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Immobilization of chiral phosphine ligands on silica gel by means of the allylsilane method and their use for catalytic asymmetric reactions

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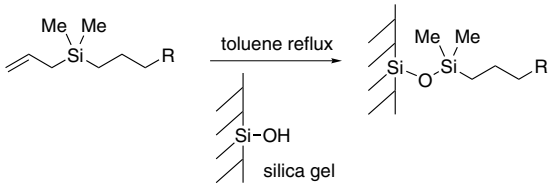
Abstract—Three chiral phosphine ligands containing an allylsilyl group at the terminus of the side chain were prepared and immobilized on a silica gel surface by use of the allylsilane modification method. The silica-supported chiral phosphine ligands were used for rhodium-catalyzed hydrogenation and palladium-catalyzed allylic alkylation and showed high enantioselectivity.

1. Introduction

We have recently reported a new method for the modification of silica gel surfaces by use of organic compounds containing an allylsilane moiety.[1] In contrast to the organosilicon compounds used for the modification, which are mostly those containing an alkoxy leaving group (R_nSiX_{4-n}: X = OR′),[2] the allylsilanes can be handled under hydrolytic conditions and can be purified by silica gel chromatography if necessary. Despite such stability, deallylation of the allylsilane takes place in refluxing toluene to form the Si–O–Si bond with the silicon on the silica gel (Scheme 1). Here we report the application of this allylsilane modification method to the immobilization of chiral phosphine ligands on silica gel surfaces and their use for some catalytic asymmetric reactions. The advantages of immobilized chiral catalysts are well-documented in literatures.[3]



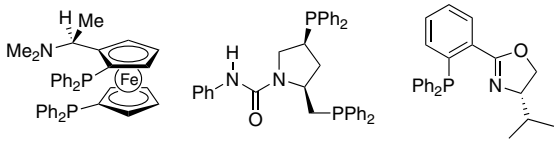
Scheme 1.

2. Results and discussion

2.1. Preparation of silica gel-supported chiral phosphine ligands

As chiral phosphine ligands to be immobilized on silica gel, we chose ferrocenylbisphosphine [(*S*)-(*R*)-bppfa],[4] bisphosphine derived from hydroxyproline [(2*S*,4*S*)-capp],[5] and phosphinooxazoline [(*S*)-*i*-Pr-phox][6] (Scheme 2), in addition to (*R*)-binap[7] whose immobilization has been already reported.[1]

We designed and prepared some allyl(dimethyl)(propyl)silanes bearing functionalized groups at the terminus of the propyl group (Scheme 3). They are expected to connect the chiral phosphine moiety with the allylsilyl group. The allylsilane containing 3-bromopropyl group **2** was prepared in a high yield by the iridium-catalyzed hydrosilylation of 2-propenyl bromide with methyldichlorosilane followed by treatment of the resulting 3-bromopropyldimethyl(chloro)silane **1** with the allyl Grignard reagent. *N*-Methyl-3-aminopropyldimethyl(allyl)silane **3** was obtained by the amination of



(*S*)-(*R*)-bppfa (2*S*,4*S*)-capp (*S*)-*i*-Pr-phox

Scheme 2.

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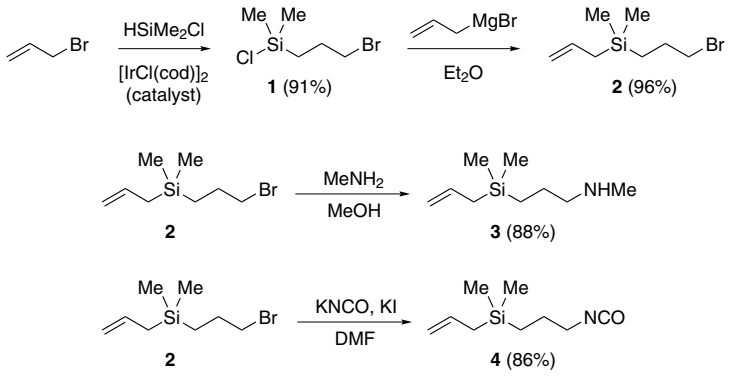
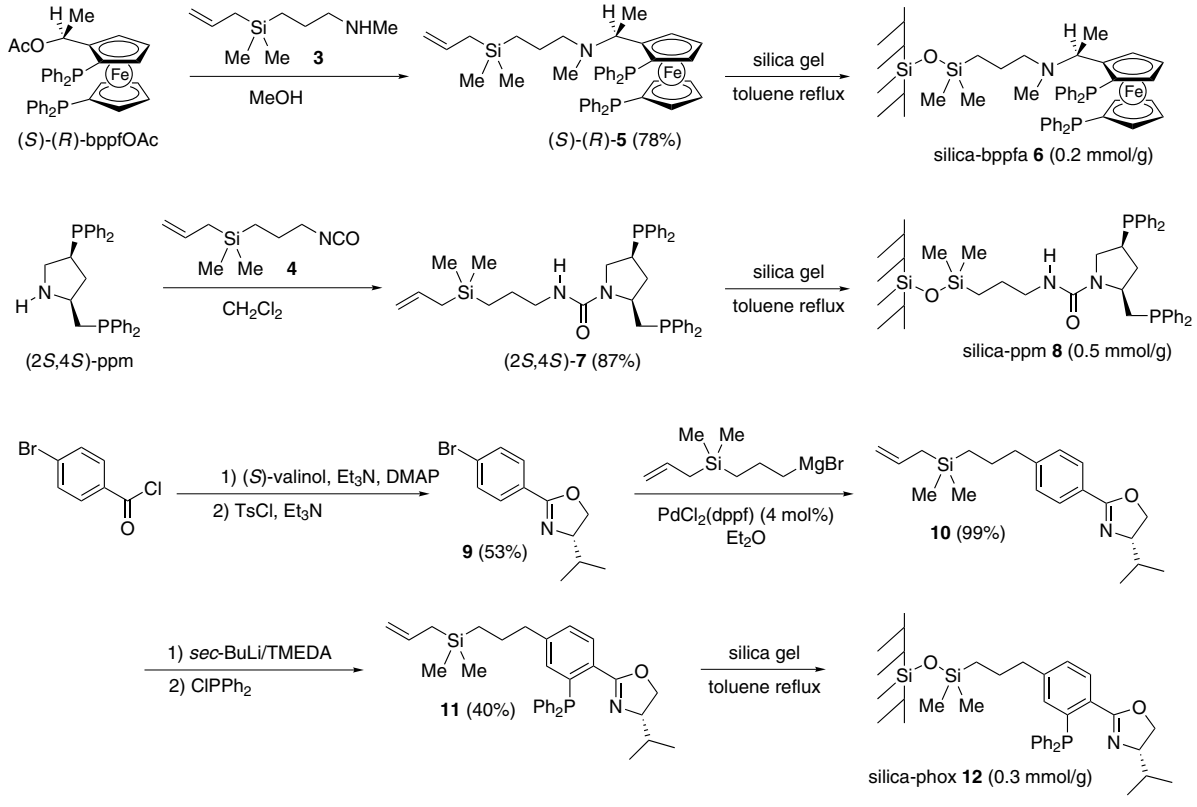


Scheme 3.

bromide **2** with methylamine in methanol. The substitution of bromide in **2** with potassium isocyanate was efficiently performed in the presence of potassium iodide in DMF to give 86% yield of the silylpropyl isocyanate **4**. The Grignard reagent generated from bromide **2** was also used for the introduction of the allylsilyl moiety on one of the chiral phosphines (vide supra).

Scheme 4 summarizes the connection of the allylsilane moiety with the three types of chiral phosphines shown above. It has been reported that the substitution of the acetoxy group in bppfOAc[4] with nucleophiles including amino groups takes place with retention of configuration at the ferrocenylmethyl position.[4] The nucleophilic substitution of (*S*)-(*R*)-bppfOAc with *N*-methyl-3-aminopropyldimethyl(allyl)silane **3** in refluxing methanol gave the ferrocenylbisphosphine bearing the allylsilyl group (*S*)-(*R*)-**5**, which was purified by silica gel chromatography (hexane/ethyl acetate = 4/1) keeping the allylsilane moiety intact. Treatment of the allylsilane (*S*)-(*R*)-**5** with an amorphous silica gel in toluene at reflux for 15 h gave silica-supported chiral phosphine (silica-bppfa **6**), which contains 0.2 mmol/g of the ferrocenylbisphosphine unit. A similar type of supported bppfa has been previously reported by Thomas and co-workers[8] to be obtained by use of a ferrocenylphosphine analogous to **5** but containing a trimethoxysilyl group in place of the allyldimethylsilyl group.

For connection of the pyrrolidinobisphosphine with the allylsilane moiety, isocyanate **4** was conveniently used. Thus, the reaction of (2*S*,4*S*)-ppm[5,9] with a slight excess



Scheme 4.

of isocyanate **4** in dichloromethane at room temperature gave, after purification by silica gel chromatography (hexane/ethyl acetate = 4/1), 87% yield of the pyrrolidinobisphosphine (2*S*,4*S*)-**7**, which possesses the allylsilyl group at the terminus of urea side chain. In a similar manner to the immobilization of **5**, allylsilane **7** was treated with silica gel in refluxing toluene to give silica-ppm **8** (0.5 mmol/g loading). The immobilization of pyrrolidinobisphosphine has been also reported by Pugin[10] using triethoxysilyl group for the connection with silica gel.

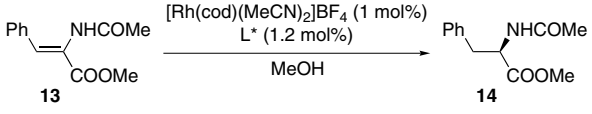
There have been no examples of solid support of phosphinooxazoline ligands represented by (*S*)-*i*-Pr-phox.[6] The key compound **11**, which is the phosphinooxazoline bearing allylsilyl group was prepared by way of the palladium-catalyzed Grignard cross-coupling of 3-(allyldimethylsilyl)propylmagnesium bromide. Thus, (*S*)-4-oxazolylbromobenzene derived from amide **9** was subjected to the cross-coupling in the presence of 4 mol% of $PdCl_2(dppf)$[11] to give a quantitative yield of the allylsilane **10**. Lithiation of **10** with *sec*-butyllithium and TMEDA in THF followed by addition of chlorodiphenylphosphine gave allylsilane-linked (*S*)-*i*-Pr-phox **11**. Silica gel-supported phosphinooxazoline (silica-phox **12**) (0.5 mmol/g loading) was obtained by the reaction with silica gel in a similar manner.

2.2. Catalytic asymmetric reactions using silica-supported chiral phosphine ligands

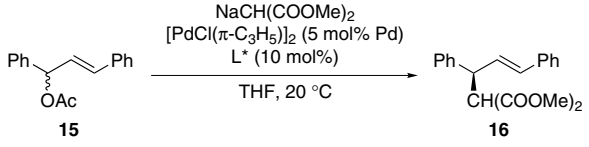
Rhodium-catalyzed asymmetric hydrogenation of methyl (*Z*)-α-(acetamido)cinnamate **13** was examined by use of silica-ppm **8** (Scheme 5, Table 1). A mixture of rhodium catalyst precursor $[Rh(cod)(MeCN)_2]BF_4$ (1 mol%), silica-ppm **8**, and **13** was stirred in methanol under 2 atm of hydrogen pressure for 10 h. The silica-rhodium catalyst was separated by decantation and the hydrogenation product *N*-acetylphenylalanine **14**, which is an *R* isomer of 93% ee, was obtained from the liquid phase in 97% isolated yield. The enantioselectivity is not lower than that reported with the silica-supported ppm ligand reported by Pugin.[10] The second run using the recovered silica catalyst was not as effective as the first run. The yield was lower even after a prolonged reaction time, although the enantioselectivity was kept high (entry 1). Addition of $[Rh(cod)(MeCN)_2]BF_4$ (0.5 mol%) at the second run recovered the catalytic activity of the silica-rhodium catalyst without loss of the enantioselectivity (entry 2).

The phosphinooxazoline ligand (*S*)-*i*-Pr-phox is known to be one of the most enantioselective ligands for the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate **15** with a malonate anion (Scheme 6).[6] The palladium catalyst coordinated with the silica-phox **12** showed high catalytic activity and enantioselectivity for the asymmetric allylic alkylation (Table 2). Thus, the reaction of **15** with a sodium salt of dimethyl malonate, generated from dimethyl malonate and sodium hydride in THF, was completed within 6 h at 20 °C in the presence of 5 mol% of the palladium catalyst prepared by mixing $[PdCl(\pi\text{-}C_3H_5)]_2$ with silica-phox **12**. After centrifuging and the removal of the solution phase with syringe, the recovered silica-phox **12**/palladium catalyst was used directly for the next run. From the solution phase, a quantitative yield of (*S*)-dimethyl 1,3-diphenyl-2-propenylmalonate **16** was obtained in 81% ee. Although the recovered silica-phox **12**/palladium catalyst was less active than the original catalyst, it gave (*S*)-**16** of the same or even higher enantiomeric purity at the second or third run.

To summarize, we have successfully applied our allylsilane modification method to the preparation of some silica-supported chiral phosphine ligands and used them as chiral ligands for rhodium-catalyzed asymmetric hydrogenation and palladium-catalyzed asymmetric



Scheme 5.



Scheme 6.

Table 1. Rhodium-catalyzed asymmetric hydrogenation of methyl (*Z*)-α-(acetamido)cinnamate **13** with silica-ppm **8**[a]

Entry	Ligand	Run	Time (h)	Yield[b] (%)	Ee (%)[c] (config)
1	Silica-ppm **8**	First	10	97	93 (*R*)
		Second	60	91	91 (*R*)
2	Silica-ppm **8**	First	10	98	93 (*R*)
		Second[d]	15	97	90 (*R*)
3	(2*S*,4*S*)-capp	First[e]	10	91	94 (*R*)

[a] The hydrogenation was carried out with **13** (0.70 mmol), $[Rh(cod)(MeCN)_2]BF_4$ (7.1 mmol), and silica-ppm **8** or (2*S*,4*S*)-capp (8.4 μmol) in 7.0 mL of methanol under 2 atm hydrogen. The catalyst recovered by decantation was used for the second run.

[b] Isolated yield by silica gel chromatography.

[c] Determined by HPLC with a chiral stationary phase column.

[d] $[Rh(cod)(MeCN)_2]BF_4$ (3.6 mmol) was added at the second run.

[e] Homogeneous reaction.

Table 2. Palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate **15** with dimethyl malonate in the presence of silica-phox **12**[a]

Entry	Ligand	Run	Time (h)	Conversion[b] (%)	Ee (%)[c] (config)
1	Silica-phox **12**	First	6	100	81 (*S*)
		Second	34	100	82 (*S*)
		Third	34	100	90 (*S*)
2	(*S*)-*i*-Pr-phox	First[d]	6	100	98 (*S*)

[a] The allylic alkylation was carried out with **15** (0.20 mmol), dimethyl sodiomalonate (0.60 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (10 mmol Pd), and silica-phox **13** or (*S*)-*i*-Pr-phox (20 mmol) in 2.0 mL of THF at 20 °C. The catalyst recovered by centrifuging was used for the next run.
[b] Determined by ^1H NMR spectra of the reaction mixture.
[c] Determined by HPLC with a chiral stationary phase column.
[d] Homogeneous reaction.

allylic alkylation. We are now in a position to immobilize various types of organic molecules on the silica support.

3. Experimental

3.1. General

All moisture sensitive manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5. NMR spectra were recorded on a JEOL JNM LA500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C, 100 MHz for ^{29}Si, and 200 MHz for ^{31}P). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H and ^{29}Si NMR, and chloroform-*d* (δ 77.0) for ^{13}C NMR and external 85% H_3PO_4 standard for ^{31}P NMR.

3.2. Materials

Silica gel (Davisil), with a particle diameter range of 100–200 mesh and a surface area of 480 m^2/g, was purchased from Aldrich. It was refluxed with concd HCl for 6 h, filtered, washed with water, and dried at 140 °C for 17 h under vacuum at 10^{-5} mmHg. (*S*)-(*R*)-bppfa,[4] (2*S*,4*S*)-capp,[5] $[IrCl(cod)]_2$,[12] (*S*)-1-[(*R*)-1′,2-bis(diphenylphosphino)ferrocenyl]-ethyl acetate [(*S*)-(*R*)-bppfOAc],[4] (2*S*,4*S*)-4-(diphenylphosphino)-2-[(diphenylphosphino)-methyl]pyrrolidine ((2*S*,4*S*)-ppm),[9] $PdCl_2$(dppf),[11] methyl (*Z*)-α-(acetamido)cinnamate **13**,[13] $[Rh(cod)(CH_3CN)_2]BF_4$,[14] (±)-1,3-diphenyl-2-propenyl acetate **15**,[15] $[PdCl(\pi\text{-}C_3H_5)]_2$[16] were prepared according to the reported procedures. 4-Brombenzoyl chloride was prepared from 4-bromobenzoic acid and thionyl chloride. (*S*)-(+)-2-Amino-3-methyl-1-butanol (*S*-valinol) was prepared by reduction of (*S*)-valine with $LiAlH_4$.

3.3. Preparation of 2-chloro(3-bromopropyl)dimethylsilane 1

This compound was prepared according to the reported procedures.[10,17] To a mixture of $[IrCl(cod)]_2$ (0.8 mg, 0.001 mmol Ir), allyl bromide (1.0 mL, 11.6 mmol), and 1,5-cyclooctadiene (5 μL, 0.04 mmol) was added chlorodimethylsilane (1.5 mL, 13.5 mmol) at 35 °C, and the mixture was stirred at 40 °C for 17 h. The mixture was distilled under reduced pressure to give 2.3 g (91% yield) of chloro(3-bromopropyl)dimethylsilane. ^1H NMR ($CDCl_3$) δ 0.44 (s, 6H), 0.96 (m, 2H), 1.97 (m, 2H), 3.43 (t, $J = 6.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 1.47, 17.97, 26.86, 35.27; ^{29}Si NMR ($CDCl_3$) δ 30.38. Anal. Calcd for $C_5H_{12}BrClSi$: C, 27.86; H, 5.61. Found: C, 27.65; H, 5.48.

3.4. Preparation of 2-propenyl(3-bromopropyl)dimethylsilane 2

To a solution of chloro(3-bromopropyl)dimethylsilane **1** (8.6 g, 40.0 mmol) in Et_2O (100 mL) was added allylmagnesium bromide in Et_2O (1 M, 50.0 mL, 50.0 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 11 h. The mixture was quenched with saturated ammonium chloride solution and extracted with Et_2O. The organic layer was washed with saturated sodium bicarbonate solution and brine. After drying over $MgSO_4$, the solvent was removed in vacuo and the residue was chromatographed on silica gel (hexane/ethyl acetate = 4/1) to give 8.40 g (96% yield) of 2-propenyl(3-bromopropyl)dimethylsilane **2**. ^1H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.64 (m, 2H), 1.53 (ddd, $J = 8.2$, 1.3, 1.1 Hz, 2H), 1.85 (m, 2H), 3.38 (t, $J = 7.2$ Hz, 2H), 4.84 (ddt, $J = 10.2$, 2.1, 1.0 Hz, 1H), 4.85 (ddt, $J = 16.9$, 2.0, 1.5 Hz, 1H), 5.77 (ddt, $J = 16.9$, 10.2, 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −3.89, 14.17, 23.04, 27.94, 35.85, 113.19, 134.21; ^{29}Si NMR ($CDCl_3$) δ 1.49. Anal. Calcd for $C_8H_{17}BrSi$: C, 43.44; H, 7.75. Found: C, 43.73; H, 7.74.

3.5. Preparation of 2-propenyl(3-methylaminopropyl)dimethylsilane 3

Prepared from 2-propenyl(3-bromopropyl)dimethylsilane **2** according to the procedure for amination of 3-chloropropyl group.[18] 2-Propenyl(3-bromopropyl)dimethylsilane (664 mg, 3.0 mmol) was stirred in a methanol solution of methylamine at 80 °C for 12 h. After removal of the solvent under reduced pressure, the residue was extracted with Et_2O. After drying over $MgSO_4$, organic solvent was removed in vacuo to give 569 mg (88% yield) of 2-propenyl(3-methylaminopropyl)dimethylsilane **3**. ^1H NMR ($CDCl_3$) δ −0.01 (s, 6H), 0.52 (m, 2H), 1.17 (br s, 1H), 1.48 (m, 2H), 1.52 (ddd, $J = 8.2$, 1.3, 1.0 Hz, 2H), 2.43 (s, 3H), 2.56 (t,

$J = 7.2$ Hz, 2H), 4.82 (ddt, $J = 10.0$, 2.2, 0.9 Hz, 1H), 4.84 (ddt, $J = 17.4$, 2.2, 1.4 Hz, 1H), 5.78 (ddt, $J = 17.0$, 10.2, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.75, 11.44, 22.33, 23.24, 35.38, 54.61, 111.95, 133.76; ^{29}Si NMR ($CDCl_3$) δ −0.21. Anal. Calcd for $C_9H_{21}NSi$: C, 63.08; H, 12.35; N, 8.17. Found: C, 62.90; H, 12.55; N, 8.07.

3.6. Preparation of 2-propenyl(3-isocyanatopropyl)-dimethylsilane 4

A mixture of 2-propenyl(3-bromopropyl)dimethylsilane **2** (1.1 g, 5.0 mmol) and potassium iodide (125 mg, 0.8 mmol) in 5 mL of DMF was heated at 100 °C for 0.5 h, followed by addition of potassium isocyanate (650 mg, 8.0 mmol). The mixture was heated at 100 °C for 0.5 h. After filtration of potassium chloride precipitates, the reaction mixture was distilled under vacuum to give 0.79 g (86% yield) of 2-propenyl(3-isocyanatopropyl)dimethylsilane **4**. ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 6H), 0.57 (m, 2H), 1.54 (ddd, $J = 8.1$, 1.2, 1.0 Hz, 2H), 1.62 (m, 2H), 3.26 (t, $J = 6.8$ Hz, 2H), 4.84 (ddt, $J = 10.2$, 2.2, 0.9 Hz, 1H), 4.89 (ddt, $J = 16.9$, 2.1, 1.4 Hz, 1H), 5.77 (ddt, $J = 16.9$, 10.3, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −3.70, 12.20, 23.28, 26.67, 46.27, 113.39, 122.14, 134.50; ^{29}Si NMR ($CDCl_3$) δ 1.71. Anal. Calcd for $C_9H_{17}ONSi$: C, 58.97; H, 9.35; N, 7.64. Found: C, 58.68; H, 9.48; N, 7.58.

3.7. Preparation of (*S*)-*N*-methyl–*N*-[3-((2-propenyl)dimethylsilyl)propyl]-1-[(*R*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine 5

Prepared from (*S*)-1-[(*R*)-1′,2-bis(diphenylphosphino)-ferrocenyl]ethyl acetate ((*S*)-(*R*)-bppfOAc) according to the procedure for amination of ferrocenylethyl acetate.[5] A mixture of (*S*)-1-[(*R*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethyl acetate [(*S*)-(*R*)-bppfOAc] (314 mg, 0.50 mmol) and 2-propenyl(3-methylaminopropyl)dimethylsilane **3** (857 mg, 5.0 mmol) in 1 mL of methanol was refluxed for 19 h. After removal of the solvent, the residue was purified by silica gel chromatography (hexane/ethyl acetate = 4/1) to give 290 mg (78% yield) of the title compound **5**. $[\alpha]_D^{20} = +297$ (*c* 0.51, chloroform); ^{1}H NMR ($CDCl_3$) δ −0.13 (s, 6H), 0.19 (m, 2H), 0.83 (m, 2H), 1.17 (d, $J = 6.8$ Hz, 3H), 1.40 (d, $J = 8.2$ Hz, 2H), 1.65 (s, 3H), 2.14 (m, 1H), 2.32 (m, 1H), 3.49 (s, 1H), 3.65 (s, 1H), 3.94 (s, 1H), 4.08 (dt, $J = 11.0$, 1.0 Hz, 2H), 4.18 (m, 1H), 4.38 (d, $J = 10.0$ Hz, 2H), 4.78–4.82 (m, 2H), 5.72 (ddt, $J = 18.8$, 10.8, 8.2 Hz, 1H), 7.06–7.10 (m, 2H), 7.14–7.16 (m, 3H), 7.22–7.31 (m, 13H), 7.50 (td, $J = 7.6$, 1.9 Hz, 2H); ^{29}Si NMR ($CDCl_3$) δ 1.50; ^{31}P NMR ($CDCl_3$) δ −16.76, −22.92. Anal. Calcd for $C_{45}H_{51}NP_2SiFe$: C, 71.89; H, 6.84; N, 1.86. Found: C, 71.82; H, 6.77; N, 1.67.

3.8. Preparation of (2*S*,4*S*)-*N*-[3-((2-propenyl)dimethylsilyl)propyl]-aminocarbonyl-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine 7

To a solution of (2*S*,4*S*)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine [(2*S*,4*S*)-ppm] (907 mg, 2.0 mmol) in 15 mL of dichloromethane was added 2-propenyl(3-isocyanatopropyl)dimethylsilane **4** (513 mg, 2.8 mmol), and the mixture was stirred at room temperature for 14 h. After removal of the solvent, the residue was purified by silica gel chromatography (hexane/ethyl acetate = 4/1) to give 1.1 g (87% yield) of the title compound **7**. $[\alpha]_D^{20} = -13$ (*c* 1.00, chloroform); ^{1}H NMR ($CDCl_3$) δ −0.03 (s, 6H), 0.43 (m, 2H), 1.37 (m, 2H), 1.49 (ddd, $J = 8.1$, 1.1, 1.0 Hz, 2H), 1.89 (m, 1H), 2.16 (ddd, $J = 13.5$, 10.2, 2.2 Hz, 1H), 2.31 (m, 1H), 2.83 (m, 1H), 3.00 (dt, $J = 13.5$, 3.2 Hz, 1H), 3.06 (m, 2H), 3.20 (q, $J = 9.6$ Hz, 1H), 3.57 (br t, $J = 8.3$ Hz, 1H), 3.88–3.94 (m, 2H), 4.77–4.83 (m, 2H), 5.74 (ddt, $J = 16.9$, 10.1, 8.2 Hz, 1H), 7.26–7.41 (m, 16H), 7.43–7.47 (m, 2H), 7.54–7.57 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −3.92, 11.86, 22.98, 24.69, 34.95 (d, $J_{C-P} = 13.4$ Hz), 35.44 (d, $J_{C-P} = 9.3$ Hz), 37.19 (dd, $J_{C-P} = 16.5$, 7.8 Hz), 43.65, 50.44 (d, $J_{C-P} = 27.9$ Hz), 56.02 (dd, $J_{C-P} = 20.6$, 6.8 Hz), 112.75, 128.17 (d, $J_{C-P} = 6.8$ Hz), 128.23, 128.39 (d, $J_{C-P} = 7.8$ Hz), 128.42, 128.47, 128.48, 128.55, 128.85, 132.57 (d, $J_{C-P} = 19.0$ Hz), 132.89 (d, $J_{C-P} = 19.1$ Hz), 132.94 (d, $J_{C-P} = 19.6$ Hz), 133.12 (d, $J_{C-P} = 19.0$ Hz), 134.57, 136.71 (d, $J_{C-P} = 12.4$ Hz), 137.07 (d, $J_{C-P} = 12.9$ Hz), 137.67 (d, $J_{C-P} = 12.9$ Hz), 138.98 (d, $J_{C-P} = 12.4$ Hz), 156.31; ^{29}Si NMR ($CDCl_3$) δ 1.67; ^{31}P NMR ($CDCl_3$) δ −8.06, −22.17. Anal. Calcd for $C_{38}H_{46}N_2OP_2Si$: C, 71.67; H, 7.28; N, 4.40. Found: C, 71.39; H, 7.31; N, 4.48.

3.9. Preparation of (*S*)-4-[4-(isopropyl)oxazol-2-yl]-1-bromobenzene 9

To a solution of (*S*)-(+)-2-amino-3-methyl-1-butanol (3.0 g, 30 mmol), triethylamine (4.0 g, 40 mmol), and 4-dimethylaminopyridine (122 mg, 1.0 mmol) in dichloromethane (30 mL) was added 4-brombenzoyl chloride (4.4 g, 20.0 mmol) at 0 °C, and the reaction mixture was stirred for 12 h at room temperature. The reaction mixture was quenched with saturated aqueous sodium bicarbonate, extracted with dichloromethane, and combined organic layer was dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/ethyl acetate = 1/1) to give 3.2 g (57% yield) of (*S*)-*N*-(1-hydroxymethyl-2-methylpropyl)-4′-bromophenyl-2-carboxylamide. $[\alpha]_D^{20} = -29$ (*c* 0.56, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.02 (d, $J = 6.9$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 2.02 (m, 1H), 2.31 (t, $J = 5.4$ Hz, 1H), 3.80–3.82 (m, 2H), 3.94 (m, 1H), 6.28 (br d, $J = 7.5$ Hz, 1H), 7.58 (d, $J = 8.6$ Hz, 2H), 7.65 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 19.03, 19.59, 29.26, 57.48, 63.86, 126.27, 128.54, 131.86, 133.38, 167.26. A solution of the amide thus obtained (4.72 g, 16.5 mmol), *p*-toluenesulfonyl chloride (3.50 g, 18.2 mmol), and triethylamine (8.35 g, 82.5 mmol) in dichloromethane (110 mL) was refluxed for 17 h. Then 1.0 mL of water was added and heating continued for an additional 1 h. The organic layer was washed with water and dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/ethyl acetate = 2/1) to give 4.1 g (93% yield) of the title compound **9**. $[\alpha]_D^{20} = -60$ (*c* 0.50, chloroform);

^{1}H NMR ($CDCl_3$) δ 0.92 (d, $J = 6.8$ Hz, 3H), 1.03 (d, $J = 6.7$ Hz, 3H), 1.85 (m, 1H), 4.06–4.15 (m, 2H), 4.41 (dd, $J = 9.3$, 8.0 Hz, 1H), 7.54 (ddd, $J = 8.7$, 2.3, 1.9 Hz, 2H), 7.81 (ddd, $J = 8.7$, 2.3, 1.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 18.10, 18.91, 32.81, 70.31, 72.72, 125.80, 126.90, 129.79, 131.52, 162.56. Anal. Calcd for $C_{12}H_{14}BrNO$: C, 53.75; H, 5.26; N, 5.22. Found: C, 53.64; H, 5.25; N, 5.25.

3.10. Preparation of 4-[3-((2-propenyl)dimethylsilyl)propyl]-(*S*)-1-[4-(isopropyl)oxazol-2-yl]benzene 10

A solution of 3-[(2-propenyl)dimethylsilyl]-propylmagnesium bromide was prepared in the usual manner from 547 mg (22.5 mmol) of magnesium and 1.6 g (7.5 mmol) of 2-propenyl(3-bromopropyl)dimethylsilane **2** in 2.5 mL of diethyl ether. To a suspension of (*S*)-4-[4-(isopropyl)oxazol-2-yl]-1-bromobenzene **9** (804 mg, 3.0 mmol) and $PdCl_2$(dppf) (66.0 mg, 0.12 mmol) in 40 mL of diethyl ether was added the Grignard solution, and the mixture was refluxed for 12 h. The reaction mixture was quenched with saturated aqueous ammonium chloride, extracted with diethyl ether, and combined organic layer was dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/ethyl acetate = 7/1) to give 980 mg (99% yield) of the title compound **10**. $[\alpha]_D^{20} = -43$ (*c* 0.51, chloroform); ^{1}H NMR ($CDCl_3$) δ −0.03 (s, 6H), 0.55 (m, 2H), 0.92 (d, $J = 6.7$ Hz, 3H), 1.03 (d, $J = 6.7$ Hz, 3H), 1.50 (ddd, $J = 8.2$, 1.3, 1.2 Hz, 2H), 1.62 (m, 2H), 1.86 (m, 1H), 2.65 (t, $J = 7.6$ Hz, 2H), 4.07–4.14 (m, 2H), 4.39 (td, $J = 7.5$, 1.1 Hz, 1H), 4.80 (ddt, $J = 10.2$, 2.3, 0.9 Hz, 1H), 4.82 (ddt, $J = 16.9$, 2.2, 1.5 Hz, 1H), 5.75 (ddt, $J = 16.9$, 10.2, 8.2 Hz, 1H), 7.20 (d, $J = 8.4$ Hz, 2H), 7.86 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −3.70, 14.86, 18.25, 19.10, 23.36, 25.92, 33.18, 40.05, 70.13, 72.93, 112.97, 125.87, 128.54, 128.56, 134.95, 146.12, 163.60; ^{29}Si NMR ($CDCl_3$) δ −0.76. Anal. Calcd for $C_{20}H_{31}NOSi$: C, 72.89; H, 9.48; N, 4.25. Found: C, 72.62; H, 9.48; N, 4.02.

3.11. Preparation of 4-[3-((2-propenyl)dimethylsilyl)propyl]-(*S*)-1-[4-(isopropyl)oxazol-2-yl]-2-(diphenylphosphino)benzene 11

To a mixture of 4-[3-((2-propenyl)dimethylsilyl)propyl]-(*S*)-1-[4-(isopropyl)oxazol-2-yl]benzene **10** (247 mg, 0.8 mmol) and TMEDA (221 mg, 1.9 mmol) in THF (150 mL) was added dropwise *sec*-butyllithium (1.5 mL, 1.5 mmol) in hexane at −96 °C. After the mixture was stirred for 2 h at −96 °C, chlorodiphenylphosphine (353 mg, 1.6 mmol) was added at this temperature. The reaction mixture was stirred for 2 h at −96 °C and then for 11 h at room temperature. The reaction mixture was quenched with saturated aqueous ammonium chloride, extracted with diethyl ether. The reaction was quenched by adding 5.0 g of dry silica gel via syringe and evaporation of the solvent under reduced pressure. The residue was chromatographed on silica gel (hexane/ethyl acetate = 4/1) to give 154 mg (40% yield) of the title compound **11**. Unreacted **10** (116 mg, 0.4 mmol) was recovered by silica gel chromatography. ^{1}H NMR ($CDCl_3$) δ −0.09 (s, 6H), 0.37 (m, 2H), 0.70 (d, $J = 6.9$ Hz, 3H), 0.80 (d, $J = 6.8$ Hz, 3H), 1.39 (m, 2H), 1.44 (d, $J = 8.2$ Hz, 2H), 1.47–1.52 (m, 1H), 2.44 (t, $J = 7.5$ Hz, 2H), 3.80–3.87 (m, 1H), 4.10–4.14 (m, 2H), 4.77–4.86 (m, 2H), 5.67–5.81 (m, 1H), 6.63 (dd, $J = 4.3$, 1.5 Hz, 1H), 7.13 (dd, $J = 8.5$, 1.3 Hz, 1H), 7.28–7.33 (m, 10H), 7.81 (dd, $J = 8.0$, 4.0 Hz, 1H); ^{31}P NMR ($CDCl_3$) δ −4.71.

3.12. Loading of phosphine ligands on silica gel

The loading was carried out according to the reported procedures.[1] A typical procedure is given for the preparation of silica-ppm **8**: To a suspension of dry silica gel (280 mg) in 7.0 mL of toluene was added **7** (900 mg, 1.4 mmol), and the mixture was refluxed for 15 h. The ppm-modified silica gel was filtered and dried at 120 °C under reduced pressure (0.2 mmHg) for 15 h. Elemental analysis: Found: C, 15.86; H, 1.74; N, 1.04. From the filtrates and extracts 832 mg (1.3 mmol) of **7** was recovered.

3.13. Rhodium-catalyzed heterogeneous asymmetric hydrogenation of a dehydroamino acid using silica-ppm 8

A typical procedure is given for the reaction of methyl (*Z*)-α-(acetamido)cinnamate **13** using silica-ppm **8** as ligand (Scheme 5, Table 1, entry 1): A mixture of silica-ppm **8** (16.8 mg, 8.4 μmol ppm), $[Rh(cod)(CH_3CN)_2]BF_4$ (2.4 mg, 7.1 μmol), and methyl (*Z*)-α-(acetamido)cinnamate **13** (212.0 mg, 0.70 mmol) in MeOH (7.0 mL) was stirred at room temperature for 10 h under 2 atm of hydrogen pressure. After releasing hydrogen gas, silica-ppm **8** was recovered by decantation and used directly for the second run. After evaporation of the solvent, the residue was chromatographed on silica gel (diethyl ether) to give **14** (207.3 mg, 97% yield). The enantiomeric purity was determined to be 93.3% ee by HPLC analysis with a chiral stationary phase column, Daicel Chiralcel OD-H (hexane/2-propanol = 9/1).

3.14. Palladium-catalyzed heterogeneous asymmetric allylic alkylation of (±)-1,3-diphenyl-2-propenyl acetate 15 using silica-phox 12

A typical procedure is given for the reaction of (±)-1,3-diphenyl-2-propenyl acetate **15** with dimethyl malonate using silica-phox **12** as ligand (Scheme 6, Table 2, entry 1): To a mixture of silica-phox **12** (67 mg, 20 μmol phox), $[PdCl(\pi\text{-}C_3H_5)]_2$ (1.8 mg, 10 μmol Pd), and (±)-1,3-diphenyl-2-propenyl acetate **15** (50.5 mg, 0.20 mmol) in 1.0 mL of THF was added a solution of dimethyl malonate (79.5 mg, 0.60 mmol) and sodium hydride (14.4 mg, 0.60 mmol) in THF (1.0 mL). The reaction mixture was stirred at 20 °C for 6 h. After centrifuging and the removal of the solution phase with syringe, the recovered silica-phox **12** was used directly for the next run. The separated solution phase was washed with

saturated sodium bicarbonate and dried over anhydrous magnesium sulfate. Chromatography on silica gel (hexane/ethyl acetate = 4/1) gave **16** (53.5 mg, 83% yield). The enantiomeric purity was determined to be 80.7% ee by HPLC analysis with a chiral stationary phase column, Daicel Chiralcel OD-H (hexane/2-propanol = 98/2).

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