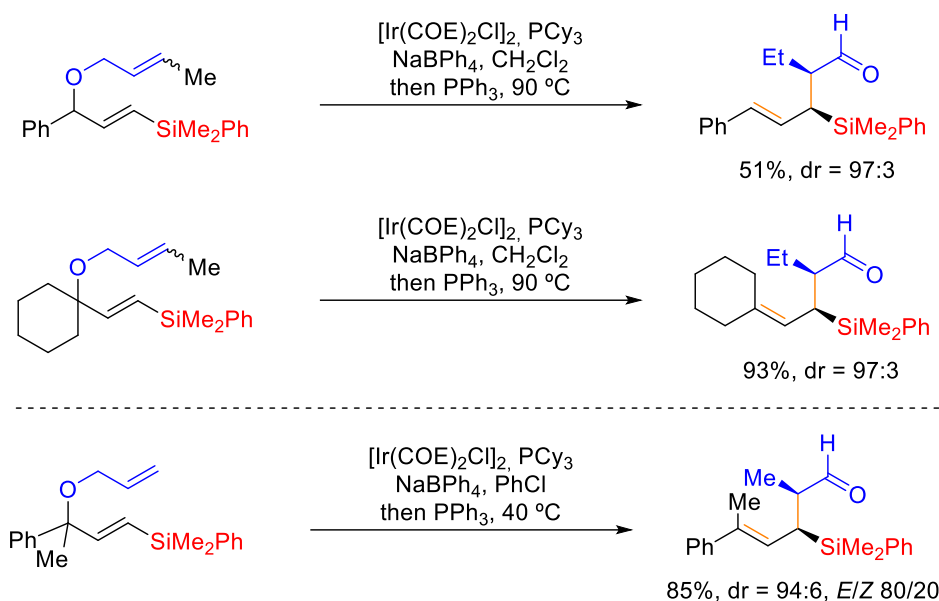
Scheme 82. *Anti*-diastereoisomer formation from (*Z*)-O-silylketene acetal.

Syn-selectivity was also obtained by performing a isomerization-Claisen rearrangement on monosilylated bis(allylic) ethers in the presence of Ir(COE)₂Cl]₂ (1 mol%), PCy₃ (6 mol%), NaBPh₄ (2 mol%) in PhCl:acetone (20:1) and then PPh₃ (6 mol%) at 90 °C.^[144] Allylethers derived from secondary alcohols with aryl or alkyl substituents, as well as tertiary alcohol derivatives were well tolerated, providing the desired 5-substituted 3-dimethylphenyl-2-alkyl-4-pentenal derivatives in good to excellent dr \geq 81:19 (**Scheme 83**). It is worthy to mention, that the longer the Claisen rearrangement takes, the lower diastereoselectivities are obtained due to the epimerization of the formed aldehydes.



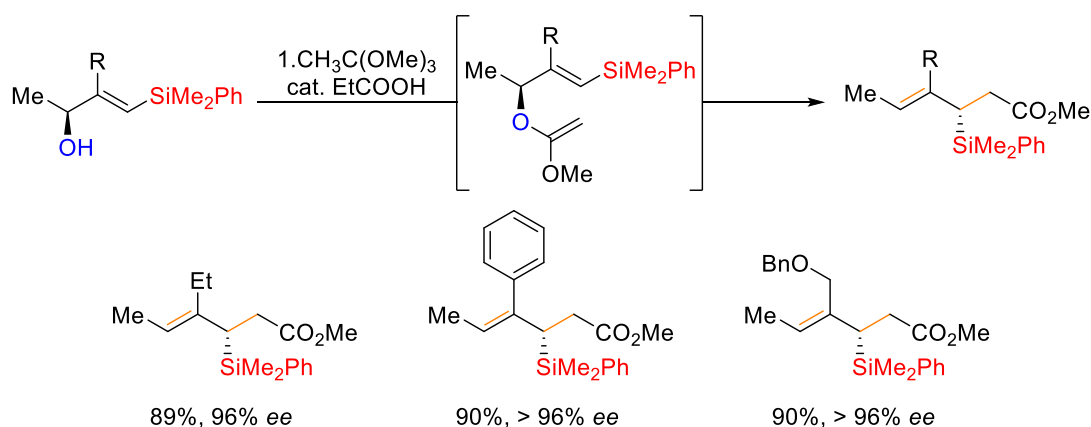
Scheme 83. Synthesis of *syn*-(*E*)-crotylsilanes.

Furthermore, mixture of *E/Z* substituted allylic ether derivatives exclusively provide (*E*)-crotylsilanes with dr = 97:3, which implies the formation of a single *E*-isomer during the isomerization process. In contrast, unsymmetrically tertiary allylic ethers provide a mixture of *E/Z* isomers even by performing the reaction at 40 °C (**Scheme 83**).



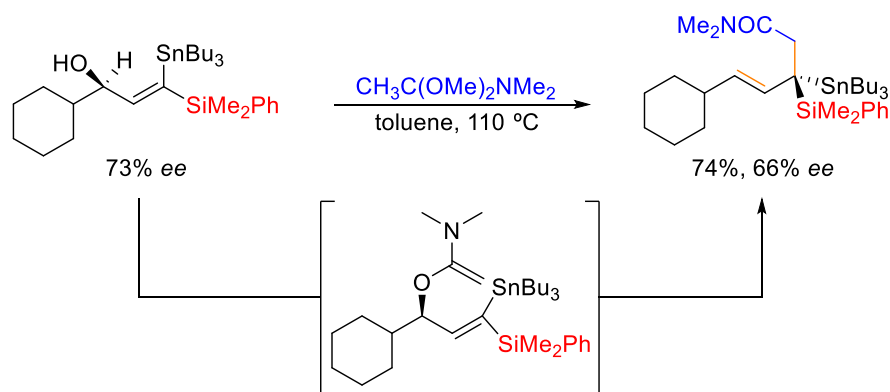
Scheme 84. Synthesis of *syn*-allylsilanes through an isomerization-Claisen rearrangement.

One example was also described where an ortho ester-Claisen rearrangement of (*S,E*)-vinyl alcohols in the presence of trimethyl orthoacetate and catalytic acetic acid in toluene under reflux furnished (*S,E*)-crotylsilanes in good yields ($\geq 78\%$) and excellent enantiomeric excesses ($ee \geq 96\%$, **Scheme 85**).^[145]



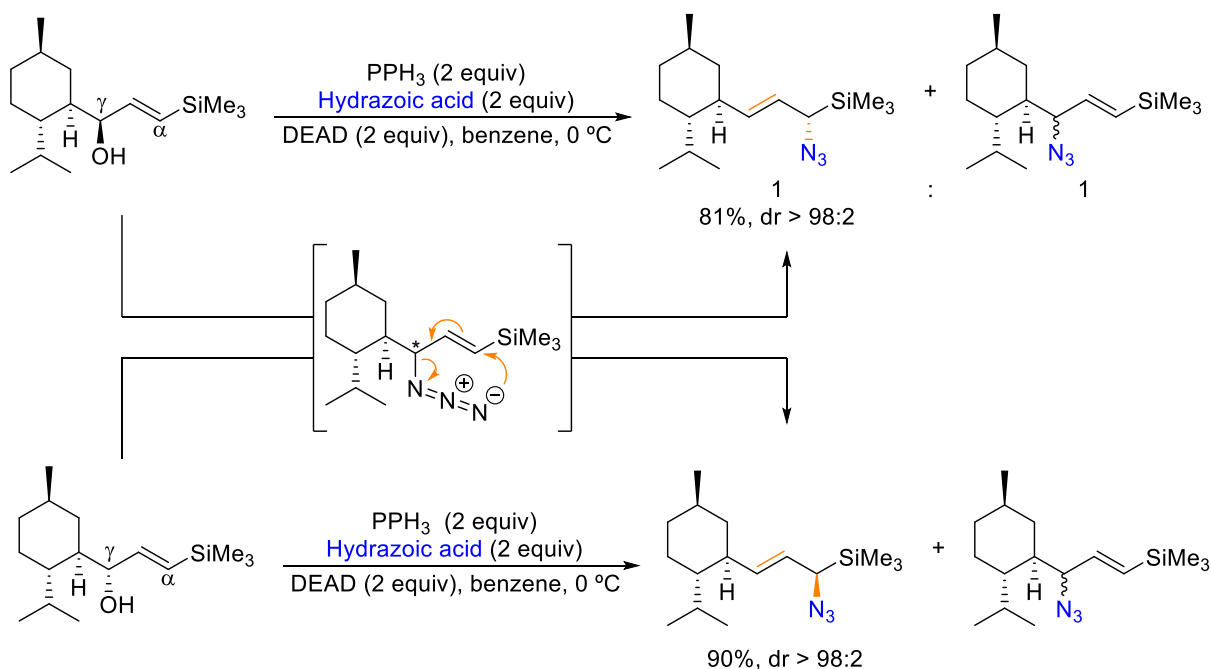
Scheme 85. Synthesis of β -substituted (*E*)-crotylsilanes.

Another method involves the preparation of one non-racemic allylsilanes from γ -cyclohexyl- γ -hydroxysilylvinylstannanes.^[146] One example was reported by treating vinylsilane with *N,N*-dimethylacetamide dimethyl acetal in toluene at reflux to provide the diorganometallic allylsilane with 66% ee (corresponding to a chirality transfer of 90%, **Scheme 86**).



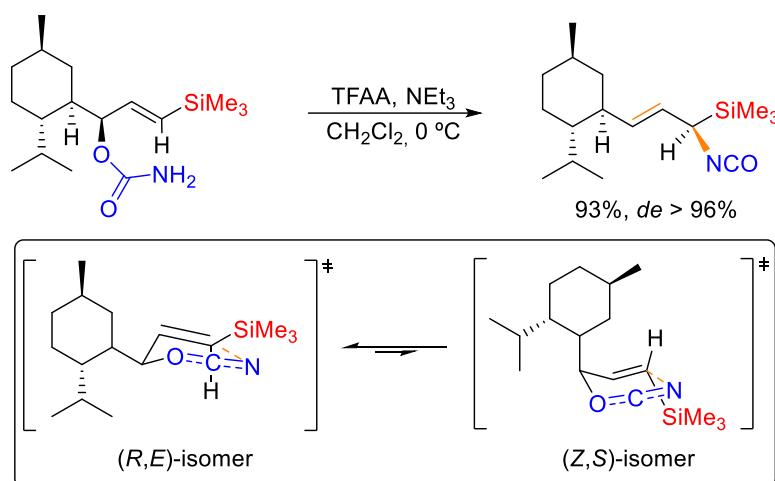
Scheme 86. Synthesis of γ,α -disubstituted allylsilylstannane.

Another two-step procedure involving a Mitsunobu reaction followed by a stereoselective [3,3]-sigmatropic rearrangement of γ -substituted allylic alcohols biased by a chiral auxiliary 3-*p*-menthane was developed.^[147] Two enantioenriched allylsilanes bearing silyl-substituted tertiary stereogenic centres were prepared with excellent diastereoselectivity ($dr > 98:2$) but low regioselectivity ($\gamma/\alpha = 1/1$) by mixing γ -hydroxyvinyltrimethylsilane with 2 equiv of PPh_3 , HN_3 and diethyl azodicarboxylate (DEAD) in benzene at 0 °C (**Scheme 87**).



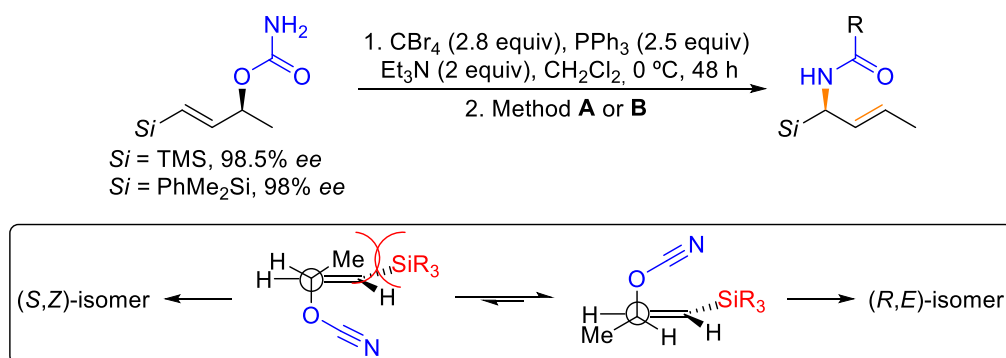
Scheme 87. Tandem Mitsunobu/[3,3]-sigmatropic rearrangement of β -alcohols.

Using the same chiral auxiliary, it was possible to access a chiral allylsilane through a [3,3]-allyl cyanate rearrangement from γ,γ -disubstituted allylic carbamate after treatment with trifluoroacetic acid anhydride and Et_3N in CH_2Cl_2 at 0 °C.^[148] The regio- and stereoselectivity of the reaction can be rationalized by a transition state wherein the TMS group lies in pseudoequatorial position in order to minimize the $A^{1,3}$ strain (**Scheme 88**).

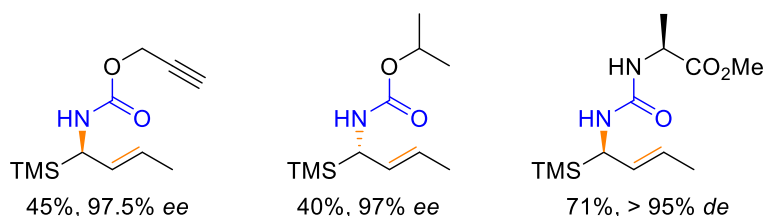


Scheme 88. Synthesis of α -isocyanate substituted allylsilane.

The plethora of allylsilanes accessed through this allyl cyanate-isocyanate rearrangement method was broadened by Carreaux *et al.* in 2016.^[149] These analogues were prepared by a one pot domino dehydration/[3,3]-sigmatropic rearrangement from enantioenriched γ -hydroxy-alkenylsilyl compounds with excellent chirality transfer ($> 96\%$). Dehydration of (*E*)-carbamate occurred in the presence of PPh_3 (2.5 equiv), Et_3N (2 equiv) and CBr_4 (2.8 equiv) in CH_2Cl_2 at $0\text{ }^\circ\text{C}$, to give the corresponding short-lived allyl cyanate that undergo the rearrangement to exclusively form the (*E*)-allylsilylisocyanates. Those intermediates are immediately trapped by different nucleophiles to provide the corresponding chiral allylsilanes. Both amine (Method **A**) and alcohol (Method **B**) derivatives are well tolerated as nucleophiles, furnishing the corresponding allylsilanes with an $ee \geq 93.8\%$ and in moderate to very good yields (45-96%) whatever the silicon moiety is, TMS or PhMe_2Si . When alcohols were used, same levels of enantioselectivity were observed, but yields were considerably eroded, especially when propargyl and isopropyl alcohols were utilized (45% and 40% yield respectively). Finally, the high chirality transfer during the [3,3]-rearrangement can be explained since conformer **A** that leads to (*S,Z*)-isocyanates is 2.1 kcal/mol less stable than the conformer **B** which leads to the (*R,E*)-isomers (**Scheme 89**).

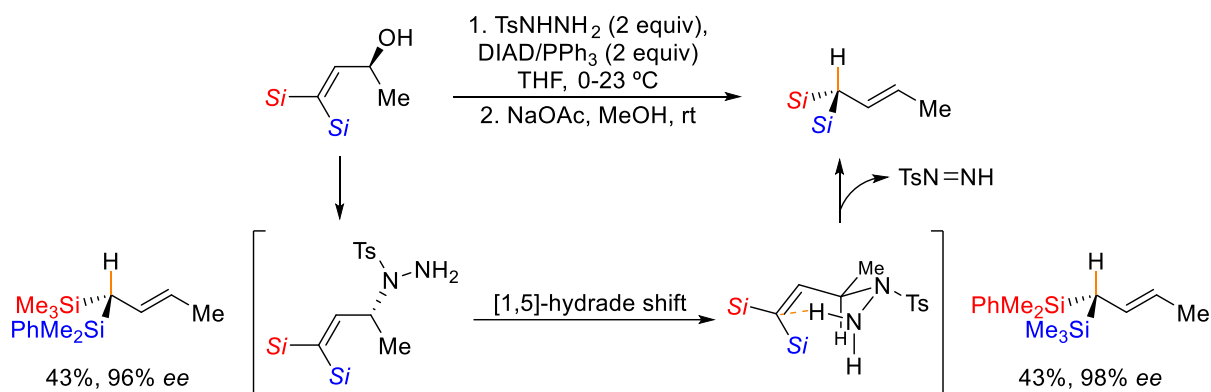
Method **A**: RNH_2 (1.5 equiv), rt, 4 hMethod **B**: ROH, DMAP (5 mol%), reflux, 18 h

Si	R	Method	Yield (%)	ee (%)
TMS	$\text{C}_6\text{H}_5\text{CH}_2\text{NH}$	A	80	98.1
TMS	$4\text{-MeOC}_6\text{H}_4\text{NH}$	A	89	94.6
TMS	$\text{MeCO}_2\text{CH}_2\text{NH}$	A	96	96.5
PhMe_2Si	MeOCH_2N	A	74	95.9
PhMe_2Si	$\text{MeCO}_2\text{CH}_2\text{NH}$	A	65	97.8
PhMe_2Si	MeO	B	87	93.8

**Scheme 89.** Synthesis of functionalized chiral α,γ -disubstituted allylsilanes.

1.2.2.8 [1,5]-hydride shift

Two chiral allyl geminal bis(silanes) were synthesized based on a sigmatropic [1,5]-hydride shift of allylic hydrazine (**Scheme 90**).^[150] Submitting bis(silyl) allylic alcohols under Mitsunobu reaction conditions utilizing TsNHNH_2 (2 equiv) as nucleophile in THF at 0 °C generated hydrazine intermediates, which suffer a NaOAc-promoted [1,5]-hydride shift in MeOH at rt to give the optically active allylic bis(silanes) in moderate yields (43%) and $ee \geq 96$.

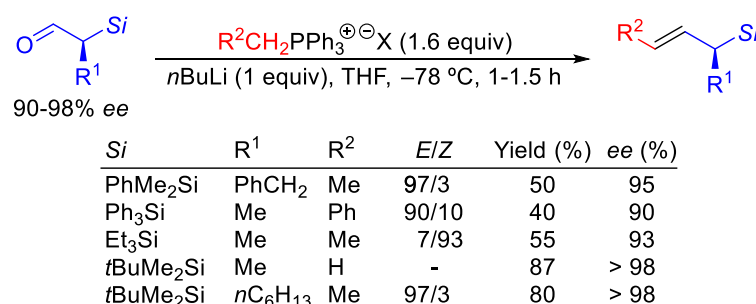
**Scheme 90.** Enantioselective synthesis of crotyl geminal bis(silanes) under Mitsunobu reaction conditions.

1.2.2.9 Olefinations

Olefinations are one of the most useful reactions for the preparation of novel carbon-carbon double bonds in organic chemistry. In the last 30 years, the potential of this transformation allowed the development of several synthetic strategies for the preparation of enantiodefined allylsilanes.

1.2.2.9.1 Wittig olefination

Firstly, phosphonium halides and non-symmetric α -substituted- α -silylated aldehydes derived from SAMP/RAMP-hydrazones were described to perform a racemization free Wittig olefination in the presence of 0.9 equiv of base in THF at $-78\text{ }^{\circ}\text{C}$. This protocol gave access to a library of allylsilanes bearing different silicon groups in moderate to good yields (40-87%) and excellent enantioselectivities ($ee > 90\%$).^[151] The regioselectivity was also very good with an E/Z ratio $\geq 90:10$, except with the Et_3Si -analogue, for which the (Z)-selectivity is favoured $E/Z = 7/93$, albeit no explanation was proposed (**Scheme 91**). $n\text{BuLi}$ was used as base for the generation of ylides instead of NaNH_2 and KDA that resulted in a partial racemization of the aldehyde, drifting in lower enantiomeric ratios.

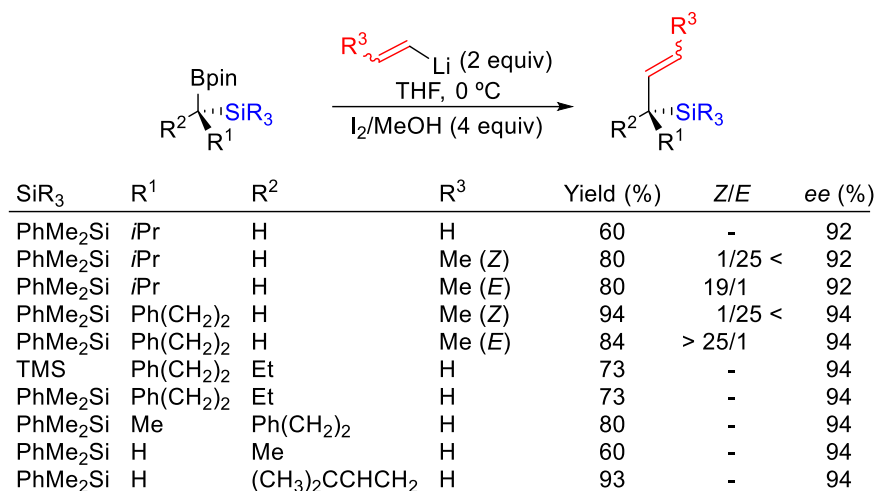


Scheme 91. Wittig reaction over α -silylaldehydes to obtain enantioenriched allylsilanes.

1.2.2.9.2 Zweifel olefination

A specific procedure for the synthesis of allylsilanes involving disubstituted silaboronate esters has been described. Chiral 1,1-silaboronates were prepared by lithiation of carbamate with $s\text{BuLi}$ in the presence of (–)-sparteine, followed by addition of $\text{PhMe}_2\text{SiBpin}$. These organometallic boronic esters reacted with simple vinyl lithium or 2-methylvinyl lithium reagents (4 equiv) in modified Zweifel olefination conditions (4 equiv of methanolic I_2 in THF at $-78\text{ }^{\circ}\text{C}$) to yield chiral crotylsilanes with high enantioselectivity ($ee > 92\%$, **Scheme 92**).^[152] Moreover, perfect levels of diastereoselectivity were observed for the allylsilanes synthesized using double bond substituted organolithium reagents as nucleophiles ($\text{R}^3 = \text{Me}$), where the double bond geometry of the allylsilane is the opposite of the alkenyllithium reagents used for their preparation. Only in the case of highly hindered (Z)- α -isopropyl allylsilane (entry 3, **Scheme 92**), a small amount of the opposite (E)-double bond geometry-isomer was observed

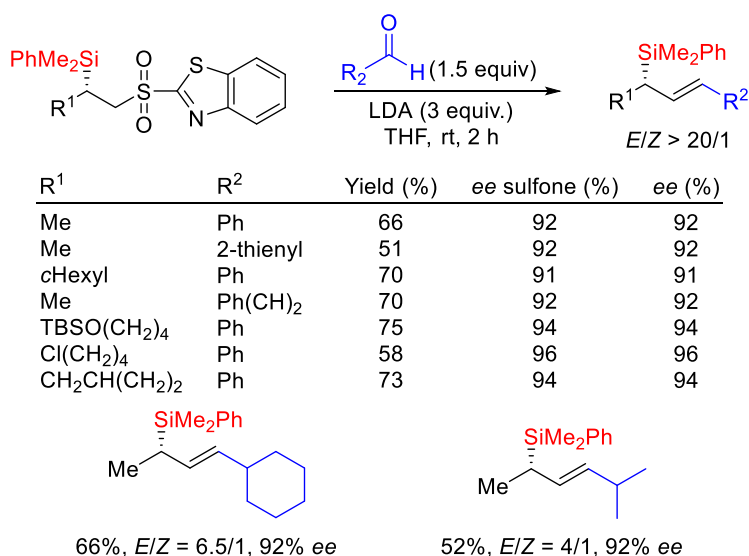
(*Z/E* = 19/1, **Scheme 92**). Same olefination strategy was also successfully applied for the preparation of quaternary α -phenethyl silanes in 60-73% yield and 94% ee.



Scheme 92. Olefination of silaboranes and synthesis of tertiary and allylsilanes bearing silyl-substituted quaternary stereogenic centres.

1.2.2.9.3 Julia olefination

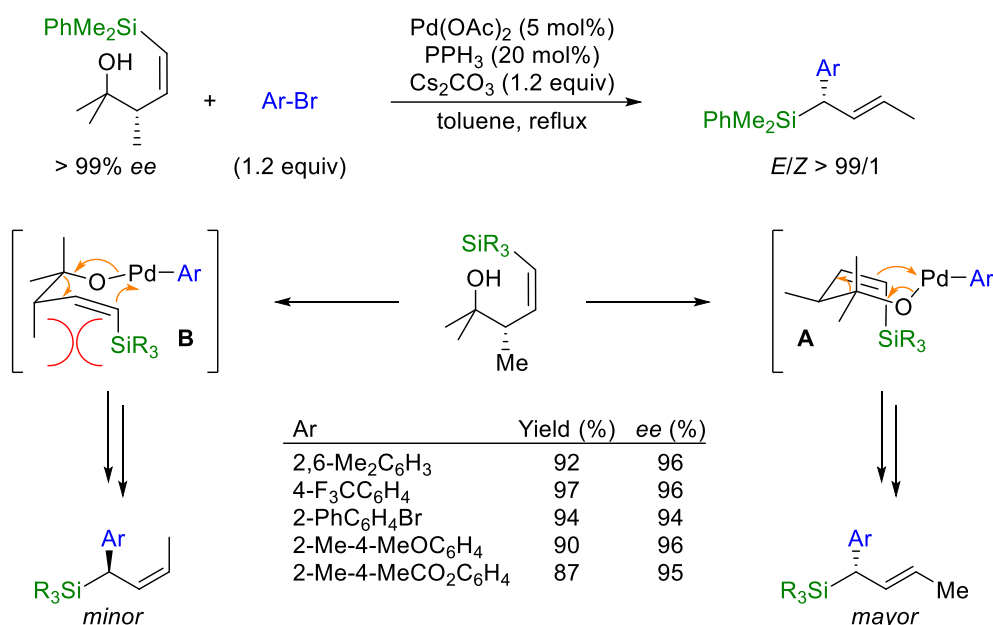
A one pot two step procedure involving a Julia-Kocienski olefination of aldehydes was described to deliver 1,3-disubstituted allylsilanes in good yields (51-75%) and high ee ($\geq 91\%$).^[153] Optically active β -substituted benzothiazole sulfones were used to perform a smooth Julia-Kocienski olefination in THF at rt for 2 h to provide the expected allylsilanes with an excellent transfer of chirality ($> 99\%$) and control of the double bond geometry (*E/Z* $> 20/1$). The reaction is however limited to non-hindered aldehydes. Cyclohexanecarboxaldehyde and isopropylaldehyde gave indeed lower *E/Z* ratios, even by decreasing the temperature to $-40\text{ }^{\circ}\text{C}$ and increasing the reaction time to 12 h, although same levels of enantioselectivity were observed.



Scheme 93. Synthesis of allylsilanes through Julia-Kocienski olefination of α,β -unsaturated BT-sulfones.

1.2.2.10 Allyl transfer from δ -silyl homoallylic alcohols

A completely different strategy was developed involving the reaction of chiral (*Z*)-4-hydroxy vinylsilanes with aryl bromides in toluene at reflux in the presence of $\text{Pd}(\text{OAc})_2$ (5 mol%), PPh_3 (20 mol%) and Cs_2CO_3 (1.2 equiv). The reaction proceeds through a retroallyl process furnishing 1-aryl-2-butenylsilanes as single (*E*)-isomers in yields up to 97% and with an excellent chirality transfer (> 98%).^[154] This ripping chirality transfer can be rationalized by comparing the two different chairlike transition states (**A** and **B**) of the retroallylation process. The formation of the (*E,S*)-product results from the favoured chair-like transition state model **A** wherein the allylic methyl substituent lies in pseudoequatorial position in order to minimize the steric interactions with the silicon moiety (**Scheme 94**).

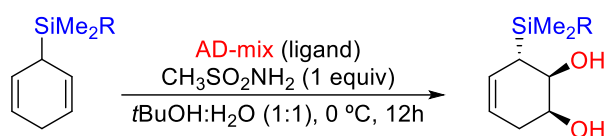


Scheme 94. Synthesis of enantioenriched allylsilanes from silyl-substituted homoallyl alcohols.

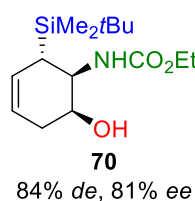
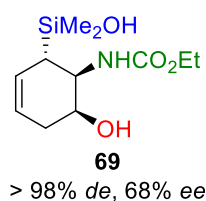
1.2.2.11 Desymmetrization of dienylsilanes

Desymmetrization of symmetrical bifunctional molecules is a powerful method to directly access asymmetric scaffolds and synthons of high value starting from easily available precursors. Among these strategies, osmium catalyzed asymmetric dihydroxylation (AD) of olefins has arisen as one of the most practical strategies to access enantiospecific diols.^[155] In this regard, dimethyl-2,5-cyclohexadiene-silanols were transformed into their *syn*-1,2-diols analogues under Sharpless conditions in *t*BuOH:H₂O (1:1) at 0 °C.^[156,157] The osmium reagent is able to differentiate between the two enantiotopic double bonds, and the silicon group to control the diastereofacial approach of the electrophiles; approach that occurs in *anti*-relative fashion. Different AD-mixes were prepared changing the ligands, with (DHQ)₂PYR-mix providing the highest enantioselectivity (ee 65%, **Scheme 95**). Performing the reaction on the

*t*BuMe₂Si- and Me₃Si- dienyilsilanes proved the method tolerance towards different silyl moieties, although an erosion in the enantioselectivity can be observed (entry 5-6, **Scheme 95**).^[157]



R	Ligand	Yield (%)	ee (%)
OH	(DHQD) ₂ Phal	-	44
OH	(DHQD)Ind	-	40
OH	(DHQD) ₂ Pyr	-	52
OH	(DHQ) ₂ Pyr	85	65
Me	(DHQ) ₂ Pyr	85	71
<i>t</i> Bu	(DHQ) ₂ Pyr	>99	60



Scheme 95. Synthesis of chiral dialcohol- and aminoalcohol allylsilanes from silyl-2,5-cyclohexadienes.

The same strategy was applied to perform the regio- and stereoselective amino-hydroxylation of allylsilanes (**69** and **70**, **Scheme 95**).^[158] Hydroxydimethylsilyl-dienylsilane reacted with Sharpless AD mixture with NH₂CO₂Et and (DHQ)₂Pyr, as nitrogen and chiral source respectively, to furnish the aminohydroxylation product with complete regio- and diastereocontrol and in 66% *ee*. The *t*BuMe₂Si- analogue was obtained with a higher *ee* (81%), but a slightly lower regioselectivity (β/γ = 92/8).

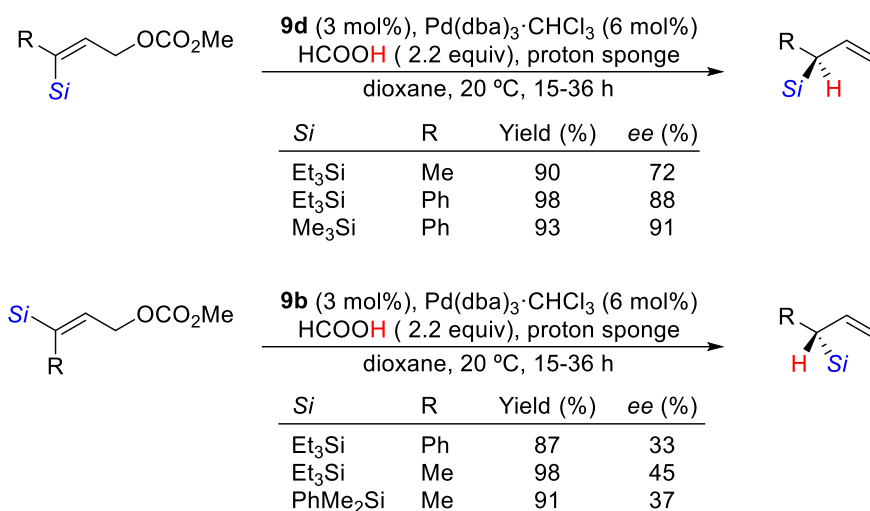
1.2.2.12 Substitution of γ -silyl-substituted allylic electrophiles

Allylic substitution of γ -silyl-substituted allylic electrophiles is a powerful reaction for the preparation of allylsilanes and has attracted much interest in the past 30 years. Consequently, many different strategies were developed depending on the nature of the nucleophile introduced during the process.

1.2.2.12.1 Reduction

One of the first methodologies developed in this field consisted in the asymmetric reduction of (*E*)- and (*Z*)-3-alkyl-3-silyl-2-propenyl methyl carbonates in dioxane with formic acid (2.2 equiv) and 1,8-bis(dimethylamino)naphthalene (1.2 equiv) in the presence 3 mol% of *in situ* prepared Pd-complex, obtained by mixing Pd₂(dba)₃·CHCl₃ and (*R*)-MOP (**9b**)/(*R*)-MOP-Ph (**9d**) (Pd:monophosphine = 1:2).^[159] The regioselective transformation tolerated different silicon

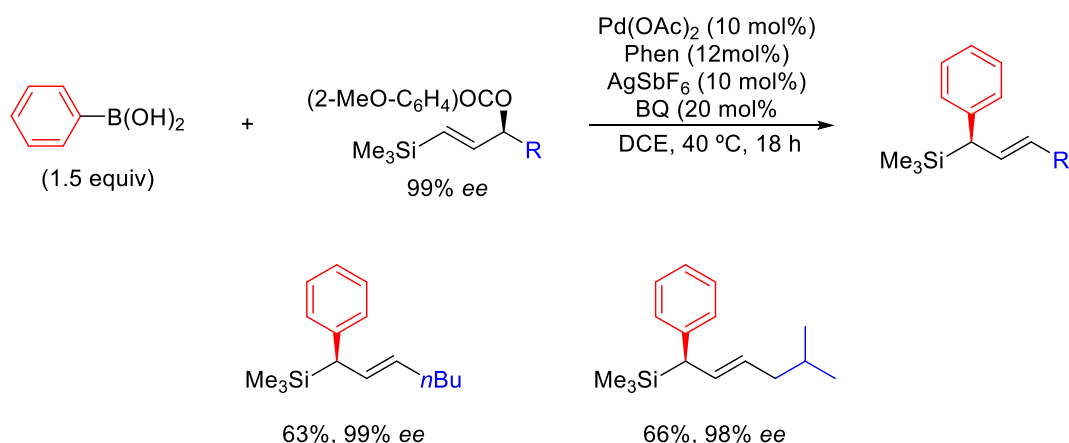
moieties such as Me₃Si-, Et₃Si- or PhMe₂Si- without having a huge impact in the yield or the enantioselectivity level of the reaction (**Scheme 96**).



Scheme 96. Synthesis of allylsilanes through asymmetric reduction with formic acid.

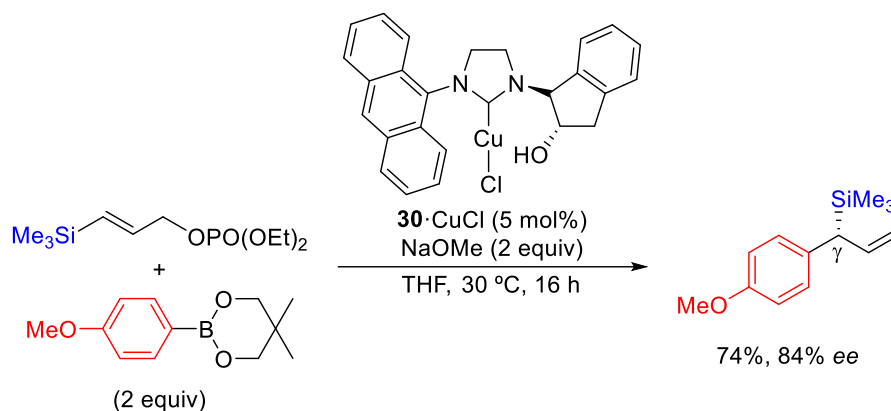
1.2.2.12.2 Arylation

γ -Silyl-allylic electrophiles can also be substituted with aryl moieties. For instance, two different examples of α -arylated allylsilanes with (*E*)-geometry were prepared by γ -selective allyl-aryl coupling between phenyl boronic acid and chiral γ,γ -disubstituted vinylsilanes.^[160] Optically active γ -alkyl substituted allylic esters reacted in a *syn*-stereochemistry manner with excellent chirality γ -to- α transfer in the presence of Pd(OAc)₂ (10 mol%) to furnish the corresponding chiral allylsilanes in good yields (63% and 69%) and excellent ee > 98% (**Scheme 97**).



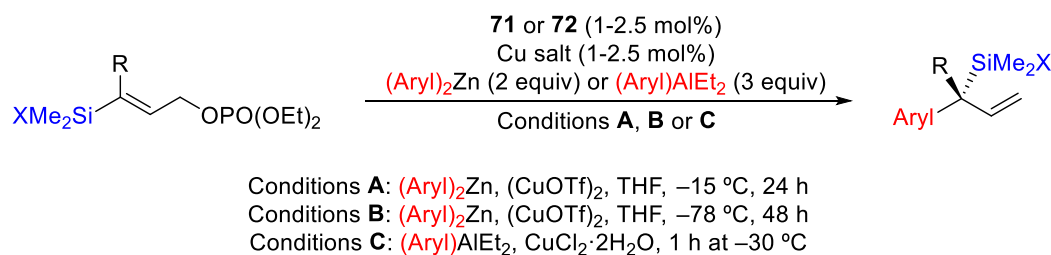
Scheme 97. Synthesis of α -substituted allylsilanes through allylic boration of γ -silyl-substituted allylic esters.

Another chiral α -aryl substituted allylsilane was prepared by the reaction of 4-methoxyphenylpinacolboronate (2 equiv) with γ -trimethylsilyl-substituted allylic diethylphosphate in the presence of NaOMe (2 equiv) and **30**·CuCl complex (5 mol%) in THF at 30 °C. The corresponding chiral allylsilane was obtained in good yield (74%) and enantioselectivity (84% ee).^[161]

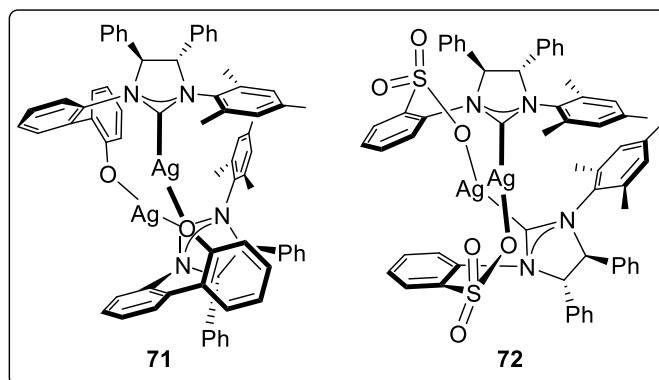


Scheme 98. Copper(I)-catalyzed allylic alkylations of γ -silyl-substituted allylic electrophile with 4-methoxyphenylpinacolboronate.

Allylsilanes bearing silyl-substituted tertiary and quaternary stereogenic centres could be prepared by asymmetric allylic arylation (AAR) with diarylzinc reagents (2 equiv) in the presence of *in situ* generated chiral NHC-copper catalysts **71** and **72** (1-2.5 mol%).^[162] The corresponding allylsilanes were formed exclusively as γ -regioisomers in moderate to good yields (72-91%) and enantioselectivities (57-92% ee, **Scheme 99**). The same NHC-silver complex **72** (1 mol%) also achieved the reaction of the same γ -silyl- γ -alkyl-disubstituted substrates with phenyl- and (4-MeOC₆H₄)diethylaluminum reagent (increasing considerably the yield and enantioselectivity achieved with catalyst **71**) and heterocycles (2-furyl)- and (3-thienyl)- analogues.^[163] Within 1 h at -30 °C, the corresponding adducts are obtained in high yields (81-97%) with a complete regioselectivity in favour of the γ -isomer and moderate to good enantioselectivity (73% and 94% ee).



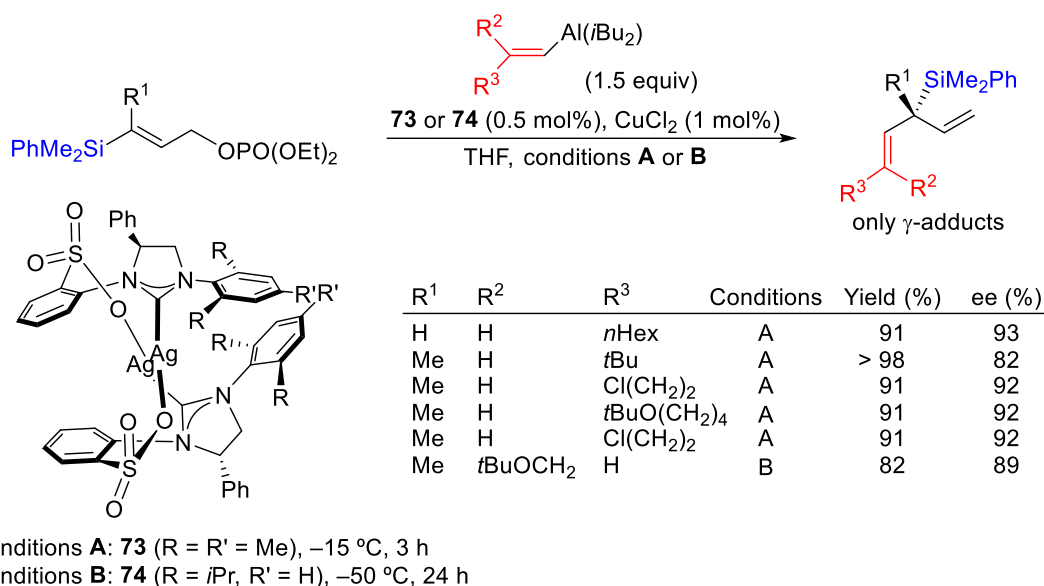
Reagent	R	Conditions	Ligand (mol %)	X	Yield (%)	ee (%)
Ph_2Zn	H	A	71 (1)	Me	91	92
Ph_2Zn	H	A	71 (1)	Ph	82	90
$(4\text{-MeOC}_6\text{H}_4)_2\text{Zn}$	H	A	71 (1)	Ph	88	91
$(4\text{-CF}_3\text{C}_6\text{H}_4)_2\text{Zn}$	H	A	71 (1)	Ph	77	57
Ph_2Zn	Me	B	72 (1)	Ph	72	85
$(4\text{-MeOC}_6\text{H}_4)_2\text{Zn}$	Me	A	72 (2.5)	Ph	80	76
PhAlEt_2	Me	C	72 (1)	Ph	81	92
$4\text{-MeOC}_6\text{H}_4\text{AlEt}_2$	Me	C	72 (1)	Ph	97	94
$(2\text{-furyl})\text{AlEt}_2$	Me	C	72 (1)	Ph	91	73
$(3\text{-thienyl})\text{AlEt}_2$	Me	C	72 (1)	Ph	95	88



Scheme 99. Copper(I)-catalyzed allylic arylation of γ -silyl-substituted allylic phosphates with diarylzinc and arylaluminium reagents.

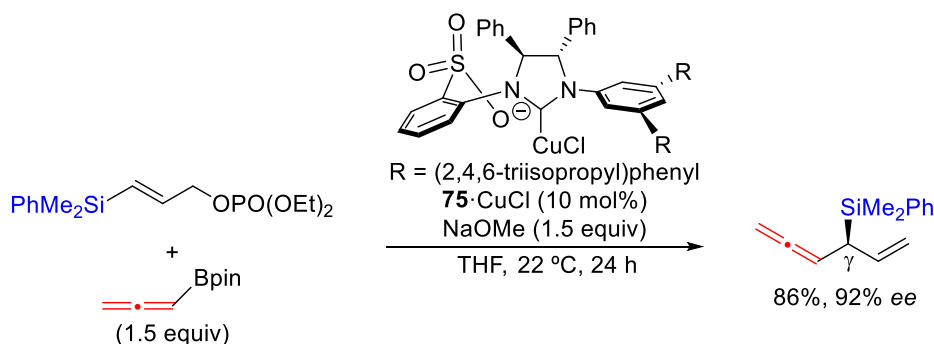
1.2.2.12.3 Vinylation

Using same γ -silyl- γ -alkyl-disubstituted allylic phosphates as starting material and NHC-silver dimer complexes analogues **73** and **74** as catalysts, alkyl-substituted vinylaluminium reagents (*in situ* prepared by hydroalumination of alkynes with DIBAL-H) were used for the preparation of enantioenriched allylsilanes (**Scheme 100**).^[164,165] Under the optimized conditions as low as 0.5 mol% of complexes **73** or **74** and 1 mol% of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, enantioenriched 3-alkyl-3-silyl-disubstituted 1,4-dienes (ee $\geq 82\%$) are obtained in high yields with full retention of the carbon-carbon bond geometry ($\geq 82\%$). With (*E*)-vinylaluminium reagents, high enantiocontrol is obtained with complex **73** in THF within 3 h at -15°C whereas the (*Z*)-isomer requires the use of complex **74** during 24 h at -50°C .



Scheme 100. Copper(I)-catalyzed allylic alkylation of γ -silyl-substituted allylic phosphates with vinylaluminum reagents.

One chiral allylsilane was prepared when allenic pinacolborane (1.5 equiv) reacted with PhMe₂Si-substituted allylic phosphate in the presence of *in situ* formed NHC-copper complex **75**·CuCl (10 mol%) and NaOMe (1.5 equiv) in THF at 22 °C (**Scheme 101**).^[166] The allenic allylsilane was isolated in excellent yield (86%) with full regioselectivity ($\gamma/\alpha > 98/2$) and high enantioselectivity (92% ee).

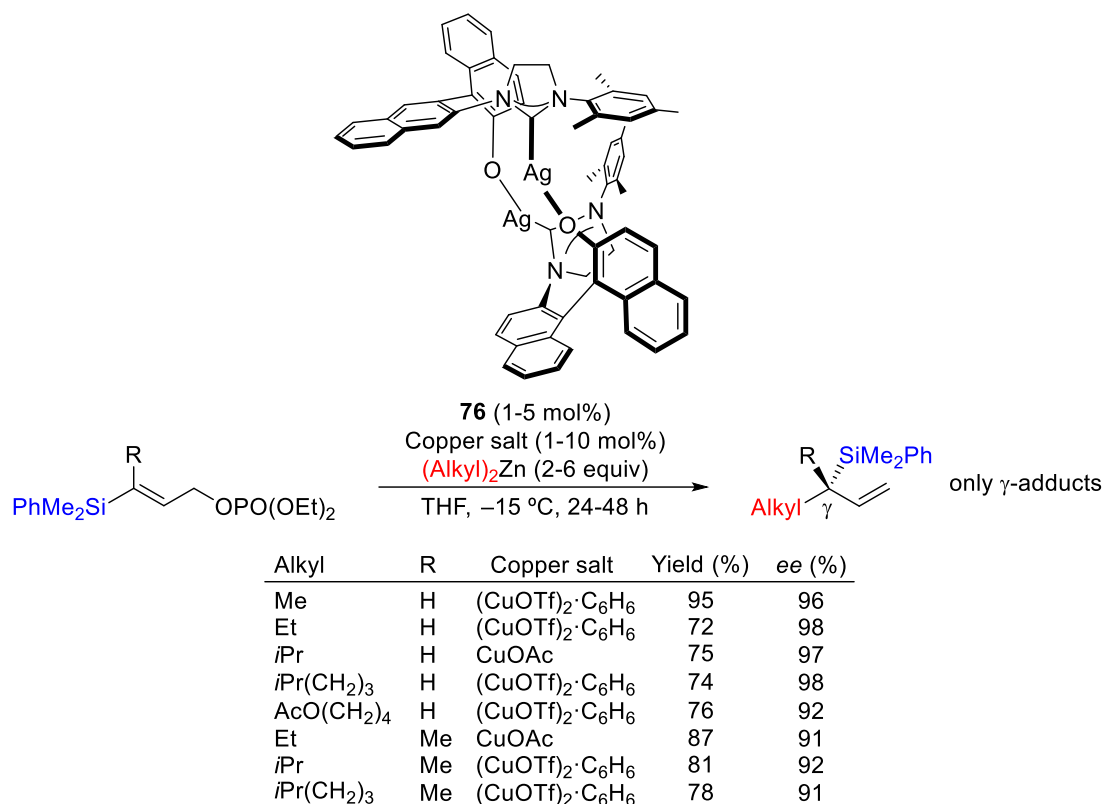


Scheme 101. Copper(I)-catalyzed allylic alkylation of γ -silyl-substituted allylic phosphates with phenylborane and allenylborane.

1.2.2.12.4 Alkylation

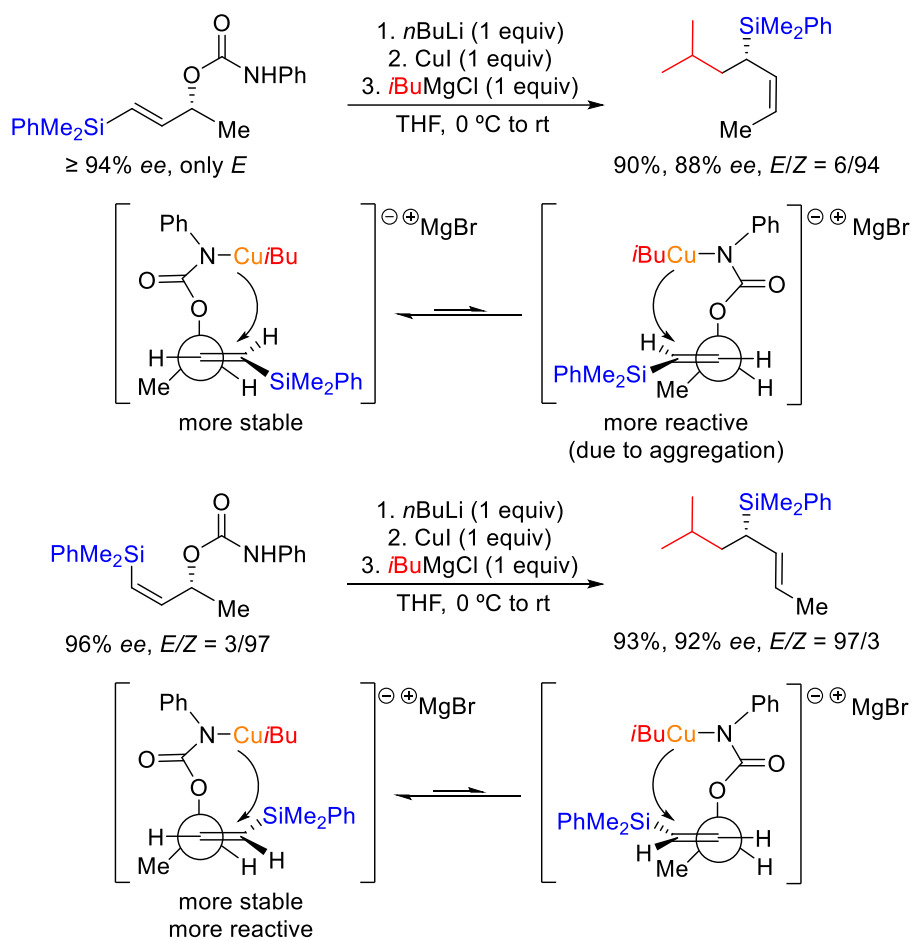
The same strategy as for the preparation of α -aryl substituted allylsilane through NHC-mediated Cu-catalyzed AAR with diarylzinc reagents was applied for the synthesis of their alkyl analogues.^[162] Asymmetric allylic alkylation (AAA) of (*E*)-phosphates with dialkylzinc reagents (2-6 equiv) in the presence of NHC-silver complex **76** (1-2 mol%) and Cu(OTf)₂·C₆H₆ or CuOAc (1-4 mol%) at -15 °C in THF furnished chiral tertiary γ -allylsilanes in good yields (72-94%) and enantiomeric excesses (ee \geq 91%). Allylic quaternary silyl-substituted centres were also accessed with similar results (75-87% yields and ee \geq 91%) from

γ -silyl- γ -alkyl-disubstituted substrates, albeit increased loads of ligand **76** (2.5-5 mol%) and copper salt (2.5-10 mol%) along with longer reaction times (48 h) were necessary (**Scheme 102**).



Scheme 102. Copper(I)-catalyzed allylic alkylation of γ -silyl-substituted allylic phosphates with dialkylzinc reagents.

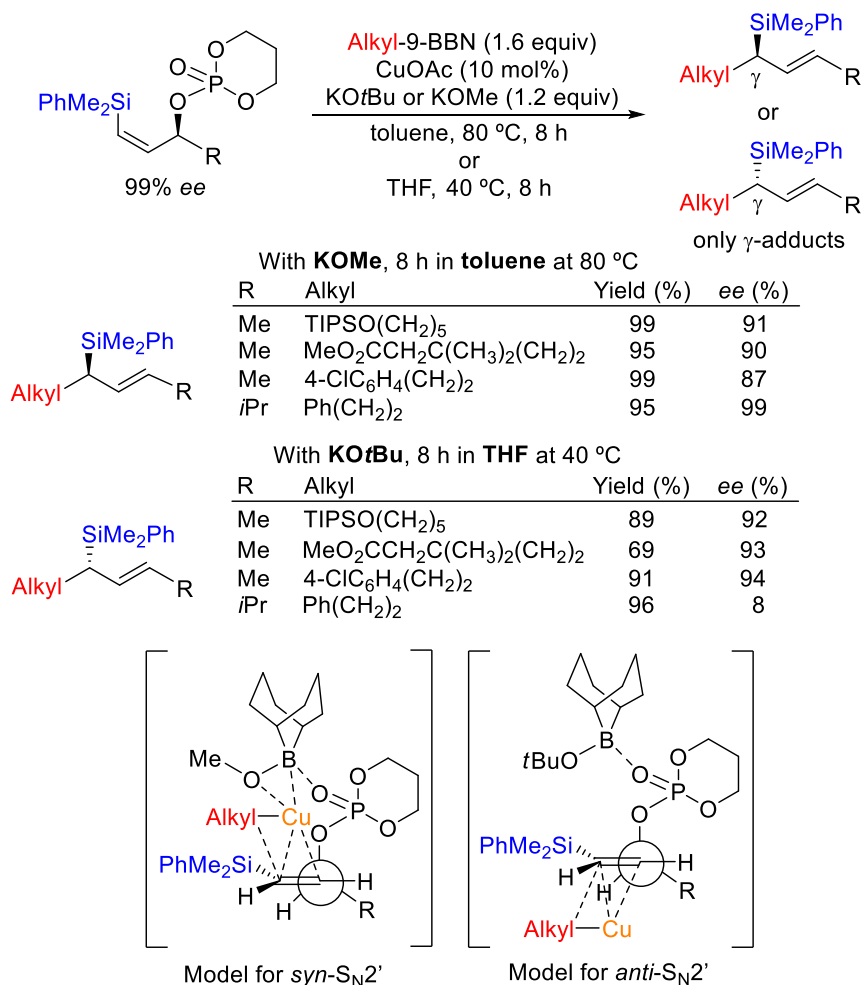
Several years before, the stereoselective copper(I)-mediated addition of Grignard reagents to nonracemic chiral γ -silyl-substituted allylic (*E*)- and (*Z*)-phenylcarbamates was reported.^[167,168] The protocol involves the deprotonation of the carbamate function with *n*BuLi (1 equiv) followed by the consecutive additions of CuI (1 equiv) and Grignard reagent (1 equiv) in THF at 0 °C and then stirring at rt for 16 h (**Scheme 103**). With both (*E*)- and (*Z*)-isomers, γ -allylsilanes are isolated in good yields ($\geq 90\%$) with excellent enantiocontrol ($ee \geq 88\%$) through a *syn*-S_N2'-pathway. The *E/Z* ratio of the γ -adducts depends on the configuration of the carbon-carbon double bond of the starting materials. Interestingly, the allylsilane double bond geometry is the opposite of the one of the starting carbamate.



Scheme 103. Allylic alkylation of nonracemic chiral γ -silyl-substituted (*E*)- and (*Z*)-allylic carbamates.

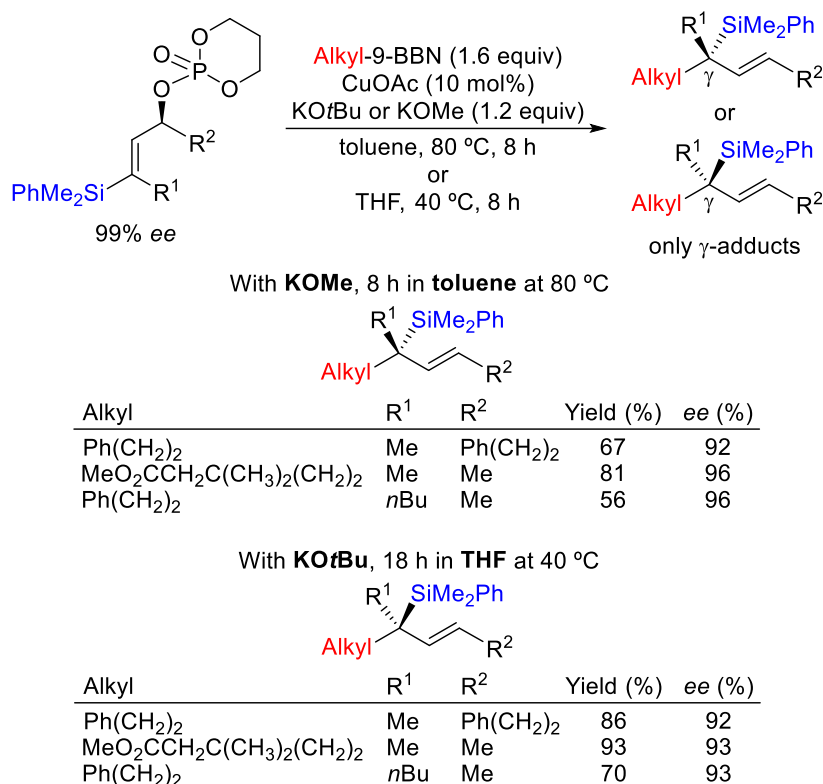
A synthetic method involving the copper(I)-catalyzed addition of primary alkylboranes to nonracemic chiral γ -silyl-substituted (*Z*)-allylic phosphates (99% ee) was also reported to access allylsilanes regio- and stereoselectively (**Scheme 104**).^[169] In all cases, a full γ -regioselectivity was observed. The stereochemical course of the reaction is however dependent on the choice of solvent and of the achiral alkoxide base needed for the activation of the alkylborane reagent. Indeed, the reaction with alkylborane (1.6 equiv, prepared in advance by hydroboration of alkenes with 9-BBN dimer), in the presence of CuOAc (10 mol%) and KOMe (1.5 equiv) in toluene at 80 °C, proceeded in a *syn*- S_N2' -fashion. On the other hand, when the bulkier base KO*t*Bu was used (instead of KOMe) at 40 °C in THF, the reaction took place in an *anti*- S_N2' -fashion. Except in the peculiar case of the substrate with the bulky isopropyl group in the α -position of the phosphate leaving group, in both conditions good to excellent yields are achieved (56-99%) with a high chirality transfer (ee $\geq 87\%$). The reversal of the *anti*:*syn* selectivity with respect to the alkoxide base has been rationalized. With KOMe, the alkoxy oxygen is assumed to be able to coordinate the copper atom, enabling a *syn*-elimination through a cyclic transition state. By contrast, the bulky *tert*-butyl group of

KOtBu prevents this coordination, leading to an *anti*-elimination through an acyclic transition state (**Scheme 104**).



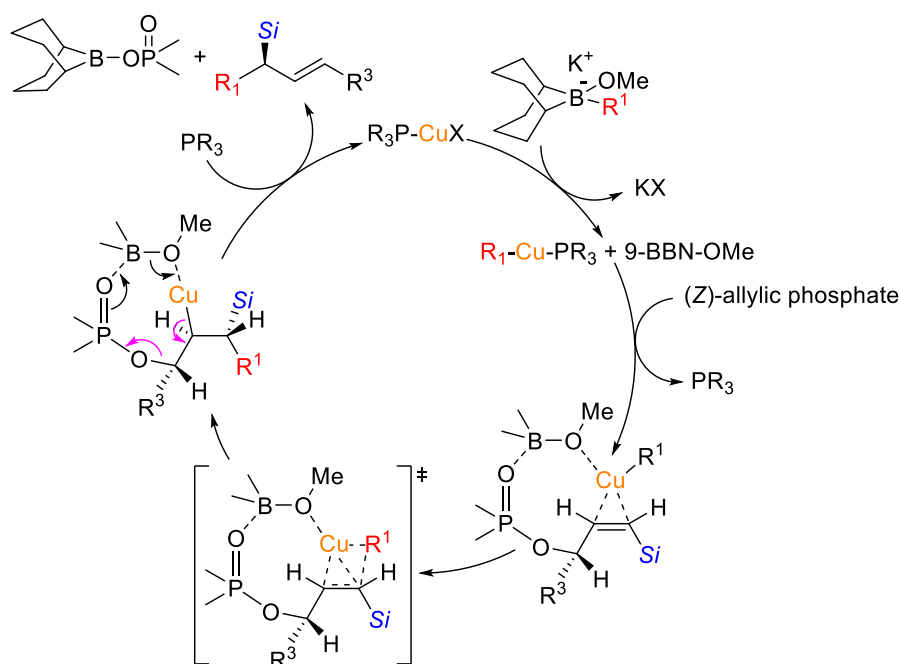
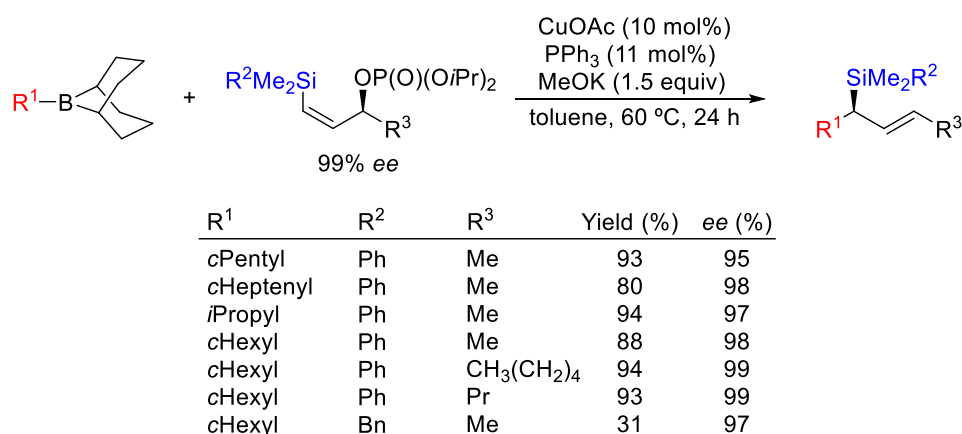
Scheme 104. Copper(I)-catalyzed allylic alkylation of nonracemic chiral γ -silyl-substituted (*Z*)-allylic phosphates with alkylboranes.

The same reversal of *anti:syn* selectivity was observed with γ -silyl- γ -alkyl-disubstituted (*E*)-allylic phosphates that afforded γ -allylsilanes with an allylic quaternary silyl-substituted stereogenic centre with similar results (56-93% yield and ee \geq 92%, **Scheme 105**). However, no secondary alkylborane was effective neither if the reaction proceeds through a 1,3-*anti* or 1,3-*syn* way, probably because of the increased steric demands of the transferring group.



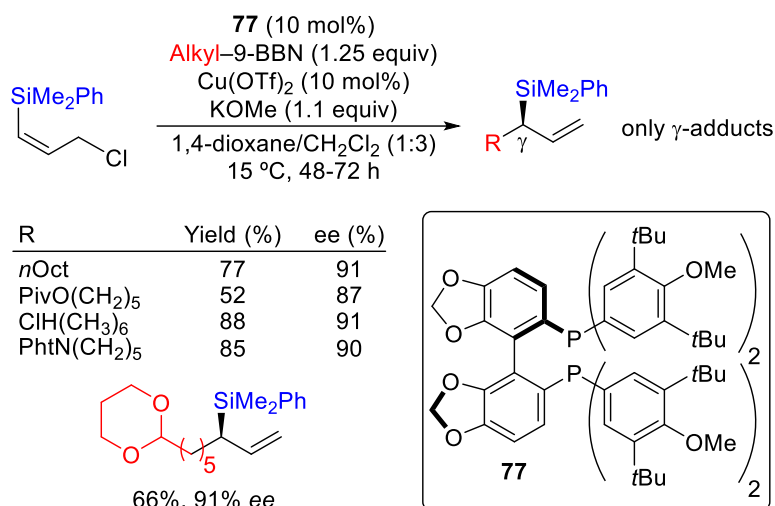
Scheme 105. Copper(I)-catalyzed allylic alkylation of nonracemic chiral γ -silyl- γ -alkyl-disubstituted allylic phosphates with alkylboranes.

This limitation regarding the exclusive use of primary alkylboranes as nucleophilic partners in the copper-catalyzed allylic cross-coupling with allylic phosphates was shortly after overcome.^[170] A new copper catalytic system with secondary alkylboronates proceeded with complete γ -(*E*)-selectivity and preferential 1,3-*syn* stereoselectivity with γ -silicon-substituted (*Z*)-allylic phosphates in the presence of CuOAc (10 mol%), PPh₃ (11 mol%) and MeOK (1.5 equiv) in toluene at 60 °C. Unlike with primary alkylborane procedures, when the sterically more demanding base *t*BuOK was used, no reaction took place. The scope of the ligand and other theoretical studies showed that the stereochemistry and yield of the reaction was highly dependent on the coordination abilities of the ligand towards the copper centre. This high phosphine dependency was explained by DFT calculations suggesting that tertiary monophosphines would not be able to coordinate to the copper centre in the cyclic organocopper addition-elimination transition state because of steric effects. Enantioenriched allylsilanes bearing α -stereogenic centres are obtained in poor to good yields (31-96%) and excellent enantiomeric excess $\geq 93\%$ through a *syn*-elimination process (**Scheme 106**).



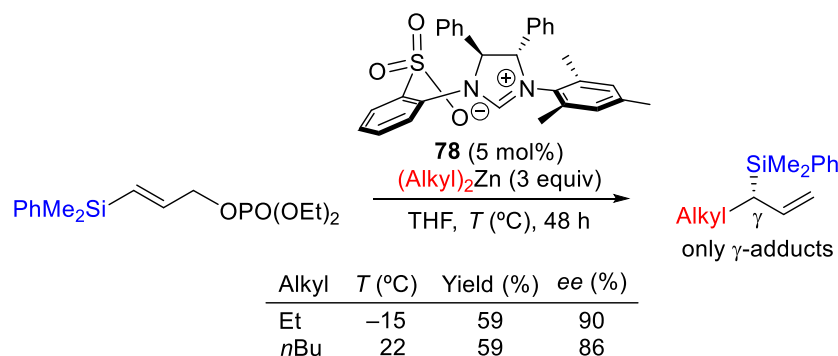
Scheme 106. Copper(I)-catalyzed γ -selective and stereospecific allylic cross-coupling with secondary alkylboranes.

Alkylboranes were also employed in the enantioselective copper(I)-catalyzed allylic substitution of γ -silyl-substituted (*Z*)-allylic chlorides (**Scheme 107**).^[171] When alkyl boranes were set in the presence of the allylic chlorides with Cu(OTf)₂ (5 mol%), 3,5-di-*tert*-butyl-4-methoxyphenyl-SEGPHOS **71** (10 mol%) and KOMe (1.1 equiv) in a 1:3 mixture of 1,4-dioxane/CH₂Cl₂ at 15 °C, γ -allylsilanes adducts were formed as single regioisomers, with high yields ($\geq 87\%$) and enantiocontrol (ee $\geq 87\%$).



Scheme 107. Copper(I)-catalyzed allylic alkylation of (*Z*)- γ -silyl-substituted allylic chlorides with alkylboranes.

Interestingly, the copper-free asymmetric allylic alkylation reaction of (*E*)- γ -dimethylphenylsilyl substituted allylic diethylphosphate has been reported using NHC-zinc complexes obtained from mixing imidazolium sulfonate **78** (5 mol%) and dialkylzinc reagents (3 equiv) in THF (**Scheme 108**).^[172] The desired products were isolated in high enantiomeric excesses (86 and 90% ee) and moderate yields (59%).



Scheme 108. Copper-free allylic alkylation of γ -silyl-substituted allylic phosphates.

1.3 Conclusion

As illustrated in this section, the synthesis of chiral allylsilanes has been widely investigated and many different strategies to access them have been unveiled. Nevertheless, the library of different allylsilanes that can be accessed remain quite limited as most of these protocols have been chiefly implemented to access PhMe₂Si- containing molecules except in a few rare cases.

PART II:

RESULTS AND DISCUSSION

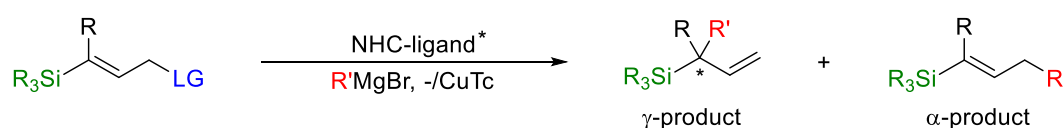
2 Results and discussion

2.1 Objectives and purpose of the project

Although asymmetric allylsilanes are potential building blocks of great interest because of the large number of transformations they can undergo through their silyl moiety, the double bond or other functions present in the molecule (halogen, ester, amine, alcohol, ether, ketone, acid), their preparation is still limited nowadays, and a general procedure to access them has not yet been established. This is the reason why the development of a direct and flexible route for their synthesis that allows an easy variation of its structure (including the nature of the silyl moiety, olefin geometry, absolute stereochemistry and the α -substituents regarding the silicon atom) is of great interest, albeit it remains as a great challenge for the synthetic and organic chemists.

As demonstrated by our literature survey, most of the methods described, particularly those based on an asymmetric allylic alkylation approach, require the presence of a transition metal such as Pd, Cu, Rh, Ir or Fe to successfully take place. Nevertheless, metal-based methods entail some disadvantages compared to the transition-metal free ones. Among them, we can highlight the high price of transition metals, their toxicity (removal of trace amounts of transition-metal residues from desired products is quite costly and challenging, while crucial, especially in the pharmaceutical industry) and the need (not always) of co-catalyst and/or special additives to increase the effectiveness in the reaction. These drawbacks coupled with an incipient society concern about the environmental impact of human activities, green chemistry and sustainable development have led the metal free methods to attract the most attention in recent years. Nevertheless, nowadays, those approaches that do not required the presence of a transition metal catalyst although highly desirable, are still limited and confront challenges to some extent.

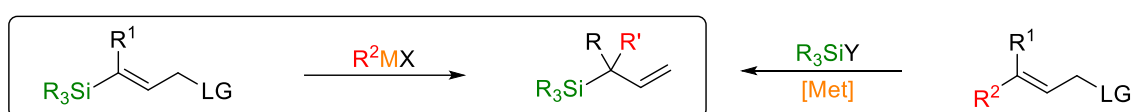
It was in this breeding ground where we thought about unveiling a novel attractive transition-metal free strategy involving the synthesis of stereodefined allylsilanes. Still with the idea of developing a platform that allows an easy modulation of the allylsilanes, we planned to study the asymmetric allylic substitution (AAS) of silicon-substituted allylic electrophiles with Grignard reagents using NHC-ligand as chiral inductors (**Scheme 109**).



Scheme 109. General synthesis method for the preparation of various allylsilanes through AAS

Based on previous studies developed by Hoveyda^[172,173] and Alexakis^[174–180] about copper-free processes where organometallic reagents can be activated by the NHC Lewis base ligands, we also envisioned the possibility of developing a new access to chiral allylsilanes through an asymmetric allylic substitution in the absence of copper. Hence, our efforts were focused on merging three different topics i.e., copper-free catalysis, synthesis of stereodefined allylsilanes and asymmetric allylic substitution, in one unique strategy.

Allylsilanes can be obtained by several synthetic strategies, for instance, through the silylation of allylic electrophiles. As for us, we envisioned their synthesis through addition of organometallics onto vinylsilanes bearing appropriate leaving groups in the α -position (**Scheme 110**).



Scheme 110. Two different strategies to access chiral allylsilanes from allylic electrophiles.

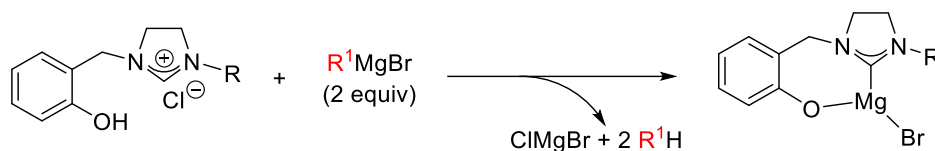
As it was exposed by the literature precedents reviewed before, near exclusive dimethylphenylsilyl moiety has been used in the preparation of the enantioenriched silanes. In our strategy we foresee, seeking the easy modification of the allylsilanes scaffold, the usage of several silyl groups to evaluate if the catalytic method can be applied over a large number of silicon substrates. This will be important, as the silyl part will certainly have an impact on the further reactivity of the allylsilanes. The leaving group will also be evaluated in order to look for the one that provide best results in terms of yield, regio- and enantioselectivity. Special interest will be placed on phosphates and halides as they have already been described as substrates in copper-free methodologies.

On the other hand, in order to achieve an asymmetric transformation, NHC-type ligand will be used as chiral inductor. Among all the different possible imidazolium-skeletons, the family of bidentate imidazolium salt precursors bearing a side hydroxy group was envisioned as the most suitable one, where the coordination hydroxyl function of this ligand is expected to play a key role in the improvement of the reaction enantioselectivity. The use of this specific type of ligand is not only intended for the introduction of the stereochemical information, but also it is expected to proceed as a Lewis base in the activation of the organometallic reagents, allowing to perform the reaction in the absence of Cu.

Last but not least, Grignard reagents were envisioned to be good organometallic partners for this transformation although they had not yet been reported for this type of asymmetric reactions. Despite their less functional tolerance than other organometallic nucleophiles such as dialkylzinc reagents, they are more atom economical, user friendly and less expensive.

Furthermore, as a huge plethora of Grignard reagents are weather commercially available or easily prepared in the laboratory, the versatility of our method will be enhanced by their use.

Another advantage of these organometallic reagents is that they can directly deprotonate *in situ* a Lewis base (in the form of imidazolium salts) without requiring a preformed copper or silver carbene, to form an active catalyst (**Scheme 111**).



Scheme 111. Deprotonation of Alexakis-type NHC-ligand by Grignard reagents.

In the next section, copper-free asymmetric allylic substitution will be briefly reviewed. Subsequently, the applicability of our novel copper-free catalytic system will be assessed in the preparation allylsilanes bearing silyl-substituted tertiary and quaternary stereogenic centres.

2.2 Copper-free asymmetric allylic substitution

Copper-catalyzed AAS has been widely developed in the last 40 years and countless publications can be found where the *in situ* formed copper reagent governs the reactivity and selectivity of the carbon-carbon bond formation, furnishing a variety of enantiopure compounds. Performing the same enantioselective reaction in the absence of the first-row transition metal or any other metal, although possible, has been scarcely described. Nevertheless, it is extremely interesting since it will allow to achieve reactivity and selectivity profiles that are inaccessible by organocopper systems.

It is well known that the properties of some organometallic reagents can be altered by the coordination of a Lewis base such as solvent or a chelating group, as well as the complexation with other organic or inorganic molecules such as LiCl or Li(acac)₂.^[181–184] Copper-free catalytic methods rely on the direct activation of the organometallic reagent (Mg-, Zn- or Al-based) by its association with a nucleophilic Lewis base (LB). This coordination is expected to cause a redistribution of the molecule electron density, affording as in the case of Grignard reagents, a LB·RMgX complex that exhibits enhanced nucleophilicity (**Figure 4**).^[185]

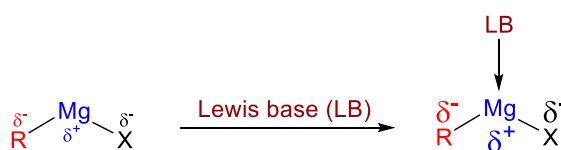


Figure 4. Lewis base association affording organometallic species with increased nucleophilicity and possible altered reactivity vs. RMgX.

First evidence of copper-free AAS appeared in 2006,^[173] although a year before copper-free ACA of Et_2Zn over acyclic enones was also described.^[186] AAA of γ -chloro- α,β -unsaturated esters with Grignard reagents was performed in the presence of bifunctional NHC-ligand **79** (Figure 5). Generally, the effectiveness of these bifunctional catalysts depends on the cooperation of both enhancing effects, which individually may not be enough to promote the particular transformation. Nevertheless, Lewis acidity and basicity have to be in accordance with the reactivity of the alkylmetal reagents, as otherwise, the alkylation may take place directly without requiring both activations, causing a diminution in regio- and/or stereoselectivity.^[172]

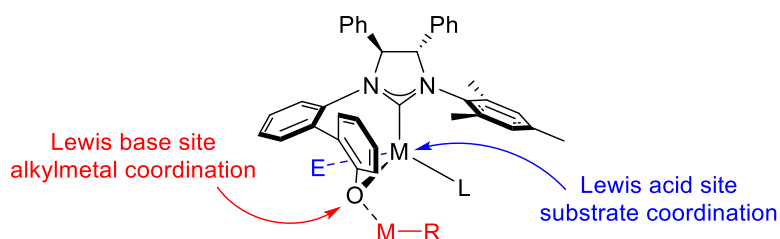
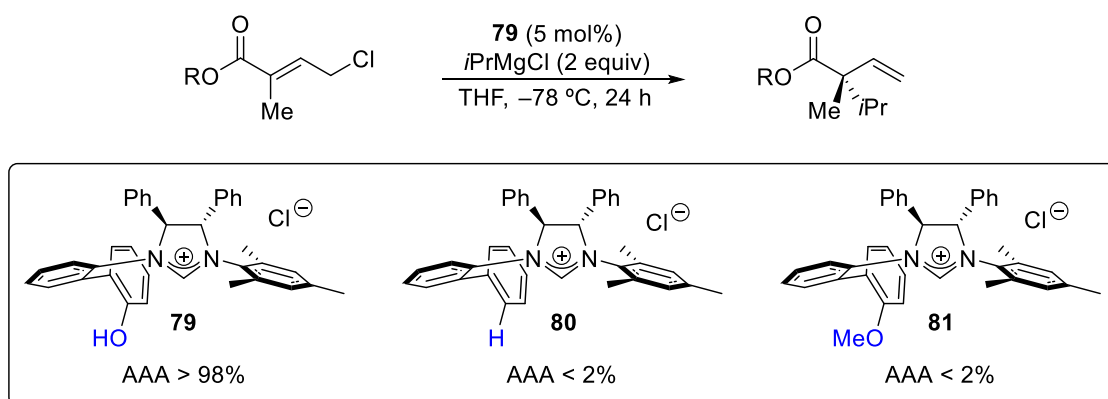


Figure 5. Asymmetric bidentate metal complex as bifunctional catalyst.

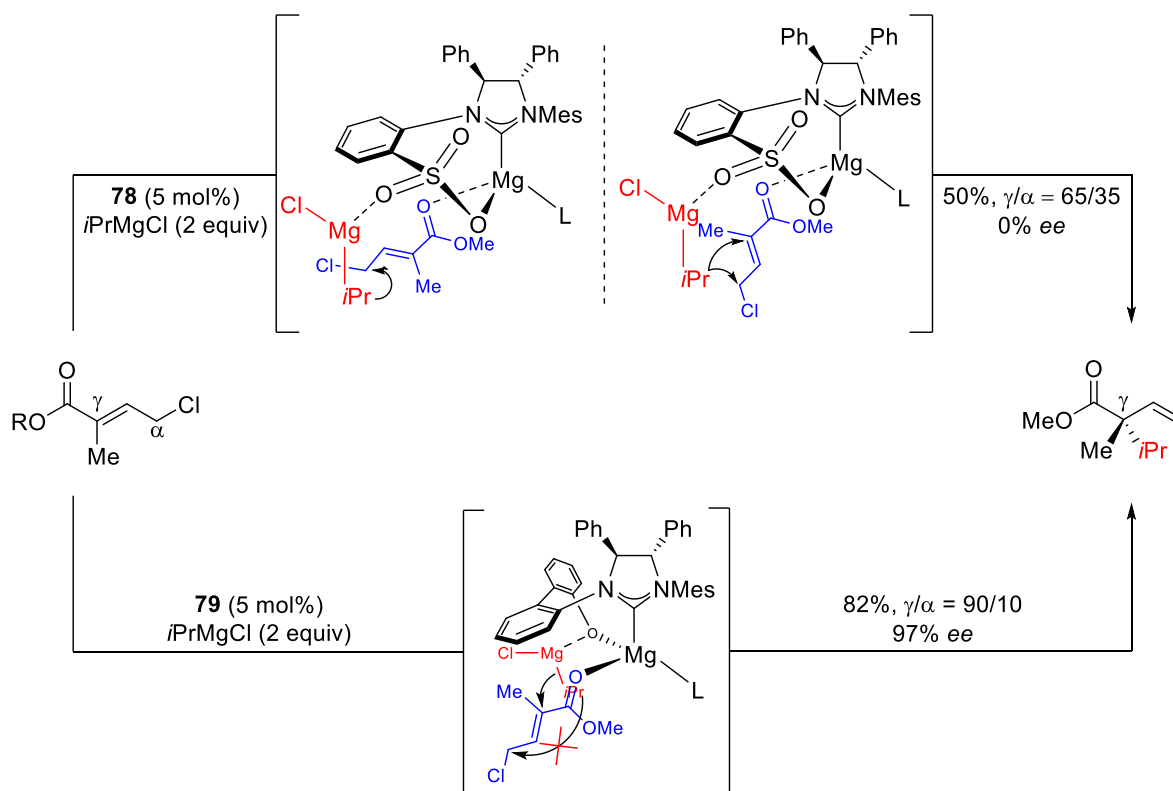
In the specific case of **79**, the phenolic hydroxyl plays a key role in the reaction, since loss of activity is observed (< 2% AAA) from the same chiral imidazolium salts bearing an H- or MeO- groups as in ligands **80** and **81** (Scheme 112). This was in accordance with the mechanistic studies that demonstrated that the phenoxy oxygen along with the carbon from the imidazolium salt were responsible for activating together the organometallic reagents to alkylate the allylic chloride.^[172]



Scheme 112. AAA studies with different imidazolium salts.

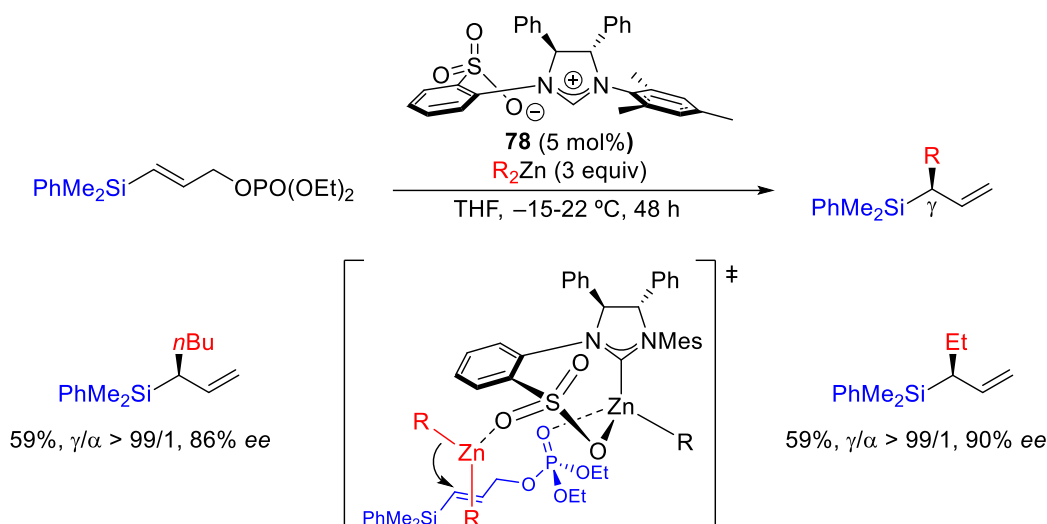
Not only the presence of an alkoxy group is necessary for the optimal operation of the reaction, but also the geometrical disposition that they induce plays a key role since it directs the addition of the alkylmetal reagent onto the electrophile. For instance, the NHC-sulfonate analogue **78** used in the copper-free AAA of allylic phosphates with Zn- and Al-based metal reagents, provide unsatisfactory results in terms of chemo-, regio- and enantioselectivity when applied with the ester-Grignard system. The complex formed by mixing NHC-ligand **78**,

isopropylmagnesium chloride and the allylic electrophile (ester) does not allow the easy delivery of the isopropyl substituent because of an undesired relative orientation of the sulfonate group related to the electrophile, leading to poor regioselectivity ($\gamma/\alpha = 65/35$) and no enantioselectivity (**Scheme 113**). On the other hand, in the complex formed with NHC-ligand **79**, the Grignard reagent and the allylic ester, they are positioned in such way that the α -attack of the Grignard reagent is much more hindered, leading to a high γ -selective ($\gamma/\alpha = 90/10$) and enantioselective (97% ee) AAA.



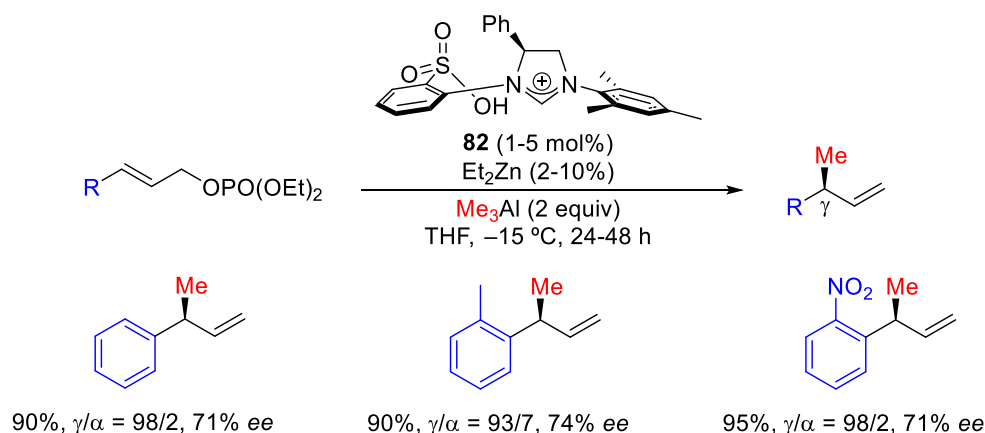
Scheme 113. Effect of the NHC-complex structure on the AAA of allylic esters.

By contrast, sulfonate imidazolium salt **78** was successfully employed for the preparation of tertiary and quaternary stereogenic centres using Zn-reagents and allylic phosphates as substrates, although a very small array of molecules was synthesized. In this particular case, ligand **79** did not promote the reaction (conversion < 18%, probably because it is not enough Lewis acid to activate the alkyl reagent).^[172] As in the previous case, ligand **78** lost its catalytic activity when there is no free oxygen in the sulphate moiety to coordinate to the metal centre (conversion < 5%). In this framework, two asymmetric allylsilanes bearing tertiary silicon-substituted stereogenic centres were synthesized in moderate yield (59%), and good regio- and enantioselectivity ($\gamma/\alpha > 99/1$ and $\geq 86\%$ ee), being the only ones prepared through a copper-free AAA method to the date (**Scheme 114**). Nevertheless, no quaternary allylsilanes analogues were reported.



Scheme 114. NHC-Zn-catalyzed EAA of silicon substituted allylic phosphates and proposed transition state.

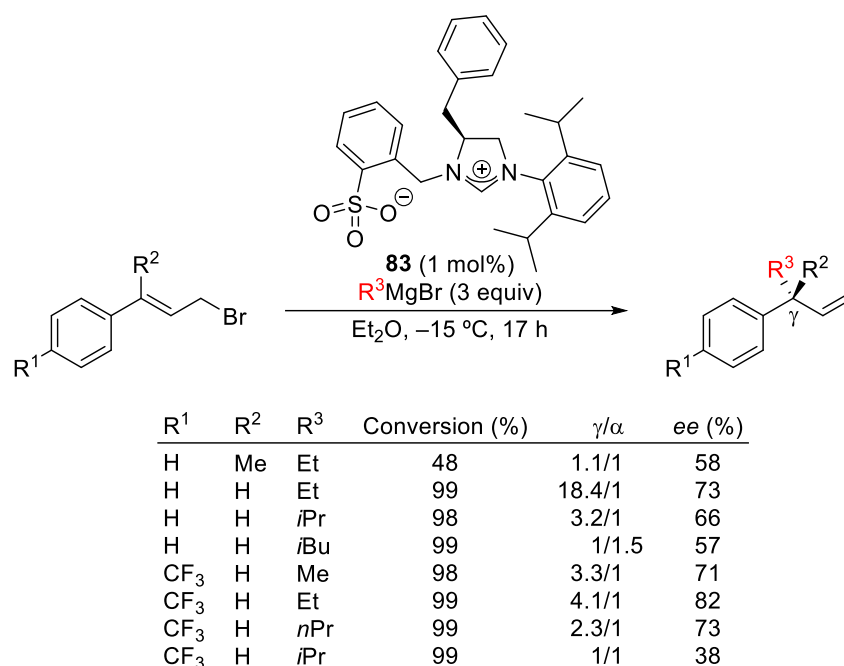
Although trialkyl-aluminium reagents were also used instead of their Zn-analogues to perform AAA, a considerable erosion in the enantioselectivity was observed.^[172] Furthermore, as NHC-Al(III) complex cannot be accessed by directly mixing the corresponding aluminium reagent and the imidazolium salt, so that NHC **82** has to be previously mixed with Et_2Zn to generate the NHC-Zn(II) complex, that will subsequently undergo a partial ligand exchange when treated with 2 equiv of Me_3Al (**Scheme 115**).



Scheme 115. EAA of allylic phosphates with (trialkyl)aluminium reagents.

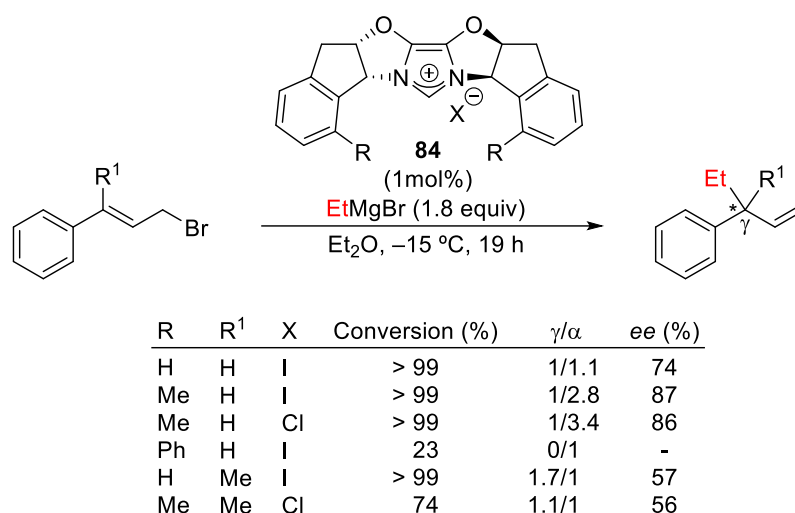
This methodology developed by Hoveyda based on the use of a bidentate sulfonate ligand, although successful when applied using organozinc/aluminium reagents, could not be applied on Grignard reagents, regardless of the leaving group nature on the electrophile. Nevertheless, contrary to Hoveyda's investigations, Woodward and co-workers were able to combine NHC-bidentate ligand **83** bearing a sulfonate moiety with Grignard reagents to successfully perform a copper-free AAA on cinnamyl bromides (**Scheme 116**).^[187] Different molecules bearing tertiary stereogenic centres were synthesized in poor regio- ($\gamma/\alpha > 40/60$) and

enantioselectivities (32-82% ee). This method was also applied for the preparation of a more sterically congested quaternary analogue, but low conversion was achieved (48%) along with almost no regioselectivity ($\gamma/\alpha = 1.1/1$) and modest enantioselectivity (58% ee).



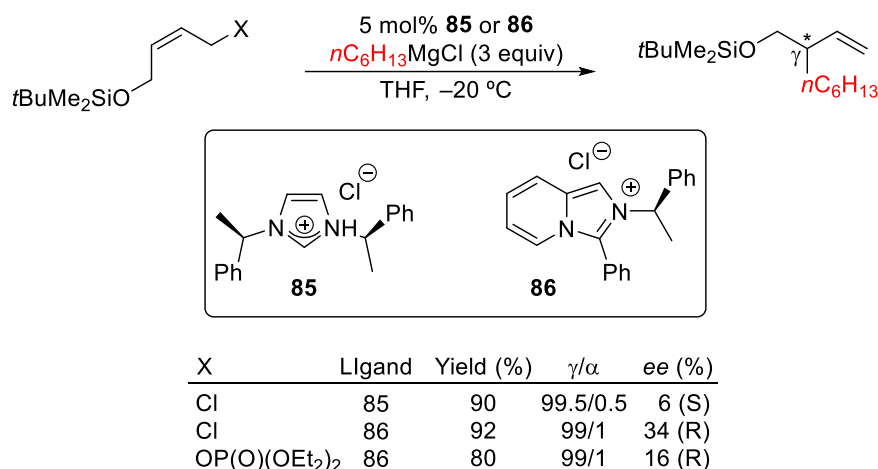
Scheme 116. Copper-free Grignard addition to allylbromides.

Other NHC-based type ligand compatible with Grignard reagents was also described to catalyze the same reaction with EtMgBr, providing higher levels of enantioselectivity (up to 86% ee), but worse γ -selectivity (up to $\gamma/\alpha = 1/1.1$).^[188] In the case of NHC-**84**, no chelating groups were present on the ligand (**Scheme 117**). Ligand **84** was also applied to the preparation of products bearing quaternary stereogenic centres ($R \neq H$, **Scheme 117**). In this case, a slight improvement of the regioselectivity (up to $\gamma/\alpha = 1.7/1$) was observed at the expense of a low enantioselectivity (56-57% ee). Contrary to other methods were the counterion of the ligand does not play any role in the stereoutcome of the reaction, here it exhibits a significant effect on both the regio- and enantioselectivity levels. The R substituents of the ligand also seems to have an effects (**Scheme 117**).



Scheme 117. AAA for the preparation of tertiary and quaternary enantioenriched molecules.

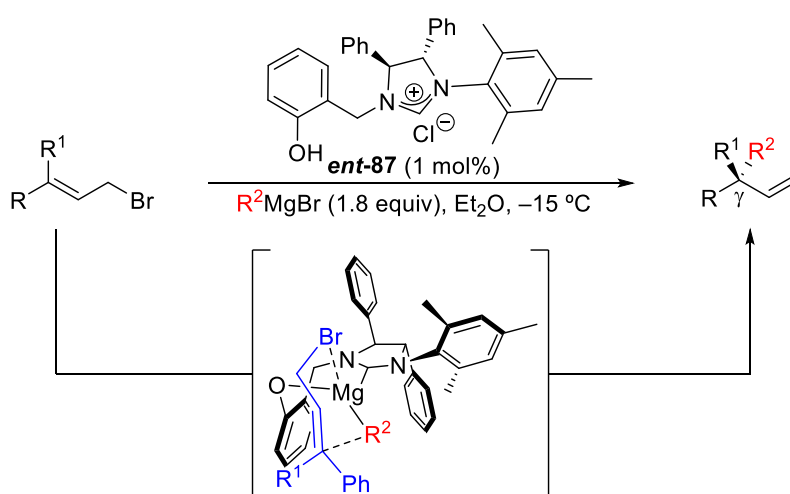
Other non-containing chelating group NHC-ligands were used efficiently to promote a copper-free AAA with organomagnesium reagents.^[189] The presence of imidazole-2-ylidene **85** and imidazole-4-ylidene **86** catalyzed the stereocontrolled Grignard allylic substitution on allylic phosphates and chlorides, to obtain the corresponding molecules as almost exclusive γ-products but very low enantiomeric excesses (6-34% ee, **Scheme 118**).



Scheme 118. Asymmetric reactions from allylic electrophiles in the presence of NHC-ligands without chelating groups.

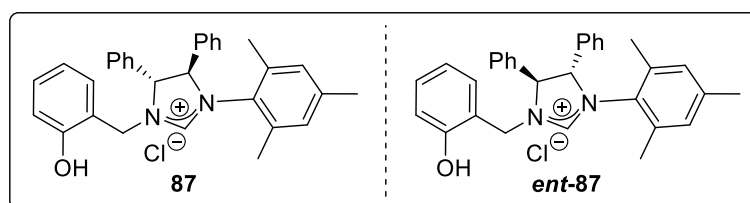
This lack of regio- and/or enantioselectivity observed when organomagnesium reagents were used was outstripped by Alexakis and co-workers. They were able to develop different catalytic systems that enable to perform the AAA of allylbromides with Grignard reagents in the absence of copper.^[174] Indeed, although it was Hoveyda who firstly discovered and exploited this type of reactivity by developing AAS protocols for the combination of allylic phosphates with Zn- and Al-based reagents, it was Alexakis *et al.* who most contributed to this field.

Alexakis and co-workers utilized convoluted NHC-ligand complexes, similar to those employed by Hoveyda (**78** and **79**) but changing the aromatic group on the nitrogen atom of the left part for a more flexible benzylic moiety (**ent-87**, **Scheme 119**), to alkylate γ -substituted cinnamyl bromides derivatives in the presence of different Grignard reagents.^[175,176] In Et₂O at $-15\text{ }^{\circ}\text{C}$, AAA proceeds smoothly with various combination of substrates and Grignard reagents to afford the corresponding products with tertiary stereogenic centres, in moderate yields and high levels of regio- and enantioselectivity (up to $\gamma/\alpha = 98/2$ and 91% ee). It is worthy to mention that this procedure was also applied for the preparation of quaternary stereogenic carbon centres with excellent γ -regioselectivity ($\gamma/\alpha > 98/2$) and same levels of enantioselectivity than those observed for tertiary centres.



R	R ¹	R ²	Yield (%)	γ/α	ee (%)
Ph	H	Et	82	76/24	85
Ph	H	<i>i</i> Bu	86	84/16	82
Ph	H	Ph(CH ₂) ₂	97	88/12	86
Me	H	Ph(CH ₂) ₂	94	86/14	33
BrCH ₂	H	Ph(CH ₂) ₂	98	> 98/2	61
1-Naphthyl	H	Et	88	74/26	91
Ph*	Me	Et	70	> 98/2	89
<i>t</i> Bu	Me	Ph(CH ₂) ₂	65	> 98/2	73

*From a mixture of *E/Z* isomers (4/1).



Scheme 119. AAA of γ -substituted cinnamyl bromides and tentative complex to explain the stereochemistry.

Later ligand studies indicated that the NHC-ligands used by Alexakis *et al.* should have some intrinsic properties to exhibit efficient catalytic activity.^[176] For instance, a three-carbon spacer on the left arm between the nitrogen of the imidazolium core and the oxygen of the chelating group was required. A library of ligands bearing some modifications regarding the

back-bone and/or blocking-aryl part (right arm) and/or benzyl part (left arm) and/or chelating group were tested (**Figure 6**). The best results were obtained with **ent-88** ($R^1 = R^5 = \text{H}$, $R^2 = R^3 = \text{Ph}$, $R^4 = R^6 = \text{Et}$), where the key change is the increase of the steric bulk in the right arm of the ligand (blocking part).

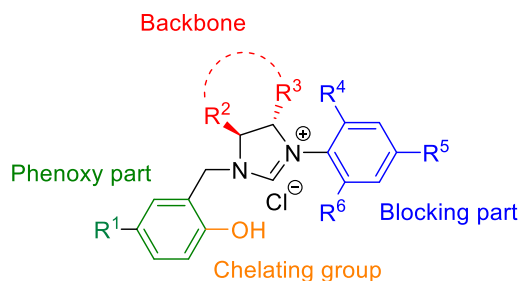
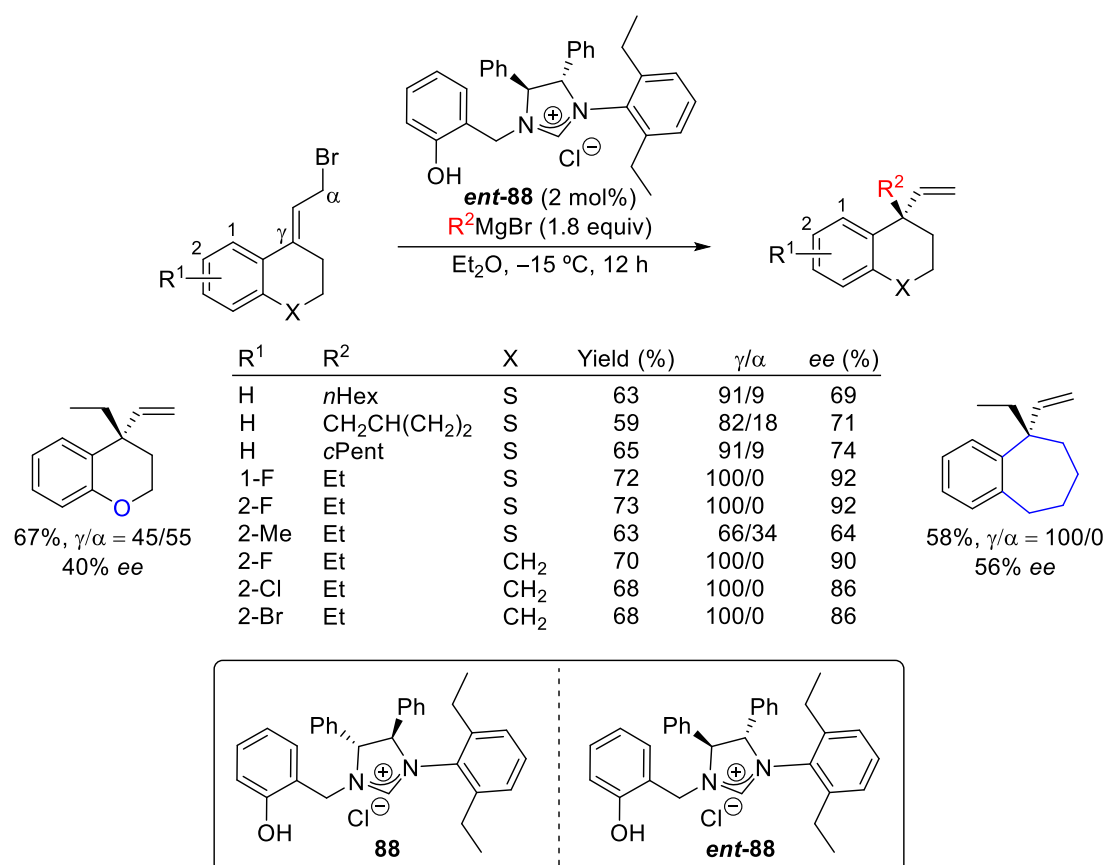


Figure 6. General structure of Alexakis type NHC-ligand and its different modifiable parts.

With this new ligand in hand, in most cases, slightly better results were obtained in term of enantioselectivity, along with a substantial improvement of the regioselectivity.

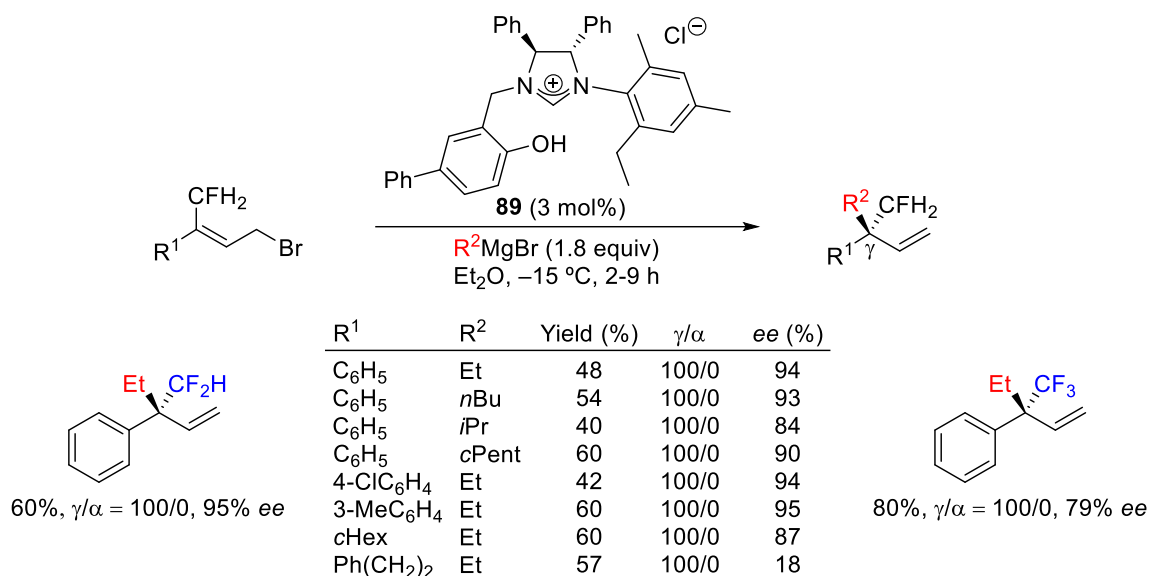
Using the same imidazolium salt **ent-88**, several exocyclic allylbromides derivatives were tested in the NHC-copper-free AAA catalytic system (**Scheme 120**).^[177] Under the optimization conditions, i.e., in the presence of 2 mol% of ligand **ent-88** at $-15\text{ }^{\circ}\text{C}$ in Et_2O , cyclic substituted allylbromides derived from Thiochroman-4-one and α -Tetralone furnished the corresponding bicyclic dialkyl-substituted products bearing a quaternary stereogenic centre in good yields (59-73%), high regioselectivity (up to $\gamma/\alpha = 100/0$) and moderate to high enantioselectivity (up to 92% ee).

These bicyclic skeletons bearing a quaternary stereogenic centre along with an exocyclic vinyl chain, represented good precursors for the synthesis of some biologically active compounds such as Eptazocine or Aphanorphine. Some limitations of this reaction were related with the six-membered ring system (seven-membered-ring resulted in a huge erosion of the ee), and the substituent in its 4 position (O instead of CH_2 or S atom resulted in a loss of enantio- and regioselectivity).



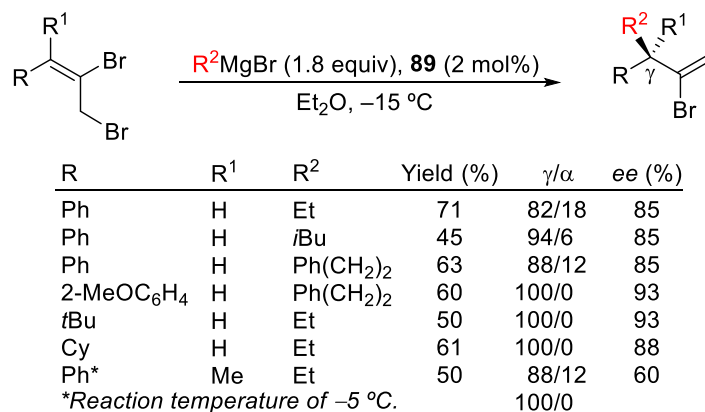
Scheme 120. Scope of substituted allylbromides with different Grignard reagents.

From γ -fluoroalkyl substituted vinylbromide derivatives, products bearing a quaternary stereogenic centre with C_nF_{3-n} substituent ($n = 0, 1$ or 2) can be prepared by the same transition-metal free AAA approach.^[178] NHC-ligand **89** with a phenyl moiety in the *para*-position of the hydroxyl group and a dissymmetric blocking part in the right arm, provided the best results in terms of yield, regio- and enantioselectivity. Perfect levels of regioselectivity ($\gamma/\alpha = 100/0$) and good levels of enantioselectivity (84-95% ee) were observed regardless of the Grignard reagent with cinnamyl bromide derivatives and vinyl bromides with a hindered alkyl substituent in the γ -position. By contrast, a poor ee of 18% was achieved when the vinyl bromide bears a non-bulky alkyl substituent in the γ -position (**Scheme 121**).



Scheme 121. Copper-free NHC-catalyzed AAA for the construction of CFH₂, CF₂H and CF₃ quaternary centres.

With NHC-ligand **89** and primary Grignard reagents, (*E*)-β-bromo cinnamyl derivatives were shown to be unreactive under copper-free conditions (< 8% conversion), while (*Z*)-analogues provided the corresponding products in moderate yields (up to 71%) and excellent regio- and enantioselectivity (up to γ/α 100/0 and 93% ee respectively).^[179] The same reaction can also be applied to the formation of quaternary centres with a considerable erosion on the enantioselectivity.

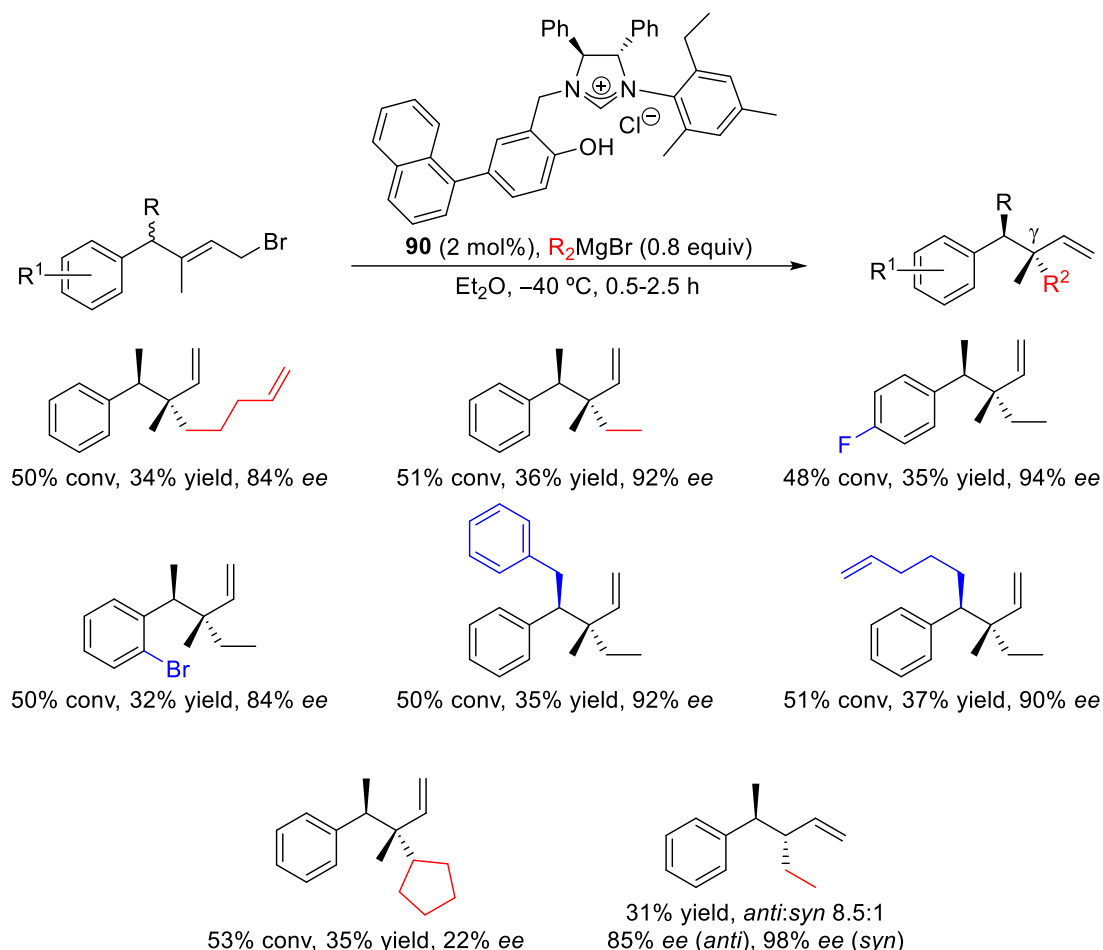


Scheme 122. AAA of (*Z*)-vinyl bromides with Grignard reagents.

It is worthy to mention that the above reactions reported with NHC-ligand **89** do not work in a conventional transition-metal-catalyzed AAA, proving that the transition-metal free AAA can be a complementary alternative to the traditional Cu-catalyzed method.

Finally, to demonstrate the wide applicability of this new synthesis approach, olefines with two contiguous stereogenic centres were synthesized in a diastereo- and enantioselective manner.^[180] This congested stereochemical structures were prepared from racemic allylic bromides bearing a tertiary centre in the α-position of the attacked carbon through a kinetic

resolution process. The resolution proceeds through AAA at low catalyst loadings (2 mol% of **90**) to furnish the corresponding γ -products exclusively with good to excellent levels of enantioselectivity ($\geq 84\%$ ee), except when secondary bulky Grignards reagent (22% ee, **Scheme 123**). Nevertheless, the formation of contiguous tertiary/tertiary stereocentres resulted in mixture of *anti:syn* diastereoisomers (8.5:1) indicating solely a partial ligand control of **90** in the reaction.



Scheme 123. Scope of vinyl-substituted quaternary and tertiary stereogenic centres.

After reviewing the described copper-free AAS literature, it can be observed that all the methods have been focused and tested to access carbonated molecules except for a very few specific examples, such as the two tertiary α -alkyl- α -dimethylphenyl-allylsilanes synthesized by Hoveyda. In this regard, as there is still a lot of room for improvement, we foresee that the development of a method based on this copper-free AAS strategy to easily access not only allylsilanes bearing silyl-substituted tertiary stereogenic centres, but also quaternary ones, would be of particular interest.

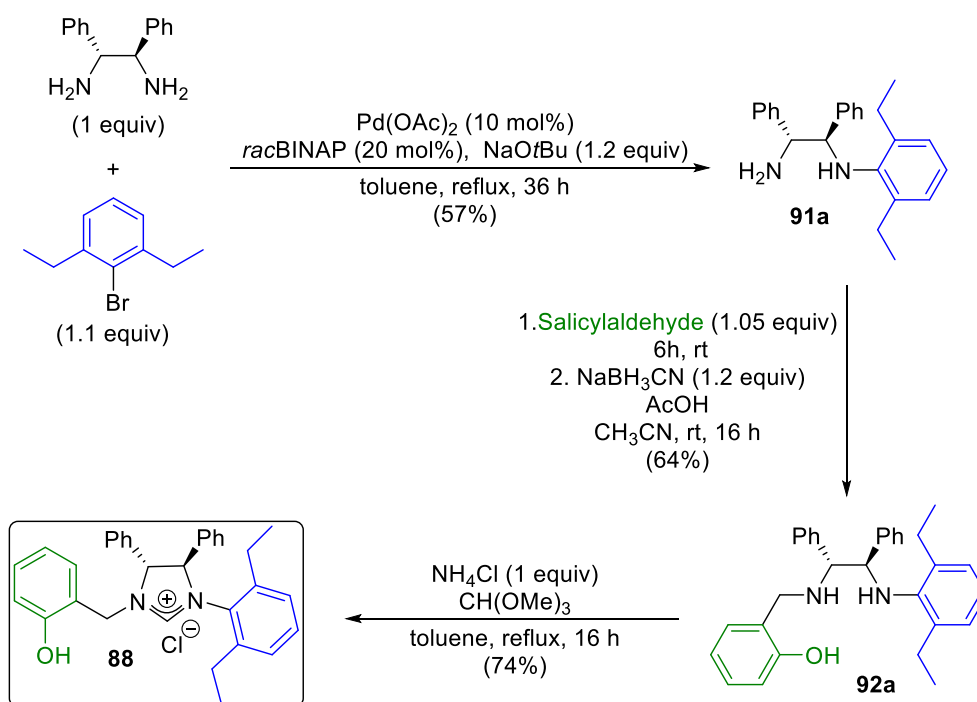
2.3 Allylsilanes bearing tertiary silyl-substituted stereogenic centres

As previously discussed, we want to propose a novel synthetic route to access enantioenriched allylsilanes through an asymmetric allylic substitution. In order to reach this objective, silyl-substituted allylic electrophiles were chosen as starting materials, Grignard reagents as nucleophiles and NHC-ligands as chiral inductors. Firstly, we will study the behavior of our model reaction in the presence and absence of copper for the preparation of allylsilanes bearing tertiary silyl-substituted stereogenic centre. Then the optimization of several parameters (such as leaving group, ligand, temperature or catalyst loading) will be investigated, to finally assess the compatibility of our method with different silicon moieties and the introduction of different alkyl and aryl substituents. Lastly, the protocol would be implemented for the preparation of the more complex allylsilanes bearing quaternary stereogenic centres. It should be noted that only a few examples of those molecules have been described in literature, revealing the great arduousness to access them.

2.3.1 Copper-free reaction evaluation

Based on previous studies developed by Alexakis and co-workers,^[175,176] we firstly evaluated our model reaction using NHC-ligand **88** as catalyst and dimethylphenylsilyl allylic bromide as electrophile.

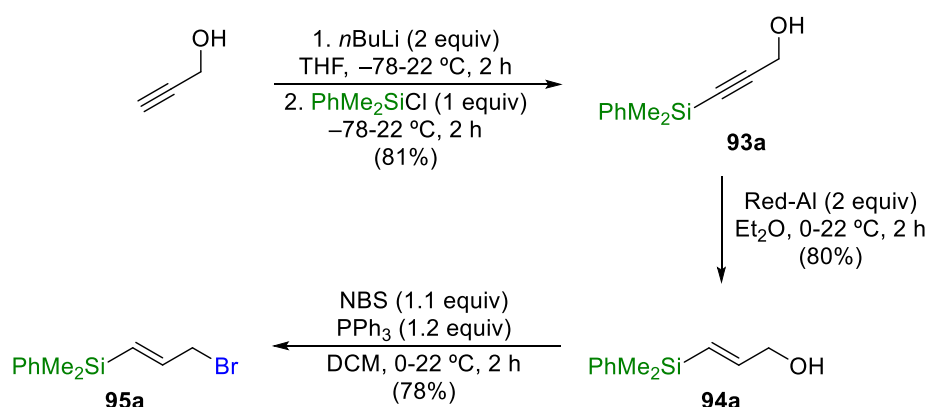
The asymmetric imidazolium salt precursor **88** was accessed through a synthesis strategy reported in the literature starting from (*R,R*)-Corey diamine. The three-step procedure begins with the introduction of the 2,6-diethylphenyl substituent under Buchwald amination conditions by utilizing Pd(OAc)₂ (10 mol%), *rac*BINAP (20 mol%) and NaOtBu (1.2 equiv). Subsequently, the coupling product **91a** reacts with salicylaldehyde (0.7 equiv) in acetonitrile under classical reductive amination conditions to form the diamine **92a** that finally cyclized into the desired imidazolium salt **88** in the presence of ammonium chloride and trimethyl orthoformate (**Scheme 124**). A recrystallization step in cold ether is necessary to precipitate the corresponding chiral-carbene as a yellow powder in 27% overall yield.



Scheme 124. Preparation of asymmetric imidazolium salt **88**.

As most of the methodologies described in the literature use PhMe_2Si - group as the silicon moiety, we decided to evaluate the effect of copper and to look for the optimized conditions using PhMe_2Si -substituted allylic electrophiles.

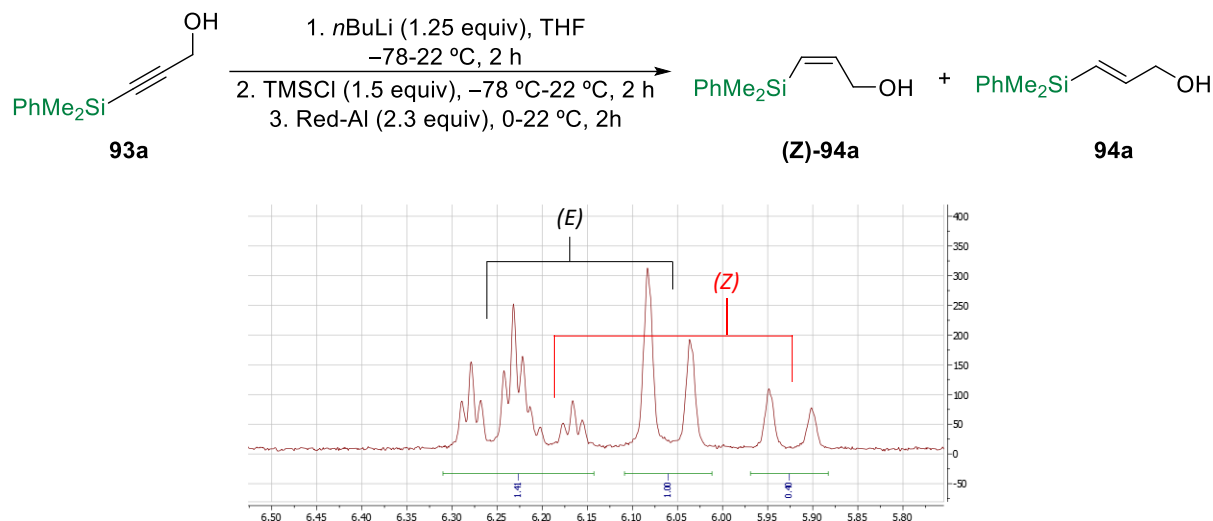
In this regard, (*E*)-allylbromide **95a** was directly prepared from alcohol **94a**, that was itself synthesized in good yield (64%) through a two-step procedure involving the silylation of propargylic alcohol with PhMe_2SiCl , followed by the stereoselective reduction of the carbon-carbon triple bond with Red-Al (**Scheme 125**). Finally, the alcohol **94a** was transformed in the presence of triphenylphosphine and NBS to obtain **95a** in 78%.



Scheme 125. Synthesis of vinyl silane **95a**.

We also wanted to evaluate the influence of the starting material double bond geometry on the reaction outcome. For that, (**Z**)-**94a** that will subsequently allow us to access the corresponding (*Z*)-allylbromide, it was envisioned to be prepared by regioselective reduction

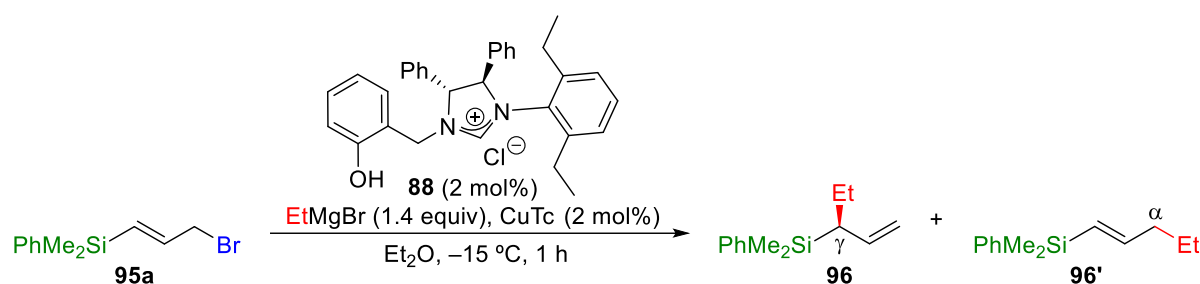
of **93a**. Nevertheless, O-protection of **93a** with TMSCl (to prevent coordination of the aluminium centre by the oxygen atom) followed by reduction of the triple bond with Red-Al led to an inseparable mixture of (*E*)- and (*Z*)-alcohols (**94a** and (**Z**)-**94a**) with Z/E ratio of 28:72 (**Scheme 126**).



Scheme 126. Synthesis attempt of (**Z**)-**94a** and ^1H NMR spectroscopy of the isolated mixture (**Z**)-**94a** and **94a**.

Other strategies such as performing the Red-Al reduction directly on the silicon-substituted 3-bromo-1-(dimethylphenylsilyl)-1-propyne resulted unsuccessful since no trace of the desired vinylsilane was observed.

Then the feasibility of our protocol in the absence of copper was assessed (**Table 1**) using the optimized conditions reported in literature.^[175] Initial tests were performed where EtMgBr (1.4 equiv) and allylbromide **95a** (1 equiv) reacted in the presence of variable loads of NHC-ligand **88** and CuTc (0 to 2 mol%) for 1 h in Et₂O at -15 °C.



Entry	Ligand (mol%)	CuTc (mol%)	Conversion (%) ^a	γ/α^a	er ^b
1	2	2	100	83/17	88:12
2	2	0	100	86/14	90:10
3	0	2	100	31/69	50:50
4	0	0	50	1/99	n.d

^aDetermined by ^1H NMR spectroscopy

^bDetermined by GC (Cyclosil-B)

Table 1. Initial tests.

Gratifyingly, the ligand **88**-CuTc complex was shown quite effective catalyzing the AAS reaction as full conversion was achieved along with good levels of γ -regio- and

enantioselectivity (**Table 1**, entry 1). Interestingly, the system gave slightly better results in the absence of copper (**Table 1**, entry 2), demonstrating the great effectiveness of the NHC ligand. On the other hand, in the exclusive presence of CuTc that theoretically favours the γ -regioselectivity (**Table 1**, entry 3), the racemic product was obtained with a γ/α ratio of 31/69, much lower than the one obtained with NHC-ligand-**88**, demonstrating its great effectiveness to promote the S_N2' reaction. When neither CuTc nor NHC-ligand **88** were employed (**Table 4**, entry 4), only 50% of conversion was achieved within 1 h giving exclusively the undesired α -regioisomer.

The absolute (S)-configuration of 3-(dimethylphenylsilyl)-1-penten-3-ol (**96**) was determined from its $[\alpha]_D^{20}$ which was earlier reported in literature.^[162] This implies the nucleophilic attack of the ethyl group on the *Si*-face of the allylic electrophile (**Figure 7**), result that was consistent with previously reported studies.

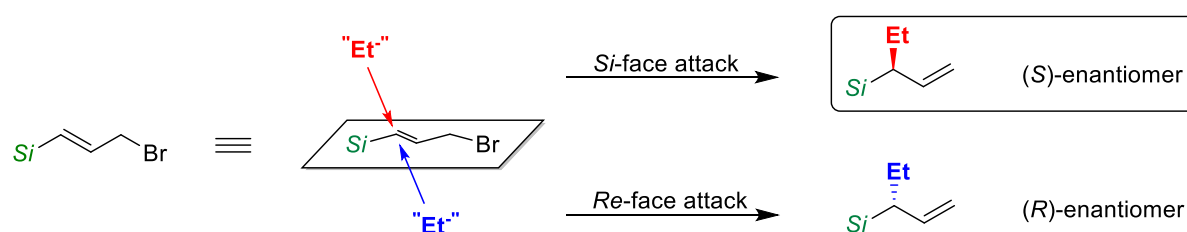


Figure 7. Attack face of Grignard reagent.

Having proved the effectiveness of our catalytic system in the absence of copper, optimization of the reaction conditions was undertaken.

2.3.2 Optimization studies

2.3.2.1 Preparation and screening of Alexakis type NHC-ligands

Even though different types of imidazolium salt precursors have been utilized for the promotion of copper-free AAS (precursors **78-90**), we decided to focus on the ones developed by Alexakis and co-workers. Since the effectiveness of these bifunctional catalysts depends on the substrate and alkylating reagent, a proper combination of both is crucial for the successful stereoselective development of the reaction. In this regard, previous studies from Alexakis *et al.* revealed a strong compatibility of their carbenes to develop copper-free asymmetric allylic alkylation of cinnamyl bromide derivatives with Grignard reagents. Therefore, we envisioned the possibility of using these ligands as chiral inductors in our silicon model, reason why **88** was present since the beginning in our experiments.

In these Alexakis family imidazolium salts, various parts can be differentiated (**Figure 8**):

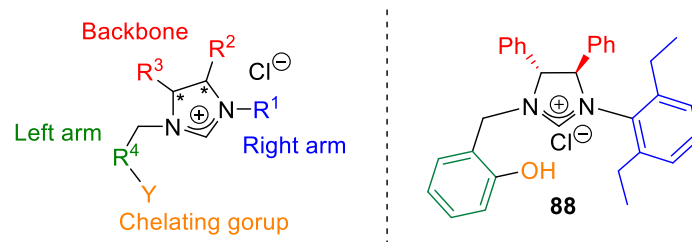


Figure 8. Structure of Alexakis carbene ligands and comparison with NHC-**88**.

- Backbone: part of the molecule which endows the ligand with chirality.
- Left arm: plays a key role bearing the chelating group.
- Chelating group: it is assumed to coordinate to the magnesium centre of the Grignard reagent enhancing its reactivity and disposing it in a specific conformation.
- Right arm: is considered the blocking part of the molecule, usually bears an aryl-substituent that have a strong influence on the reaction regio- and stereoselectivity.

Previous investigations reported in literature proved that, in order for those ligands to exhibit efficient catalytic activity, some intrinsic properties have to be present.^[176] Among them, a chelating group is required in the left arm of the imidazolium salt (hydroxyl group was demonstrated to be widely more effective than other groups such as sulfonamide-derivatives). The presence of a phenylethane diamine backbone is also required (for instance cyclohexyl backbone proved ineffective) along with a three-carbon spacer on the left arm between the carbene core and the chelating hydroxyl group. Those features are essential for the NHC ligand to play its role in an efficient and effective way.

These compulsory characteristics of the imidazolium salt, along with some synthetic limitations, did not let much room for the imagination and improvement, letting the right blocking arm as the only part that could be tuneable in order to examine its impact on the reaction.

Taking everything into consideration, three different chiral imidazolium salts were prepared (including NHC-ligand-**88**) following the same three-step procedure described before (**Scheme 124**) but exclusively changing the aryl bromide introduced in the Buchwald amination reaction (**Figure 9**).

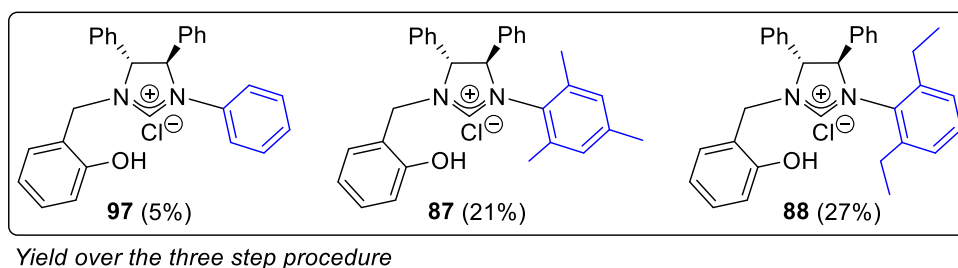
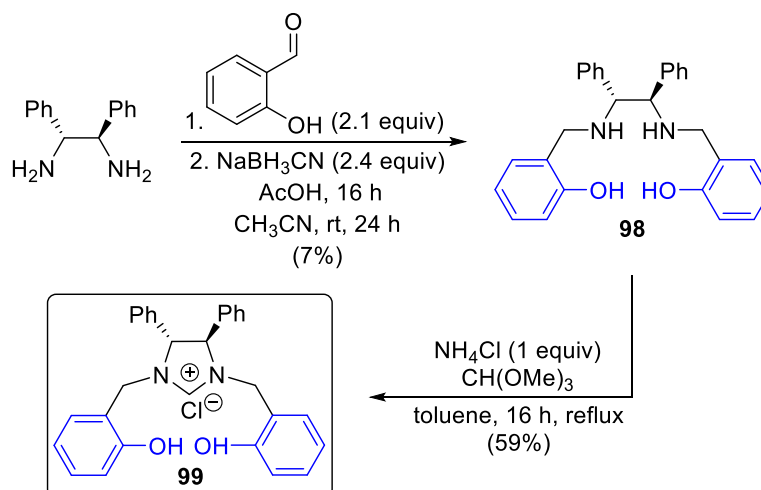


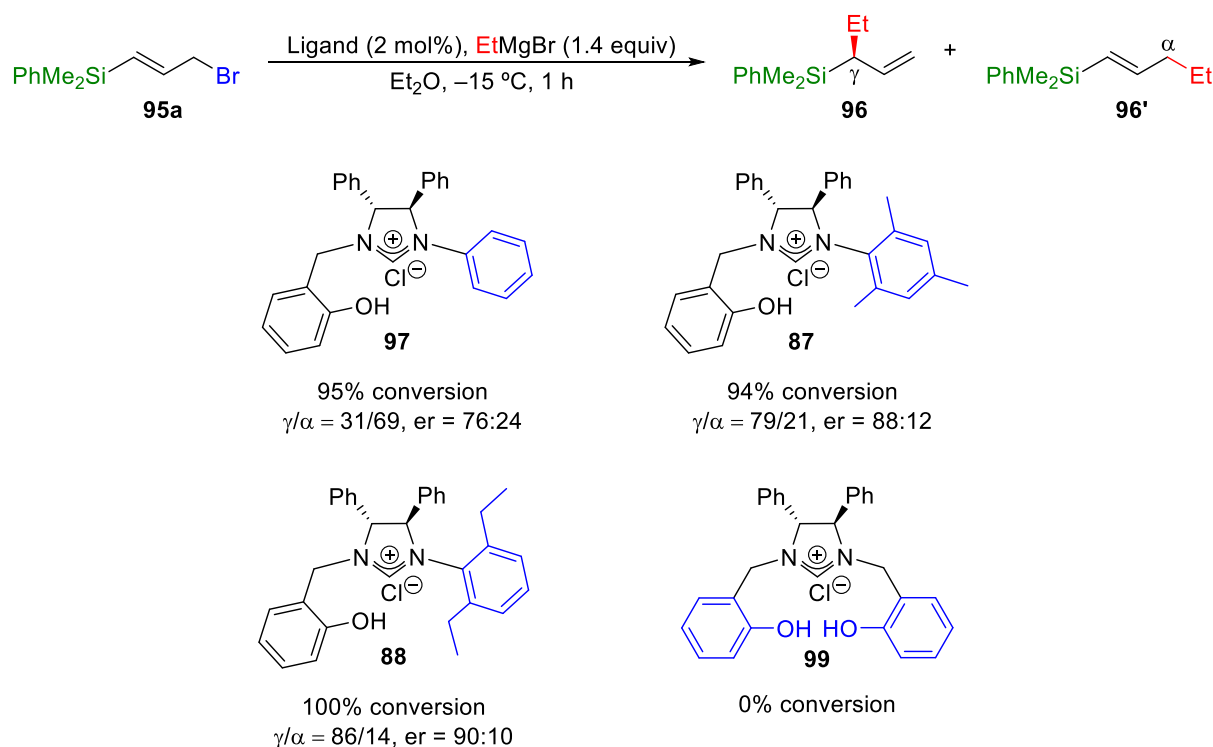
Figure 9. Preparation of asymmetric NHC chiral imidazolium salts.

As the presence of an hydroxyl group was mandatory for the effective performance of the ligand, we wondered about the impact of a C₂-symmetric double chelating imidazolium salt such as **99** in our reaction. For its preparation, alternative double simultaneous aminoreduction between (*R,R*)-Corey diamine and salicylaldehyde was performed to obtain diamine **98** that was subsequently subjected to similar cyclization conditions, i.e. NH₄Cl (1 equiv) and CH(OMe)₃ in toluene at reflux overnight (**Scheme 127**).



Scheme 127. Synthesis of bi-chelating chiral carbene ligand **99**.

With all the NHC-ligands in hand, we tested their performance on the AAS of allylbromide **95a** under the optimized conditions of our model reaction (**Scheme 128**).



Scheme 128. Screening of different bidentate and tridentate chiral carbene ligands.

A reaction time of 1 h at $-15\text{ }^{\circ}\text{C}$ was enough to achieve almost full conversion with ligands **97** and **87** (95% and 94%, respectively). As it could be observed, the nature of the ligand blocking part plays a crucial role regarding the stereoselective outcome of the reaction. In the case of **97**, reverse regioselectivity (compared to the one obtained with **87** and **88**) favourable to the α -product was observed ($\gamma/\alpha = 31/69$), along with a modest $er = 76:24$. Increasing the steric bulk in the blocking part of the ligand replacing the phenyl ring by a mesityl group, led to a huge increase in both the regio- and enantioselectivity (from $\gamma/\alpha = 79/21$ and $er = 88:12$). This different regio- and enantioselectivity observed for the NHC-**97**, **87** and **88** can be rationalize on the base of the distinct spatial geometry of the reaction site where the AAS take place (**Figure 10**). In the case of **101**, the steric hindrance in the surroundings of the Mg atom is increased (when compared with **100**) so the reaction must take place with a specific 3D disposition in order to minimize the steric constraints that can arise from the interaction between the substrate, the nucleophile and the ligand. This leads to higher levels of regio- and enantioselectivity than those promoted by complex **100**. Same reasoning could be applied to explain the increased stereospecificity observed for NHC-ligand-**88** when compared with NHC-ligand-**87**. Although in complex **102**, the *para*-substituent of the phenyl ring is suppressed (it hardly exerts any influence on the reaction site of the complex), the bulkier *ortho*-ethyl substituents create a more effective chiral environment surrounding the Mg (bulkier groups are close to the reaction site), exacerbating the steric repulsions when the reaction substrate approach in the less favourable way that leads to the α -regioisomer or the (*R*)-enantiomer.

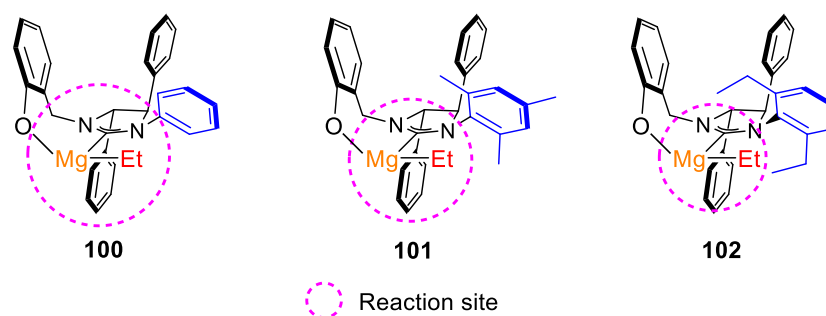
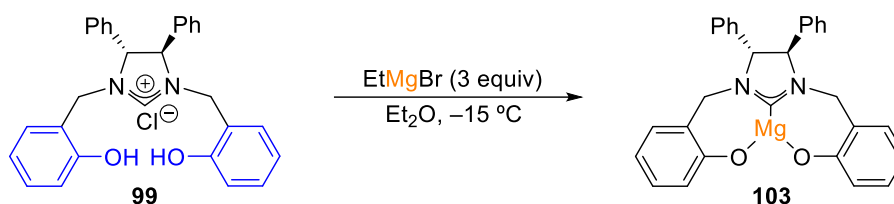


Figure 10. Comparison of the different reaction sites created by the distinct ligands.

By contrast, chiral dihydroxy ligand **99** was found ineffective (no product was observed by ^1H NMR) and the starting material could be recovered. The triple deprotonation of **99** by the Grignard reagent gives the magnesium carbene **103**, wherein the magnesium centre is coordinated by the two oxygen atoms and the carbene moiety of the ligand, precluding the transmetalation by another Grignard reagent (**Scheme 129**).



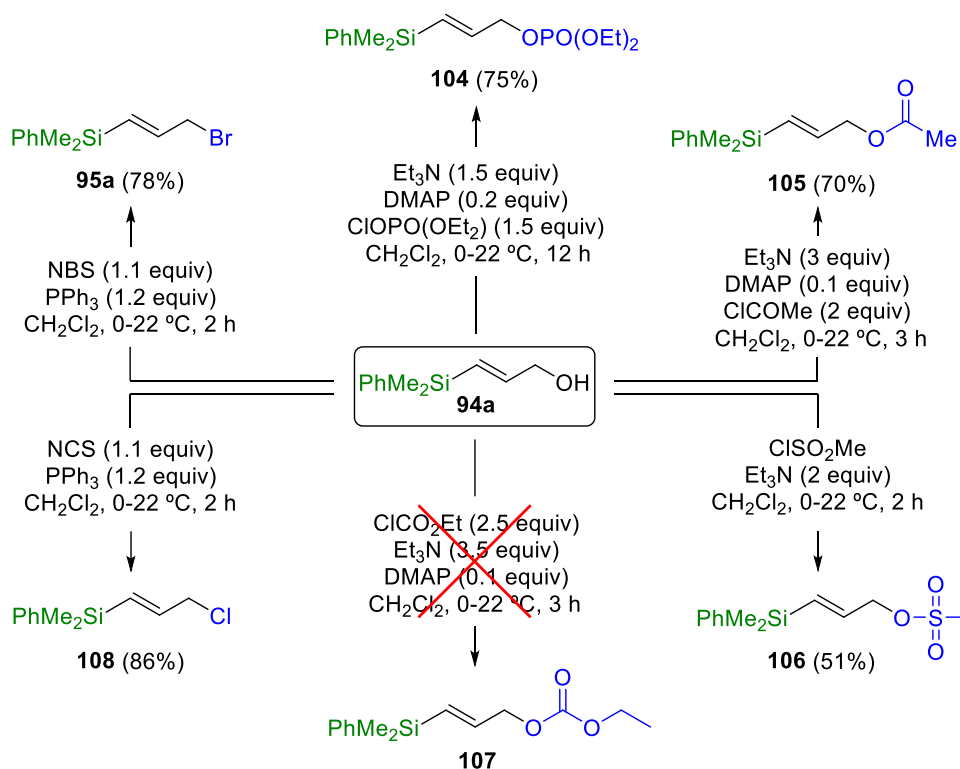
Scheme 129. Triple deprotonation of **99** and formation of magnesium-carbene **103**.

It is also worthy to mention that since the nature of the counterion employed has a negligible effect, as it was proved by previous studies, we decided to keep chloride as the anion for all the different imidazolium salts.

2.3.2.2 Preparation and screening of silyl-substituted allylic electrophiles

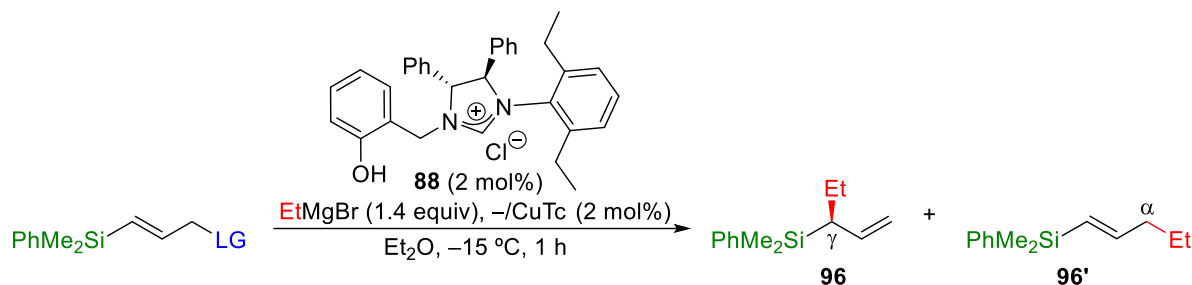
As it was discussed before, the related AAS reactions based on hard nucleophiles strongly depends on the nature of the leaving group that plays a key role in the reaction outcome. Therefore, various PhMe_2Si -vinylsilanes bearing different leaving groups such as halogen, phosphate, acetate or mesylate were prepared.

To access these vinylsilanes, the derivatization of the hydroxyl function of alcohol **94a** was undertaken (**Scheme 130**). Under classical conditions, allylic phosphate **104**, acetate **105**, mesylate **106** and chloride **108** were prepared in moderate to good yields (51-86%), whereas the ethyl carbonate analogue **107** could not be isolated (**Scheme 130**).



Scheme 130. Synthesis of silicon-substituted allylic electrophiles.

With all the substrates in hand, their impact on the reaction outcome in the presence and absence of copper was tested (**Table 2**). Preliminary investigations were performed with EtMgBr (1.4 equiv) as nucleophile and in the presence of 2 mol% of NHC-ligand **88**, inspired by conditions reported in literature.^[175]



Entry	Leaving group	Electrophile	CuTc (mol%)	Conversion (%) ^a	γ/α ^a	er ^b
1	OPO(OEt) ₂	104	2	> 98	74/26	53:47
2	Acetate	105	2	> 98	82/18 ^c	56:44
3	Mesylate	106	2	100	55/45	71:29
4	Br	95a	2	100	83/17	88:12
5	Cl	108	2	> 98	98/2	90:10
6	OPO(OEt) ₂	104	-	67	93/7	70:30
7	Acetate	105	-	82	28/72 ^d	52:48
8	Mesylate	106	-	100	60/40	92:8
9	Br	95a	-	100	86/14	90:10
10	Cl	108	-	0	-	-

^aDetermined by ¹H NMR spectroscopy

^bDetermined by GC (Cyclosil-B)

^c17% of the allylic electrophile was converted into alcohol

^d55% of the allylic electrophile was converted into alcohol

Table 2. NHC-Cu(II) catalyzed and copper-free AAS of different allylic electrophiles.

In the presence of 2 mol% of CuTc, full conversion was achieved in all cases whatever the leaving group (**Table 2**, entries 1-5). Good to high levels of γ -selectivity (γ/α ration ranging from 72/26 to 93/7) were observed for phosphate, acetate and bromide (**Table 2**, entries 1, 2 and 4). By contrast, mesylate led to almost no regioselectivity (**Table 2**, entry 3) and moderate enantioselectivity (er = 71:29). Moreover, careful analysis by ¹H NMR of the crude reaction mixture revealed that 17% of the starting material was converted into the corresponding alcohol **94a** (**Table 2**, entry 2). Particularly encouraging were the results obtained with the allylic chloride and bromide (**Table 2**, entries 4 and 5), as not only good γ -regioselectivity was observed, but also good levels of enantioselectivity (er ranging from 80:12 to 90:10), unlike with allylic phosphate where stereochemical information was hardly introduced (**Table 2**, entry 1).

Continuously, the same electrophiles were tested in the absence of copper (**Table 2**). On one hand, vinyl phosphate, contrary to some described literature and although 1 h-reaction did not allow a complete consumption of the starting material (only 67% conversion), the copper-free AAS reaction worked giving the desired allylsilane in excellent γ -selectivity (γ/α = 93/7) but with a modest er = 70:30 (**Table 2**, entry 6). The use of acetate led to a

preferred α -selectivity ($\gamma/\alpha = 28/72$) and an increased amount of side product (from 17% to 55%) when comparing with the Cu-method results. On the other hand, incredible better results were obtained from the mesylate electrophile in terms of enantioselectivity (from $er = 71:29$ to $er = 92:8$), although a poor ratio 60:40 was observed in favour of the γ -product (**Table 2**, entry 8). Very good results were obtained from the allylic bromide regarding both regio- and enantioselectivity ($\gamma/\alpha = 84/16$ and $er = 90:10$). The results obtained in the absence of copper with allylbromide **95a** were encouraging (**Table 2**, entry 9). Bromide as leaving groups was indeed the best compromise between regio- and enantioselectivities since disappointing results were obtained for the promising chloride analogue.

2.3.2.3 Influence of temperature and catalyst loading.

Typically, temperatures below 0 °C and catalyst loadings between 2 and 5 mol% are often required to achieve highly stereoselective copper-free AAS reactions. The results previously obtained lead us to focus on NHC-**88** as the catalyst. In our reaction model, using allylbromide **95a** and EtMgBr in standard reaction conditions of –15 °C in Et₂O under the presence of 2 mol% of the above-mentioned ligand, the influence of temperature and imidazolium salt loading was investigated (**Table 3**).

Entry	Ligand (mol%)	Temperature	Conversion (%) ^a	γ/α ^a	er ^b
1	2	–15 °C	100	86/14	90:10
2	1	–15 °C	100	92/8	89:11
3	1	–78 °C	0	-	-
4	1	–40 °C	37	87/13	88:12
5	1	25 °C	100	91/9	88:12
6	1	45 °C	100	82/18	88:12

^aDetermined by ¹H NMR spectroscopy
^bDetermined by GC (Cyclosil-B)

Table 3. Temperature and catalyst loading investigations.

Reducing the amount of catalyst to 1 mol% (the lowest load of catalyst reported in copper-free AAS) while keeping the temperature at –15 °C (**Table 3**, entry 2) lead to a slight increase in the regioselectivity ($\gamma/\alpha = 92/8$) along with almost no decrease in the enantioselectivity level. Decreasing the temperature to –40 °C resulted in a poor conversion of 37% along with a slight drop in the regioselectivity ($\gamma/\alpha = 87/13$) while at –78 °C no reaction occurred (**Table 3**, entries 3 and 4). On the other hand, carrying out the reaction at 25 °C did not influence neither the γ/α ratio nor the enantioselectivity, while full conversion was observed (**Table 3**, entry 5). Finally, increasing the temperature to 45 °C led to a significantly lower amount of γ -product ($\gamma/\alpha = 82/18$) although the same level of enantioselectivity was obtained

(Table 3, entry 6). Thus, although slightly better results were observed when performing the reaction at $-15\text{ }^{\circ}\text{C}$, $25\text{ }^{\circ}\text{C}$ seemed to be the optimal temperature to performing this transformation using silyl-substituted allylic bromides (Table 3, entry 5).

These results are in contrast with those previously reported by Alexakis *et al.*,^[175] that showed an erosion of the regio- and enantioselectivity levels by simply raising the temperature from $-15\text{ }^{\circ}\text{C}$ to $0\text{ }^{\circ}\text{C}$.

With the temperature optimized, we thus focused on the influence of the catalytic loading (Table 4).

Entry	Ligand (mol%)	Temperature	Conversion (%) ^a	γ/α ^a	er ^b
1	2	$-15\text{ }^{\circ}\text{C}$	100	86/14	90:10
2	1	$25\text{ }^{\circ}\text{C}$	100	91/9	88:12
3	0.5	$25\text{ }^{\circ}\text{C}$	100	91/9	90:10
4	0.25	$25\text{ }^{\circ}\text{C}$	94	83/17	84:16

^aDetermined by ^1H NMR spectroscopy
^bDetermined by GC (Cyclosil-B)

Table 4. NHC-catalyzed catalyst loading investigation.

Gratifyingly, reducing the ligand **88** loading from 1 mol% to 0.5 mol% resulted in a full conversion with no impact on the γ -selectivity and a slight improvement of the enantioselectivity (er = 90:10, Table 4, entry 3). Ruefully, with only 0.25 mol% of catalyst loading, although almost full conversion was achieved (94%), a decrease in both regio- and enantioselectivity levels (γ/α = 83/17 and er = 84:16) were observed (Table 4, entry 4), leaving the 0.5 mol% loading as the optimal condition.

2.3.2.4 Solvent dependence and Grignard addition rate

Several solvents were then tested, using optimized conditions of 1.4 equiv of EtMgBr with allyl bromide **95a** (1 equiv) and NHC-ligand **88** (0.5 mol%) at $25\text{ }^{\circ}\text{C}$ (Table 5).

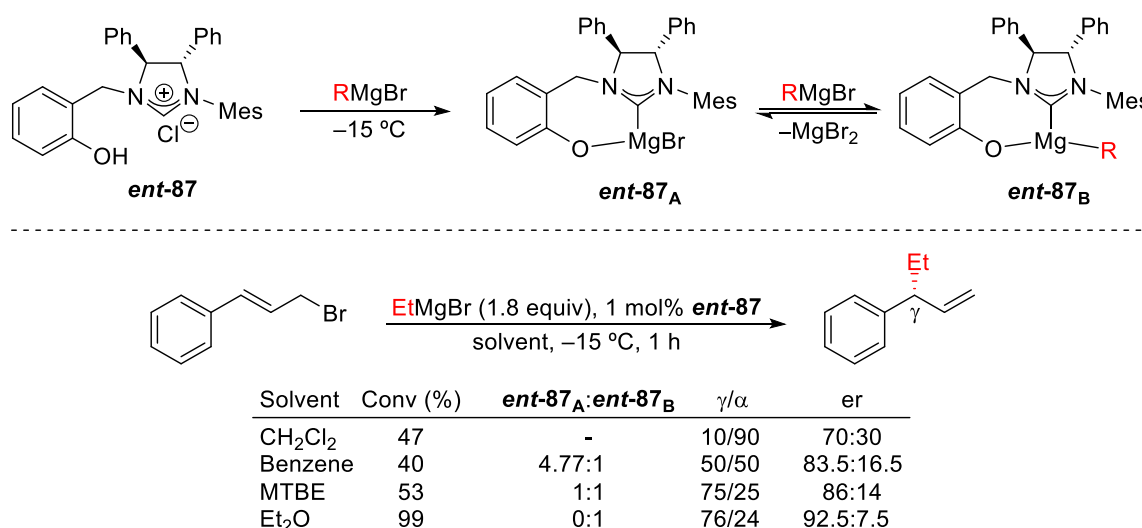
Entry	Solvent	Conversion (%) ^a	γ/α ^a	er ^b
1	Et_2O	100	91/9	90:10
2	MTBE	93	80/20	89:11
3	THF	84	43/57	66:34
4	Dioxane	78	42/58	66:34
5	CH_2Cl_2	100	32/68	53:47
6	Pentane	90	33/67	76:24

^aDetermined by ^1H NMR spectroscopy
^bDetermined by GC (Cyclosil-B)

Table 5. Solvent investigation on the NHC-**88** catalyzed AAS of allylbromide **95a**.

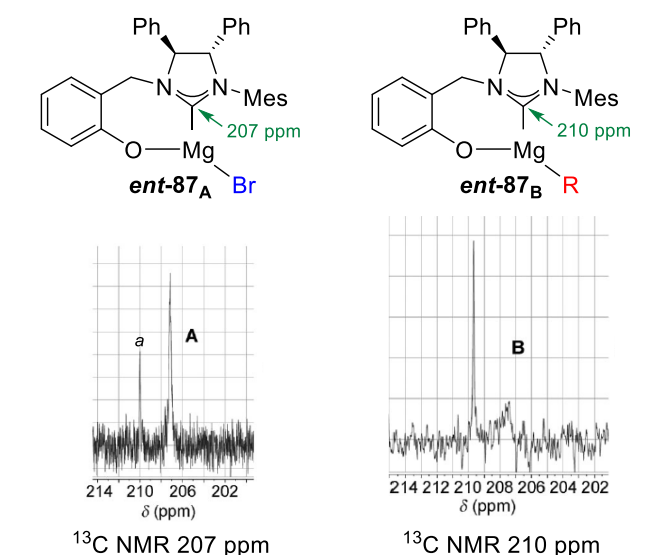
Initial attempts indicated that moderately coordinating solvents (**Table 5**, entry 1 and 2) were necessary to afford good regio- and enantioselectivities. Et₂O gave better results than MTBE, both in terms of γ -selectivity (91/9 vs. 80/20 for the γ/α ratio) and enantioselectivity (er = 90:10 vs. 89:11). More coordinating solvents, as THF and dioxane (**Table 5**, entries 3 and 4), and non-coordinating ones, such as CH₂Cl₂ and pentane (**Table 5**, entries 5 and 6) afforded bad results ($\gamma/\alpha \leq 43/57$ and er $\leq 76/24$) with partial conversion in most cases.

From this investigation, it could be concluded that the solvent plays a key role in the reaction. This was in accordance with the previously reported results when performing copper-free asymmetric allylic alkylation of cynamyl bromide in the presence of NHC-ligand **ent-87**.^[176] NMR spectroscopic experiments, demonstrated that two different magnesium-NHC species **ent-87_A** and **ent-87_B** coexist in equilibrium when mixing **ent-87** with RMgBr. A strong dependence between the number of species **ent-87_B** present in the reaction mixture and the conversion, γ/α ratio and enantiomeric ratio was established (**Scheme 131**). The solvent by displacing the equilibrium towards the catalytic active magnesium-carbene species plays a key role in the reaction.



Scheme 131. Correlation between **87_A**:**87_B** ratio and the AAS of cinnamyl bromide selectivity.

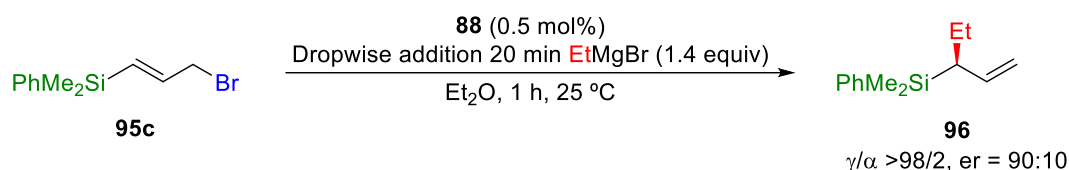
It is worth to mention, that in the same studies, intermediates **ent-87_A** and **ent-87_B** that differ only by one ligand in the coordination sphere of the magnesium (bromide for **ent-87_A** vs. ethyl R group for **ent-87_B**) were identified by ¹³C NMR analysis according to chemical shifts of C_a (207 ppm for the specie **ent-87_A** and 210 for the specie **ent-87_B**, **Figure 11**).



^aThis peak correspond to the Mg-carbene specie **ent-87_B** as **ent-87_A** could not be isolated alone

Figure 11. ¹³C NMR spectra of the intermediates **ent-87_A** and **ent-87_B**.

Finally, as there were still room for the improvement and following some information encountered in literature suggesting that regioselectivity could be influenced by the addition rate of the organometal reagent, we evaluated this parameter. Since α -product was exclusively formed by the direct S_N2 reaction between the organomagnesium reagent and the allylbromide without the influence of the ligand, avoiding the excess of Grignard in the reaction mixture by slowing the addition rate would increase the presence of the active magnesium-carbene species in front of free Grignard reagent in the system, eventually leading to an scenario where the undesired S_N2 reaction can be limited if not eliminated. In this regard, the reaction was performed under the optimized conditions, i.e. NHC-ligand **88** (0.5 mol%), in Et₂O at 25 °C for 1 h, by adding 1.4 equiv of EtMgBr dropwise over a period of 20 min (**Scheme 132**).



Scheme 132. Improvement of regioselectivity by dropwise addition of Grignard reagent for 20 min.

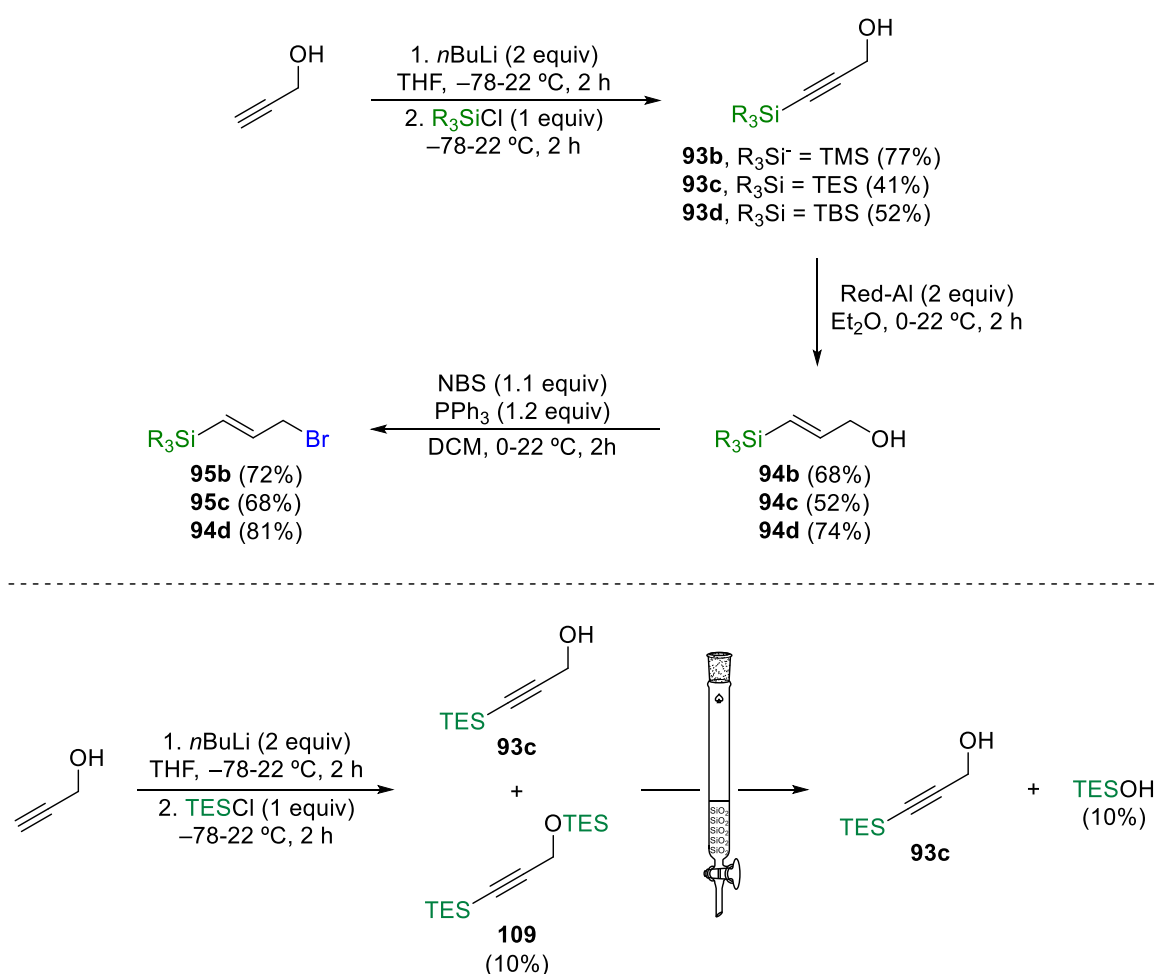
As expected, the slow addition of the Grignard reagent had an impact on the stereoselective outcome as γ -product was formed as the only regioisomer ($\gamma/\alpha > 98/2$ vs. $\gamma/\alpha = 91/9$) without affecting the levels of enantioselectivity (er = 90:10).

It is noteworthy to mention that the amount of organomagnesium equivalents was also investigated. Reducing the number of Grignard reagent until 1.1 equivalent did not have an impact neither the γ/α ratio nor the enantiomeric ratio. Finally, we decided to keep 1.5 equivalents as the standard amount for practical reasons due to the scale level.

2.3.3 Influence of the silyl group

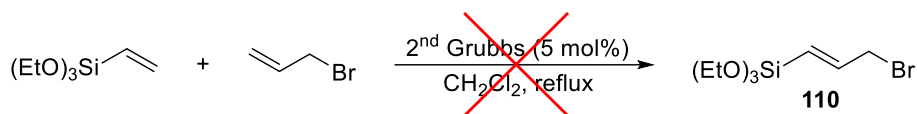
As it has been mentioned in section “Objectives and purpose of the project” (p. 101), one of our main goals consisted in the development of a strategy that allows to easily access allylsilanes bearing different silicon moieties, and not only the dimethylphenylsilyl one. Thus, we next focused our attention on assessing different silyl electrophiles and their influence over the stereoselective outcome of the reaction.

TMS- and *t*BuMe₂Si -analogues of allylbromide **95** (**95b** and **95d**) were prepared following the three-step synthesis strategy described in **Scheme 125**, consisting in the propargyl alcohol acetylenic position silylation followed by the stereoselective reduction of the carbon-carbon triple bond with Red-Al and the final derivatization of the hydroxy group (**Scheme 133**). In the case of the silylation of propargyl alcohol with TESCl, a mixture of the desired product **93c** accompanied by bis-silylated adduct **109** (10%) was obtained. Fortunately, column chromatography promoted the cleavage of the O-Si bond, affording **93c** along with TESOH (10%) that could be subsequently removed by distillation after the regioselective reduction of the triple bond.



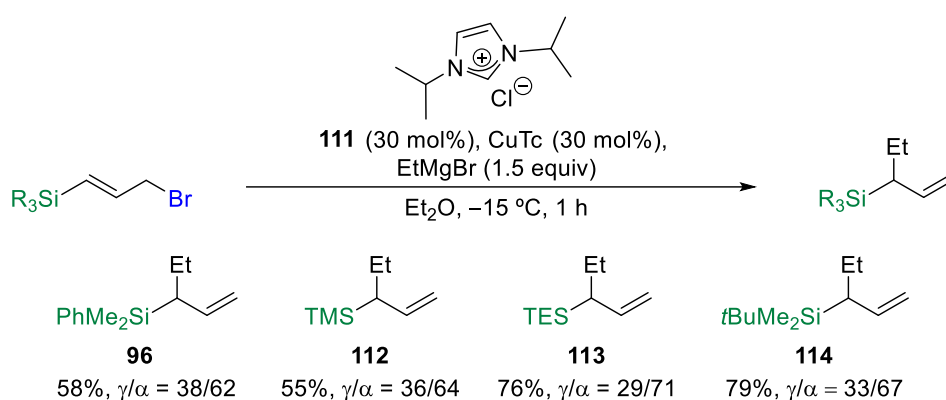
Scheme 133. Synthesis of allylic electrophiles bearing different silicon moieties and TES-substituted propargylic alcohol **93c**.

We also envisioned to introduce trialkoxysilyl moieties. Unfortunately, all our efforts to perform the metathesis between trialkoxyvinylsilane and allyl bromide in the presence of 5 mol% of Grubbs II catalyst to obtain allylbromide **110** were unsuccessful (**Scheme 134**).



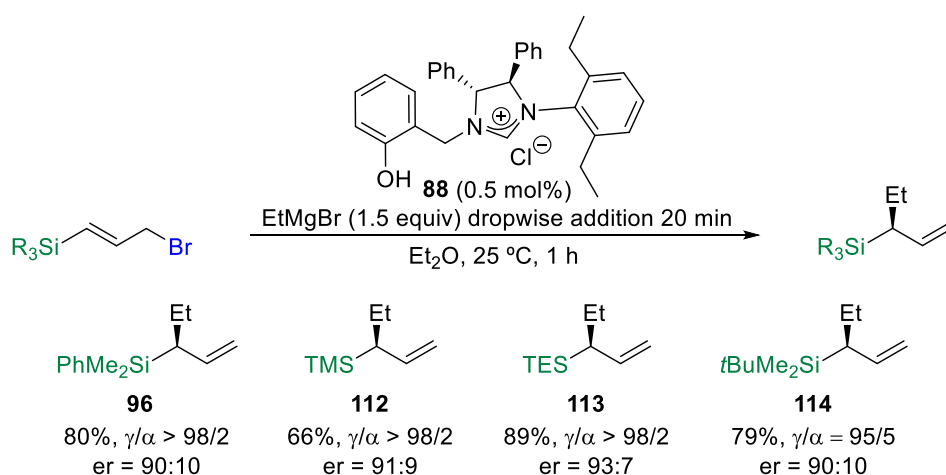
Scheme 134. Failed synthesis of triethoxysilyl-substituted allylic bromide.

In order to evaluate the influence of the different silicon moieties on the reaction enantioselectivity, the corresponding racemates were previously synthesized by performing the AAS reaction in the presence of CuTc (30 mol%) and 1,3-diisopropylimidazolium chloride **111** (30 mol%) in Et₂O at -15 °C (**Scheme 135**)



Scheme 135. Preparation of racemic allylsilanes bearing different silyl moieties.

Subsequently, the same silicon-substituted allylic bromides, were subjected to the copper-free optimized conditions to evaluate their compatibility with our model reaction and the influence they exert on the regio- and enantioselectivity levels (**Scheme 136**).



Scheme 136. Allylsilanes bearing different silyl moieties.

Pleasantly, the reaction turn out to be tolerant to a wide range of silicon groups (**Scheme 136**). In all cases, the reaction was completed within 1 h, proving the high reactivity

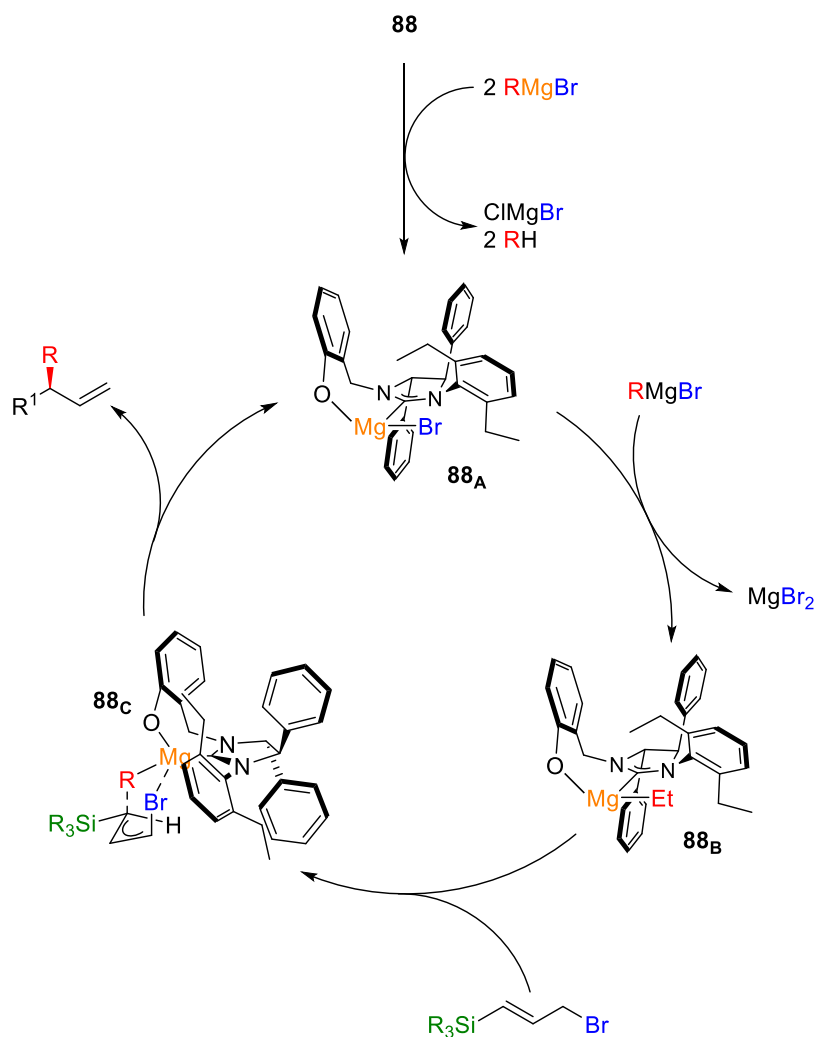
of all electrophiles under our conditions. Allylsilanes **96** and **114** containing dimethylphenylsilyl- and *tert*-butyldimethylsilyl- moieties respectively, are obtained in good isolated yields (80% and 79% respectively). Gratifyingly, for the triethylsilyl- analogue **113**, a substantial higher yield was observed (89%), contrary to the trimethylallylsilane **112** that was isolated in a moderate 66% yield (presumably because its high volatility). The same levels of enantioselectivity, around *er* = 90:10, were also shared by the quartet of allylsilanes, highlighting the remarkable increase to *er* = 93:7 exhibited by allylsilane **113**.

All these results, allow us to conclude that the silyl moiety has a small impact on the reaction stereo-outcome, as various allylsilanes bearing different silyl moieties can be accessed through our copper-free AAS model reaction in good yields, γ/α ratio > 95/5 and noteworthy enantiomeric ratio up to 93:7.

2.3.4 Proposed mechanism and NHC-magnesium models

In the light of our own observations, along with the experimental and computational studies performed by Alexakis *et al.*^[176] and Halbert *et al.*^[190] respectively, for the copper-free allylic alkylation with Grignard reagents in the presence of NHC-ligands, we therefore proposed a mechanism to explain the stereochemical outcome of the reaction.

According to the proposed mechanism in the literature,^[175,176] consistent with the DFT results reported by Albert *et al.*,^[190] a double deprotonation of the starting imidazolium salt by the Grignard reagent takes place to form *in situ* the intermediate **88_A** (mono-insertion into the OH bond was never observed). Subsequently, **88_A** undergoes transmetalation with another equivalent of Grignard affording the intermediate **88_B**, which was assumed to be the catalytic active specie. Finally, the interaction between **88_B** and the allylbromide leads to the formation of a pseudo-chair transition state **88_C**, wherein the alkyl R group bonded to the magnesium centre undergoes a S_N2'-attack, giving the desired γ -allylsilane and regenerating intermediate **88_A** (Scheme 137).



Scheme 137. Proposed mechanism for the copper-free AAS of silyl-substituted allylic bromides.

Recently, computational studies performed by Halbert and Poblador-Bahamonde shed some light into the proposed mechanism (**Scheme 137**) and the effect of Alexakis-NHC ligands in this reaction.^[190]

All these computational studies were done on the basis of previously validated models where the backbone phenyl substituent as well as the aryl-blocking ring and the R group of the Grignard reagent were replaced by methyl groups (**Figure 12**).

NBO analysis carried out for **A_m** and **B_m**, demonstrated the high ionic nature of the bonding around the magnesium centre in these carbene species. In this regard, according to MP2 calculations, donor-acceptor interactions arise between the lone pairs of both, the imidazolium carbon atom and the alcoholate, and the unoccupied orbital of the magnesium centre. Moreover, in **B_m**, a stabilizing contribution of 78.4 kcal/mol can be observed from the transfer of partial electron density from the lone pair of the carbon atom of the methyl substituent to the magnesium centre.

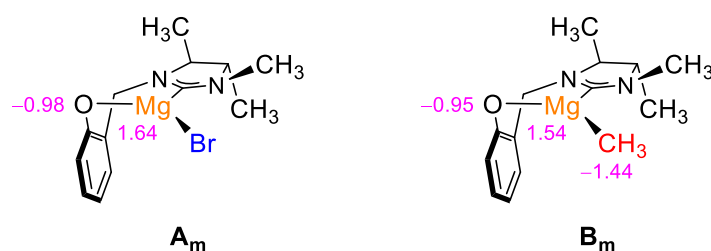
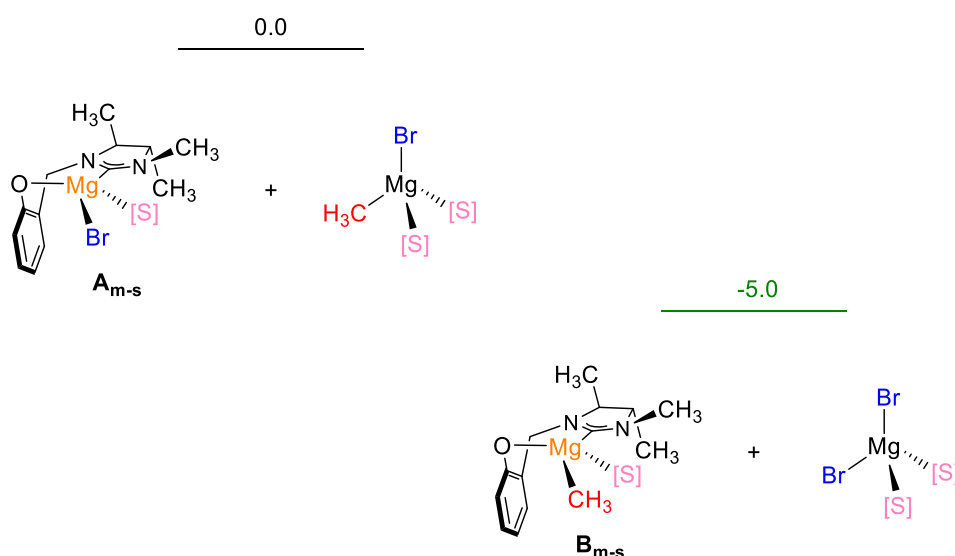


Figure 12. Validated models used for calculations.

The ionic character of Mg-C_{NHC}, Mg-O and Mg-CH₃ bonds were in accordance with the NBO calculated natural atomic charges (**Figure 12**). This analysis revealed a positive charge around 1.6 for the magnesium centre and around -1.0 for the oxygen atom of the alcoholate in **A_m** and **B_m**, along with a negligible charge on the carbon atom of the imidazolium. Finally, on **B_m** species, a charge of -1.44 was calculated for the methyl group contrasting with the -0.96 charge calculated on the free Grignard reagent. From these results, it can be concluded that the nucleophilicity of the Mg-R bond increases in the presence of the Lewis base type ligand, which activates the Lewis acid character of Mg as a result of the electron density transfer from the lone pair of the NHC ligand to the unoccupied orbital of Mg.

This study also explained the favoured transmetalation step between **88_A** and **88_B**, since MP2 and coupled cluster single-point energy calculations in the gas phase confirmed the favourable **B_m** formation by a Gibbs free energy of -5.5 kcal/mol (MP2) and -7.4 kcal/mol (coupled cluster single-point). Particularly interesting are the results provided by DFT calculations that showed the need to include explicit solvent molecules in the first solvation shell (as already observed for organolithium compounds)^[191] due to the important solute-solvent interactions to accurately reproduce the thermodynamics of this reaction (**Scheme 138**).



Scheme 138. Gibbs free energy profiles [kcal/mol] for the transmetalation step from **A_{m-s}** to **B_{m-s}** considering the explicit solvation model ([S] = (CH₃)₂O).

Calculations performed on transition states **TS_α** and **TS_γ** (**Figure 13**) showed a shortening of the Mg-Br bond (0.406 Å for **TS_α** and 0.380 Å for **TS_γ**) and a moderate elongation of the Mg-R (0.097 Å for **TS_α** and 0.090 Å for **TS_γ**) bond, what is in accordance with a nucleofuge activation and the above-mentioned nucleophilic enhancement. These structural features thus confirmed the bifunctional role of magnesium activating both the bromide (leaving group) and the Grignard reagents (nucleophile).

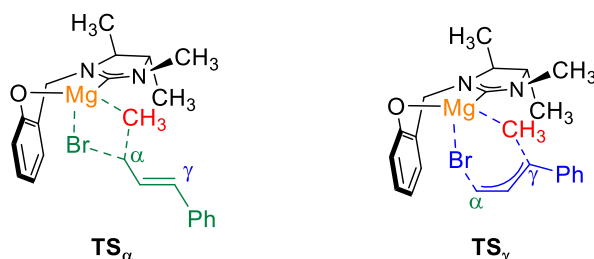


Figure 13. Proposed transition state that would lead to the corresponding α - and γ -products.

The favoured γ -selectivity for the copper-free NHC-catalyzed allylic alkylation can be explained by the energy barriers of **TS_α** and **TS_γ**. **TS_α** which leads to the α -isomer through a four-membered metallacycle has a higher energy barrier than **TS_γ** that leads to the γ -isomer through a much less constrained six-membered metallacycle. This indicates that γ -isomer is the kinetically favoured product.

Although these computational studies explained the preferred γ -selectivity, they did not do any reference regarding the enantioselectivity. We thus proposed some intuitive models based on sterical repulsions between the allylic electrophile and the magnesium-carbene ligand to rationalize the high stereoselective induction observed in our model system. Considering a chair-like transition state and a frontal approach of the allylic electrophile on the magnesium centre, two transition states **TS_{S₈₈}** and **TS_{R₈₈}** can be envisioned (**Figure 14**).

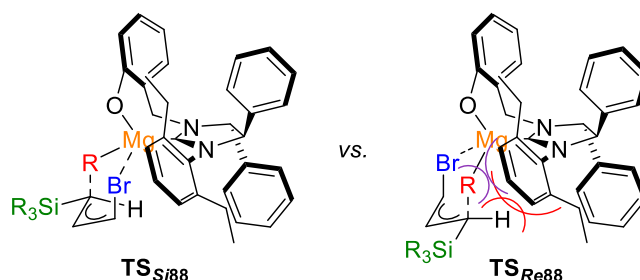
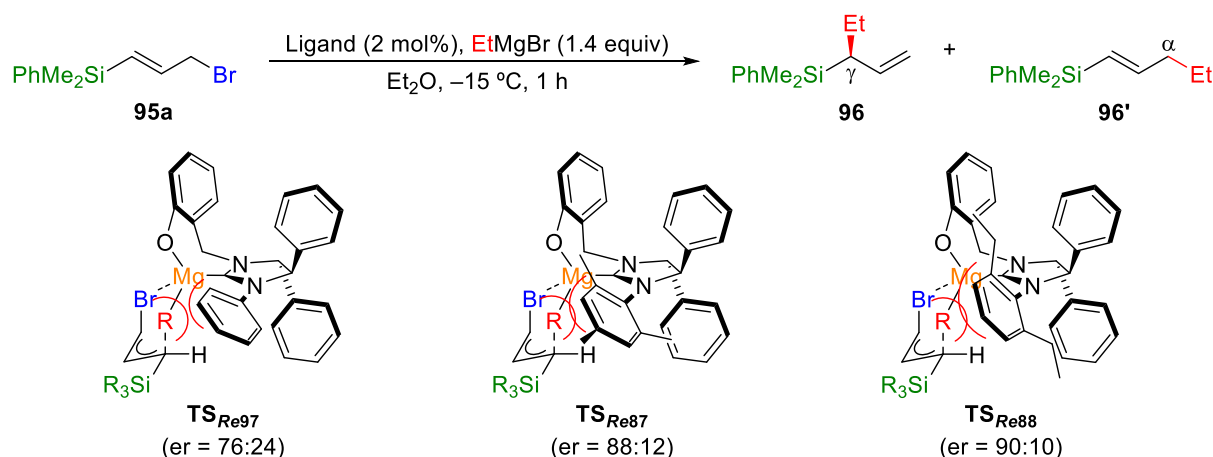


Figure 14. NHC-magnesium-allylbromide models to explain the high enantioselectivity.

In **TS_{S₈₈}**, the bromine atom is coordinated to the magnesium centre from the front-down right part, allowing the magnesium to adopt a favoured distorted tetrahedral configuration that was depicted as its preferred geometry by computational studies. In this approach, the Grignard reagent lies frontally to the magnesium centre and the pseudo-chair is perpendicular to the NHC skeleton plane. The silicon moiety is far from any atom of the imidazolium salt,

what minimizes the sterical interactions between the substrate and the ligand affording the major (*S*)-enantiomer. On the contrary, **TS_{Re88}** that leads to the minor (*R*)-enantiomer, is disfavoured due to the proximity between the Grignard reagent and the blocking aryl part, giving rise to steric repulsions (**Figure 14**).

The variation of the enantioselectivity observed for the different NHC-ligands screened can also be explained by these two transition states. In this regard, the more disfavoured **TS_{Re}** is, the less (*R*)-enantiomer will be observed and higher the enantiomeric excess will be (**Scheme 139**).



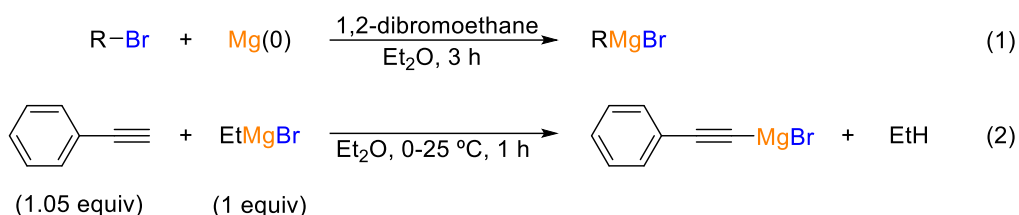
Scheme 139. Different NHC-ligand transition state and the corresponding er observed.

Varying the right arm phenyl ring substituents of the ligand would result in different steric hindrances and interactions impacting the enantioselectivity level. In the case of **TS_{Re97}**, a considerable erosion of the enantioselectivity was observed with respect to **TS_{Re88}** (er = 76:24 vs. er = 90:10) as a consequence of the unsubstituted phenyl ring, that results in lower interactions and a lower enantiomeric ratio. For **TS_{Re87}**, the slight decrease in the enantioselectivity was also in good agreement with the smaller size of the methyl *ortho*-substituents on the phenyl ring compared with its bulkier diethyl analogue in **TS_{Re88}**. In conclusion, the bulkier the *ortho*-substituents on the phenyl ring, the better the enantiodifferentiation. Nevertheless, increasing too much the bulkiness on the *ortho*-position of the phenyl ring can prevent the $\text{S}_{\text{N}}2'$ attack from happening, as shown by Alexakis and co-workers.^[176]

2.3.5 Grignard reagent scope and limitations

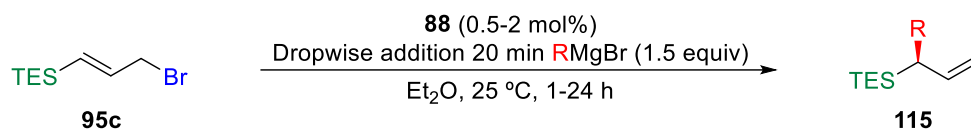
The scope of the reaction regarding the Grignard reagent was undertaken with γ -triethylsilyl-substituted allylbromide **95c** that was shown to give the best results both in terms of yield and enantioselectivity (**Scheme 136**).

Almost all the commercially Grignard reagents are available in THF solutions. However, as we have demonstrated that THF is detrimental in our reaction, we then decided to use homemade Grignard reagents, that were prepared under classical conditions from the corresponding bromine (**Scheme 140**). Worthy of note, phenylethynylmagnesium bromide was prepared by deprotonation of phenylacetylene with EtMgBr in Et₂O.



Scheme 140. Preparation of Grignard reagents.

With all the Grignard reagents in hand, the alkylation of allylbromide **95c** was studied under optimized conditions. In the classic protocol, 1.5 equiv of Grignard reagent was slowly added over 20 min to a solution of NHC-ligand **88** (0.5 to 2 mol%) in Et₂O at 25 °C, that is then stirred for 1 to 24 h (**Scheme 141**). After work-up, the regioselectivity was determined by ¹H NMR and the enantiomeric ratio by chiral GC or HPLC analysis. In some cases (those whose enantiomers could not be separated by GC), due to the polarity of the products, the allylsilanes obtained had to be derivatized by hydroboration-oxidation of the carbon-carbon double bond (see section 2.3.6.1, p. 141) in order to increase the polarity of these silanes and allow the determination of its enantiomeric ratio by HPLC. It is worthy of not, that this sequence is well documented to not lead to epimerization.



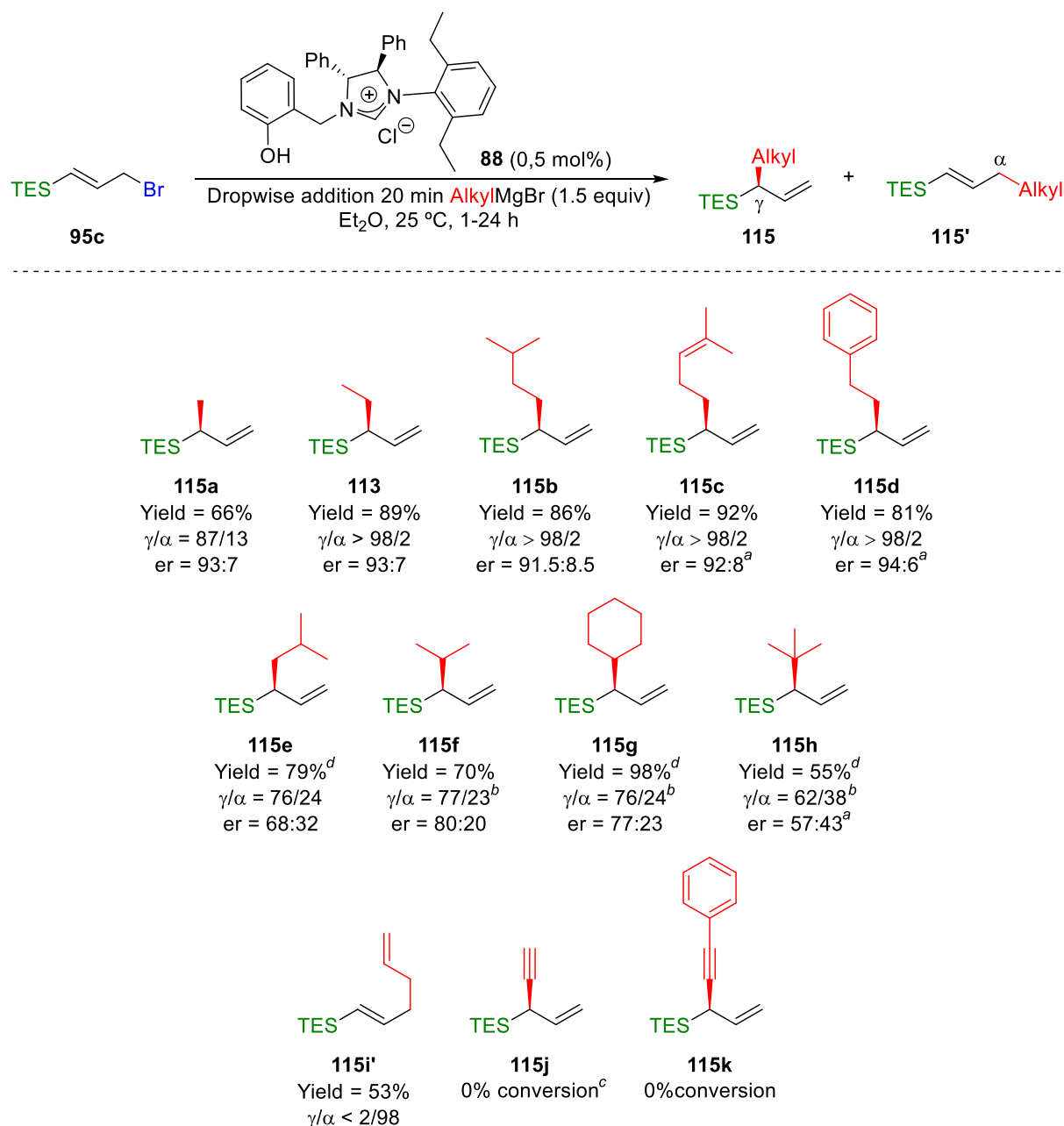
Scheme 141. Copper-free AAS of **95c** with Grignard reagents under optimized conditions.

This scope was firstly performed with primary, secondary and tertiary alkyl Grignard reagents, then applied with aryl analogues.

2.3.5.1 Alkyl and alkynyl Grignard reagents

The alkylation process was initially intended to be developed mainly with primary, secondary and tertiary Grignard reagents (**Scheme 142**). Alkyl substituted allylsilanes were

prepared in its racemic form by performing the AAS in Et₂O at 25 °C, in the presence of CuTc (30 mol%) and 1,3-diisopropylimidazolium chloride **111** (30 mol%) instead of NHC-ligand **88** (see **Scheme 135**, p. 128).



Yield for the inseparable mixture of α - and γ -product

γ/α ratio determined by ¹H NMR spectroscopy

er determined by GC or HPLC

^aer determined by chiral HPLC analysis of the derived alcohol

^bDetection of side product.

^cFrom commercial THF solution of ethynylmagnesium bromide

^d2 mol% of NHC-**88** was used

Scheme 142. Primary, secondary and tertiary Grignard reagents scope.

Satisfyingly, our model reaction showed a good tolerance towards all primary Grignard reagents tested. Non-hindered Grignard reagents afforded the corresponding γ -allylsilanes

113 and **115a-d** in good yields (66-92%) and excellent γ -regio- and enantioselectivity ($\gamma/\alpha \geq 87/13$ and $er \geq 91.5:8.5$). The result obtained for compound **115a** is particularly interesting since MeMgBr is well known for its lack of selectivity and low enantioselectivity in copper catalyzed-systems.

More hindered primary, secondary and tertiary Grignard reagents gave the corresponding allylsilanes **115e-h** in similar yields (55-98%) but with lower γ -regio- and enantioselectivity ($\gamma/\alpha \leq 77/23$ and $er \leq 80:20$). Unexpectedly, 1-buten-3-yl magnesium bromide afforded allylsilanes **115i'** as the only regioisomer ($\gamma/\alpha < 2/98$). Disappointingly, with alkynyl Grignard reagents, no reaction occurred.

On one hand, the decrease in regioselectivity observed with secondary and tertiary Grignard reagents, could be rationalized by their high reactivity that allow them to directly react with allylbromide **95c** through a four-member ring transition state (see **Figure 13**, p. 132) without requiring the ligand activation. On the other hand, the drop in the enantioselectivity could also be attributed to steric effects arising from the 1,3-diaxial interaction of the hindered Grignard reagents with the phenoxy group of the NHC-ligand, that would favour less the transition state **TS_{Sibulky}** when compared to transition state **TS_{Sinon-bulky}** (**Figure 15**).

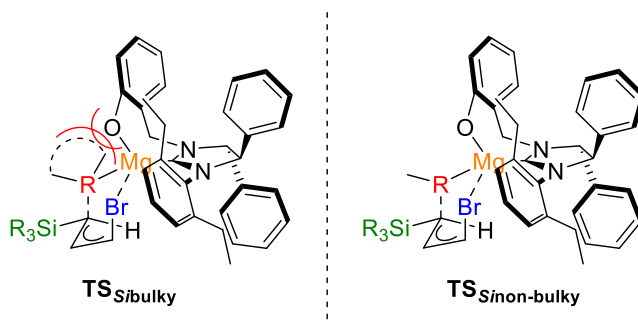
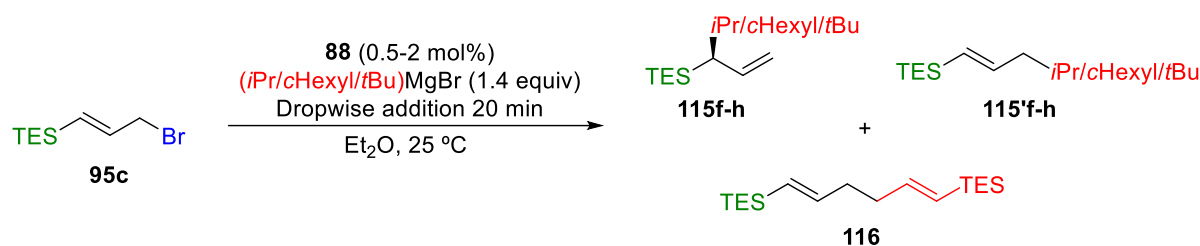
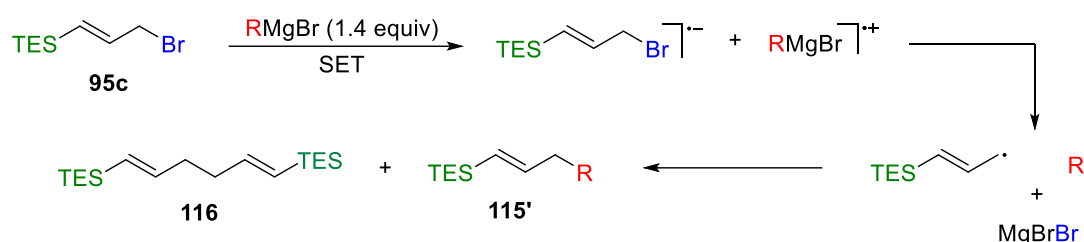


Figure 15. Comparison between **TS_S** generated with bulky (**TS_{Sibulky}**) and primary (**TS_{Sinon-bulky}**) Grignard reagents.

Furthermore, in contrast with primary alkyl Grignard reagents, allylic alkylation with secondary and tertiary analogues, give rise to the formation of a side product detected by ^1H NMR, in proportions of 9% for **115f**, 7% for **115g** and 21% for **115h**. This side product was assumed to be compound **116**, that corresponds to the allylic dimer that we hypothesized that could arise from the homocoupling between *in situ* generated allyl radical species (SET mechanism, **Scheme 143**).

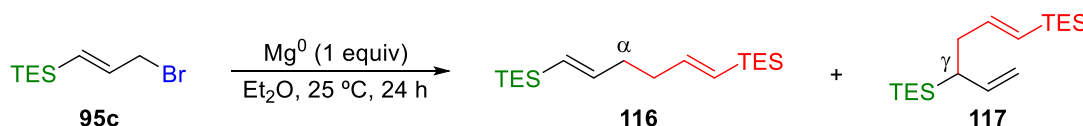


Proposed SET mechanism



Scheme 143. Copper-free AAS of secondary and tertiary Grignard reagents over silyl-substituted allylic bromide and proposed SET mechanism for the **116** formation.

We could confirm the identity of the side product after carrying out a reaction between **95c** and activated magnesium in Et_2O at 25 °C. Under these reaction conditions, *in situ* formed allylic Grignard reagent reacted with **95c**, affording a mixture of α - and γ -regioisomers ($\gamma/\alpha = 61/39$) in 56% yield (**Scheme 144**). ^1H NMR spectroscopy analysis of the mixture allowed us to confirm our hypothesis by comparison of spectrum with those obtained for allylsilanes synthesized from secondary and tertiary Grignard reagents (same dimer peaks were identified in the spectrum of **115f-h**).



Scheme 144. Reaction between **95c** and Mg^0 .

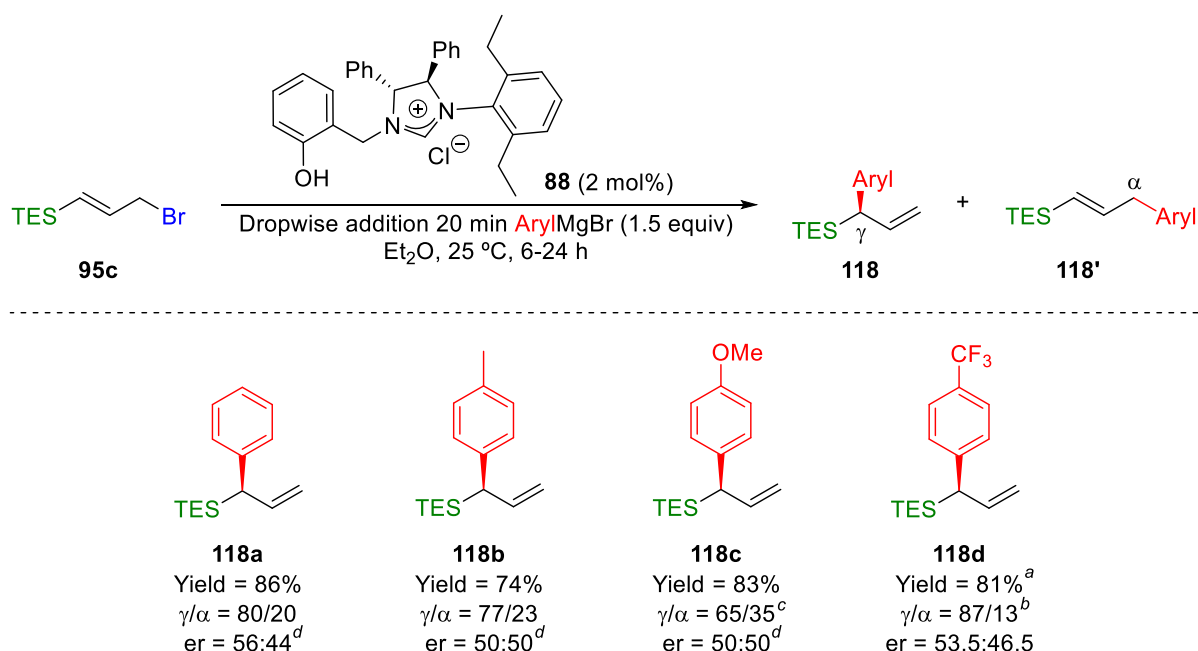
It is worthy to mention that although compound **117**, arising from the $\text{S}_{\text{N}}2'$ -attack of allylic Grignard over **95c** was detected in this reaction, no traces of it were observed in any of the reactions performed using isopropyl, cyclohexyl or *tert*-butyl Grignard reagent.

As a general trend, it can be observed that allylic alkylation with primary Grignard provides γ -allylsilanes with good levels of enantioselectivity (**Scheme 142**). Even derivatized primary analogues were successfully introduced (**115b**, **115c** and **115d**) on the condition of a two-carbon spacer between the Mg and the derivatization as it was proved by the results obtain for the isobutyl analogue (lower γ/α ratio and er). In this aspect, our synthesis strategy showed some limitations since secondary and tertiary nucleophiles were well tolerated but depicting lower levels of regio- and enantioselectivity, especially for the *tert*-butyl analogue **115h** which yield was also eroded.

2.3.5.2 Aryl Grignard reagents

The reaction scope was also extended to aromatic Grignard reagents. Because of the lower reactivity of these organometallics, 2 mol% of NHC-ligand **88** were used and longer reaction times were necessary (6 to 24 h) to achieve a complete conversion. Both electron-donating and electron-withdrawing groups were introduced on the *para*-position of the phenyl ring to study the impact of the electronic effects on the reaction.

As before, the racemates were obtained by performing the AAS in Et_2O at 25 °C, in the presence of CuTc (30 mol%) and 1,3-diisopropylimidazolium chloride **111** (30 mol%) instead of NHC-ligand **88** (see **Scheme 135**, p. 128). Also, as it was already mentioned, the enantiomeric ratios were determined by chiral GC or HPLC. In some cases, for the determination of the enantiomeric ratios, the allylsilanes obtained needed to be converted into their alcohol analogues through a hydroboration-oxidation transformation.



Yield for the inseparable mixture of α - and γ -product

γ/α ratio determined by ^1H NMR spectroscopy

er determined by GC or HPLC

^aReaction in pentane, when performed in Et_2O $\gamma/\alpha = 8/92$

^b γ/α after purification by silica-gel column chromatography

^c $\gamma/\alpha = 92/8$ after purification by silica-gel column chromatography

^der determined by chiral HPLC analysis of the derived alcohol

Scheme 145. Aryl Grignard scope.

All the allylsilanes obtained were isolated in good yields ($\geq 74\%$) whatever the *para*-substituent of the phenyl ring. Nevertheless, although decent to good γ/α ratios were attained (γ/α up to 87/13), the aryl-substituted allylsilanes displayed a complete loss of enantioselectivity ($\text{er} \leq 56:44$). This could be rationalized by 1,3-diaxial interaction as before.

In this case, a transition state **TS_{Siaromatic}**, higher in energy than transition state **TS_{Stbulky}** (see **Figure 15**, p. 136), can be envisioned due to the rigidity of the aryl rings (**Figure 16**).

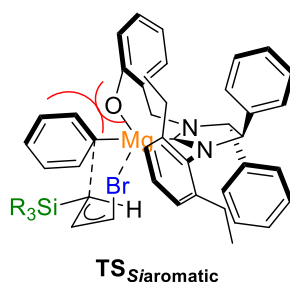
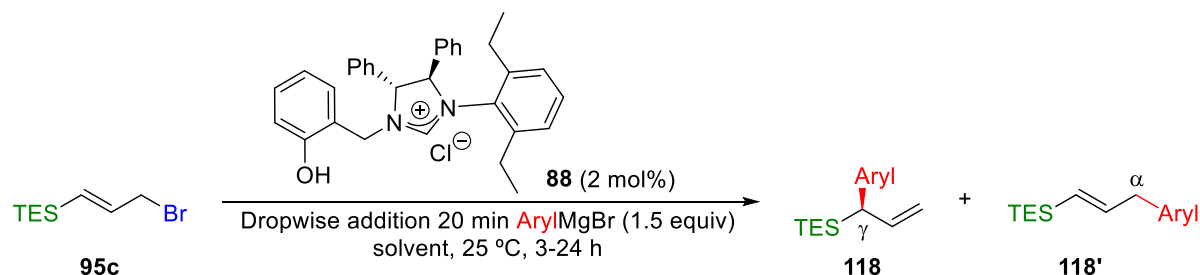


Figure 16. Disfavoured *Si*-face attack transition state in the presence of Grignard aryl reagents.

As seen in **Scheme 145**, electron-donating groups in the para-position of the phenyl ring led to a decline in the regioselectivity. The more electron-donor the group is, the greater the erosion on the regioselectivity (from $\gamma/\alpha = 80/20$ for **118a** to 77/23 for **118b** and 65/35 for **118c**).

Surprisingly, in the presence of an electron-withdrawing group in the para-position, a high regioselectivity in favour of the α -isomer was observed, as exemplified with **118d** ($\gamma/\alpha = 8/92$). Unexpectedly, the regioselectivity could be reversed by carrying out the reaction in pentane giving the γ -allylsilane as the main isomer ($\gamma/\alpha = 87/13$). This astonishing result prompted us to evaluate if the change of solvent also favored the γ -selectivity with the other aryl Grignard reagents (**Table 6**).



Entry	Aryl	Solvent	Conversion (%) ^a	γ/α ^a
1	C ₆ H ₅	Et ₂ O	100	80/20
2	C ₆ H ₅	Pentane	76	29/71
3	<i>p</i> -CH ₃ C ₆ H ₄	Et ₂ O	100	77/23
4	<i>p</i> -CH ₃ C ₆ H ₄	Pentane	63	33/67
5	<i>p</i> -MeOC ₆ H ₄	Et ₂ O	100	65/35
6	<i>p</i> -MeOC ₆ H ₄	Pentane	0	-
7	<i>p</i> -CF ₃ C ₆ H ₄	Et ₂ O	100	8/92
8	<i>p</i> -CF ₃ C ₆ H ₄	Pentane	100	87/13

^aDetermined by ¹H NMR spectroscopy

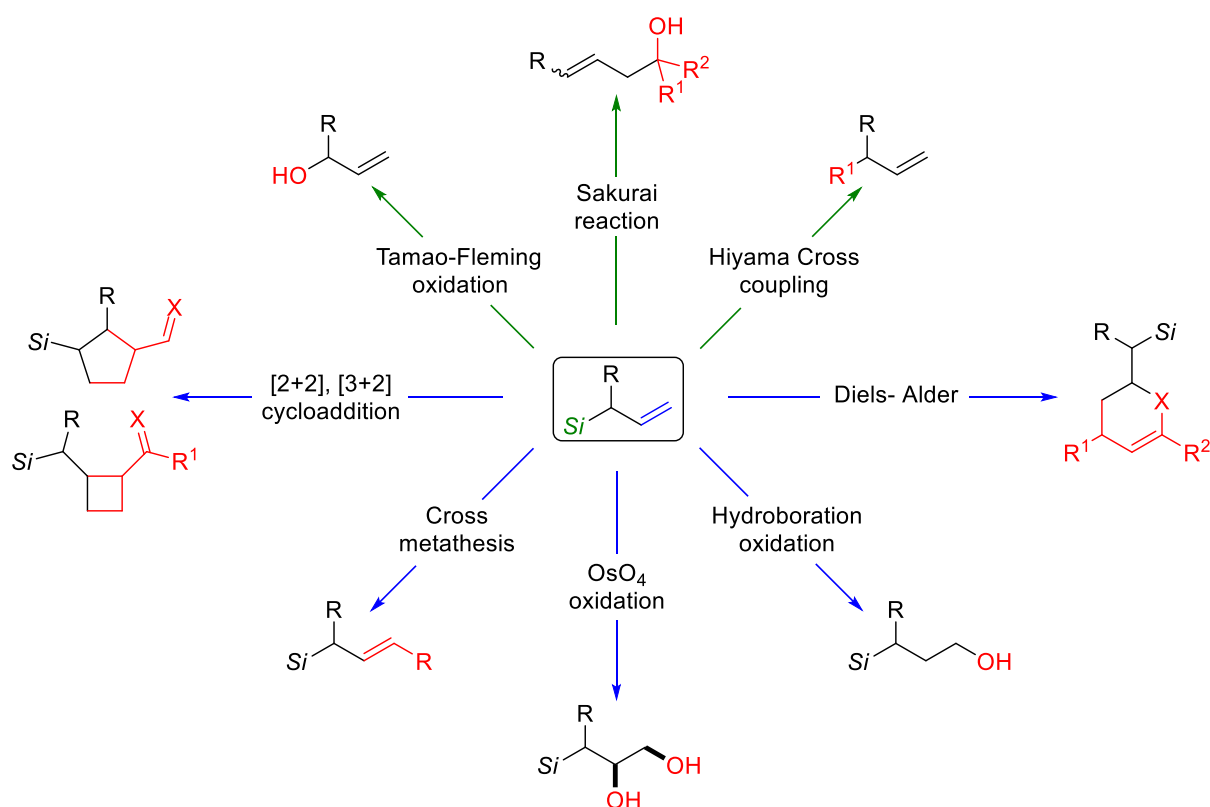
Table 6. Solvent dependence of copper-free asymmetric allylic arylation.

As expected (see **Table 5**, p. 124), γ/α ratios were substantially eroded with most of the other aryl Grignard reagents (**Table 6**). Noteworthy, no reaction took place in the case of the methoxy-substituted one (**Table 6**, entry 6).

As conclusion, γ -silyl- γ -aryl substituted allylsilanes were synthesized in good yields and moderate to good γ -regioselectivities but almost no enantioselectivity. Worthy of note is the peculiar case of allylsilane **118d**, since it was obtained in high γ -selectivity by performing the corresponding AAR of **95c** in pentane instead of Et₂O.

2.3.6 Functionalization of allylsilanes bearing tertiary silyl-substituted stereogenic centres

One of the main reasons why the synthesis of asymmetric allylsilanes has been widely develop in the last 40 years is because of the high synthetic potential of these molecules. Among all the transformations that can be envisioned with allylsilanes, the Hiyama cross-coupling, the Tamao-Fleming oxidation and the Hosomi-Sakurai allylation are the most used. Moreover, allylsilanes can also be subjected to cycloaddition reactions, Diels-Alder,^[192] hydroboration-oxidation sequences and olefin metathesis through their intrinsic double bond (**Scheme 146**).^[193]

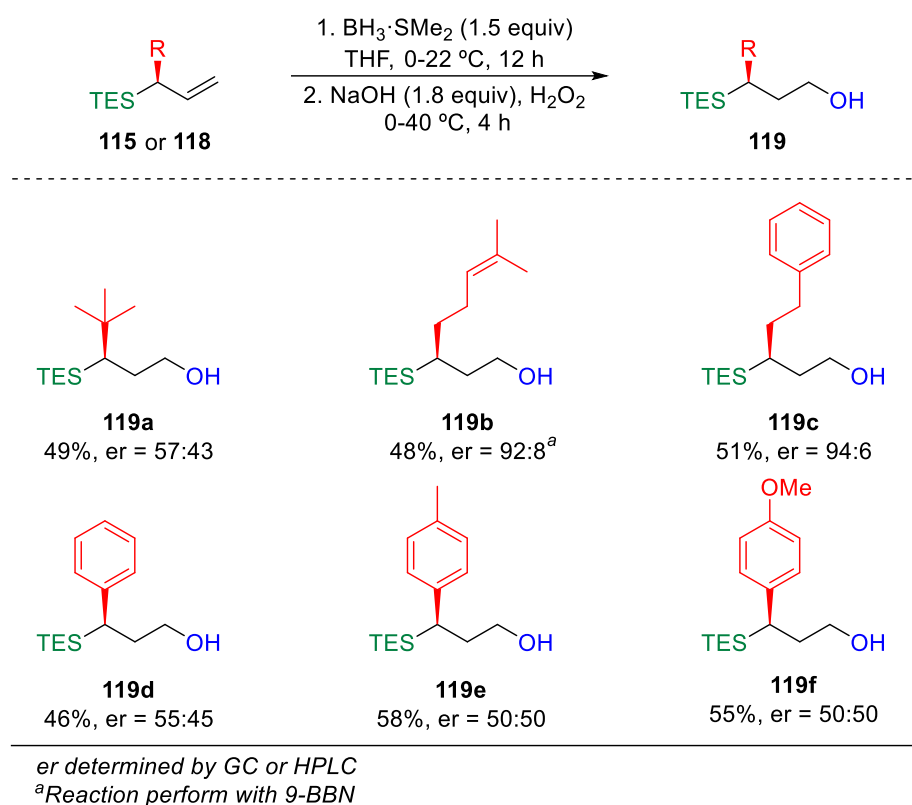


Scheme 146. Possible γ -allylsilane functionalizations.

We then planned to demonstrate the synthetic utility of our γ -substituted enantioenriched allylsilanes bearing tertiary silyl-substituted stereogenic centre. For that, we envisioned its derivatizations through its two functions, both double bond and silicon moiety.

2.3.6.1 Hydroboration-oxidation

We envisioned the preparation of chiral γ -silyl-substituted primary alcohols through the classic hydroboration-oxidation sequence. In this way, our method could be envisioned as a synthetic platform to access an array of chiral saturated γ,γ -disubstituted alcohols. $\text{BH}_3\cdot\text{SMe}_2$ and 9-BBN have been used under described literature conditions to provide exclusively the desired *anti*-Markovnikov alcohols in moderate isolated yields (46-58%, **Scheme 147**).



Scheme 147. γ -silyl-substituted alcohols accessed from chiral allylsilanes.

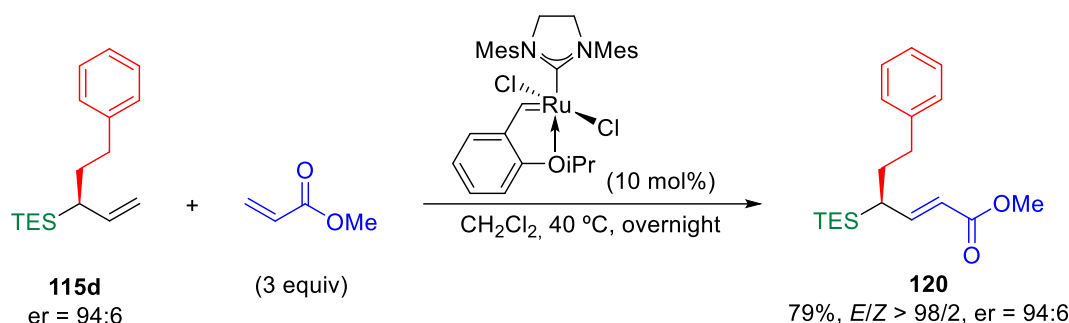
$\text{BH}_3\cdot\text{SMe}_2$ was used as the general source of borane, while hindered 9-BBN had to be employed only in the case of allylsilane **115c** (led to compound **119b**) in order to prevent the double hydroboration.

2.3.6.2 Cross-metathesis reactions

Allylsilanes can also be used as olefins in cross-metathesis and ring-closing metathesis (RCM). In the presence of a catalyst, usually based on transition metals such as Mo, Ru, Re or W, redistribution of olefin fragments take place by the scission and regeneration of carbon-carbon double bonds.^[194]

In this regard, we wanted to exemplify the ability of our γ -allylsilanes to perform this transformation with **115d** as model. Its reaction with methylacrylate (3 equiv) and 10 mol% of Grubbs II catalyst in CH_2Cl_2 at 40 °C afforded the corresponding chiral acrylate derivative **120**

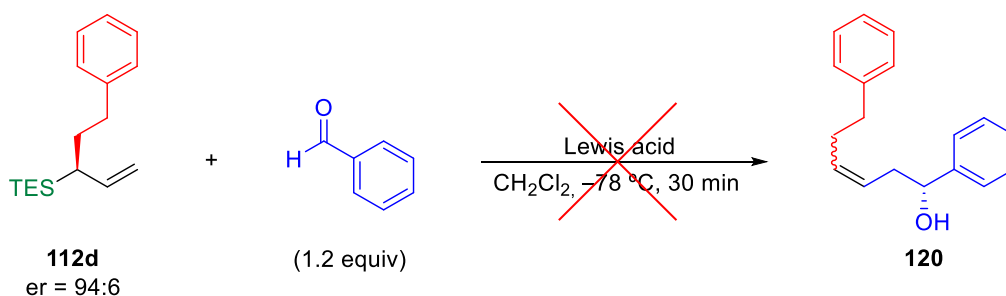
in 79% isolated yield. Full control of the carbon-carbon double bond geometry ($E/Z > 98/2$) along with no eroded enantioselective ratio was observed (**Scheme 148**).



Scheme 148. Preparation of functionalized allylsilane **120** through olefin metathesis of **115d** with methyl acrylate.

2.3.6.3 Hosomi-Sakurai reaction

We next studied the possibility of performing Hosomi-Sakurai allylation using our γ-allylsilanes. Allylsilane **115d** was thus reacted with benzaldehyde (1.2 equiv) in the presence of Lewis acid in CH_2Cl_2 at $-78\text{ }^\circ\text{C}$, that are the classical conditions of the Hosomi-Sakurai reaction (**Scheme 149**).



Scheme 149. Lewis acid catalyzed Sakurai-Hosomi reaction using allylsilane **115d**.

Under Lewis acid catalysis of TiCl_4 , ^1H NMR evidenced the disappearance of the starting material double bond while the characteristic signals of the TES group were still present in the crude mixture. However, no trace of the desired homoallylic alcohol **120** could be observed. Using $\text{BF}_3 \cdot \text{Et}_2\text{O}$ instead of TiCl_4 as Lewis acid led to a similar result. Studies are ongoing to set the reaction conditions.

2.3.7 Partial conclusion

In summary, we have developed a strategy for the copper-free allylic alkylation of vinylsilanes with Grignard reagents in the absence of Cu. This relatively simple process which represents the first copper-free AAS strategy regarding the preparation of enantioenriched allylsilanes is catalyzed by NHC-**88** ligand. This imidazolium salt bears a bulky (diethyl)phenyl substituent in its right arm that served as blocking part to avoid the $\text{S}_{\text{N}}2$ -attack, and a phenoxy group with a carbon spacer relative to the imidazolium core in its left arm that will coordinate

to the Grignard reagent enhancing its nucleophilicity and placing it in the appropriate position to perform the desired S_N2' -attack. For the imidazolium salt double deprotonation, no external base is needed since the Grignard reagents basicities are high enough to perform it.

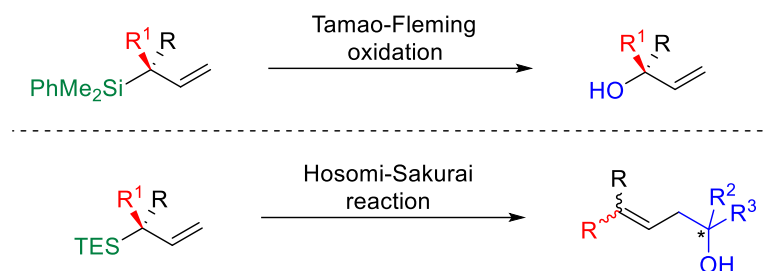
Our developed synthesis strategy although highly tolerant towards different silyl groups (**Scheme 136**), is strongly dependent on the nature of the Grignard reagent. In this regard, non-hindered primary alkyl Grignard reagents allow the synthesis of chiral allylsilanes with high γ -regio- and enantioselectivity. By contrast, hindered alkyl Grignard reagents (mainly secondary and tertiary ones) afford the corresponding allylsilanes in lower γ -regioselectivities and an eroded enantiomeric ratio, while aryl Grignard reagents furnish the corresponding allylsilanes in moderate regioselectivities but as racemates.

In the next section, taking into account the promising results obtained for allylsilanes bearing tertiary silicon-substituted stereogenic centres, we will expand and implement our methodology for the preparation of the much more challenging quaternary analogues.

2.4 Allylsilanes bearing quaternary silyl-substituted stereogenic centres

As mentioned throughout the manuscript, the final target of our project is the development of a method to access enantioenriched allylsilanes bearing silyl-substituted quaternary stereogenic centres. This objective is quite ambitious, and only four strategies in the last 20 years have focused on the preparation of these congested molecules.^[87,162,165,169] Moreover, to the best of our knowledge, all the examples described in the precedent literature contain exclusively the dimethylphenylsilyl group.

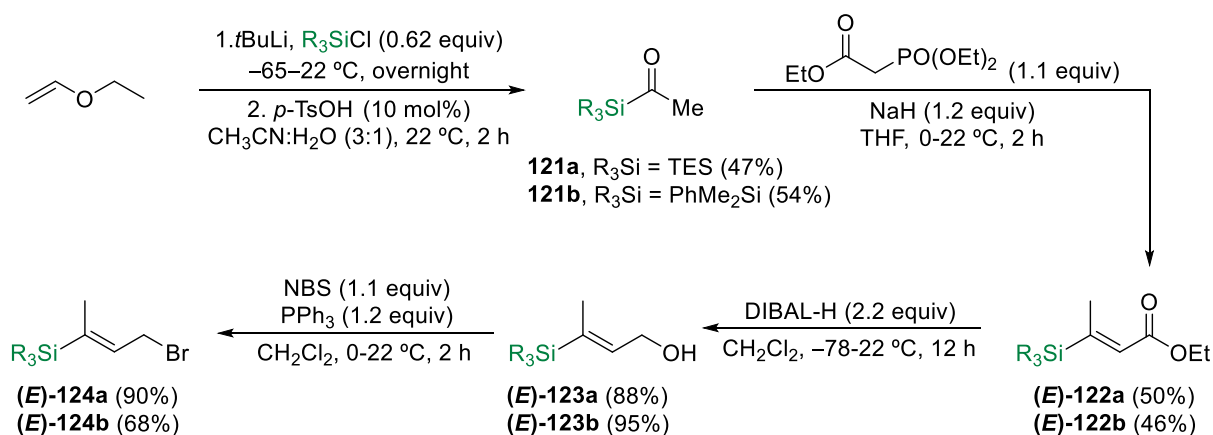
In this section, we will attempt to apply our copper-free chemistry not only to access triethylsilyl-substituted allylsilanes (continuing our previous investigation on this type of products, see section 1.1, p. 114) but also dimethylphenylsilyl containing ones. As these substituents will present different reactivity towards the posterior derivatization of the silane, it will allow us to have access to distinct type of complex molecules. Particularly, we envisioned the approach to chiral tertiary alcohols through the Tamao-Fleming oxidation from dimethylphenylsilyl-adducts and to stereodefined homoallylic alcohols through the Sakurai-Hosomi allylation from triethylsilyl-analogues (**Scheme 150**).



Scheme 150. Possible functionalization of allylsilanes bearing silyl-substituted quaternary stereogenic centres.

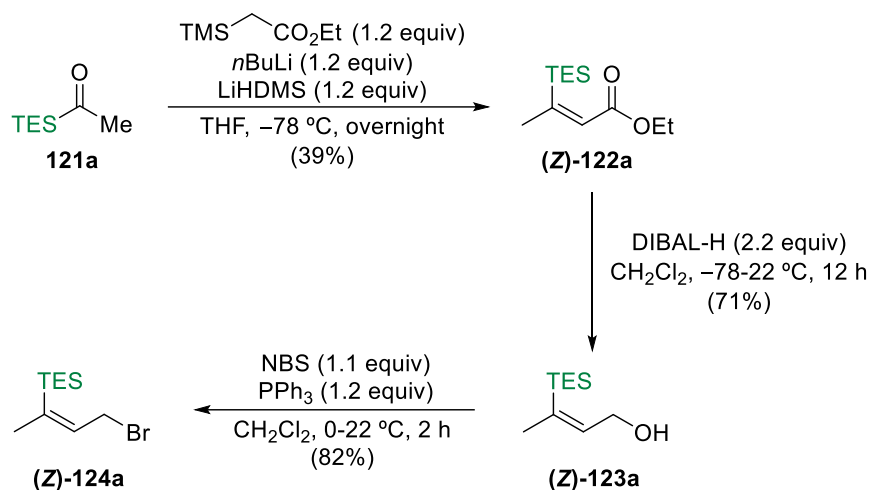
2.4.1 Preparation of α -substituted- γ -bromo vinylsilanes

Owing to the leaving group optimization performed during the preparation of tertiary enantioenriched allylsilanes, we directly focused on the exclusive synthesis of allylic bromides following reported protocols. Methyl-substituted vinylsilanes (**E**)-**124** were accessed through a four-step procedure (**Scheme 151**) starting from commercially available ethylvinylether that was transformed into the corresponding acylsilane **121** after deprotonation with *tert*-butyl lithium in the presence of silylchloride (PhMe_2SiCl or TESCl) followed by catalytic acid hydrolysis. Subsequently, **121** was subjected to a Horner-Wadsworth-Emmons type reaction by addition of (triethyl)phosphonoacetate in the presence of NaH to furnish the corresponding ester (**E**)-**122** that was reduced under DIBAL-H classical conditions to yield alcohol (**E**)-**123**. Finally, alcohol activation was performed by NBS and triphenylphosphine to obtain γ -bromovinylsilane (**E**)-**124**.



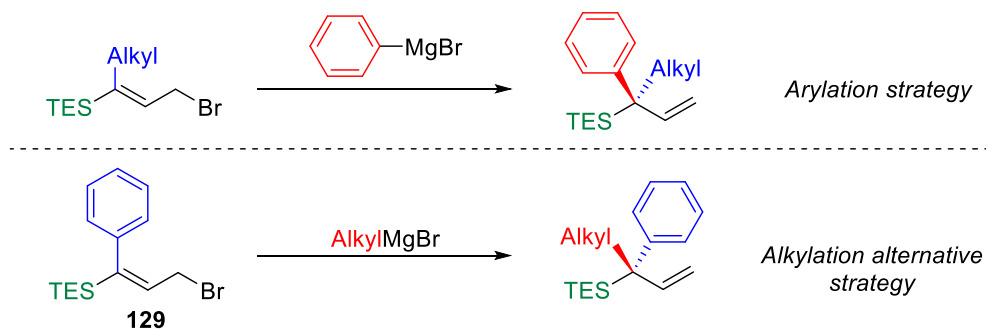
Scheme 151. Synthesis of PhMe_2Si - and TES- substituted allylic bromides (**E**)-**124**.

Unlike the study of allylsilanes bearing tertiary silyl-substituted stereogenic centres in which we failed to prepare the (*Z*)-starting material, we succeeded in the preparation of (**Z**)-**124a**. A Peterson olefination procedure in the presence of the *in situ* prepared lithium carbanion of ethyl (trimethylsilyl)acetate was used to control the double bond geometry, furnishing allylacetate (**Z**)-**122a** in low yield (39%). Subsequently DIBAL-H reduction and NBS bromination afforded allylbromide (**Z**)-**124a** (**Scheme 152**).



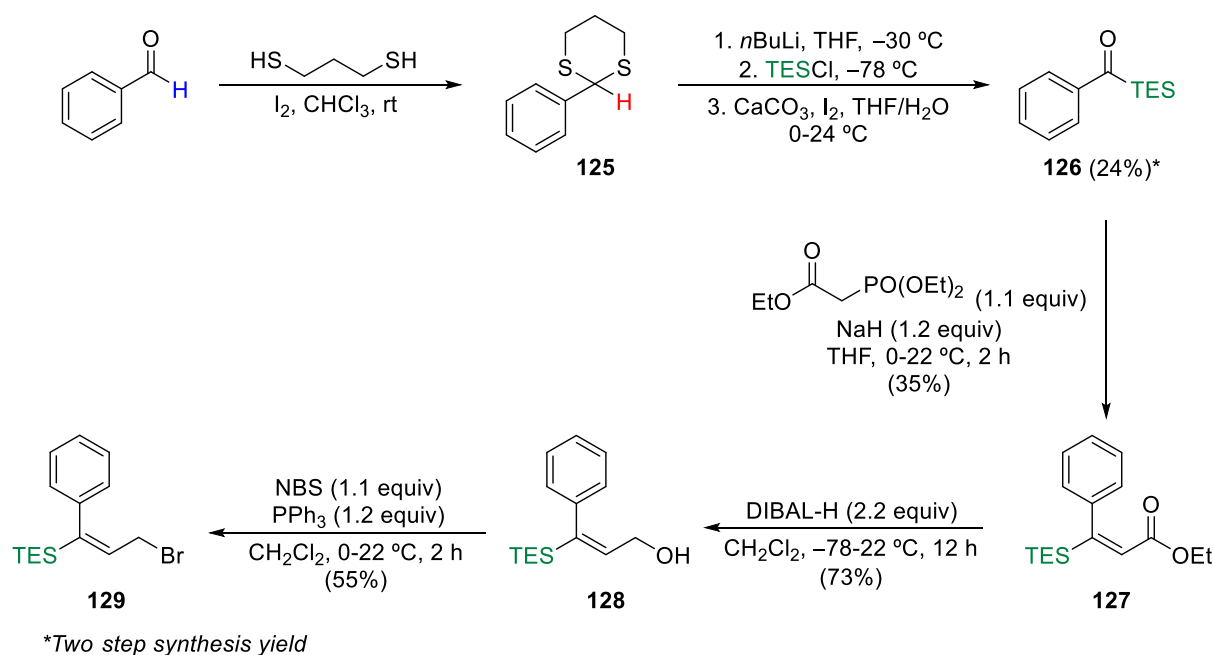
Scheme 152. Peterson olefination sequence to access allylic bromide **(Z)-124a**.

On the other hand, we also envisioned the possibility of performing copper-free asymmetric allylic alkylation on aryl-substituted allylbromide **129** in order to obtain chiral γ -aryl-substituted allylsilanes (**Scheme 153**). Furthermore, alkylation of **129** could emerge as a possible alternative to overcome the low enantioselectivity observed for the preparation of enantioenriched allylsilanes when aryl Grignard reagents were involved (see **Scheme 145**, p. 138).



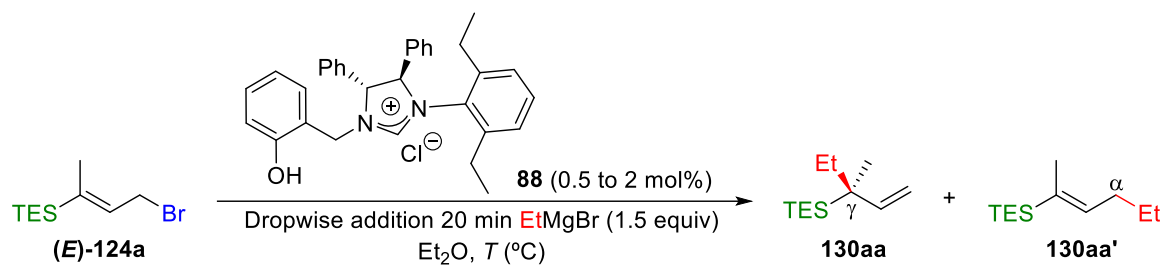
Scheme 153. Different synthesis strategies to access aryl substituted quaternary stereogenic centres.

This α -phenyl substituted vinylsilane **129** was prepared from its corresponding acylsilane **126** following the same synthesis sequence exemplified before (**Scheme 151**). In turn, an umpolung strategy was applied on benzaldehyde to access phenyl(triethyl)silyl ketone **126** in a two-step synthesis (**Scheme 154**).


 Scheme 154. Synthesis of allylbromide **129**.

2.4.2 Optimization conditions

Initial tests were performed starting from the optimized conditions developed for the copper-free asymmetric allylic allylation of γ -silyl-substituted allylbromides to access allylsilanes bearing silyl-substituted tertiary stereogenic centres. While Et_2O and NHC-**88** were kept as the optimal solvent-ligand combination, some parameters as the catalytic loading and the temperature were investigated (**Table 7**). The racemate to measure the enantiomeric ratio was prepared, as before, by performing the AAS in Et_2O at $-15\text{ }^\circ\text{C}$, in the presence of CuTc (30 mol%) and 1,3-diisopropylimidazolium chloride **111** (30 mol%). The absolute (S)-configuration of the allylsilanes bearing quaternary stereogenic centre was assigned by comparison of the $[\alpha]_{\text{D}}^{20}$ measured for 3-(Dimethylphenylsilyl)-3-methyl-1-pentene **130ba** with data reported in literature.^[162] This measurement was in agreement with our previous investigations over the tertiary analogues, as it was expected the Grignard reagent to attack the *Si*-face of the allylbromide.



Entry	Ligand (mol%)	T (°C)	Time (h)	Conversion (%) ^a	γ/α ^a	er ^b
1	0.5	25	1	56	70/30	87:13
2	1	25	1	95	95/5	88:12
3	2	25	1	100	98/2	87.5:12.5
4	2	-15	1	50	> 98/2	97.5:2.5
5	2	-15	5	100	> 98/2	98:2
6 ^c	2	-15	5	100	> 98/2	> 98:2

^aDetermined by ¹H NMR spectroscopy.

^bDetermined by GC (DEX-CB).

^cPerformed over vinylsilane (E)-124b (PhMe₂Si-)

Table 7. NHC-catalyzed copper-free AAS temperature, catalyst loading and time optimization.

Encouraging results in terms of regio- ($\gamma/\alpha = 70/30$) and enantioselectivity (er = 87:13) were obtained with the standard reaction conditions, although not full conversion was achieved within 1 h (**Table 7**, entry 1). In order to achieve complete conversion, NHC-ligand **88** loading was increased. When the reaction was performed in the presence of 1 mol% of ligand **88**, a conversion of 95% was achieved along with a huge increase in the regioselectivity ($\gamma/\alpha = 95/5$), while the enantiomeric ratio remained almost unchanged (**Table 7**, entry 2). Finally, with 2 mol% of ligand **88**, γ -product was obtained as the only isomer ($\gamma/\alpha > 98/2$) with the same levels of enantioselectivity (**Table 7**, entry 3). The correlation between these two parameters (catalytic loading and regioselectivity), can be rationalized on the basis of the active Mg-carbene species amount existing in the middle. Considering that in the presence of our NHC-**88** ligand, S_N2' reaction is kinetically favoured in front of the classical S_N2,¹ the last will only take place if the Grignard concentration in the reaction mixture is too high in front of the ligand.

Satisfactorily, by lowering the reaction temperature to -15 °C, the corresponding γ -allylsilane was obtained in excellent 98:2 er, although a modest 50% conversion was achieved within the 1 h (**Table 7**, entry 4). Nevertheless, this hassle was easily overcome by increasing the reaction time to 5 h without observing any degradation while the regio- and enantioselectivity were maintained (**Table 7**, entry 5).

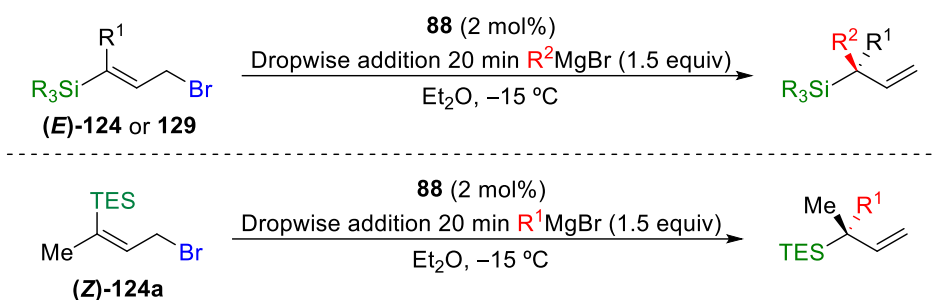
Finally, these reaction conditions were successfully applied to the PhMe₂Si- bromide analogue (E)-124b, obtaining the corresponding allylsilane **130ba** in excellent yield (96%) and perfect γ -regio- and enantioselectivity (**Table 7**, entry 6). All these results indicated, as it was

¹ We considered that by analogy with the computational studies performed by Halbert *et al.*^[190]

expected, that different silyl groups are well tolerated by our catalytic system without detriment of the reaction outcome.

2.4.3 Grignard reagent scope and limitations

In the optimized procedure, alkyl or aryl Grignard reagent (1.5 equiv) was slowly added over a period of 20 min to a solution of γ -bromovinylsilane **124** or **129** in the presence of NHC-ligand **88** (2 mol%) at $-15\text{ }^{\circ}\text{C}$ in Et_2O (**Scheme 155**)

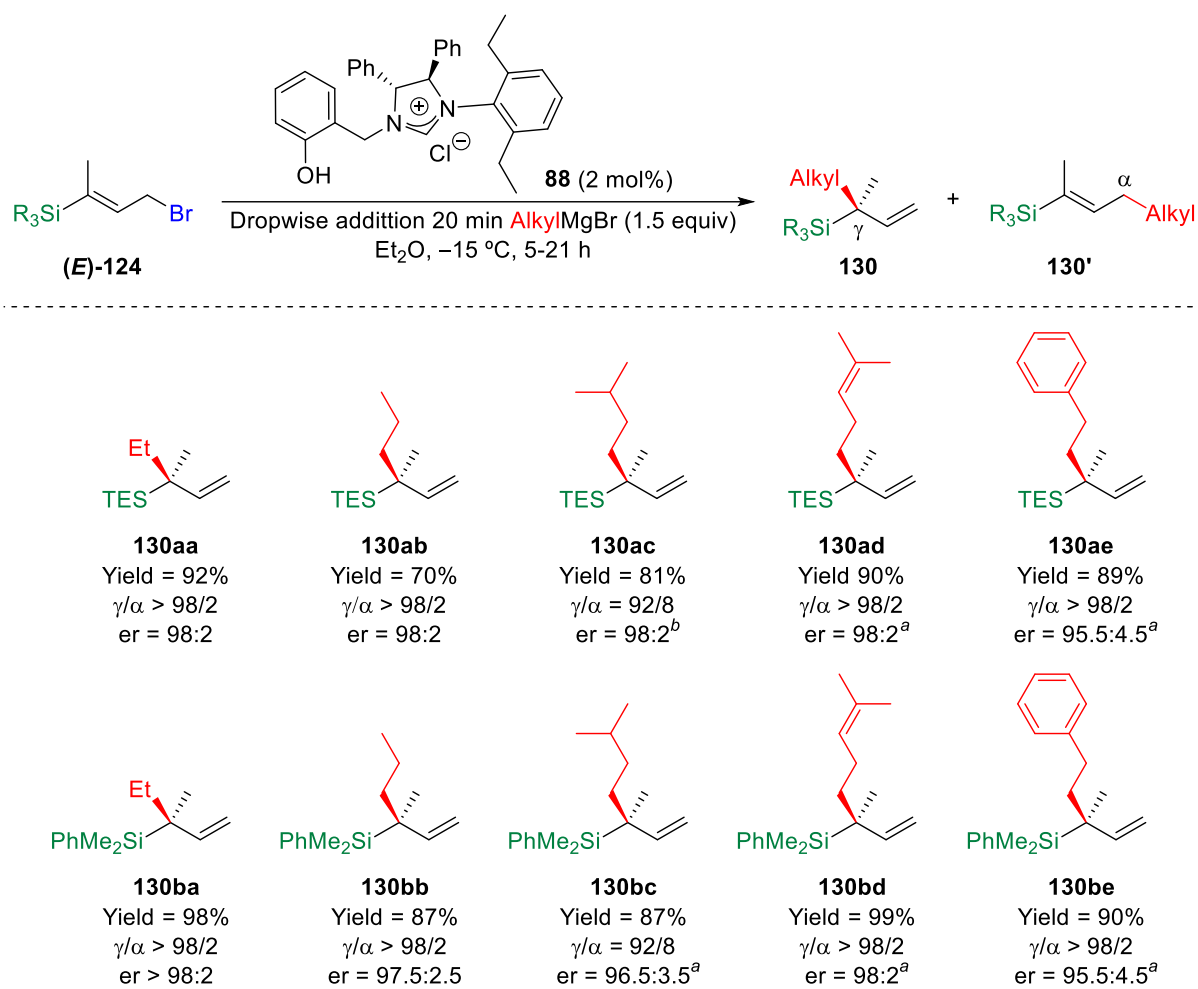


Scheme 155. Copper-free AAS of γ -bromovinylsilanes 123 and 124.

As before, in some cases the enantiomeric ratio could not be determined by chiral GC or HPLC analysis of the allylsilanes obtained. In these cases, the determination of the enantiomeric ratio needed the derivatization of the allylsilanes into the corresponding primary alcohols by hydroboration-oxidation of the double bond (see section 2.4.4.2.1, p. 155) and eventually, subsequent esterification with acryloyl chloride (see section 2.4.4.2.2, p. 156).

2.4.3.1 Alkyl Grignard reagents

Owing to the results obtained during the preparation of allylsilanes bearing tertiary silyl-substituted stereogenic centres with primary Grignard reagents and taking into account the initial studies during the optimization process, excellent results for both TES- and PhMe_2Si - adducts were expected when utilizing alkyl Grignard reagents. As before, allylsilane racemates were obtained by performing the AAS in Et_2O at $25\text{ }^{\circ}\text{C}$ in the presence of CuTc (30 mol%) and 1,3-diisopropylimidazolium chloride **111** (30 mol%) instead of NHC-ligand **88**. Alternatively, due to the low γ -regioselectivity this copper system displayed towards the preparation of several allylsilane racemates, achiral NHC-ligand **87** was prepared in their racemic form and used under copper-free reaction conditions to furnish the desired racemates.



Yield for the inseparable mixture of α and γ -products

γ/α ratio determined by ^1H NMR spectroscopy

er determined by GC or HPLC

^aer determined by chiral HPLC analysis of the derived alcohol

^ber determined by chiral HPLC analysis of the acryloyl ester (esterification of derived alcohol)

Scheme 156. Primary Grignard reagents scope.

Pleasantly, the reaction of non-hindered alkyl Grignard reagents with γ -bromovinylsilanes (**(E)-124**) afforded a wide range of enantioenriched allylsilanes (er \geq 95.5:4.5) bearing a silyl-substituted quaternary stereogenic centre in high yields (up to 99%) and exclusive γ -regioselectivity except for the isopentyl-substituted allylsilanes **130ac** and **130bc** where a very small amount of α -isomer ($\gamma/\alpha \geq 92/8$) was observed (**Scheme 156**).

Interestingly, when compared with their tertiary analogues, allylsilanes bearing silicon-substituted quaternary stereogenic centres were furnished in higher γ -regio- and enantioselectivity. However, especially interesting was the huge augmentation observed regarding the chiral selectivity, a fact that could be rationalized by the two transition state models previously envisioned. In these models (**TS_{ReMe}** and **TS_{ReH}**), the bulkier the γ -substituent in the allylbromide, the higher the steric strains between the ethyl substituents of the right-arm phenyl group in NHC-ligand **88** and the substrate (steric interactions of

$\text{TS}_{\text{ReMe}} \gg \text{TS}_{\text{ReH}}$), enhancing the disadvantage regarding the formation of the (*R*)-enantiomer when compared with the γ -unsubstituted **95c** used for the preparation of tertiary allylsilanes (Figure 17).

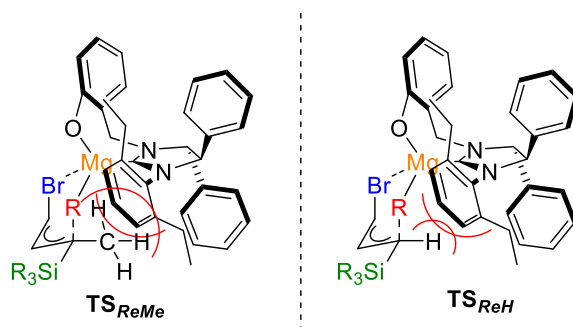
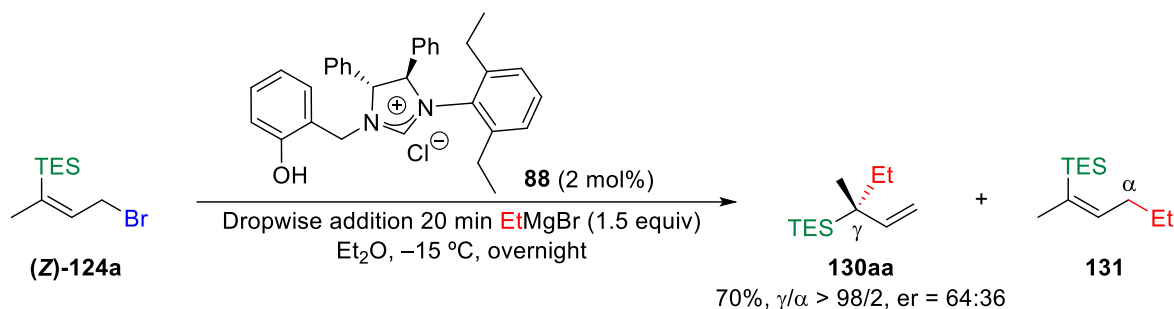


Figure 17. Steric interaction comparison between tertiary and quaternary substrates with the NHC-ligand **88**.

To explore the impact of the double bond geometry on the stereo-outcome of the reaction, copper-free AAS method was applied over (**Z**)-**124a**. Surprisingly, although the reaction took place exclusively through the desired $\text{S}_{\text{N}}2'$ -pathway isolating the allylsilane **130aa** in 70% yield without any trace of the α -isomer ($\gamma/\alpha > 98/2$), a poor *er* = 64:36 was favourable to the (*R*)-enantiomer.



Scheme 157. Copper-free AAS of (**Z**)-**124a**.

The low enantiomeric excess and the inversion of the stereoselectivity observed for allylsilane **130aa** when compared with the same compound obtained from (**E**)-**124a** could be explained by steric considerations in the two possible transition states $\text{TS}_{\text{Re(Z)}}$ and $\text{TS}_{\text{Si(Z)}}$ leading to opposite enantiomers (Figure 18). The less difference in the steric constraints between both models, makes none of the two much favourable unlike for the transition states $\text{TS}_{\text{Re(E)}}$ and $\text{TS}_{\text{Si(E)}}$ formed with (**E**)-**124a** that led to an excellent enantioselectivity for **130aa** (*er* = 98:2).

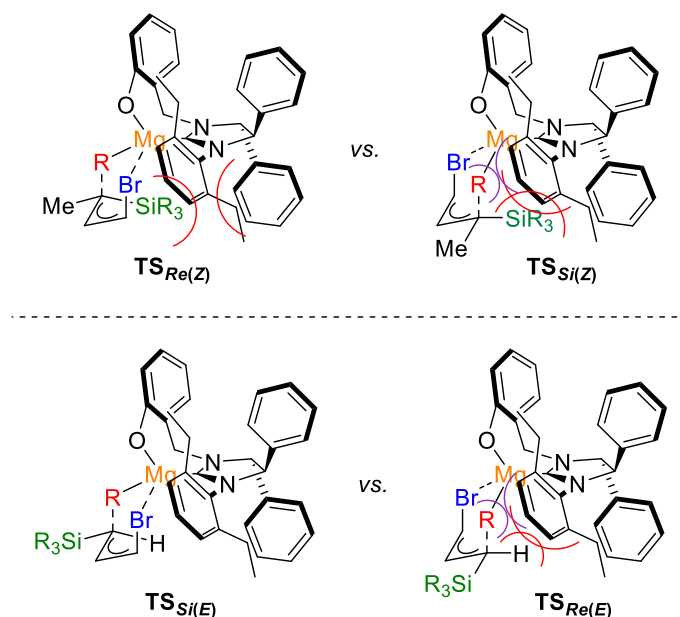
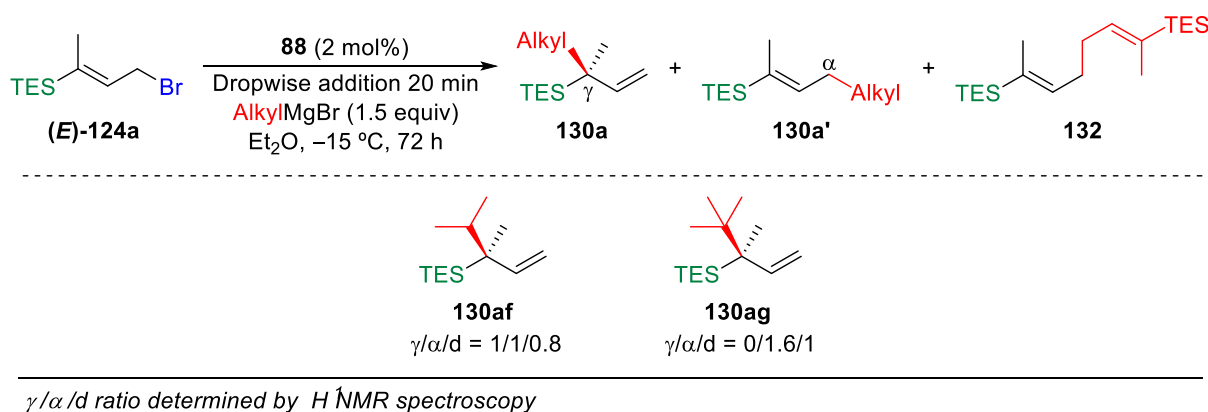


Figure 18. Proposed transition states for the copper-free AAS of Grignard reagents with **(Z)**-124a and **(E)**-124a as substrate.

In both **TS_{Re(Z)}** and **TS_{Si(Z)}**, although the R_3Si - groups are placed in the less steric demanding equatorial positions of the pseudo-chair, both transition states present steric repulsions. However, **TS_{Re(Z)}** leading to the (*R*)-enantiomer present less steric interactions (silyl moiety with backbone phenyl ring) than **TS_{Si(Z)}** leading to the (*S*)-enantiomer (silyl moiety and Grignard reagent with aryl blocking part), resulting in a *er* = 64:36 favourable to the (*R*)-enantiomer (**Figure 18**).

On the other hand, this strategy also showed some limitations regarding secondary and tertiary alkyl Grignard reagents. Attempts of allylic alkylation with isopropylmagnesium bromide led to a mixture of α - and γ -products along with a dimer side product **132** (**Scheme 158**). Although we were not able to isolate these side product by column chromatography due to its low polarity, comparison of 1H NMR spectrum with the ones corresponding to **115f**, **115g** and **115h** (*i*Propyl-, *c*Hexyl- and *t*Bu-substituted allylsilanes) indicated the formation of the dimer **132**. The use of the bulkier *tert*-butylmagnesium bromide was also considered. Nevertheless, a mixture of α -isomer and dimer **132** products was observed with no trace of the desired γ -product (**Scheme 162**).

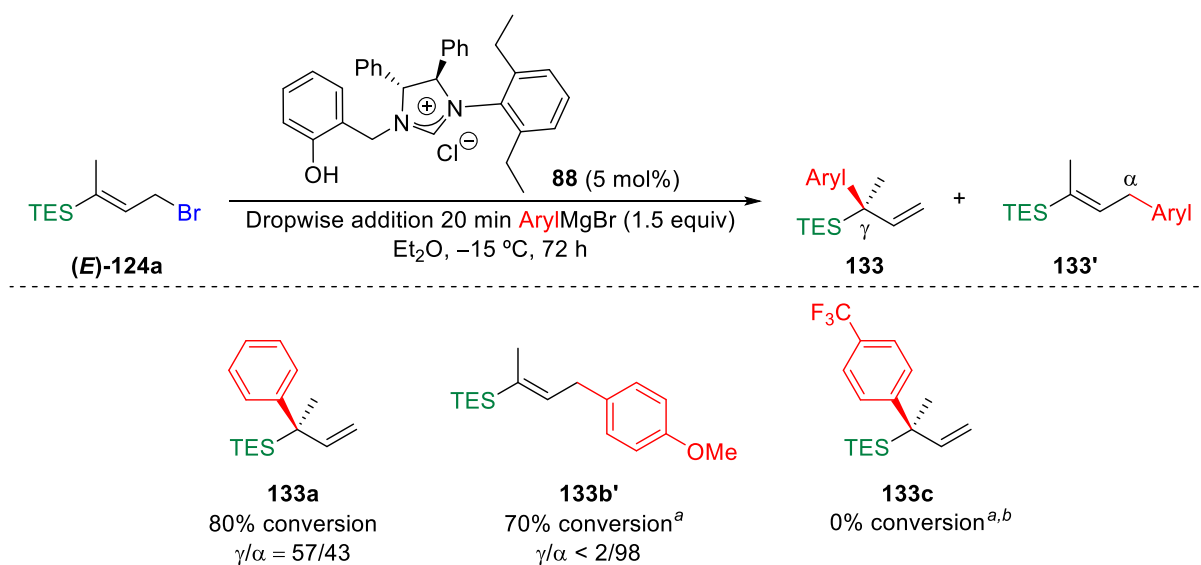


Scheme 158. Copper-free AAS of **(E)-124a** with secondary and tertiary alkyl Grignard reagents.

As conclusion, enantioenriched allylsilanes bearing a silyl-substituted quaternary stereogenic centre were successfully prepared from primary alkyl Grignard reagents in excellent γ -regio and enantioselectivities (up to $\gamma/\alpha > 98/2$ and $er > 98:2$). Bulkier secondary and tertiary Grignard reagents were not well tolerated leading to complex mixture of α - and γ -isomers along with dimer product. Finally, it was highlighted the essential role played in the stereoselective outcome of the reaction by the carbon-carbon double bond geometry of the allylic electrophiles, since only (*E*)-allylbromides led to high enantioselective ratios.

2.4.3.2 Aryl Grignard reagents

The copper-free AAS was next studied with different *p*-substituted aryl Grignard reagents under the prior-mentioned optimized conditions but with an increased NHC-ligand **88** loading from 2% to 5% (**Scheme 159**).



γ/α ratio determined by ^1H NMR spectroscopy

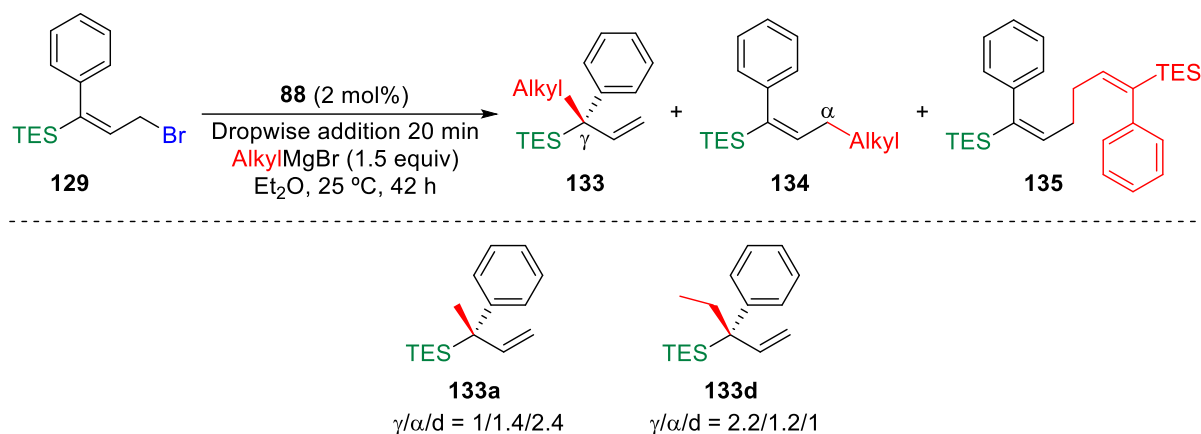
^aReaction performed at 25 °C.

^bReaction performed in pentane

Scheme 159. Preparation of allylsilanes bearing a quaternary silyl-substituted stereogenic centre through copper-free asymmetric allylic arylation.

By contrast to previous aryl-substituted tertiary analogues, increase of the NHC-ligand **88** loading to 5 mol% and longer reaction time (up to 72 h) did not allow to achieve full conversion. When phenylmagnesium bromide was used, 80% of conversion was achieved furnishing the desired allylsilane **133a** as an inseparable mixture of α - and γ -products in low regioselectivity ($\gamma/\alpha = 57/43$). When the electron-donor methoxy group was introduced in the *para*-position of the phenyl ring, no reaction took place at $-15\text{ }^{\circ}\text{C}$ while 70% conversion was attained when the reaction temperature was increased to $25\text{ }^{\circ}\text{C}$, affording however the α -isomer **133b'** as the only product. As for the electron-withdrawing trifluoromethyl group, it led to no reaction neither at $-15\text{ }^{\circ}\text{C}$ nor as $25\text{ }^{\circ}\text{C}$ (**Scheme 160**).

After these disappointing results, we envisioned an alternative method consisting in the copper-free AAS of α -phenyl- β -bromovinylsilane **129** with alkyl Grignard reagents for the preparation of allylsilanes **133** bearing aryl- and silyl-substituted quaternary stereogenic cents (**Scheme 160**).



$\gamma/\alpha/d$ ratio determined by ^1H NMR spectroscopy.

Scheme 160. Copper-free AAS of aryl-substituted vinylsilane **129** with alkyl Grignard reagents.

At $-15\text{ }^{\circ}\text{C}$, no transformation was observed while increasing the reaction temperature to $25\text{ }^{\circ}\text{C}$ resulted in full conversion within 24 h. Unfortunately, complex mixtures of α - and γ -isomers, dimer **135** and other unidentified products precluded the desired allylsilane **133a** and **133d** to be isolated (**Scheme 160**).

This lack of regioselectivity can be explained by the two transition state models **TS_{Re129}** and **TS_{Si129}**, that both exhibit high steric repulsions precluding the favorable formation of the γ -isomer (**Figure 19**).

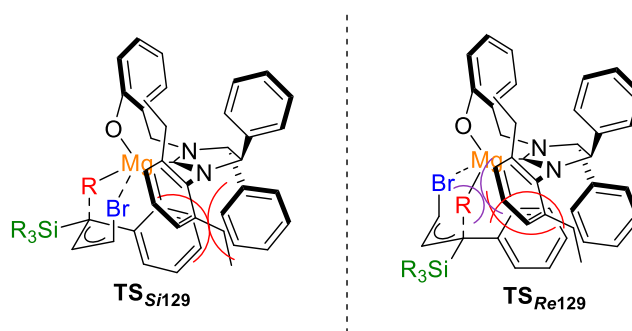


Figure 19. Disfavoured transitions states leading to branch allylsilane.

2.4.4 Derivatization of allylsilanes bearing quaternary silyl-substituted stereogenic centres

The synthetic potential of allylsilanes bearing silyl-substituted quaternary stereogenic centres was investigated. Since those molecules present two different functional groups that offer distinct types of transformations and derivatizations, a large number of different molecules can be accessed from them.

In spite of their great synthetic potential, these molecules have been however involved only in a few transformations, not only because of the high complexity to access them, but also due to the high congestion regarding the quaternary stereogenic centre. Because of that, many transformations are thus difficult if not impossible to carry out such as the cross metathesis.^[118]

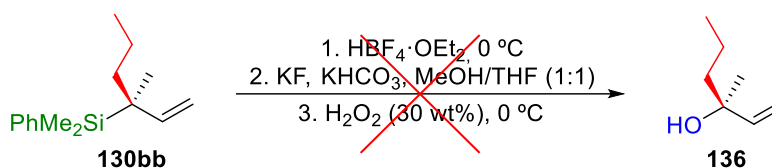
2.4.4.1 Silyl moiety derivatization

In our project, triethylsilyl and dimethylphenylsilyl groups, were envisioned as the silicon moieties not only to demonstrate the high tolerance of our reaction towards different silicon groups but also because they could provide access to different type of interesting molecules. We visualized the PhMe_2Si -substituted allylsilanes as a platform to access tertiary enantioenriched chiral alcohols through the Tamao-Fleming oxidation while the TES-substituted ones will allow to synthesize stereodefined homoallylic alcohols or amines, as they are ideal substrates to perform a Hosomi-Sakurai reaction (under investigation in the laboratory).

2.4.4.1.1 Tamao-Fleming oxidation

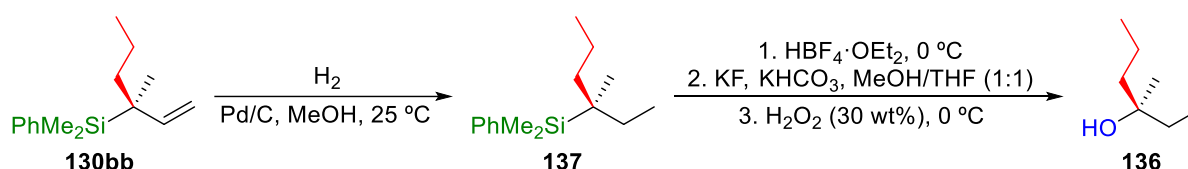
Since Tamao-Fleming oxidation was firstly described by Fleming *et al.* in 1984,^[195] the PhMe_2Si - group has extensively been used as a masked hydroxyl group (silicon groups possess certain properties complementary to hydroxy groups or any protected form of them). This transformation allows the synthesis of alcohol from silanes through the conversion of the C-Si bond into the C-O bond with possible retention of the stereogenic carbon atom configuration.

Unfortunately, under described conditions of $\text{HBF}_4 \cdot \text{OEt}_2$ (2.5 equiv) in CH_2Cl_2 at $0\text{ }^\circ\text{C}$ for 1h, KF (2.1 equiv) and KHCO_3 (5.7 equiv) in THF/MeOH at $0\text{ }^\circ\text{C}$ for 30 min then addition of H_2O_2 at $0\text{ }^\circ\text{C}$ for 5 h, allylsilane **130bb** did not give the desired alcohol **136** (**Scheme 161**).



Scheme 161. Tamao-Fleming oxidation of allylsilane **130bb**.

Considering some reported literature^[162] and ^1H NMR analysis of the crude that showed the disappearance of the carbon-carbon double bond and the methyl substituents of the silicon atom, same reaction was tested after reduction of the corresponding double bond (**Scheme 162**).



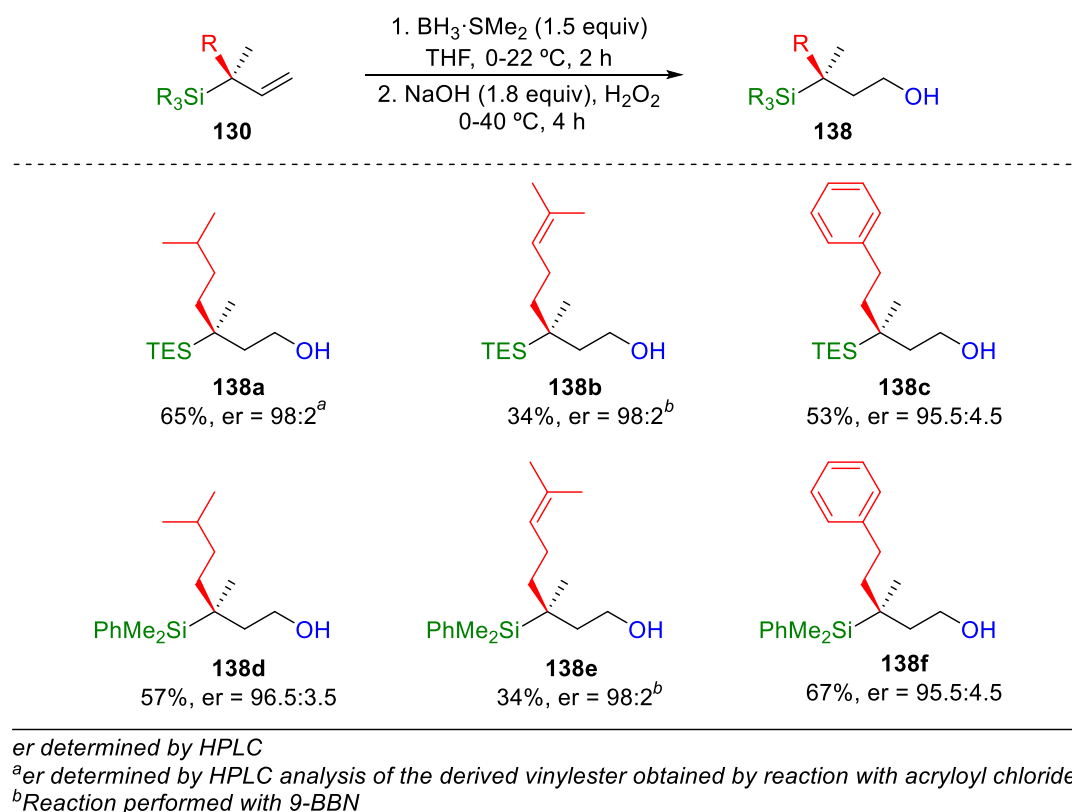
Scheme 162. Synthesis sequence for the preparation of alcohol **132** through a Tamao-Fleming oxidation reaction.

The ^1H NMR analysis of the crude **136** did not show any trace of the $\text{PhMe}_2\text{Si-}$ moiety, indicating a possible successful Tamao-Fleming oxidation. However, the desired alcohol could not be isolated after column and further experiments are under investigation in the laboratory.

2.4.4.2 Double bond functionalization

2.4.4.2.1 Hydroboration-oxidation

Based on previous results, *anti*-Markovnikov γ -alkyl- γ -silyl alcohol derivatives were synthesized through the hydroboration-oxidation sequence using $\text{BH}_3 \cdot \text{SMe}_2$ as the boron source. In the cases where a double hydroboration was possible (allylsilanes **130ad** and **130bd**), 9-BBN was employed instead of $\text{BH}_3 \cdot \text{SMe}_2$ (**Scheme 147**).

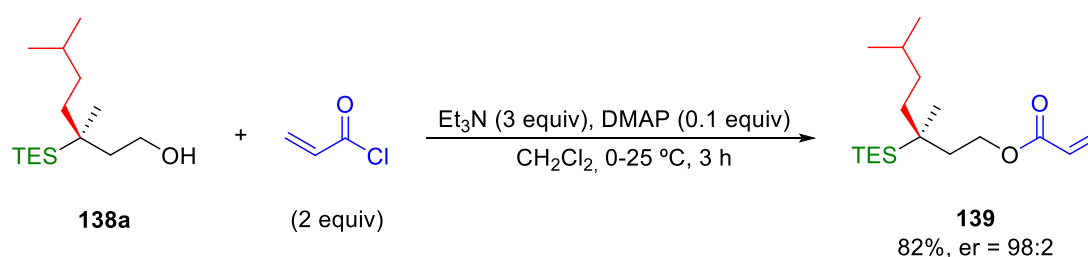


Scheme 163. Palette of alcohols accessed through hydroboration oxidation sequence on allylsilanes bearing silyl-substituted quaternary stereogenic centres.

The targeted γ -silyl-substituted chiral alcohols were isolated in moderate to good yields (34-67%) and perfect regioselectivity without observing any trace of their corresponding Markovnikov adducts.

2.4.4.2.2 Esterification

Interestingly, we also demonstrated their utility as suitable alcohols to perform esterifications in the presence of carbonyl chloride derivatives. When alcohol **138a** was set in the presence of 2 equiv of acryloyl chloride, 3 equiv triethylamine and 0.1 equiv of DMAP in CH_2Cl_2 at 0 °C then 3 h at rt, ester **139** was obtained in 82% yield and er = 98:2 (**Scheme 164**).



Scheme 164. Synthesis of vinyl ester **139** from chiral allylsilane **138a**.

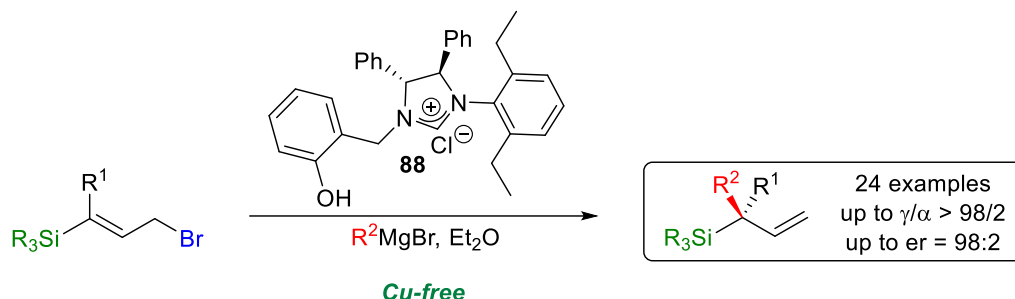
2.4.5 Partial conclusion

The copper-free AAS was successfully implemented to access enantioenriched allylsilanes bearing silyl-substituted quaternary stereogenic centres. In this regard, two set of allylsilanes bearing different silyl moieties were prepared. In comparison with the previous investigated tertiary analogues, better levels of enantioselectivity have been observed when primary alkyl Grignard reagents were used in the reaction. The main limitation of the reaction is that aryl-substituted stereogenic quaternary centres cannot be accessed enantioselectively. The double bond geometry of the allylic electrophile was also demonstrated to play a key role in the stereo-outcome of the reaction as only (*E*)-isomers led to both high regio- and enantioselective levels.

The functionalization of these molecules was not achieved. Nevertheless, γ -silyl substituted alcohols could be prepared through hydroboration-oxidation.

General Conclusion and Outlook

This PhD work relates the development of a copper-free AAS method for the preparation of chiral enantioenriched allylsilanes bearing tertiary and quaternary silyl-substituted stereogenic centres. The asymmetric allylic substitution of allylbromides could be performed in the absence of copper by using Alexakis type NHC-ligand and Grignard reagents as chiral inductors and nucleophile respectively (**Scheme 165**).

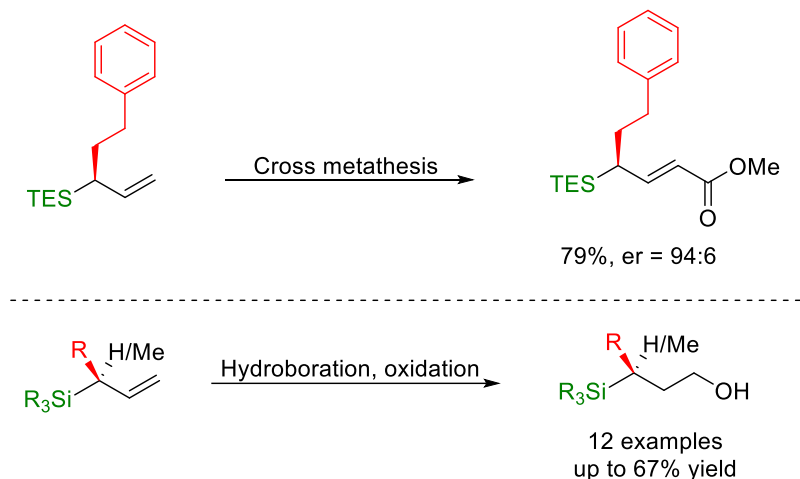


Scheme 165. Preparation of enantioenriched allylsilanes by copper-free AAS of allylic bromides.

Firstly, this work was devoted to the development and optimization of this AAS reaction for the preparation of allylsilanes bearing tertiary silyl-substituted stereogenic centres. Several ligand and electrophile investigations determined imidazolium salt **88** and bromide as the most suitable ligand and leaving group to perform the reaction. Subsequently, the high tolerance of the reaction towards different silicon moieties were proved. Four different silyl groups (Me_2PhSi -, TMS-, TES- and $t\text{BuMe}_2\text{Si}$ -) were successfully introduced, obtaining the corresponding allylsilanes in excellent γ -selectivity (up to $\gamma/\alpha > 98/2$) and remarkable enantiomeric excess (up to er = 93:7). Subsequently, the reaction scope was expanded and different primary, secondary and tertiary Grignard reagents were successfully tested, furnishing the corresponding allylsilanes with different levels of regio- (up to $\gamma/\alpha > 98/2$) and enantioselectivities (up to er = 94:6). As a general trend, higher the bulkiness of the Grignard reagents, lower levels of regio- and enantioselectivity were observed. This trend was exacerbated for aryl Grignard reagents, as almost completely lost of enantioselectivity was observed (er < 56:44%).

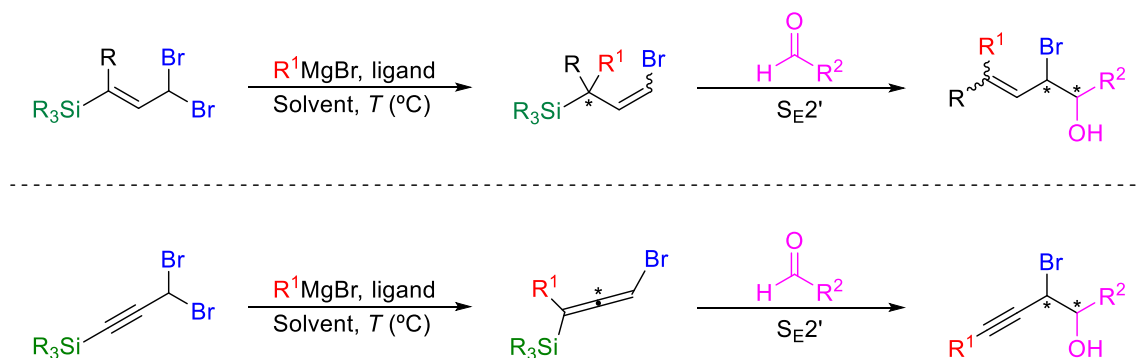
Having tested the success of the reaction for the preparation of allylsilanes bearing tertiary silyl-substituted stereogenic centres, their applicability to the synthesis their quaternary analogues was implemented. In this regard, two sets of compounds bearing PhMe_2Si - and TES-moieties were obtained with primary alkyl Grignard reagents. The corresponding quaternary analogues were obtained in better regio- and enantioselective levels than those described in literature, exhibiting perfect γ -selectivity and er up to > 98:2. On the contrary, bulky Grignard reagents (secondary, tertiary and aromatic) were less tolerated when compared to their tertiary analogues. The preparation of allylbromide (**Z**-**124a**) allowed us to evaluate the impact of the double bond geometry on the reaction outcome, revealing that it plays a key role regarding the enantioselective outcome of the reaction.

Finally, although these valuable molecules can be subjected to many different transformations and functionalizations through their silicon moiety or through their double bond, only cross-metathesis and hydroboration-oxidation transformations were successfully developed (**Scheme 166**).



Scheme 166. Chiral allylsilane derivatization and functionalization.

On the base of the results obtained, it can be envisioned to apply the copper free AAS to allylic dihalides and prochiral propargylic dihalides. In the first case, substituted allylic silanes would be generated with a defined stereocentre and controlled carbon-carbon bond geometry in a single step, while the propargylic halide would furnish enantioenriched haloallenylsilanes. In both cases, they would be useful versatile scaffolds to perform further functionalizations. For instance, they could be used to access complex molecules with two contiguous stereogenic centres through S_E2' reactions with aldehydes (**Scheme 167**).



Scheme 167. Copper-free AAS preparation of γ -substituted allyl- and allenylsilanes. Functionalization through S_E2' reaction with aldehydes.

PART III:

EXPERIMENTAL SECTION

3 Experimental section

3.1 General information

All reactions were carried out under argon atmosphere unless otherwise stated. Reactions were run in flask or Schlenk tubes with magnetic stirrings. Glassware was dried under vacuum or taken directly from the oven and let cool under vacuum prior to use.

Reagents and solvents were purchased from commercial sources and generally used without purification. Et₂O and CH₂Cl₂ were dried on a Mbraun purification system MB SPS-800. THF from the MB SPS-800 was distilled over sodium and benzophenone under nitrogen flow prior to utilization.

NMR spectra (¹H, ¹³C) were recorded on a Bruker AM 300 MHz or a Bruker AVANCE 400 MHz spectrometer. NMR experiments were carried out at room temperature in CDCl₃. Chemical shifts are given in parts per million (ppm) using the CDCl₃ residual non-deuterated signals as reference (δ ¹H = 7.26 ppm; δ ¹³C = 77.16 ppm). The terms m, s, d, t and q represent multiplet, singlet, doublet, triplet and quartet, respectively. The term (br.) is used when the peak is broad, and the correct multiplicity cannot be assigned unambiguously. Coupling constants (*J*) are given in Hertz (Hz). For previously unknown compounds, a combination of ¹H, ¹³C and 2D experiment was used.

IR spectra were recorded with a Tensor 27 (ATR diamond) Bruker spectrometer and reported as characteristic bands (cm⁻¹). High-resolution mass spectra (ESI-MS, APCI-MS) were acquired using an LTQ-Orbitrap XL from Thermo Scientific (Thermo Fisher Scientific, Courtaboeuf, France) operated in positive ionization mode.

TLC were performed on Merck 60 F254 silica gel and revealed with either an ultra-violet lamp (λ = 254 nm) or a specific color reagent (potassium permanganate, *p*-anisaldehyde, etc.). A silica gel Merck Geduran(*R*) SI 60 (40-63 μ m) was used for flash column chromatography along with the indicated solvents.

Optical rotations were measured on JASCO P-2000 polarimeter at 25 °C in a 10 cm cell in the stated solvent with $[\alpha]_D$ values reported in 10⁻¹ (°·cm² g⁻¹); concentration *c* given as g/100 mL.

Enantiomeric excesses were determined by chiral gas chromatography (GC) measurement on an Agilent GC 7890A (Injector: 220 °C, split ratio 20, FID detector: 300 °C, H₂ as vector gas) equipped with a CP-Chirasil Dex CB (25m × 0.32 mm × 0.25 μ m) or Cyclosil-B (30m × 0.25 mm × 0.25 μ m). Temperature programs are described as follows: initial T (°C) - initial times (min) - temperature gradient (°C/min) - final T (°C); retention times (RT) are given

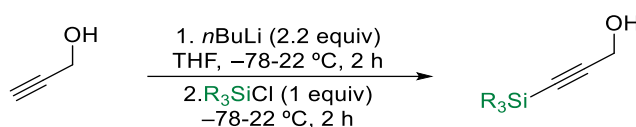
in min. In some cases, the enantiomeric excess was determined by High-performance liquid chromatography (HPLC) measurement on a Shimadzu SIL-20AHT instrument, with appropriated program in a chiral stationary phase using Daicel Chiralcel OD-H (4.6 x 250 mm) or Daicel Chiralcel AD-H (4.6 x 250 mm) column (hexane/iPrOH mixtures as solvent) in comparison with authentic racemic materials.

The absolute configuration was determined by comparison with described compounds. For the new products it was assigned by analogy.

3.2 Preparation of starting materials

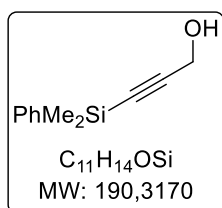
3.2.1 (*E*)- γ -Silyl-substituted allylic electrophiles

3.2.1.1 Preparation of silylated propargyl alcohols

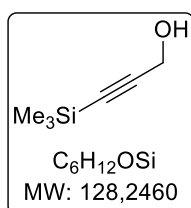


General procedure GP1: Following reported procedures,^[162] in a flame-dried flask under Argon atmosphere, propargyl alcohol (1 equiv) is diluted in dry THF (to reach 0.2 M) and cool down to $-78\text{ }^{\circ}\text{C}$ (liquid nitrogen/acetone bath). *n*BuLi (2.2 equiv from a solution in hexanes) is added dropwise through a syringe and the reaction is allowed to slowly warm to room temperature. After 2 h at room temperature, the mixture is allowed to cool down to $-78\text{ }^{\circ}\text{C}$ (liquid nitrogen/acetone bath) and the corresponding chlorosilane (1 equiv) is added dropwise through a syringe. The solution is allowed to warm to room temperature over 12 h. The reaction mixture is quenched with HCl (1 M) and diluted with Et₂O. The layers are separated and the aqueous layer is extracted three times with Et₂O. The combined organic fractions are washed with brine, dried over MgSO₄, filtered and concentrated under reduce pressure. The residue is purified by silica gel chromatography.

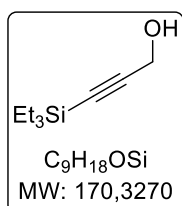
3-(Dimethylphenylsilyl)-prop-2-yn-1-ol (**93a**)



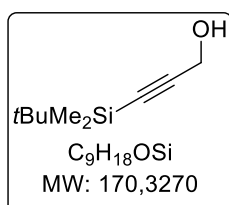
Prepared according to **GP1** from the reaction of propargyl alcohol (2.0 mL, 34.4 mmol) with *n*BuLi (27.5 mL of a 2.5 M solution in hexanes, 68.8 mmol) and PhMe₂SiCl (5.9 mL, 34.4 mmol) in dry THF (172 mL). The residue is purified by flash column chromatography (from pentane to pentane:Et₂O 9:1, *R_f* = 0.4) to afford the desired product **93a** (5.20 g, 27.9 mmol) in 81% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.65-7.61 (m, 2H), 7.41-7.37 (m, 3H), 4.31 (d, *J* = 6.2 Hz, 2H), 1.72 (t, *J* = 6.2 Hz, 1H, OH), 0.44 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 136.6, 133.8, 129.7, 128.1, 105.6, 88.9, 51.9, -0.9 . These data are in good agreement with those reported in literature.^[118]

3-(Trimethylsilyl)-prop-2-yn-1-ol (93b)

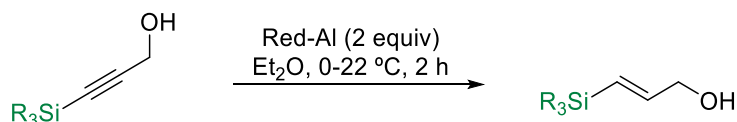
Prepared according to **GP1** from the reaction of propargyl alcohol (1.0 mL, 17.2 mmol) with *n*BuLi (22.5 mL of a 1.6 M solution in hexanes, 68.8 mmol) and $(\text{CH}_3)_3\text{SiCl}$ (2.2 mL, 17.2 mmol) in dry THF (85 mL). The residue is concentrated to afford the desired product **96b** (1.83 g, 14.2 mmol) in 81% yield and used without further purification. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.26 (s, 2H), 0.18 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 104.0, 90.8, 51.8, -0.1 . These data are in good agreement with those reported in literature.^[118,196]

3-(Triethylsilyl)-prop-2-yn-1-ol (93c)

Prepared according to **GP1** from the reaction of propargyl alcohol (2.5 mL, 43.0 mmol) with *n*BuLi (37.8 mL of a 2.5 M solution in hexanes, 94.6 mmol) and $(\text{CH}_3\text{CH}_2)_3\text{SiCl}$ (7.1 mL, 43.0 mmol) in dry THF (215 mL). The residue is purified by flash column chromatography (from pentane to pentane:Et₂O 95:5, R_f = 0.35) to afford the desired product **93c** (5.25 g, 30.8 mmol) in 71% yield along with 10% of TES-OH. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.26 (d, J = 6.1 Hz, 2H), 2.02 (t, J = 6.1 Hz, 1H, OH), 0.99 (t, J = 8.0 Hz, 6H, TES-OH), 0.95 (t, J = 8.2 Hz, 6H), 0.60 (q, J = 8.0 Hz, 9H, TES-OH), 0.58 (q, J = 7.8 Hz, 9H). No $^{13}\text{C NMR}$. Commercially available.²

3-(*tert*-Butylsilyl)-prop-2-yn-1-ol (93d)

Prepared according to **GP1** from the reaction of propargyl alcohol (2.0 mL, 34.4 mmol) with *n*BuLi (27.5 mL of a 2.5 M solution in hexanes, 68.8 mmol) and *t*BuMe₂SiCl (5.2 g, 34.4 mmol) in dry THF (172 mL). The residue is purified by flash column chromatography (from pentane to pentane:Et₂O 9:1, R_f = 0.3) to afford the desired product **93d** (2.11 g, 12.4 mmol) in 36% yield. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.27 (d, J = 6.0 Hz, 2H), 1.83 (t, J = 6.1 Hz, 1H), 0.93 (s, 9H), 0.11 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 104.6, 89.0, 51.8, 26.2, 16.6, -4.6 . These data are in good agreement with those reported in literature.^[196]

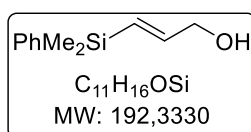
3.2.1.2 Preparation of (*E*)- γ -silyl substituted allylic alcohols

General procedure GP2: Following reported procedures,^[118] to a stirred solution of the appropriate silylated propargylic alcohols (1 equiv) in Et₂O (to reach 0.5 M) at 0 °C (ice-bath),

² Supplier: Ambinter, ABCR Gute Chemie or Aurora Fine Chemicals LLC.

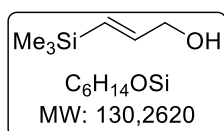
Red-Al (2 equiv from a 3.54 M solution in toluene) are added dropwise through a syringe as a solution in Et₂O (to reach 0.3 M). The solution is allowed to warm at room temperature over 3 h and then slowly quenched at 0 °C by the addition of H₂O and H₂SO₄ (3.6 M). The resulting solution is diluted with Et₂O and H₂O. The layers are separated and the aqueous layer washed with Et₂O three times. The combined organic layers are washed with a saturated solution of brine, dried over MgSO₄, filtered and concentrated under reduce pressure. The residue is purified.

(*E*)-1-Dimethylphenylsilyl-prop-1-en-2-ol (**94a**)



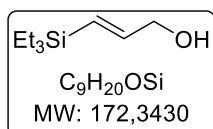
Prepared according to **GP2** from the reaction of propargyl alcohol **93a** (3.61 g, 19.0 mmol) and Red-Al (10.7 mL, 38.0 mmol, diluted in 8.7 mL of Et₂O) in dry Et₂O (43.9 mL). The residue is purified by flash column chromatography (from pentane to pentane:Et₂O 5:1, R_f = 0.3) to afford the desired product **94a** (2.93 g, 15.2 mmol) in 80% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.57-7.53 (m, 2H), 7.40-7.36 (m, 3H), 6.26 (dt, *J* = 18.7, 4.2 Hz, 1H), 6.07 (dt, *J* = 18.9, 1.7 Hz, 1H), 4.22 (ddd, *J* = 6.0, 4.2, 1.7 Hz, 2H), 1.49 (t, *J* = 6.0 Hz, 1H, OH), 0.37 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 146.8, 138.6, 134.0, 129.2, 128.0, 127.3, 65.6, -2.5. These data are in good agreement with those reported in literature.^[118]

(*E*)-1-(Trimethylsilyl)-prop-1-en-2-ol (**94b**)



Prepared according to **GP2** from the reaction of propargyl alcohol **93b** (2.73 g, 21.3 mmol) and Red-Al (12.1 mL, 42.6 mmol, diluted in 9.8 mL of Et₂O) in dry Et₂O (49.2 mL). The residue is purified by flash column chromatography (from pentane to pentane:Et₂O 5:1, R_f = 0.3) to afford the desired product **94b** (1.88 g, 14.5 mmol) in 68% yield. ¹H NMR (400 MHz, CDCl₃) δ 6.19 (dt, *J* = 18.8, 4.3 Hz, 1H), 5.92 (dt, *J* = 18.8, 1.8 Hz, 1H), 4.18 (br. s, 2H), 1.44 (br. s, 1H, OH), 0.08 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 144.9, 129.7, 65.7, -1.2. These data are in good agreement with those reported in literature.^[118,197]

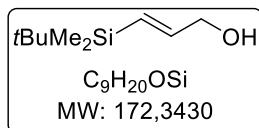
(*E*)-1-(Triethylsilyl)-prop-1-en-2-ol (**94c**)



Prepared according to **GP2** from the reaction of propargyl alcohol **93c** (contained TESOH) (5.25 g, 30.5 mmol) and Red-Al (17.2 mL, 61.0 mmol, diluted in 14.0 mL of Et₂O) in dry Et₂O (70.5 mL). The residue is purified by distillation (150 °C, 70 torr) to afford the desired product **94c** (2.31 g, 13.4 mmol) in 44% yield. ¹H NMR (400 MHz, CDCl₃) δ 6.21 (dt, *J* = 18.9, 4.4 Hz, 1H), 5.85 (dt, *J* = 18.9, 1.8 Hz, 1H), 4.19 (ddd, *J* = 6.1, 4.4, 1.8 Hz, 2H), 1.43 (t, *J* = 6.0 Hz, 1H, OH), 0.94 (t, *J* = 7.9 Hz, 9H), 0.58

(q, $J = 7.9$ Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 146.2, 125.9, 65.9, 7.5, 3.5. These data are in good agreement with those reported in literature.^[198]

(*E*)-1-(*tert*-Butyldimethylsilyl)-prop-1-en-2-ol (**94d**)

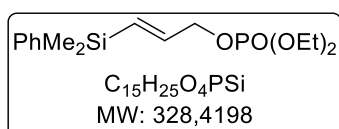


Prepared according to **GP2** from the reaction of propargyl alcohol **93d** (4.23 g, 25.7 mmol) and Red-Al (14.5 mL, 51.5 mmol, diluted in 11.8 mL of Et_2O) in dry Et_2O (59.3 mL). The residue is purified by flash column chromatography (from pentane to pentane: Et_2O 5:1, $R_f = 0.3$) to afford the desired product **94d** (3.26 g, 14.5 mmol) in 74% yield. ^1H NMR (400 MHz, CDCl_3) δ 6.20 (dt, $J = 18.8$, 4.4 Hz, 1H), 5.92 (dt, $J = 18.9$, 1.7 Hz, 1H), 4.20 (ddd, $J = 5.8$, 4.1, 1.7 Hz, 2H), 1.43 (t, $J = 5.6$ Hz, 1H, OH), 0.88 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 146.3, 126.8, 65.8, 26.6, 16.6, -6.0 . These data are in good agreement with those reported in literature.^[199]

3.2.1.3 Preparation of (*E*)-Allylic electrophiles

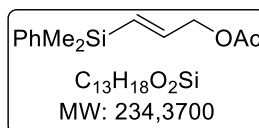
(*E*)-3-(Diethoxyphosphoryloxy)-1-(dimethylphenylsilyl)-1-propene (**104**)

To a stirred solution of **94a** (0.192 g, 1.0 mmol) in CH_2Cl_2 (2.5 mL) place in a dry flask under Argon atmosphere, DMAP (26.0 mg, 0.21 mmol) and Et_3N (0.21 mL, 1.5 mmol) are added. Chlorodiethylphosphate (0.23 mL, 1.5 mmol) is added at 0 °C (ice bath) and the reaction is allowed to stir at 22 °C for 12 h. The mixture is quenched by the addition of a saturated solution of NH_4Cl (10 mL) and diluted with CH_2Cl_2 (10 mL). The layers are separated and the aqueous layer is washed three times with CH_2Cl_2 . The combined organic layers are washed with brine, dried over Mg_2SO_4 and concentrated in vacuo. The resulting yellow oil is



purified by silica gel chromatography (from cyclohexane: EtOAc 3:1 to 1:1 $R_f = 0.25$) to obtain **104** (245 mg, 0.75 mmol) in 75% as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.52-7.48 (m, 2H), 7.37-7.34 (m, 3H), 6.13 (br. s, 2H), 4.57 (ddd, $J = 8.0$, 2.2, 1.0 Hz, 2H), 4.11 (m, 4H), 1.32 (dt, $J = 7.1$, 1.0 Hz, 6H), 0.36 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 141.5, 141.4, 138.1, 133.9, 131.0, 129.3, 128.0, 69.5, 69.4, 64.0, 63.9, 16.3, 16.2, -2.7 . These data are in good agreement with those reported in literature.^[118]

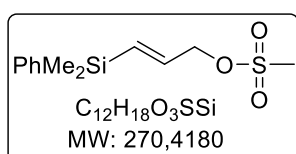
(*E*)-3-Acetate-1-(dimethylphenylsilyl)-1-propene (**105**)



To a stirred solution of **94a** (0.192 g, 1.0 mmol) in CH_2Cl_2 (4.0 mL) place in a dry flask under Argon atmosphere, DMAP (12.5 mg, 0.1 mmol) and Et_3N (0.43 mL, 3.0 mmol) are added. Acetyl chloride (0.15 mL, 2 mmol) is added during 2-3 minutes at 0 °C. After stirring at room temperature for 3 h, the reaction mixture is quenched with saturated aqueous NH_4Cl (5 mL). The layers are

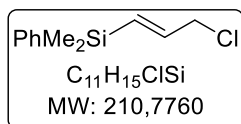
separated and the aqueous layer is washed three times with CH_2Cl_2 . The combined organic extracts are washed with brine. Finally, the organic layer is dried over MgSO_4 , the solvent is removed under reduced pressure. The residue is purified by silica gel chromatography (from pentane to pentane: Et_2O 20:1 R_f = 0.2) to obtain **105** (0.154 g, 0.70 mmol) in 70% as a yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 7.54-7.50 (m, 2H), 7.38-7.36 (m, 3H), 6.14 (dt, J = 18.6, 4.4 Hz, 1H), 6.06 (dt, J = 18.8, 1.1 Hz, 1H), 4.63 (dd, J = 4.3, 1.0 Hz, 2H), 2.10 (s, 3H), 0.37 (s, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 170.8, 141.2, 138.2, 134.0, 131.1, 129.3, 128.0, 66.8, 21.1, -2.6. **IR**: ν (cm^{-1}) 3069, 2954, 1743, 1624, 1428, 1361, 1231, 1113, 1028, 837, 822, 786, 732, 700. **HRMS**: m/z calculated for $\text{C}_{13}\text{H}_{22}\text{O}_2\text{SiN}$ $[\text{M}+\text{NH}_4]^+$ 252.1414, found 252.1416.

(*E*)-3-Methylsulfonyl-1-(dimethylphenylsilyl)-1-propene (**106**)

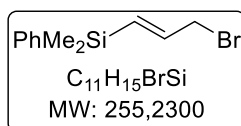


To a stirred solution of **94a** (0.192 g, 1.0 mmol) in CH_2Cl_2 (4.3 mL) is added Et_3N (0.35 mL, 2.5 mmol) at 0 °C. Methanesulfonyl chloride (0.15 mL, 2.0 mmol) is added at 0 °C (ice bath) and the reaction is allowed to stir at 22 °C for 4 h. The mixture is quenched by the addition of water and diluted with CH_2Cl_2 (10 mL). The layers are separated and the organic layer is washed three times with Et_2O . The combine organic layers are washed with brine, dried over Mg_2SO_4 and concentrate under reduced pressure. The resulting yellow oil is purified by silica gel chromatography (pentane: Et_2O 4:1 R_f = 0.25) to obtain **106** (138,2 mg, 0.51 mmol) in 51% as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 7.54-7.48 (m, 2H), 7.40-7.36 (m, 3H), 6.24 (dt, J = 18.6, 1.4 Hz), 6.12 (dt, J = 18.6, 5.0 Hz), 4.74 (dd, 5.1, 1.2 Hz), 2.89 (s, 3H), 0.39 (s, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 138.7, 137.5, 134.8, 133.9, 129.5, 128.1, 71.7, 38.1, -2.8. **IR**: ν (cm^{-1}) 2957, 2918, 2850, 1625, 1428, 1356, 1174, 1113, 1044, 935, 818, 731, 701. **HRMS**: m/z calculated for $\text{C}_{12}\text{H}_{22}\text{O}_3\text{SSiN}$ $[\text{M}+\text{NH}_4]^+$ 288.1084, found 288.1084.

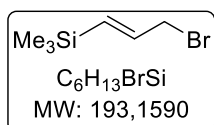
(*E*)-3-Chloro-1-(dimethylphenylsilyl)-1-propene (**108**)



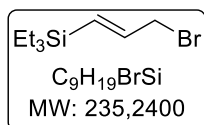
To a stirred solution of **94a** (192 mg, 1.0 mmol) in dry CH_2Cl_2 (2.0 mL) place in a dry flask under Argon atmosphere, NCS (214 mg, 1.6 mmol) and PPh_3 (393 mg, 1.5 mmol) are sequentially added at 0 °C. After 10 minutes, the bath is removed and the mixture is allowed to warm to 22 °C over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug with pentane to obtain **108** (181.8 mg, 0.86 mmol) in 86% as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 7.53-7.49 (m, 2H), 7.39-7.35 (m, 3H), 6.21-6.06 (m, 2H), 4.10 (d, J = 4.5 Hz), 0.38 (s, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 142.3, 138.0, 134.0, 132.7, 129.34, 128.0, 47.3, -2.7. These data are in good agreement with those reported in literature.^[200]

(E)-3-Bromo-1-(dimethylphenylsilyl)-1-propene (95a)

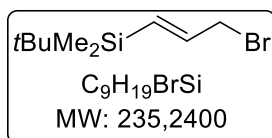
To a stirred solution of **94a** (192 mg, 1.0 mmol) in dry CH₂Cl₂ (2.0 mL) place in a dry flask under Argon atmosphere, NBS (195 mg, 1.1 mmol) and PPh₃ (314 mg, 1.2 mmol) are sequentially added at 0 °C. After 10 minutes, the bath is removed and the mixture is allowed to warm to 22 °C over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug with pentane to obtain **95a** (183.5 mg, 0.86 mmol) in 78% as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 7.56-7.48 (m, 2H), 7.40-7.34 (m, 3H), 6.33 (dt, 18.3, 6.4 Hz, 1H), 6.08 (d, 18.1 Hz), 3.98 (dd, *J* = 6.6, 1.5 Hz), 0.37 (s, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 142.5, 137.9, 134.0, 133.7, 129.4, 128.0, 35.1, -2.7. **IR**: ν (cm⁻¹) 3069, 3013, 2956, 2899, 1611, 1428, 1250, 1201, 1113, 1048, 984, 894, 837, 786, 731, 699, 647. **HRMS**: Ongoing experiments.

(E)-3-Bromo-1-(trimethylsilyl)-1-propene (95b)

To a stirred solution of **94b** (130 mg, 1.0 mmol) in dry CH₂Cl₂ (2.0 mL) place in a dry flask under Argon atmosphere, NBS (195 mg, 1.1 mmol) and PPh₃ (314 mg, 1.2 mmol) are sequentially added at 0 °C. After 10 minutes, the bath is removed and the mixture is allowed to warm to 22 °C over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug with pentane to obtain **95b** (70.5 mg, 0.37 mmol) in 37% as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 6.14 (dt, *J* = 18.2, 6.5 Hz, 1H), 5.95 (d, *J* = 18.4 Hz, 1H), 3.95 (dd, *J* = 6.8, 1.3 Hz), 0.09 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 140.8, 135.9, 35.4, -1.4. These data are in good agreement with those reported in literature.^[197]

(E)-3-Bromo-1-(triethylsilyl)-1-propene (95c)

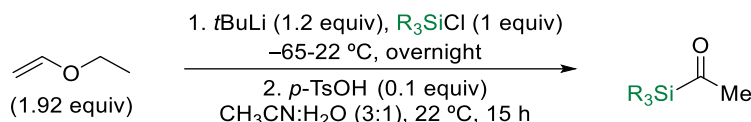
To a stirred solution of **94c** (0.430 g, 2.5 mmol) in dry CH₂Cl₂ (5.0 mL) place in a dry flask under Argon atmosphere, NBS (0.490 g, 2.8 mmol) and PPh₃ (0.787 g, 3.0 mmol) are sequentially added at 0 °C. After 10 minutes, the bath is removed and the mixture is allowed to warm to 22 °C over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug with pentane to obtain **95c** (0.538 g, 2.25 mmol) in 91% as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 6.17 (dt, *J* = 18.4, 6.9 Hz, 1H), 5.89 (d, *J* = 18.4 Hz, 1H), 3.97 (dd, 6.9, 1.1 Hz, 2H), 0.94 (t, *J* = 7.9 Hz, 2H), 0.59 (q, *J* = 7.9 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 142.2, 132.3, 35.5, 7.4, 3.4. **IR**: ν (cm⁻¹) 2954, 2910, 2875, 1610, 1458, 1416, 1252, 1200, 1046, 1016, 785, 756, 720. **HRMS**: Ongoing experiments.

(E)-3-Bromo-1-(*tert*-butylsilyl)-1-propene (95d)

To a stirred solution of **94d** (0.862 g, 5.0 mmol) in dry CH_2Cl_2 (10.0 mL) place in a dry flask under Argon atmosphere, NBS (0.978 g, 5.5 mmol) and PPh_3 (1.573 g, 6.0 mmol) are sequentially added at 0 °C. After 10 minutes, the bath is removed and the mixture was allowed to warm to 22 °C over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug with pentane to obtain **95d** (0.949 g, 4.05 mmol) in 81% as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 6.17 (dt, $J = 18.3, 6.8$ Hz, 1H), 5.95 (d, $J = 18.2$, 1H), 3.97 (dd, $J = 6.9, 1.4$ Hz, 2H), 0.88 (s, 9H), 0.04 (s, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 142.2, 133.2, 35.4, 26.5, 16.7, -6.1. These data are in good agreement with those reported in literature.^[201]

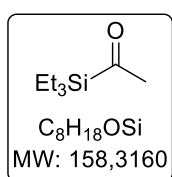
3.2.2 γ -Silyl- γ -substituted allylic electrophiles

3.2.2.1 Preparation of acylsilanes



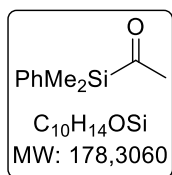
General procedure GP3: Following reported procedures,^[118] in a flame-dried flask, ethyl vinyl ether (1.92 equiv) is dissolved in dry THF (to reach 1.4 M) and cool at $-65\text{ }^{\circ}\text{C}$ (dry ice/acetone bath). *t*BuLi (1.2 equiv from a 1.7 M solution in pentane) is added dropwise through a syringe. The solution is allowed to warm to $0\text{ }^{\circ}\text{C}$. After 1 h the solution is allowed to recool to $-78\text{ }^{\circ}\text{C}$ (dry ice/acetone bath) and the corresponding silyl chloride (1 equiv) is added slowly. The solution was allowed to warm to $22\text{ }^{\circ}\text{C}$ and allowed to stir for 15 h. The reaction is quenched by the addition of HCl (1 M) and the resulting solution is diluted with Et₂O and poured into a separatory funnel. The layers are separated and the aqueous layer washed with Et₂O three times. The combined organic layers are washed with brine, dried with MgSO₄, filtered and concentrated to yield the corresponding unpurified 1-(trialkylsilyl)-1-ethoxyethene as a yellow oil. The yellow oil was dissolved in CH₃CN:H₂O (3:1, to reach 0.3 M) and *p*-TsOH (0.1 equiv) is added. The solution is allowed to stir for 1 h, at which time it was poured into a separatory funnel and washed three times with EtOAc, brine, dried with MgSO₄, filtered and concentrated in vacuo. The resulting yellow oil is purified.

1-(Triethylsilyl)-ethanone (**121a**)



Prepared according to **GP3** from the reaction of ethyl vinyl ether (20.0 mL, 209 mmol) with *t*BuLi (76.6 mL), triethylsilyl chloride (18.0 mL, 108 mmol) and *p*-TsOH (3.58 g, 21 mmol). The residue is purified by flash column chromatography (cyclohexane:Et₂O 95:5, $R_f = 0.3$) to obtain **121a** (8.06 g, 50.95 mmol) in 47% as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.24 (s, 3H), 0.97 (t, $J = 7.9$ Hz, 9H), 0.73 (q, $J = 7.9$ Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 247.4, 37.5, 7.3, 2.2. These data are in good agreement with those reported in literature.^[202]

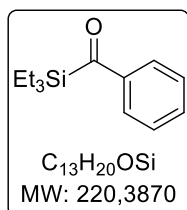
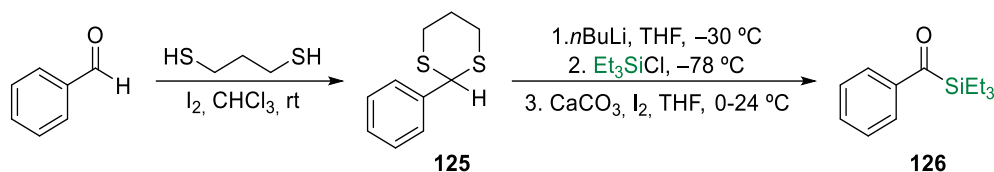
1-(Dimethylphenylsilyl)-ethanone (**121b**)



Prepared according to **GP3** from the reaction of ethyl vinyl ether (2.5 mL, 26.0 mmol) with *t*BuLi (16.3 mL), dimethylphenylsilyl chloride (2.3 mL, 13.6 mmol) and *p*-TsOH (0.51 g, 2.6 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 95:5, $R_f = 0.4$) to obtain **121b** (1.30 g, 7.3 mmol) in 54% as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.58-7.54 (m, 2H), 7.47-7.36

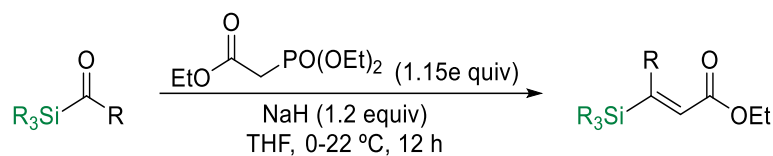
(m, 3H), 2.24 (s, 3H), 0.50 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 245.5, 134.4, 134.1, 130.1, 128.3, 36.1, -4.7. These data are in good agreement with those reported in literature.^[118]

Benzoyltriethylsilane (**126**)



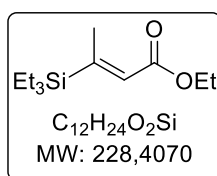
Following reported procedures,^[203] to a stirred solution of benzaldehyde (2.5 mL, 25.5 mmol) and 1,3-propanedithiol (2.8 mL, 27.5 mmol) in CHCl_3 (100.0 mL) at room temperature, I_2 (0.634 g, 2.5 mmol) is added. After 1 h, the reaction is quenched with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$, the layers are separated and the aqueous layer washed with CHCl_3 three times. The combined organic layers are washed with brine, dried with MgSO_4 , filtered and concentrated to yield the **125**, that is diluted in dry THF (60 mL). The reaction mixture is allowed to cool until $-30\text{ }^\circ\text{C}$ and $n\text{BuLi}$ (13.1 mL of a 2.3 M solution in hexanes, 30.1 mmol) is added dropwise. After 2 h at room temperature, the reaction is allowed to cool down to $-78\text{ }^\circ\text{C}$ (dry ice/acetone bath) and triethylsilyl chloride (5.5 mL, 32.8 mmol) is added dropwise, then the reaction is allowed to warm to $0\text{ }^\circ\text{C}$. After 12 h at this temperature, the reaction is quenched with a saturated solution of NH_4Cl , the layers are separated and the aqueous layer washed with CHCl_3 three times. The combined organic layers are washed with brine, dried with MgSO_4 , filtered and concentrated. The residue is diluted in THF: H_2O (4:1) and the reaction mixture is cool down to $0\text{ }^\circ\text{C}$, then CaCO_3 (8.1 equiv) and I_2 (6.1 equiv) are added. After 2 h at room temperature, the reaction is quenched with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$, the layers are separated and the aqueous layer washed with CH_2Cl_2 three times. The combined organic layers are washed with brine, dried with MgSO_4 , filtered and concentrated. The residue is purified by flash column chromatography (pentane: Et_2O 99:1, $R_f = 0.8$) to obtain **126** (1.37 g, 6.22 mol) in 24% as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.82-7.78 (m, 2H), 7.56-7.44 (m, 3H), 1.03-0.96 (m, 9H), 0.95-0.87 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 142.6, 132.8, 128.8, 127.3, 7.6, 3.8. These data are in good agreement with those reported in literature.^[204]

3.2.2.2 Preparation of γ -silyl- γ -substituted α,β -unsaturated esters



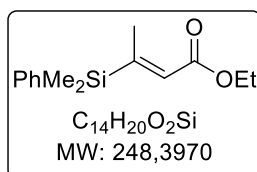
General procedure GP4: Following reported procedures,^[118] to a stirred solution of NaH (1.2 equiv) in dry THF (to reach 0.3 M) is added triethylphosphonoacetate (1.15 equiv) at 0 °C (ice bath). After 0.5 h, the corresponding acylsilane (1 equiv) is added through a syringe and the mixture is allowed to warm to 22 °C over 12 h. The reaction is quenched by the addition of a saturated solution of NH_4Cl and diluted with Et_2O . The layers were separated, and the aqueous layer washed three times with Et_2O , brine, dried with MgSO_4 , filtered and concentrated in vacuo. The resulting yellow oil is purified.

(*E*)-Ethyl 3-(triethylsilyl)-but-2-enoate (**(E)-122a**)

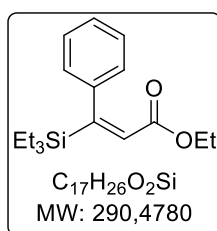


Prepared according to **GP4** from the reaction of NaH (0.50 g, 12.4 mmol), triethylphosphonoacetate (2.36 mL, 11.9 mmol) and acylsilane **121a** (1.63 g, 10.3 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 99:1, R_f = 0.4) to obtain **(E)-122a** (1.18 g, 5.15 mmol) in 50% as pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 6.00 (q, J = 1.8 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.20 (d, J = 1.7 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.9 Hz, 9H), 0.65 (q, J = 7.9 Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.7, 160.1, 127.5, 59.8, 17.9, 14.5, 7.4, 2.3. These data are in good agreement with those reported in literature.^[205]

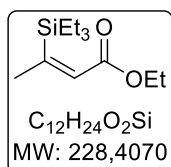
(*E*)-Ethyl 3-(dimethylphenylsilyl)-but-2-enoate (**122b**)



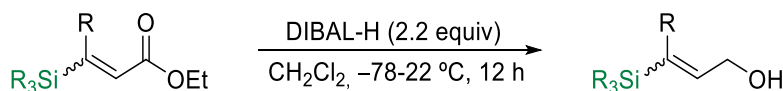
Prepared according to **GP4** from the reaction of NaH (1.35 g, 33.8 mmol), triethylphosphonoacetate (6.4 mL, 32.4 mmol) and acylsilane **121b** (5.02 g, 28.2 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 99:1, R_f = 0.35) to obtain **122b** (3.22 g, 12.95 mmol) in 46% as pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.53-7.46 (m, 2H), 7.41-7.33 (m, 3H), 6.09 (q, J = 1.8 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 2.19 (d, J = 1.8 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H), 0.42 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.8, 160.0, 136.3, 134.2, 129.6, 128.1, 127.9, 17.64, 14.5, -3.8. These data are in good agreement with those reported in literature.^[118]

(E)-Ethyl-3-phenyl-3-(triethylsilyl)acrylate (127)

Prepared according to **GP4** from the reaction of NaH (298 mg, 7.5 mmol), triethylphosphonoacetate (1.41 mL, 7.2 mmol) and acylsilane **126** (1.63 g, 10.3 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 99:1, *R_f* = 0.4) to obtain **127** (0.61 g, 2.17 mmol) in 35% as pale yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 7.31-7.26 (m, 2H), 7.20 (tt, *J* = 7.4, 1.2 Hz, 1H), 6.93 (dd, *J* = 7.2, 1.3 Hz, 2H), 6.19 (s, 1H), 3.95 (q, *J* = 7.1 Hz, 2H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.63 (q, *J* = 8.1 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.3, 161.2, 142.2, 129.3, 127.9, 126.0, 60.0, 14.0, 7.3, 2.5. **IR:** ν (cm⁻¹) 2954, 2910, 2876, 1731, 1710, 1416, 1344, 1239, 1190, 1073, 1037, 734, 718, 700. **HRMS:** *m/z* calculated for C₁₇H₂₇O₂Si [M+H]⁺ 291.1775, found 291.1775.

(Z)-Ethyl-3-(triethylsilyl)-but-2-enoate ((Z)-122a)

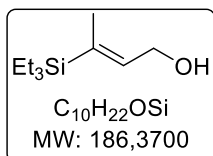
To a stirred solution of 1,1,1,3,3,3-hexamethyldisilazane (0.76 mL, 3.6 mmol) in THF (10 mL) is added *n*BuLi (1.40 mL, 3.6 mmol from a 2.5 M in hexanes) at 0 °C (ice-bath). After 20 min, the reaction is allowed to cool down to -78 °C (dry ice/acetone bath) and ethyl (trimethylsilyl)acetate (0.66 mL, 3.6 mmol) in dry THF (3.0 mL) is added, continuing the stirring for 15 min. Then, acylsilane **121a** (0.50 g, 3.0 mmol) in dry THF (3.0 mL). After 1 h, the reaction is allowed to warm to room temperature and let stirring overnight. The reaction is quenched by the addition of a saturated solution of NH₄Cl. The layers were separated, and the aqueous layer washed three times with Et₂O, brine, dried with MgSO₄, filtered and concentrated in vacuo. The resulting yellow oil is purified by silica gel chromatography (pentane:Et₂O 99:1, *R_f* = 0.40) to obtain **(Z)-122a** (0.27 g, 1.17 mmol) in 39% as a yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 6.37 (q, *J* = 1.7 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.98 (d, *J* = 1.8 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 9H), 0.78 (q, *J* = 7.7 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.7, 160.0, 131.7, 60.0, 27.2, 14.4, 3.3. **IR:** ν (cm⁻¹) 2953, 2910, 2874, 1719, 1601, 1445, 1368, 1330, 1193, 1108, 1044, 1007, 975, 869, 730, 686. **HRMS:** *m/z* calculated for C₁₀H₁₉O₂Si [M-C₂H₅]⁺ 199.1149, found 199.1152.

3.2.2.3 Preparation of γ -silyl- γ -substituted allylic alcohols

General procedure GP5: Following reported procedures,^[118] a solution of the corresponding enoate (1 equiv) in dry CH₂Cl₂ (to reach 0.5 M) is added dropwise to DIBAL-H (2.2 equiv from a 1 M solution in hexanes) solution in CH₂Cl₂ at -78 °C (dry ice/acetone bath).

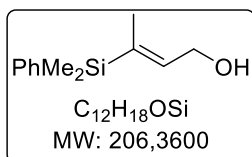
After 4 h, the reaction mixture is allowed to warm to 22 °C over 12 h. The reaction is quenched at –78 °C (dry ice/acetone bath) by the addition of a saturated solution of NaHCO₃ and the mixture is allowed to stir for 15 minutes before being filtered through a celite pad. The celite pad is rinsed with CH₂Cl₂ and the recovered solvent is dried over MgSO₄, filtered and concentrated under reduced pressure. The resulting colorless oil is purified or used without further purification.

(*E*)-3-(Triethylsilyl)-but-2-en-1-ol ((*E*)-123^a)



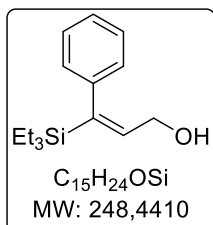
Prepared according to **GP5** from the reaction of (***E***-122^a) (1.12 g, 4.9 mmol) and DIBAL-H (10.8 mL, 10.8 mmol). The product (***E***-123^a) (0.81 g, 4.33 mmol) is obtained in 88% as a colorless oil and used without further purification. ¹H NMR (400 MHz, CDCl₃) δ 5.86 (tq, *J* = 5.6, 1.7 Hz, 1H), 4.28 (dd, *J* = 5.9, 1.0 Hz, 2H), 1.69 (dt, *J* = 1.8, 0.9 Hz, 2H), 1.20 (br. s, 1H, OH), 0.92 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.7 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 139.3, 136.7, 59.9, 15.5, 7.5, 2.6. (note: quaternary C peak missing). Commercially available.³

(*E*)-3-(Dimethylphenylsilyl)-but-2-en-1-ol ((*E*)-123^b)



Prepared according to **GP5** from the reaction of (**122^b**) (3.67 g, 14.8 mmol) and DIBAL-H (32.6 mL, 32.6 mmol). The product (***E***-123^b) (2.91 g, 14.1 mmol) is obtained in 95% as a colorless oil and used without further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.52-7.48 (m, 2H), 7.39-7.33 (m, 3H), 5.96 (tq, *J* = 5.9, 1.7 Hz, 1H), 4.29 (dd, *J* = 6.0, 0.9 Hz, 7H), 1.70 (dt, *J* = 1.9, 0.9 Hz, 3H), 1.31 (br. s, 1H, OH) 0.36 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 139.9, 138.0, 137.5, 134.1, 129.1, 127.9, 59.9, 15.1, –3.6. These data are in good agreement with those reported in literature.^[118]

(*E*)-3-Phenyl-3-(triethylsilyl)-prop-2-en-1-ol (**128**)

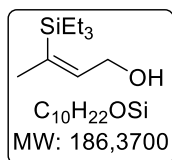


Prepared according to **GP5** from the reaction of **127** (0.58 g, 2.0 mmol) and DIBAL-H (4.4 mL, 4.4 mmol). The residue is purified by silica gel chromatography (pentane:Et₂O 9:1, R_f = 0.3) to obtain **128** (0.36 g, 1.46 mmol) in 73% as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.26 (m, 2H), 7.19 (tt, *J* = 7.4, 1.3 Hz, 1H), 6.93 (dd, *J* = 7.7, 1.3 Hz, 2H), 6.12 (t, *J* = 6.0 Hz, 1H), 4.04 (dd, *J* = 6.2, 3.5 Hz), 1.31 (br. s, 1H, OH), 0.92 (t, *J* = 7.9 Hz, 9H), 0.60 (m, *J* = 8.0 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 144.4, 142.0, 140.9, 128.3, 127.3, 125.9, 61.0, 7.4. IR: ν (cm^{–1}) 3335, 2954, 2910, 2875, 1596, 1490, 1458, 1417, 1237, 1019,

³ Supplier: Aurora Fine Chemicals LLC.

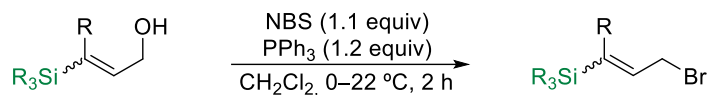
764, 732, 718, 702, 683. **HRMS**: m/z calculated for $C_{15}H_{24}SiO$ $[M+H]^+$ 249.1669, found 249.1669.

(*Z*)-3-(Triethylsilyl)-but-2-en-1-ol ((*Z*)-123a)



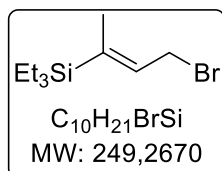
A solution of (**Z**)-122a (1.26 g, 6.8 mmol) in dry CH_2Cl_2 (14.0 mL) is added dropwise to DIBAL-H (14.9 mL, 14.9 mmol from a 1 M solution in hexanes) solution in CH_2Cl_2 (9 mL) at $-78\text{ }^\circ\text{C}$ (dry ice/acetone bath). After 4 h, the reaction mixture is allowed to warm to $22\text{ }^\circ\text{C}$ over 12 h. The reaction is quenched at $-78\text{ }^\circ\text{C}$ (dry ice/acetone bath) by the addition of a saturated solution of $NaHCO_3$ and the mixture is allowed to stir for 15 minutes before being filtered through a celite pad. The celite pad is rinsed with CH_2Cl_2 and the recovered solvent are dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue is purified by silica gel chromatography (pentane:Et₂O 9:1, $R_f = 0.3$) to obtain (**Z**)-123a (0.895 g, 4.79 mmol) in 71% as a colorless oil. **¹H NMR** (400 MHz, $CDCl_3$) δ 6.23 (tq, $J = 7.0, 1.8$ Hz, 1H), 4.13 (m, 2H), 1.81 (s, 3H), 1.22 (t, $J = 5.5$ Hz, 1H, OH), 0.94 (t, $J = 7.9$ Hz, 9H), 0.66 (q, $J = 7.9$ Hz, 4H). **¹³C NMR** (101 MHz, $CDCl_3$) δ 141.5, 137.5, 62.3, 25.4, 7.6, 4.2. These data are in good agreement with those reported in literature.^[206]

3.2.2.4 Preparation of γ -silyl- γ -substituted allylic bromides

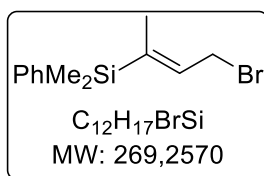


General procedure GP6: To a stirred solution of the corresponding alcohol (1 equiv) in dry CH_2Cl_2 (to reach 0.5 M) place in a dry flask under Argon atmosphere, NBS (1.1 equiv) and PPh_3 (1.2 equiv) are sequentially added at $0\text{ }^\circ\text{C}$. After 10 minutes, the bath is removed and the mixture is allowed to warm to $22\text{ }^\circ\text{C}$ over 2 h. The resulting solution is diluted with pentane and filtered through a silica plug to recover the corresponding bromide after evaporation.

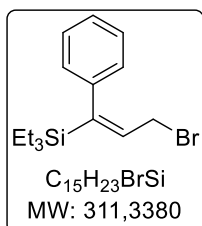
(*E*)-1-(Bromo)-3-(triethylsilyl)-2-butene ((*E*)-124^a)



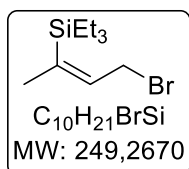
Prepared according to **GP6** from the reaction of (**E**)-123a (1.34 g, 7.2 mmol), NBS (1.41 g, 7.9 mmol) and PPh_3 (2.26 g, 8.7 mmol). The product (**E**)-124a (1.61 g, 6.47 mmol) is obtained in 90% as a colorless oil. **¹H NMR** (400 MHz, $CDCl_3$) δ 6.00 (tq, $J = 7.9, 1.8$ Hz, 1H), 4.03 (d, $J = 7.9$ Hz, 2H), 1.77 (d, $J = 1.8$ Hz, 3H), 0.92 (t, $J = 7.9$ Hz, 9H), 0.61 (q, $J = 7.9$ Hz, 6H). **¹³C NMR** (101 MHz, $CDCl_3$) δ 141.7, 134.7, 27.5, 14.8, 7.4, 2.5. **IR**: ν (cm^{-1}) **HRMS**: 2953, 2910, 2875, 1609, 1457, 1417, 1201, 1008, 735, 716, 670. **HRMS**: Ongoing experiments.

(E)-1-(Bromo)-3-(dimethylsilyl)-2-butene ((E)-124b)

Prepared according to **GP6** from the reaction of **(E)-123b** (0.64 g, 3.1 mmol), NBS (0.61 g, 3.4 mmol) and PPh₃ (0.90 g, 3.7 mmol). The product **(E)-124b** (0.565 g, 2.12 mmol) is obtained in 68% as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.53-7.47 (m, 2H), 7.40-7.34 (m, 3H), 6.10 (tq, *J* = 7.9, 1.8 Hz, 1H), 4.04 (d, *J* = 7.9 Hz, 2H), 1.78 (d, *J* = 1.8 Hz, 3H), 0.38 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 142.4, 137.5, 135.2, 134.1, 129.3, 27.4, 14.6, -3.6. These data are in good agreement with those reported in literature.^[207]

(E)-1-(Bromo)-3-phenyl-3-(triethylsilyl)-2-propene (129)

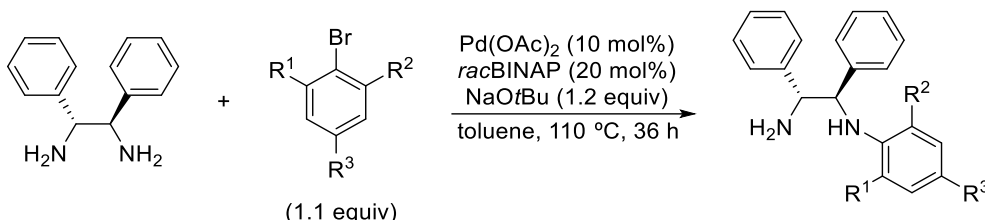
Prepared according to **GP6** from the reaction of **128** (0.36 g, 1.5 mmol), NBS (0.28 g, 1.6 mmol) and PPh₃ (0.46 g, 1.7 mmol). The product **129** (0.25 g, 0.82 mmol) is obtained in 55% as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.22 (tt, *J* = 7.5, 1.3 Hz, 1H), 6.99 (dd, *J* = 8.2, 1.4 Hz, 2H), 6.21 (t, *J* = 7.8 Hz, 1H), 3.80 (d, *J* = 7.8 Hz, 2H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.59 (q, *J* = 7.9 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 147.6, 140.7, 136.4, 128.4, 127.2, 126.2, 29.4, 7.3, 2.8. IR: ν (cm⁻¹) 3026, 2953, 2910, 2875, 1602, 1488, 1204, 734, 718, 689. HRMS: *m/z* calculated for C₁₅H₂₄SiBr [M+H]⁺ 311.0825, found 311.0823.

(Z)-1-(bromo)-3-triethylsilyl-2-butene ((Z)-124a)

Prepared according to **GP6** from the reaction of **(Z)-123a** (0.66 g, 2.7 mmol), NBS (0.52 g, 2.9 mmol) and PPh₃ (0.84 g, 3.2 mmol). The product **(Z)-124a** (0.539 g, 2.19 mmol) is obtained in 82% as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 6.28 (tq, *J* = 8.5, 1.7 Hz, 1H), 4.02 (d, *J* = 8.5 Hz, 2H), 1.84 (dt, *J* = 1.7, 0.9 Hz, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.71 (q, *J* = 8.0 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 140.7, 137.9, 32.6, 25.4, 7.6, 4.0. IR: ν (cm⁻¹) 2953, 2910, 2875, 1698, 1458, 1201, 1006, 732, 718, 702, 677. HRMS: Ongoing experiments.

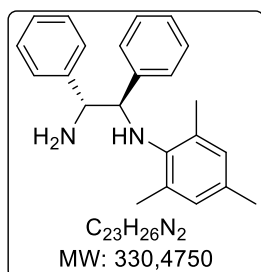
3.2.3 Synthesis of NHC ligands

3.2.3.1 Preparation of (*R,R*)-*N*-aryl-1,2-diphenylethylenediamines



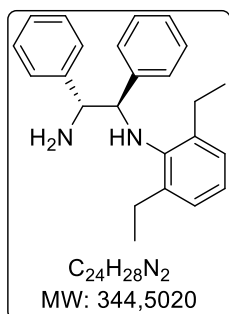
General procedure GP7: Following reported procedures,^[175] in a flame-dried flask under Argon atmosphere equipped with a stir bar, Pd(OAc)₂ (10 mol %), *rac*BINAP (20 mol %) and NaOtBu (1.2 equiv) are placed and stirred for 1 h in toluene (to reach 0.2 M) at room temperature. Parallely, the (+)-(*R,R*)-1,2-diphenylethylenediamine (1 equiv) and aryl-bromide (1.1 equiv) are dissolved in toluene (to reach 0.2 M) and heated at 110 °C for 15 min, then added to the Pd solution. The mixture is allowed to stir vigorously at 110 °C for 36 h. The mixture is cooled to room temperature and filtered through a celite pad using CH₂Cl₂. The solvent is removed under reduced pressure. The resulting yellow oil was purified.

(*R,R*)-*N*-mesityl-1,2-diphenylethylenediamine (**91c**)



Prepared according to **GP7** from the reaction of (*R,R*)-1,2-diphenyl-1,2-ethylene diamine (1.06 g, 5.0 mmol) and mesetyl bromide (0.83 mL, 5.5 mmol) in the presence of Pd(OAc)₂ (113 mg, 0.5 mmol), *rac*BINAP (0.62 g, 1.0 mmol) and NaOtBu (0.77 g, 8.0 mmol). The residue is purified by flash column chromatography (cyclohexene:Et₂O 6:1, R_f = 0.3) to obtain **91c** (0.93 g, 2.8 mmol) in 56% as pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.7 Hz, 2H), 7.14 (m, 4H), 7.05 (dd, *J* = 7.6, 2.0 Hz, 2H), 6.65 (s, 2H), 4.54 (d, *J* = 6.4 Hz, 0H), 4.42 (d, *J* = 6.3 Hz, 0H), 2.12 (s, 3H), 1.44 (s, 6H). These data are in good agreement with those reported in literature.^[176]

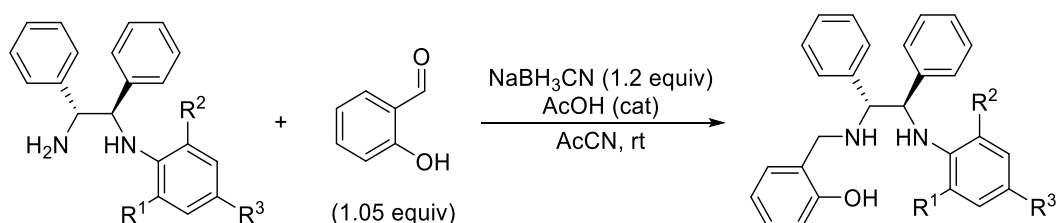
(*R,R*)-*N*-(2,6-diethylphenyl)-1,2-diphenylethylenediamine (**91a**)



Prepared according to **GP7** from the reaction of (*R,R*)-1,2-diphenyl-1,2-ethylene diamine (2.25 g, 10.6 mmol) and 2,6-diethylphenyl bromide (1.97 mL, 5.5 mmol), Pd(OAc)₂ (238 mg, 1.1 mmol), *rac*BINAP (1.46 g, 2.34 mmol) and NaOtBu (1.80 g, 18.7 mmol). The residue is purified by flash column chromatography (cyclohexene:Et₂O 6:1, R_f = 0.3) to obtain **91a** (2.04 g, 5.94 mmol) in 56% as pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.33 (m, 2H), 7.28-7.03 (m, 8H), 6.87 (d, *J*

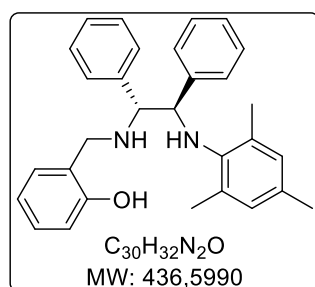
= 7.3 Hz, 2H), 6.78 (t, $J = 7.3$ Hz, 1H), 4.54 (d, $J = 5.9$ Hz, 2H), 4.46 ($J = 5.6$ Hz, 2H), 2.53 (dq, $J = 7.5, 4.6$ Hz, 4H), 1.13 (t, $J = 7.5$ Hz, 6H). These data are in good agreement with those reported in literature.^[176]

3.2.3.2 Preparation of (*R,R*)-*N*-aryl-*N'*-(2-hydroxybenzyl)-1,2-diphenylethylenediamines

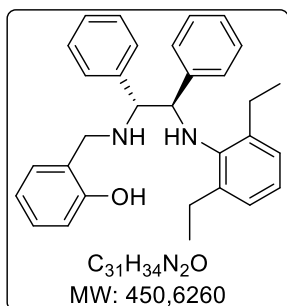


General procedure GP8: Following reported procedures,^[175] in a flame-dried flask under Argon, a solution of the appropriate diamine **91** (1 equiv) in dry CH₃CN (to reach 0.1 M) containing activated molecular sieves is added salicylaldehyde dropwise (1.05 equiv). The mixture is stirred at room temperature for 6 h, then NaBH₃CN (1.2 equiv) and AcOH are added. The mixture is stirred overnight at room temperature. The next day, the reaction was quenched with a saturated solution of NaHCO₃ at room temperature. After 15 min, the layers are separated and the aqueous layer is extracted three times with CH₂Cl₂. The combined organic fractions are washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. The resulting dark yellow oil was purified.

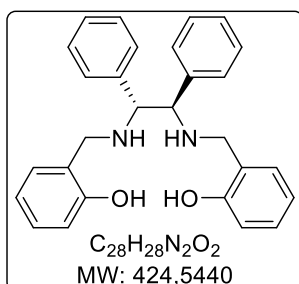
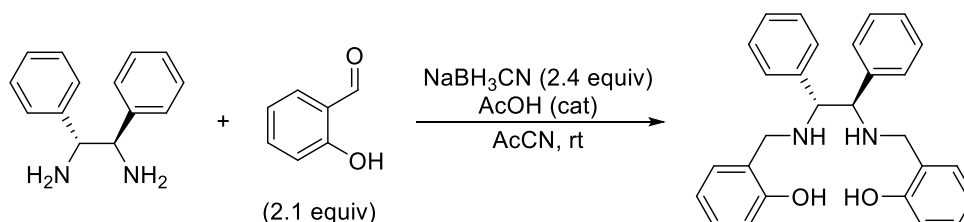
(*R,R*)-*N*-mesityl-*N'*-(2-hydroxybenzyl)-1,2-diphenylethylenediamine (**92c**)



Prepared according to **GP8** from the reaction of **91c** (0.93 g, 2.8 mmol), salicylaldehyde (0.32 mL, 3.0 mmol), NaBH₃CN (0.21 g, 3.4 mmol) and AcOH (0.33 mL). The residue is purified by flash column chromatography (cyclohexene:EtOAc 9:1, $R_f = 0.4$) to obtain **92c** (0.77 g, 1.8 mmol) in 63% as pale yellow bubbled rubber. ¹H NMR (400 MHz, CDCl₃) δ 7.23-7.11 (m, 5H), 7.1-7.04 (m, 3H), 6.95 (d, $J = 7.2$ Hz), 6.93-6.87 (m, 2H), 6.85 (d, $J = 7.8$ Hz, 1H), 6.74 (t, 7.4 Hz, 1H), 6.67 (s, 1H), 4.44 (d, $J = 9.5$ Hz, 1H), 4.15 (d, $J = 9.5$ Hz, 1H), 3.89 (d, $J = 13.4$ Hz, 1H), 3.78 (d, $J = 13.4$ Hz, 1H), 2.14 (s, 3H), 2.09 (s, 6H). These data are in good agreement with those reported in literature.^[176]

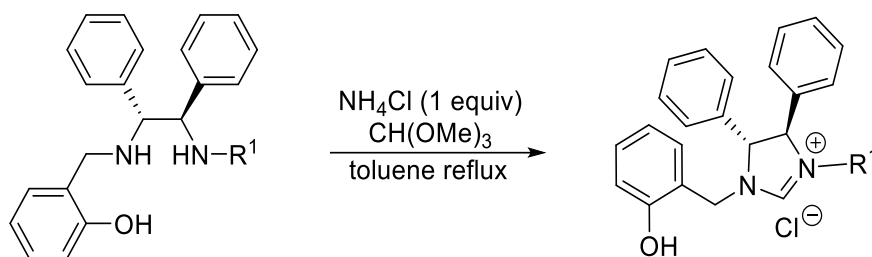
(*R,R*)-*N*-(2,6-diethylphenyl)-*N'*-(2-hydroxybenzyl)-1,2-diphenylethylenediamine (92a)

Prepared according to **GP8** from the reaction of **91a** (2.04 g, 5.92 mmol), salicylaldehyde (0.65 mL, 6.2 mmol), $NaBH_3CN$ (0.45 g, 7.7 mmol) and AcOH (0.70 mL). The residue is purified by flash column chromatography (cyclohexene:EtOAc 9:1, R_f = 0.4) to obtain **92a** (1.69 g, 1.75 mmol) in 64% as pale yellow bubbled rubber. 1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.10 (m, 6H), 7.10-7.03 (m, 3H), 6.98-6.81 (m, 7H), (td, J = 7.4, 1.2 Hz, 2H), 4.43 (t, J = 10.1 Hz, 1H), 4.21 (d, J = 9.4 Hz, 1H), 3.77 (d, J = 13.3 Hz, 1H), 3.52 (d, J = 11.5 Hz, 1H), 2.47 (qd, J = 7.5, 1.3 Hz, 4H), 1.11 (t, J = 7.5 Hz, 6H). These data are in good agreement with those reported in literature.^[176]

3.2.3.3 Preparation of diphenylethylenediamine **98**

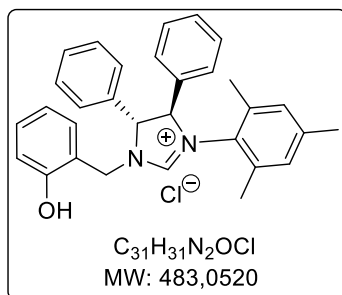
In a flame-dried flask under Argon, a solution (*R,R*)-1,2-diphenyl-1,2-ethylene diamine (0.42 g, 2.0 mmol) in dry CH_3CN (to reach 0.1 M) containing activated molecular sieves is added salicylaldehyde dropwise (0.44 mL, 4.2 mmol). The mixture is stirred at room temperature for 6 h, then $NaBH_3CN$ (0.28 g, 4.8 mmol) and AcOH are added. The mixture is stirred overnight at room temperature. The next day, the reaction is quenched with a saturated solution of $NaHCO_3$ at room temperature. After 15 min, the layers are separated and the aqueous layer is extracted three times with CH_2Cl_2 . The combined organic fractions are washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting dark yellow oil was purified by flash column chromatography (pentane:Et₂O 2:1) to obtain **98** (59 mg, 0.014 mmol) in 7% as pale yellow bubbled rubber. 1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.21 (m, 6H), 7.22-7.11 (m, 2H), 6.94 (m, 4H), 6.87 (d, J = 8.1 HZ, 2H), 6.76 (m, 4H), 4.02 (s, 2H), 3.86 (d, J = 13.7 Hz, 2H), 3.61 (d, J = 13.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 137.5, 129.1, 128.7, 128.6, 128.2, 122.3, 119.4, 116.6, 66.5, 50.3. These data are in good agreement with those reported in literature.^[208]

3.2.3.4 Preparation of chloride imidazolium salts



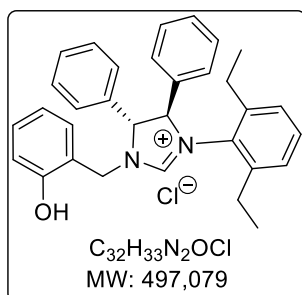
General procedure GP9: Following reported procedures, in a flame-dried flask under Argon equipped with a condenser, the appropriate diamine (1 equiv) and dry NH_4Cl (1.1 equiv) are charged and dissolved in dry toluene (to reach 0.25 M). $\text{CH}(\text{OMe})_3$ (23 equiv) are added and the mixture is heated to reflux for 16 h. The reaction is allowed to cool to room temperature and the solvent is removed under reduced pressure. The bubbled solid is triturated with Et_2O using ultrasound bath and filtered. The recovered solid is washed with cold Et_2O and dried into high vacuum. Due to hygroscopic property of the imidazolium salt, it must be kept under inert atmosphere. They were kept in the freezer at -22°C .

Imidazolium salt (87)



Prepared according to **GP** from the reaction of **92c** (0.771 g, 1.77 mmol), NH_4Cl (95 mg, 1.77 mmol) and $\text{CH}(\text{OMe})_3$ (4.42 mL, 40.62 mmol). The residue is triturated in Et_2O to obtain **87** (504 mg, 1.04 mmol) in 59% as pale yellow powder. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.68 (br. s, 1H), 9.60 (s, 1H), 7.52-7.22 (m, 4H), 7.38-7.30 (m, 2H), 7.29-7.14 (m, 4H), 6.98 (m, 2H), 6.75-6.60 (m, 3H), 6.44 (m, 1H), 5.18 (d, $J = 8.5$ Hz, 1H), 5.08 (d, $J = 8.5$ Hz, 1H), 2.38 (s, 3H), 2.08 (s, 3H), 1.88 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 159.0, 157.1, 139.6, 136.9, 135.4, 134.5, 133.7, 131.0, 130.8, 130.2, 130.1, 130.1, 130.0, 129.9, 129.8, 128.7, 127.3, 126.5, 119.3, 117.9, 117.8, 75.3, 69.6, 66.0, 48.5, 31.0, 21.0, 19.0, 18.5, 15.4. $[\alpha]_D^{20}$ 74.560 ($c = 0.500$, CHCl_3) These data are in good agreement with those reported in literature.^[176]

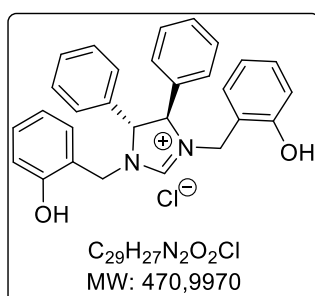
Imidazolium salt (88)



Prepared according to **GP** from the reaction of **92a** (1.69 g, 3.75 mmol), NH_4Cl (0.201 g, 3.75 mmol) and $\text{CH}(\text{OMe})_3$ (9.4 mL, 86.25 mmol). The residue is triturated in Et_2O to obtain **88** (1.39 g, 2.78 mmol) in 74% as pale yellow powder. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.50 (br. s, 1H), 9.59 (s, 1H), 7.58 (d, $J = 8.2$ Hz, 1H), 7.48 (m, 3H), 7.34-7.14 (m, 7H), 7.07 (d, $J = 7.4$ Hz, 1H), 6.95 (d, $J = 7.4$ Hz, 2H), 6.85 (dd, $J = 7.6$ Hz, 1H), 6.70 (m, 1H), 6.64 (m, 1H), 5.84 (d, $J = 14.3$ Hz, 1H), 5.29 (d,

$J = 8.4$ Hz, 1H), 5.06 (d, $J = 8.4$ Hz, 1H), 4.08 (d, $J = 14.3$ Hz, 1H), 2.78 (dq, $J = 15.1$, 7.6 Hz, 1H), 2.61 (dq, $J = 14.9$, 7.5 Hz, 1H), 2.44 (dq, $J = 15.0$, 7.4 Hz, 1H), 1.99 (dq, $J = 15.1$, 7.5 Hz, 1H), 1.32 (t, $J = 7.5$ Hz, 3H), 0.79 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.8, 157.3, 143.4, 140.7, 135.4, 133.3, 131.0, 130.9, 130.2, 130.2, 130.1, 130.0, 130.0, 129.4, 128.8, 127.2, 127.1, 126.7, 119.4, 118.2, 118.1, 76.3, 69.4, 58.4, 48.6, 31.0, 24.6, 23.6, 18.5, 15.1, 14.9. $[\alpha]_{\text{D}}^{20}$ 99.120 ($c = 0.500$, CHCl_3) These data are in good agreement with those reported in literature.^[176]

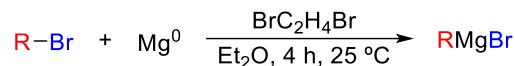
Imidazolium salt (**99**)



Prepared according to **GP** from the reaction of **98** (59 mg, 0.143 mmol), NH_4Cl (8 mg, 0.146 mmol) and $\text{CH}(\text{OMe})_3$ (0.363 mL, 3.36 mmol). The residue is triturated in Et_2O to obtain **99** (41 mg, 0.09 mmol) in 59% as pale yellow powder. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.40 (br. s, 2H), 9.17 (s, 1H), 7.46-7.35 (m, 6H), 7.24-7.11 (m, 6H), 7.03 (d, $J = 8.1$ Hz, 2H), 6.96 (dd, $J = 7.5$, 1.7 Hz, 2H), 6.74 (t, $J = 7.2$ Hz, 2H), 4.85 (d, $J = 14.4$ Hz, 2H), 4.70 (s, 2H), 4.10 (d, $J = 14.4$ Hz, 2H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 158.3, 156.2, 135.9, 130.8, 130.2, 129.5, 129.4, 127.1, 119.1, 118.8, 115.7, 71.4, 46.0. HRMS: m/z calculated for $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 435.2067, found 435.2064. $[\alpha]_{\text{D}}^{20}$ +81.130 ($c = 1.500$, DMSO). These data are in good agreement with those reported in literature.^[209]

3.2.4 Synthesis of Grignard reagents.

3.2.4.1 Classical preparation of Grignard reagents



In a dried three neck flask under Argon atmosphere equipped with a stir bar and a condenser, magnesium (1.46 g, 60.0 mmol) and four drops of 1,2-dibromoethane are covered with dry Et₂O (2.0 mL). After letting the mixture stir 5 minutes at 25 °C, the bromide solution in Et₂O (30.0 mmol, adjusted to 13.0 mL) is added with a syringe pump over 3 h. The reaction mixture is stirred 4 h at 25 °C. The solution is transferred to a septum-closed dry flask or Schlenk under argon by a syringe equipped with a filter, and store in the fridge at 3 °C.

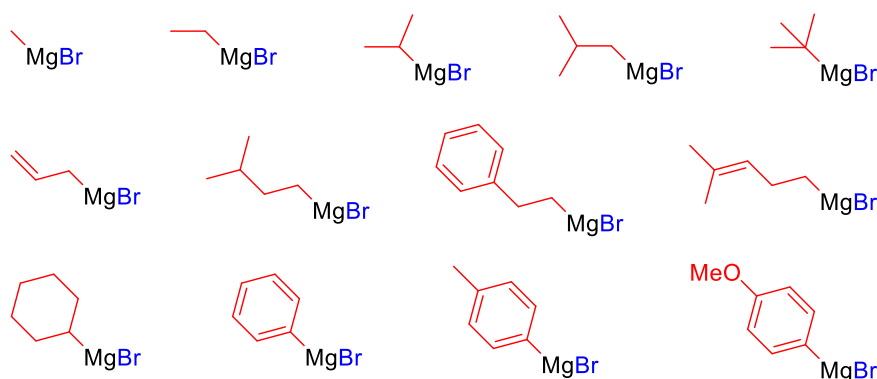
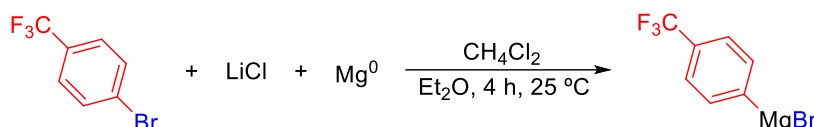


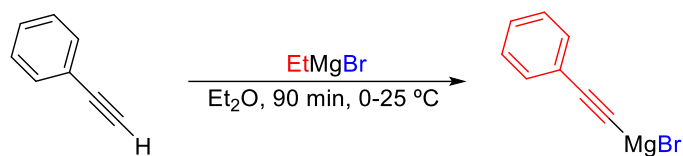
Figure 20: Chart of Grignard reagents synthesized via this procedure.

3.2.4.2 Preparation of Bromo[4-(trifluoromethyl)phenyl]magnesium reagent.



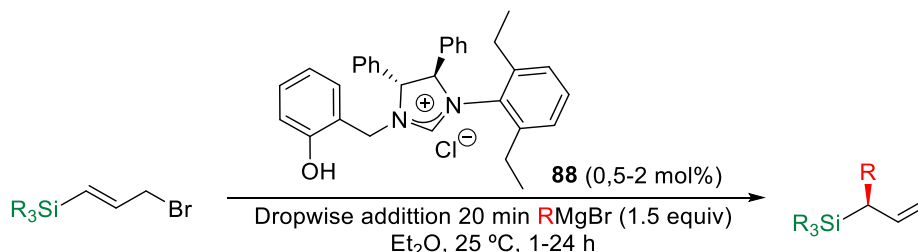
In a dried three neck flask under Argon atmosphere equipped with a stir bar and a condenser, magnesium (1.46 g, 60.0 mmol), dry LiCl (0.38 g, 9.0 mmol) and four drops of CH₂Cl₂ are covered with dry Et₂O (2.0 mL). After letting the mixture stir 5 minutes at 25 °C, the bromide solution in Et₂O (30.0 mmol, adjusted to 13.0 mL) was added with a syringe pump over 3 h. The reaction mixture was stirred 4 h at 25 °C. The solution is transfer to a septum-closed dry flask or Schlenk under argon by a syringe equipped with a filter, and store in the fridge at 3 °C.

3.2.4.3 Preparation of phenylalkynyl Grignard reagent

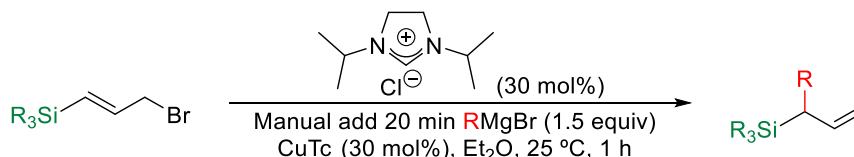


To a stirred solution of phenylacetylene (3.29 mL, 30.0 mmol) in Et₂O (11.7 mL) was slowly added EtMgBr (11 mL of a 2.6 M solution in Et₂O) at 0 °C. After 10 min the mixture is allowed to warm to 25 °C over 1 h. The solution is transfer to a septum-closed dry flask or Schlenk under argon by a syringe and store in the fridge at 3 °C.

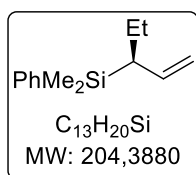
3.3 Synthesis of allylsilanes bearing tertiary silyl-substituted stereogenic centres



General procedure GP10: In a flame-dried Schlenk under Argon atmosphere equipped with a stir bar, the appropriate allylbromide derivative (0.3 mmol) and NHC-ligand **88** (0.5-2 mol%) are suspended in dry Et_2O (adjusted to 1.4 mL depending on the Grignard reagent volume) and stir at 25°C . A solution of Grignard reagent RMgBr (1.5 equiv in Et_2O) is added dropwise over 20 min. After complete conversion, the mixture is diluted with 1 mL of THF and quenched by addition of K_2CO_3 (23.5 mg, 0.17 mmol) and benzylamine (0.02 mL, 0.19 mmol). After 15 min, the mixture is diluted with 2 mL of Et_2O and 5 mL of H_2O . The aqueous layer is separated and extracted with Et_2O (3 x 5 mL). The combined organic fractions are washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue is purified by flash column chromatography to offer a mixture of $\text{S}_{\text{N}}2'$ and $\text{S}_{\text{N}}2$ products.

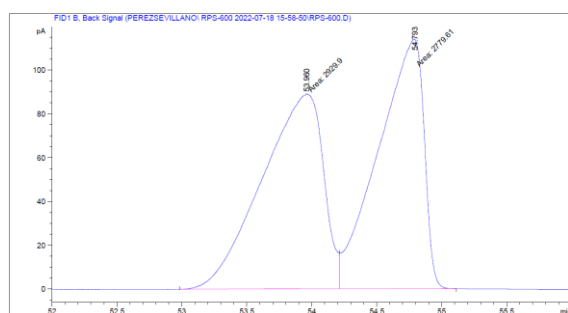


For the preparation of tertiary allylsilane racemates, same procedure **GP10** was used but in the presence of CuTc (30 mol%) and 1,3-diisopropyl imidazolium salt (30 mol %). Desired racemates are obtained with γ/α ratios ranging from 9/91 to 98/2 depending on the substrate.

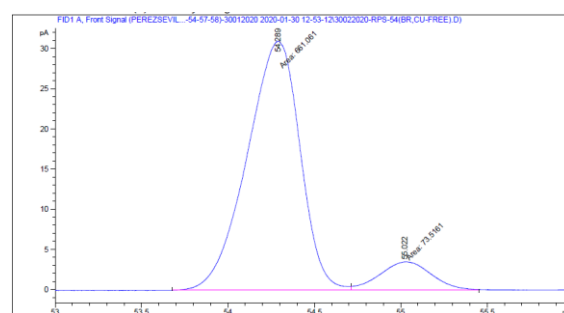
(+)-(S)-3-(Dimethylphenylsilyl)-1-pentene (96)

 Mixture $\gamma/\alpha > 98/2$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95a** (76.6 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **96** (49.1 mg, 0.24 mmol) in 80% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.57-7.47 (m, 2H), 7.39-7.31 (m, 3H), 5.59 (m, 1H), 4.91 (dd, $J = 10.3, 2.1$ Hz, 1H), 4.83 (dd, $J = 17.0, 1.9$ Hz, 1H), 1.68-1.30 (m, 3H), 0.87 (t, $J = 7.3$ Hz, 3H), 0.28 (s, 3H), 0.27 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 139.8, 138.2, 134.2, 129.0, 127.7, 112.8, 36.8, 21.8, 14.3, -43, -5.0. These data are in good agreement with those reported in literature.^[118] The absolute configuration of **96** was assigned by comparison of the optical rotation with a reported value.^[118]

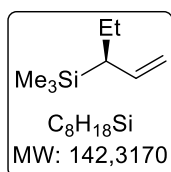
Enantiomeric ratio of 90:10 was determined by chiral GC analysis (CycloSil-B column: 60-0-87-37-25-200). Chromatograms are illustrated below: 54.29 (S), 55.02 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	53.960	MF	0.5484	2929.90479	89.03850	51.31618
2	54.793	FM	0.4068	2779.61011	113.87227	48.68382



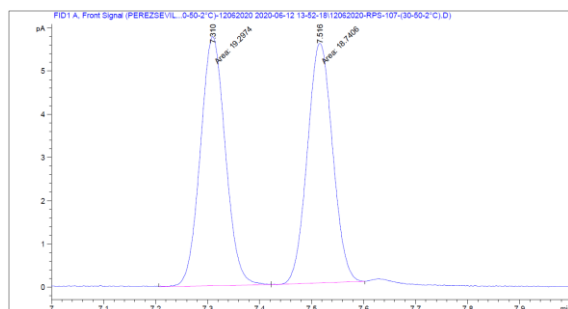
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	54.289	MF	0.3553	661.06134	31.00733	89.99205
2	55.022	FM	0.3471	73.51612	3.52985	10.00795

(+)-(S)-3-(Trimethylsilyl)-1-pentene (112)

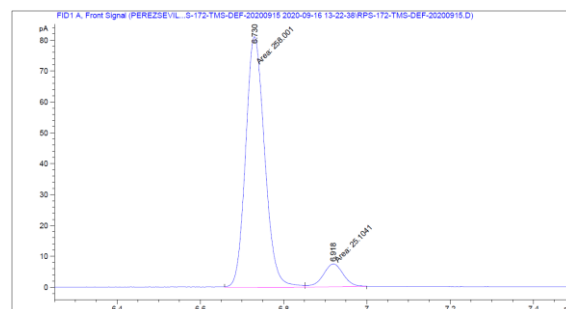
Mixture $\gamma/\alpha > 98/2$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95b** (58.0 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **112** (29.1 mg, 0.20 mmol) in 66% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.60 (ddd, $J = 16.9, 8.9, 2.6$ Hz, 1H), 4.88 (dd, $J = 10.3, 2.2$ Hz, 1H), 4.82 (dd, $J = 17.0, 2.1$ Hz, 1H), 1.60-1.34 (m, 3H), 0.92 (t, $J = 7.1$ Hz, 3H), -0.03 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 140.4, 112.0, 37.3, 21.7, 14.4, -3.1. HRMS: m/z calculated for C₈H₁₉Si [M+H]⁺ 143.1251, found 143.1254. $[\alpha]_D^{20} = +10.54$ ($c = 0.200$ CHCl₃) for a 82% ee sample.

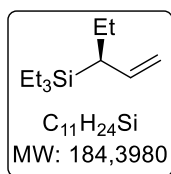
Enantiomeric ratio of 91:9 was determined by chiral GC analysis (CycloSil-B column: 30-0-2-50-25-200). Chromatograms are illustrated below: 6.73 (S), 6.92 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	7.310	MM	0.0558	19.29737	5.76731	50.73183
2	7.516	MM	0.0563	18.74062	5.54800	49.26817



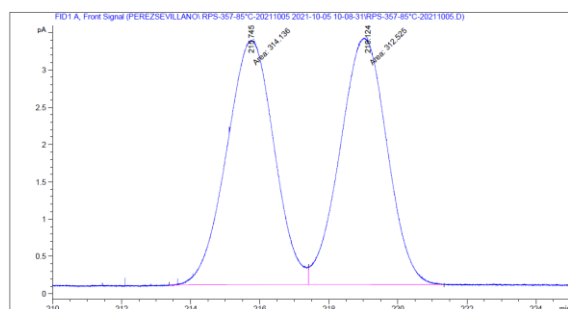
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	6.730	MF	0.0529	258.00067	81.26006	91.13257
2	6.918	FM	0.0564	25.10412	7.41249	8.86743

(+)-(S)-3-(Triethylsilyl)-1-pentene (113)

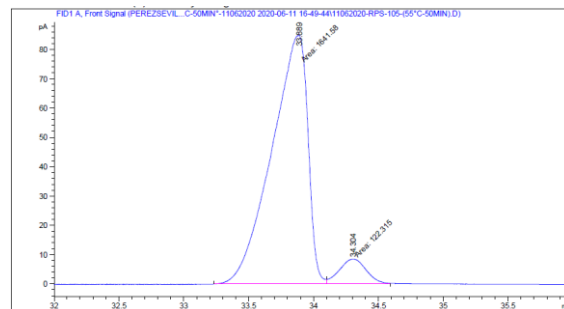
Mixture $\gamma/\alpha > 98/2$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **99** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **113** (49.2 mg, 0.27 mmol) in 89% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.64 (m, 1H), 4.90-4.79 (m, 2H), 1.59-1.49 (m, 2H), 1.46-1.33 (m, 1H), 0.94 (t, $J = 7.9$ Hz, 9H), 0.91 (t, $J = 7.6$ Hz, 3H), 0.55 (q, $J = 8.0$ Hz, 7H). ¹³C NMR (101 MHz, CDCl₃) δ 140.6, 111.9, 34.6, 22.0, 14.5, 7.7. HRMS: m/z calculated for C₁₁H₂₅Si [M+H]⁺ 185.1720, found 185.1729. $[\alpha]_D^{20} = 0.290$ ($c = 1.000$, CHCl₃) for a 86% ee sample.

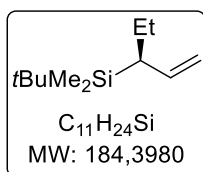
Enantiomeric ratio of 93:7 was determined by chiral GC analysis (CycloSil-B column: 55-50-25-200). Chromatograms are illustrated below: 33.89 (S), 34.3 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	33.669	MF	0.2816	331.70828	19.63446	49.58392
2	34.296	FM	0.2737	337.27530	20.53922	50.41608



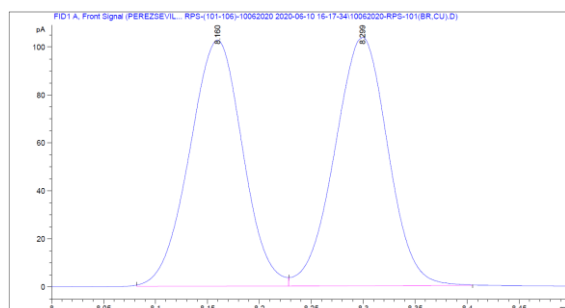
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	33.889	MF	0.3223	1641.57581	84.88284	93.06559
2	34.304	FM	0.2400	122.31549	8.49492	6.93441

(-)-(S)-3-(tert-Butyldimethylsilyl)-1-pentene (114)

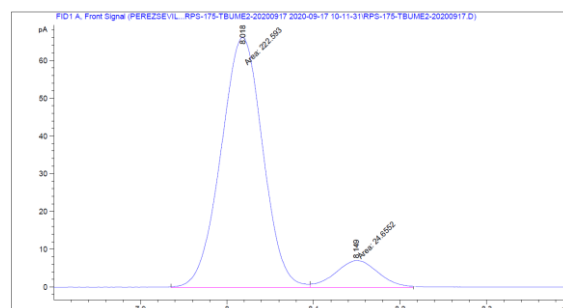
Mixture $\gamma/\alpha = 95/5$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95d** (70.6 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **114** (43.7 mg, 0.24 mmol) in 79% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.65 (m, 1H), 4.89 (dd, $J = 10.3, 2.1$ Hz, 1H), 4.84 (dd, $J = 17.1, 2.1$ Hz, 1H), 1.66-1.51 (m, 2H), 1.42-1.30 (m, 1H), 0.91 (s, 9H), -0.06 (s, 3H), -0.07 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 140.9, 112.5, 35.4, 27.5, 22.5, 14.3, -6.9, -7.0. HRMS: m/z calculated for C₁₁H₂₅Si [M+H]⁺ 185.1720, found 185.1729. $[\alpha]_D^{20} = -2.85$ ($c = 0.320$ CHCl₃) for a 80% ee sample.

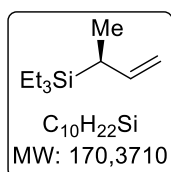
Enantiomeric ratio of 90:10 was determined by chiral GC analysis (CycloSil-B column: 70-0-1-85-0-25-200). Chromatograms are illustrated below: 8.02 (S), 8.15 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.160	BV	0.0545	364.72318	102.54730	49.67987
2	8.299	VB	0.0557	369.42368	103.38477	50.32013



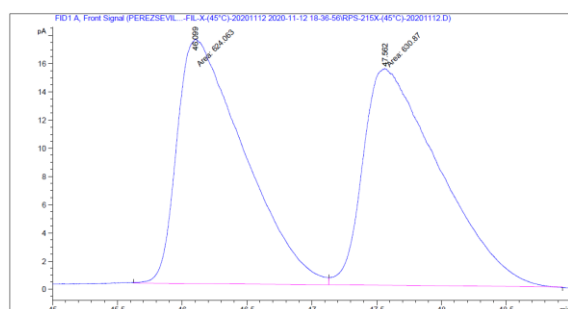
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.018	MF	0.0560	222.59297	66.28313	90.02816
2	8.149	FM	0.0577	24.65519	7.12617	9.97184

(-)-(S)-3-(Triethylsilyl)-1-butene (115a)

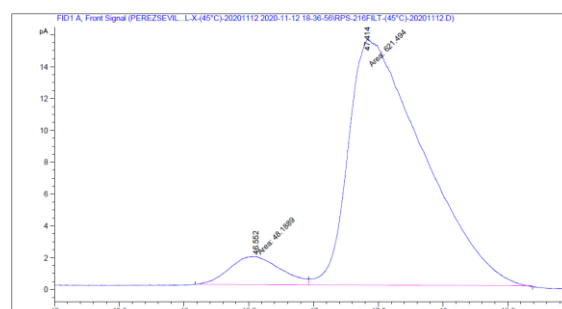
Mixture $\gamma/\alpha = 93/7$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with MeMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115a** (33.7 mg, 0.2 mmol) in 66% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 6.12 (dt, $J = 18.7$, 6.0 Hz, 1H, S_{N2}), 5.93 (m, 1H, S_{N2'}), 5.57 (dt, $J = 18.6$, 1.6 Hz, 1H, S_{N2}), 4.83 (m, 2H, S_{N2'}), 2.16 (m, 1H, S_{N2}), 1.77 (m, 1H, S_{N2}), 1.09 (d, $J = 7.2$ Hz, 3H, S_{N2} and S_{N2'}), 0.95 (t, $J = 8.0$ Hz, 9H, S_{N2} and S_{N2'}), 0.56 (q, $J = 7.9$, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 150.3 (S_{N2}), 142.2 (S_{N2'}), 124.3 (S_{N2}), 109.8 (S_{N2'}), 29.9 (S_{N2'}), 24.9 (S_{N2'}), 13.5 (S_{N2'}), 13.2 (S_{N2}), 7.7 (S_{N2'}), 7.5 (S_{N2}), 3.7 (S_{N2}), 2.2 (S_{N2'}). HRMS: Ongoing experiments. $[\alpha]_D^{20} = -31.74$ ($c = 0.220$ CHCl₃) for a 86% ee sample.

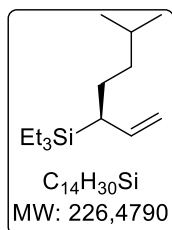
Enantiomeric ratio of 93:7 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 45-50-25-200). Chromatograms are illustrated below: 46.55 (*R*), 47.42 (*S*).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	46.099	MF	0.6001	624.06311	17.33118	49.72880
2	47.562	FM	0.6836	630.86987	15.38158	50.27120



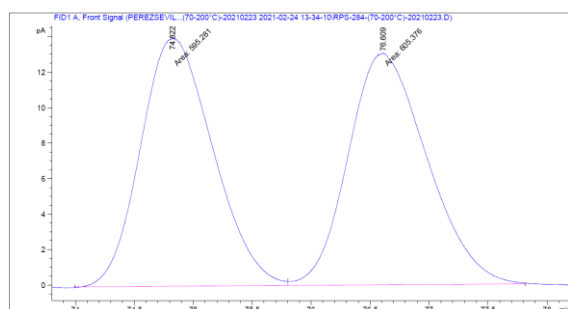
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	46.552	MF	0.4545	48.18892	1.76718	7.19578
2	47.414	FM	0.6707	621.49402	15.44284	92.80422

(+)-(S)-6-Methyl-3-(triethylsilyl)-1-heptene (115b)

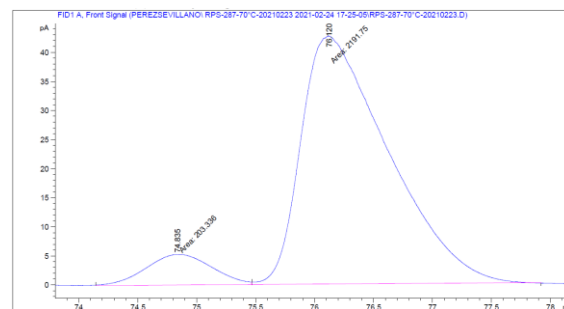
Mixture $\gamma/\alpha > 98/2$. Reaction time 5 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with *i*PentMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115b** (58.4 mg, 0.26 mmol) in 86% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 5.64 (m, 1H), 4.82 (m, 2H), 1.65-1.25 (m, 5H), 1.08 (m, 1H), 0.95 (t, $J = 7.9$ Hz, 9H), 0.87 (d, $J = 6.2$ Hz, 3H), 0.85 (d, $J = 6.2$ Hz, 3H), 0.55 (q, $J = 7.9$ Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 141.0, 111.6, 39.1, 32.5, 28.0, 26.5, 23.1, 22.4, 7.7, 2.4. **HRMS**: m/z calculated for $C_{14}H_{31}Si$ [M+H]⁺ 227.2190, found 227.2198. $[\alpha]_D^{20} = +5.98$ ($c = 0.400$ CHCl₃) for a 83% ee sample.

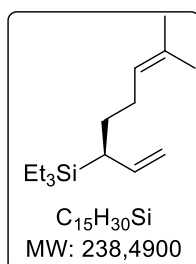
Enantiomeric ratio of 91.5:8.5 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 70-85-25-200). Chromatograms are illustrated below: 74.84 (*R*), 76.12 (*S*).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	74.822	MF	0.7109	595.28107	13.95533	49.57961
2	76.609	FM	0.7717	605.37598	13.07391	50.42039



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	74.835	MF	0.6440	203.33588	5.26239	8.48972
2	76.120	FM	0.8565	2191.74634	42.65122	91.51028

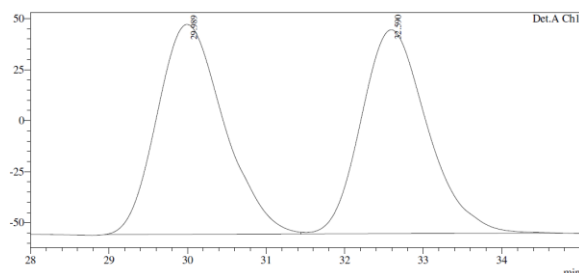
(-)-(S)-7-Methyl-3-(triethylsilyl)-octa-1,6-diene (115c)

Mixture $\gamma/\alpha > 98/2$. Reaction time 90 min.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $(\text{CH}_3)_2\text{CCH}(\text{CH}_2)_2\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115c** (65.8 mg, 0.28 mmol) in 92% yield as a colorless oil.

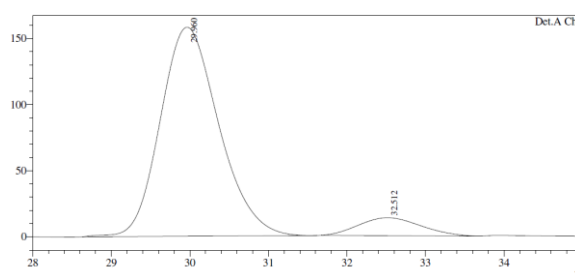
^1H NMR (400 MHz, CDCl_3) δ 5.66 (m, 1H), 5.10 (t, $J = 6.9$ Hz, 1H), 4.85 (m, 2H), 2.07 (m, 1H), 1.85 (m, 1H), 1.69 (s, 3H), 1.67 (m, 1H), 1.59 (s, 3H), 1.45 (m, 2H), 0.94 (t, $J = 7.9$ Hz, 9H), 0.55 (q, $J = 7.9$ Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 140.7, 131.7, 124.8, 111.9, 32.0, 29.1, 28.0, 25.9, 17.9, 7.7, 2.4. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -0.53$ ($c = 0.400$ CHCl_3) for a 83% ee sample.

Enantiomeric ratio of 92:8 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99.5% hexane: 0.5% *i*PrOH, 0.5 mL/min) of the derived alcohol **119b** obtained by hydroboration of the olefin with 9-BBN in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 29.96 (S), 32.51 (R).



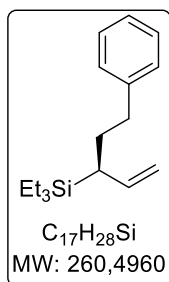
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	29.989	6081126	102831	50.980
2	32.590	5847380	99855	49.020
Total		11928506	202687	100.000



Detector A Ch1 214nm

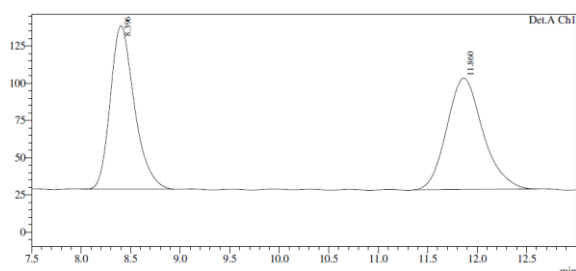
Peak#	Ret. Time	Area	Height	Area %
1	29.960	8176653	157997	91.657
2	32.512	744278	13557	8.343
Total		8920931	171554	100.000

(+)-(S)-3-Phenethyl-3-(triethylsilyl)-1-propene (115d)

Mixture $\gamma/\alpha > 98/2$. Reaction time 3h.

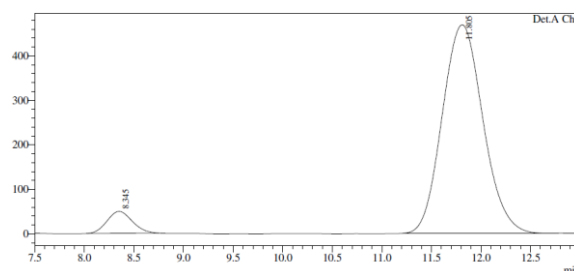
Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $\text{C}_6\text{H}_5(\text{CH}_2)_2\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115d** (63.30 mg, 0.24 mmol) in 81% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.31-7.15 (m, 5H), 5.73 (m, 1H), 4.95 (dd, $J = 10.3, 2.1$ Hz, 1H), 4.90 (dd, $J = 17.0, 1.9$ Hz, 1H), 2.79 (m, 1H), 2.45 (m, 1H), 1.74 (m, 3H), 0.92 (t, $J = 7.9$ Hz, 9H), 0.55 (q, $J = 7.9$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 143.0, 140.4, 128.7, 128.4, 125.7, 112.4, 35.8, 32.0, 31.0, 7.7, 2.3. **HRMS**: m/z calculated for $\text{C}_{17}\text{H}_{28}\text{SiNa}$ $[\text{M}+\text{Na}]^+$ 283.1852, found 283.1853. $[\alpha]_D^{20} = +8.60$ ($c = 0.500$ CHCl_3) for a 88% ee sample.

Enantiomeric ratio 94:6 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 95% hexane: 5% *i*PrOH, 1 mL/min) of the derived alcohol **119c** obtained by hydroboration of the olefin with $\text{BH}_3 \cdot \text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 8.34 (*R*), 11.81 (*S*).



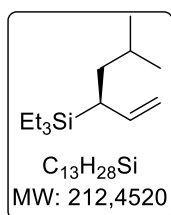
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	8.396	1854226	109621	49.421
2	11.860	1897662	74667	50.579
Total		3751888	184288	100.000



Detector A Ch1 214nm

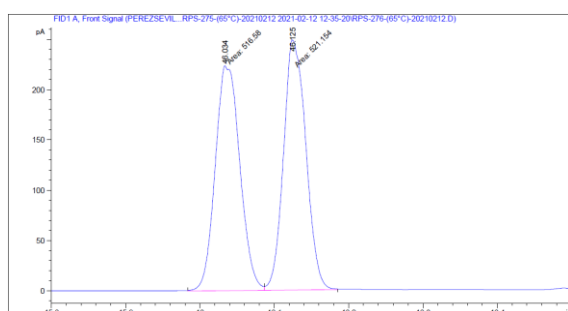
Peak#	Ret. Time	Area	Height	Area %
1	8.345	873244	49355	6.130
2	11.805	13372628	468706	93.870
Total		14245872	518062	100.000

(+)-(S)-3-Isobutyl-3-(triethylsilyl)-1-propene (115e)

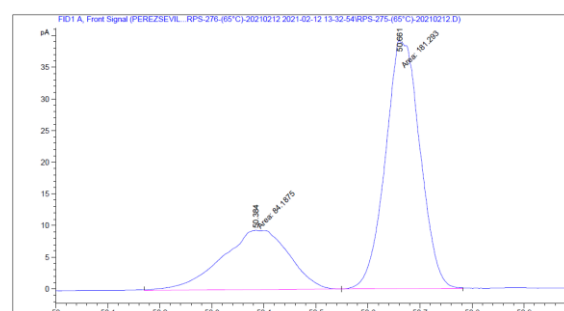
Mixture $\gamma/\alpha = 76/24$. Reaction time 5 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $t\text{BuMgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115e** (50.4 mg, 0.24 mmol) in 79% yield as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 6.11-6.01 (dt, $J = 18.7, 6.32$ Hz, 1H, $\text{S}_{\text{N}2}$), 5.65 (dt, $J = 16.9, 10.3$ Hz, 1H, $\text{S}_{\text{N}2'}$), 5.56 (dd, $J = 18.7, 1.2$ Hz, 1H, $\text{S}_{\text{N}2}$), 4.89-4.80 (m, 2H $\text{S}_{\text{N}2'}$), 2.12 (m, 2H, $\text{S}_{\text{N}2}$), 1.81 (m, 1H, $\text{S}_{\text{N}2'}$), 1.60 (m, 1H, $\text{S}_{\text{N}2'}$), 1.55 (m, 1H, $\text{S}_{\text{N}2}$), 1.46 (m, 1H, $\text{S}_{\text{N}2'}$), 1.30 (m, 2H, $\text{S}_{\text{N}2}$), 1.12 (m, 1H, $\text{S}_{\text{N}2'}$), 1.0-0.92 (m, 9H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 0.91 (d, $J = 6.6$ Hz, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 0.82 (d, 3H, $J = 6.5$ Hz, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 0.61-0.53 (m, 6H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$). **^{13}C NMR** (101 MHz, CDCl_3) δ 149.1 ($\text{S}_{\text{N}2}$), 140.9 ($\text{S}_{\text{N}2'}$), 125.4 ($\text{S}_{\text{N}2}$), 111.5 ($\text{S}_{\text{N}2'}$), 38.3 ($\text{S}_{\text{N}2}$), 38.1 ($\text{S}_{\text{N}2'}$), 35.1 ($\text{S}_{\text{N}2}$), 30.0 ($\text{S}_{\text{N}2'}$), 27.7 ($\text{S}_{\text{N}2}$), 26.6 ($\text{S}_{\text{N}2'}$), 24.2 ($\text{S}_{\text{N}2'}$), 22.6 ($\text{S}_{\text{N}2}$), 20.7 ($\text{S}_{\text{N}2'}$), 7.7 ($\text{S}_{\text{N}2'}$), 7.5 ($\text{S}_{\text{N}2}$), 3.7 ($\text{S}_{\text{N}2}$), 2.3 ($\text{S}_{\text{N}2'}$). **HRMS**: Ongoing experiments. $[\alpha]_{\text{D}}^{20} = +4.960$ ($c = 1.000$, CHCl_3) for a 36% ee sample.

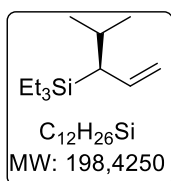
Enantiomeric ratio 68:32 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 65-55-25-200). Chromatograms are illustrated below: 108.70 (*R*), 110.68 (*S*).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	46.034	MF	0.0385	516.58044	223.80081	49.77964
2	46.125	FM	0.0349	521.15387	249.10416	50.22036



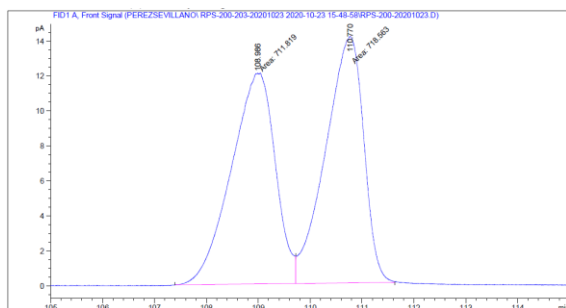
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	50.384	MF	0.1495	84.18748	9.38598	31.71135
2	50.661	FM	0.0770	181.29314	39.22598	68.28865

(+)-(S)-3-Isopropyl-3-(triethylsilyl)-1-propene (115f)

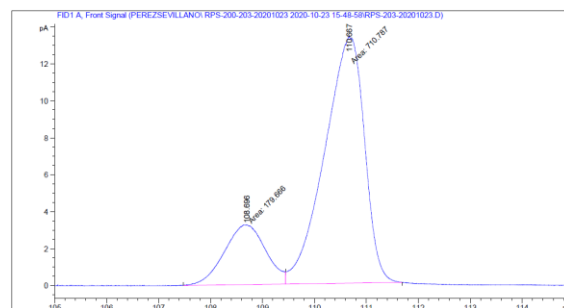
Mixture $\gamma/\alpha = 77/23$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with *i*PrMgBr (1.5 equiv) in the presence of NHC-ligand **88** (0.75 mg, 1.5×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115f** (41.7 mg, 0.21 mmol) in 70% yield as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 6.08-5.99 (m, 2H, dimer), 6.03-5.95 (m, 1H, $\text{S}_{\text{N}2}$), 5.72 (dt, $J = 16.8, 10.6$ Hz, 1H, $\text{S}_{\text{N}2'}$), 5.56 (m, 2H, dimer), 5.54 (m, 1H, $\text{S}_{\text{N}2}$), 4.88 (dd, $J = 10.2, 2.4$ Hz, $\text{S}_{\text{N}2'}$), 4.83 (dd, $J = 16.9, 2.26$ Hz, $\text{S}_{\text{N}2'}$), 2.25-2.22 (m, 4H, dimer), 2.01 (t, $J = 6.8$ Hz, 2H, $\text{S}_{\text{N}2}$), 1.89 (m, 1H, $\text{S}_{\text{N}2'}$), 1.66 (m, 1H, $\text{S}_{\text{N}2}$), 1.58 (dd, 1H, $J = 11.1, 4.9$ Hz, $\text{S}_{\text{N}2'}$), 0.98 (m, 15H, $\text{S}_{\text{N}2}$, $\text{S}_{\text{N}2'}$ and dimer), 0.63-0.50 (m, 6H, $\text{S}_{\text{N}2}$, $\text{S}_{\text{N}2'}$ and dimer). **^{13}C NMR** (101 MHz, CDCl_3) δ 147.9 (dimer), 147.7 ($\text{S}_{\text{N}2}$), 138.0 ($\text{S}_{\text{N}2'}$), 127.2 ($\text{S}_{\text{N}2}$), 126.2 (dimer), 113.4 ($\text{S}_{\text{N}2'}$), 46.8 ($\text{S}_{\text{N}2}$), 40.4 ($\text{S}_{\text{N}2'}$), 36.3 (dimer), 28.2 ($\text{S}_{\text{N}2}$), 28.1 ($\text{S}_{\text{N}2'}$), 24.0 ($\text{S}_{\text{N}2'}$), 22.4 ($\text{S}_{\text{N}2'}$), 21.2 ($\text{S}_{\text{N}2}$), 7.9 ($\text{S}_{\text{N}2'}$), 7.5 ($\text{S}_{\text{N}2}$), 7.5 (dimer), 3.7 ($\text{S}_{\text{N}2}$), 3.7 (dimer), 3.4 ($\text{S}_{\text{N}2'}$). **HRMS**: $\text{C}_{12}\text{H}_{27}\text{Si}$ $[\text{M}+\text{H}]^+$ 199.1877, found 199.1855. $[\alpha]_{\text{D}}^{20} = +0.120$ ($c = 0.100$ CHCl_3) for a 60% ee sample.

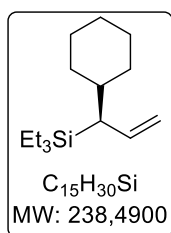
Enantiomeric ratio 80:20 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 45-125-25-200). Chromatograms are illustrated below: 108.70 (*R*), 110.68 (*S*).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	108.986	MF	0.9858	711.81866	12.03394	49.76424
2	110.770	FM	0.8506	718.56317	14.07983	50.23576



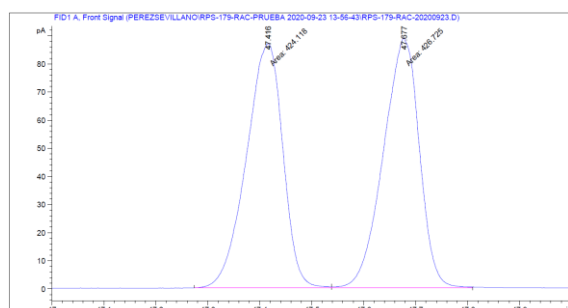
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	108.696	MF	0.9259	179.66640	3.23406	20.17696
2	110.667	FM	0.8865	710.78693	13.36354	79.82304

(-)-(R)-3-Cyclohexyl-3-(triethylsilyl)-1-propene (115g)

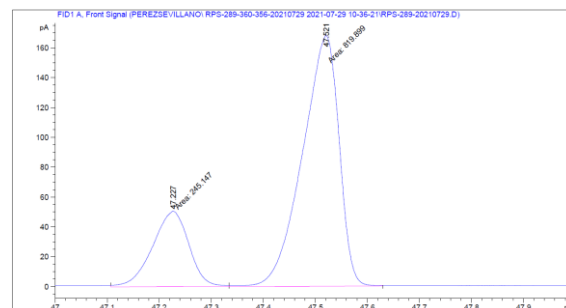
Mixture $\gamma/\alpha = 76/24$. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with cHexMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **115g** (74.2 mg, 0.29 mmol) in 98% yield as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 6.09-5.96 (m, 2H, dimer), 6.04-5.96 (dt, $J = 18.6, 6.7$ Hz, 1H, $\text{S}_{\text{N}2}$), 5.72 (ddd, $J = 16.8, 11.1, 10.0$ Hz, 1H, $\text{S}_{\text{N}2'}$), 5.59-5.53 (m, 2H, dimer), 5.50 (dt, $J = 18.5, 1.4$ Hz, 1H, $\text{S}_{\text{N}2}$), 4.85 (dd, $J = 10.1, 2.4$ Hz, $\text{S}_{\text{N}2'}$), 4.79 (ddd, $J = 16.8, 2.4, 0.7$ Hz, 1H, $\text{S}_{\text{N}2'}$), 2.25-2.22 (m, 4H, dimer), 2.02 (dt, $J = 6.7, 1.5$ Hz, 2H, $\text{S}_{\text{N}2}$), 1.80-1.44 (m, 6H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 1.35-0.98 (m, 6H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 1.0-0.91 (m, 9H, $\text{S}_{\text{N}2}$, $\text{S}_{\text{N}2'}$ and dimer), 0.64-0.52 (m, 6H, $\text{S}_{\text{N}2}$, $\text{S}_{\text{N}2'}$ and dimer). **^{13}C NMR** (101 MHz, CDCl_3) δ 147.9 (dimer), 147.5 ($\text{S}_{\text{N}2}$), 138.8 ($\text{S}_{\text{N}2'}$), 127.1 ($\text{S}_{\text{N}2}$), 126.2 (dimer), 112.9 ($\text{S}_{\text{N}2'}$), 45.5 ($\text{S}_{\text{N}2}$), 40.1 ($\text{S}_{\text{N}2'}$), 38.5 ($\text{S}_{\text{N}2'}$), 36.3 (dimer), 34.4 ($\text{S}_{\text{N}2'}$), 33.3 ($\text{S}_{\text{N}2}$), 31.8 ($\text{S}_{\text{N}2'}$), 27.1 ($\text{S}_{\text{N}2'}$), 26.8 ($\text{S}_{\text{N}2}$), 26.6 ($\text{S}_{\text{N}2}$), 26.4 ($\text{S}_{\text{N}2'}$), 7.9 ($\text{S}_{\text{N}2'}$), 7.6 ($\text{S}_{\text{N}2}$), 7.5 ($\text{S}_{\text{N}2}$), 3.6 (dimer), 3.5 ($\text{S}_{\text{N}2'}$). **HRMS**: Ongoing experiments. $[\alpha]_{\text{D}}^{20} = -2.74$ ($c = 0.200$ CHCl_3) for a 54% ee sample.

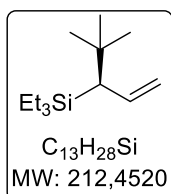
Enantiomeric ratio 77:23 was determined by chiral GC analysis (CycloSil-B column: 40-0-2-150-0-25-200). Chromatograms are illustrated below: 47.22 (S), 47.52 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	47.416	MF	0.0814	424.11780	86.81710	49.84680
2	47.677	FM	0.0803	426.72482	88.56643	50.15320



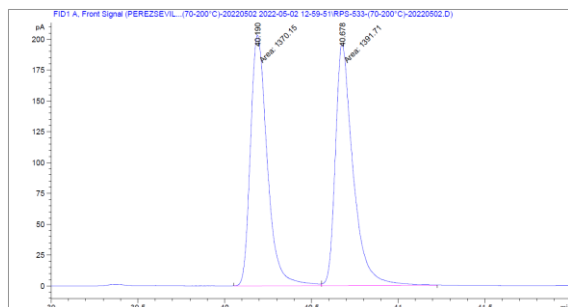
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	47.227	MF	0.0808	245.14651	50.55634	23.01748
2	47.521	FM	0.0813	819.89868	168.00340	76.98252

(+)-(R)-3-*tert*-Butyl-3-(triethylsilyl)-1-propene (115h)

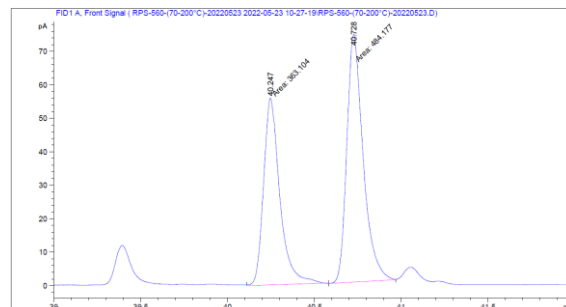
Mixture γ/α = 62/38. Reaction time 1 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with *t*-ButylMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0x10⁻³ mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, R_f = 0.98) to afford the desired product **115h** (35.1 mg, 0.17 mmol) in 55% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 6.12-5.94 (m, 2H, dimer), 6.05 (dt, *J* = 18.6, 7.1 Hz, 1H, S_{N2}), 5.76 (dt, *J* = 16.6, 11.1 Hz, 1H, S_{N2'}), 5.56 (m, 2H, dimer), 5.55 (dt, *J* = 18.5, 1.2 Hz, 1H, S_{N2}), 4.89 (dd, *J* = 10.1, 2.5 Hz, 1H S_{N2'}), 4.81 (dd, *J* = 16.9, 2.0 Hz, 1H, S_{N2'}), 2.25-2.22 (m, 4H, dimer), 2.01 (dd, *J* = 7.1, 1.3 Hz, 2H, S_{N2}), 1.57 (d, *J* = 11.6 Hz, 1H, S_{N2'}), 1.01-0.90 (m, 9H, S_{N2} and S_{N2'}), 0.96 (s, 9H, S_{N2}, S_{N2'} and dimer) 0.68-0.47 (m, 6H, S_{N2}, S_{N2'} and dimer). ¹³C NMR (101 MHz, CDCl₃) δ 147.9 (dimer), 146.2 (S_{N2}), 139.0 (S_{N2'}), 128.8 (S_{N2}), 126.3 (dimer), 113.6 (S_{N2'}), 52.1 (S_{N2}), 46.0 (S_{N2'}), 36.3 (dimer), 33.3 (S_{N2'}), 31.0 (S_{N2}) 30.8 (S_{N2'}), 29.5 (S_{N2}) 7.9 (S_{N2'}), 7.6 (S_{N2}), 7.5 (dimer) 4.6 (S_{N2'}), 3.8 (S_{N2}), 3.7 (dimer). HRMS: Ongoing experiments. $[\alpha]_D^{20}$ = +0.440 (*c* = 1.000 CHCl₃) for a 14% ee sample.

Enantiomeric ratio 57:43 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 70-0-2-200) of the derived alcohol **119a** obtained by hydroboration of the olefin with BH₃-SMe₂ in THF, followed by oxidation with H₂O₂/NaOH. Chromatograms are illustrated below: 40.28 (S), 40.73 (R).

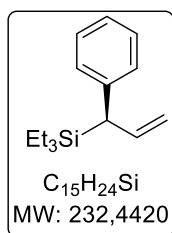


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.190	MF	0.1124	1370.15344	203.13458	49.60967
2	40.678	FM	0.1190	1391.71399	194.91705	50.39033



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.247	MM	0.1083	363.10446	55.86544	42.85523
2	40.728	MM	0.1089	484.17706	74.08640	57.14477

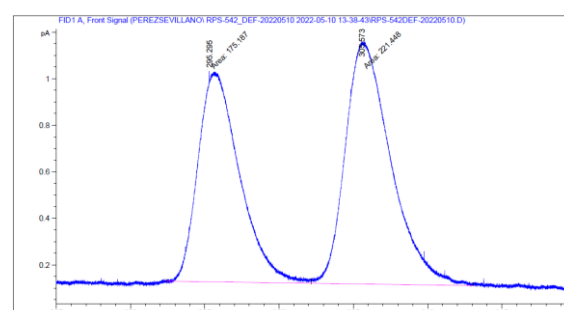
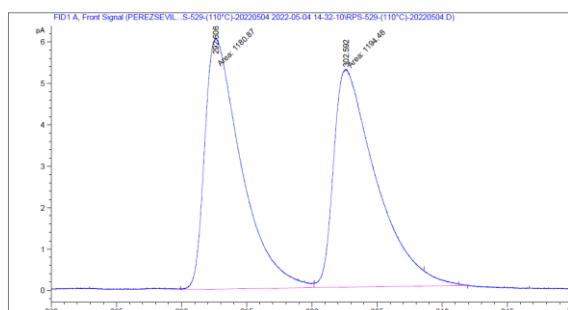
(+)-(R)-3-Phenyl-3-(triethylsilyl)-1-propene (**118a**)

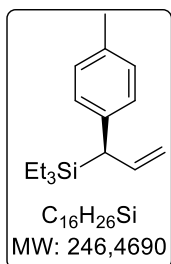


Mixture $\gamma/\alpha = 80/20$. Reaction time 6 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $\text{C}_6\text{H}_5\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **118a** (55.78 mg, 0.24 mmol) in 80% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33-7.16 (m, 3H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 7.13-7.07 (m, 2H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 6.22 (m, 1H, $\text{S}_{\text{N}2'}$), 6.17 (dt, $J = 18.3$, 6.6 Hz, 1H, $\text{S}_{\text{N}2}$), 5.66 (dt, $J = 18.5$, 1.4 Hz, 1H, $\text{S}_{\text{N}2}$), 4.96 (m, 2H, $\text{S}_{\text{N}2'}$), 3.46 (dd, $J = 6.3$, 1.5 Hz, 2H, $\text{S}_{\text{N}2}$), 3.12 (d, $J = 9.8$ Hz, 1H, $\text{S}_{\text{N}2'}$), 0.94 (t, $J = 8.0$ Hz, 9H, $\text{S}_{\text{N}2}$), 0.90 (t, $J = 8.0$ Hz, 9H, $\text{S}_{\text{N}2'}$), 0.57 (q, $J = 7.8$ Hz, 6H, $\text{S}_{\text{N}2}$), 0.55 (q, $J = 8.0$ Hz, 9H, $\text{S}_{\text{N}2'}$). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 146.5 ($\text{S}_{\text{N}2}$), 142.7 ($\text{S}_{\text{N}2'}$), 138.8 ($\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 128.8 ($\text{S}_{\text{N}2}$), 128.5 ($\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 127.5 ($\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 126.1 ($\text{S}_{\text{N}2}$), 124.7 ($\text{S}_{\text{N}2'}$), 112.3 ($\text{S}_{\text{N}2'}$), 43.7 ($\text{S}_{\text{N}2}$), 42.0 ($\text{S}_{\text{N}2'}$), 7.6 ($\text{S}_{\text{N}2}$), 7.5 ($\text{S}_{\text{N}2'}$), 3.6 ($\text{S}_{\text{N}2}$), 2.4 ($\text{S}_{\text{N}2'}$). **HRMS**: m/z calculated for $\text{C}_{15}\text{H}_{24}\text{SiNa}$ $[\text{M}+\text{Na}]^+$ 255.1539, found 255.1540. $[\alpha]_{\text{D}}^{20} = +3.65$ ($c = 0.450$ CHCl_3) for a 12% ee sample.

Enantiomeric ratio 56:44 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 110-315-25-200) of the derived alcohol **119d** obtained by hydroboration of the olefin with $\text{BH}_3\cdot\text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 295.30 (S), 305.57 (R).

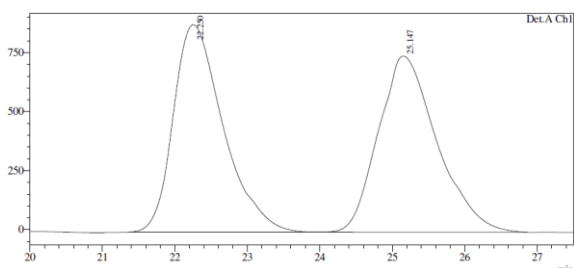


(R)-3-(4-Methylphenyl)-3-(triethylsilyl)-1-propene (118b)

Mixture $\gamma/\alpha = 77/23$. Reaction time 12 h.

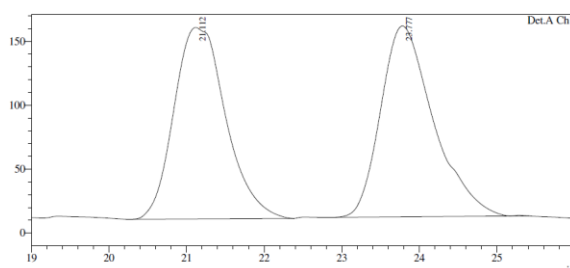
Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $\text{CH}_3\text{-C}_6\text{H}_4\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **118b** (54.22 mg, 0.22 mmol) in 74% yield as a colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 7.13-6.97 (m, 4H, $\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 6.19 (m, 1H, $\text{S}_{\text{N}2'}$), 6.15 (dt, $J = 18.9, 6.2$ Hz, 1H, $\text{S}_{\text{N}2}$), 5.65 (dt, $J = 18.5, 1.5$ Hz, 1H, $\text{S}_{\text{N}2}$), 4.94 (m, 2H, $\text{S}_{\text{N}2'}$), 3.44 (dd, $J = 6.2, 1.5$ Hz, 2H, $\text{S}_{\text{N}2}$), 3.08 (d, $J = 9.8$ Hz, 1H, $\text{S}_{\text{N}2'}$), 2.33 (s, 3H, $\text{S}_{\text{N}2}$), 2.30 (s, 3H, $\text{S}_{\text{N}2'}$), 0.94 (t, $J = 8.0$ Hz, 9H, $\text{S}_{\text{N}2}$), 0.91 (t, $J = 8.0$ Hz, 9H, $\text{S}_{\text{N}2'}$), 0.57 (q, $J = 7.9$ Hz, 6H, $\text{S}_{\text{N}2}$), 0.55 (t, $J = 7.9$ Hz, 9H, $\text{S}_{\text{N}2'}$). **^{13}C NMR** (101 MHz, CDCl_3) δ 146.9 ($\text{S}_{\text{N}2}$), 139.4 ($\text{S}_{\text{N}2'}$), 139.0 ($\text{S}_{\text{N}2'}$), 137.2 ($\text{S}_{\text{N}2}$), 135.7 ($\text{S}_{\text{N}2}$), 134 ($\text{S}_{\text{N}2'}$) 129.2 ($\text{S}_{\text{N}2}$), 129.1 ($\text{S}_{\text{N}2'}$) 128.7 ($\text{S}_{\text{N}2}$), 127.6 ($\text{S}_{\text{N}2}$), 127.4 ($\text{S}_{\text{N}2'}$), 112.0 ($\text{S}_{\text{N}2'}$), 43.3 ($\text{S}_{\text{N}2}$), 41.4 ($\text{S}_{\text{N}2'}$), 21.2 ($\text{S}_{\text{N}2}$), 21.0 ($\text{S}_{\text{N}2'}$), 7.6 ($\text{S}_{\text{N}2}$ and $\text{S}_{\text{N}2'}$), 3.8 ($\text{S}_{\text{N}2}$) 2.5 ($\text{S}_{\text{N}2'}$). **HRMS**: Ongoing experiments. $[\alpha]_{\text{D}}^{20} = 0$ ($c = 1.000$ CHCl_3) for a 0% ee sample.

Enantiomeric ratio 50:50 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99% hexane: 2% *i*PrOH, 1 mL/min) of the derived alcohol **119e** obtained by hydroboration of the olefin with $\text{BH}_3\text{-SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 21.11, 23.77.



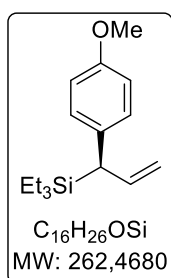
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	22.250	41956964	877453	50.020
2	25.147	41923727	744950	49.980
Total		83880690	1622403	100.000



Detector A Ch1 214nm

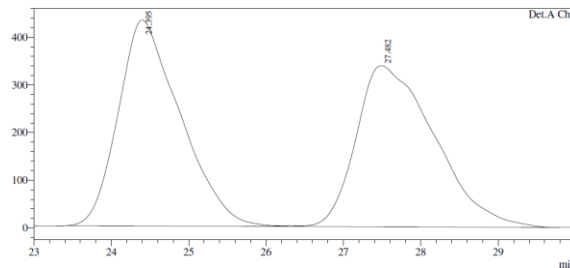
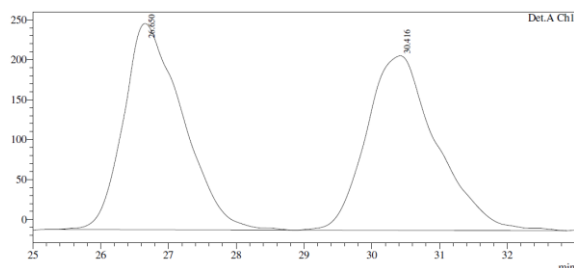
Peak#	Ret. Time	Area	Height	Area %
1	21.112	6965886	149804	49.612
2	23.777	7074914	149345	50.388
Total		14040801	299148	100.000

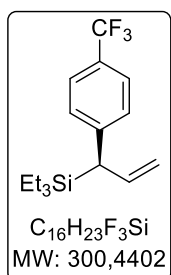
(R)-3-(4-Methoxyphenyl)-3-(triethylsilyl)-1-propene (118c)

Mixture $\gamma/\alpha = 65/35$ (after column $\gamma/\alpha = 92/8$). Reaction time 24 h.

Prepared according to **GP10** from the reaction of allylbromide **95c** (70.7 mg, 0.3 mmol) with $\text{MeO-C}_6\text{H}_4\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.9$) to afford the desired product **118c** (65.4 mg, 0.25 mmol) in 83% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.02 (d, $J = 8.6$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 6.16 (m, 1H), 4.94 (ddd, $J = 13.1$, 1.9, 1.0 Hz, 1H), 4.91 (ddd, $J = 6.4$, 1.9, 1.0 Hz, 1H), 3.78 (s, 3H), 3.05 (d, $J = 9.6$ Hz, 1H), 0.91 (t, $J = 7.9$ Hz, 9H), 0.54 (q, $J = 7.7$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 157.1, 139.2, 134.6, 128.4, 114.0, 112.0, 55.4, 40.7, 7.6, 2.5. **HRMS**: $\text{C}_{16}\text{H}_{27}\text{SiO}$ $[\text{M}+\text{H}]^+$ 263.1826, found 263.1826 $[\alpha]_D^{20} = 0$ ($c = 0.600$ CHCl_3) for a 0% ee sample.

Enantiomeric ratio 50:50 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99% hexane: 2% *i*PrOH, 1 mL/min) of the derived alcohol **119g** obtained by hydroboration of the olefin with $\text{BH}_3\cdot\text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 24.40, 27.48.

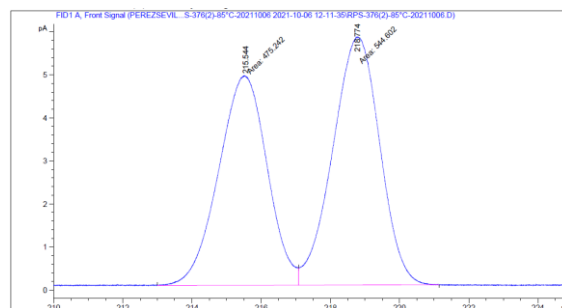
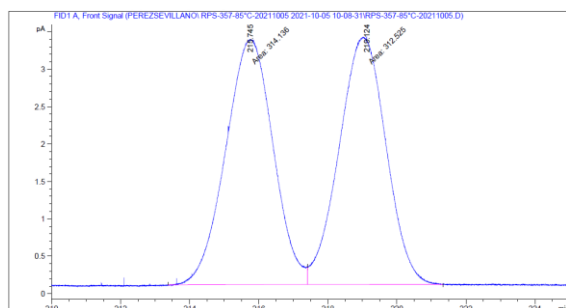


(-)-(R)-3-(Triethylsilyl)-3-(4-trifluoromethylphenyl)-1-propene (118d)

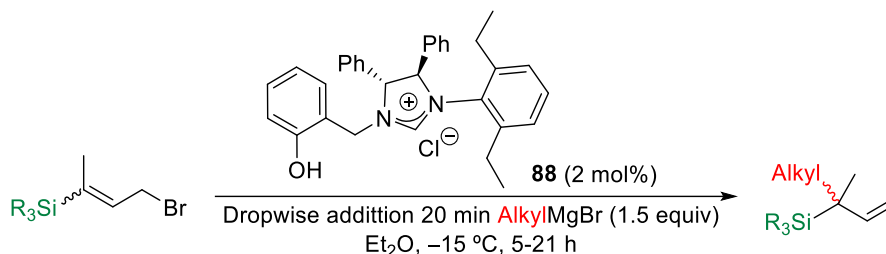
Mixture $\gamma/\alpha = 87/13$. Reaction time 24 h.

Following a reported procedure,^[175] in a flame-dried Schlenk under Argon atmosphere equipped with a stir bar, the allylbromide **95c** derivative (70.7 mg, 0.3 mmol) and NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) are suspended in pentane (adjusted to 1.4 mL depending on the Grignard reagent volume) and stir at 25 °C. A solution $\text{F}_3\text{C}-\text{C}_6\text{H}_4\text{MgBr}$ in Et_2O (1.5 equiv) is added dropwise over 20 min. After complete conversion, the mixture is diluted with 1 mL of THF and quenched by addition of K_2CO_3 (23.5 mg, 0,17 mmol) and benzylamine (0.02 mL, 0.19 mmol). After 15 min, the mixture was diluted with 2 mL of Et_2O and 5 mL of H_2O . The aqueous layer is separated and extracted with Et_2O (3 x 5 mL). The combined organic fractions are washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **118d** (72.11 mg, 0.24 mmol) in 81% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl_3) δ 7.55 (d, $J = 8.1$ Hz, 2H, $\text{S}_{\text{N}2}$), 7.51 (d, $J = 8.1$ Hz, 2H, $\text{S}_{\text{N}2'}$), 7.29 (d, $J = 8.1$ Hz, 2H, $\text{S}_{\text{N}2}$), 7.20 (d, $J = 8.1$ Hz, 2H, $\text{S}_{\text{N}2'}$), 6.2 (dt, $J = 17.3, 9.8$ Hz, 1H, $\text{S}_{\text{N}2'}$), 6.14 (dt, $J = 18.7, 6.1$ Hz, 1H, $\text{S}_{\text{N}2}$), 5.68 (dt, $J = 18.6, 1.6$ Hz, 1H, $\text{S}_{\text{N}2}$), 4.99 (m, 2H, $\text{S}_{\text{N}2'}$), 3.52 (d, $J = 6.3$ Hz, 2H, $\text{S}_{\text{N}2}$), 3.20 (d, $J = 9.9$ Hz, 1H, $\text{S}_{\text{N}2'}$), 0.94 (t, $J = 8.1$ Hz, 9H, $\text{S}_{\text{N}2}$), 0.91 (t, $J = 7.9$ Hz, 9H, $\text{S}_{\text{N}2'}$), 0.57 (q, $J = 7.9$ Hz, 6H, $\text{S}_{\text{N}2}$), 0.55 (q, $J = 7.5$ Hz, 9H, $\text{S}_{\text{N}2'}$). **¹³C NMR** (101 MHz, CDCl_3) δ 147.2, 137.6, 127.6, 125.4, 113.2, 42.2, 7.5, 2.3. **HRMS**: Ongoing experiments. $[\alpha]_{\text{D}}^{20} = -3.36$ ($c = 0.600$ CHCl_3) for a 7% ee sample.

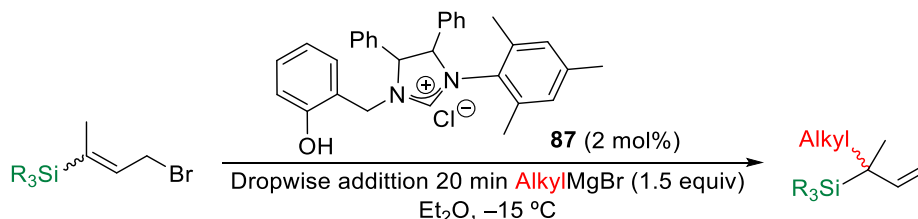
Enantiomeric ratio 53.5:46.5 was determined by chiral GC analysis (CycloSil-B column: 70-0-1-85-215-25-200). Chromatograms are illustrated below: 215.54 (S), 218.77 (R).



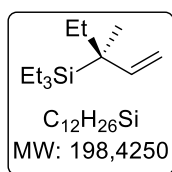
3.4 Synthesis of allylsilanes bearing quaternary silyl-substituted stereogenic centres



General procedure GP11: Following a reported procedure,^[175] in a flame-dried Schlenk under Argon atmosphere equipped with a stir bar, the appropriate allylbromide derivative (0.3 mmol) and NHC-ligand **88** (2 mol%) are suspended in dry Et_2O (adjusted to 1.4 mL depending on the Grignard reagent volume) and stir at $-15\text{ }^{\circ}C$. A solution of Grignard reagent $RMgBr$ in Et_2O (1.5 equiv) is added dropwise over 20 min. After complete conversion, the mixture is diluted with 1 mL of THF and quenched by addition of K_2CO_3 (23.5 mg, 0.17 mmol) and benzylamine (0.02 mL, 0.19 mmol). After 15 min, the mixture is diluted with 2 mL of Et_2O and 5 mL of H_2O . The aqueous layer is separated and extracted with Et_2O (3 x 5 mL). The combined organic fractions are washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue is purified by flash column chromatography to offer a mixture of S_N2' and S_N2 products.



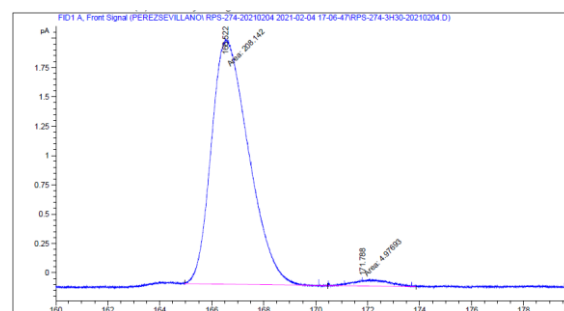
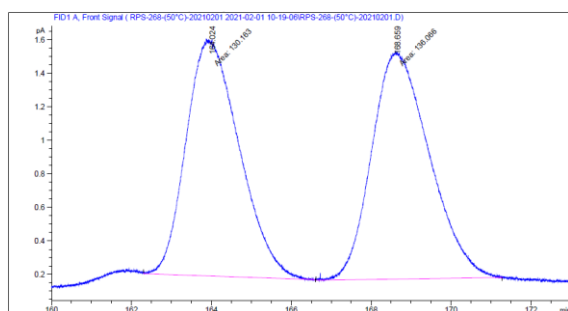
For the preparation of allylsilane bearing quaternary racemates, same procedure **GP10** was used but in the presence of $CuTC$ (30 mol%) and 1,3-diisopropyl imidazolium salt (30 mol %) or procedure **GP11** was used but in the presence of racemate NHC-ligand **87** (prepared from racemic 1,2-diphenylethylenediamine).

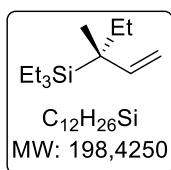
(-)-(S)-3-Methyl-3-(triethylsilyl)-1-pentene (130aa)

Mixture $\gamma/\alpha > 98/2$. Reaction time 6 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124a** (72.6 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130aa** (54.8 mg, 0.28 mmol) in 92% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 5.80 (dd, $J = 17.4$, 10.7 Hz, 1H), 4.92 (dd, $J = 10.9$, 1.1 Hz, 1H), 4.71 (dd, $J = 17.4$, 1.2 Hz, 1H), 1.61 (dq, $J = 14.6$, 7.4 Hz, 1H), 1.46 (dq, $J = 14.3$, 7.3 Hz, 1H), 1.00 (s, 3H), 0.97 (t, $J = 8.1$ Hz, 9H), 0.75 (t, $J = 7.3$ Hz, 3H), 0.58 (q, $J = 8.0$ Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 145.7, 110.3, 32.0, 28.7, 17.1, 8.3, 7.8, 1.9. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -12.35$ ($c = 0.400$ CHCl₃) for a 96% ee sample.

Enantiomeric ratio 98:2 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 50-180-25-200). Chromatograms are illustrated below: 166.52 (S), 171.78 (R).

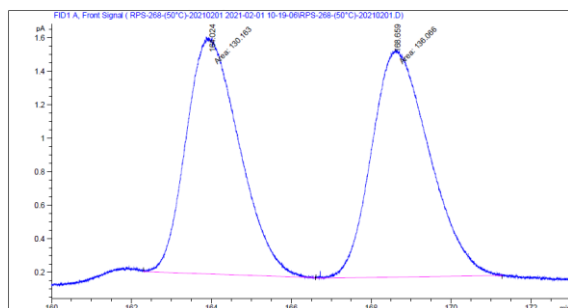


(+)-(R)-3-Methyl-3-(triethylsilyl)-1-pentene (130aa)

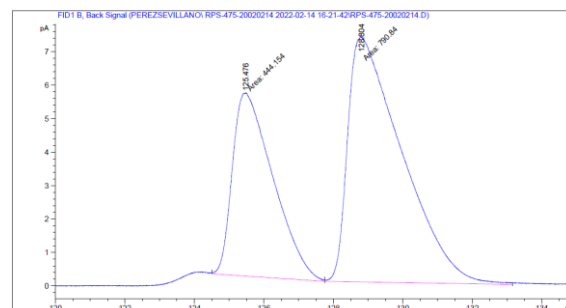
Mixture $\gamma/\alpha > 98/2$. Reaction time 6 h.

Prepared according to **GP11** from the reaction of allylbromide **(Z)-124a** (72.6 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130aa** (41.7 mg, 0.21 mmol) in 70% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 5.80 (dd, $J = 17.4$, 10.7 Hz, 1H), 4.92 (dd, $J = 10.8$, 1.7 Hz, 1H), 4.71 (dd, $J = 17.3$, 1.7 Hz, 1H), 1.61 (dq, $J = 14.7$, 7.4 Hz, 1H), 1.46 (m, 1H), 1.00 (s, 3H), 0.97 (t, $J = 8.0$ Hz, 9H), 0.75 (t, $J = 7.4$ Hz, 3H), 0.58 (q, $J = 8.1$ Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 145.7, 110.3, 32.0, 28.7, 17.1, 8.3, 7.8, 1.9. These data are in good agreement with those reported above.

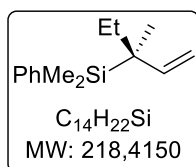
Enantiomeric ratio 64:36 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 50-180-25-200). Chromatograms are illustrated below: 125.48 (S), 128.80 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	164.024	MM	1.5336	130.16321	1.41461	48.89143
2	168.659	MM	1.6725	136.06590	1.35595	51.10857



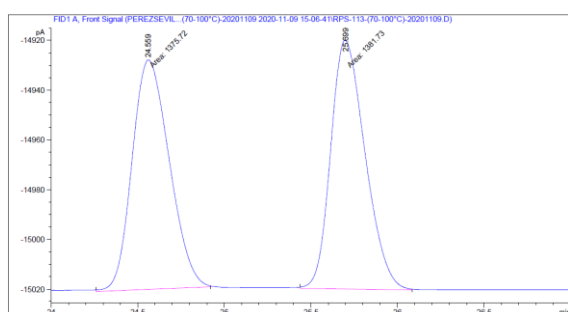
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	125.476	MM	1.3516	444.15366	5.47680	35.96404
2	128.804	MM	1.7982	790.84027	7.33005	64.03596

(+)-(S)-3-(Dimethylphenylsilyl)-3-methyl-1-pentene (130ba)

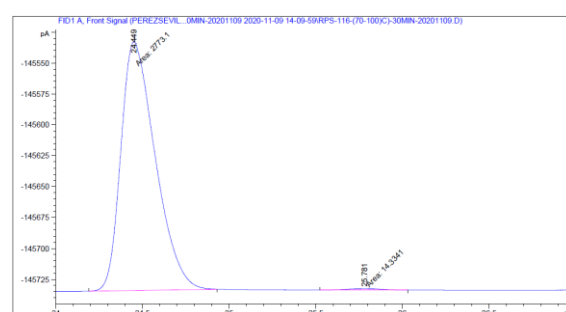
Mixture $\gamma/\alpha > 98/2$. Reaction time 5 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124b** (80.8 mg, 0.3 mmol) with EtMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et₂O. The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130ba** (76.6 mg, 0.29 mmol) in 98% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.52-7.47 (m, 2H), 7.39-7.31 (m, 3H), 5.71 (dd, $J = 17.4, 10.8$ Hz, 1H), 4.99 (dd, $J = 10.8, 1.6$ Hz, 1H), 4.70 (dd, $J = 17.4, 1.6$ Hz, 1H), 1.56 (m, 1H), 1.42 (m, 1H), 0.98 (s, 3H), 0.72 (t, $J = 7.3$ Hz, 3H), 0.27 (s, 3H), 0.26 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 137.3, 134.9, 129.0, 127.5, 111.3, 31.0, 28.0, 16.5, 7.9, -5.9, -6.0. $[\alpha]_D^{20} = +13.4$ ($c = 0.500$ CHCl₃) for a 96% ee sample. These data are in good agreement with those reported in literature.^[118] The absolute configuration of **130ba** was assigned by comparison of the optical rotation with a reported value.^[118]

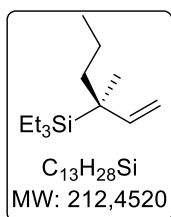
Enantiomeric ratio > 98:2 was determined by chiral GC analysis CP-ChiraSil DEX-CB column: 70-0-5-100-24-25-200). Chromatograms are illustrated below: 22.49 (S), 25.78 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.559	MM	0.2483	1375.72302	92.32710	49.89100
2	25.699	MM	0.2304	1381.73450	99.97314	50.10900



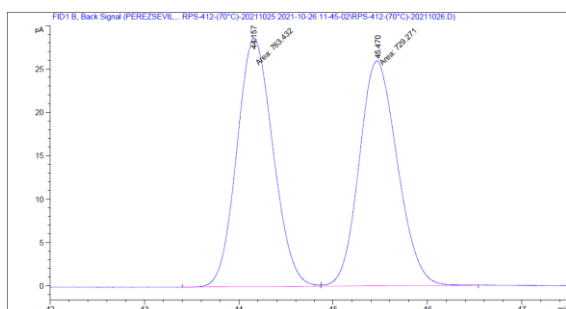
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.449	MM	0.2298	2773.09644	201.11420	99.48576
2	25.781	MM	0.2132	14.33413	1.12074	0.51424

(+)-(S)-3-Methyl-3-(triethylsilyl)-1-hexene (130ab)

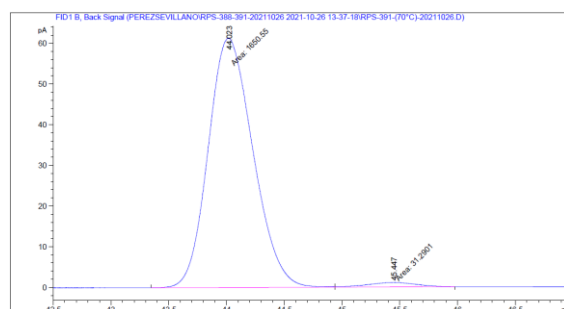
Mixture $\gamma/\alpha > 98/2$. Reaction time 6 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124a** (72.6 mg, 0.3 mmol) with $n\text{PrMgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130ab** (44.6 mg, 0.21 mmol) in 70% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.84 (dd, $J = 17.4, 10.7$ Hz, 1H), 4.89 (dd, $J = 10.7, 1.7$ Hz, 1H), 4.69 (dd, $J = 17.4, 1.7$ Hz, 1H), 1.52-1.34 (m, 2H), 1.30-1.08 (m, 2H), 1.02 (s, 3H), 0.97 (t, $J = 7.9$ Hz, 9H), 0.86 (t, $J = 7.3$ Hz, 3H), 0.59 (q, $J = 7.5$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 146.1, 109.8, 39.0, 32.2, 17.9, 16.7, 15.1, 8.4, 1.9. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = +21.84$ ($c = 0.750$ CHCl_3) for a 96% ee sample.

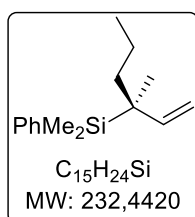
Enantiomeric ratio $> 98:2$ was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 70-50-25-200). Chromatograms are illustrated below: 40.02 (S), 45.45 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	44.157	MF	0.4438	763.43158	28.67328	51.14427
2	45.470	FM	0.4683	729.27063	25.95198	48.85573



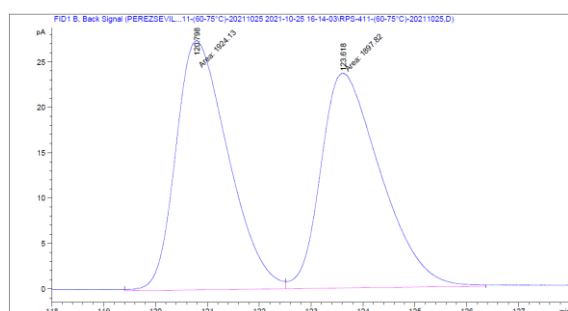
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	44.023	MF	0.4492	1650.55127	61.24148	98.13953
2	45.447	FM	0.4888	31.29012	1.06698	1.86047

(+)-(S)-3-(Dimethylphenylsilyl)-3-methyl-1-hexene (130bb)


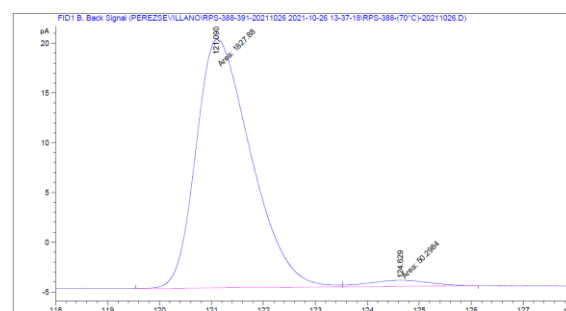
Mixture $\gamma/\alpha > 98/2$. Reaction time 6 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124b** (80.8 mg, 0.3 mmol) with $n\text{PrMgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130bb** (60.7 mg, 0.26 mmol) in 87% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.53-7.48 (m, 2H), 7.39-7.31 (m, 3H), 5.75 (dd, $J = 17.4, 10.7$ Hz, 1H), 4.96 (dd, $J = 10.8, 1.6$ Hz, 1H), 4.68 (dd, $J = 17.5, 1.6$ Hz, 1H), 1.43 (m, 1H), 1.33 (m, 1H), 1.28-1.07 (m, 2H), 1.00 (s, 3H), 0.83 (t, $J = 7.3$ Hz), 0.27 (s, 3H), 0.26 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 145.0, 137.3, 134.9, 129.0, 127.5, 110.8, 38.0, 31.2, 17.2, 16.9, 15.0, -6.0. **HRMS**: m/z calculated for $\text{C}_{15}\text{H}_{25}\text{Si}$ $[\text{M}+\text{H}]^+$ 233.1720, found 233.1720. $[\alpha]_D^{20} = +6.52$ ($c = 0.750$ CHCl_3) for a 96% ee sample.

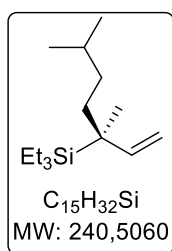
Enantiomeric ratio 97.5:2.5 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 60-0-2-75-25-20-200). Chromatograms are illustrated below: 121.09 (S), 124.63 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	120.798	MF	1.1664	1924.12500	27.49383	50.34412
2	123.618	FM	1.3362	1897.82068	23.67205	49.65588



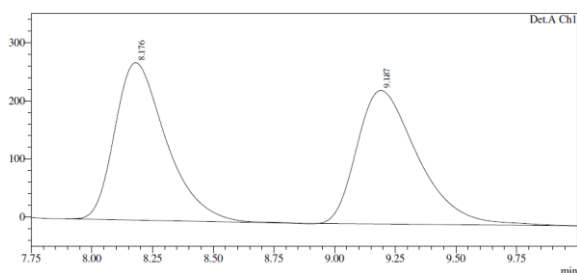
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	121.090	MF	1.2190	1827.88147	24.99201	97.32196
2	124.629	FM	1.3379	50.29839	6.26562e-1	2.67804

(–)-(S)-3-Isopentyl-3-(triethylsilyl)-1-butene (130ac)

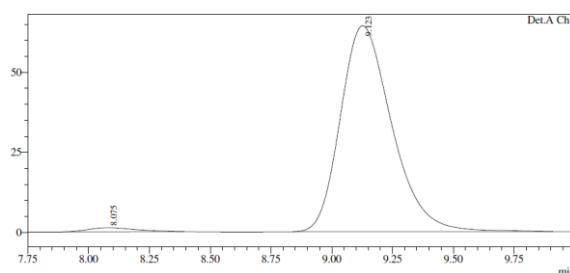
Mixture $\gamma/\alpha = 92/8$. Reaction time 21 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124a** (72.6 mg, 0.3 mmol) with *i*PentMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130bc** (58.6 mg, 0.24 mmol) in 81% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.81 (dd, $J = 17.4, 10.8$ Hz, 1H), 4.90 (dd, $J = 10.7, 1.7$ Hz, 1H), 4.69 (dd, $J = 17.4, 1.7$ Hz, 1H), 1.55–1.36 (m, 3H), 1.08 (m, 1H), 1.01 (s, 3H), 0.97 (t, $J = 7.9$ Hz, 9H), 0.91 (m, 1H), 0.86 (d, $J = 6.6$ Hz, 6H), 0.59 (q, $J = 7.8$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 146.1, 109.9, 34.1, 32.4, 31.7, 28.9, 22.9, 22.8, 17.8, 8.4, 1.9. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -16.68$ ($c = 1.000$ CHCl_3) for a 96% ee sample.

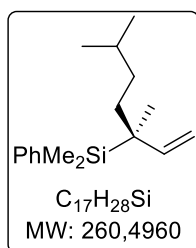
Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.9% hexane: 0.1% *i*PrOH, 0.5 mL/min) of the derived ester **139**, obtained by hydroboration of the olefin with $\text{BH}_3 \cdot \text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$ to obtain alcohol **138a**, used to perform esterification with acryloyl chloride in the presence of DMAP and Et_3N in CH_2Cl_2 . Chromatograms are illustrated below: 8.08 (*R*), 9.12 (*S*).



Peak#	Ret. Time	Area	Height	Area %
1	8.176	3989341	270391	49.905
2	9.187	4004577	229448	50.095
Total		7993918	499839	100.000



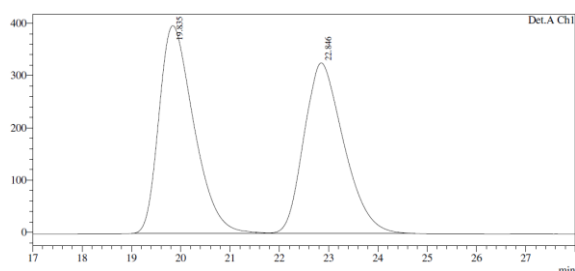
Peak#	Ret. Time	Area	Height	Area %
1	8.075	17120	1260	1.779
2	9.123	945184	64272	98.221
Total		962304	65532	100.000

(+)-(S)-3-(Dimethylphenylsilyl)-3-isopentil-1-butene (130bc)

Mixture $\gamma/\alpha = 92/8$. Reaction time 21 h.

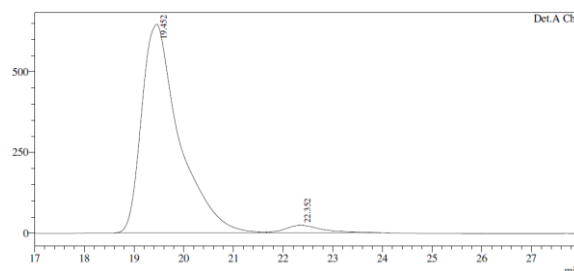
Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124b** (80.8 mg, 0.3 mmol) with *i*PentMgBr (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130bc** (68.0 mg, 0.26 mmol) in 87% yield as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.53-7.47 (m, 2H), 7.39-7.31 (m, 3H), 5.73 (dd, $J = 17.4, 10.8$ Hz, 1H), 4.96 (dd, $J = 10.8, 1.6$ Hz, 1H), 4.67 (dd, $J = 17.3, 1.6$ Hz, 1H), 1.52-1.31 (m, 1H), 1.04 (m, 1H), 0.99 (s, 3H), 0.88 (m, 1H), 0.82 (d, $J = 6.6$ Hz, 6H), 0.28 (s, 3H), 0.27 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 145.0, 137.3, 134.9, 129.0, 127.5, 110.9, 33.3, 32.6, 30.7, 28.8, 22.8, 22.8, 17.2, -5.9. HRMS: m/z calculated for $\text{C}_{17}\text{H}_{29}\text{Si}$ $[\text{M}+\text{H}]^+$ 261.2033, found 261.2031. $[\alpha]_D^{20} = +5.12$ ($c = 1.000$ CHCl_3) for a 93% ee sample.

Enantiomeric ratio 96.5:3.5 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min) of the derived alcohol **138d** obtained by hydroboration of the olefin with $\text{BH}_3\cdot\text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 19.45 (S), 22.35 (R).



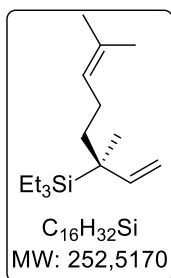
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	19.835	19526072	397698	51.527
2	22.846	18368655	326422	48.473
Total		37894727	724120	100.000



Detector A Ch1 220nm

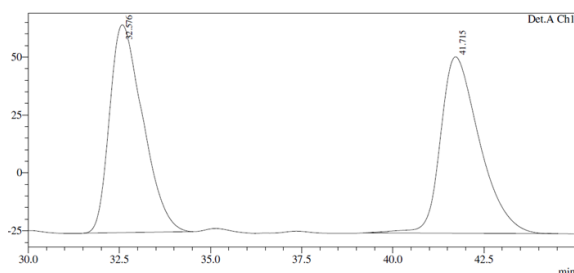
Peak#	Ret. Time	Area	Height	Area %
1	19.452	33937989	646764	96.576
2	22.352	1203175	23212	3.424
Total		35141163	669975	100.000

(-)-(S)-3,7-Dimethyl-3-(triethylsilyl)-octa-2,6-diene (130ad)

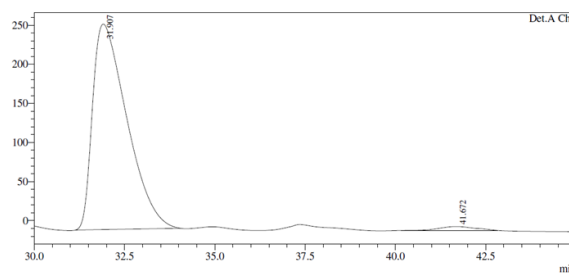
Mixture $\gamma/\alpha > 98/2$. Reaction time 21 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124a** (72.6 mg, 0.3 mmol) with $(\text{CH}_3)_2\text{CCH}(\text{CH}_2)_2\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130ad** (68.2 mg, 0.27 mmol) in 90% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.84 (dd, $J = 17.4, 10.7$ Hz, 1H), 5.10 (m, 1H), 4.92 (dd, $J = 10.7, 1.6$ Hz, 1H), 4.72 (dd, $J = 17.4, 1.8$ Hz, 1H), 1.93-1.75 (m, 2H), 1.68 (d, $J = 1.4$ Hz, 3H), 1.58 (d, $J = 1.3$ Hz, 3H), 1.52 (m, 1H), 1.43 (m, 1H), 1.05 (s, 3H), 0.97 (t, $J = 7.9$ Hz, 9H), 0.59 (q, $J = 8.2$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 145.7, 131.2, 125.4, 110.1, 36.5, 32.0, 25.9, 22.2, 17.7, 8.4, 1.9. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -39.63$ ($c = 1.000$ CHCl_3) for a 96% ee sample.

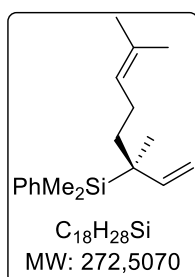
Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min) of the derived alcohol **138b** obtained by hydroboration of the olefin with 9-BBN in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 31.91 (S), 41.67 (R).



Peak#	Ret. Time	Area	Height	Area %
1	32.576	5693213	89688	50.038
2	41.715	5684557	76153	49.962
Total		11377770	165841	100.000



Peak#	Ret. Time	Area	Height	Area %
1	31.907	17358612	262808	98.085
2	41.672	338875	4973	1.915
Total		17697488	267781	100.000

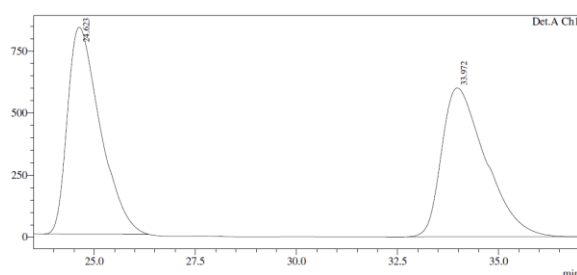
(–)-(S)-3,7-Dimethyl-3-(triethylsilyl)-octa-2,6-diene (130bd)


Mixture $\gamma/\alpha > 98/2$. Reaction time 21 h.

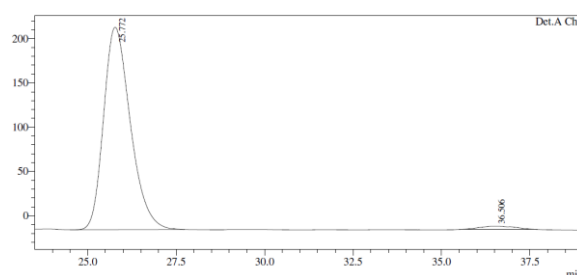
Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124b** (80.8 mg, 0.3 mmol) with $(\text{CH}_3)_2\text{CCH}(\text{CH}_2)_2\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130bd** (81.5 mg, 0.29 mmol) in 99% yield as a colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 7.51-7.47 (m, 2H), 7.39-7.31 (m, 3H), 5.75 (dd, $J = 17.4, 10.7$ Hz, 1H), 5.04 (m, 1H), 4.98 (dd, $J = 10.8, 1.6$ Hz, 1H), 4.67 (dd, $J = 17.4, 1.6$ Hz, 1H), 1.93-1.71 (m, 2H), 1.65 (d, $J = 1.3$ Hz, 3H), 1.53 (d, $J = 1.3$ Hz, 3H), 1.48 (m, 1H), 1.36 (m, 1H), 1.02 (s, 3H), 0.27 (s, 3H), 0.26 (s, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 144.6, 137.1, 134.9, 131.2, 129.0, 127.5, 125.3, 111.1, 35.6, 25.9, 22.3, 17.7, 17.1, –6.0. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -12.85$ ($c = 1.000$ CHCl_3) for a 96% ee sample.

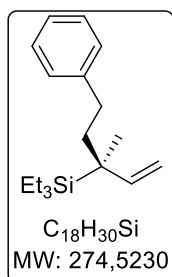
Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min) of the derived alcohol **138e** obtained by hydroboration of the olefin with 9-BBN in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 25.77 (S), 36.51 (R).



Peak#	Ret. Time	Area	Height	Area %
1	24.623	46974726	833744	50.800
2	33.972	45495517	599796	49.200
Total		92470243	1433540	100.000



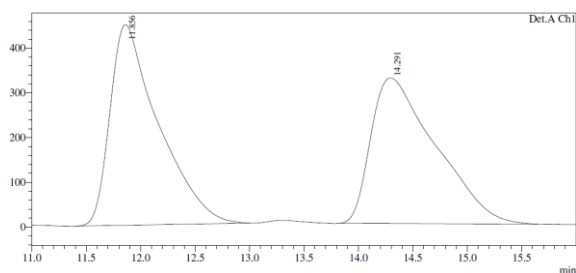
Peak#	Ret. Time	Area	Height	Area %
1	25.772	12043899	228616	97.918
2	36.506	256114	3574	2.082
Total		12300013	232190	100.000

(-)-(S)-3-Phenetyl-3-(triethylsilyl)-1-butene (130ae)

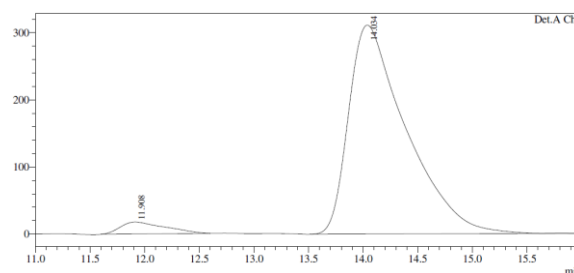
Mixture $\gamma/\alpha > 98/2$. Reaction time 21 h.

Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124a** (72.6 mg, 0.3 mmol) with $\text{C}_6\text{H}_5(\text{CH}_2)_2\text{MgBr}$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130ae** (73.3 mg, 0.27 mmol) in 89% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.30-7.24 (m, 2H), 7.20-7.13 (m, 3H), 5.92 (dd, $J = 17.4, 10.7$ Hz, 1H), 5.00 (dd, $J = 10.7, 1.6$ Hz, 1H), 4.80 (dd, $J = 17.3, 1.6$ Hz, 1H), 2.53 (td, $J = 12.3, 5.5$ Hz, 1H), 2.43 (td, $J = 13.0, 4.2$ Hz, 1H), 1.82 (td, $J = 13.5, 4.6$ Hz, 1H), 1.73 (td, $J = 12.5, 5.6$ Hz, 1H), 1.15 (s, 3H), 0.97 (t, $J = 8.0$ Hz, 9H), 0.60 (q, $J = 8.0$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 145.5, 143.8, 128.5, 128.5, 125.6, 110.6, 38.9, 32.1, 30.0, 17.8, 8.3, 1.9. **HRMS**: Ongoing experiments. $[\alpha]_D^{20} = -49.08$ ($c = 0.800$ CHCl_3) for a 91% ee sample.

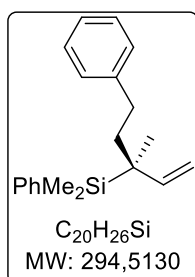
Enantiomeric ratio 95.5:4.5 was determined by chiral HPLC analysis (Chiral Technologies ADH, 214 nm, 98% hexane: 2% *i*PrOH, 1 mL/min) of the derived alcohol **138c** obtained by hydroboration of the olefin with $\text{BH}_3 \cdot \text{SMe}_2$ in THF, followed by oxidation with $\text{H}_2\text{O}_2/\text{NaOH}$. Chromatograms are illustrated below: 11.91 (*R*), 14.03 (*S*).



Peak#	Ret. Time	Area	Height	Area %
1	11.856	13894349	448778	50.819
2	14.291	13446733	325296	49.181
Total		27341083	774075	100.000



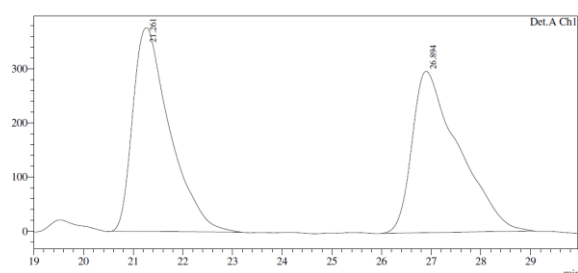
Peak#	Ret. Time	Area	Height	Area %
1	11.908	504569	17888	4.243
2	14.034	11387475	311060	95.757
Total		11892044	328947	100.000

(-)-(S)-3-(Dimethylphenylsilyl)-3-(Phenethyl)-1-butene (130be)

Mixture $\gamma/\alpha > 98/2$. Reaction time 21h.

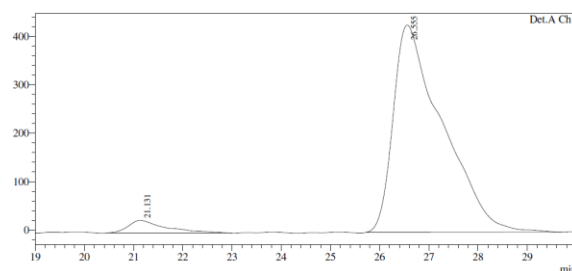
Prepared according to **GP11** from the reaction of allylbromide (**E**)-**124b** (80.8 mg, 0.3 mmol) with $C_6H_5(CH_2)_2MgBr$ (1.5 equiv) in the presence of NHC-ligand **88** (2.98 mg, 6.0×10^{-3} mmol) in Et_2O . The residue is purified by a (rapid) flash column chromatography (pentane, $R_f = 0.98$) to afford the desired product **130be** (79.5 mg, 0.27 mmol) in 90% yield as a colorless oil. 1H NMR (400 MHz, $CDCl_3$) δ 7.53-7.47 (m, 2H), 7.40-7.23 (m, 5H), 7.22-7.09 (m, 3H), 5.84 (dd, $J = 17.4, 10.7$ Hz, 1H), 5.06 (dd, $J = 10.8, 1.5$ Hz, 1H), 4.79 (dd, $J = 17.4, 1.5$ Hz, 1H), 2.55-2.37 (m, 2H), 1.80 (td, $J = 12.8, 5.1$ Hz, 1H), 1.68 (td, $J = 12.8, 5.6$ Hz, 2H), 1.18 (s, 3H), 0.29 (s, 3H), 0.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 143.6, 136.9, 134.9, 129.1, 128.5, 128.4, 127.6, 125.7, 111.6, 38.0, 31.2, 30.2, 17.2, -5.9. HRMS: m/z calculated for $C_{20}H_{26}Si$ $[M+H]^+$ 295.1877, found 295.1873. $[\alpha]_D^{20} = -28.87$ ($c = 1.000$ $CHCl_3$) for a 91% ee sample.

Enantiomeric ratio 95.5:4.5 was determined by chiral HPLC analysis (Chiral Technologies ADH, 214 nm, 98.5% hexane: 1.5% *i*PrOH, 1 mL/min) of the derived alcohol **138f** obtained by hydroboration of the olefin with $BH_3 \cdot SMe_2$ in THF, followed by oxidation with $H_2O_2/NaOH$. Chromatograms are illustrated below: 21.13 (*R*), 26.55 (*S*).



Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	21.261	19495929	376805	49.984
2	26.894	19508499	298258	50.016
Total		39004428	675063	100.000

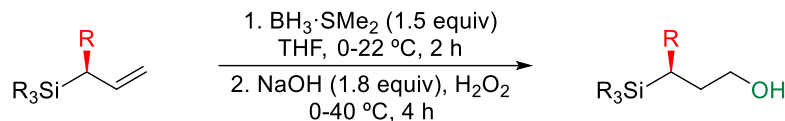


Detector A Ch1 214nm

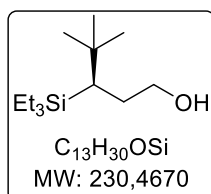
Peak#	Ret. Time	Area	Height	Area %
1	21.131	1381512	26080	4.429
2	26.555	29807820	428172	95.571
Total		31189333	454252	100.000

3.5 Hydroboration-oxidation of allylsilanes

3.5.1.1 With $\text{BH}_3\cdot\text{SMe}_2$



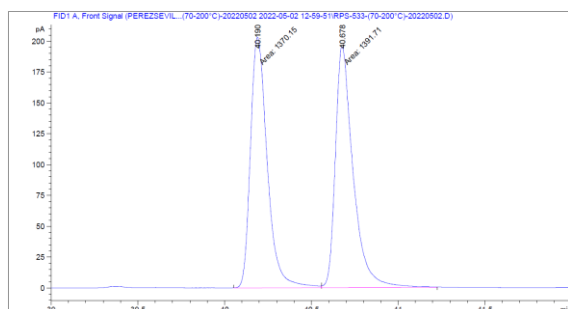
General procedure GP12: In a flame-dried Schlenk under Argon atmosphere equipped with a stir bar is placed the corresponding allylsilane (1 equiv) and is dissolved in freshly distilled THF (0.25 M adjusted depending on the borane). The solution is cooled to $-15\text{ }^\circ\text{C}$ and then $\text{BH}_3\cdot\text{SMe}_2$ (1.5 equiv of 0.5 M in THF) is added dropwise. After addition is complete, the solution is allowed to stir 5 min at $0\text{ }^\circ\text{C}$ (ice bath). After 2 h at $25\text{ }^\circ\text{C}$, the mixture is allowed to cool to $0\text{ }^\circ\text{C}$ (ice bath) and H_2O_2 (9 equiv of 35% w/t solution in H_2O) along with NaOH (1.8 equiv of 3 M solution in H_2O) are added dropwise through a syringe. After 5 min at $0\text{ }^\circ\text{C}$, the mixture is stirred 4 h at $40\text{ }^\circ\text{C}$. The mixture is cold down at room temperature and diluted with 5 mL of Et_2O and 5 mL of H_2O . The layers are separated and the aqueous phase extracted with three times with Et_2O (3 x 5 mL). The combined organic layers are washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue is purified by flash column chromatography to offer exclusively the *anti*-Markovnikov product.

(+)-(R)-3-*tert*-Butyl-3-(triethyl)silyl-propan-1-ol (119a)

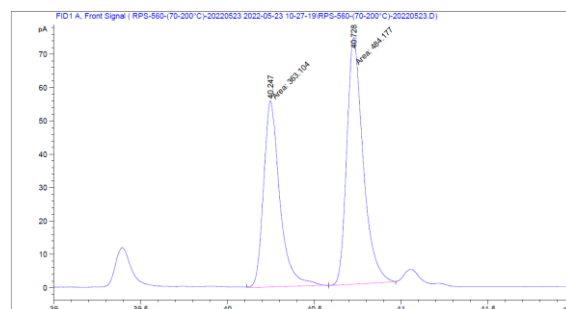
Prepared according to **GP12** from the reaction of **115h** (50.6 mg, 0.23 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.7 mL, 0.35 mmol) in THF (0.22 mL), previous addition of H_2O_2 (0.17 mL, 2.07 mmol) and NaOH (0.14 mL, 0.41 mmol).

The residue is purified by flash column chromatography (pentane: Et_2O 4:1, $R_f = 0.3$) to afford the desired product **119a** (25.9 mg, 0.11 mmol) in 49% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.60 (td, $J = 9.6, 7.6$ Hz, 1H), 3.48 (td, $J = 9.4, 7.7$ Hz, 1H), 1.69-1.59 (m, 2H), 1.32 (br. s, 1H, OH), 0.97 (t, $J = 7.8$ Hz, 9H), 0.95 (s, 9H), 0.64 (q, $J = 8.0$ Hz, 6H), 0.43 (t, $J = 4.6$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 65.3, 34.5, 31.4, 31.2, 30.7, 8.10, 4.8. **HRMS**: m/z calculated for $\text{C}_{11}\text{H}_{25}\text{OSi}$ $[\text{M}-\text{C}_2\text{H}_5]^+$ 201.1669, found 201.1667. $[\alpha]_D^{20} = +0.92$ ($c = 0.800$ CHCl_3) for a 14% ee sample.

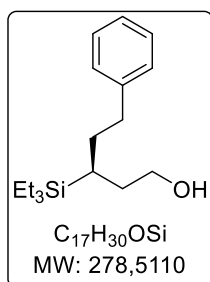
Enantiomeric ratio 57:43 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 70-0-2-200). Chromatograms are illustrated below: 40.28 (*R*), 40.73 (*S*).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.190	MF	0.1124	1370.15344	203.13458	49.60967
2	40.678	FM	0.1190	1391.71399	194.91705	50.39033

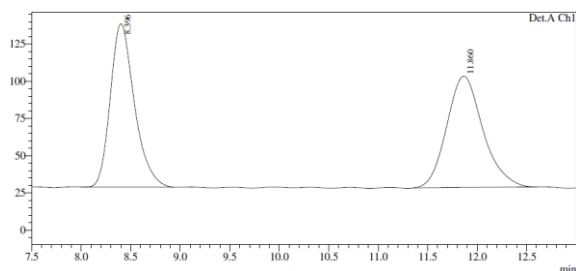


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.247	MM	0.1083	363.10446	55.86544	42.85523
2	40.728	MM	0.1089	484.17706	74.08640	57.14477

(+)-(S)-3-Phenetyl-3-(triethylsilyl)-propan-1-ol (119c)

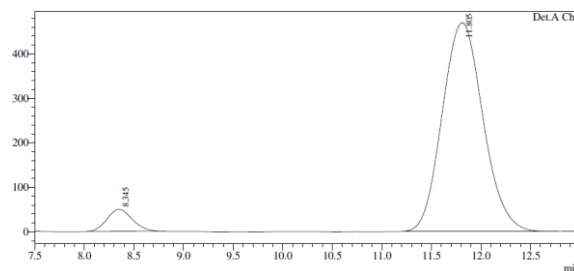
Prepared according to **GP12** from the reaction of **115d** (88.1 mg, 0.34 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (1.02 mL, 0.51 mmol) in THF (0.34 mL), previous addition of H_2O_2 (0.26 mL, 3.04 mmol) and NaOH (0.20 mL, 0.61 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 4:1, $R_f = 0.3$) to afford the desired product **119c** (48.1 mg, 0.172 mmol) in 51% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.31-7.25 (m, 2H), 7.22-7.14 (m, 3H), 3.70 (m, 1H), 3.63 (m, 1H), 2.70 (m, 1H), 2.57 (m, 1H), 1.80 (m, 1H), 1.60 (m, 1H), 1.2 (br. s, 1H), 0.95 (t, $J = 7.9$ Hz, 9H), 0.83 (tt, $J = 8.4, 4.5$ Hz, 1H), 0.59 (q, $J = 7.8$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 142.9, 128.5, 125.9, 62.9, 36.4, 33.5, 32.5, 18.6. **HRMS**: m/z calculated for $\text{C}_{15}\text{H}_{25}\text{OSi}$ [$\text{M}-\text{C}_2\text{H}_5$] $^+$ 249.1669, found 249.1667. $[\alpha]_D^{20} = +3.68$ ($c = 1.000$ CHCl_3) for a 88% ee sample.

Enantiomeric ratio 94:6 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 95% hexane: 5% $i\text{PrOH}$, 1 mL/min). Chromatograms are illustrated below: 8.34 (R), 11.81 (S).



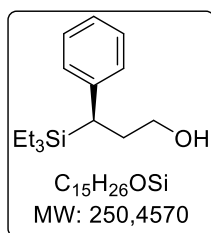
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	8.396	1854226	109621	49.421
2	11.860	1897662	74667	50.579
Total		3751888	184288	100.000



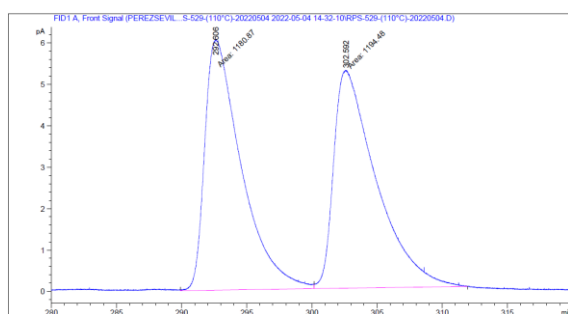
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	8.345	873244	49355	6.130
2	11.805	13372628	468706	93.870
Total		14245872	518062	100.000

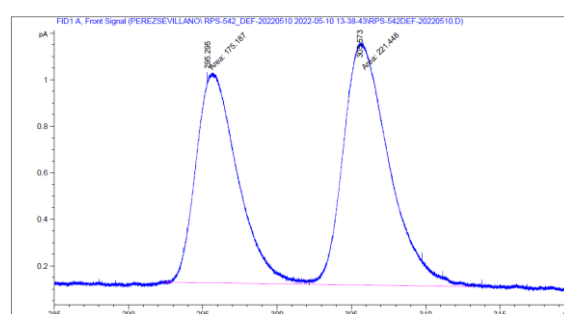
(-)-(R)-3-Phenyl-3-(triethylsilyl)propan-1-ol (119d)

Prepared according to **GP12** from the reaction of **118a** (42.1 mg, 0.18 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.54 mL, 0.27 mmol) in THF (0.20 mL), previous addition of H_2O_2 (0.14 mL, 1.61 mmol) and NaOH (0.11 mL, 0.33 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 4:1, R_f = 0.3) to afford the desired product **125d** (20.5 mg, 0.082 mmol) in 46% yield as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.25-7.20 (m, 2H), 7.12-7.04 (m, 3H), 3.57 (m, 1H), 3.45 (m, 1H), 2.30 (dd, J = 12.6, 3.2 Hz, 1H), 2.10 (m, 1H), 1.97 (m, 1H), 1.18 (br. s, 1H, OH), 0.89 (t, J = 7.9 Hz, 9H), 0.52 (q, J = 7.8 Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 143.2, 128.4, 128.0, 124.7, 62.6, 32.8, 30.2, 7.6, 2.4. HRMS: m/z calculated for $\text{C}_{15}\text{H}_{27}\text{OSi}$ $[\text{M}+\text{H}]^+$ 251.1826, found 251.1825. $[\alpha]_D^{20}$ = -4.38 (c = 1.000 CHCl_3) for a 12% ee sample.

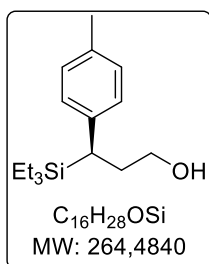
Enantiomeric ratio 56:44 was determined by chiral GC analysis (CP-ChiraSil DEX-CB column: 110-315-25-200). Chromatograms are illustrated below: 295.30 (S), 305.57 (R).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	292.606	MF	3.2504	1180.86902	6.05503	49.71352
2	302.592	FM	3.7796	1194.47900	5.26726	50.28648

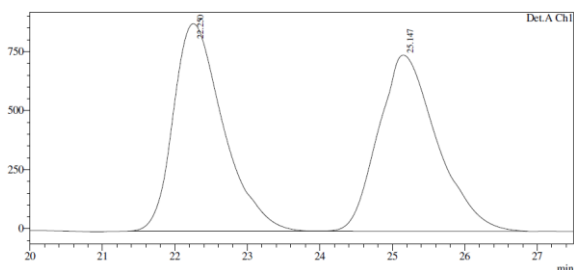


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	295.295	MF	3.2076	175.18674	9.10273e-1	44.16823
2	305.573	FM	3.5441	221.44847	1.04139	55.83177

3-(4-methylphenyl)-3-(triethylsilyl)-propan-1-ol (119e)

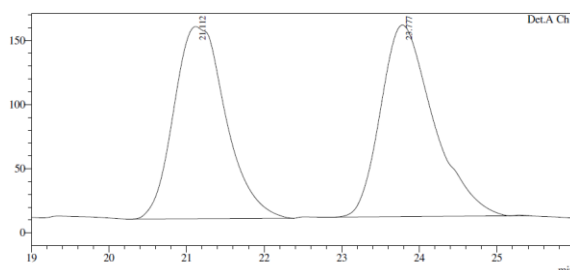
Prepared according to **GP12** from the reaction of **118b** (30.1 mg, 0.12 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.37 mL, 0.18 mmol) in THF (0.11 mL), previous addition of H_2O_2 (0.09 mL, 1.10 mmol) and NaOH (0.07 mL, 0.22 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 4:1, $R_f = 0.4$) to afford the desired product **119e** (18.7 mg, 0.071 mmol) in 58% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.04 (d, $J = 7.9$ Hz, 2H), 6.96 (d, $J = 8.0$ Hz, 2H), 3.57 (m, 1H), 3.45 (m, 1H), 2.29 (s, 3H), 2.25 (dd, $J = 12.6, 3.2$ Hz, 1H), 2.11–1.91 (m, 2H), 1.19 (br. s, 1H, OH), 0.90 (t, $J = 7.9$ Hz, 9H), 0.51 (q, $J = 7.9$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 139.9, 134.1, 129.1, 127.8, 62.6, 32.8, 29.6, 21.1, 7.7, 2.4. **HRMS**: m/z calculated for $\text{C}_{16}\text{H}_{28}\text{OSi}$ $[\text{M}+\text{H}]^+$ 265.1982, found 265.1981. $[\alpha]_D^{20} = 0$ ($c = 0.700$ CHCl_3) for a 0% ee sample.

Enantiomeric ratio 50:50 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99% hexane: 2% $i\text{PrOH}$, 1 mL/min). Chromatograms are illustrated below: 21.11, 23.77.



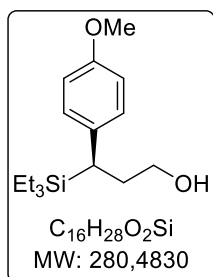
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	21.112	41956964	877453	50.020
2	23.777	41923727	744950	49.980
Total		83880690	1622403	100.000



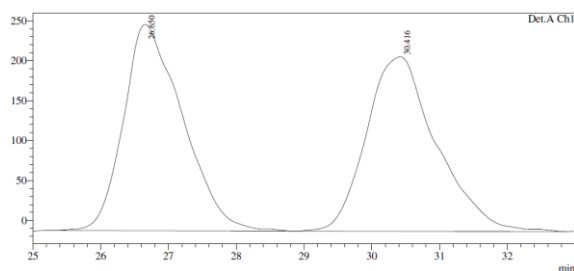
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	21.112	6965886	149804	49.612
2	23.777	7074914	149345	50.388
Total		14040801	299148	100.000

3-(4-methoxyphenyl)-3-(triethylsilyl)-propan-1-ol (119f)

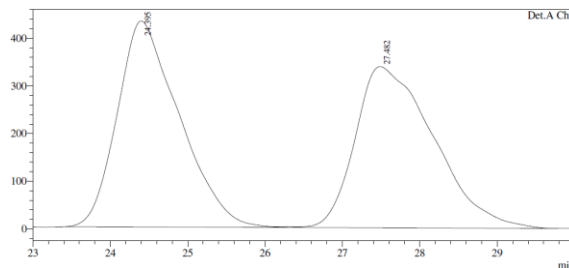
Prepared according to **GP12** from the reaction of **118c** (46.8 mg, 0.18 mmol) with $BH_3 \cdot SMe_2$ (0.54 mL, 0.27 mmol) in THF (0.18 mL), previous addition of H_2O_2 (0.14 mL, 1.60 mmol) and NaOH (0.11 mL, 0.32 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 4:1, R_f = 0.4) to afford the desired product **119f** (27.3 mg, 0.099 mmol) in 55% yield as a colorless oil. 1H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.7 Hz, 2H), 3.78 (s, 3H), 3.56 (m, 1H), 3.45 (m, 1H), 2.23 (dd, J = 11.8, 4.0 Hz, 1H), 2.10-1.88 (m, 2H), 1.26 (br. s, 1H, OH), 0.89 (t, J = 7.9 Hz, 9H), 0.51 (q, J = 7.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 135.0, 128.7, 113.9, 62.6, 55.4, 33.0, 29.0, 7.7, 2.4. HRMS: m/z calculated for $C_{16}H_{28}O_2SiNa$ $[M+Na]^+$ 303.1751, found 303.157. $[\alpha]_D^{20}$ = 0 (c = 0.500 $CHCl_3$) for a 0% ee sample.

Enantiomeric ratio 50:50 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99% hexane: 2% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 24.40, 27.48.



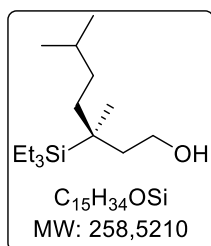
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	26.650	15679183	258190	49.939
2	30.416	15717505	218466	50.061
Total		31396688	476656	100.000



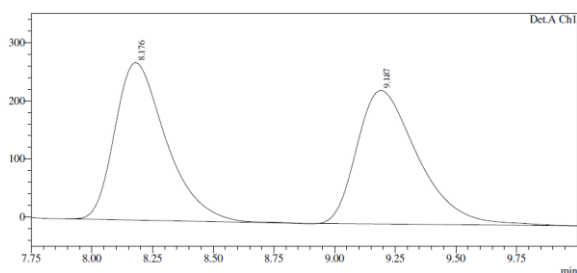
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	24.395	24111728	432216	50.282
2	27.482	23840845	338319	49.718
Total		47952573	770535	100.000

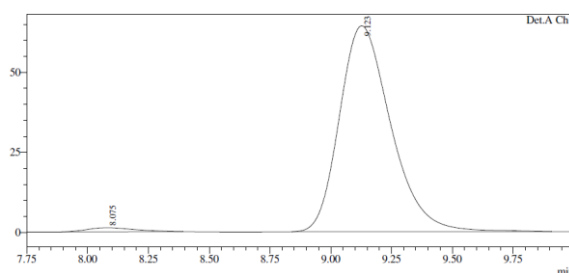
(+)-(S)-3-Isopentyl-3-(triethylsilyl)-butan-1-ol (138a)

Prepared according to **GP12** from the reaction of **130ac** (52.9 mg, 0.22 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.66 mL, 0.33 mmol) in THF (0.22 mL), previous addition of H_2O_2 (0.17 mL, 1.98 mmol) and NaOH (0.13 mL, 0.40 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 5:1, $R_f = 0.5$) to afford the desired product **138a** (37.5 mg, 0.143 mmol) in 65% yield as a colorless oil. $^1\text{H NMR}$ (400 MHz, CDCl_3) 3.86 (m, 2H), 1.73-1.57 (m, 2H), 1.46-1.09 (m, 5H), 1.25 (br. s, 1H, OH), 0.99 (t, $J = 7.9$ Hz, 9H), 0.94 (s, 3H), 0.88 (d, $J = 6.6$ Hz, 6H), 0.61 (q, $J = 7.9$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 60.1, 40.3, 35.6, 33.5, 29.2, 23.6, 23.0, 8.5, 3.0. **HRMS**: m/z calculated for $\text{C}_{15}\text{H}_{34}\text{OSi}$ $[\text{M}-\text{C}_2\text{H}_5]^+$ 229.1982, found 229.1982. $[\alpha]_D^{20} = +0.12$ ($c = 0.500$ CHCl_3) for a 96% ee sample.

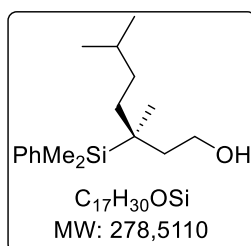
Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.9% hexane: 0.1% *i*PrOH, 0.5 mL/min) of the derived ester **139**, obtained by esterification with acryloyl chloride in the presence of DMAP and Et_3N in CH_2Cl_2 . Chromatograms are illustrated below: 8.08 (*R*), 9.12 (*S*).



Peak#	Ret. Time	Area	Height	Area %
1	8.176	3989341	270391	49.905
2	9.187	4004577	229448	50.095
Total		7993918	499839	100.000

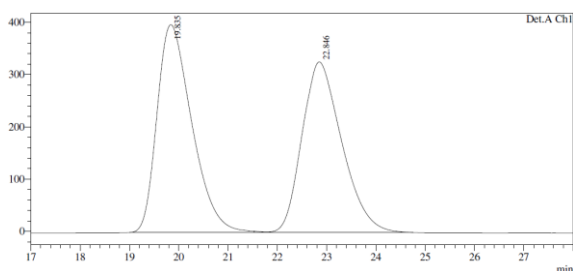


Peak#	Ret. Time	Area	Height	Area %
1	8.075	17120	1260	1.779
2	9.123	945184	64272	98.221
Total		962304	65532	100.000

(–)-(S)-3-(Dimethylphenylsilyl)-3-isopentyl-butan-1-ol (138d)

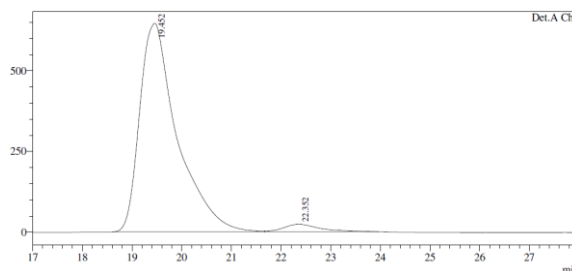
Prepared according to **GP12** from the reaction of **130bc** (45.3 mg, 0.17 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.52 mL, 0.26 mmol) in THF (0.16 mL), previous addition of H_2O_2 (0.13 mL, 1.56 mmol) and NaOH (0.11 mL, 0.31 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 4:1, R_f = 0.35) to afford the desired product **138d** (27.6 mg, 0.197 mmol) in 57% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 7.56-7.52 (m, 2H), 7.39-7.35 (m, 3H), 3.62 (t, J = 8.0 Hz, 2H), 1.73-1.55 (m, 2H), 1.45-1.06 (m, 6H, OH), 0.93 (s, 3H), 0.84 (dd, J = 6.6, 1.6 Hz, 6H), 0.32 (s, 3H), 0.31 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 138.3, 134.7, 129.0, 127.7, 59.9, 39.4, 34.9, 33.5, 29.1, 22.8, 22.8, 22.7, 22.4, –4.2, –4.3. **HRMS**: m/z calculated for C₁₁H₂₅OSi [M-C₆H₅]⁺ 201.1669, found 201.1669. $[\alpha]_D^{20}$ = –0.54 (c = 0.600 CHCl₃) for a 93% ee sample.

Enantiomeric ratio 96.5:3.5 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 19.45 (S), 22.35 (R).



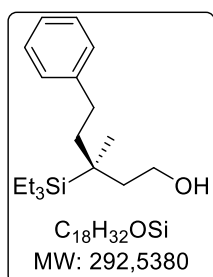
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	19.835	19526072	397698	51.527
2	22.846	18368655	326422	48.473
Total		37894727	724120	100.000



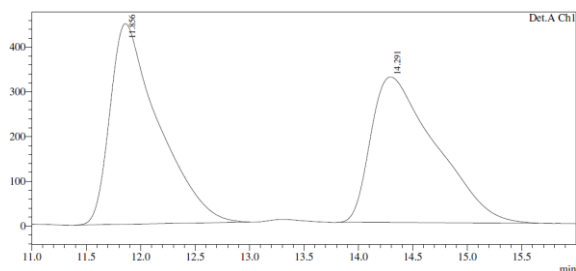
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	19.452	33937989	646764	96.576
2	22.352	1203175	23212	3.424
Total		35141163	669975	100.000

(–)-(S)-(3-(triethyl)silyl-3-phenethyl)butan-1-ol (138c)

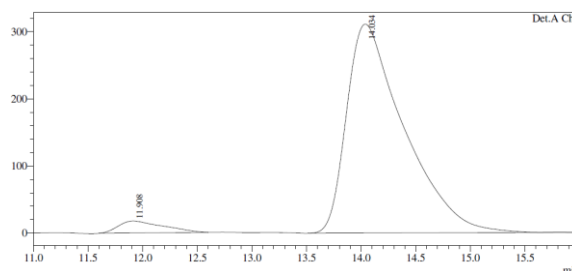
Prepared according to **GP12** from the reaction of **130ae** (37.2 mg, 0.14 mmol) with $\text{BH}_3\cdot\text{SMe}_2$ (0.41 mL, 0.20 mmol) in THF (0.16 mL), previous addition of H_2O_2 (0.11 mL, 1.22 mmol) and NaOH (0.08 mL, 0.24 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 4:1, R_f = 0.35) to afford the desired product **138c** (21.1 mg, 0.198 mmol) in 53% yield as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.25 (m, 2H), 7.21-7.15 (m, 3H), 3.76 (m, 2H), 2.60 (m, 2H), 1.85-1.56 (m, 4H), 1.26 (br. s, 1H, OH), 1.06 (s, 3H), 1.03 (t, J = 7.9 Hz, 9H), 0.67 (q, J = 8.0 Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 143.5, 128.5, 128.4, 125.8, 60.1, 40.2, 3.2, 24.1, 22.9, 8.5, 3.0. HRMS: m/z calculated for $\text{C}_{18}\text{H}_{36}\text{OSiN}$ $[\text{M}+\text{NH}_4]^+$ 310.2561, found 310.2560. $[\alpha]_D^{20}$ = -3.64 (c = 0.900 CHCl_3) for a 91% ee sample.

Enantiomeric ratio 95.5:4.5 was determined by chiral HPLC analysis (Chiral Technologies ADH, 214 nm, 98% hexane: 2% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 11.91 (R), 14.03 (S).



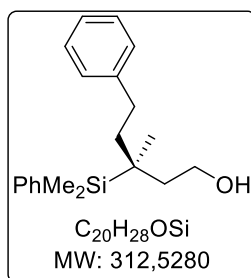
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	11.856	13894349	448778	50.819
2	14.291	13446733	325296	49.181
Total		27341083	774075	100.000



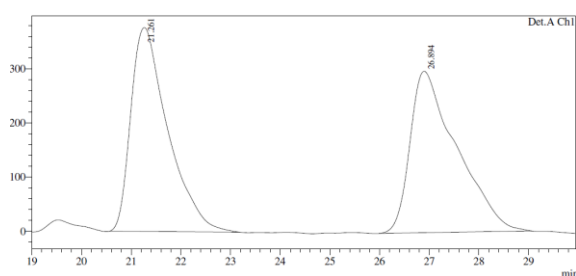
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	11.908	504569	17888	4.243
2	14.034	11387475	311060	95.757
Total		11892044	328947	100.000

(-)-(S)-3-(Dimethylphenylsilyl)-3-phenethyl-butan-1-ol (138f)

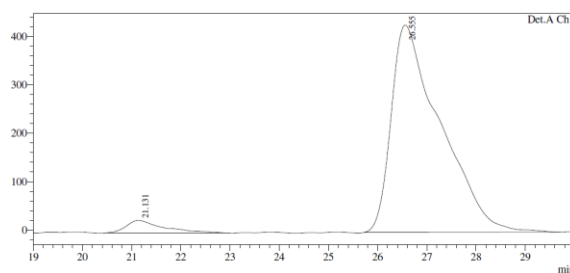
Prepared according to **GP12** from the reaction of **139be** (55.7 mg, 0.20 mmol) with BH₃·SMe₂ (0.60 mL, 0.20 mmol) in THF (0.2 mL), previous addition of H₂O₂ (0.15 mL, 1.80 mmol) and NaOH (0.12 mL, 0.36 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 4:1, R_f = 0.35) to afford the desired product **138f** (41.8 mg, 0.123 mmol) in 67% yield as a colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 7.58-7.53 (m, 2H), 7.39-7.34 (m, 3H), 7.29-7.24 (m, 2H), 7.20-7.14 (m, 1H), 7.12-7.08 (m, 2H), 3.70 (t, *J* = 7.9 Hz, 2H), 2.56 (m, 2H), 1.81-1.55 (m, 4H), 1.13 (br.s, 1H, OH), 1.04 (s, 3H), 0.37 (s, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 143.3, 138.0, 134.7, 129.1, 128.5, 128.4, 127.8, 125.8, 59.9, 39.8, 39.4, 31.1, 22.3, -4.2, -4.3. **HRMS**: *m/z* calculated for C₂₀H₃₂OSiN [M+NH₄]⁺ 330.2248, found 330.2247. [α]_D²⁰ = -5.86 (*c* = 0.800 CHCl₃) for a 91% ee sample.

Enantiomeric ratio 95.5:4.5 was determined by chiral HPLC analysis (Chiral Technologies ADH, 214 nm, 98.5% hexane: 1.5% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 21.13 (*R*), 26.55 (*S*).



Detector A Ch1 214nm

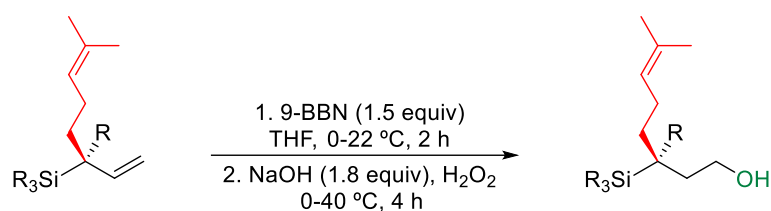
Peak#	Ret. Time	Area	Height	Area %
1	21.261	19495929	376805	49.984
2	26.894	19508499	298258	50.016
Total		39004428	675063	100.000



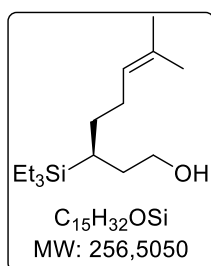
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	21.131	1381512	26080	4.429
2	26.555	29807820	428172	95.571
Total		31189333	454252	100.000

3.5.1.2 With 9-BBN

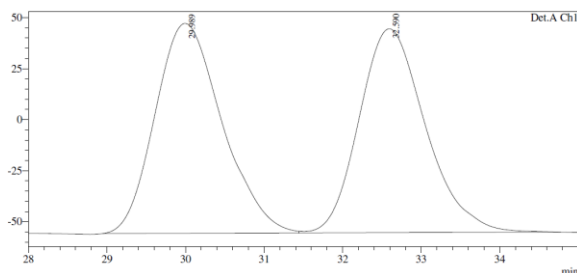


General procedure GP13: In a flame-dried Schlenk under Argon atmosphere equipped with a stir bar, is placed the corresponding allylsilane (1 equiv) and dissolved in freshly distilled THF (0.25 M adjusted depending on the borane). The solution is cooled to $-15\text{ }^\circ\text{C}$ and then 9-BBN (1.5 equiv of 0.5 M in THF) was added dropwise. After addition is complete, the solution is allowed to stir 5 min at $0\text{ }^\circ\text{C}$ (ice bath). After 2 h at $25\text{ }^\circ\text{C}$, the mixture is allowed to cool to $0\text{ }^\circ\text{C}$ (ice bath) and H_2O_2 (9 equiv of 35% w/t solution in H_2O) along with NaOH (1.8 equiv of 3 M solution in H_2O) are added dropwise through a syringe. After 5 min at $0\text{ }^\circ\text{C}$, the mixture is stirred 4 h at $40\text{ }^\circ\text{C}$. The mixture is cold down at room temperature and diluted with 5 mL of Et_2O and 5 mL of H_2O . The layers are separated and the aqueous phase extracted three times with Et_2O (3 x 5 mL). The combined organic layers are washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue is purified by flash column chromatography to offer exclusively the *anti*-Markovnikov product.

(-)-(S)-7-Methyl-3-(triethylsilyl)-oct-6-ene-1-ol (119b)

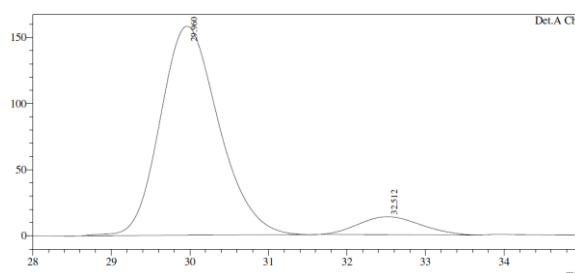
Prepared according to **GP13** from the reaction of **115c** (65.5 mg, 0.276 mmol) with 9-BBN (0.83 mL, 0.41 mmol) in THF (0.27 mL), previous addition of H₂O₂ (0.22 mL, 2.48 mmol) and NaOH (0.17 mL, 0.50 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 5:1, R_f = 0.25) to afford the desired product **125b** (24.3 mg, 0.091 mmol) in 48% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.09 (tt, *J* = 7.0, 1.4 Hz, 1H), 3.65 (m, 2H), 1.98 (m, 2H), 1.75 (m, 1H), 1.70 (d, *J* = 1.3 Hz, 3H), 1.61 (d, *J* = 1.3 Hz, 3H), 1.58-1.44 (m, 2H), 1.35-1.19 (m, 1H), 1.24 (br. s, 1H, OH), 0.95 (t, *J* = 7.9 Hz, 9H), 0.75 (tt, *J* = 8.4, 4.5 Hz, 1H), 0.58 (q, *J* = 7.9 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 131.8, 124.9, 63.0, 33.5, 30.4, 28.5, 25.9, 18.5, 17.9, 7.9, 2.9. HRMS: *m/z* calculated for C₁₅H₃₃OSi [M+H]⁺ 257.2295, found 257.2293. [α]_D²⁰ = -1.04 (*c* = 1.000 CHCl₃) for a 84% ee sample.

Enantiomeric ratio 91.5:8.5 was determined by chiral HPLC analysis (Chiral Technologies ODH, 214 nm, 99.5% hexane: 0.5% *i*PrOH, 0.5 mL/min). Chromatograms are illustrated below: 29.96 (S), 32.51 (R).



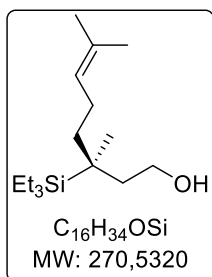
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	29.989	6081126	102831	50.980
2	32.590	5847380	99855	49.020
Total		11928506	202687	100.000



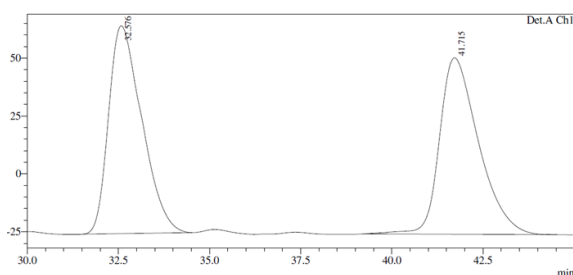
Detector A Ch1 214nm

Peak#	Ret. Time	Area	Height	Area %
1	29.960	8176653	157997	91.657
2	32.512	744278	13557	8.343
Total		8920931	171554	100.000

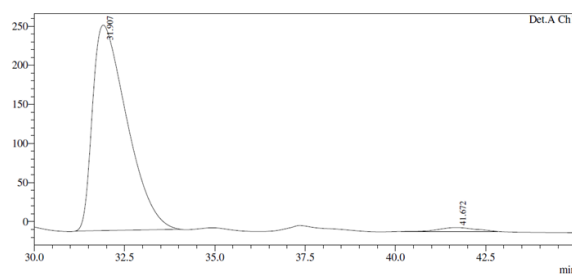
(+)-(S)-3,7-Dimethyl-3-(triethylsilyl)-oct-6-ene-1-ol (138b)

Prepared according to **GP13** from the reaction of **139ad** (63.6 mg, 0.266 mmol) with 9-BBN (0.80 mL, 0.40 mmol) in THF (0.24 mL), previous addition of H_2O_2 (0.21 mL, 2.29 mmol) and NaOH (0.16 mL, 0.48 mmol). The residue is purified by flash column chromatography (pentane:Et₂O 5:1, R_f = 0.4) to afford the desired product **138b** (23.5 mg, 0.091 mmol) in 34% yield as a colourless oil. 1H NMR (400 MHz, $CDCl_3$) δ 5.09 (m, 1H), 3.73 (m, 2H), 1.97 (m, 2H), 1.78-1.64 (m, 2H), 1.68 (s, 3H), 1.63 (s, 3H), 1.44-1.30 (m, 3H), 1.03 (t, J = 8.0 Hz, 9H), 0.65 (q, J = 7.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.3, 125.2, 60.2, 40.3, 38.0, 25.9, 23.8, 23.2, 22.8, 17.8, 8.5, 2.9. HRMS: m/z calculated for $C_{16}H_{35}OSi$ $[M+H]^+$ 271.2452, found 271.2451. $[\alpha]_D^{20}$ = +0.38 (c = 0.500 $CHCl_3$) for a 96% ee sample.

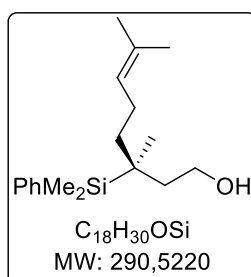
Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 31.91 (S), 41.67 (R).



Peak#	Ret. Time	Area	Height	Area %
1	32.576	5693213	89688	50.038
2	41.715	5684557	76153	49.962
Total		11377770	165841	100.000

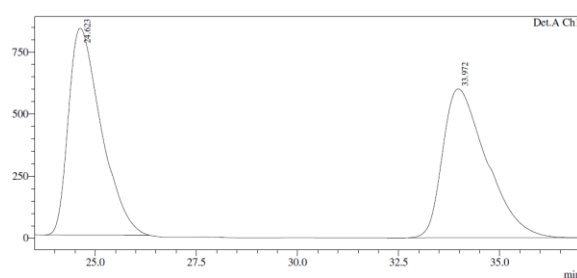


Peak#	Ret. Time	Area	Height	Area %
1	31.907	17358612	262808	98.085
2	41.672	338875	4973	1.915
Total		17697488	267781	100.000

(-)-(S)-3,7-Dimethyl-3-(dimethylphenylsilyl)-oct-6-ene-1-ol (138e)

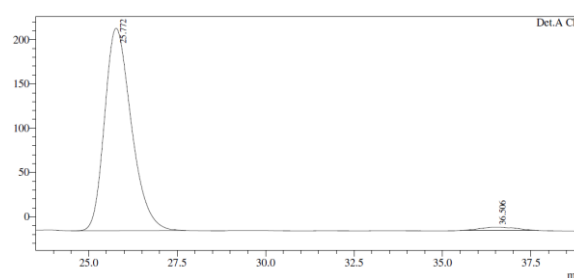
Prepared according to **GP13** from the reaction of **130bd** (20.3 mg, 0.074 mmol) with 9-BBN (0.22 mL, 0.11 mmol) to in THF (0.12 mL), previous addition of H_2O_2 (57 μL , 0.67 mmol) and NaOH (44 μL , 0.13 mmol). The residue is purified by flash column chromatography (pentane: Et_2O 4:1, R_f = 0.3) to afford the desired product **138e** (7.3 mg, 0.066 mmol) in 34% yield as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.49 (m, 2H), 7.37-7.33 (m, 3H), 5.03 (m, 1H), 3.64 (m, 2H), 1.92 (m, 2H), 1.73-1.59 (m, 2H), 1.67 (s, 3H) 1.56 (s, 3H), 1.40-1.24 (m, 3H), 0.96 (s, 3H), 0.33 (s, 3H), 0.32 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 138.2, 134.7, 131.3, 129.0, 127.8, 125.1, 60.0, 39.5, 37.2, 25.8, 23.2, 22.0, 22.1, 17.8, -4.3. HRMS: m/z calculated for $\text{C}_{18}\text{H}_{31}\text{OSi}$ $[\text{M}+\text{H}]^+$ 291.2139, found 291.2137. $[\alpha]_D^{20}$ = -0.48 (c = 0.350 CHCl_3) for a 96% ee sample.

Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.5% hexane: 0.5% *i*PrOH, 1 mL/min). Chromatograms are illustrated below: 25.77 (S), 36.51 (R).



Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	24.623	46974726	833744	50.800
2	33.972	45495517	599796	49.200
Total		92470243	1433540	100.000

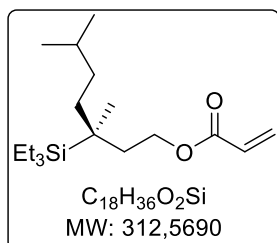


Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	25.772	12043899	228616	97.918
2	36.506	256114	3574	2.082
Total		12300013	232190	100.000

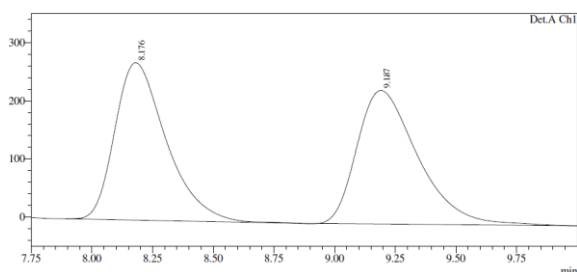
3.6 Esterification of (+)-(*S*)-3-Isopentyl-3-(triethylsilyl)-butan-1-ol

3.6.1 Preparation of acrylate **139**

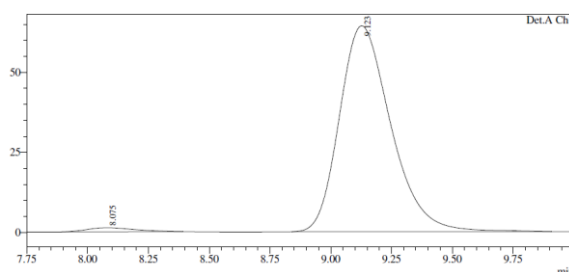


Following a reported procedure,^[210] a flame-dried Schlenk under Argon equipped with a stir bar is charged with **138a** (21.0 mg, 0.08 mmol), DMAP (0.99 mg, 0.008 mmol) and Et_3N (32 μL , 0.24 mmol) in CH_2Cl_2 (1 mL, 0.08 M). The solution is cool to 0 °C (ice-bath) and acryloyl chloride (13 μL , 0.16 mmol) is added dropwise over 5 min. The solution was allowed to slowly warm up to 25 °C over 3 h. After this time, the mixture is quenched by addition of $\text{NH}_4\text{Cl}_{\text{sat}}$ (3 mL), diluted with CH_2Cl_2 (2 mL) and stirred at room temperature for 20 min. The layers are separated and the aqueous phase extracted three times with Et_2O (3 x 5 mL). The combined organic layers are washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue is purified by flash column chromatography (pentane: Et_2O 97.5:2.5, R_f = 0.5) to afford the desired product **139** (20.5 mg, 0.066 mmol) in 82% yield as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.39 (dd, J = 17.3, 1.5 Hz, 1H), 6.11 (dd, J = 17.3, 10.4 Hz, 1H), 5.81 (dd, J = 10.4, 1.5 Hz, 1H), 4.20 (m, 2H), 1.80-1.64 (m, 2H), 1.48-1.29 (m, 3H), 1.23-1.10 (m, 2H), 1.00 (t, J = 7.9 Hz, 9H), 0.97 (s, 3H), 0.88 (dd, J = 6.6, 0.7 Hz, 6H), 0.63 (q, J = 7.8 Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.5, 130.6, 128.8, 62.2, 35.5, 35.2, 33.6, 29.2, 23.6, 22.9, 22.8, 8.5, 2.9. HRMS: m/z calculated for $\text{C}_{18}\text{H}_{40}\text{O}_2\text{SiN}$ $[\text{M}+\text{NH}_4]^+$ 330.2823, found 330.2823. $[\alpha]_D^{20}$ = +0.94 (c = 0.500 CHCl_3) for a 96% ee sample.

Enantiomeric ratio 98:2 was determined by chiral HPLC analysis (Chiral Technologies ODH, 220 nm, 99.9% hexane: 0.1% *i*PrOH, 0.5 mL/min). Chromatograms are illustrated below: 8.08 (*R*), 9.12 (*S*).



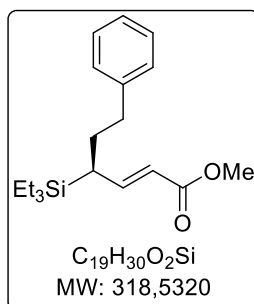
Peak#	Ret. Time	Area	Height	Area %
1	8.176	3989341	270391	49.905
2	9.187	4004577	229448	50.095
Total		7993918	499839	100.000



Peak#	Ret. Time	Area	Height	Area %
1	8.075	17120	1260	1.779
2	9.123	945184	64272	98.221
Total		962304	65532	100.000

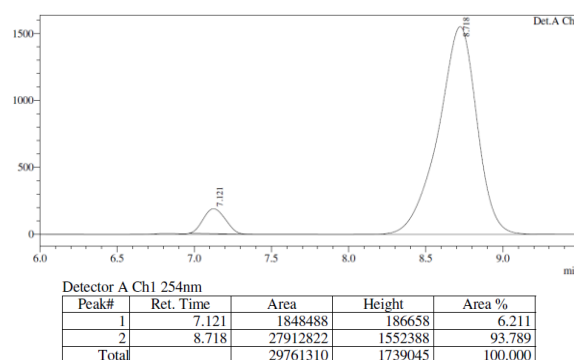
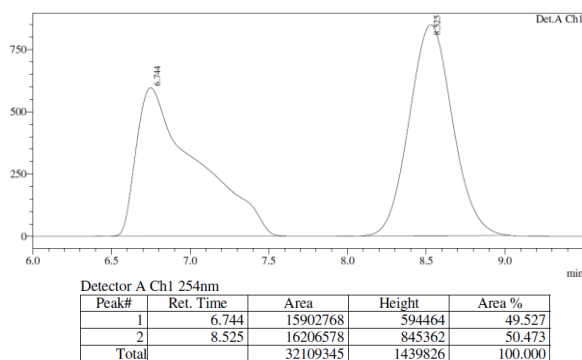
3.7 Cross-metathesis of (+)-(S)-3-Phenethyl-3-(triethylsilyl)-1-propene

3.7.1 Preparation of acrylate **120**



Following a reported procedure,^[118] a flame-dried round bottom flask under Argon equipped with a stir bar and condenser is charged with silane **115d** (66.3 mg, 0.255 mmol), methyl acrylate (69.3 μL , 0.765 mmol) and CH_2Cl_2 (1,25 mL, 0.2 M). 2nd Grubbs generation Ru-catalyst (16.9 mg, 0.026 mmol) is added to the solution and the dark-green mixture is heat to 40 °C overnight. Next day, the mixture is allowed to cool at room temperature and the dark green solution is concentrated under reduced pressure. The residue is purified by flash column chromatography (pentane: Et_2O , R_f = 0.5) to afford the desired product **120** (57.7 mg, 0.19 mmol) in 79% yield as a colorless oil. ¹H NMR (400 MHz, CDCl_3) δ 7.31-7.25 (m, 2H), 7.21-7.11 (m, 3H), 7.05 (dd, J = 15.6, 9.7 Hz, 1H), 5.72 (dd, J = 15.6, 1.1 Hz, 1H), 3.75 (s, 3H), 2.75 (ddd, J = 13.8, 9.0, 5.0 Hz, 1H), 2.4 (dt J = 13.3, 8.2 Hz, 1H), 1.97 (m, 1H), 1.92-1.75 (m, 2H), 0.91 (t, J = 7.9 Hz, 9H), 0.56 (q, J = 8.1 Hz, 6H). ¹³C NMR (101 MHz, CDCl_3) δ 128.6, 128.5, 51.4, 36.2, 32.4, 30.7, 7.6, 2.4. HRMS: m/z calculated for $\text{C}_{19}\text{H}_{31}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$ 319.2088, found 319.2087. $[\alpha]_D^{20}$ = -7.88 (c = 1.000 CHCl_3) for a 88% ee sample.

Enantiomeric ratio 94:6 was determined by chiral HPLC analysis (Chiral Technologies ODH, 254 nm, 99.5% hexane: 0.5% *i*PrOH, 1.0 mL/min). Chromatograms are illustrated below: 7.12 (R), 8.72 (S).



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Copper-free asymmetric allylic substitution with Grignard reagents: a new route to enantioenriched allylsilanes

This thesis work has unveiled a novel synthesis strategy based on a copper-free asymmetric allylic substitution (AAS) of allylbromides to access enantioenriched allylsilanes bearing tertiary and quaternary silyl-substituted stereogenic centres. The key feature of this novel approach was the possibility of performing the AAS in the absence of copper thanks to the Lewis-base activation of the Grignard reagents by an asymmetric NHC-ligand. This novel approach was implemented using a large number of alkyl and aryl Grignard reagents to access chiral allylsilanes bearing four different silyl-moieties (PhMe₂Si-, Me₃Si-, Et₃Si- and *t*BuMe₂Si-) in excellent γ -regioselectivities (up to $\gamma/\alpha > 98/2$) and enantiomeric ratios (up to $er > 98:2$). This work merged two different topics such as transition-metal free catalysis and asymmetric allylic substitution in one unique strategy, opening a new sustainable route to access stereodefined allylsilanes.

Keywords: Organic catalysis, Lewis-base activation, regioselectivity, enantioselectivity, enantioenriched allylsilanes

Substitution allylique asymétrique sans cuivre avec des réactifs de Grignard: une nouvelle voie d'accès aux allylsilanes énantioenrichis

Ce travail de thèse a mis en relief une nouvelle stratégie de synthèse basée sur substitution allylique asymétrique (SAA) de bromure d'allyles pour accéder à des allylsilanes énantioenrichis portant des centres stéréogéniques tertiaires et quaternaires substitués par un groupe silylé. La caractéristique principale de cette nouvelle approche est la possibilité de réaliser la SAA en absence de cuivre grâce à l'activation par base de Lewis des réactifs de Grignard à l'aide d'un ligand NHC asymétrique. Cette nouvelle approche a été mise en œuvre en utilisant un grand nombre de réactifs de Grignard alkyles et aryles pour accéder aux allylsilanes chiraux portant quatre parties silylées différents (PhMe₂Si-, Me₃Si-, Et₃Si- et *t*BuMe₂Si-) avec d'excellentes γ -régiosélectivités (jusqu'à $\gamma/\alpha > 98/2$) et rapports énantiomérique (jusqu'à $er > 98:2$). Ce travail a fusionné deux sujets différents tels que la catalyse sans métaux de transition et la substitution allylique asymétrique dans une stratégie unique, ouvrant une nouvelle voie durable pour accéder aux allylsilanes stéréodéfinis.

Mots clés: Catalyse organique, activation par base de Lewis, régiosélectivité, énantiosélectivité, allylsilanes énantioenrichis