DOI: 10.1002/chem.201202693

Illuminating the Mechanism of the Borane-Catalyzed Hydrosilylation of Imines with Both an Axially Chiral Borane and Silane

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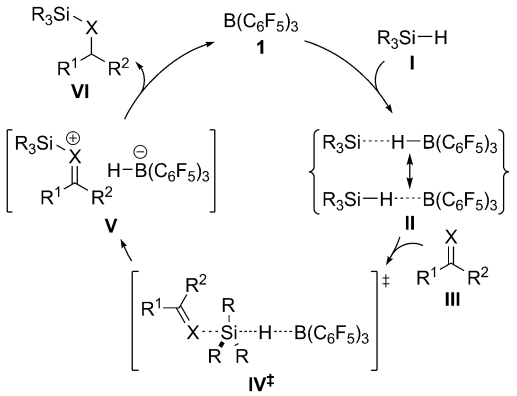
Abstract: The reduction of C=O groups with silanes catalyzed by electron-deficient boranes follows a counterintuitive mechanism in which the Si–H bond is activated by the boron Lewis acid prior to nucleophilic attack of the carbonyl oxygen atom at the silicon atom. The borohydride thus formed is the actual reductant. These steps were elucidated by using a silicon-stereogenic silane, but applying the same technique to the related reduction of C=N groups was inconclusive due to racemization of the silicon atom. The present investigation now proves by the deliberate combination of our axially chiral borane catalyst and axially chiral silane reagents (in both enantiomeric forms) that the mechanisms of these hydrosilylations are essentially identical. Unmistakable stereochemical outcomes for the borane/silane pairs show that both participate in the enantioselectivity-determining hydride-transfer step. These experiments became possible after the discovery that our axially chiral C_6F_5-substituted borane induces appreciable levels of enantioinduction in the imine hydrosilylation.

Keywords: boron · hydrosilylation · Lewis acids · reaction mechanisms · silicon

Introduction

Small-molecule activation by main-group elements, the new chemistry of frustrated Lewis pairs (FLPs) in particular, is currently garnering tremendous attention.[1,2] The deliberate combination of a strong (usually boron-based) Lewis acid and various Lewis bases enables the heterolytic splitting of Si–H and even H–H bonds.[3] This intriguing activation mode was initially found to be operative in the $B(C_6F_5)_3$-catalyzed hydrosilylation of C=O and C=N groups,[4] and a related imine hydrogenation was later developed.[5] The Piers group showed by careful analysis that $B(C_6F_5)_3$ (**1**) activates the Si–H bond of **I** rather than the C=X group of **III** (**I**→**II**; Scheme 1),[6] and our laboratory clarified the mechanism of the actual activation step (for X=O) with the aid of a silicon-stereogenic silane (**II**→**IV**‡→**V**; Scheme 1).[7] The catalytic cycle closes with a conventional borohydride reduction of the intermediate silylcarboxonium ion (**V**→**VI**; Scheme 1), thereby releasing the electron-deficient borane **1**.

The counterintuitive mechanism of the $B(C_6F_5)_3$-catalyzed Si–H bond activation with subsequent carbonyl reduction (X=O) is therefore sufficiently understood.[6,7] Conversely, solid evidence for the cognate imine reduction (X=NR) to follow the same steps is still pending. With regards to recent



Scheme 1. Mechanism of the $B(C_6F_5)_3$-catalyzed hydrosilylation of ketones (X=O, reported) and imines (X=NR, proposed).

efforts to render these metal-free reductions enantioselective, the unclear mechanism represents a significant gap. Just a few months ago, a single example was reported by the Klankermayer group.[8] The chiral borane used in this work indeed induces decent enantioselectivity but only in the presence of a bulky phosphane. No asymmetric induction is seen with the chiral borane alone. It is assumed that a boron/phosphorus frustrated Lewis pair (FLP) forms, then cleaving the Si–H bond without the involvement of the imine.[9] The mechanism of the asymmetric reduction step as well as the role of the phosphane (or silylphosphonium ion) remains unclear. We disclose here conclusive insight into the borane-catalyzed imine reduction by using the axially chiral, electron-deficient borane (*S*)-**2**·THF recently introduced by us (Figure 1, left).[10] Our investigation was triggered by the observation that (*S*)-**2**·THF alone yields significant levels of enantioselection and displays distinct matched/mismatched

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201202693.

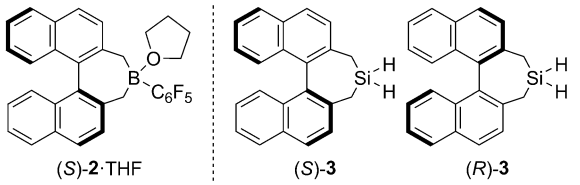
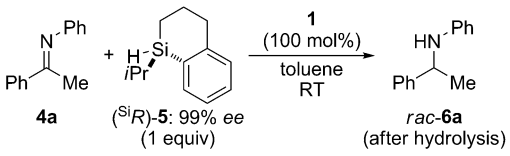


Figure 1. Axially chiral borane (*S*)-**2**·THF as well as silanes (*S*)-**3** and (*R*)-**3** as stereochemical probes.

selectivities with axially chiral silanes (*S*)-**3** and (*R*)-**3** (Figure 1, right).

Results and Discussion

As mentioned above, we had verified the S_N2-Si mechanism of the Si–H bond activation with silicon-stereogenic silane (^{Si}R)-**5** (see **IV**$^+$ with X = O in Scheme 1).[7] Subsequent cleavage of the Si–O bond with retention of the configuration[11] liberated (^{Si}S)-**5**, which corresponds to a Walden inversion at the silicon atom in the heterolytic Si–H splitting.[7] Importantly, the alcohol formed in the reductive Si–O cleavage was enantiomerically enriched (38% *ee* with (^{Si}R)-**5** (90% *ee*) for R^1 = Ph and R^2 = Me, not shown), thus demonstrating considerable reagent control of the chiral silane through single-point binding.[7,12] An attempt to prove the mechanism of the imine reduction by the same strategy failed. Reduction of a representative imine with (^{Si}R)-**5** was stoichiometric in **1** to afford the amine in racemic form (**4a**→*rac*-**6a**; Scheme 2).[12]



Scheme 2. $B(C_6F_5)_3$-mediated imine reduction with a silicon-stereogenic silane.

This unexpected outcome brought us to consider another reduction pathway. As one equivalent of the borane Lewis acid is present, the formation of its imine adduct is not unlikely.[13] Reduction of the $B(C_6F_5)_3$-activated imine (Figure 2, path a) rather than silyliminium ion (Figure 2, path b) by the borohydride is, therefore, at least conceivable. The former path would proceed without any involvement of the chiral silicon moiety.

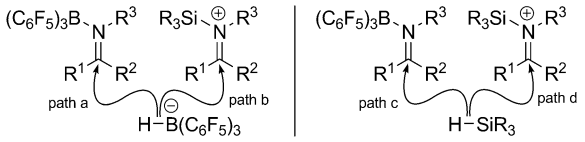
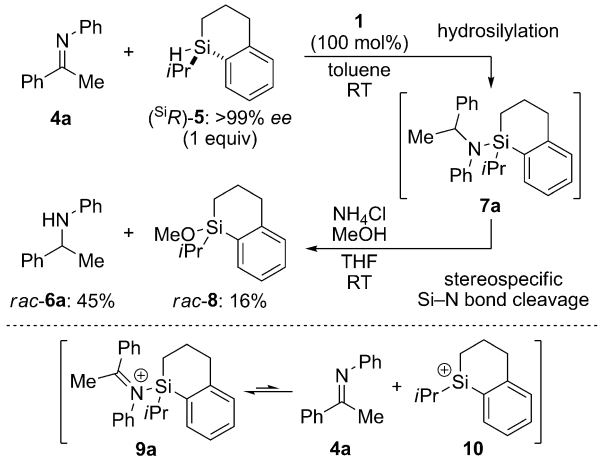


Figure 2. Possible hydride-transfer scenarios.

To gain more insight into the above experiment, the configurational stability of an asymmetrically substituted silicon atom attached to an imine nitrogen atom will be crucial (see **V** with X = NR in Scheme 1). Moreover, the stereochemical course of the Si–N bond cleavage must be determined to assign the absolute configuration at the silicon atom. It turned out that little is known about the chemistry of amino-substituted silicon-stereogenic silanes.[11,14] We therefore had to elaborate a protocol for the stereospecific cleavage of an Si–N bond (see the Supporting Information for details) and found that NH_4Cl and MeOH transform an Si–N into an Si–O bond with complete inversion of the configuration. This setup was applied to the amino-substituted silane intermediate **7a** after $B(C_6F_5)_3$-mediated imine hydrosilylation to afford the methoxy-substituted silane in racemic form [(^{Si}R)-**5**→*rac*-**8**; Scheme 3, top]. As shown by Piers



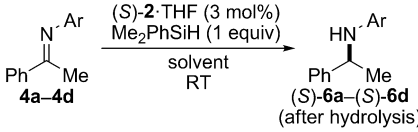
Scheme 3. Probing the stereochemical course at the silicon atom (upper) and potential racemization process (lower).

et al., the borohydride reduction becomes rate-determining in reactions with sterically demanding reactants.[4b] The slow borohydride reduction might account for dissociation of the silyliminium intermediate **9a**, thus resulting in a transient planar (i.e., achiral) silylium ion **10** (Scheme 3, bottom). These results clearly show that, unlike the C=O reduction,[7] silicon-stereogenic silanes cannot be used as stereochemical probes in the C=N reduction.[12]

We have recently reported the preparation and detailed characterization of the axially chiral, electron-deficient borane (*S*)-**2** that is conveniently isolated as its THF adduct (*S*)-**2**·THF (Figure 1, left).[10] It was designed as a chiral analogue of $B(C_6F_5)_3$ (**1**), and we were delighted to see that (*S*)-**2**·THF was indeed able to activate Si–H bonds but there was either no asymmetric induction in carbonyl hydrosilylation[10] or numbers were low.[15] In turn, imine hydrosilylation catalyzed by (*S*)-**2**·THF without the addition of another Lewis base produced promising enantioselectivities, sufficiently high for mechanistic investigations. We note here that, compared to Klankermayer's observation,[8] the presence of bulky phosphanes such as Mes_3P had no effect.

We focused on imines with various aryl substituents at the nitrogen atom in our systematic screening (Table 1). An attempt in toluene, the commonly used solvent for $B(C_6F_5)_3$-catalyzed reactions, with phenyl-substituted imine **4a** afforded disappointing 2% *ee* at low reaction rate (Table 1, entry 1). Minor improvement was seen when the reaction was run without solvent (Table 1, entry 2). The solvent polarity had a strong effect, and enantiomeric excesses increased significantly in polar aprotic solvents such as CH_2Cl_2 and 1,2-$C_6H_4F_2$ (Table 1, entries 3 and 4). An enantiomeric excess of 2% (Table 1, entry 1) versus 33% (Table 1, entry 4) is an unprecedented solvent effect in borane-catalyzed hydrosilylation reactions. We next turned to electronic and steric effects of the aryl protecting group.[4b] The reaction rate for 4-anisyl-substituted imine **4b** was slower with almost identical enantiomeric excess (Table 1, entry 5). The decreased rate is likely to be due to the formation of a stronger borane–imine adduct with an electron-richer nitrogen atom in **4b** than in **4a**, thereby making less free borane available for the silane activation.[4b] Conversely, more steric bulk around the nitrogen donor as in **4c** (with 2-tolyl) or **4d** (with 1-naphthyl) substantially increased the reaction rate, thereby resulting in full conversion in less than one day (Table 1, entries 6 and 7). Moreover, slightly enhanced enantioinduction is also obtained (36 and 41% *ee*).[16] Similar observations in the racemic series were made by Piers et al. for $B(C_6F_5)_3$ (**1**),[4b] and these strongly support the Si–H bond-activation mode and exclude a Lewis acid activation mechanism (see Figure 2, path c). We do have, however, no explanation yet for the pronounced solvent effect on asymmetric induction. The effect on the reaction rate is rationalized by better stabilization of **V** (Scheme 1) in more polar solvents. For example, imine **4d** also reacts slowly in toluene, again with little enantioselectivity (7 versus 41% *ee*; Table 1, entries 8 and 7, respectively). Another observation worth mentioning is that asymmetric induction is independent of conversion and catalyst loading. Hence, thermal *E*/*Z* isomerization of imines in the presence of the borane catalyst[13] seems not to interfere in the reduction of imines **4a**–**4d** catalyzed by (*S*)-**2**·THF.

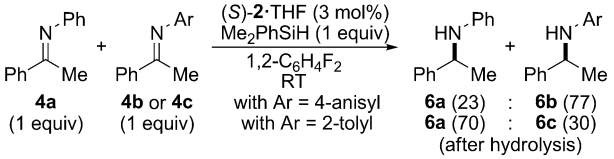
Table 1. Enantioselective imine hydrosilylation catalyzed by (*S*)-**2**.[a]



	Ar	Solvent[b]	*t* [h]	Conv. [%][c]	Yield [%][d]	*ee* [%][e,f]
1	Ph (**4a**)	toluene	74	70	53	2
2	Ph (**4a**)	neat[g]	45	80	62	9
3	Ph (**4a**)	CH_2Cl_2	74	66	50	33
4	Ph (**4a**)	1,2-$C_6H_4F_2$	66	84	78	33
5	4-anisyl (**4b**)	1,2-$C_6H_4F_2$	68	55	52	30
6	2-tolyl (**4c**)	1,2-$C_6H_4F_2$	17	quant	94	36
7	1-Np (**4d**)	1,2-$C_6H_4F_2$	18	quant	97	41
8	1-Np (**4d**)	toluene	120	47	n.d.	7

[a] 0.1 or 0.2 mmol scale. Np = naphthyl, n.d. = not determined, quant = quantitative. [b] 1.0 M solutions. [c] Determined by GLC analysis using tetracosane as internal standard. [d] Isolated yield after flash column chromatography. [e] Determined by HPLC analysis using chiral stationary phases. [f] Absolute configurations of **6c** and **6d** were assigned by comparison with **6a** and **6b**. [g] Me_2PhSiH (2.0 equiv) used.

The electronic and steric effects exerted by the aryl nitrogen substituent on the reaction rate were further verified in two competition experiments (Scheme 4).[6] We subjected an equimolar mixture of imine **4a** and electron-rich imine **4b** to borane catalysis. Remarkably, more nucleophilic **4b** reacts faster than **4a**, whereas **4b** is reduced at a slower rate than **4a** when reacted separately (Table 1, entries 4 and 5). A similar situation is seen in the competition experiment with phenyl-substituted **4a** and sterically hindered **4c**. Less-hindered **4a** reacts faster than **4c** in its presence, whereas **4c** is the fast-reacting imine in the separate experiment (Table 1, entries 4 and 6). These results are interpreted as a reflection of the different borane–imine adduct strengths and the ability of the imine to attack the silicon atom from the backside in the Si–H bond-activation step. The more nucleophilic (as for **4a**/**4b**) and less-hindered imines (as for **4a**/**4c**) win in competitive experiments but lose in the individual setups. These results support a mechanism in which the Si–H bond is activated by the borane followed by the preferred backside attack of a nucleophilic and unhindered imine at the silicon atom.



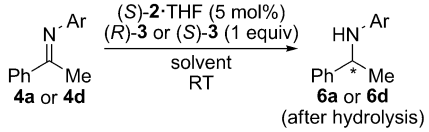
Scheme 4. Competition experiments between imines **4a** and **4b** as well as **4a** and **4c** (ratios based on conversion of imines determined by GLC analysis with tetracosane as internal standard after >97% conversion of Me_2PhSiH).

Doubts remained about the stereochemistry-determining hydride-transfer step (see Figure 2). We exclude path c, as Lewis acid activation of the imine was disproven. The significant enantioselectivities obtained in reduction with the chiral borane (*S*)-**2** (Table 1) make path d, that is, hydride transfer from another equivalent of the silane, seem more than unlikely. If path d were the actual hydride-transfer mode, asymmetric induction would arise from a chiral borohydride counteranion. Polar solvents have been shown to be detrimental to enantioinduction in asymmetric counteranion catalysis,[17] and enantioselectivity even increases from nonpolar (toluene) to polar (CH_2Cl_2 and 1,2-$C_6H_4F_2$) solvents in our case. To finally distinguish between path a and path b, or, in other words, to prove the participation of both the borane and the silicon reactant in the hydride transfer, we prepared both enantiomers of the new axially chiral silane **3**[18] (Figure 1, right). Combination with (*S*)-**2** ought to form matched/mismatched pairs for reduction path b, and the out-

come would not be blurred by racemization of the chiral silane.

We performed the catalyses with a slightly increased loading of (*S*)-**2** (5 mol%) and tested the influence of the configuration of **3** with **4a** and **4d** (unhindered and hindered imines) in 1,2-$C_6H_4F_2$ and toluene (polar and nonpolar solvents).[19] As observed before (see Table 1), reactions of **4d** were generally faster than those of **4a** (Table 2). We were

Table 2. Matched/mismatched scenarios in the imine hydrosilylation with either enantiomer of axially chiral silane **3** catalyzed by (*S*)-**2**.[a]



	Ar	3	Solvent[b]	*t* [h]	Conv [%][c]	*ee* [%][d,e]
1	Ph (**4a**)	*R*	1,2-$C_6H_4F_2$	96	57	22 (*S*)
2	Ph (**4a**)	*S*	1,2-$C_6H_4F_2$	96	60	2 (*R*)
3	1-Np (**4d**)	*R*	1,2-$C_6H_4F_2$	22	92	13 (*S*)
4	1-Np (**4d**)	*S*	1,2-$C_6H_4F_2$	23	90	16 (*R*)
5	Ph (**4a**)	*R*	toluene	160	26	18 (*S*)
6	Ph (**4a**)	*S*	toluene	160	16	16 (*R*)
7	1-Np (**4d**)	*R*	toluene	69	53	29 (*S*)
8	1-Np (**4d**)	*S*	toluene	69	29	18 (*R*)

[a] 0.05 or 0.1 mmol scale. [b] 0.5 M solutions. [c] Determined by GLC analysis using tetracosane as internal standard. [d] Determined by HPLC analysis using chiral stationary phases. [e] Major enantiomer of **6a** and **6d**, respectively, in parentheses.

delighted to find unmistakable stereochemical outcomes for both (*S*)-**2**/(*R*)-**3** and (*S*)-**2**/(*S*)-**3** pairs with all imine/solvent combinations. We consider those cases matched when the same absolute configuration is seen as with achiral Me_2PhSiH. The matched/mismatched cases are also clear from the reaction rates with toluene but not 1,2-$C_6H_4F_2$ as solvent. This observation might be again interpreted by a better stabilization of ion pair **V** (Scheme 1) in polar solvents, thus making the matched/mismatched effect more pronounced in a nonpolar solvent with **V** being less stabilized. Gratifyingly, (*R*)-**3** invariably produced (*S*)-**6** (matched), whereas (*S*)-**3** always afforded (*R*)-**6** (mismatched). Hence, axially chiral **3** determines the absolute configuration of the resulting amine. This considerable reagent control is absolutely remarkable because $B(C_6F_5)_3$-catalyzed imine reductions that employed chiral **3** exclusively yielded racemic amines. Without ambiguity, these data prove that reduction path b is the predominant hydride-transfer mechanism (Figure 2, left).

Conclusion

To recap, we demonstrated the potential of our borane (*S*)-**2** as a chiral analogue of $B(C_6F_5)_3$ (**1**) to induce 33% *ee* for a phenyl-substituted imine (Table 1, entry 4) and even 62% *ee* for a benzyl-substituted imine.[16] These values were achieved due to the discovery of a strong solvent effect not only on enantioinduction but also reaction rate. The enantiomeric excesses were sufficiently high for mechanistic investigations, and combinations of the borane (*S*)-**2** and the new axially chiral silanes **3** [(*S*)-**2**/(*R*)-**3** and (*S*)-**2**/(*S*)-**3** pairs] displayed distinct matched/mismatched selectivities (Table 2). By this, we now confirmed the tentative mechanism for this imine reduction, and our data are in accordance with the mechanistic picture originally proposed by the Piers group and refined by us (Scheme 1). We regard the present study as a useful basis for the development of improved Lewis acid catalyzed asymmetric hydrosilylation reactions.

Experimental Section

All reactions were performed in flame-dried glassware using an M. Braun glovebox ($O_2 < 0.5$ ppm, $H_2O < 0.5$ ppm) or conventional Schlenk techniques under a static pressure of nitrogen. Liquids and solutions were transferred with syringes. Solvents (THF, Et_2O, toluene, 1,2-$C_6H_4F_2$, *n*-hexane, and CH_2Cl_2) were purified and dried following standard procedures. Technical-grade solvents for extraction or chromatography (cyclohexane, *tert*-butyl methyl ether, Et_2O, and ethyl acetate) were distilled prior to use. CCl_4, Cl_2, MeOH, *n*BuLi (in hexanes), TfOH, $LiAlH_4$, imidazole, DMAP, NH_4Cl, and $Ph(H)SiCl_2$ were purchased from commercial suppliers and used without further purification. *N*,*N*,*N*′,*N*′-Tetramethylenediamine (TMEDA) and dibenzylamine were dried over sodium and distilled prior to use. $MePh_2SiH$ and Ph_2SiH_2 were dried over $LiAlH_4$ and distilled prior to use. Imines **4a**–**4d** were prepared according to known procedures and spectroscopic data agreed with reported data. Borane (*S*)-**2**·THF was prepared according to our previously reported procedure.[10] $B(C_6F_5)_3$ was prepared according to the procedure of Erker et al.[20] (^{Si}R)-1-Isopropyl-1,2,3,4-tetrahydro-1-silanaphthalene [(^{Si}R)-**5**] was prepared according to our previously reported procedure.[21] Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F254 glass plates by Merck. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by Merck using the indicated solvents. ^1H, ^{13}C, and ^{29}Si NMR spectra were recorded in $CDCl_3$ using Bruker AV400 and Bruker AV500 instruments. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent resonance as the internal standard ($CDCl_3$: $\delta = 7.26$ and 77.2 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m_c = centrosymmetric multiplet, m = multiplet, br = broad), coupling constants (Hz), and integration. Gas liquid chromatography (GLC) was performed using an Agilent 7820A gas chromatograph equipped with an HP-5 capillary column (30 m × 0.32 mm, 0.25 μm film thickness) by Agilent Technologies using the following program: N_2 carrier gas, injection temperature 250 °C, detector temperature 300 °C; temperature program: start temperature 40 °C, heating rate 10 °C min^{-1}, end temperature 280 °C for 10 or 30 min. Enantiomeric excesses were determined by analytical high-pressure liquid chromatography (HPLC) analysis using an Agilent 1200 Series instrument with a chiral stationary phase using a Daicel Chiralcel OJ-RH column (MeCN/H_2O mixtures as solvent), a Daicel Chiralcel OJ-H column (*n*-heptane/*i*PrOH mixtures as solvent), or a Daicel Chiralcel OD-H column (*n*-heptane/*i*PrOH mixtures as solvent). Optical rotations were measured using a Schmidt and Haensch Polartronic H 532 polarimeter. Mass spectrometry (MS) was obtained from the Analytical Facility at the Institut für Chemie, Technische Universität Berlin.

Preparation of (*S*)-4,5-dihydro-3*H*-dinaphtho[2,1-*c*:1′,2′-*e*]silepine ((*S*)-3): A solution of *n*-butyllithium (1.5 M in hexanes, 8.19 mL, 12.3 mmol, 2.50 equiv) was concentrated under vacuum to an oil and diluted in Et_2O (10 mL). A solution of (*S*)-2,2′-dimethyl-1,1′-binaphthalene (1.39 g, 4.92 mmol, 1.00 equiv) in Et_2O (10 mL) was added to this dropwise at 0 °C followed by TMEDA (1.87 mL, 12.6 mmol, 2.55 equiv). The mixture

was maintained at room temperature for 20 h to result in a deep red suspension. The liquid was removed by filtration, and the residue was dried under full vacuum to furnish a red/brown solid (1.25 g, 2.37 mmol). The solid was dissolved in THF (15 mL) and cooled to −78 °C. $Ph(H)SiCl_2$ (0.52 mL, 3.56 mmol, 1.50 equiv based on metalated intermediate) was added in one portion, and a color change from deep red to yellow was observed. The solution was slowly warmed to room temperature and quenched by the addition of water. The aqueous layer was extracted with *tert*-butyl methyl ether, and the combined organic layers were washed with brine. The organic layer was dried over $MgSO_4$, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (cyclohexane) to yield (*S*)-4-phenyl-4,5-dihydro-3*H*-dinaphtho[2,1-*c*:1′,2′-*e*]silepine as a white solid. Yield: 660 mg (1.71 mmol, 35% overall yield; 72% based on metalated intermediate). M.p. 151–152 °C (cyclohexane); R_f = 0.14 (cyclohexane); GLC (HP-5): t_R = 44.1 min; $[\alpha]_D^{20}$ = +71.0 (*c* = 0.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.25 (d, AB spin system, ^2J = 13.6 Hz, 1H), 2.28 (dd, AB spin system, ^2J = 13.3 Hz, ^3J = 7.1 Hz, 1H), 2.31 (dd, AB spin system, ^2J = 13.6 Hz, ^3J = 2.3 Hz, 1H), 2.36 (dd, AB spin system, ^2J = 13.3 Hz, ^3J = 2.1 Hz, 1H), 4.69 (ddd, ^3J = 7.1 Hz, ^3J = 2.3 Hz, ^3J = 2.1 Hz, 1H), 7.13 (dm, ^3J = 8.5 Hz, 1H), 7.17 (dm, ^3J = 8.7 Hz, 1H), 7.18–7.24 (m, 2H), 7.30–7.35 (m, 3H), 7.37–7.43 (m, 5H), 7.55 (d, ^3J = 8.4 Hz, 1H), 7.84 (d, ^3J = 8.2 Hz, 1H), 7.89–7.94 ppm (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.37, 20.42, 124.6, 126.0, 126.1, 126.48, 126.53, 127.7, 128.1 (2C), 128.19, 128.21, 128.3 (2C), 130.1, 132.1, 132.2, 132.6, 132.7, 132.8, 132.9, 134.0, 134.7, 135.6, 136.0 ppm; ^{29}Si NMR (99 MHz, $CDCl_3$): δ = −2.0 ppm; IR (ATR): $\tilde{\nu}$ = 3056 (m), 2130 (s), 1618 (m), 1592 (m), 1507 (s), 1427 (m), 1404 (m), 1355 (m), 1327 (m), 1242 (m), 1141 (s), 1112 (s), 1024 (m), 964 (s), 925 (m), 836 (s), 815 (s), 737 (s), 693 cm^{-1} (s); HRMS (EI): *m*/*z*: calcd for $C_{28}H_{22}Si$ [M^+]: 386.14853; found: 386.14918. According to the protodesilylation reported by Hayashi and Shintani et al.,[22] TfOH (0.17 mL, 1.9 mmol, 3.5 equiv) was added to a solution of (*S*)-4-phenyl-4,5-dihydro-3*H*-dinaphtho[2,1-*c*:1′,2′-*e*]silepine (210 mg, 0.543 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL), and the mixture was stirred at room temperature. After 1 h, all volatiles were removed under full vacuum, and the residue was dissolved in CH_2Cl_2 (5 mL) and again subjected to full vacuum for 30 min. The foamy residue was dissolved in Et_2O (8 mL), and $LiAlH_4$ (102 mg, 2.69 mmol, 4.95 equiv) was carefully added in three portions. The suspension was stirred at room temperature for 2 h and was then carefully quenched with water. After extraction of the aqueous layer with *tert*-butyl methyl ether, the combined organic layers were dried over $MgSO_4$, and the solvents were removed under reduced pressure. Purification by flash column chromatography on silica gel (cyclohexane) followed by recrystallization from cyclohexane at 4 °C yielded the title compound (*S*)-**3** as colorless crystals. Yield: 101 mg (0.33 mmol, 60%). M.p. 182–183 °C (cyclohexane); R_f = 0.29 (cyclohexane); GLC (HP-5): t_R = 27.7 min; $[\alpha]_D^{20}$ = +413.7 (*c* = 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (dt, AB spin system, ^2J = 13.5 Hz, ^3J = 5.0 Hz, 2H), 2.15 (dt, AB spin system, ^2J = 12.8 Hz, ^3J = 1.1 Hz, 2H), 4.09 (tt, ^3J = 4.5 Hz, ^3J = 1.0 Hz, 2H), 7.09 (dm, ^3J = 8.5 Hz, 2H), 7.18 (ddd, ^3J = 8.2 Hz, ^3J = 6.7 Hz, ^4J = 1.3 Hz, 2H), 7.38 (ddd, ^3J = 8.1 Hz, ^3J = 6.7 Hz, ^4J = 1.3 Hz, 2H), 7.46 (d, ^3J = 8.4 Hz, 2H), 7.87 (d, ^3J = 8.1 Hz, 2H), 7.89 ppm (dm, ^3J = 8.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.9, 124.6, 125.9, 126.3, 127.3, 128.1, 128.3, 132.0, 132.5, 132.7, 136.0 ppm; ^{29}Si NMR (99 MHz, $CDCl_3$): δ = −22.6 ppm; IR (ATR): $\tilde{\nu}$ = 3040 (w), 2130 (s), 1616 (w), 1590(m), 1506 (m), 1411 (m), 1352 (m), 1328 (m), 1241 (m), 1221 (w), 1135 (m), 1055 (w), 971 (m), 920 (s), 846 (m), 823 cm^{-1} (s); HRMS (EI): *m*/*z*: calcd for $C_{22}H_{18}Si$ [M^+]: 310.11723; found: 310.11648.

The enantiomer of the title compound (*R*)-**3** was prepared from (*R*)-2,2′-dimethyl-1,1′-binaphthalene and analytical data matched those of (*S*)-**3**. $[\alpha]_D^{20}$ ((*R*)-**3**) = −417.9 (*c* = 0.28, $CHCl_3$).

$B(C_6F_5)_3$-catalyzed imine hydrosilylation with silicon-stereogenic silane (^{Si}*R*)-5 followed by stereospecific Si−N bond cleavage: In a glovebox, a 2 mL vial equipped with a magnetic stir bar was charged with $B(C_6F_5)_3$ (86.0 mg, 0.168 mmol, 1.00 equiv). A solution of imine **4a** (32.8 mg, 0.168 mmol, 1.00 equiv) and silane (^{Si}*R*)-**5** (>99% *ee*, 32.0 mg, 0.168 mmol, 1.00 equiv) in toluene (1.5 mL) was added to the borane in one portion and the vial was closed. After 46 h (full conversion of silane), the vial was taken out of the glovebox, and the reaction mixture was diluted with *tert*-butyl methyl ether (1 mL). The solution was filtered over a small pad of silica gel, and all solvents of the filtrate were removed under reduced pressure. GLC-MS analysis of the crude product showed a peak that corresponded to the aminosilane intermediate **7a**. Crude **7a** was then dissolved in THF (1 mL), and MeOH (20.5 mg, 0.640 mmol, 3.81 equiv) and NH_4Cl (10.5 mg, 0.196 mmol, 1.17 equiv) were added. After 40 h, GLC analysis indicated full conversion of aminosilane **7a**. The reaction mixture was filtered over a short sand/cotton pad to remove the solids, and the solvents were removed under reduced pressure. Flash column chromatography on silica gel (cyclohexane/ethyl acetate 99:1) afforded amine *rac*-**6a** (15 mg, 76 μmol, 45%) and silyl ether *rac*-**8** (5.9 mg, 27 μmol, 16%) both in racemic form. For the analytical data of **6a**, see below. For the analytical data of **8**, see the Supporting Information.

General procedure for borane-catalyzed imine hydrosilylation: In a glovebox, a 2 mL vial equipped with a magnetic stir bar was charged with (*S*)-**2**·THF (3–5 mol%). A solution of the indicated imine **4** (0.050–0.20 mmol, 1.0 equiv), the silane (1.0 equiv), and tetracosane (internal standard for GLC analysis, 0.5–2.0 mg) in the indicated solvent (0.5–1 M) was added to the borane in one portion, and the vial was closed. The mixture was stirred for the indicated time (conversion monitored by GLC analysis) and subsequently subjected to flash column chromatography on silica gel (cyclohexane/ethyl acetate mixtures) to afford amines **6** as solids or oils.

***N*-(1-Phenylethyl)aniline (6a)**: Prepared according to the general procedure. Analytical data: isolated as colorless oil. R_f = 0.70 (cyclohexane/ethyl acetate 4:1); GLC (HP-5): t_R = 17.4 min; HPLC (Daicel Chiralcel OD-H, 20 °C, *n*-heptane/*i*PrOH 90:10, flow rate 0.7 mL min^{-1}, λ = 230 nm): t_R = 8.8 min ((*S*)-**6a**), 10.0 min ((*R*)-**6a**); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (d, ^3J = 6.7 Hz, 3H), 4.13 (br s, 1H), 4.50 (q, ^3J = 6.7 Hz, 1H), 6.53 (dd, ^3J = 8.6 Hz, ^4J = 1.0 Hz, 2H), 6.66 (tt, ^3J = 7.3 Hz, ^4J = 1.0 Hz, 1H), 7.10 (m_c, 2H), 7.20–7.27 (m, 1H), 7.29–7.42 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.2, 53.6, 113.4, 117.4, 126.0, 127.0, 128.8, 129.2, 145.3, 147.4 ppm; IR (ATR): $\tilde{\nu}$ = 3410 (s), 3053 (m), 3024 (m), 2967 (m), 2924 (m), 2868 (m), 1601 (s), 1505 (s), 1449 (m), 1428 (w), 1373 (w), 1353 (w), 1318 (m), 1258 (m), 1206 (w), 1180 (w), 1140 (w), 750 (s), 701 cm^{-1} (s); HRMS (ESI): *m*/*z*: calcd for $C_{14}H_{15}NH$ [M+H]$^+$: 198.1277; found: 198.1277.

4-Methoxy-*N*-(1-phenylethyl)aniline (6b): Prepared according to the general procedure. Analytical data: isolated as yellow oil. R_f = 0.20 (cyclohexane/ethyl acetate 20:1); GLC (HP-5): t_R = 20.1 min; HPLC (Daicel Chiralcel OD-H, 20 °C, *n*-heptane/*i*PrOH 98:2, flow rate 0.7 mL min^{-1}, λ = 230 nm): t_R = 25.1 min ((*R*)-**6b**), 28.3 min ((*S*)-**6b**); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, ^3J = 6.7 Hz, 3H), 3.70 (s, 3H), 4.20 (br s, 1H), 4.42 (q, ^3J = 6.7 Hz, 1H), 6.46–6.51 (m, 2H), 6.68–6.73 (m, 2H), 7.23 (tt, ^3J = 7.1 Hz, ^4J = 1.5 Hz, 1H), 7.30–7.40 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 25.3, 54.4, 55.9, 114.7, 114.9, 126.0, 127.0, 128.7, 141.7, 145.6, 152 ppm; IR (ATR): $\tilde{\nu}$ = 3402 (s), 2963 (m), 2832 (m), 1617 (w), 1508 (s), 1449 (m), 1406 (w), 1372 (w), 1294 (w), 1231 (s), 1177 (m), 1139 (m), 1035 (s), 816 (s), 752 (s), 699 cm^{-1} (s); HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{17}NOH$ [M+H]$^+$: 228.1380; found: 228.1383.

2-Methyl-*N*-(1-phenylethyl)aniline (6c): Prepared according to the general procedure. Analytical data: isolated as colorless oil. R_f = 0.48 (cyclohexane/ethyl acetate 20:1); GLC (HP-5): t_R = 18.1 min; HPLC (Daicel Chiralcel OJ-H, 20 °C, *n*-heptane/*i*PrOH 97:3, flow rate 0.5 mL min^{-1}, λ = 230 nm): t_R = 21.5 min ((*S*)-**6c**), 26.1 min ((*R*)-**6c**); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (d, ^3J = 6.7 Hz, 3H), 2.25 (s, 3H), 3.87 (br s, 1H), 4.56 (q, ^3J = 6.7 Hz, 1H), 6.39 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1H), 6.62 (ddd, ^3J = 7.4 Hz, ^3J = 7.4 Hz, ^4J = 1.2 Hz, 1H), 6.98 (ddd, ^3J = 8.0 Hz, ^3J = 7.4 Hz, ^4J = 1.6 Hz, 1H), 7.07 (ddd, ^3J = 7.3 Hz, ^4J = 1.8 Hz, ^5J = 0.9 Hz, 1H), 7.24 (tt, ^3J = 7.1 Hz, ^4J = 1.5 Hz, 1H), 7.31–7.41 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 17.8, 25.4, 53.4, 111.2, 117.0, 121.7, 125.9, 127.0, 127.1, 128.8, 130.1, 145.3, 145.4 ppm; IR (ATR): $\tilde{\nu}$ = 3433 (m), 3023 (w), 2965 (m), 2923 (w), 2866 (w), 1604 (s), 1508 (s), 1446 (s), 1372 (m), 1313 (s), 1259 (s), 1212 (m), 1144 (m), 1050 (w), 1017 (w), 984 (w), 920 (w), 838 (w), 743 (s), 698 cm^{-1} (s); HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{17}NH$ [M+H]$^+$: 212.1434; found: 212.1432.

***N*-(1-Phenylethyl)naphthalen-1-amine (6d)**: Prepared according to the general procedure. Analytical data: isolated as white solid. M.p. 95–96 °C (cyclohexane); $R_f = 0.47$ (cyclohexane/ethyl acetate 20:1); GLC (HP-5): $t_R = 23.3$ min; HPLC (Daicel Chiralcel OD-H, 20 °C, *n*-heptane/*i*PrOH 98:2, flow rate 0.7 mL min^{-1}, $\lambda = 230$ nm): $t_R = 22.9$ min ((*S*)-**6d**), 36.8 min ((*R*)-**6d**); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.69$ (d, $^3J = 6.7$ Hz, 3H), 4.71 (q, $^3J = 6.7$ Hz, 1H), 4.76 (br s, 1H), 6.41 (m_c, 1H), 7.19–7.23 (m, 2H), 7.26 (tt, $^3J = 7.3$ Hz, $^4J = 1.3$ Hz, 1H), 7.32–7.37 (m, 2H), 7.43–7.52 (m, 4H), 7.79–7.84 (m, 1H), 7.93–7.98 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 25.4$, 53.7, 106.1, 117.4, 119.9, 123.4, 124.8, 125.8, 125.9, 126.7, 127.1, 128.8, 128.9, 134.4, 142.2, 145.0 ppm; IR (ATR): $\tilde{\nu} = 3434$ (m), 2973 (m), 2866 (w), 1575(s), 1523 (s), 1476 (s), 1446 (m), 1408 (s), 1370 (m), 1345 (m), 1279 (s), 1220 (m), 1139 (s), 1102 (w), 1026 (w), 765 (s), 703 cm^{-1} (s); HRMS (ESI): *m/z:* calcd for $C_{18}H_{17}NH$ $[M+H]^+$: 248.1434; found: 248.1431.

***N*-Benzyl-1-phenylethanamine**:[16] Prepared according to the general procedure. Analytical data: isolated as colorless oil. $R_f = 0.25$ (cyclohexane/ethyl acetate 4:1); GLC (HP-5): $t_R = 17.9$ min; HPLC (Daicel Chiralcel OD-H, 20 °C, *n*-heptane/*i*PrOH 99:1, flow rate 0.75 mL min^{-1}, $\lambda = 230$ nm): $t_R = 8.6$ min (*R*), 9.4 min (*S*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.38$ (d, $^3J = 6.6$ Hz, 3H), 1.93 (br s, 1H), 3.60 (d, $^2J = 13.2$ Hz, 1H), 3.67 (d, $^2J = 13.2$ Hz, 1H), 3.82 (q, $^3J = 6.6$ Hz, 1H), 7.22–7.42 ppm (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 24.4$, 51.5, 57.4, 126.7, 126.9, 126.9, 128.2, 128.3, 128.5, 140.4, 145.3 ppm; IR (ATR): $\tilde{\nu} = 3062$ (w), 3026 (m), 2963 (m), 2925 (w), 1493 (m), 1452 (s), 1369 (w), 1201 (w), 1124 (s), 700 cm^{-1} (s); HRMS (ESI): *m/z*: calcd for $C_{15}H_{17}NNa$ $[M+Na]^+$: 212.1434; found: 212.1440.

Acknowledgements

This research was supported by the Deutsche Forschungsgemeinschaft (Oe 249/6-1). M.O. is indebted to the Einstein Foundation (Berlin) for an endowed professorship. We thank Professor Warren Piers (University of Calgary) for suggesting to us that racemization of the silicon-stereogenic silane might explain our previous preliminary observations.

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[16] We would like to mention here that acetophenone-derived imine with a benzyl protection group is reduced by (*S*)-**2**·THF with promising 62% *ee*. Optimization of the enantiomeric excess is not the purpose of the present investigation but ongoing efforts in our laboratory are directed toward the modification of the borane catalyst.

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[18] For details of its preparation, see the Experimental Section. A related silepine structure was reported before: M. E. Jung, K. T. Hogan, *Tetrahedron Lett.* **1988**, *29*, 6199–6202.

[19] Dihydrosilane **3** is assumed to react as a monohydride, thereby avoiding more complicated selectivity effects due to another hydride transfer. Experiments with Ph_2SiH_2 showed that one equivalent is completely consumed under the reaction conditions of Table 1 (26% *ee* with imine **4a** in 1,2-$C_6H_4F_2$).

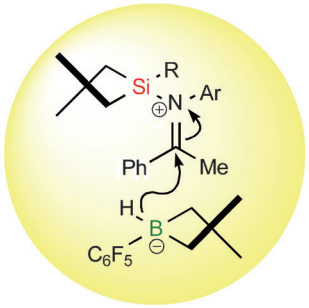
[20] C. Wang, G. Erker, G. Kehr, K. Wedeking, R. Fröhlich, *Organometallics* **2005**, *24*, 4760–4773.

[21] a) M. Oestreich, U. K. Schmid, G. Auer, M. Keller, *Synthesis* **2003**, 2725–2739; b) S. Rendler, M. Oestreich, C. P. Butts, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2007**, *129*, 502–503.

[22] R. Shintani, K. Moriya, T. Hayashi, *J. Am. Chem. Soc.* **2011**, *133*, 16440–16443.

Received: July 27, 2012
Published online: ■■ ■■, 0000

Chiral detectives: Borane-catalyzed imine hydrosilylation is investigated with the aid of an axially chiral borane (catalyst) and silane (reactant). Their uses in separate experiments as well as (mis)matched combinations offer conclusive evidence of a mechanism identical to that of related $B(C_6F_5)_3$-catalyzed carbonyl hydrosilylation. Both the borane and silane participate in the selectivity-determining hydride-transfer step (see figure).



Reaction Mechanisms

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Illuminating the Mechanism of the Borane-Catalyzed Hydrosilylation of Imines with Both an Axially Chiral Borane and Silane