DOI: 10.1002/adsc.200606071

Preparation of a Privileged Silicon-Stereogenic Silane: Classical *versus* Kinetic Resolution

Sebastian Rendler,[a] Gertrud Auer,[a] Manfred Keller,[a] and Martin Oestreich[a, b,*]

[a] Institut für Organische Chemie und Biochemie, Albert-Ludwigs-Universität Freiburg, Albertstrasse 21, 79104 Freiburg im Breisgau, Germany
Fax: (+49)-761-203-6100; e-mail: martin.oestreich@orgmail.chemie.uni-freiburg.de or keller@organik.chemie.uni-freiburg.de (X-ray)

[b] Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany
Fax: (+49)-251-83-33271; e-mail: martin.oestreich@uni-muenster.de

Received: February 27, 2006; Accepted: May 11, 2006

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: The cyclic silicon-stereogenic silane (Si*R*)-**5** decorated with three different substituents of distinct steric demand is an exceptionally useful chiral reagent in asymmetric organosilicon chemistry. Several approaches for its large-scale preparation in optically pure form have been investigated. These hinge upon the resolution of racemic silane *rac*-**5** which, in turn, is accessible in multi-gram quantities by a straightforward one-pot two-step reaction sequence. For this, a classical as well as a novel kinetic resolution *via* its diastereomeric silyl ethers derived from enantiopure secondary alcohols as resolving agents has been elaborated: (1) the use of (−)-menthol [(−)-**7**] allowed for a quantitative separation of silyl ethers (Si*S*)-**10** and (Si*R*)-**10** by practical fractional crystallization and (2) a diastereoselective copper-catalyzed dehydrogenative silicon-oxygen coupling using pyridyl alcohols (*S*)-**16** or (*R*)-**16** capable of two-point binding has been devised and assessed as a novel kinetic resolution strategy for the synthesis of a silane with silicon-centered chirality. Subsequent stereospecific reductive cleavage of the silicon-oxygen bond enabled the preparation of (Si*R*)-**5** and (Si*S*)-**5** in excellent enantiomeric excesses of up to 99% *ee*.

Keywords: alcohols; asymmetric catalysis; copper; kinetic resolution; silicon

Introduction

The synthetic potential of silicon-stereogenic silanes has been literally ignored for decades since initial setbacks corroborated a reputation for being poor stereoinductors.[1] This is particularly remarkable in the light of the detailed investigation of the stereochemical course of reactions at asymmetrically substituted silicon.[2] A handful of substrate-controlled transformations with the silicon moiety functioning as a chiral auxiliary are known[3] whereas the first successful applications of asymmetrically substituted silanes as reagents in stereoselective synthesis were only reported recently.[4] In this context, the elusive chirality transfer was independently realized in both an inter-[5] and an intramolecular[6] scenario by Oestreich et al. and Leighton et al., respectively. Moreover, we devised a novel concept for the non-enzymatic kinetic resolution of chiral secondary alcohols employing asymmetrically substituted silanes as recyclable resolving agents.[7]

A rationale for the notorious track record of failure[4] is probably provided by the structure of standard silane (Si*R*)-**1**[8] (Figure 1), which illustrates the pivotal features intrinsically connected with asymmet-

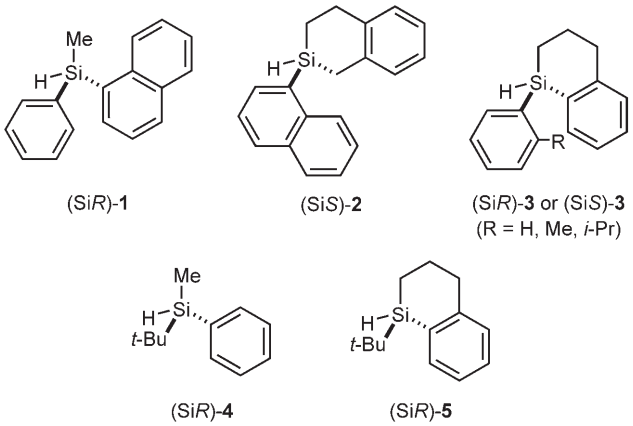


Figure 1. Asymmetrically substituted triorganosilanes.

rically substituted silanes:[4] (1) relatively long carbon-silicon bonds thwarting compact stereochemistry-determining transition states and (2) insufficient stereochemical differentiation at silicon. In order to create more conformational rigidity as a measure against the detrimental carbon-silicon bond length, the silicon center might be embedded into a cyclic framework [(Si*S*)-**2**[9] and (Si*R*)-**3**/(Si*S*)-**3**,[10] Figure 1)].[11] In all these silanes, at least two of the three carbon ligands attached to the stereogenic silicon are of comparable steric demand. This particular structural peculiarity is likely to serve as a reason for the limited success of these readily available acyclic and cyclic silanes. Conversely, *tert*-butyl-substituted silane (Si*R*)-**4**, devoid of this shortcoming, is acyclic and its preparation is rather capricious.[12] The structurally related (Si*R*)-**5** combines this attractive substitution pattern with the conformational rigidity of a cyclic framework. Gratifyingly, the structural features of (Si*R*)-**5** allowed for stereoselective transformations that had failed for its congeners before.[5,7]

An additional challenging obstacle is the restricted number of procedures for the preparation of enantiomerically enriched silanes **A** (Figure 2).[13] In principle, silicon-element double bond-containing molecules **B** are attractive prochiral precursors for reagent- as well as catalyst-controlled asymmetric construction of **A** by enantiofacial discrimination. These highly reactive intermediates are still rather uncommon in synthetic organosilicon chemistry.[14] Thus, in sharp contrast to the asymmetric formation of stereogenic carbons, sp^2-hybridized prochiral silicon compounds **B** cannot be considered as conceivable precursors for the (catalytic) asymmetric synthesis of silanes with silicon-centered chirality.

This clear limitation promoted interest in using stable prochiral substrates **C** (Figure 2) with enantiotopic groups at sp^3-hybridized silicon leading to two efficient catalytic asymmetric processes. Originally introduced by Corriu et al.,[1,15] the diastereoselective, transition metal-catalyzed, dehydrogenative silicon-oxygen coupling[16,17] of **C** (X = H) with enantiopure secondary alcohols **D** was considerably improved in a recent investigation by Leighton et al.[6] (**D** → **F**, Scheme 1). The otherwise low to moderate diastereoselectivities seen for silyl ethers **F** were substantially enhanced in the presence of chirally modified catalysts.[1,6,15] The same class of products was accessed by catalytic asymmetric hydrosilylation of ketones **E** with **C** again using chirally modified transition metal complexes (**E** → **F**, Scheme 1).[1] Moderate to excellent enantio- and diastereoselectivities were reported by Corriu et al.[18a], Kumada et al.[18b] and, later, by Takaya et al.[18c]. The alkoxy moiety in **F** is then replaced by a Grignard reagent affording the desired enantiomerically enriched triorganosilanes **A**.

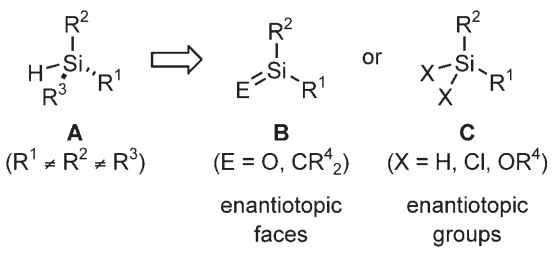
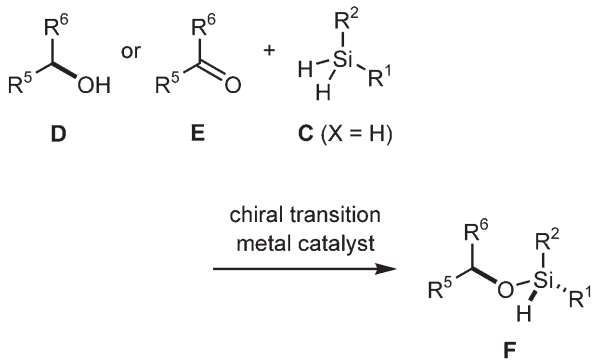


Figure 2. Conceivable prochiral precursors for silicon-stereogenic silanes.

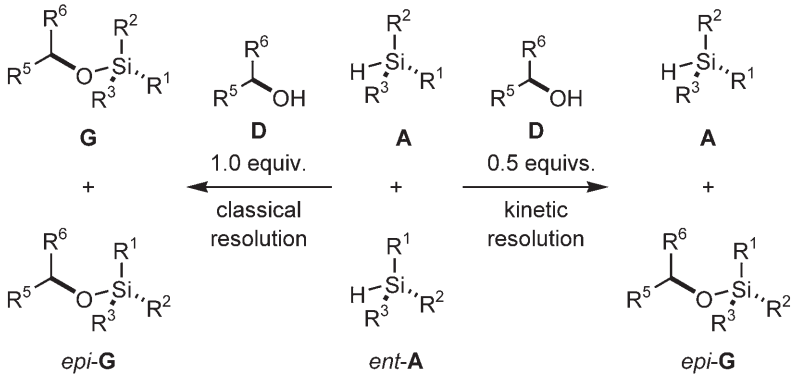


Scheme 1. Dihydrosilane **C** as a prochiral precursor.

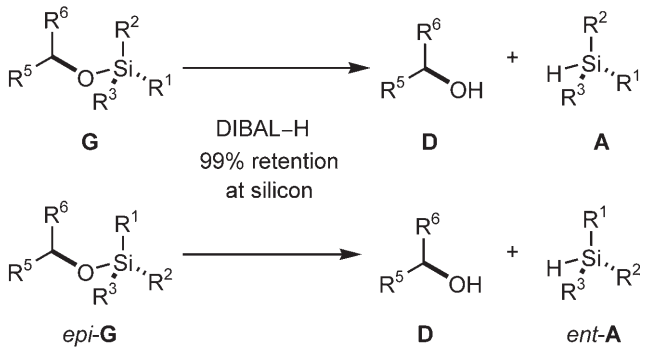
Although these asymmetric syntheses of silyl ethers **F** are highly attractive, the common strategy is still the chemical derivatization of *rac*-**A** with enantiopure resolving agents **D** (Scheme 2, left).[8–10,12] For this purpose, *rac*-**A** is optionally transformed into the corresponding chloro- or alkoxysilane followed by reaction or transetherification with **D**. After separation of diastereomers **G** and *epi*-**G**, which is usually achieved by classical techniques (fractional crystallization and chromatography), the ethers **G** and *epi*-**G** are individually converted into enantiopure **A** and *ent*-**A**, respectively by reduction without racemization at silicon (*vide infra*).

This comparison of the currently available methods unveils a third concept, which has not been realized so far (Scheme 2, right): the "transcription" of *enantiotopic groups* in a single molecule **C** (Scheme 1) into two *enantiomeric molecules* **A** and *ent*-**A** (Scheme 2). This opens the possibility of an unprecedented kinetic resolution[19] of *rac*-**A** with **D** by means of a direct dehydrogenative silicon-oxygen coupling furnishing enantioenriched **A** and diastereoenriched *epi*-**G** (Scheme 2, right). As in the classical resolution, reductive cleavage of the silicon-oxygen linkage in *epi*-**G** should then eject the optical antipode *ent*-**A** along with the resolving reagent **D**. This novel two-step procedure[20] complements our recent kinetic resolution of racemic alcohols with enantiomerically enriched silanes **A**.[7]

As indicated above, the reductive cleavage of the silyl ethers **G** with aluminum hydrides such as



Scheme 2. Classical *versus* kinetic resolution.



Scheme 3. Stereospecific reduction of silyl ethers **G**.

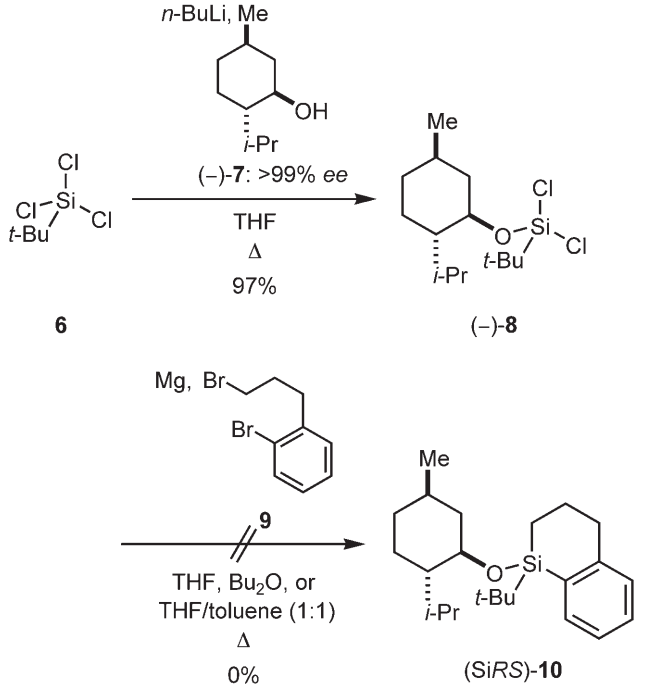
DIBAL-H liberates the corresponding silanes **A** with complete preservation of stereochemical information at silicon (Scheme 3). The observed retention of the configuration is rationalized by an S_Ni-Si mechanism[2] and was recently secured for silane (Si*S*)-**3** (R = *i*-Pr) by X-ray analysis.[10b]

In this paper, we report on our efforts towards the asymmetric synthesis of priviledged silane **5**. Two independent protocols were developed to access enantiopure **5** in multi-gram quantities: (1) a classical resolution pathway *via* stoichiometric formation of diastereomers and (2) a novel non-enzymatic kinetic resolution based on a diastereoselective copper-catalyzed dehydrogenative silicon-oxygen coupling.[21]

Results and Discussion

Synthesis of Racemic Silane *rac*-5

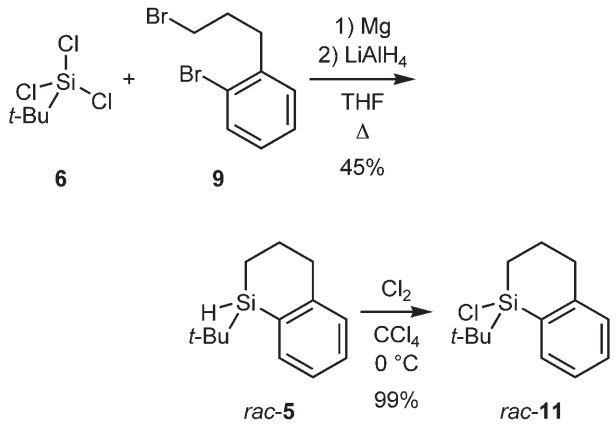
In analogy to our previously reported modular and convergent assembly of 1-aryl-1,2,3,4-tetrahydro-1-silanaphthalenes **3** (Figure 1),[10] we attempted the preparation of *rac*-**5** (Scheme 4).[22] The preparation of dichlorosilane (−)-**8** from *tert*-butyltrichlorosilane (**6**)[23] and the lithium alkoxide derived from (−)-menthol [(−)-**7**] proceeded cleanly in nearly quantitative yield. It is important to note that single and



Scheme 4. Attempted cyclization following our convergent approach.

double nucleophilic displacements of chloride are usually observed for substitutions at aryltrichlorosilanes.[10] This already indicates the increased steric bulk of the *tert*-butyl group disfavoring a two-fold nucleophilic attack. It is presumably for this reason that we were not able to join dichlorosilane (−)-**8** and dibromide **9** together to form the six-membered ring (Si*RS*)-**10** [(−)-**8** → (Si*RS*)-**10**, Scheme 4]. The established Barbier-type reaction conditions[10] at elevated temperatures using THF/toluene solvent mixtures as well as high-boiling di-*n*-butyl ether or the addition of catalytic amounts of copper(I) cyanide[24] (not shown) failed to produce the desired product (Si*RS*)-**10**.

These observations prompted us to reinvestigate a variant that had proven fruitless in earlier studies directed towards the synthesis of **3**.[25] Hindered tri-



Scheme 5. Direct one-pot assembly of the racemic silane *rac*-**5** and subsequent chlorination.

chlorosilane **6** was used directly in the above Grignard reaction with dibromide **9** (**6** → *rac*-**5**, Scheme 5). A dilute 1:1 mixture of **6** and **9** in THF was slowly syringed to thermally and mechanically activated magnesium turnings thereby suppressing competing formation of oligomers. In order to circumvent isolation of the intermediate halosilanes – which comprises bromo- and chlorosilanes –, the reaction mixture was immediately exposed to excess $LiAlH_4$. After aqueous work-up and subsequent distillation, *rac*-**5** was obtained in reasonable yield. By this procedure, *tert*-butyl-substituted silane *rac*-**5** is now available in multi-gram quantities (100-mmol scale).

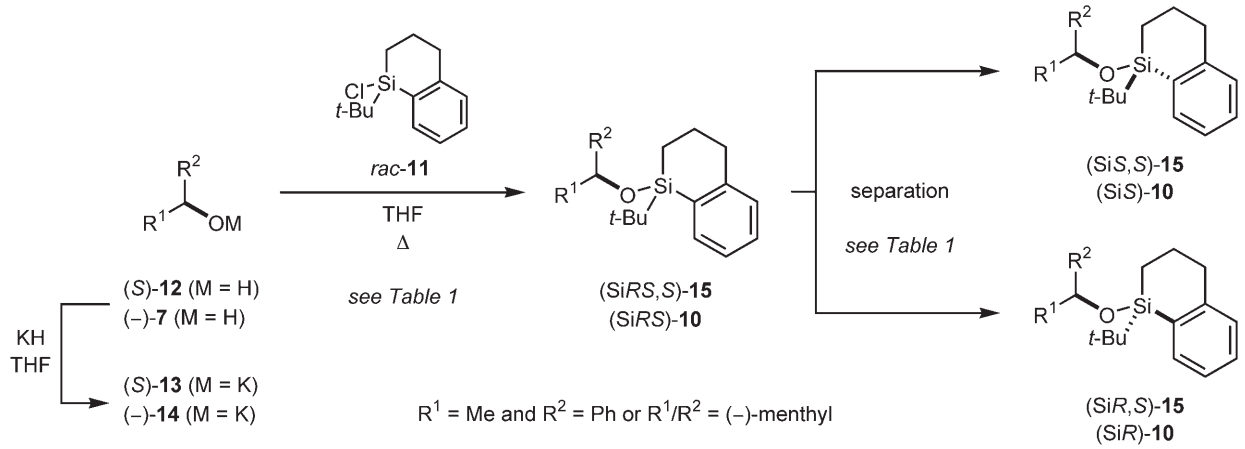
For the following installation of a chiral alcohol, we transformed *rac*-**5** into the intermediate chlorosilane *rac*-**11** by chlorination with a saturated solution of chlorine gas in carbon tetrachloride (*rac*-**5** → *rac*-**11**, Scheme 5).[8,10] Freshly prepared *rac*-**11** was then reacted with potassium alkoxides.

Classical Resolution *via* Silyl Ethers (Si*RS*)-10 and (Si*RS,S*)-15

As depicted in Scheme 4, we were not able to incorporate the preferred chiral auxiliary (−)-**7** by the one-step assembly using dichlorosilane (−)-**8**. Thus, we initially decided to test a sterically less demanding alcohol, namely 1-phenylethanol [(*S*)-**12**] (Scheme 6, Table 1). Reaction of its corresponding potassium alkoxide (*S*)-**13** with *rac*-**11** gave the silyl ether (Si*RS*,*S*)-**15** as a mixture of diastereomers in good yield (Scheme 6, Table 1, Entry 1). Diastereomeric (Si*S*,*S*)-**15** and (Si*R*,*S*)-**15** were partially separable by flash column chromatography on silica gel. Although these ethers **15** were not prone to hydrolysis in pure hydrocarbon eluents, a quantitative separation was still difficult and the diastereomeric ratio of synthetically useful amounts hardly exceeded 93:7.

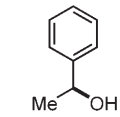
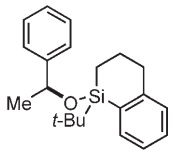
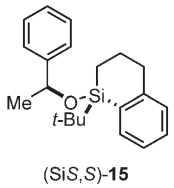
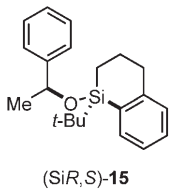
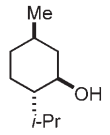
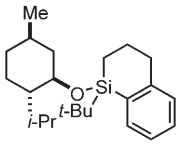
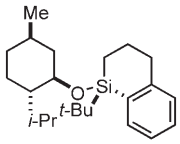
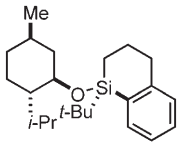
All attempts to crystallize diastereomerically enriched silyl ethers (Si*S*,*S*)-**15** or (Si*R*,*S*)-**15** derived from enantiopure (*S*)-**12** were unsuccessful. Conversely, a sample of *racemic*, diastereomerically enriched silyl ether (Si*S**,*S**)-**15** crystallized nicely. X-ray analysis unambiguously secured the relative configuration (Figure 3). Correlation with HPLC data of racemic and enantiopure samples of known absolute configuration at C–O enabled the assignment of the absolute configurations of all four stereoisomers (see Supporting Information for a detailed illustration).

The crystal structure of (Si*S**,*S**)-**15** shows an expanded half-chair conformation for the silicon-containing six-membered ring, in which the *tert*-butyl substituent occupies a pseudo-axial position. This conformation is also characterized by a *syn*-periplanar orientation of the equatorial protons at the benzylic carbon and the carbon α to silicon resulting in a ^4J coupling, which was detected in the ^{1}H NMR spectrum at room temperature. This so-called W coupling is also seen in



Scheme 6. Synthesis and separation of silyl ethers (see Table 1).

Table 1. Classical resolution *via* silyl ethers **10** and **15**.

Entry	Chiral alcohol	Product	Yield [%][a]	Method[b]	Silyl ether[c]		Yield [%][d]	*dr*[e]
1[f]	 (*S*)-**12**: >99% *ee*	 (Si*RS*,*S*)-**15**: *dr* = 50:50	71	**A**	 (Si*S*,*S*)-**15**	viscous oil	24[g]	93:7
					 (Si*R*,*S*)-**15**	viscous oil	10[g]	11:89
2[f]	 (–)-**7**: >99% *ee*	 (Si*RS*)-**10**: *dr* = 50:50	76	**B**	 (Si*S*)-**10**	viscous oil	43[h]	>99:1
					 (Si*R*)-**10**	crystalline solid	46[h]	1:99

[a] Yield of analytically pure product (*dr* = 50:50).
[b] **A**: separation by flash chromatography on silica gel with cyclohexane as eluent; **B**: separation by fractional crystallization from *n*-pentane and flash chromatography of the mother liquors on silica gel with cyclohexane as eluent.
[c] Configurations were assigned by combined HPLC and X-ray analysis of **15** and by X-ray analysis of **10**.
[d] Yield based on (Si*RS*,*S*)-**15** or (Si*RS*)-**10**.
[e] Determined by HPLC on chiral stationary phase using a Daicel Chiralcel OJ-R column, column temperature 20 °C, solvent MeCN:H_2O = 60:40, flow rate 0.5 mL min^{-1} for (Si*RS*,*S*)-**15** or Daicel Chiralcel OJ-R column, column temperature 35 °C, solvent EtOH:H_2O = 70:30, flow rate 0.4 mL min^{-1} for (Si*RS*)-**10**.
[f] Conditions: see Experimental Section.
[g] Yield after a single chromatography along with a diastereomeric mixture of (Si*RS*,*S*)-**15** reisolated in 66% yield.
[h] (Si*S*)-**10**: yield after flash chromatography of mother liquors; (Si*R*)-**10**: yield after fractional crystallization.

related derivatives including the parent compound **5**. This provides strong evidence for the rigid, conformationally locked nature of **5** and congeners thereof.

We then assessed a variety of commercially available alcohols and amino alcohols from the *chiral pool* in the resolution of *rac*-**11** but none showed the required physical properties. Despite our concerns we returned to sterically encumbered (–)-**7**. Treatment of *rac*-**11** with potassium alkoxide (–)-**14** of (–)-menthol [(–)-**7**] under the standard reaction conditions resulted in clean formation of the silyl ethers (Si*S*)-**10** and (Si*R*)-**10** (Scheme 6, Table 1, Entry 2). Fortunately, (Si*S*)-**10** and (Si*R*)-**10** displayed substantially different R_f values and we succeeded in quantitatively separating these by flash column chromatography on silica gel. Importantly, diastereoenriched fractions (*dr* < 10:90) of the more polar diastereomer (Si*R*)-**10** readily crystallized from *n*-pentane solutions or in substance. This crystalline material could be used for seeding less diastereoenriched solutions (*dr* ≤ 50:50) in *n*-pentane at –18 °C. These crystallizations afforded nearly diastereopure, crystalline (Si*R*)-**10**. Further flash chromatography of the mother liquors yielded the opposite diastereomer (Si*S*)-**10**, a highly viscous oil, in pure form as well. Several grams of each diastereomer were made available by this procedure. The absolute configuration was unambiguously assigned by crystallographic analysis of a suitable single crystal of (Si*R*)-**10** (Figure 4). The molecular structure reflects those features already discussed for (Si*S**,*S**)-**15**.

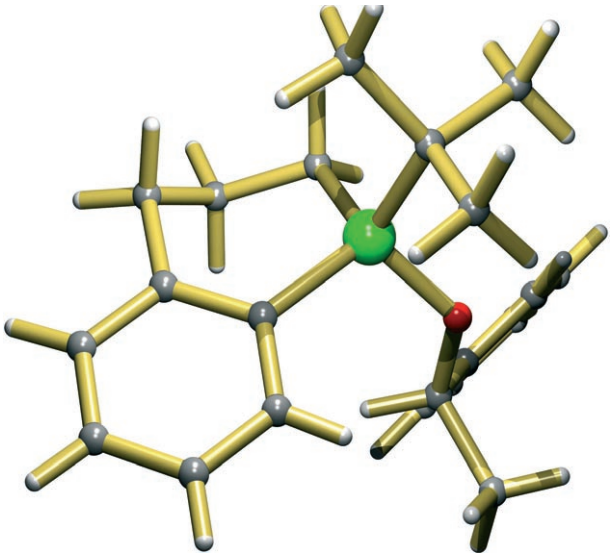


Figure 3. Molecular structure of (Si*S**,*S**)-**15**.

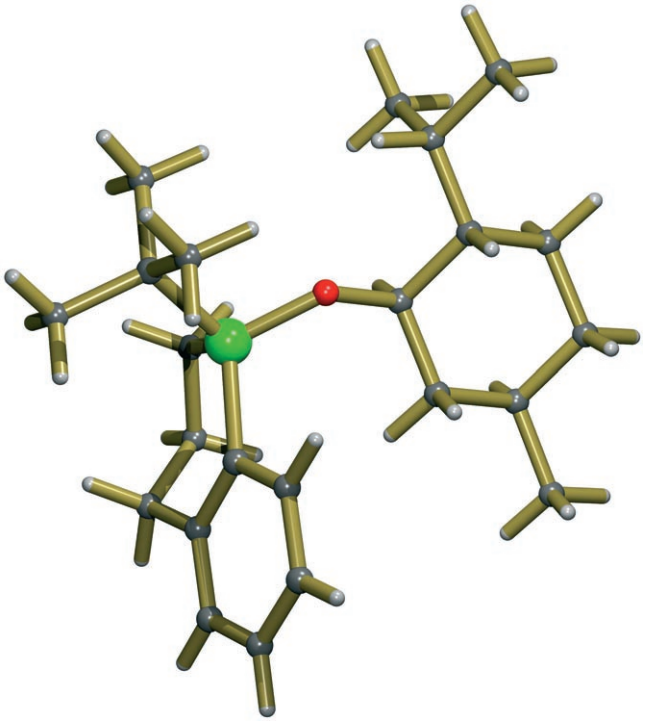


Figure 4. Molecular structure of (Si*R*)-**10**.

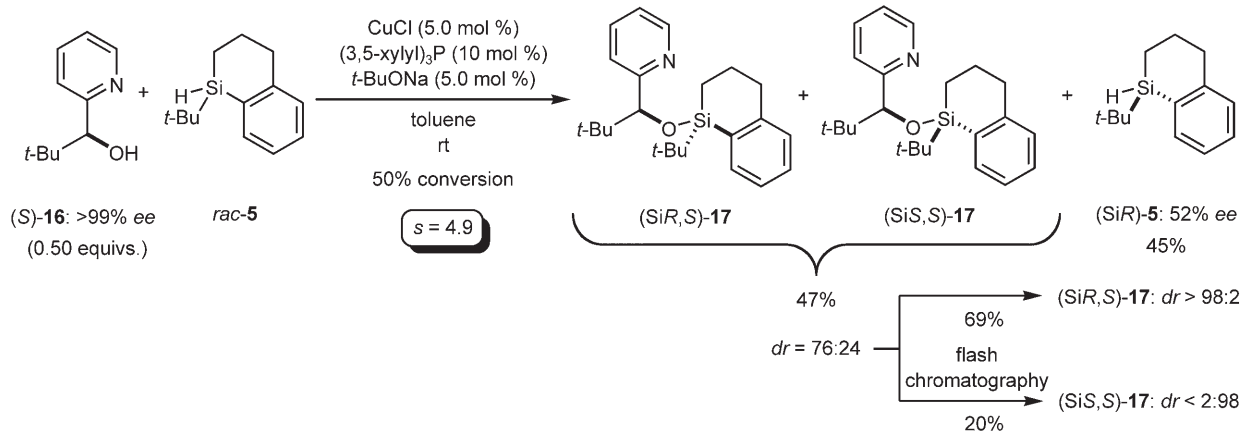
Kinetic Resolution by Copper-Catalyzed Si–O Coupling

The classical resolution employing alcohol (–)-**7** from the *chiral pool* represents a practicable solution for the preparation of enantioenriched silane **5**. Nevertheless, a non-enzymatic kinetic resolution process as outlined in the introductory section is intellectually appealing (Scheme 2). Furthermore, this approach would render the detour *via* the chlorosilane *rac*-**11** superfluous thereby avoiding hazardous chlorine gas and potassium hydride as well as stoichiometric formation of salts. In turn, separation of highly enantio- (remaining silane) and diastereomerically (formed silyl ether) enriched products by chromatography or distillation is extremely simple due to the widely different polarities and boiling points.

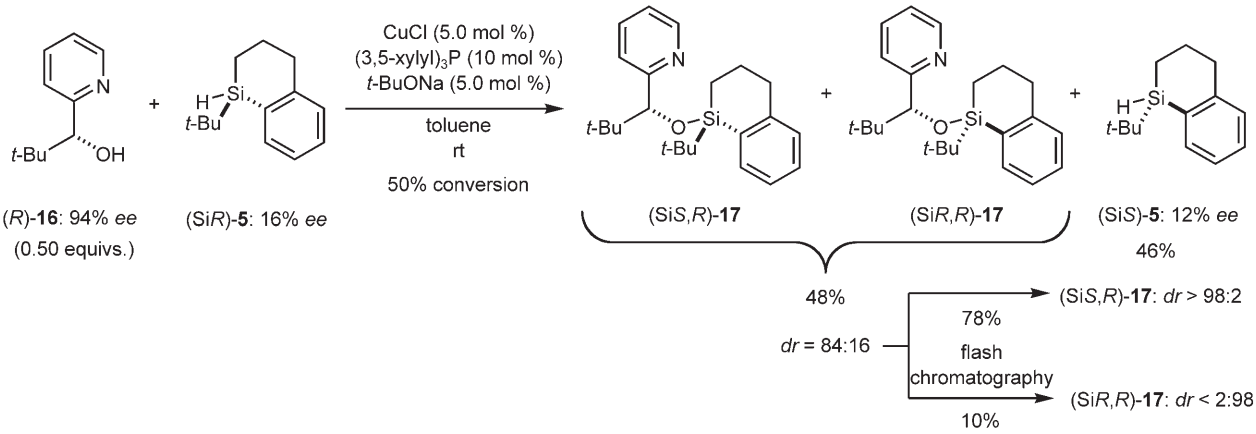
Our recently reported kinetic resolution of chiral non-racemic alcohols using silicon-stereogenic silanes as resolving agents revealed three requirements for the alcohol:[7] (1) the alcohol must incorporate a pending donor, which provides a temporary residence site for the copper catalyst; (2) such an alcohol must be readily available in enantiomerically pure form; and (3) the formed diastereomeric silyl ethers should be separable by chromatography or fractional crystallization to enable further enrichment of stereoisomers.

According to these premises, we were not able to identify a suitable resolving reagent from the *chiral pool* (e.g., cinchonine, prolinol, pseudoephedrine and derivatives thereof). However, within our previous study of the inverted scenario we became aware of *tert*-butyl-substituted pyridylmethanol **16** as a reasonably efficient resolving reagent.[7,26] Alcohol **16** is one of the few synthetically accessible compounds whose structural motif resembles our requirements and which is available in (both) enantiopure form(s), (*S*)-**16** and (*R*)-**16**.[27] The resolution of *rac*-**16** has been achieved by chromatographic separation of the corresponding diastereomeric (–)-(1*S*)-ketopinate esters,[27a] both of which afforded crystalline material suitable for the elucidation of the relative and, hence, absolute configuration of **16** by X-ray analysis.

With optically pure (*S*)-**16** at hand, we subjected silane *rac*-**5** to a dehydrogenative silicon-oxygen coupling in the presence of the in situ generated catalyst system[28,29] consisting of copper(I) chloride (5 mol%), (3,5-xylyl)$_3$P (10 mol%) and freshly prepared *t*-BuONa (5 mol%)[7] using 0.5 equivs. of (*S*)-**16** (>99% *ee*) (Scheme 7). We were pleased to find that this inverse kinetic resolution set-up proceeded cleanly with moderate diastereoselectivity. The formed silyl ether (Si*R*,*S*)-**17**[30] (*dr*=76:24) and the remaining enantioenriched silane (Si*R*)-**5** (52% *ee*) were isolated in excellent yield. The observed enantiomeric excess of (Si*R*)-**5** at 50% conversion corresponds to a selectivity factor $s=4.9$.[31] Importantly for our purposes, (Si*R*,*S*)-**17** and (Si*S*,*S*)-**17** were separable by flash column chromatography on silica gel enabling further enrichment of the initially obtained diastereomeric mixtures in nearly quantitative yield and excellent diastereomeric purity. Substantially better diastereoselectivities (*dr*=92:8) would have been possible using pyridylethanol derivatives,[7] if gram quantities of these would be easily accessible in enantiopure form.



Scheme 7. Kinetic resolution with pyridyl alcohol (*S*)-**16**.



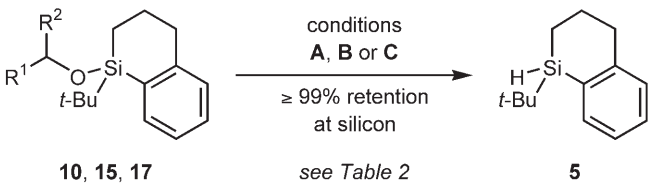
Scheme 8. Kinetic resolution with pyridyl alcohol (*R*)-**16**.

The moderately enantioenriched silane (Si*R*)-**5** together with *rac*-**5** were resubjected to another kinetic resolution that was performed with the optical antipode (*R*)-**16** (94% *ee*) affording a markedly higher diastereoselectivity of 84:16 for (Si*S*,*R*)-**17** (Scheme 8).

Stereospecific Reductive Cleavage

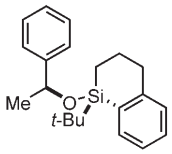
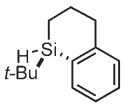
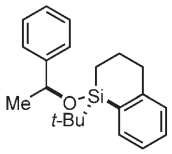
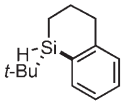
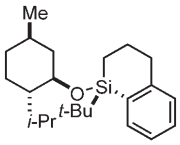
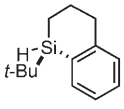
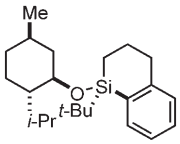
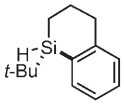
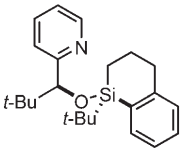
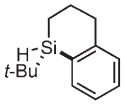
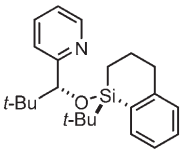
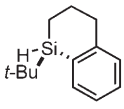
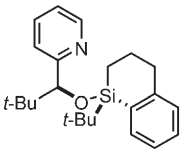
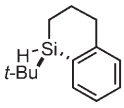
The preceding sections were devoted to the preparation of highly diastereomerically enriched and – depending on the alcohols **7**, **12**, and **16** – enantiomerically pure silyl ethers **10**, **15** and **17**. To complete the preparation of optically enriched silane **5**, these ethers were cleaved under the recently reported conditions.[10] The steric bulk of the *tert*-butyl substituent and, in the case of the pyridyl moiety, the additional nitrogen donor had a profound effect on the rate of the cleavage (Scheme 9, Table 2).

Moderately diastereoenriched silyl ethers (Si*S*,*S*)-**15** (*dr* = 93:7) and (Si*R*,*S*)-**15** (*dr* = 20:80) derived from phenylethanol [(*S*)-**12**] required quite forcing conditions (excess DIBAL-H in *n*-Bu$_2$O/*n*-hexane at 100 °C); nevertheless, (*R*)-**5** or (*S*)-**5**, respectively, were isolated in reasonable yields (Entries 1 and 2, Table 2). As expected, the stereochemical information at silicon was completely preserved. The enantiomeric excesses of (Si*R*)-**5** (93% *ee*) and (Si*S*)-**5** (60% *ee*) correlated perfectly with the diastereomeric ratio of the used silyl ethers **15**. Applying similar conditions to the (−)-menthyl ethers (Si*S*)-**10** and (Si*R*)-**10**, we obtained good yields similar to those of the reduction of **15** (Entries 3 and 4, Table 2). The excellent diastereomeric ratios of (Si*S*)-**10** or (Si*R*)-**10**, respectively,



Scheme 9. Stereospecific reductive cleavage (see Table 2).

Table 2. Reduction of silyl ethers **10**, **15** and **17**.

Entry	Silyl ether	*dr*[a]	Conditions[b]	Silane[c]	Yield [%][d]	*ee* [%][e]
1	 (Si*S*,*S*)-**15**	93:7	**A**	 (Si*R*)-**5**	84	85[f] (Si*R*)
2	 (Si*R*,*S*)-**15**	20:80	**A**	 (Si*S*)-**5**	77	60[f] (Si*S*)
3	 (Si*S*)-**10**	>99:1	**B**	 (Si*R*)-**5**	79	99[f] (Si*R*)
4	 (Si*R*)-**10**	1:99	**B**	 (Si*S*)-**5**	85	98[f] (Si*S*)
5	 (Si*R*,*S*)-**17**	>98:2	**C**	 (Si*S*)-**5**	96 [g]	96[f] (Si*S*)
6	 (Si*S*,*R*)-**17**	>98:2	**C**	 (Si*R*)-**5**	92 [g]	91[f] (Si*R*)
7	 (Si*S*,*S*)-**17**	3:97	**C**	 (Si*R*)-**5**	89	93[f] (Si*R*)

[a] Determined by HPLC on chiral stationary phase for **10** and **15** and by ^{1}H NMR by integration of baseline-separated signals at 4.38 ppm for (Si*S*,*S*)-**17** at 4.49 ppm for (Si*R*,*S*)-**17**.
[b] Conditions **A**: DIBAL-H (1.0 M in *n*-hexane, 5.0 equivs.), Bu_2O, 100 °C, 30 h; **B**: DIBAL-H (1.0 M in *n*-hexane, 4.0 equivs.), Bu_2O, 100 °C, 20 h; **C**: DIBAL-H (1.0 M in *n*-hexane, 2.0 equivs.), CH_2Cl_2, room temperature, 16 h.
[c] Absolute configuration assigned by correlation with the known configuration of the corresponding silyl ether.
[d] Yield of analytically pure product after flash chromatography on silica gel.
[e] Determined by HPLC on a chiral stationary phase using a Daicel Chiralcel OJ-R column, column temperature 20 °C, solvent EtOH:H_2O = 80:20, flow rate 0.3 mL min^{-1}.
[f] >99 % *ee* for (*S*)-**12**, (−)-**7**, and (*S*)-**16** and 94 % *ee* for (*R*)-**16** as resolving reagent.
[g] (*S*)-**16** reisolated in 88 % yield (99 % *ee*); (*R*)-**16** reisolated in 78 % yield (93 % *ee*).

translated stereospecifically into the enantiomeric excesses of (Si*R*)-**5** and (Si*S*)-**5** (98–99% *ee*) without any erosion of stereochemical information. This completes a practical synthesis of both enantiomeric forms of **5** in 52–60% overall yield for each enantiomer based on *rac*-**5**.

The products of the kinetic resolution process **17** were also subjected to the reduction (Entries 5–7, Table 2). Not unexpectedly, the reductive cleavage already occurred under mild conditions at ambient temperature in CH_2Cl_2. This might be attributed to the aluminum-coordinating ability of the pyridyl moiety in **17**. The reduction of (Si*R*,*S*)-**17** and (Si*S*,*R*)-**17** as well as the minor diastereomer (Si*S*,*S*)-**17** proceeded in excellent yields following a stereoretentive process. The somewhat lower enantiomeric purities of (Si*S*)-**5** (96% *ee*) and (Si*R*)-**5** (91% *ee* and 93% *ee*) are explained by slightly lower diastereomeric ratios (Entries 5–7, Table 2) and optical purity of starting alcohols (*R*)-**16** or (*S*)-**16** (Entries 6 and 7, Table 2). In some of these cases, we also recovered the resolving reagent (*S*)-**16** or (*R*)-**16**. The optical purity (99% or 93% *ee*) was virtually identical with the values for the initially used alcohol.

Conclusions

In summary, we have developed a practical protocol for the synthesis of the important silicon-stereogenic silane **5** in excellent enantiomeric purities by a classical resolution. Using (−)-menthol [(−)-**7**] as resolving reagent enables a scalable synthesis of both enantiomers (Si*R*)-**5** and (Si*S*)-**5** in excellent optical purities $\geq$ 98% *ee* and in high yields since fractional crystallization is used as separation technique. Relative and absolute configurations were secured by crystallographic analysis.

In addition, we were able to realize the first example of a kinetic resolution of an asymmetrically substituted silane with a moderate selectivity value $s = 4.9$. This resolution is based on a copper-catalyzed dehydrogenative silicon-oxygen coupling with recyclable chiral pyridyl alcohols (*S*)-**16** or (*R*)-**16**. Future efforts will be devoted to the refinement of this kinetic resolution process mainly by variation of the resolving reagent.

These approaches to the reliable preparation of enantiopure **5** should provide a solid footing for its future applications in asymmetric catalysis involving silicon-based stereogenicity and thus stimulate further research in this area.

Experimental Section

General Remarks

Reagents obtained from commercial suppliers were used without further purification unless otherwise noted. *tert*-Butyltrichlorosilane (**6**),[23] 1-bromo-2-(3-bromopropyl)benzene (**9**),[10a] as well as (*S*)- and (*R*)-2,2-dimethyl-1-(2-pyridyl)propan-1-ol [(*S*)-**16** and (*R*)-**16**][27a] were prepared according to known procedures. All reactions were performed in flame-dried glassware under a static pressure of argon. Liquids and solutions were transferred with syringes or double-ended needles. Solvents were dried prior to use following standard procedures (THF, CH_2Cl_2, toluene) or used as purchased (Bu_2O, CCl_4). Technical grade solvents for extraction or chromatography (cyclohexane, *tert*-butyl methyl ether) were distilled before use. Analytical thin layer chromatography was performed on silica gel SIL G-25 glass plates by Macherey–Nagel (Germany) and flash chromatography on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by Merck (Germany) using the indicated solvents. High vacuum distillations (10^{-6} mbar) were performed using standard glassware and an Edwards turbo molecular pump. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AM 400 and DRX 500 instruments. Analytical HPLC analysis on a chiral stationary phase using a Daicel Chiralcel OD-H column (*n*-heptane:2-propanol mixtures as solvent) or Daicel Chiralcel OJ-R (EtOH:H_2O or MeCN:H_2O mixtures) provided baseline separation of enantiomers and/or diastereomers, respectively.

Characterization data for all reported compounds are available in the Supporting Information.

(−)-*tert*-Butyldichloro-[(1*R*,2*S*,5*R*)-menthyloxy]silane [(−)-8]

n-BuLi (7.20 mL, 18.0 mmol, 1.22 equivs., 2.5 M solution in *n*-hexane) was added dropwise to a solution of (−)-menthol [(−)-**7**] (2.81 g, 18.0 mmol, 1.22 equivs.) in THF (25 mL). After complete addition, the mixture was maintained for further 20 min at room temperature. To this solution trichlorosilane **6** (2.94 g, 14.7 mmol, 1.00 equiv.) in THF (10 mL) was added and the mixture was subsequently heated at reflux for 5 h. Then, the volume was reduced by 50% until a major portion of salts had precipitated. The solids were removed by suction filtration using Schlenk techniques. After complete removal of remaining solvent, the residue was distilled under vacuum (bp 82–85 °C at 0.5 mbar) providing analytically pure dichlorosilane (−)-**8**; yield: 4.44 g (97%).

rac-1-*tert*-Butyl-1,2,3,4-tetrahydro-1-silanaphthalene (*rac*-5)

A 1 L, three-necked flask equipped with a reflux condenser, a 500 mL pressure-equalizing dropping funnel, an argon inlet and a magnetic stirring bar was charged with magnesium turnings (24.3 g, 1.00 mol, 10.0 equivs.). The flask was

subsequently flame dried under vacuum (3 times) with vigorous stirring, backfilled with argon and stirring was continued for 12 h. Then, the magnesium turnings were suspended in THF (150 mL) and a solution of 1,2-dibromoethane (8.80 mL, 18.8 g, 100 mmol, 1.00 equiv.) in THF (50 mL) was added dropwise. After complete addition, the mixture was heated to reflux and a solution of dibromide **9**[10a] (27.8 g, 100 mmol, 1.00 equiv.) and trichlorosilane **6**[23] (19.2 g, 100 mmol, 1.00 equiv.) in THF (400 mL) was added slowly over a period of 4 h. The reaction mixture was maintained for further 24 h at reflux. The resulting solution was transferred to another 1 L, three-necked flask equipped with a reflux condenser, an argon inlet and a magnetic stirring bar, containing a suspension of $LiAlH_4$ (6.83 g, 180 mmol, 1.80 equivs.) in THF (100 mL). Heating at reflux for 20 h was followed by careful quenching of the resulting mixture with acetone (50 mL), water (400 mL) and, finally, concentrated HCl (100 mL) under ice cooling until pH 4–5 was reached. The organic layer was separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4×150 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered and volatiles were evaporated under reduced pressure. The crude product was distilled under vacuum (bp 72–74 °C at 0.5 mbar) affording the silane *rac*-**5** as a colorless liquid; yield: 9.20 g (45 %).

rac-1-*tert*-Butyl-1-chloro-1,2,3,4-tetrahydro-1-silanaphthalene (*rac*-11)

A saturated solution of Cl_2 in CCl_4 (20 mL) was added to a solution of *rac*-**5** (4.09 g, 20.0 mmol, 1.00 equiv.) in CCl_4 (20 mL) at 0 °C until a permanent pale yellow color appeared. After 4 min the reaction mixture was purged with argon. Evaporation of the solvent under reduced pressure provided crude *rac*-**11** as a colorless oil which was used without further purification; yield: 4.73 g (99 %).

(Si*RS*,*S*)-1-*tert*-Butyl-1-[(1*S*)-1-phenylethoxy]-1,2,3,4-tetrahydro-1-silanaphthalene [(Si*RS*,*S*)-15]

The alcohol (*S*)-**12** (1.75 g, 14.3 mmol, 1.50 equivs., > 99 % *ee*) was added dropwise to a suspension of oil-free potassium hydride (670 mg, 16.7 mmol, 1.75 equivs.) in THF (16 mL) at 0 °C. To ensure complete deprotonation, the mixture was stirred for further 30 min at room temperature. This mixture was then treated with a solution of chlorosilane *rac*-**11** [freshly prepared from *rac*-**5** (1.95 g, 9.54 mmol, 1.00 equiv.)] in THF (16 mL). Heating at reflux for 3 h was followed by cooling to ambient temperature. Water (20 mL) and then 2 M HCl were added until pH 7 was reached. The organic layer was separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3×75 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered and the volatiles were evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with cyclohexane as eluent achieving partial separation of the diastereomeric silyl ethers (Si*S*,*S*)-**15** [yield: 518 mg (17 %; 24 % based on isolated **15**), *dr* = 93:7] and (Si*R*,*S*)-**15** [yield: 206 mg (7 %; 10 % based on isolated **15**), *dr* = 11:89] along with (Si*R*,*S*)-**15** [yield: 625 mg (20 %; 28 % based on isolated **15**), *dr* = 20:80] and (Si*RS*,*S*)-**15** [yield: 860 mg (28 %; 39 % based on isolated **15**), *dr* = 50:50] (72 % yield overall). Both diastereomers were obtained as viscous oils.

(Si*RS*)-1-*tert*-Butyl-1-[(1*R*,2*S*,5*R*)-1-menthyloxy]-1,2,3,4-tetrahydro-1-silanaphthalene [(Si*RS*)-10]

A solution of (−)-menthol [(−)-**7**] (4.69 g, 30.0 mmol, 1.50 equivs., > 99 % *ee*) in THF (40 mL) was added to a suspension of oil-free potassium hydride (1.40 g, 35.0 mmol, 1.75 equivs.) in THF (10 mL) at room temperature. To ensure complete deprotonation, the mixture was heated at reflux for 1 h. Subsequently, the mixture was treated portionwise with a solution of chlorosilane *rac*-**11** [freshly prepared from *rac*-**5** (4.09 g, 20.0 mmol, 1.00 equiv.)] in THF (50 mL) at ambient temperature. Heating at reflux for 4 h was followed by cooling to ambient temperature, quenching with water (100 mL) and then 2 M HCl until pH 7 was reached. The organic layer was separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4×100 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), filtered and the volatiles were evaporated under reduced pressure. The crude product optionally was distilled under high vacuum (bp 142–146 °C at 10^{-6} mbar) to remove excess (−)-menthol [(−)-**7**] furnishing (Si*RS*)-**10** as a colorless, viscous oil; yield: 5.42 g (76 %, *dr* = 50:50).

Crystalline (Si*R*)-**10** (*dr* = 1:99) suitable for seeding was obtained by a single flash column chromatography on silica gel with cyclohexane as eluent. Highly diastereomerically enriched fractions of (Si*R*)-**10** solidified spontaneously. For crystallization the 1:1-mixture of diastereomers was dissolved in the two-fold volume of *n*-pentane, seeded with crystals of (Si*R*)-**10** and cooled to −18 °C for 24 h. The mother liquor was removed by a pipette and remaining crystalline (Si*R*)-**10** was washed with cold *n*-pentane. Diastereomerically pure (Si*S*)-**10** was obtained from the mother liquors by flash chromatography on silica gel with cyclohexane as eluent. Repeating this process with the remaining mixture of diastereomers, (Si*R*)-**10** [yield: 2.50 g, 46 % based on (Si*RS*)-**10**, *dr* = 1:99] was obtained as a white, crystalline solid (mp 72 °C); in addition (Si*S*)-**10** [yield: 2.24 g, 43 % based on (Si*RS*)-**10**, *dr* > 99:1] was isolated as a colorless, viscous oil.

Kinetic Resolution of *rac*-5 by Dehydrogenative Coupling: (Si*R*,*S*)-2-[1-(1-*tert*-Butyl-1,2,3,4-tetrahydro-1-silanaphthalinyloxy)-2,2-dimethylpropyl]pyridine [(Si*R*,*S*)-17 and (Si*R*)-5]

To a 100 mL Schlenk flask charged with CuCl (26.4 mg, 0.267 mmol, 0.0500 equivs.), $(3,5\text{-xylyl})_3P$ (185 mg, 0.534 mmol, 0.100 equiv.) and degassed toluene (20 mL) was added solid *t*-BuONa (25.6 mg, 0.267 mmol, 0.0500 equivs.). The resulting pale yellow solution was stirred for 2 min. Subsequently, a solution of alcohol (*S*)-**16**[27a] (441 mg,

2.67 mmol, 0.500 equivs., >99% *ee*) in toluene (15 mL) and silane *rac*-**5** (1.09 g, 5.34 mmol, 1.00 equiv.) in toluene (5 mL) were added in one portion. The color immediately changed to bright yellow and then darkened to orange within 2 h. Stirring was continued for 24 h until ^{1}H NMR analysis of an aliquot indicated complete conversion of (*S*)-**16** to (Si*R*,*S*)-**17** (*dr* = 76:24). The mixture was transferred to a round-bottom flask and silica gel was added. The solvent was evaporated under reduced pressure. Purification by flash column chromatography on silica gel with cyclohexane/*tert*-butyl methyl ether (100:0 → 97:3) as eluent gave enantioenriched (Si*R*)-**5** [yield: 491 mg (45%), 52% *ee*] and (Si*R*,*S*)-**17** [yield: 923 mg (47%), *dr* = 76:24]. Major amounts were obtained as highly enriched diastereomers (Si*S*,*S*)-**17** [yield: 185 mg (20% based on **17**), *dr* < 2:98] and (Si*R*,*S*)-**17** [yield: 636 mg (69% based on **17**), *dr* > 98:2].

Starting with (*R*)-**16** (94% *ee*) and (Si*R*)-**5** (16% *ee*) the optical antipodes (Si*R*,*R*)-**17** (*dr* < 2:98) and (Si*S*,*R*)-**17** (*dr* > 98:2) as well as (Si*S*)-**5** (12% *ee*) were prepared by the same procedure (*dr* = 84:16 before separation).

Preparation of (Si*R*)-5 from Silyl Ether (Si*S*,*S*)-15

A 25 mL Schlenk flask equipped with a magnetic stirring bar and a reflux condenser was charged with (Si*S*,*S*)-**15** (210 mg, 1.00 equiv., *dr* = 93:7, >99% *ee*) and di-*n*-butyl ether (5 mL). DIBAL-H (3.20 mL, 3.20 mmol, 5.00 equivs., 1.0 M in *n*-hexane) was added, the reaction mixture was subsequently heated to 100 °C, and maintained at this temperature for 30 h. The reaction was quenched at ambient temperature by careful addition of water (20 mL) followed by 2 M HCl (10 mL) until pH 7 was reached. The organic layer was separated and the aqueous phase extracted with *tert*-butyl methyl ether (4 × 20 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered and volatiles were evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with cyclohexane as eluent furnishing the analytically pure, enantiomerically enriched silane (Si*R*)-**5** as a colorless liquid; yield: 110 mg (84%), 85% *ee*.

Starting with (Si*R*,*S*)-**15** (*dr* = 20:80, >99% *ee*) the optical antipode (Si*S*)-**5** (60% *ee*) was prepared by the same procedure.

Preparation of (Si*R*)-5 from Silyl Ether (Si*S*)-10

A 25 mL Schlenk flask equipped with a magnetic stirring bar and a reflux condenser was charged with (Si*S*)-**10** (589 mg, 1.64 mmol, 1.00 equiv., *dr* < 1:99) and di-*n*-butyl ether (15 mL). DIBAL-H (6.60 mL, 6.60 mmol, 4.00 equivs., 1.0 M in *n*-hexane) was added, the reaction mixture was subsequently heated to 100 °C and maintained at this temperature for 20 h. The reaction was quenched at ambient temperature by careful addition of water (40 mL) followed by 2 M HCl (25 mL) until pH 7 was reached. The organic layer was separated and the aqueous phase extracted with *tert*-butyl methyl ether (4 × 40 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered and volatiles were evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with cyclohexane as eluent, furnishing the analytically pure, highly enantiomerically enriched silane (Si*R*)-**5** as a colorless liquid; yield: 264 mg (79%), 99% *ee*.

Starting with (Si*R*)-**10** (*dr* = 99:1) the optical antipode (Si*S*)-**5** (98% *ee*) was prepared by the same procedure.

Preparation of (Si*S*)-5 from Silyl Ether (Si*R*,*S*)-17

A 10 mL Schlenk tube equipped with a magnetic stirring bar was charged with (Si*R*,*S*)-**17** (128 mg, 0.348 mmol, 1.00 equiv., *dr* > 98:2) and CH_2Cl_2 (1.5 mL). DIBAL-H (0.696 mL, 0.696 mmol, 2.00 equivs., 1.0 M in *n*-hexane) was added, the reaction mixture was subsequently stirred at ambient temperature for 16 h. The reaction was carefully quenched with water (10 mL) followed by 2 M HCl (5 mL) until pH 7 was reached. The organic layer was separated and the aqueous phase extracted with *tert*-butyl methyl ether (5 × 15 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and volatiles were evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with cyclohexane/*tert*-butyl methyl ether (100:0 → 70:30) furnishing analytically pure, enantioenriched (Si*S*)-**5** as a colorless liquid [yield: 69 mg (96%), 96% *ee*] and (*S*)-**16** as a yellowish oil [yield: 51 mg (88%), 99% *ee*].

Starting with (Si*S*,*R*)-**17** (*dr* > 98:2) the optical antipode (Si*R*)-**5** (91% *ee*) along with (*R*)-**16** (93% *ee*) was prepared by the same procedure. Alternatively, the minor diastereomer (Si*S*,*S*)-**17** was used as well.

X-Ray Crystallographic Study

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-299831 [(Si*R*)-**10**], CCDC-299828 [(Si*S**,*S**)-**15**], CCDC-299829 [(−)-(1*S*)-ketopinate ester of (*S*)-**16**], and CCDC-299830 [(−)-(1*S*)-ketopinate ester of (*R*)-**16**]. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336–033; E-mail: deposit@ccdc.cam.ac.uk]

Acknowledgements

*The research was supported by the Deutsche Forschungsgemeinschaft (Emmy Noether program, Oe 249/2–3 and Oe 249/2–4), the Fonds der Chemischen Industrie (pre-doctoral fellowship to S. R.), and the Aventis Foundation (Karl Winnacker fellowship to M. O.). The authors thank Gerd Fehrenbach for performing the HPLC analyses and Ilona Hauser for the large-scale preparation of racemic silane rac-**5**. Generous donations of chemicals from BASF AG, Ludwigshafen/Germany, Lanxess AG, Leverkusen/Germany, as well as Symrise, Holzminden/Germany are gratefully acknowledged.*

References

[1] C. A. Maryanoff, B. E. Maryanoff, in: *Asymmetric Synthesis*, Vol. 4, (Eds.: J. D. Morrison, J. W. Scott), Academic Press, Orlando, **1984**, pp. 355–374.

[2] a) L. H. Sommer, *Stereochemistry, Mechanism and Silicon*, McGraw-Hill, New York, **1965**; b) L. H. Sommer, *Intra-Sci. Chem. Rep.* **1973**, *7*, 1–44; c) R. J. P. Corriu, C. Guérin, J. J. E. Moreau, in: *Topics in Stereochemistry*, Vol. 15, (Ed.: E. L. Eliel), Wiley, New York, **1984**, pp. 43–198.

[3] S. Bienz, *Chimia* **1997**, *51*, 133–139.

[4] For a survey, see: M. Oestreich, *Chem. Eur. J.* **2006**, *12*, 30–37 and references cited therein.

[5] M. Oestreich, S. Rendler, *Angew. Chem.* **2005**, *117*, 1688–1691; *Angew. Chem. Int. Ed.* **2005**, *44*, 1661–1664.

[6] D. R. Schmidt, S. J. O'Malley, J. L. Leighton, *J. Am. Chem. Soc.* **2003**, *125*, 1190–1191.

[7] S. Rendler, G. Auer, M. Oestreich, *Angew. Chem.* **2005**, *117*, 7793–7797; *Angew. Chem. Int. Ed.* **2005**, *44*, 7620–7624.

[8] a) L. H. Sommer, C. L. Frye, *J. Am. Chem. Soc.* **1959**, *81*, 1013; b) L. H. Sommer, C. L. Frye, G. A. Parker, K. W. Michael, *J. Am. Chem. Soc.* **1964**, *86*, 3271–3276.

[9] a) R. J. P. Corriu, J. P. Massé, *J. Chem. Soc., Chem. Commun.* **1967**, 1287–1288; b) R. Corriu, B. Henner, J. Massé, *Bull. Soc. Chim. Fr.* **1968**, 3013–3023.

[10] a) M. Oestreich, U. K. Schmid, G. Auer, M. Keller, *Synthesis* **2003**, 2725–2739; b) M. Oestreich, G. Auer, M. Keller, *Eur. J. Org. Chem.* **2005**, 184–195.

[11] For known, difficult-to-obtain silanes with silicon-centered chirality, see: a) D. N. Roark, L. H. Sommer, *J. Am. Chem. Soc.* **1974**, *95*, 969–971; b) J. M. Lefour, A. Loupy, *Tetrahedron* **1978**, *34*, 2597–2605.

[12] a) P. Jankowski, E. Schaumann, J. Wicha, A. Zarecki, G. Adiwidjaja, *Tetrahedron: Asymmetry* **1999**, *10*, 519–526; b) P. Jankowski, E. Schaumann, J. Wicha, A. Zarecki, G. Adiwidjaja, M. Asztemborska, *Chem. Commun.* **2000**, 1029–1030. It must be noted that we had not assessed the usefulness of (Si*R*)-**4** (Figure 1) as a chiral reagent in our previous projects.[5,7]

[13] Besides the methods discussed herein, an access based on a reductive enzymatic kinetic resolution of acyl silanes is available: a) R. Tacke, S. Brakmann, F. Wuttke, J. Fooladi, C. Syldatk, D. Schomburg, *J. Organomet. Chem.* **1991**, *403*, 29–41; b) M. Trzoss, J. Shao, S. Bienz, *Tetrahedron: Asymmetry* **2004**, *15*, 1501–1505.

[14] H. Ottosson, P. G. Steel, *Chem. Eur. J.* **2006**, *12*, 1576–1585.

[15] R. J. P. Corriu, J. J. E. Moreau, *J. Organomet. Chem.* **1976**, *120*, 337–346.

[16] For a tabulated summary, see: J. Y. Corey, in: *Advances in Silicon Chemistry*, Vol. 1, (Ed.: G. Larson), JAI Press, Greenwich, **1991**, pp. 327–387.

[17] For some recent examples, see: a) C. N. Scott, C. S. Wilcox, *Synthesis* **2004**, 2273–2276; b) R. L. Miller, S. V. Maifeld, D. Lee, *Org. Lett.* **2004**, *6*, 2773–2776; c) H. Ito, A. Watanabe, M. Sawamura, *Org. Lett.* **2005**, *7*, 1869–1871; d) H. Ito, K. Takagi, T. Miyahara, M. Swamura, *Org. Lett.* **2005**, *7*, 3001–3004.

[18] a) R. J .P. Corriu, J. J. E. Moreau, *J. Organomet. Chem.* **1974**, *64*, C51–54; b) T. Hayashi, K. Yamamoto, M. Kumada, *Tetrahedron Lett.* **1974**, 331–334; c) T. Ohta, M. Ito, A. Tsuneto, H. Takaya, *J. Chem. Soc., Chem. Commun.* **1994**, 2525–2526.

[19] H. B. Kagan, J. C. Fiaud, in: *Topics in Stereochemistry*, Vol. 18, (Eds.: E. L. Eliel, S. H. Wilen), Wiley, New York, **1988**, pp. 249–330.

[20] To the best of our knowledge, a single kinetic resolution process of racemic silyl ethers based on the reductive cleavage of the silicon-oxygen bond by chiral hydride reagents has been reported so far. However, enantiomeric excesses were determined from the optical rotatory power, which emerges as being sensitive towards impurities of the chiral ligand. In our hands, application of this method to a derivative of *rac*-**5** provided only marginal optical enrichment ($<1\%$ *ee*): a) A. Holt, A. W. P. Jarvis, G. J. Jarvis, *Tetrahedron Lett.* **1968**, 4087–4088; b) A. Holt, A. W. P. Jarvis, G. J. Jarvis, *J. Chem. Soc., Perkin Trans. 2* **1973**, 114–122.

[21] A catalytic asymmetric access as depicted in Scheme 2 was not considered since the synthesis of the requisite precursor, 1,2,3,4-tetrahydro-1-silanaphthalene, has not been accomplished yet.

[22] Early reports of related cyclizations: a) H. Gilman, O. L. Marrs, *J. Org. Chem.* **1964**, *29*, 3175–3179; b) H. Gilman, O. L. Marrs, *J. Org. Chem.* **1965**, *30*, 325–328.

[23] L. J. Tyler, L. H. Sommer, F. C. Whitmore, *J. Am. Chem. Soc.* **1948**, *70*, 2876–2878.

[24] Acceleration by copper(I) cyanide for otherwise sluggish Grignard reactions has been reported: P. J. Lennon, D. P. Mack, Q. E. Thompson, *Organometallics* **1989**, *8*, 1121–1222.

[25] U. K. Schmid, *Diploma Thesis*, Albert-Ludwigs-Universität, Freiburg, **2003**.

[26] S. Rendler, M. Oestreich, unpublished results, **2005**.

[27] a) M. Ishizaki, K. Fujita, M. Shimamoto, O. Hoshino, *Tetrahedron: Asymmetry* **1994**, *5*, 411–424; b) reduction with rather expensive (−)-Ipc_2BCl provided only poor yields and 94% *ee*: C. Bolm, M. Ewald, M. Felder, G. Schlinghoff, *Chem. Ber.* **1992**, *125*, 1169–1190.

[28] In analogy to a previously reported procedure: D. H. Appella, Y. Moritani, R. Shintani, E. M. Ferreira, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 9473–9474.

[29] Air-sensitive $[CuH(PPh_3)]_6$[29b] has been previously used: a) C. Lorenz, U. Schubert, *Chem. Ber.* **1995**, *128*, 1267–1269; b) D. M. Bestrensky, D. E. Huseland, C. McGettigan, J. M. Stryker, *Tetrahedron Lett.* **1988**, *29*, 3749–3752.

[30] Relative and absolute configurations were assigned based on a stereoretentive reductive cleavage of **15b** and the known configuration of the alcohol **16**.[27]

[31] The *s* value was calculated by the following equation: $\ln[1-\text{conv.}/100][1-ee_{(\text{Si}R)-\mathbf{5}}/100]/\ln[1-\text{conv.}/100][1+ee_{(\text{Si}R)-\mathbf{5}}/100]$.[19] To our regret, the equation in ref.[7] is reproduced incorrectly.

