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Catalytic enantioselective *N*-silylation of sulfoximine

Xingfen Huang[a], Jiefeng Zhu[a], Chuan He[a,b,*]

[a] *Shenzhen Grubbs Institute and Department of Chemistry, Guangdong Provincial Key Laboratory of Catalysis, Southern University of Science and Technology, Shenzhen 518055, China*

[b] *Key Laboratory of Organosilicon Chemistry and Material Technology of Ministry of Education, Hangzhou Normal University, Hangzhou 311121, China*

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ABSTRACT

A rhodium/diphosphine-catalyzed asymmetric cross-dehydrogenative coupling between sulfoximines and dihydrosilanes has been achieved. This is the first report on the enantioselective *N*-silylation of sulfoximines. The protocol gives access to a variety of Si-stereogenic *N*-silylated sulfoximines in decent yield (up to 99%) with excellent stereoselectivity (up to 99%), featuring high atom economy, and a cleaner manner with H_2 as the sole byproduct. The obtained bis-Si-stereogenic monohydrosilane product can be further converted into the corresponding chiral polymer with pendant sulfoximine groups.

Sulfoximines, isosteres of sulfones, are valuable motifs in many scenarios [1–3]. Besides the traditional utilization as catalysts and ligands in synthetic chemistry [4–9], sulfoximines are also intensively investigated in medicinal chemistry as key pharmacophores (Scheme 1a, left) [10–14]. In addition, studies on sulfoximines have also branched out into materials science. For example, Takata and Bolm introduced sulfoximine units into polymers (Scheme 1a, middle) [15,16]; Yang *et al.* designed a sulfoximine unit as a new acceptor for thermally activated delayed fluorescence (TADF) emitters featuring tunable electron-accepting ability (Scheme 1a, right) [17,18]. What goes beyond sulfones is that sulfoximines can conveniently regulate physicochemical properties through N-H functionalization. Synthetic protocols for *N*-functionalization of sulfoximines have been widely explored, such as *N*-phosphorylation, acylation, halogenation, alkynylation, alkylation, arylation [19–22]. Despite vast established methods for N-H functionalization, *N*-silylation of sulfoximines has been less explored. Traditionally, chlorosilanes or silylamine reagents are used to conduct silylation of sulfoximines, which usually have problems due to the hygroscopically sensitive starting materials [23–27]. In 2015, Cheng and co-workers reported a direct oxidative cross-coupling reaction towards *N*-silylated sulfoximines *via* a copper-catalyzed *N*-silylation of sulfoximines with various 3° silanes in the presence of stoichiometric DTBP (Scheme 1b) [28].

To the best of our knowledge, the enantioselective *N*-silylation of sulfoximine is still unknown to date. In fact, there is currently a lack of an efficient catalytic asymmetric synthesis to access Si-stereogenic silylamine compounds. Few attempts could provide Si-stereogenic silylamine derivatives with enantiomeric excess of around 30% after stabilization *via* a one-pot deprotonation/boronation procedure [29,30]. The challenges may lie in the following aspects: (a) Si-N bond is usually unstable due to the high moisture sensitivity of silylamines [31–34]; (b) a longer Si-N bond (1.74 Å) compared with C-N bond (1.47 Å) would prevent the formation of compact transition states, making it difficult to achieve high enantiocontrol [35–38]. Given the unique properties and versatile utilities of both sulfoximines and Si-stereogenic silanes, the development of efficient enantioselective *N*-silylation of sulfoximine is highly demanded.

Owing to the electrostatic attractions between sulfur and nitrogen, as well as the severe lone-pair lone-pair repulsions between oxygen and nitrogen, NH in sulfoximine is acidic and the silylated Si-N bond is relatively stable for separation and identification [39]. Meanwhile, during the past few years, a handful of elegant methods have been developed for constructing Si-stereogenic centers [40–48], especially the direct desymmetrization of dihydrosilanes *via* catalytic asymmetric dehydrogenative coupling towards Si-stereogenic compounds (Si-CADC) [49–51]. Herein, we report a rhodium/diphosphine-catalyzed enantioselective *N*-silylation of sulfoximines. This protocol gives access to a variety of Si-stereogenic *N*-silylated sulfoximines in decent yield (up to 99%) with excellent stereoselectivity (up to 99%), featuring high atom

* Corresponding author at: Shenzhen Grubbs Institute and Department of Chemistry, Guangdong Provincial Key Laboratory of Catalysis, Southern University of Science and Technology, Shenzhen 518055, China.
E-mail address: hec@sustech.edu.cn (C. He).

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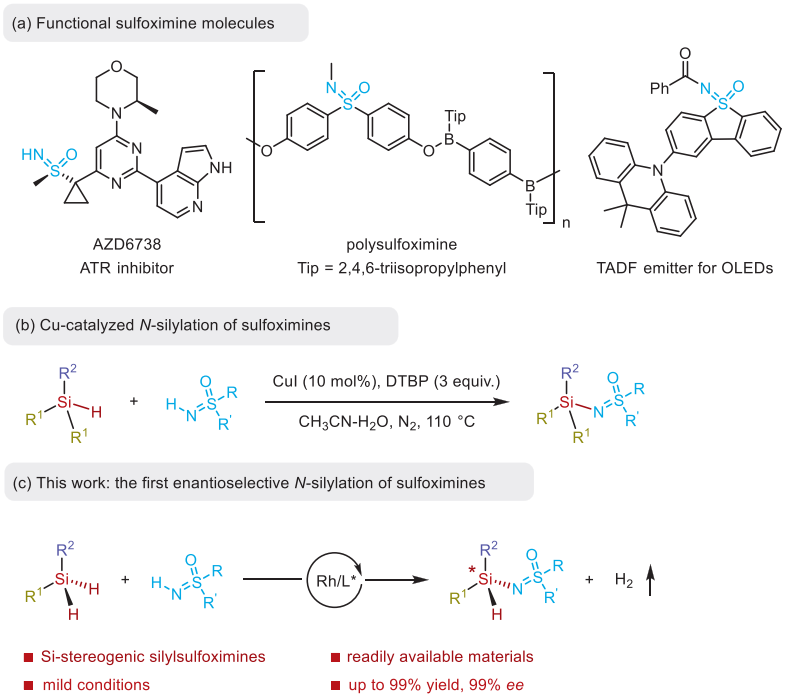


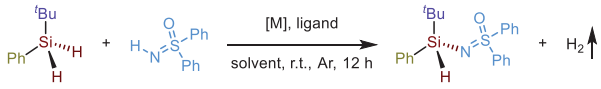
Scheme 1. Inspiration for enantioselective *N*-silylation of sulfoximine.

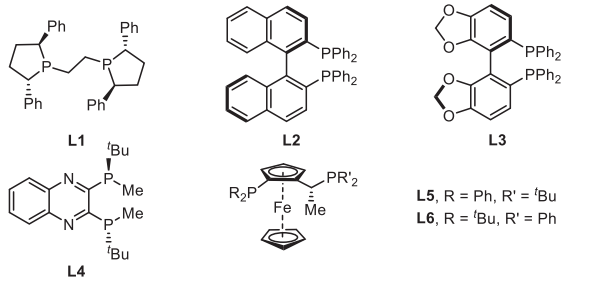
economy, and a cleaner manner with H_2 as the sole byproduct (Scheme 1c).

At the outset of our studies, we examined this cross-coupling reaction between *tert*-butylphenylsilane **1a** and diphenylsulfoximine **2a** using copper or rhodium as the catalyst with chiral phosphine ligands. Under copper catalysis, we could obtain good yields of the targeted cross-coupling product **3aa**, albeit with poor stereocontrol (Table 1, entries 1 and 2). When we moved on to rhodium catalyst, an obvious increase of enantioselectivity was observed using $[Rh(cod)Cl]_2$ combined with BINAP **L2** as the catalyst and chiral ligand respectively (Table 1, entry 4). To our delight, when Josiphos **L5** was applied with $[Rh(cod)Cl]_2$ in this reaction, both the yield and enantioselectivity could be obtained from moderate to good (Table 1, entry 7). Further switching the substituted groups on the phosphorus atoms of the Josiphos ligand, almost quantitative yield and enantiomeric excess (*ee*) were obtained (Table 1, entry 8). Under the rhodium-catalyzed conditions, other diphosphine ligands such as Ph-BPE **L1**, Segphos **L3**, and QuinoxP* **L4** gave barely stereocontrol with low to moderate yields (Table 1, entries 3, 5 and 6). More polar solvents such as THF, and DCE did not show a positive impact on the reaction (Table 1, entries 9 and 10). It is worth mentioning that, the reaction could proceed smoothly without the use of any ligand under $[Rh(cod)Cl]_2$-catalyzed conditions with a high yield (Table 1, entry 11). In summary, the best reaction conditions we identified is that starting material dihydrosilane **1a** and sulfoximine **2a** could react with each other to give desired coupling product **3aa** with both quantitative yield and *ee* in the presence of $[Rh(cod)Cl]_2$ catalyst with Josiphos **L6** as chiral ligand at room temperature in the solvent of toluene.

With the optimized conditions in hand, next we investigated the substrate scope to establish a general methodology for the construction of enantioenriched *N*-silylated sulfoximines (Scheme 2). First, functional group tolerance on the aromatic ring of dihydrosilane substrates was tested. Both electron-donating methyl (**1b**), methoxy (**1c**), trimethylsilyl (**1d**), and electron-withdrawing fluorine (**1e**), chlorine (**1f**) groups all proceeded robustly with diphenylsulfoximine **2a** to afford the corresponding

Table 1
Condition optimization.[a]

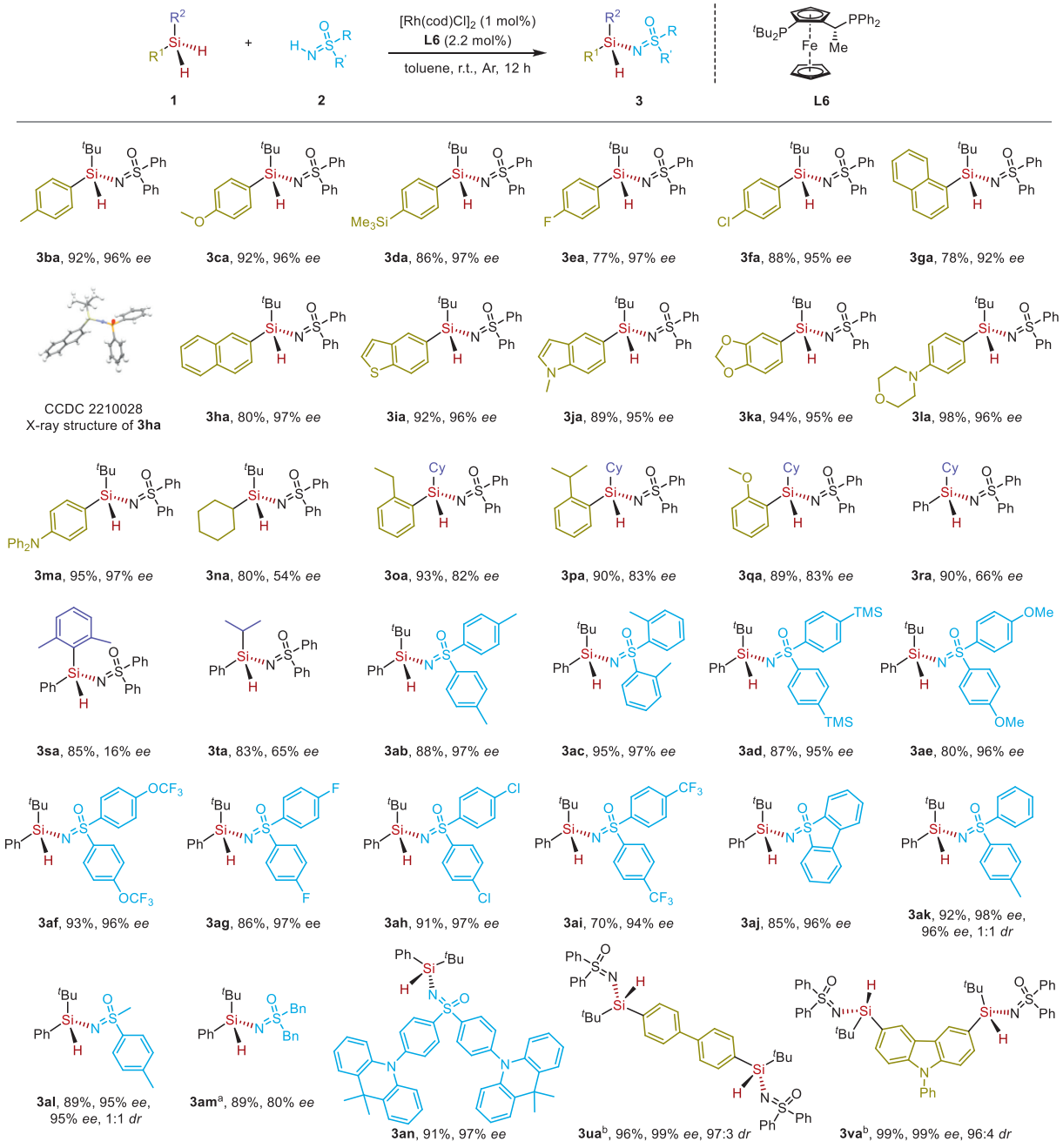




Entry	[M] (x mol%)	Ligand (x mol%)	Solvent	Yield (%)	*ee* (%)
1	$Cu(OAc)_2$ (5)	**L1** (6)	THF	88	30
2	$Cu(OAc)_2$ (5)	**L6** (6)	THF	86	15
3	$[Rh(cod)Cl]_2$ (1)	**L1** (2.2)	Toluene	75	1
4	$[Rh(cod)Cl]_2$ (1)	**L2** (2.2)	Toluene	42	62
5	$[Rh(cod)Cl]_2$ (1)	**L3** (2.2)	Toluene	71	10
6	$[Rh(cod)Cl]_2$ (1)	**L4** (2.2)	Toluene	12	0
7	$[Rh(cod)Cl]_2$ (1)	**L5** (2.2)	Toluene	73	78
8	$[Rh(cod)Cl]_2$ (1)	**L6** (2.2)	Toluene	98	98
9	$[Rh(cod)Cl]_2$ (1)	**L6** (2.2)	THF	60	95
10	$[Rh(cod)Cl]_2$ (1)	**L6** (2.2)	DCE	50	85
11	$[Rh(cod)Cl]_2$ (1)	-	Toluene	96	0

[a] **1a** (0.24 mmol), **2a** (0.2 mmol), in 2.0 mL solvent under argon atmosphere at room temperature for 12 h. Isolated yields. The *ee* values were determined by chiral HPLC.

silicon-stereogenic sulfoximine products **3ba**-**3fa** in good yields (77%-92%) with excellent enantioselectivities (95%-97% *ee*). Extended aromatic rings such as 1-naphthyl (**1g**), and 2-naphthyl (**1h**) groups were also well accommodated in this transformation. This catalytic system is also suitable for heterocycles such as ben-



Scheme 2. Substrate scope. Reaction conditions: **1** (0.24 mmol), **2** (0.2 mmol), $[Rh(cod)Cl]_2$ (1 mol%), **L6** (2.2 mol%) in 2.0 mL toluene under argon atmosphere at room temperature for 12 h, isolated yields. [a] Reacted for 36 h; [b] **1** (0.1 mmol), **2** (0.2 mmol), $[Rh(cod)Cl]_2$ (2 mol%), **L6** (4.4 mol%) in 2.0 mL toluene under argon atmosphere at room temperature for 12 h, isolated yields. X-ray crystallographic analysis of **3ha** allowed us to determine the absolute configuration, and configurations of the product **3** were assigned by analogy.

zothiophene (**1i**), indole (**1j**), and benzodioxole (**1k**), which provided the corresponding chiral *N*-silylated sulfoximine products with excellent yields (89%-94%) and stereoselectivities (95%-96% *ee*). Morpholine (**1l**) and triphenylamine (**1m**) units which frequently appeared in material molecules as donors also proceeded smoothly, and afforded the target products **3la** and **3ma** with almost quantitative yields and *ee*, indicating a promising application potential of this methodology in material area. Nonaromatic *tert*-butyl dihydrosilane substrate **1n** was submitted to the reaction, however, only 54% *ee* of the product **3na** was obtained. *Ortho*-substituted phenyl cyclohexyl dihydrosilanes maintained to give products **3oa**-**3qa** with good *ee* around 83%, while phenyl cyclohexyl dihydrosilane could only yield desired product **3ra** with 66% *ee*. Replacing the *tert*-butyl group with isopropyl, cyclohexyl, and 2,5-dimethylphenyl groups reduced the stereoselectivity comparing product **3aa** with **3ra**-**3ta**. Meanwhile, a range of diaryl sulfoximines **2b**-**2i** bearing electron-donating and withdrawing groups were tested in the reaction. The corresponding enantioenriched *N*-silylated sulfoximines **3ab**-**3ai** could be generated in decent yields with excellent *ee*. In addition, cyclic sulfoximine **2j** also went through the reaction smoothly without a significant drop in efficiency. Non-symmetric sulfoximines **2k** and **2l** functioned well under the catalytic conditions, but without the control of the sulfur-stereogenic center. Changing the phenyl substituent to benzyl group on sulfoximine (**2m**) reduced both the reactivity and enantioselectivity.

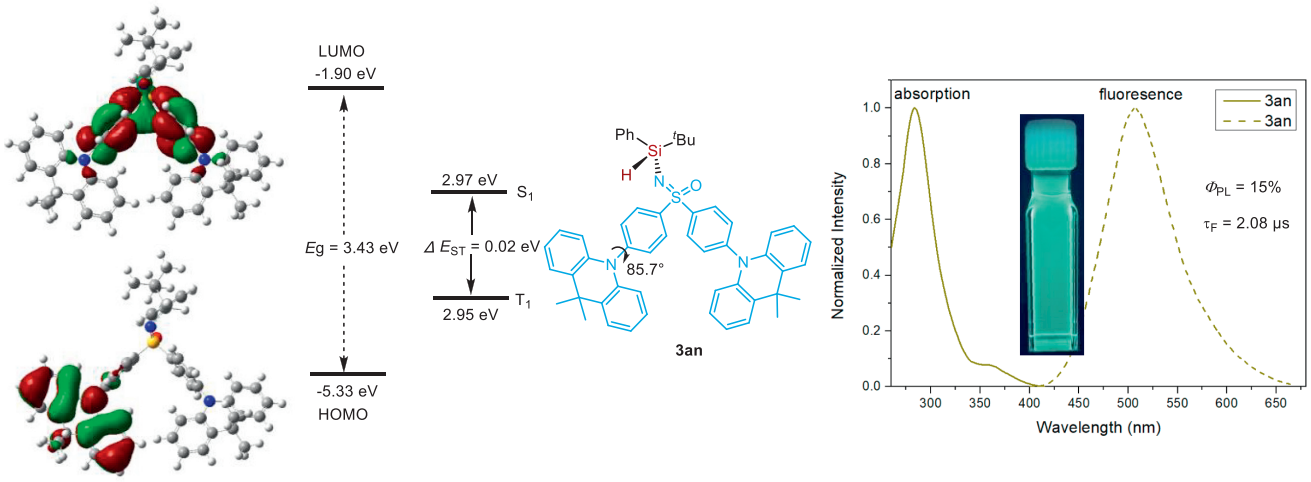
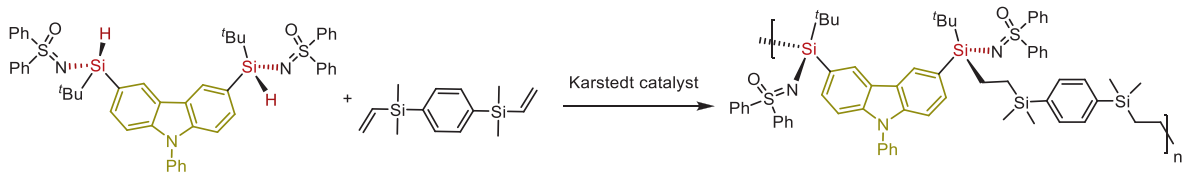


Fig. 1. DFT calculation and photophysical properties investigation of **3an** in CH_2Cl_2 (10^{-5} mol/L).



Scheme 3. Polymerization of bis-silicon-stereogenic sulfoximine. **3va** (0.1 mmol), 1,4-bis(dimethyl(vinyl)silyl)benzene (0.1 mmol) in THF (0.2 mol/L) with Karstedt catalyst (1 mol%) at 120 °C for 5 h, isolated yields; M_n and PDI were measured by GPC.

To illustrate the utility of this methodology, we designed a sulfoximine substrate **2n** featuring a 9,9-dimethyl-9,10-dihydroacridine unit as a typical donor (D) and a sulfoximine unit itself as an elegant acceptor (A). Under the standard reaction conditions, the corresponding enantioenriched *N*-silylated sulfoximine product **3an** was obtained in 91% yield with 97% *ee*. Molecular modeling of **3an** by DFT revealed an almost perpendicular D-A conformation with a dihedral angle of 85.7° in the ground state (Fig. 1). Efficient spatial separation of HOMO and LUMO distribution in the ground state, together with a small singlet-triplet energy gap (ΔE_{ST}) of 0.02 eV were disclosed by theoretical calculation. These properties showed a potential possibility for the entitled product to find utility in TADF materials [52–56]. Moreover, a microsecond level of fluorescent lifetime $\tau_F = 2.08$ μs for **3an** in CH_2Cl_2 (10^{-5} mol/L) was detected at room temperature (Section 6 in Supporting information). The photophysical properties of **3an** elucidate that the UV-vis absorption maxima and emission maxima of **3an** are around 284 and 504 nm, respectively, thus featuring a large Stokes shift of 220 nm. Meanwhile, Φ_{PL} of **3an** in CH_2Cl_2 (10^{-5} mol/L) at room temperature was measured to be 15% by integrating sphere.

To extend the scope of this enantioselective *N*-silylation of sulfoximines, we evaluated the reaction between bis-dihydrosilanes **1u**, **1v**, and sulfoximine **2a**. Under the standard conditions, the enantioenriched bis-silicon-stereogenic sulfoximine **3ua** and **3va** could be successfully obtained by the double dehydrogenative coupling reaction. Notably, the bis-silicon-stereogenic sulfoximine featuring Si-H bonds can readily be utilized as the chiral monomer for the polymerization reaction. Given the important application of sulfoximine unit, the direct transformation of bis-silicon-stereogenic sulfoximine **3va** into its corresponding polymer **4va** was conducted (Scheme 3). When **3va** and 1,4-bis(dimethyl(vinyl)silyl) benzene were charged with Karstedt catalyst in THF at 120 °C, the hydrosilylation polymerization proceeded efficiently providing the chiral polymer **4va** in 75% yield with number-average molecular weights $M_n = 7.3$ kg/mol, and small polymer dispersity index (PDI = 1.1). This chiral organosilicon polymer featuring sulfoximine pendants could be highly attractive to organic material chemists [57–61].

In summary, we have developed the first enantioselective *N*-silylation of sulfoximines *via* a rhodium/diphosphine-catalyzed asymmetric dehydrogenative cross-coupling, which gave access to a variety of chiral *N*-silylated sulfoximines featuring versatile Si-H bonds in good yields with excellent enantioselectivities. Sulfoximine featuring a D-A structure which frequently appeared as functional material fragments proceeded in this reaction smoothly. Moreover, chiral sulfoximine-containing polymer could be accessed conveniently from the enantiopure bis-Si-stereogenic *N*-silylated sulfoximine. We believe that this operational benign and effective methodology for constructing silicon-stereogenic *N*-silylated sulfoximines will embrace potential applications in different scenarios.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2023.108783.

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