

SPSiPs, A New Class of Biphosphine Ligands Based on SPSiOL with a Large Dihedral Angle

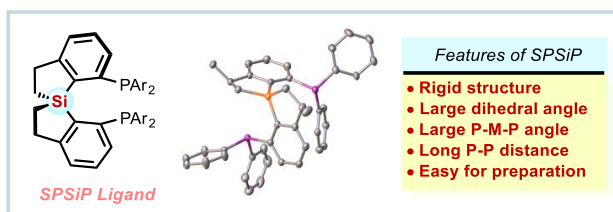
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Supporting Information Placeholder

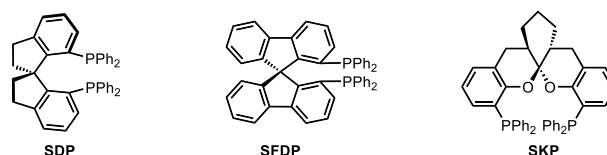


ABSTRACT: Here, we demonstrate the development and the synthetic applications of a novel class of diphosphine ligands (SPSiP) based on chiral spirocyclic diol (SPSiOL). Starting from SPSiOL, the biphosphine ligands could be readily prepared in three steps with high efficiency. This novel class of biphosphine ligands features rigid configuration, a large dihedral angle, a large P-M-P angle, and a long P-P distance, which might possess unique catalytic reactivities. The potentials of SPSiPs in asymmetric catalysis have also been preliminarily disclosed by Rh-catalyzed asymmetric hydrogenation, Rh-catalyzed tandem hydrosilylation, and Pd-catalyzed asymmetric allylic alkylation.

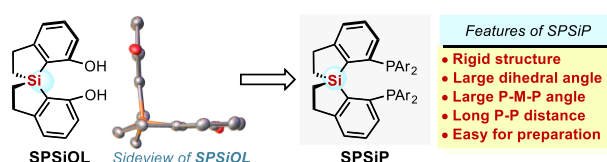
The chiral ligands have played indispensable roles in the transition-metal catalyzed asymmetric reactions, which could significantly modulate the reactivities and enhance the stereoselection.¹ Therefore, the design and development of new chiral ligands is crucial in the development of metal catalyzed asymmetric catalysis. Of the reported chiral ligands, diphosphine ligands are the most popular one with outstanding chiral induction ability in many different asymmetric reactions, and a large number of efficient chiral diphosphine ligands have been developed.² In this context, significant progresses have been made in the development of *C*₂-symmetric spirocycle-based diphosphine ligands pioneered by Zhou and coworkers³⁻⁷ in the last two decades. Given the rigid conformation of spirocyclic scaffold, a series of corresponding chiral diphosphine ligands, including SDP⁴, SFDP⁵, SKP⁶, and SPIRAP⁷ etc., have been prepared and applied in various transition-metal catalyzed asymmetric reactions with superb performance. However, the major progress relies on the use of carbon-centered spirocyclic scaffolds, and conformationally more constrained silicon-centered spirocycle-based diphosphine ligand is not disclosed to date.⁸ To further develop structurally tunable diphosphine ligands will merit the ligand and catalyst diversity,

Scheme 1. Synopsis for the Development of SPSiP Ligands.

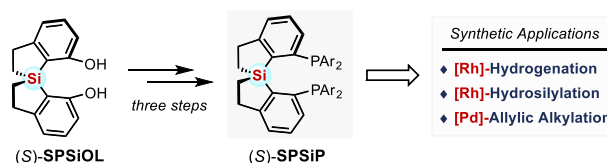
a. Previliged Spirocycle-Based Diphosphine Ligands



b. Design of Spirocycle-Based Bisphosphine Ligand



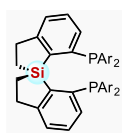
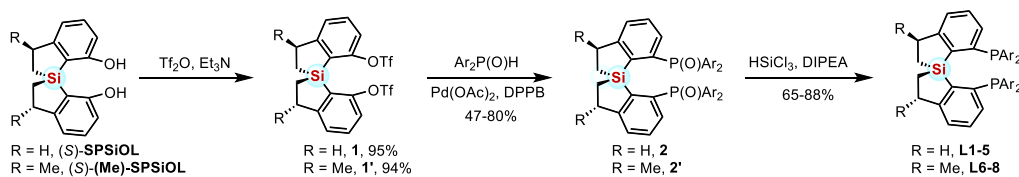
c. Preparation of SPSiPs and Their Synthetic Applications



thus bringing remarkable opportunities for novel asymmetric reaction development.

Recently, our group has proven the chiral spiroisilacyclic-based scaffolds are versatile architectures for chiral ligand development.⁹ Those spiroisilacyclic-based scaffolds are easy to prepare, and feature a longer C–Si bond, a larger Si atom radius, and a vertical and rigid configuration. For example, preliminary studies on SPSiOL-based SPSiPhos^{9a} and SPSiPO^{9c} ligands unveiled remarkable stereo-induction abilities in transition-metal catalysis. Based on the gained knowledges of SPSiOL (long O–O distance, 5.155 Å), we believe that the corresponding diphosphine ligands (SPSiP) should possess a constrained chiral-core with a large

Scheme 2. Preparation of SPSiP Ligands.



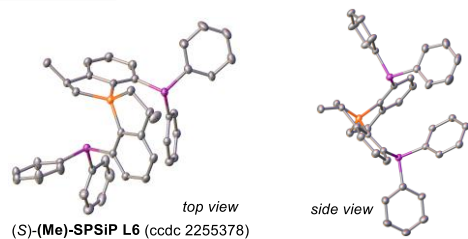
Ar = Ph
 p -CH₃C₆H₄-
 p -MeOC₆H₄-
3,5-(Me)₂C₆H₃-
3,5-(^tBu)₂C₆H₃-

SPSiP (L1), 77%
Tol-SPSiP (L2), 73%
An-SPSiP (L3), 67%
Xyl-SPSiP (L4), 71%
DTB-SPSiP (L5), 88%



Ar = Ph
 p -CH₃C₆H₄-
 p -MeOC₆H₄-

(Me)-SPSiP (L6), 83%
(Me)-Tol-SPSiP (L7), 77%
(Me)-An-SPSiP (L8), 65%



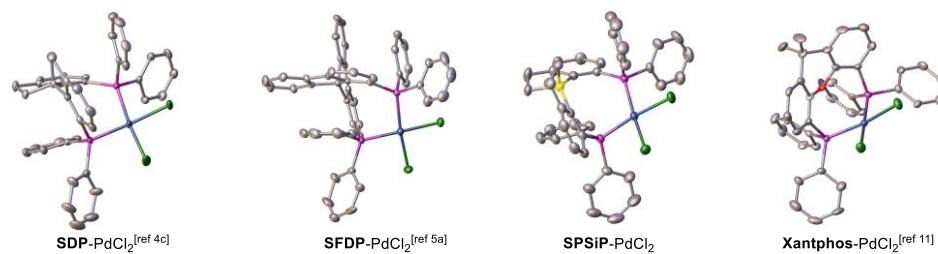
Diphosphine Ligand	(S)-SPSiOL ^[ref 9a]	(S)-(Me)-SPSiP
Length of Si-C or C-C [Å] ^[a]	1.86 (1.87)	1.84 (1.83)
Dihedral Angel [°] ^[b]	92.2	88.2
O-O or P-P distance [Å]	5.155	5.104

^[a]The length of Si-C bond or C-C bond at the phenol side;

^[b]Dihedral angel between the two phenol-side phenyl rings.

We first explored the preparation of SPSiP ligands from the enantiopure (S)-SPSiOLs. The corresponding (S)-SPSiOL triflate and (S)-(Me)-SPSiOL triflate could be readily accessed in 95% and 94% yields, respectively. Then, the installation of bis(diarylphosphine oxide) was achieved with Pd(OAc)₂/dppb as the combined catalyst in 47–80% yields. The reduction of bis(diarylphosphine oxide) (**2** and **2'**) with HSiCl₃ in the presence of DIPEA gave the (S)-SPSiP ligands (**L1-8**) in 65–88% yields. Notably, despite the installation of two diarylphosphines in axially chiral scaffolds normally requires a four-step procedure (install the phosphine oxide

Scheme 3. Structure Properties of SPSiP-PdCl₂ Complex.



Ligand-PdCl ₂	SDP-PdCl ₂	SFDP-PdCl ₂	SPSiP-PdCl ₂	Xantphos-PdCl ₂
∠ P-Pd-P [°]	96.01	96.62	102.71	101.19
Dihedral Angel [°] ^[a]	61.38	60.99	53.51	---
P-P distance [Å]	3.361	3.418	3.548	3.542
Pd-P distance [Å]	2.282 (2.241)	2.299 (2.279)	2.282 (2.260)	2.295 (2.289)

^[a]Dihedral angel between the two phosphine-side phenyl rings.

dihedral angle, a long P–P distance, which will result in a significantly larger P–M–P bite angle. Herein, we report our efforts on the preparation of SPSiP ligands and their synthetic applications. From enantiopure SPSiOL, the SPSiP ligands could be readily prepared in three steps in high efficiency. Preliminary studies unveiled that SPSiP ligands possess a large dihedral angle (88.2°), a large P–M–P bite angle (102.7°) and a long P–P distance (5.104 Å), which might have different catalytic properties in transition-metal catalyzed asymmetric reactions. The catalytic performance of SPSiPs has been evaluated in Rh-catalyzed asymmetric hydrogenation reaction, asymmetric tandem hydrosilylation, and Pd-catalyzed asymmetric allylic alkylation.

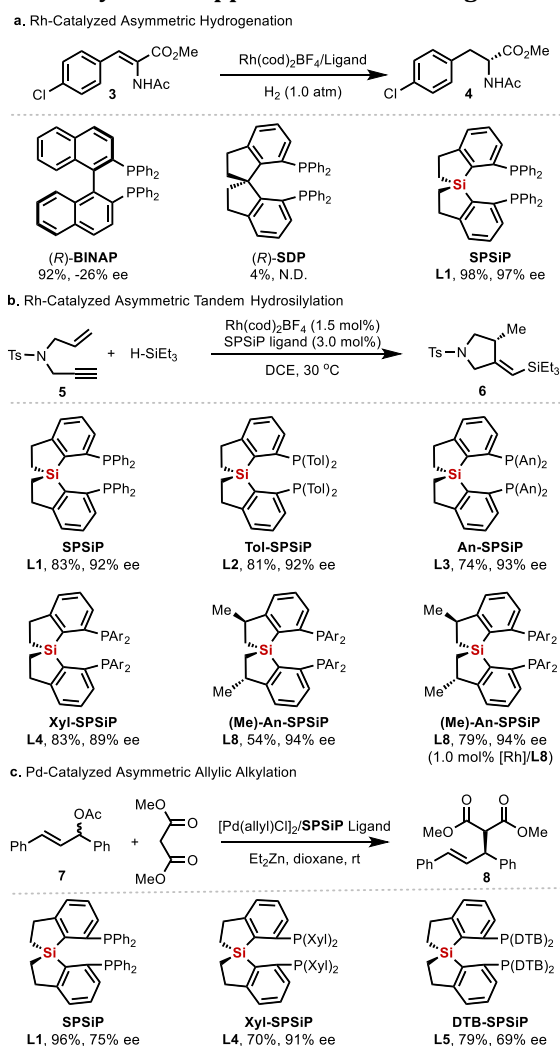
In the area of diphosphine ligand-involved transition metal-catalysis, the bite angle (P–M–P angle) has been well-recognized as one of the key geometric parameters for classification of the diphosphine ligands, as this value is related to profound differences in the performance of a metallic catalyst.¹⁰ Therefore, we next checked the corresponding P–M–P bite angle of our SPSiP ligands by obtaining its SPSiP–PdCl₂ complex, and the analysis of the structural parameters of its X-ray structure. As showed in Scheme 3, the P–Pd–P bite angle in SPSiP–PdCl₂ complex is significantly larger than that in SDP–PdCl₂ or SFDP–PdCl₂ complexes (102.7° vs 96.0° for SDP and 96.6° for SFDP), and the longer P–P distance was also observed (3.548 Å vs 3.361 Å and 3.418 Å). Interesting, the dihedral angle between the two-phosphine side phenyl rings in SPSiP–PdCl₂ complex is remarkable smaller than that in SDP–PdCl₂ or SFDP–PdCl₂ complexes (53.51° vs 61.38° for SDP and 60.99° for SFDP), probably due to the longer C–Si bond. This structural property might indicate a flexible chiral pocket which might be suitable for many asymmetric reactions, despite of the vertical configuration of SPSiP without the ligation of transition metals (dihedral angle, 88.2°, see Scheme 2). Notably, the structural properties of SPSiP–PdCl₂ complex are quite similar to that of Xantphos–PdCl₂ complex¹¹ with a similar P–Pd–P bite angle

(102.7° vs 101.2°) and a P–P distance (3.548 Å vs 3.542 Å), which might be seen as the three-dimensional version of two-dimensional Xantphos ligand.

To preliminarily check the potentials of the SPSiP ligands in asymmetric catalysis, the well-studied Rh-catalyzed asymmetric hydrogenation of dehydrogenative amino acids was first carried out (Scheme 4a). To our delighted, 97% ee was obtained with SPSiP **L1**, while the reaction with (*R*)-BINAP proceeded in high efficiency with low enantioselectivity. The hydrogenation barely occurred under the current conditions in the presence of (*R*)-SDP, highlighting the difference of SPSiP ligand with its carbon analogue. We next turned to evaluate a series of SPSiP ligands in the Rh-catalyzed asymmetric tandem hydrosilylation (Scheme 4b). The better performance on chiral induction was found with more electron-rich SPSiP ligand (**L3** vs **L1-2**). Moreover, the steric hinderance on the aryl motif of the ligand affect enantioselectivity and a slight decrease on ee value was observed with more steric hindered ligand **L4**. The highest enantioselectivity was found in the presence of (Me)-An-SPSiP (**L8**) albeit with a slighted lower reactivity. This result indicates our method^{9a} for preparation of SPSiOL could provide a new site on the ligand backbone for tuning the reactivities of chiral ligands. Delightedly, the yield could be improved to 79% with a low catalyst loading (1.0 mol% of Rh) when the reaction time was prolonged to 3 hours. Furthermore, Pd-catalyzed asymmetric allylic alkylation reaction was performed (Scheme 4c). Using the Xyl-SPSiP **L4** as the optimal ligand, we are pleased to find the reaction could proceed smoothly with 91% ee while the steric less hindrance SPSiP **L1** resulted in high yield (96%) with moderate ee value. These promising outcomes indicate the great potentials of SPSiP ligands in transition metal catalysis, and encourage us to further explore the applications in asymmetric catalysis.

In summary, we report the design, preparation, and preliminary applications of a new class of biphosphine ligands, SPSiPs. Detailed structure properties are presented by the analysis of their SPSiP–PdCl₂ complex. The ease of preparation, the availability of new sites for tuning, and the outstanding performance of (*S*)-SPSiP suggest that it could be a widely used and successful ligand in asymmetric catalysis. To develop efficient and highly stereoselective asymmetric reactions using SPSiP ligands is ongoing in our laboratory.

Scheme 4. Synthetic applications of SPSiP ligands.



ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its online Supporting Information.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, complete characterization data, copies of ¹H and ¹³C NMR spectra (PDF).

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Notes

P. Wang and Y. Wu are inventors on a patent related to this

work (CN114478632) filed by Shanghai Institute of Organic Chemistry (SIOC). The authors declare no other competing interests.

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