Copper catalyzed asymmetric addition of Grignard reagents to ketones and ketimines
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Chapter 2
Asymmetric Alkylation of Acylsilanes

The Cu(I)/ferrocenyl diphosphine catalyzed highly enantioselective addition of Grignard reagents to acylsilanes is described. This transformation affords benzylic and allylic α-silylated tertiary alcohols with up to 95% yield and 96% e.e.. The competing Meerwein-Ponndorf-Verley reduction is suppressed by applying a mixture of Lewis acid additives.

Part of this chapter has been published:
2.1 Introduction
2.1.1 Chemistry of acylsilanes
As important organosilicon reagents in organic synthesis, the preparation and application of acylsilanes have received massive attention from the scientific community.\(^1\) The properties of acylsilanes combine the inherent reactivity of the carbonyl group and the influence of the C-Si bond. Compared with ketones and aldehydes, the \(^{13}\)C-NMR of acylsilanes shows a downfield shift of the carbonyl group, which suggests that the silicon atom introduces a significant inductive effect.\(^2\) On one hand, the bulky tetra-substituted silyl group increases the steric hindrance near the carbonyl group. On the other hand, the C-Si bond is longer than the C-C or C-H bond, which partially relieves this steric hindrance.\(^3\) Some of the selected chemistry specific to acylsilanes is highlighted below.

It is not surprising that the carbonyl group of acylsilanes reacts with various nucleophiles in a similar way as aldehydes and ketones to form silyl alkoxide 2, which can be hydrolyzed to \(\alpha\)-silylated alcohols 3. The difference is that due to the presence of the silicon atom, the silyl alkoxides may undergo a Brook rearrangement to form a carbanion intermediate 4, which could be hydrolyzed or trapped by an electrophile to form silyl ethers 6 (Scheme 1).\(^4\)

With respect to stereochemistry, nucleophilic addition to \(\alpha\)- and \(\beta\)-chiral acylsilanes shows excellent diastereoselectivity when compared to additions to corresponding aldehydes or ketones.\(^5,6\) This enhanced diastereoselectivity is caused by the steric hindrance introduced by the silyl group. E.g., addition of \(n\)-BuLi to \(\alpha\)-chiral acylsilane 7 results in the \(\alpha\)-silyl alcohol 8 with perfect diastereoselectivity. Upon treatment of product 8 with TBAF the desilylated chiral alcohol 9 is obtained with full retention of the configuration. In contrast, adding \(n\)-BuLi to the corresponding chiral aldehyde 10 leads to product 9 with only 5:1 diastereomeric ratio (Scheme 2)\(^6\)

Apart from the special reactivity of the carbonyl group, the C-Si bond allows acylsilanes to be used as acyl anions.\(^7\) Treatment of aryl acyl trimethyl silanes with fluoride anions in the presence of
organic halids allows transformation of acylsilanes into ketones (Scheme 3). The driving force of this transformation is the high Si-F bond dissociation energy (142 kcal/mol).  

![Scheme 3. Synthesis of ketones from acylsilanes](image)

A different type of transformation is induced by a softer cyanide anion which is able to attack the carbonyl group instead of the silyl group.  

![Scheme 4. Catalytic silyl benzoin reaction](image)

Acylsilanes also participate in transition metal catalyzed hydrogenations and cross-coupling reactions. In 1991, Panek et al. developed a palladium catalyzed hydrogenolysis of acylsilanes to aldehydes (Scheme 5).  

![Scheme 5. Pd-catalyzed hydrogenolysis of acylsilanes](image)

Acylsilanes can also be used in synthesis to introduce an acyl group by cross-coupling reactions. In 2001, Tsuij and co-workers reported Pd-catalyzed acylation of allylic trifluoroacetates 24 with acylsilanes 23 (Scheme 6a) and recently, the group of Krska developed Pd-catalyzed acylation of aryl bromides to synthesize unsymmetrical diaryl ketones 26 (Scheme 6b).
2.1.2 Preparation of acylsilanes

Acylsilanes have gained increasing interest not only because of their applications in organic synthesis, but also because of their ready availability. Versatile methods have been developed to access this class of molecules. In this introduction, we only show a few representative examples (Scheme 7). Acylsilanes can be synthesized by the addition of silyl lithium reagents to an aldehyde, followed by oxidation of the corresponding α-silylated alcohols (Scheme 7a). Adding nucleophilic silyl reagents to carboxylic acid derivatives is another straightforward strategy to access acylsilanes. Acyl chlorides are another class of convenient precursors, which upon addition of silyl-copper based reagent $(SiR_3)_2CuCN(ZnCl)_2$ provide acylsilanes. Readily available zincates were proven to be very practical in reactions with acyl chlorides to produce acylsilanes (Scheme 7b). Another reliable method to obtain phenyl acylsilanes starts with benzyl silanes. Reacting benzyl silanes with NBS reagent leads to the corresponding dibromide compounds 27 which can be oxidized to acylsilanes by AgOAc (Scheme 7c). Lithiation of dithianes and subsequent reaction with TMSCl, followed by hydrolytic deprotection (Scheme 7d) affords acylsilanes in three steps. The reverse Brook rearrangement (Scheme 7e) is an elegant way to synthesize α,β-unsaturated acylsilanes 32. Treatment of allyl silyl ethers 30 with tBuLi can trigger reverse Brook rearrangement, leading to the corresponding α-silylated alcohols 31, which can be oxidized to acylsilanes 32 as in Scheme 7a. Alkynes are important starting materials for acylsilanes as well. A three-step procedure was reported for the synthesis of various alkyl acylsilanes 36: Pd-catalyzed silyl-stannation of alkynes; cross-coupling with organohalides, and TFA catalyzed hydrolysis (Scheme 7f).
### 2.1.3 Applications of chiral α-silylated alcohols in synthesis

Optically active α-silylated alcohols are chiral organometallic compounds that contain a functional group, and therefore they are important building blocks in stereoselective carbon-carbon bond forming and rearrangement reactions.\(^{1a,20}\)

In 2003, chiral α-silylated secondary alcohols were applied as chiral auxiliaries in oxocarbenium ion reactions (Scheme 8).\(^{21a}\) They were investigated in the reaction between allyl trimethyl silanes and aldehydes under conditions developed by Marko and coworkers.\(^{21b}\) Good diastereoselectivity was found with aliphatic aldehydes; however, moderate selectivity was obtained for aromatic and unsaturated aldehydes.

**Scheme 8.** Chiral α-silylated secondary alcohols as chiral auxiliaries

Claisen rearrangement is an important transformation to utilize chiral α-silylated allylic alcohols for the synthesis of complex chiral molecules. The α-silyl group was envisaged to serve as a “chirality-inducing group”. Ireland and co-workers initially discovered chiral α-silylated allylic alcohols as a “chiral primary alcohol equivalent” in 1984. The chirality could be fully transferred after Claisen rearrangement in the prostanoid synthesis (Scheme 9a).\(^{22a}\) In 1989, in the total synthesis towards the antimalarial agent (+)-artemisinin, this transformation was established as the key step to build the C/D ring fragment (Scheme 9b).\(^{22b}\) The group of Jacobi also designed a similar strategy to access chiral alkyne acids, which are employed in Ring-C construction of the precursors of Vitamin B12 (Scheme 9c).\(^{22c}\) Later, Riccardis et al. applied this reaction in the preparation of N,O-diprotected (2S,3S)-N-methyl-hydroxyisoleucine, a noncoded amino acid of halipeptin A (Scheme 9d).\(^{22d}\)

**Scheme 9.** Transformations of chiral α-silylated secondary alcohols by Claisen rearrangement
In 2007, Knochel and co-workers developed a highly diastereoselective methodology to obtain (E)-alkenylsilanes 51 bearing an α-chiral center from protected chiral α-silylated vinyl alcohols 50 by a copper mediated SN₂ allylic substitution.²³ This method is fairly practical because these chiral (E)-alkenylsilanes are versatile intermediates which can be transformed to α,β-unsaturated ketones 52, alkenyl boronates 53, etc. (Scheme 10).

Scheme 10. Preparation and application of (E)-alkenylsilanes

Last but not least, one of the truly attractive, but still challenging applications of chiral α-silylated alcohols, especially chiral α-silylated tertiary alcohols 55 is to generate a chiral (tertiary substituted) carbanion 58 via 1,2-Brook rearrangement²⁴ and then trap it stereospecifically by an electrophile (Scheme 11). This transformation would allow access to various functionalized chiral (tertiary) alcohols 59 from chiral α-silylated tertiary alcohols.

Scheme 11. 1,2-Brook rearrangement and nucleophilic trapping

The equilibrium of the 1,2-Brook rearrangement is determined by the stability of alkoxide 56 and carbanion 58.²⁵ It has been shown in the literature that by introducing alkenyl, alkynyl, or phenyl as the R group the resulting carbanion becomes relatively stabilized.²⁵ However, this thermodynamic stabilization of the chiral carbanion will also be responsible for a rapid racemization, therefore the reactivity of the carbanion toward the electrophile is crucial. The first reported exploration of this research area is a three-component coupling reaction of silylglyoxylates 60, alkynes, and aldehydes. The reaction proceeds in an “asymmetric alkynylation - Brook rearrangement - trapping with aldehyde” sequence. Although the chemoselectivity is excellent, only moderate enantioselectivity was obtained, probably caused by the racemization of the carbanion intermediate (Scheme 12a).²⁶a

In 2013, Marek and co-workers unveiled a very delicate and complicated design to avoid this racemization problem. After asymmetric alkynylation of acylsilane 62, the product 63 undergoes an allenyl-Zn-Brook rearrangement to from a chiral allene intermediate 64. This intermediate can undergo an intramolecular Zn-ene-allene carbocyclization and be trapped by an electrophile to produce 65. The subsequent Tamao-Fleming oxidation was performed to obtain the desilylated product 66 with full retention of the e.e. from 63 (Scheme 12b).²⁶b
2.1.4 Asymmetric synthesis of chiral $\alpha$-silylated alcohols

Several strategies have been reported for the preparation of enantiopure $\alpha$-silylated secondary alcohols, based on the non-catalytic asymmetric reduction of acylsilanes. However, catalytic methods are still scarce. In 2008 the group of Ohkuma reported, for the first time, catalytic asymmetric synthesis of chiral $\alpha$-silylated secondary alcohols via a highly enantioselective Ru-catalyzed asymmetric hydrogenation of acylsilanes (Scheme 13a). Various $\alpha$-silylated aliphatic, allylic and benzylic alcohols were obtained with excellent yields and up to 99% e.e. Moreover, the substrate to catalyst ratio of this reaction can reach 10,000 under 10 atm of $H_2$. In 2013 the group of Riant published a method for Cu(I)-catalyzed asymmetric addition of silaboranes to aldehydes (Scheme 13b). The optimized catalyst involved a chiral diphosphine Cu(I)-complex with a unique bifluoride counterion (FHF$^-$), which was suggested to play a role in activating the Si-B reagent and lead to a faster transmetalation. The reaction featured a very broad substrate scope. Various chiral $\alpha$-silylated secondary alcohols were obtained with up to 99% e.e. starting from both aliphatic and aromatic aldehydes.

Scheme 12. Transformation of chiral $\alpha$-silylated alcohols by Brook rearrangement

Scheme 13. Catalytic asymmetric synthesis of chiral $\alpha$-silylated secondary alcohols

Either the nature of this reaction or reactivity issues, prevent these methods from being applied to the synthesis of chiral $\alpha$-silylated tertiary alcohols. The most straightforward approach towards these compounds would be the catalytic asymmetric addition of organometallic reagents to acylsilanes. So far the only reported such system was the catalytic enantioselective alkynylation of...
alkyl acylsilanes. The group of Chan developed a Zinc-Salen-catalyst L3 which enables alkynylation of acylsilane 70 with up to 88% e.e. (Scheme 14).\textsuperscript{28} Marek et al. introduced a prophenol type ligand L4 which could achieve excellent e.e. (Scheme 14).\textsuperscript{26b} However, the substrate scope of this reaction is narrow and only alkyl acylsilanes could be applied.

**Scheme 14. Asymmetric alkynylation of acylsilanes**

Compared with alkynylation, alkylation of acylsilanes is proven to be problematic. In 2012, Xu and co-workers attempted the asymmetric alkylation of acylsilanes by applying the well-known method of Ti-catalyzed alkylation of aldehydes and ketones by diethylzinc, but a non-catalytic Meerwein–Ponndorf–Verley (MPV) type reduction of the carbonyl moiety was discovered as the major pathway (Scheme 15).\textsuperscript{29} The formation of the reduction product 73 was rationalized by the low rate of the catalytic addition of an organometallic reagent, due to the increased steric hindrance of the substrate 72 introduced by the tetrasubstituted silyl group. The competing β-hydride transfer from the organometallic reagent that results in the reduction product is sterically less demanding.\textsuperscript{30}

**Scheme 15. Attempt of asymmetric alkylation of acylsilanes**

### 2.2 Aim

In our group, a highly selective catalytic system has been developed for the asymmetric alkylation of various aryalkyl, vinyl aryl and vinyl alkyl ketones using Grignard reagents.\textsuperscript{31} Compared with the previously developed Ti-catalyzed asymmetric addition of R₂Zn to ketones,\textsuperscript{32} this robust catalytic system enables excellent enantioselectivities and yields within a short reaction time. However, the reaction also suffers from several drawbacks: bulky Grignard reagents (β-branched) such as i-BuMgBr are required for high enantioselectivity and; with linear Grignard reagents a significant decrease in enantioselectivities was observed.

In this project, we aimed to develop a catalytic asymmetric method for the synthesis of α-silylated tertiary alcohols via the addition of Grignard reagents to acylsilanes, based on our experience of asymmetric alkylation of ketones. We hoped that our efficient catalytic system could overcome the reduction pathway observed previously with these substrates, and that the steric hindrance introduced by the bulky silyl group could enhance the face discrimination by the chiral catalyst, and thus improving the enantioselectivity in the addition of linear Grignard reagents.
2.3 Results and Discussion

We began our studies by investigating the catalytic asymmetric alkylation of acylsilane 75a (Table 1). Initial attempts comprised the use of iBuMgBr (2 equiv., 2 h addition time), CuBr·SMe2 (5 mol%) and various chiral ligands L (6 mol%) in MTBE at -78 °C.

Chiral ferrocenyldiphosphine ligands L5-L11, BINAP L6, as well as the phosphoramidite L11, were studied in this reaction (Table 1). The combination of chiral ferrocenyldiphosphine ligand L5 and CuBr·SMe2 as the Cu(I) salt proved to be an efficient catalyst for this reaction and the desired α-silylated alcohol 76a was obtained with a high e.e. (90%). As expected, the selectivity of the reaction was disappointing, with 77a originating from the non-catalyzed reduction pathway (Entry 1). In the absence of a copper catalyst only reduction product was observed.

When ligand L6, in which the positions of the alkyl and aryl phosphine groups are exchanged, was used instead of L5, product 76a was obtained with lower selectivity (76a:77a = 1:8.5) and e.e. (Entry 2). Unfortunately, with all other ligands tested, L7-L11, alkylation products were not formed. Instead of the desired product 76a, the secondary racemic α-silylated alcohol 77a was obtained (Entry 3).

Having established L5 as the optimal chiral ligand for this reaction and with the aim to improve the selectivity, we studied the effect of the solvent on the reaction outcome. Dichloromethane and toluene provided product 76a with slightly lower enantiomeric ratios but a similar selectivity compared to MTBE (Entries 4 and 5). In Et2O and THF (Entry 6), however, only reduction product was obtained. Increasing or decreasing the reaction temperature from -78 °C to -100 °C or to -30 °C did not improve the selectivity either (Entries 7 and 8). To test the role of the bulkiness of the silyl moiety we evaluated the related substrates with SiMe2Ph, SiPh3 and SiEt3 moieties.21 With SiMe2Ph, the e.e. was 80% and the selectivity was improved to 1:1:3. Surprisingly, both the acylsilane with the more bulky SiPh3 and the less bulky SiEt3 moiety provided the reduction products only. Assuming that the reduction reaction is a result of the activation of the carbonyl moiety of the acylsilane through coordination with the magnesium ion of the Grignard reagent, followed by β-hydride transfer,30 we predicted that reduction could be avoided by using Lewis acid additives.30a Lewis acids would be expected to prevent the coordination of the magnesium to the carbonyl moiety, thereby allowing the catalytic pathway to outcompete reduction.33 A survey of Lewis acids (Entries 9-13), demonstrated that in the presence of CeCl3, both the selectivity and enantioselectivity improved (compare entries 1 and 9). The best selectivity (76a:77a = 3:1) was obtained when BF3·Et2O was used as an additive, but at the cost of a drop of the e.e. to 86% (Entry 13). Remarkably, a mixture of BF3·Et2O:CeCl3 = 1:1, resulted in a dramatic decrease in reduction, and provided both a high selectivity and enantiomeric ratio (Entry 14).

We have also tested other Lewis acids such as BBr3·SMe2, BCl3·SMe2, BF3·SMe2, BF2·OTf, TCl4, ZnCl2, TMSOTf, CeBr3, Cel3, Ti(OiPr)4 but none of them could improve our reaction.

With optimized reaction conditions in hand, the acylsilane scope was explored (Table 2). Application of the optimized conditions to a wide range of substituted acylsilanes afforded the alkylation products in moderate to excellent yields and with good to excellent enantiomeric ratios. For instance, aromatic acylsilanes bearing alkyl substituents in the para- and meta- position provided the corresponding α-silylated tertiary alcohols with good yields and enantiomeric excess of up to 92% (Entries 1-5). The presence of halogens in the aromatic ring decreased the selectivity of the alkylation, while maintaining high levels of stereoselectivity (Entries 6-8). Unexpectedly, the presence of a p-OMe substituent in the acylsilane 76j resulted in a decrease in the e.e. to 26%, whereas for m-OMe substituted 76k an e.e. of 86% was obtained (Entries 10 and 11). With the o-Me substituted substrate, neither alkylation nor reduction was observed. Aryl acylsilanes bearing phenyl substituents in the para- and meta- position furnished the corresponding α-silylated tertiary alcohols with good yields and e.e. of 90% (Table 2, Entries 12 and 13).
Table 1. Catalytic Asymmetric Alkylation of Acylsilanes: Selected Optimization Results

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Lewis acid; equiv.</th>
<th>Addition: reduction, $76a:77a$</th>
<th>e.e. (%) $76a$</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>L5</td>
<td>MTBE</td>
<td>-78</td>
<td>none</td>
<td>1:2</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>L6</td>
<td>MTBE</td>
<td>-78</td>
<td>none</td>
<td>1:8.5</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>L7-L11</td>
<td>MTBE</td>
<td>-78</td>
<td>none</td>
<td>0:1</td>
<td>n.d.</td>
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<tr>
<td>4</td>
<td>L5</td>
<td>CH₂Cl₂</td>
<td>-78</td>
<td>none</td>
<td>1:2.2</td>
<td>44</td>
</tr>
<tr>
<td>5</td>
<td>L5</td>
<td>toluene</td>
<td>-78</td>
<td>none</td>
<td>1:3.2</td>
<td>84</td>
</tr>
<tr>
<td>6</td>
<td>L5</td>
<td>Et₂O or THF</td>
<td>-78</td>
<td>none</td>
<td>0:1</td>
<td>n.d.</td>
</tr>
<tr>
<td>7</td>
<td>L5</td>
<td>MTBE</td>
<td>-100</td>
<td>none</td>
<td>1:5</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>L5</td>
<td>MTBE</td>
<td>-30</td>
<td>none</td>
<td>1:9</td>
<td>70</td>
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<td>MTBE</td>
<td>-78</td>
<td>CeCl₃; 1.3</td>
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<td>92</td>
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<tr>
<td>10</td>
<td>L5</td>
<td>MTBE</td>
<td>-78</td>
<td>TMSCl; 2</td>
<td>1:1.2</td>
<td>92</td>
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<td>11</td>
<td>L5</td>
<td>MTBE</td>
<td>-78</td>
<td>CeBr₃; 1</td>
<td>1:1.5</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
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<td>MgCl₂; 2</td>
<td>1:2</td>
<td>92</td>
</tr>
<tr>
<td>13</td>
<td>L5</td>
<td>MTBE</td>
<td>-78</td>
<td>BF₃·Et₂O; 2</td>
<td>3:1</td>
<td>86</td>
</tr>
<tr>
<td>14</td>
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<td>MTBE</td>
<td>-78</td>
<td>BF₃·Et₂O·CeCl₃; 1:1</td>
<td>5:1</td>
<td>90</td>
</tr>
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[a] Conditions: iBuMgBr (1.2-1.5 M) was added over 2 h; [b] Full conversion was achieved in all entries; [c] The ratio of $76a:77a$ was determined by $^1$H-NMR; [d] The e.e. was determined by chiral HPLC analysis.

The further expansion of the substrate scope was carried out with α,β-unsaturated acylsilanes (enoyl silanes). Notably, for these substrates, the conjugate addition of the Grignard reagent is another potential reaction, in addition to the reduction and alkylation pathways. However, using our catalytic system, only the desired 1,2-addition product was observed. Remarkably, the corresponding α-silylated tertiary vinylic alcohols were obtained with excellent yields and enantiomeric excess (Entries 14-18). Furthermore, as Meerwein-Ponndorf-Verley reduction was less pronounced for these substrates, the amount of the Lewis acid mixture needed was reduced to 0.25 equiv.
Table 2. Substrate Generality$^{[a],[b]}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>75</th>
<th>76</th>
<th>Yield (%)$^c$</th>
<th>e.e. (%)$^d$</th>
<th>Entry</th>
<th>75</th>
<th>76</th>
<th>Yield (%)$^c$</th>
<th>e.e. (%)$^d$</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>75a</td>
<td>76a</td>
<td>74</td>
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<td>75j</td>
<td>76j</td>
<td>67</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>75b</td>
<td>76b</td>
<td>70</td>
<td>88</td>
<td>11</td>
<td>75k</td>
<td>76k</td>
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<td>75c</td>
<td>76c</td>
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<td>5</td>
<td>75e</td>
<td>76e</td>
<td>59</td>
<td>84</td>
<td>14$^{[l]}$</td>
<td>75n</td>
<td>76n</td>
<td>90</td>
<td>96</td>
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<tr>
<td>6</td>
<td>75f</td>
<td>76f</td>
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<td>90</td>
<td>15$^{[l]}$</td>
<td>75o</td>
<td>76o</td>
<td>91</td>
<td>96</td>
</tr>
<tr>
<td>7$^{[e]}$</td>
<td>75g</td>
<td>76g</td>
<td>52</td>
<td>92</td>
<td>16$^{[l]}$</td>
<td>75p</td>
<td>76p</td>
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<td>80</td>
<td>18$^{[l]}$</td>
<td>75q</td>
<td>76q</td>
<td>66</td>
<td>94</td>
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[a-d] As for Table 1; [e] 15 mol% CuBr SMe$_2$, 18 mol% L5 were used; [f] 0.25 equiv. of CeCl$_3$, 0.25 equiv. BF$_3$ Et$_2$O were used. [g] Reaction was performed with a chiral catalyst (Cu(I)-complex) recovered from a previous reaction (see Scheme 16).

The scope in Grignard reagents was subsequently studied using 75p and 75c as substrates (Table 3). We found that the reaction tolerates linear, β-branched as well as functionalized Grignard reagents (Entries 1-11). In all cases, high yields and good to excellent stereoselectivities were obtained. A low conversion and racemic product were obtained with MeMgBr, probably due to lack of reactivity and steric hindrance.
Table 3. Grignard Reagent Scope[a],[b]

<table>
<thead>
<tr>
<th>Entry</th>
<th>RMgBr</th>
<th>Yield(%)</th>
<th>e.e.(%)</th>
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<tr>
<td>1</td>
<td>75p</td>
<td>95</td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td>75p</td>
<td>93</td>
<td>84</td>
</tr>
<tr>
<td>3[e]</td>
<td>75p</td>
<td>90</td>
<td>96</td>
</tr>
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<tr>
<td>9[g]</td>
<td>75p</td>
<td>88</td>
<td>70</td>
</tr>
<tr>
<td>10[g]</td>
<td>75p</td>
<td>52</td>
<td>60</td>
</tr>
<tr>
<td>11[g]</td>
<td>75c</td>
<td>96</td>
<td>70</td>
</tr>
</tbody>
</table>

[a]-[d] As for Table 1; [e] 0.25 equiv. of CeCl₃, 0.25 equiv. of BF₃Et₂O used. [f] 1 equiv. of CeCl₃ was used. [g] 1 equiv. of CeCl₃, 1 equiv. of BF₃Et₂O used.

To further demonstrate the potential of this method, the alkylation of 75p with iPentMgBr was carried out on 500 mg scale; product 76t was obtained in an excellent 98% yield with e.e. 86% (Scheme 16). The catalyst was recovered as the Cu(I)-complex by column chromatography with 87% yield and used repeatedly without any loss of catalytic activity (Scheme 16a and 16b).

Scheme 16. Practical aspects
The effect of mixed Lewis acids is remarkable, in particular, the high e.e. and selectivity obtained in the presence of BF$_3$·Et$_2$O and three metals (Mg, Cu, Ce). Performing the addition of iBuMgBr to 75c in the absence of the Cu(I)-catalyst and the Lewis acid mixture led to the reduction product exclusively. A similar result was obtained in the presence of only the Lewis acid mixture, albeit at a slower reaction rate. While it is not yet possible to provide a detailed mechanistic picture, the involvement of an organocerium species as a nucleophile and BF$_3$·Et$_2$O as a Lewis acid should be considered. To test this hypothesis, the isobutylcerium reagent was synthesized$^{34}$ and tested. The reduction product was obtained both in the presence and in the absence of the Cu(I)-catalyst. These results indicate that organocerium species are probably not involved but instead a new Lewis acidic species compatible with the copper catalyst is formed upon mixing BF$_3$·Et$_2$O and CeCl$_3$. Future studies will have to be performed to elucidate the precise role of the Lewis acids.

2.4 Conclusion
In summary, we have developed an unprecedented catalytic asymmetric strategy to access valuable benzylic and allylic $\alpha$-silylated alcohols with tetrasubstituted chiral carbon with high yields and enantioselectivities. The competing Meerwein-Ponndorf-Verley reduction can be suppressed by applying a mixture of Lewis acid additives. The chiral catalyst can be recovered as a Cu(I)-complex and used repeatedly without any loss of catalytic activity. Studies toward the synthetic applications of newly synthesized $\alpha$-silylated tertiary alcohols, the elucidation of the mechanism of this transformation and the effect of the Lewis acid mixture are currently in progress.

2.5 Experimental Section
2.5.1 General information
Flash chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV and phosphomolybdic acid staining (phosphomolybdic acid 30 g, ethanol 1000 mL)
High-resolution mass spectra (HRMS) were recorded on an Orbitrap XL (Thermo Fisher Scientific) mass spectrometer. $^1$H- and $^{13}$CNMR were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) using CDCl$_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl$_3$: $\delta$ 7.24 for $^1$H, $\delta$ 77.23 for $^{13}$C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Enantiomeric excess (e.e.) were determined by chiral HPLC analysis using a Shimadzu LC-10ADVP HPLC equipped with a Shimadzu SPD-M10AVP diode array detector or SFC analysis using a TharSFC Investigator II.

All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. MTBE was dried and distilled from sodium; All chemicals were purchased from Sigma Aldrich. HexMgBr (2 M in Et$_2$O) was purchased from Sigma Aldrich. All the Grignard reagents were prepared from corresponding alkyl bromides and Mg activated with I$_2$ in MTBE. CuBrSMe$_2$ was purchased from Sigma Aldrich, and used without further purification. Ligands L5 - L10 were purchased from Sigma Aldrich, Ligand L11 was synthesized according to the reported procedure.$^{35}$ Racemic 76a - 76g, 76i - 76m were synthesized by alkylation of acylsilanes with iBu$_3$MgLi.$^{30c}$ Racemic 76h, 76n - 76w were obtained by mixing enantiomers of alkylation products isolated from the catalytic asymmetric reactions using each enantiomer of L5. Reduction product was determined as racemic by comparing with reported HPLC data.$^{27}$ The following substrates were synthesized according to literature procedure: 75a,$^{21}$ 75b - 75m,$^{15}$ 75n - 75q.$^{36}$
2.5.2 Substrate synthesis

Synthesis method of substrate 75a

\[
\begin{align*}
&\text{1) Mg, THF} \quad \text{reflux 1 h} \\
&\text{2) Ph}_3\text{MeSiCl} \quad 0 \degree C - r.t.12 h
\end{align*}
\]

Synthesis method of substrate 75b - 75m

2.5.3 Characterization of acylsilane substrates

(Methyldiphenylsilyl)(phenyl)methanone, 75a

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3 \text{)} & \delta 7.85 \text{ (d, J = 7.2 Hz, 2H), 7.66 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 7.7 Hz, 2H), 7.51 - 7.39 (m, 7H), 7.37 (t, J = 7.6 Hz, 2H), 0.94 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3 \text{)} & \delta 232.0, 141.8, 135.2, 133.81, 133.0, 130.1, 128.6, 128.3, 128.3, -3.2.
\end{align*}
\]


(Methyldiphenylsilyl)(p-tolyl)methanone, 75b

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3 \text{)} & \delta 7.72 \text{ (d, J = 8.1 Hz, 2H), 7.67 - 7.56 (d, J = 7.8 Hz, 4H), 7.48 - 7.32 (m, 6H), 7.15 (d, J = 7.9 Hz, 2H), 2.34 (s, 3H), 0.88 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3 \text{)} & \delta 231.1, 143.9, 139.8, 135.3, 134.2, 130.1, 129.4, 128.6, 128.4, 21.8, -3.0.
\end{align*}
\]


(4-(tert-Butyl)phenyl)(methyldiphenylsilyl)methanone, 75c

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3 \text{)} & \delta 7.73 \text{ (d, J = 8.4 Hz, 2H), 7.60 (d, J = 7.7 Hz, 2H), 7.59 (d, J = 7.9 Hz, 2H), 7.45 - 7.33 (m, 8H), 1.28 (s, 9H), 0.86 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3 \text{)} & \delta 231.2, 156.8, 139.7, 135.4, 134.2, 130.1, 128.4, 128.4, 125.7, 35.3, 31.3, -3.0.
\end{align*}
\]


(Methyldiphenylsilyl)(m-tolyl)methanone, 75d

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3 \text{)} & \delta 7.65 - 7.58 (m, 6H), 7.47 - 7.35 (m, 6H), 7.28 (d, J = 7.5 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 2.29 (s, 3H), 0.90 (s, 3H). \\
\text{13C NMR (101 MHz, CDCl}_3 \text{)} & \delta 232.3, 142.1, 138.5, 135.3, 134.1, 133.8, 130.2, 128.5, 128.4, 128.4, 126.2, 21.5, -3.1.
\end{align*}
\]

(Dimethylphenyl)(methyl diphenylsilyl)methanone, 75e

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.58 (d, J = 7.0 Hz, 4H), 7.46 – 7.29 (m, 8H), 7.08 (s, 1H), 2.21 (s, 6H), 0.85 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 232.5, 142.4, 138.3, 135.4, 134.71, 134.3, 130.2, 128.4, 126.3, 21.4, -3.1.

HRMS (ESI+, m/z): calcd for C$_{22}$H$_{22}$OSi Na[M+Na]$^+$: 353.1332; found: 353.1330.

(4-Fluorophenyl)(methyl diphenylsilyl)methanone, 75f

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.78 (dd, J = 8.7, 5.7 Hz, 2H), 7.64 – 7.53 (m, 4H), 7.48 – 7.31 (m, 6H), 6.99 (t, J = 8.6 Hz, 2H), 0.85 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 230.1, 165.7 (d, J$_{C-F}$ = 255.1 Hz), 138.6 (d, J$_{C-F}$ = 2.8 Hz), 135.3, 133.8, 131.0 (d, J$_{C-F}$ = 9.3 Hz), 130.4, 128.5, 115.9 (d, J$_{C-F}$ = 21.9 Hz), -3.1.

HRMS (ESI+, m/z): calcd for C$_{20}$H$_{17}$FOSi Na[M+Na]$^+$: 343.0925; found: 343.0922.

(3-Fluorophenyl)(methyl diphenylsilyl)methanone, 75g

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.60 (d, J = 6.6 Hz, 4H), 7.54 (d, J = 7.7 Hz, 1H), 7.49 – 7.36 (m, 7H), 7.30 (td, J = 7.9 Hz, 5.6, 1H), 7.16 (td, J = 8.2, 2.6 Hz, 1H), 0.88 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 231.0, 163.1 (d, J$_{C-F}$ = 248.7 Hz), 143.9 (d, J$_{C-F}$ = 5.1 Hz), 135.3, 133.5, 130.4, 130.4 (d, J$_{C-F}$ = 7.6 Hz), 128.5, 124.9 (d, J$_{C-F}$ = 2.9 Hz), 120.1 (d, J$_{C-F}$ = 21.8 Hz), 114.0 (d, J$_{C-F}$ = 21.7 Hz), -3.2.

HRMS (ESI+, m/z): calcd for C$_{20}$H$_{17}$FOSi Na[M+Na]$^+$: 343.0925; found: 343.0916.

(4-Bromophenyl)(methyl diphenylsilyl)methanone, 75h

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.62 (d, J = 8.6 Hz, 2H), 7.60 – 7.55 (m, 4H), 7.47 (d, J = 8.6 Hz, 2H), 7.46 – 7.35 (m, 6H), 0.86 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 231.0, 140.4, 135.3, 133.6, 132.1, 130.4, 129.8, 128.5, 128.3, -3.2.

HRMS (ESI+, m/z): calcd for C$_{20}$H$_{17}$BrOSi Na[M+Na]$^+$: 403.0124; found: 403.0120.

Methyl diphenylsilyl)(naphthalen-2-yl)methanone, 75i

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.22 (s, 1H), 7.88 (dd, J = 8.6 Hz, 1.4, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.70-7.60 (m, 5H), 7.53 (t, J = 7.5 Hz, 1H), 7.48-7.33 (m, 7H), 0.92 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 231.8, 139.5, 135.7, 135.4, 134.2, 132.7, 132.6, 130.3, 129.9, 128.7, 128.7, 128.5, 128.0, 126.8, 122.8, -3.1.

HRMS (ESI+, m/z): calcd for C$_{24}$H$_{20}$OSi Na[M+Na]$^+$: 375.1176; found: 375.1173.

(4-Methoxyphenyl)(methyl diphenylsilyl)methanone, 75j

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.78 (d, J = 8.9 Hz, 2H), 7.60 (d, J = 7.8 Hz, 2H), 7.59 (d, J = 7.9 Hz, 2H), 7.45 – 7.34 (m, 6H), 6.81 (d, J = 8.9 Hz, 2H), 3.79 (s, 3H), 0.85 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 229.1, 163.5, 135.9, 135.3, 134.4, 130.9, 130.1, 128.4, 113.9, 55.6, -3.0.

HRMS (ESI+, m/z): calcd for C$_{21}$H$_{20}$O$_2$Si Na[M+Na]$^+$: 355.1525; found: 355.1122.
Chapter 2

(3-Methoxyphenyl)(methyldiphenylsilyl)methanone, 75k

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.66 - 7.59 (m, 4H), 7.43 (m, 7H), 7.31 (s, 1H), 7.27 (d, J = 7.4 Hz, 1H), 7.04 (dd, J = 8.2, 1.8 Hz, 1H), 3.67 (s, 3H), 0.89 (s, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 231.8, 160.0, 143.3, 135.4, 134.1, 130.3, 129.7, 128.5, 121.7, 120.5, 111.4, 55.4, -3.1. \]

HRMS (ESI+, m/z): Calc. for C\textsubscript{21}H\textsubscript{20}O\textsubscript{2}SiNa [M+Na]+: 355.1125, found: 355.1108

[1,1'-Biphenyl]-4-yl(methyldiphenylsilyl)methanone, 75l

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.84 (d, J = 8.1 Hz, 2H), 7.63 - 7.59 (dd, J = 7.8, 1.4 Hz, 4H), 7.57 - 7.54 (dd, J = 8.4, 1.6 Hz, 4H), 7.46 - 7.32 (m, 9H), 7.31 (t, J = 7.0 Hz, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 231.5, 145.7, 140.7, 140.1, 135.4, 134.0, 130.3, 129.1, 129.0, 128.5, 128.4, 127.4, -3.0. \]

HRMS (ESI+, m/z): calcd for C\textsubscript{26}H\textsubscript{22}OSiNa [M+Na]+: 401.1332; found: 401.1328.

[1,1'-Biphenyl]-3-yl(methyldiphenylsilyl)methanone, 75m

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.99 (s, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.3 Hz, 4H), 7.46 - 7.33 (m, 9H), 7.31 (t, J = 7.0 Hz, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 232.2, 142.4, 141.5, 140.1, 135.4, 134.1, 131.5, 130.3, 129.3, 129.0, 128.5, 128.0, 127.8, 127.2, 126.6, -3.2. \]

HRMS (ESI+, m/z): calcd for C\textsubscript{26}H\textsubscript{22}OSiNa [M+Na]+: 401.1332; found: 401.1328.

(E)-2-Methyl-1-(methyldiphenylsilyl)but-2-en-1-one, 75n

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.60 - 7.55 (m, 4H), 7.43 - 7.35 (m, 6H), 6.76 - 6.69 (dq, J = 6.9, 0.62 Hz, 1H), 1.78 (d, J = 6.9 Hz, 3H), 1.74 (s, 3H), 0.80 (s, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 231.9, 146.2, 145.6, 135.1, 134.9, 129.9, 128.2, 150.0, 9.7, -2.5. \]

HRMS (ESI+, m/z): calcd for C\textsubscript{18}H\textsubscript{20}OSi [M+Na]+: 303.1175; found: 303.1175.

(E)-2,4-Dimethyl-1-(methyldiphenylsilyl)pent-2-en-1-one, 75o

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.53 (d, J = 9.3 Hz, 1H), 2.73 - 2.49 (m, 1H), 1.68 (s, 3H), 0.76 (d, J = 6.6 Hz, 6H), 0.74 (s, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 232.7, 159.0, 141.7, 135.2, 129.9, 128.2, 21.8, 9.8, -2.7. \]

HRMS (ESI-, m/z): calcd for C\textsubscript{20}H\textsubscript{23}OSi [M-H]: 307.1513; found: 307.1524.

(E)-3-Cyclohexyl-2-methyl-1-(methyldiphenylsilyl)prop-2-en-1-one, 75p

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.53 (d, J = 7.2 Hz, 4H), 7.37 (m, 6H), 6.42 (d, J = 9.3 Hz, 1H), 2.42 - 2.24 (m, 1H), 1.69 (s, 3H), 1.61-1.38 (m, 5H), 1.29-1.13 (m, 2H), 1.14-0.99 (m, 1H), 0.85 - 0.76 (m, 2H), 0.74 (s, 3H). \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 232.7, 157.5, 142.2, 135.2, 135.2, 129.9, 128.2, 37.9, 31.6, 25.9, 25.3, 9.9, -2.7. \]

HRMS (ESI+, m/z): calcd for C\textsubscript{23}H\textsubscript{28}OSiNa [M+Na]+: 371.1802; found: 371.1801.
(E)-2-Methyl-1-(methylidiphenylsilyl)-4-phenylbut-2-en-1-one, **75q**

1H NMR (400 MHz, CDCl3) δ 7.48 (d, J = 6.8 Hz, 4H), 7.37 (t, J = 7.3 Hz, 2H), 7.30 (t, J = 7.3 Hz, 4H), 7.17 – 7.13 (m, 3H), 6.79 (d, J = 3.2 Hz, 2H), 6.77 (t, J = 7.2 Hz, 1H), 3.49 (d, J = 7.2 Hz, 2H), 1.78 (s, 3H), 0.72 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 232.4, 149.2, 144.6, 138.6, 135.2, 134.7, 134.1, 129.9, 128.7, 128.3, 126.4, 35.2, 10.1, -2.8.


2.5.4 Cu-catalyzed asymmetric alkylation of acysilanes

General procedure for synthesis of racemic products

To 1 ml dry THF iBuMgBr (0.15 mmol, 1.5 M in MTBE solution) and iBuLi (0.32 mmol, 1.6 M in heptane solution) were added at -78 °C under nitrogen atmosphere. This solution was stirred at that temperature for 1 hour. Then 40 mg acylsilane (75a-g, 75i-m) in 1 ml THF was added. The mixture was stirred for 15 min, quenched by saturated aqueous NH₄Cl solution and extracted with ether. The combined organic layers were dried with anhydrous MgSO₄, filtered and the solvent was evaporated. The crude product was purified by flash chromatography on silica gel using a mixture of pentane and Et₂O as eluent.

Cu-catalyzed asymmetric synthesis of chiral α-silylated tertiary alcohols

In a dry Schlenk flask, CuBr.SMe² and ligand (S,RFe)-L⁵ were dissolved in dry MTBE under nitrogen and the solution was stirred at room temperature for 10 min. The acysilane 75 in 1 ml MTBE and CeCl₃ (solid) were added. The mixture was stirred for another 30 min before being cooled to -78 °C. BF₃·Et₂O was added to the cooled mixture directly and the resulting mixture was stirred for another 30 min, followed by slow addition (over 2 h by syringe pump) of a corresponding Grignard reagent. After 1 h of additional stirring, the reaction was quenched with saturated aqueous NH₄Cl solution and warmed up to room temperature. The reaction mixture was extracted with Et₂O (3* 10 ml). The combined organic layers were dried with anhydrous MgSO₄, filtered and the solvent was evaporated. The crude product was purified by flash chromatography on silica gel using a mixture of pentane and Et₂O as eluent. The main side product to be separated was the reduction product.

2.5.5 Characterization of α-silylated tertiary alcohols

1-(Methyldiphenylsilyl)-1-phenylbutan-1-ol, **76a**

The reaction was performed with 0.3 mmol **75a**, iBuMgBr (0.6 mmol, 1.4M in MTBE), CuBr.SMe² (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L⁵ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃ (74 mg, 0.3 mmol) and BF₃·Et₂O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76a was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 95:5), [74% yield, 90% e.e.].

1H NMR (400 MHz, CDCl₃) δ 7.55 (d, J = 6.7 Hz, 2H), 7.46 (d, J = 6.8 Hz, 2H), 7.40 (t, J = 6.8 Hz, 1H), 7.36 – 7.31 (m, 3H), 7.28 – 7.25 (m, 2H), 7.17 (t, J = 7.39 Hz, 2H), 7.09 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 8.2 Hz, 2H), 2.15 (dd, J = 14.7, 5.0 Hz, 1H), 1.97 (dd, J = 14.7, 7.2 Hz, 1H), 1.69- 1.59 (m, 2H), 0.86 (d, J = 6.6 Hz, 3H), 0.62 (d, J = 6.7 Hz, 3H), 0.50 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 144.9, 135.9, 135.7, 134.4, 133.9, 129.5, 129.3, 127.7, 127.5, 127.5, 125.3, 125.1, 74.4, 45.7, 24.7, 24.5, 23.8, -6.2.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel AD-H column, n-heptane/i-PrOH 99:1, 40 °C, 0.5 ml/min, detection at 254 nm. Retention times 19.3 min (major) and 20.1 min (minor).
4-Methyl-1-(methyldiphenylsilyl)-1-(p-tolyl)butan-1-ol, 76b

The reaction was performed with 0.3 mmol 75b, iBuMgBr (0.6 mmol, 1.3M in MTBE), CuBrSMe₂ (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L₅ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃ (74 mg, 0.3 mmol) and BF₃·Et₂O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76b was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [70% yield, 88% e.e.].

1H NMR (400 MHz, CDCl₃) δ 7.56 (d, J = 6.6 Hz, 2H), 7.47 (d, J = 6.7 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.36-7.30 (m, 3H), 7.26 (t, J = 7.7 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.2 Hz, 2H), 2.28 (s, 3H), 2.11 (dd, J = 14.7, 4.8 Hz, 1H), 1.96 (dd, J = 14.7, 7.2 Hz, 1H), 1.68 – 1.57 (m, 2H), 0.86 (d, J = 6.6 Hz, 3H), 0.63 (d, J = 6.7 Hz, 3H), 0.49 (s, 3H).

13C NMR. (100 MHz, CDCl₃) δ 141.8, 135.9, 135.8, 134.6, 134.5, 134.2, 129.5, 129.3, 128.3, 127.7, 127.5, 125.3, 74.3, 24.8, 24.5, 23.7, 21.0, -6.1.

HRMS (ESI+, m/Z): calcd for C₂₄H₂₈O₅Si [M-OH]+: 357.2033; found: 357.2039.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.6:0.4, 0.3 mL/min, 40 °C, detection at 230 nm. Retention times 35.3 min (major) and 38.5 min (minor).

1-(4-(tert-Butyl)phenyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76c

The reaction was performed with 0.3 mmol 75c, iBuMgBr (0.6 mmol, 1.4M in MTBE), CuBrSMe₂ (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L₅ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃ (74 mg, 0.3 mmol) and BF₃·Et₂O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76c was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 95:5), [85% yield, 90% e.e.].

1H NMR (400 MHz, CDCl₃) δ 7.55 (d, J = 6.6 Hz, 2H), 7.41-7.35 (m, 3H), 7.26-7.20 (m, 2H), 7.17 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.5 Hz, 2H), 2.12 (dd, J = 14.7, 4.7 Hz, 1H), 1.96 (dd, J = 14.6, 7.2 Hz, 1H), 1.71-1.59 (m, 2H), 1.28 (s, 9H), 0.87 (d, J = 6.6 Hz, 3H), 0.64 (d, J = 6.7 Hz, 3H), 0.49 (s, 3H).

13C NMR. (101 MHz, CDCl₃) δ 148.2, 141.9, 136.1, 135.9, 134.9, 134.4, 129.6, 129.4, 127.8, 127.6, 125.2, 124.6, 74.7, 45.8, 34.5, 31.7, 25.1, 24.8, 24.0, -5.8.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 230 nm. Retention times (major) 12.3 min and (minor) 13.7 min.

3-Methyl-1-(methyldiphenylsilyl)-1-(m-tolyl)butan-1-ol, 76d

The reaction was performed with 0.3 mmol 75d, iBuMgBr (0.6 mmol, 1.2M in MTBE), CuBrSMe₂ (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L₅ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃ (74 mg, 0.3 mmol) and BF₃·Et₂O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76d was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 95:5), [53% yield, 92% e.e.].

1H NMR (400 MHz, CDCl₃) δ 7.57 (d, J = 6.6 Hz, 2H), 7.50 (d, J = 6.7 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.29 (t, J = 7.5 Hz, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.5 Hz, 1H), 6.87 (d, J = 7.8 Hz, 1H), 6.77 (s, 1H), 2.21 (s, 3H), 2.16 (dd, J = 14.7, 4.9 Hz, 1H), 2.00 (dd, J = 14.7, 7.2 Hz, 1H), 1.76 – 1.62 (m, 2H), 0.90 (d, J = 6.6 Hz, 3H), 0.66 (d, J = 6.7 Hz, 3H), 0.52 (s, 3H).

13C NMR. (100 MHz, CDCl₃) δ 144.8, 136.9, 135.9, 135.8, 134.5, 134.0, 129.5, 129.3, 127.6, 127.5, 127.4, 126.3, 125.8, 122.4, 74.5, 45.5, 24.8, 24.6, 23.8, 21.6, -6.2.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 220 nm. Retention times 9.7 min (minor) and 10.9 min (major).

1-(3,5-Dimethylphenyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76e

The reaction was performed with 0.3 mmol 75e, iBuMgBr (0.6 mmol, 1.2M in MTBE), CuBrSMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,R)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76e was obtained as colorless oil after column chromatography (SiO2, pentane:Et2O 97.5:2.5), [59% yield, 84% e.e.].

1H NMR (400 MHz, CDCl3) δ 7.56 (d, J = 6.6 Hz, 2H), 7.51 (d, J = 7.7 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.35 (m, 3H), 7.30 (t, J = 7.2 Hz, 2H), 6.76 (s, 1H), 6.59 (s, 2H), 2.19 (s, 3H), 2.14 (dd, J = 14.7, 4.8 Hz, 1H), 2.00 (dd, J = 14.7, 7.2 Hz, 1H), 1.76 – 1.62 (m, 2H), 0.91 (d, J = 6.6 Hz, 3H), 0.68 (d, J = 6.7 Hz, 3H), 0.51 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 144.8, 136.9, 136.2, 136.0, 134.8, 134.3, 129.6, 129.5, 127.8, 127.6, 126.9, 123.6, 74.7, 45.6, 25.1, 24.8, 24.1, 21.7, -6.1.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 240 nm. Retention times 9.6 min (minor) and 11.3 min (major).

1-(4-Fluorophenyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76f

The reaction was performed with 0.3 mmol 75f, iBuMgBr (0.6 mmol, 1.3M in MTBE), CuBrSMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,R)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76f was obtained as colorless oil after column chromatography (SiO2, pentane:Et2O 97.5:2.5), [60% yield, 90% e.e.].

1H NMR (400 MHz, CDCl3) δ 7.57 (d, J = 6.6 Hz, 2H), 7.50 (d, J = 6.6 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.38-7.33 (m, 3H), 7.29 (t, J = 7.2 Hz, 2H), 6.99 (dd, J = 8.8 Hz, 5.4, 2H), 6.87 (t, J = 8.8 Hz, 2H), 2.12 (dd, J = 14.7, 5.1 Hz, 1H), 1.99 (dd, J = 14.8, 7.1 Hz, 1H), 1.72 – 1.57 (m, 2H), 0.88 (d, J = 6.6 Hz, 3H), 0.63 (d, J = 6.7 Hz, 3H), 0.52 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 160.8 (d, JC-F = 243.4 Hz), 140.6 (d, JC-F = 2.9 Hz), 136.0, 135.9, 134.3, 133.9, 129.9, 129.7, 128.0, 127.9, 126.8 (d, JC-F = 7.7 Hz), 114.3 (d, JC-F = 21.0 Hz), 74.3, 46.0, 24.9, 24.7, 23.9, -6.1.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 220 nm. Retention times (major) 12.5 min and (minor) 13.6 min.

1-(3-Fluorophenyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76g

The reaction was performed with 0.3 mmol 75g, iBuMgBr (0.6 mmol, 1.3M in MTBE), CuBrSMe2 (9.24 mg, 0.015 mmol, 15 mol%), ligand (S,R)-L5 (32.4 mg, 0.054 mmol, 18 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 10 ml MTBE. Product 76g was obtained as colorless oil after column chromatography (SiO2, pentane:Et2O 95:5), [52% yield, 92% e.e.].

1H NMR (400 MHz, CDCl3) δ 7.58 (d, J = 6.7 Hz, 2H), 7.50 (d, J = 6.8 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.40 - 7.33(m, 3H), 7.29 (t, J = 7.2 Hz, 2H), 7.12 (dt, J = 14.4, 7.7 Hz, 1H), 6.85 - 6.74 (m, 3H), 2.12 (dd, J = 14.7, 5.2 Hz, 1H), 1.99 (dd, J = 14.8, 7.0 Hz, 1H), 1.69 (s, 1H), 1.68-1.60 (m, 1H), 0.88 (d, J = 6.6 Hz, 3H), 0.63 (d, J = 6.7 Hz, 3H), 0.53 (s, 3H).
\[ ^1\text{H} \text{NMR} (400 \text{ MHz}, \text{CDCl}_3) \delta 7.77 (d, J = 8.7 \text{ Hz, 1H}), 7.68 (d, J = 8.7 \text{ Hz, 1H}), 7.63 (d, J = 8.7 \text{ Hz, 1H}), 7.60-7.55 (m, 3H), 7.52 (d, J = 7.4 \text{ Hz, 2H}), 7.45-7.31 (m, 6H), 7.27 (t, J = 7.5 \text{ Hz, 2H}), 7.09 (d, J = 8.6 \text{ Hz, 1H}), 2.30 (dd, J = 14.7, 4.9 \text{ Hz, 1H}), 2.07 (dd, J = 14.7, 7.3 \text{ Hz, 1H}), 1.84 (s, 1H), 1.71-1.60 (m, 1H), 0.90 (d, J = 6.6 \text{ Hz, 3H}), 0.63 (d, J = 6.7 \text{ Hz, 3H}), 0.54 (s, 3H). \]

\[ ^{13}\text{C} \text{NMR} (101 \text{ MHz}, \text{CDCl}_3) \delta 154.3, 136.0, 135.6, 131.9, 128.2, 127.8, 127.6, 127.0, 125.9, 125.3, 124.7, 124.0, 75.0, 54.9, 25.0, 24.7, 24.1, -5.9. \]

HRMS (APCI+, m/z): calcd for C_{28}H_{29}O_{3}Si [M-H]: 409.1882; found: 409.1877.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 265 nm. Retention times 11.3 min (minor) and 12.4 min (major).

The reaction was performed with 0.3 mmol 75j, iBuMgBr (0.6 mmol, 1.3M in MTBE), CuBr.SMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3. Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product \textit{76j} was obtained as colorless oil after column chromatography (SiO2, pentane: Et2O 95:5), [67% yield, 26% e.e.].
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\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.57 (dd, J = 8.0, 1.4 Hz, 2H), 7.49 (dd, J = 8.0, 1.3 Hz, 2H), 7.43 – 7.38 (m, 1H), 7.37 – 7.31 (m, 3H), 7.28 (t, J = 7.2 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 6.74 (d, J = 8.9 Hz, 2H), 3.77 (s, 3H), 2.11 (dd, J = 14.7, 4.9 Hz, 1H), 1.97 (dd, J = 14.7, 7.1 Hz, 1H), 1.71 – 1.59 (m, 2H), 0.88 (d, J = 6.6 Hz, 3H), 0.65 (d, J = 6.7 Hz, 3H), 0.51 (s, 3H).

\[ ^{13} \text{C NMR (101 MHz, CDCl}_3 \] \( \delta \) 157.5, 137.2, 136.1, 135.9, 134.8, 134.4, 129.7, 129.5, 129.7, 129.7, 126.6, 113.1, 74.2, 55.4, 45.9, 25.0, 24.8, 23.9, -5.9.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 230 nm. Retention times 24.2 min (major) and 26.1 min (minor).

\[ \text{1-(3-methoxyphenyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76k} \]

The reaction was performed with 0.3 mmol 75k, tBuMgBr (0.6 mmol, 1.2M in MTBE), CuBrSMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76k was obtained as colorless oil after column chromatography (SiO2, pentane:Et2O 95:5), [73% yield, 86% e.e.].

\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.59 (d, J = 7.7 Hz, 2H), 7.52 (d, J = 7.7 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.36 (m, 3H), 7.29 (t, J = 7.5 Hz, 2H), 7.11 (t, J = 7.9 Hz, 1H), 6.70 – 6.63 (m, 2H), 6.58 (s, 1H), 3.58 (s, 3H), 2.18 (d, J = 5.0 Hz, 1H), 2.01 (dd, J = 14.7, 7.1 Hz, 1H), 1.73 – 1.63 (m, 1H), 0.91 (d, J = 6.6 Hz, 2H), 0.66 (d, J = 6.7 Hz, 2H), 0.54 (s, 3H).

\[ ^{13} \text{C NMR (101 MHz, CDCl}_3 \] \( \delta \) 159.3, 147.1, 136.1, 135.9, 134.7, 134.2, 129.8, 129.6, 128.6, 127.9, 127.8, 118.0, 111.5, 116.5, 115.0, 74.8, 55.1, 46.0, 25.0, 24.8, 24.0, -6.0.

HRMS (APCI+ m/z): calcld for C_{25}H_{31}O_{2}Si [M+H]+: 391.2088; found: 391.2087.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 265 nm. Retention times 14.2 min (minor) and 18.4 min (major).

\[ \text{1-[(3-methoxycarbonyl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76l} \]

The reaction was performed with 0.3 mmol 75l, tBuMgBr (0.6 mmol, 1.2M in MTBE), CuBrSMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76l was obtained as colorless oil after column chromatography (SiO2, pentane:Et2O 95:5), [76% yield, 90% e.e.].

\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.61 (d, J = 7.7 Hz, 4H), 7.52 (d, J = 7.8 Hz, 2H), 7.48-7.32 (m, 9H), 7.29 (t, J = 7.5 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 2.21 (dd, J = 14.7, 4.9 Hz, 1H), 2.03 (dd, J = 14.7, 7.2 Hz, 1H), 1.77 – 1.65 (m, 2H), 0.92 (d, J = 6.6 Hz, 3H), 0.68 (d, J = 6.7 Hz, 3H), 0.56 (s, 3H).

\[ ^{13} \text{C NMR (101 MHz, CDCl}_3 \] \( \delta \) 144.4, 141.1, 137.9, 136.1, 136.0, 134.6, 134.1, 129.8, 129.6, 128.9, 127.9, 127.8, 127.2, 127.0, 126.3, 126.0, 74.7, 45.9, 25.0, 24.8, 24.1, -5.9.

HRMS (ESI+, m/z): calcld for C_{30}H_{32}O_{2}SiNa [M+Na]+: 459.2114; found: 459.2111.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 235 nm. Retention times 11.1 min (minor) and 12.1 min (major).

\[ \text{1-[(1,1'-biphenyl)-3-yl)-3-methyl-1-(methyldiphenylsilyl)butan-1-ol, 76m} \]

The reaction was performed with 0.3 mmol 75m, tBuMgBr (0.6 mmol, 1.2M in MTBE), CuBrSMe2 (3.08 mg, 0.015 mmol, 5 mol%), ligand (S,RFe)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3.Et2O (0.037ml, 0.3 mmol) in 6 ml MTBE. Product 76m was obtained as colorless oil after...
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column chromatography (SiO₂, pentane: Et₂O 95:5), [56% yield, 90% e.e.].

\(^1H\) NMR (400 MHz, CDCl₃) δ 7.60 (d, J = 7.4 Hz, 2H), 7.53 (d, J = 7.4 Hz, 2H), 7.46 – 7.40 (m, 1H), 7.35 (dd, J = 11.1, 7.1 Hz, 6H), 7.28 (dt, J = 16.7, 6.9 Hz, 6H), 7.20 (s, 1H), 7.08 (d, J = 7.7 Hz, 1H), 2.24 (dd, J = 14.7, 5.0 Hz, 1H), 2.04 (dd, J = 14.7, 7.3 Hz, 1H), 1.79 – 1.64 (m, 2H), 0.90 (d, J = 6.6 Hz, 3H), 0.65 (d, J = 6.7 Hz, 3H), 0.56 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl₃) δ 145.7, 141.7, 140.4, 136.1, 136.0, 134.7, 134.1, 129.8, 129.6, 128.7, 128.2, 128.0, 127.9, 127.3, 127.2, 124.7, 124.5, 124.2, 74.8, 45.9, 25.0, 24.7, 24.1, -6.0.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 275 nm. Retention times 11.2 min (major) and 13.5 min (minor).

\((E)-3,6\)-Dimethyl-4-(methyldiphenylsilyl)hept-2-en-4-ol, 76n

The reaction was performed with 0.15 mmol 75n, iBuMgBr (0.3 mmol, 1.5M in MTBE), CuBr.SMe₂ (1.54 mg, 0.0075 mmol, 5 mol%), ligand (S,RFe)-L₅ (5.4 mg, 0.009 mmol, 6 mol%), CeCl₃ (9.5 mg, 0.0375 mmol) and BF₃·Et₂O (0.005 ml, 0.0375 mmol) in 3 ml MTBE. Product 76n was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [90% yield, 96 e.e.].

\(^1H\) NMR (400 MHz, CDCl₃) δ 7.67 (dd, J = 7.7, 1.7 Hz, 2H), 7.63 (dd, J = 7.9, 1.6 Hz, 2H), 7.40 – 7.27 (m, 6H), 5.35 (qd, J = 6.7, 1.0 Hz, 1H), 1.97 – 1.89 (m, 1H), 1.75 – 1.64 (m, 2H), 1.57 (dd, J = 6.7, 0.8 Hz, 3H), 1.33 (s, 3H), 1.32 (s, 1H), 0.91 (d, J = 6.3 Hz, 3H), 0.81 (d, J = 6.5 Hz, 3H), 0.59 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl₃) δ 138.6, 135.9, 135.8, 135.7, 135.3, 129.6, 129.4, 127.9, 127.7, 117.2, 116.4, 43.7, 25.2, 24.8, 24.0, 15.2, 13.5, -5.1.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 220 nm. Retention times 9.9 min (major) and 11.1 min (minor).

\((E)-2,5,7\)-Trimethyl-4-(methyldiphenylsilyl)oct-5-en-4-ol, 76o

The reaction was performed with 0.15 mmol 75o, iBuMgBr (0.3 mmol, 1.5M in MTBE), CuBr.SMe₂ (1.54 mg, 0.0075 mmol, 5 mol%), ligand (S,RFe)-L₅ (5.4 mg, 0.009 mmol, 6 mol%), CeCl₃ (9.5 mg, 0.0375 mmol) and BF₃·Et₂O (0.005 ml, 0.0375 mmol) in 3 ml MTBE. Product 76o was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [91% yield, 96 e.e.].

\(^1H\) NMR (400 MHz, CDCl₃) δ 7.71 – 7.62 (m, 4H), 7.42 – 7.27 (m, 6H), 5.11 (d, J = 9.2 Hz, 1H), 2.47 (dq, J = 13.4, 6.6 Hz, 1H), 1.93 (q, J = 7.4, 1H), 1.76 – 1.64 (m, 2H), 1.36 (s, 3H), 1.30 (s, 1H), 0.91 (dd, J = 6.1, 3.4 Hz, 6H), 0.87 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.0 Hz, 3H), 0.62 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl₃) δ 135.9, 135.8, 135.6, 135.3, 135.2, 131.2, 129.6, 129.4, 127.9, 127.7, 117.6, 43.7, 27.4, 25.2, 24.7, 23.9, 23.3, 23.0, 15.3, -5.0.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 240 nm. Retention times 8.3 min (minor) and 8.6 min (major).

\((E)-1\)-Cyclohexyl-2,5-dimethyl-3-(methyldiphenylsilyl)hex-1-en-3-ol, 76p

The reaction was performed with 0.15 mmol 75p, iBuMgBr (0.3 mmol, 1.5M in MTBE), CuBr·SMe₂ (1.54 mg, 0.0075 mmol, 5 mol%), ligand (S,RFe)-L₅ (5.4 mg, 0.009 mmol, 6 mol%), CeCl₃ (9.5 mg, 0.0375 mmol) and BF₃·Et₂O (0.005 ml, 0.0375 mmol) in 3 ml MTBE. Product 76p was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [91% yield, 96 e.e.].

\(^1H\) NMR (400 MHz, CDCl₃) δ 7.71 – 7.62 (m, 4H), 7.42 – 7.27 (m, 6H), 5.11 (d, J = 9.2 Hz, 1H), 2.47 (dq, J = 13.4, 6.6 Hz, 1H), 1.93 (q, J = 7.4, 1H), 1.76 – 1.64 (m, 2H), 1.36 (s, 3H), 1.30 (s, 1H), 0.91 (dd, J = 6.1, 3.4 Hz, 6H), 0.87 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.0 Hz, 3H), 0.62 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl₃) δ 135.9, 135.8, 135.6, 135.3, 135.2, 131.2, 129.6, 129.4, 127.9, 127.7, 117.6, 43.7, 27.4, 25.2, 24.7, 23.9, 23.3, 23.0, 15.3, -5.0.

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after column chromatography (SiO$_2$, pentane: Et$_2$O 97.5:2.5), [90% yield, 96% e.e.].

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.71 - 7.63 (m, 4H), 7.41 - 7.27 (m, 6H), 5.14 (d, J = 9.0 Hz, 1H), 2.21 - 2.08 (m, 1H), 1.93 (q, J = 7.4 Hz, 1H), 1.78 - 1.47 (m, 8H), 1.37 (s, 3H), 1.29 - 1.12 (m, 3H), 1.02 (dt, J = 15.5, 7.7 Hz, 2H), 0.92 (d, J = 6.2 Hz, 3H), 0.82 (d, J = 6.3 Hz, 3H), 0.62 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 136.0, 135.8, 135.7, 135.6, 135.3, 129.60, 129.55, 129.4, 127.9, 127.7, 75.7, 43.7, 37.3, 33.5, 33.2, 26.4, 26.4, 26.3, 25.2, 24.7, 23.9, 15.4, -5.0.

HRMS (APCI+, m/Z): calcd for C$_{27}$H$_{37}$Si [M-OH]$^+$: 389.2659; found: 389.2653.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 220 nm. Retention times 8.2 min (minor) and 8.8 min (major).

(E)-3,6-Dimethyl-4-(methyldiphenylsilyl)-1-phenylhept-2-en-4-ol, 76q

The reaction was performed with 0.15 mmol 75q, iBuMgBr (0.3 mmol, 1.5M in MTBE), CuBr.SMe$_2$ (1.54 mg, 0.0075 mmol, 5 mol%), ligand (S,RFe)-L$_5$ (5.4 mg, 0.009 mmol, 6 mol%), CeCl$_3$ (9.5 mg, 0.0375 mmol) and BF$_3$.Et$_2$O (0.005 ml, 0.0375 mmol) in 3 ml MTBE. Product 76q was obtained as colorless oil after column chromatography (SiO$_2$, pentane: Et$_2$O 97.5:2.5), [66% yield, 94% e.e.].

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 - 7.44 (m, 4H), 7.37 - 7.14 (m, 8H), 7.10 (t, J = 7.1 Hz, 1H), 7.00 (d, J = 7.4 Hz, 2H), 5.47 (t, J = 7.2 Hz, 1H), 3.28 (d, J = 6.1 Hz, 3H), 0.77 (d, J = 6.3 Hz, 3H), 0.55 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 141.8, 139.0, 135.9, 135.8, 135.4, 135.1, 129.6, 129.5, 128.6, 128.5, 128.0, 127.8, 125.8, 122.1, 76.3, 43.9, 34.6, 25.2, 24.8, 24.0, 15.6, -5.0.

HRMS (APCI+, m/Z): calcd for C$_{28}$H$_{33}$Si [M-OH]$^+$: 397.2340; found: 397.2346.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 230 nm. Retention times 10.7 min (minor) and 15.4 min (major).

(E)-1-Cyclohexyl-2-methyl-3-(methyldiphenylsilyl)pent-1-en-3-ol, 76r

The reaction was performed with 0.15 mmol 75p, EtMgBr (0.3 mmol, 1.4 M in MTBE), CuBr.SMe$_2$ (1.54 mg, 0.0075 mmol, 5 mol%) and ligand (S,RFe)-L$_5$ (5.4 mg, 0.009 mmol, 6 mol%) in 3 ml MTBE. Product 76r was obtained as colorless oil after column chromatography (SiO$_2$, pentane: Et$_2$O 97.5:2.5), [95% yield, 84% e.e.].

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.75 - 7.65 (m, 4H), 7.44 - 7.27 (m, 6H), 5.14 (d, J = 9.0 Hz, 1H), 2.23 - 2.10 (m, 1H), 1.99 (dq, J = 14.6, 7.3 Hz, 1H), 1.84 (dq, J = 14.2, 7.1 Hz, 1H), 1.73 - 1.50 (m, 6H), 1.34 (s, 3H), 1.31 - 1.13 (m, 3H), 1.11 - 0.95 (m, 2H), 0.73 (t, J = 7.2 Hz, 3H), 0.63 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 135.89, 135.85, 135.6, 135.37, 135.35, 130.5, 129.5, 129.4, 127.9, 127.7, 74.8, 37.4, 33.7, 33.3, 28.1, 26.4, 26.3, 14.8, 5.7, -5.2.

HRMS (APCI+, m/Z): calcd for C$_{25}$H$_{33}$Si [M-OH]$^+$: 361.2346; found: 361.2346.

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 230 nm. Retention times 11.3 min (minor) and 14.1 min (major).

(E)-1-Cyclohexyl-2-methyl-3-(methyldiphenylsilyl)hept-1-en-3-ol, 76s

The reaction was performed with 0.15 mmol 75p, BuMgBr (0.3 mmol, 1.6 M in MTBE), CuBr.SMe$_2$ (1.54 mg, 0.0075 mmol, 5 mol%) and ligand (S,RFe)-L$_5$ (5.4 mg, 0.009 mmol, 6 mol%) in 3 ml MTBE. Product 76s was obtained as colorless oil after column chromatography (SiO$_2$, pentane: Et$_2$O
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97.5:2.5), [93% yield, 84% e.e.].

H NMR (400 MHz, CDCl₃) δ 7.74–7.66 (m, 4H), 7.45–7.27 (m, 6H), 5.12 (d, J = 9.0 Hz, 1H), 2.21–2.09 (m, 1H), 2.00–1.87 (m, 1H), 1.85–1.75 (m, 1H), 1.74–1.49 (m, 5H), 1.34 (s, 3H), 1.30–0.95 (m, 10H), 0.86 (t, J = 7.1 Hz, 3H), 0.63 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 135.9, 135.9, 135.8, 135.7, 135.4, 130.1, 129.5, 129.3, 127.9, 127.7, 74.8, 37.3, 35.3, 33.7, 33.3, 26.4, 26.3, 23.7, 23.3, 14.8, 14.4, -5.1.

HRMS (APCI+, m/Z): calcd for C₂₇H₃₇Si [M-OH]+: 389.2653; found: 389.2659

The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 215 nm. Retention times 9.8 min (minor) and 10.5 min (major).

(E)-1-Cyclohexyl-2,6-dimethyl-3-(methyldiphenylsilyl)hept-1-en-3-ol, 76t

The reaction was performed with 0.15 mmol 75p, iPentMgBr (0.3 mmol, 1.4 M in MTBE), CuBr·SMe2 (1.54 mg, 0.0075 mmol, 5 mol%) and ligand (S,RFe)₅-L₅ (5.4 mg, 0.009 mmol, 6 mol%) in 3 ml MTBE. Product 76t was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [89% yield, 86% e.e.].

H NMR (400 MHz, CDCl₃) δ 7.75–7.63 (m, 4H), 7.43–7.26 (m, 6H), 5.11 (d, J = 9.0 Hz, 1H), 2.14 (dd, J = 12.7, 7.5 Hz, 1H), 1.94 (td, J = 13.8, 4.2 Hz, 1H), 1.85–1.75 (m, 1H), 1.74–1.49 (m, 6H), 1.43 (td, J = 13.1, 6.6 Hz, 1H), 1.33 (s, 4H), 1.30–1.12 (m, 4H), 1.11–0.87 (m, 2H), 0.84 (dd, J = 6.5, 4.8 Hz, 6H), 0.63 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 135.89, 135.86, 135.7, 135.4, 130.4, 129.5, 129.3, 127.9, 127.7, 74.7, 37.4, 33.7, 33.3, 30.4, 28.5, 26.4, 26.3, 23.2, 22.7, 14.8, -5.1.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 220 nm. Retention times 16.9 min (minor) and 17.8 min (major).

(E)-1-Cyclohexyl-2-methyl-3-(methyldiphenylsilyl)-5-phenylpent-1-en-3-ol, 76u

The reaction was performed with 0.15 mmol 75p, Ph(CH₂)₂MgBr (0.3 mmol, 1.0 M in MTBE), CuBr·SMe² (1.54 mg, 0.0075 mmol, 5 mol%), ligand(S,RFe)₅-L₅ (5.4 mg, 0.009 mmol, 6 mol%) and CeCl₃ (37 mg, 0.15 mmol) in 3 ml MTBE. Product 76u was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [95% yield, 82% e.e.].

H NMR (400 MHz, CDCl₃) δ 7.75–7.67 (m, 4H), 7.46–7.31 (m, 6H), 7.28 (t, J = 7.5 Hz, 2H), 7.19 (t, J = 6.9 Hz, 1H), 7.16 (d, J = 7.6 Hz, 2H), 5.22 (d, J = 9.0 Hz, 1H), 2.75–2.63 (td, J = 12.5, 5.6 Hz, 1H), 2.40 (td, J = 12.5, 4.5 Hz, 1H), 2.30–2.12 (m, 3H), 1.79–1.54 (m, 5H), 1.47 (s, 3H), 1.45 (s, 1H), 1.38–1.00 (m, 5H), 0.67 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 143.1, 135.9, 135.8, 135.3, 135.2, 134.9, 130.6, 129.7, 129.5, 128.7, 128.6, 128.0, 127.0, 125.8, 75.0, 38.1, 37.4, 33.7, 33.3, 28.5, 26.4, 26.3, 14.9, -5.2.


The enantiomeric ratio was determined by chiral SFC analysis, Chiralpak IB column, 95% CO₂/5% MeOH, 150 bar, 40 °C, 2 ml/min, Retention times 10.9 min (minor) and 13.1 min (major).

(E)-1-Cyclohexyl-2-methyl-3-(methyldiphenylsilyl)hepta-1,6-dien-3-ol, 76v

The reaction was performed with 0.15 mmol 75p, but-3-en-1-ylmagnesium bromide (0.3 mmol, 1.3 M in MTBE), CuBr·SMe₂ (1.54 mg, 0.0075 mmol, 5 mol%) and ligand(S,RFe)₅-L₅ (5.4 mg, 0.009 mmol, 6 mol%) in 3 ml MTBE. Product 76v was obtained as colorless oil after column chromatography
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[SiO₂, pentane: Et₂O 97.5:2.5], [97% yield, 86% e.e.].

1H NMR (400 MHz, CDCl₃) δ 7.73-7.64 (m, 4H), 7.44 – 7.28 (m, 6H), 5.81 (ddt, J = 16.8, 10.1, 6.6 Hz, 1H), 5.13 (d, J = 9.0 Hz, 1H), 4.96 (d, J = 17.2 Hz, 1H), 4.90 (d, J = 10.1 Hz, 1H), 2.22-2.05 (m, 2H), 2.00 (bb, J = 11.8, 3.8 Hz, 1H), 1.91 (tb, J = 12.0, 4.8 Hz, 1H), 1.87-1.76 (m, 1H), 1.75 – 1.48 (m, 5H), 1.43 (s, 1H), 1.35 (s, 3H), 1.32 – 1.12 (m, 3H), 1.11 – 0.93 (m, 2H), 0.63 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 139.7, 135.9, 135.8, 135.4, 135.3, 135.1, 130.5, 129.6, 129.4, 128.0, 127.8, 114.7, 74.9, 37.4, 34.9, 33.7, 33.3, 26.7, 26.4, 26.3, 14.8, -5.2.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 254 nm. Retention times 11.5 min (minor) and 12.3 min (major).

(E)-1-Cyclohexyl-2-methyl-3-(methyldiphenylsilyl)octa-1,7-dien-3-ol, 76w

The reaction was performed with 0.15 mmol 75p, Pent-3-en-1-ylmagnesium bromide (0.3 mmol, 1.0 M in MTBE), CuBr·SMe₂ (1.54 mg, 0.0075 mmol, 5 mol%) and ligand(S,RFe)-L₅ (5.4 mg, 0.009 mmol, 6 mol%) in 3 ml MTBE. Product 76w was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 97.5:2.5), [96% yield, 90% e.e].

1H NMR (400 MHz, CDCl₃) δ 7.74-7.61 (m, 4H), 7.44 – 7.26 (m, 6H), 5.75 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 5.11 (d, J = 9.0 Hz, 1H), 4.96 (d, J = 17.1 Hz, 1H), 4.91 (d, J = 10.2 Hz, 1H), 2.21-2.08 (m, 1H), 2.06-1.89 (m, 3H), 1.85 – 1.74 (m, 1H), 1.74 – 1.48 (m, 5H), 1.48-1.36 (m, 1H), 1.33 (s, 3H), 1.30 – 0.92 (m, 7H), 0.62 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 139.0, 135.9, 135.8, 135.6, 135.5, 135.3, 130.1, 129.6, 129.4, 127.9, 127.7, 114.6, 74.8, 37.3, 35.1, 34.2, 33.7, 33.3, 26.4, 26.3, 21.0, 14.8, -5.1.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ADH column, n-heptane/i-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 254 nm. Retention times 10.8 min (minor) and 11.5 min (major).

1-(4-(tert-butyl)phenyl)-1-(methyldiphenylsilyl)pentan-1-ol, 76x

The reaction was performed with 0.3 mmol 75c, BuMgBr (0.6 mmol, 1.6 M in MTBE), CuBr·SMe₂ (3.08 mg, 0.015 mmol, 5 mol%), ligand(S,RFe)-L₅ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃ (74 mg, 0.3 mmol) and BF₃·Et₂O (0.037 ml, 0.3 mmol) in 3 ml MTBE. Product 76x was obtained as colorless oil after column chromatography (SiO₂, pentane: Et₂O 95:5), [88% yield, 70% e.e].

1H NMR (400 MHz, CDCl₃) δ δ 7.56 (d, J = 6.8 Hz, 1H), 7.45-7.34 (m, 3H), 7.314-7.27 (m, 3H), 7.17 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H). 2.23 – 1.94 (m, 2H), 2.17 (s, 1H), 1.27 (s, 9H), 1.25-1.14 (m, 3H), 1.07 – 0.85 (m, 1H), 0.77 (t, J = 7.0 Hz, 3H), 0.50 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 148.2, 141.7, 136.0, 135.9, 134.8, 134.4, 129.5, 129.4, 127.8, 127.6, 125.2, 124.6, 73.7, 37.3, 34.4, 31.6, 23.8, 23.3, 14.2, -5.8.


The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99.8:0.2, 0.5 mL/min, 40 °C, detection at 254 nm. Retention times 11.7 min (minor) and 12.2 min (major).

1-(4-(tert-butyl)phenyl)-1-(methyldiphenylsilyl)-3-phenylpropan-1-ol, 76y

The reaction was performed with 0.3 mmol 75c, Ph(CH₂)₂MgBr (0.6 mmol, 1.0 M in MTBE), CuBr·SMe₂ (3.08 mg, 0.015 mmol, 5 mol%), ligand(S,RFe)-L₅ (10.8 mg, 0.018 mmol, 6 mol%), CeCl₃
was determined by chiral HPLC analysis, Chiralcel ODH column, n-A. Carini, Nakada, 6)
128.5, 127.8, 127.7, 125.8, 125.2, 124.8, 73.8, 39.8, 34.5, 31.6, 31.5, 28.5, -5.8.
5) 1980 Commun. 1-(4-(tert-butyl)phenyl)-4-methyl-1-
and (minor) 22.0 min. 3H), 0.58 (s, 3H).
Jpn. 2) 3) 13C NMR (101 MHz, cdc13) δ 148.2, 141.6, 136.0, 135.9, 134.8, 134.4, 129.5, 129.3, 127.7, 127.6, 125.2, 124.6, 73.5, 35.2, 34.4, 31.6, 30.5, 28.5, 23.0, 22.5, -5.8.
The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99: 1, 0.5 mL/min, 40 °C, detection at 254 nm. Retention times (major) 18.8 min and (minor) 22.0 min.

1-{4-(tert-butyl)phenyl}-4-methyl-1-{(methyldiphenylsilyl)pentan-1-ol, 76z
The reaction was performed with 0.3 mmol 75c, iPentMgBr (0.6 mmol, 1.4 M in MTBE), CuBr2Me2 (3.08 mg, 0.015 mmol, 5 mol%), ligand(S,R,e)-L5 (10.8 mg, 0.018 mmol, 6 mol%), CeCl3 (74 mg, 0.3 mmol) and BF3 OEt2 (0.037 ml, 0.3 mmol) in 6 ml MTBE. Product 76z was obtained as colorless oil after column chromatography (SiO2, pentane: Et2O 95:5), [96% yield, 70% e.e.].

1H NMR (400 MHz, Chloroform-d) δ 7.65 (d, J = 6.6 Hz, 21H), 7.53 – 7.42 (m, 3H), 7.42 – 7.35 (m, 3H), 7.30 (t, J = 7.2 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 2.27-2.07 (m, 2H), 1.74 (s, 0H), 1.55-1.42 (m, 1H), 1.36 (s, 9H), 1.27-1.17 (m,1H), 0.98 – 0.89 (m, 0H), 0.85 (t, J = 6.0 Hz, 3H), 0.58 (s, 3H).

13C NMR (101 MHz, cdc13) δ 148.2, 141.6, 136.0, 135.9, 134.8, 134.4, 129.5, 129.3, 127.7, 127.6, 125.2, 124.6, 73.5, 35.2, 34.4, 31.6, 30.5, 28.5, 23.0, 22.5, -5.8.
The enantiomeric ratio was determined by chiral HPLC analysis, Chiralcel ODH column, n-heptane/i-PrOH 99.5 : 0.5, 0.5 mL/min, 40 °C, detection at 254 nm. Retention times (minor) 9.7 min and (major) 10.5 min.

2.6 References

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