Asymmetric Catalysis

Copper-Catalyzed Highly Enantioselective Carbenoid Insertion into Si-H Bonds**

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Chiral silanes are versatile intermediates for stereoselective transformations in organic synthesis.^[1] Transition-metal-catalyzed carbenoid insertion into Si-H bonds provides a direct and efficient method for the synthesis of silane-containing compounds.^[2] The most popular catalysts used in Si-H bondinsertion reactions have been copper(I) and rhodium(II) complexes.^[3] In 1996, Doyle and Moody^[4] reported the first asymmetric Si-H bond-insertion reaction of a-diazophenylacetates, catalyzed by a chiral dirhodium(II) carboxylate and carboxamidate complexes with moderate enantioselectivities (up to 47% ee). A year later, Davies and co-workers^[5] achieved high enantioselectivities (up to 95% ee) in the Si-H bond insertion of α -vinyldiazoacetates catalyzed by *N*-[*p*-(dodecylphenyl)-sulfonyl]prolinate. rhodium(II) Recently, Ge and Corey^[6] reported a Si-H bond insertion of an α -diazoketone with a N-nonafluorobutanesulfonylproline rhodium(II) catalyst to prepare 6-silyl-2-cyclohexenones with 94% ee. Several other chiral rhodium(II) catalysts have also been used in the Si-H bond-insertion reaction with different diazo compounds, with no marked improvement in enantiocontrol.^[7] Although copper catalysts had been applied to

Si–H bond-insertion reactions before rhodium catalysts,^[3] the copper-catalyzed asymmetric Si-H bond insertion has not been widely exploited. The only example of a coppercatalyzed asymmetric Si-H bond-insertion reaction was reported by Panek and Jacobsen.^[8] Using a copper chiral-Schiff-base complex as a catalyst, they obtained Si-H bondinsertion products in high yields with up to 88% ee, for the reaction of α -diazophenylacetate with trialkylsilanes. In previous studies, we accomplished highly enantioselective insertions of α-diazoesters into N-H bonds of anilines^[9] and O-H^[10] bonds of phenols and water, using copper complexes of chiral spiro-bisoxazoline ligands 1 (spirobox; Scheme 1). We report herein a copper/chiral spiro-diimine-complexcatalyzed asymmetric carbenoid insertion into the Si-H bond, with high yields and excellent enantioselectivities (up to 99% ee).

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Scheme 1. Copper-catalyzed insertion of α -diazoesters **3** into Si-H bonds. L = chiral spiro-bisoxazoline (spirobox) or spiro-diimine (SIDIM) ligand.

The reaction of methyl α -diazophenylacetate (3a) and dimethylphenylsilane (4a) was performed in CH₂Cl₂ at 25 °C with a copper catalyst generated in situ from 5 mol% CuCl and 6 mol% ligand. Firstly, we developed and examined various chiral spiro-bisoxazoline ligands (1a-d) (Scheme 1). All copper complexes of ligands 1a-d catalyzed the reaction, affording the Si-H insertion product methyl 2-dimethylphenvlsilyl-2-phenylacetate (5a), in high yields, with the ligand (R_a,S,S) -1a being the most enantioselective (81% ee)(Table 1, entry 2). Comparison of enantioselectivities of ligands (R_a, S, S) -1a and (S_a, S, S) -1a clearly revealed that the combination of chiralities in the ligand (R_a, S, S) -1 a is matched in terms of enantioselectivity (Table 1, entries 1 and 2). With ligand $(R_{a}S,S)$ -1a, the reaction conditions were then carefully optimized for maximum enantioselectivity. However, no additional positive effect was detected.

To further improve the enantioselectivity of the Si–H bond-insertion reaction, we turned our attention to new diimine ligands $2\mathbf{a}-\mathbf{e}$, incorporating a chiral spirobiindane backbone. The chiral spiro diimines $2\mathbf{a}-\mathbf{e}$ (abbreviated as SIDIM) were prepared by a facile condensation of enantiopure (*R*)-1,1'-spirobiindane-7,7'-diamine (*R*)-6^[11] with different aromatic aldehydes (Scheme 2, for detailed synthesis of ligands $2\mathbf{a}-\mathbf{e}$, see the Supporting Information).

Encouragingly, the SIDIM ligand (*R*)-**2a** had much higher activity and enantioselectivity than the spirobox ligands **1a–d** in the Si–H insertion reaction of methyl α -diazophenylacetate. The reaction was complete in 1 h at 0 °C, and the Si–H insertion product was obtained in 95% yield with 93% *ee*



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Table 1: Copper-catalyzed asymmetric Si–H insertion of methyl α -diazophenylacetate with dimethylphenylsilane: optimization of conditions.^[a]

	N ₂	Ma BhSi-H	5 mol% [Cu] 6 mol% L*		SiPhMe₂ ↓∗		
Ph	CO ₂ Me		CH_2CI_2		Ph ^C CO ₂ I	ı́ CO₂Me	
	3a	4a			5a		
Entry	Ligand	[Cu]	T [°C]	t [h]	Yield ^[b]	ee ^[c]	
	L*				[%]	[%]	
1	(S _a , S, S)- 1 a	CuCl/NaBAr	25	2	92	21	
2	$(R_a, S, S) - 1 a$	CuCl/NaBAr	25	2	95	81	
3	(R _a , S, S)- 1 b	CuCl/NaBAr _r	25	2	95	35	
4	(<i>R_a, S, S</i>)- 1 c	CuCl/NaBAr _r	25	2	96	71	
5	$(R_a, S, S) - 1 d$	CuCl/NaBAr	25	10	90	37	
6	(R)- 2 a	CuCl/NaBAr _r	. 0	1	95	93	
7	(R)- 2 b	CuCl/NaBAr _r	. 0	1	95	83	
8	(R)- 2 c	CuCl/NaBAr _r	. 0	10	93	78	
9	(R)- 2 d	CuCl/NaBAr _r	. 0	1	93	50	
10	(R)- 2 e	CuCl/NaBAr _r	. 0	10	92	69	
11	(R)- 2 a	Cu(OTf) ₂ /NaB/	Ar _F 0	1	95	93	
12	(R)- 2 a	Cu(OTf) ₂	0	1	93	93	
13	(R)- 2 a	(CuOTf) ₂ Tol	0	1	98	93	
14	(R)- 2 a	CuPF ₆ (MeCN))4 0	3	96	91	
15	(R)- 2 a	Cu(OTf) ₂	-40	5	95	97	
16	(R)- 2 a	Cu(OTf) ₂	-60	6	94	98	
17 ^[d]	(R)- 2 a	Cu(OTf) ₂	-40	20	85	93	

[a] Reaction conditions: [Cu] (0.01 mmol), ligand (0.012 mmol), and NaBAr_F (0.012 mmol, entries 1–11) were mixed in CH₂Cl₂ (2 mL) and stirred for 2 h at 25 °C. Dimethylphenylsilane (0.2 mmol) and methyl α -diazophenylacetate (0.2 mmol) were introduced and the mixture stirred at the specified temperature for the specified time. [b] Yield of isolated product. [c] Determined by chiral HPLC using a Chiralcel OD-H column. [d] With 1 mol% catalyst. Tol = toluene.



Scheme 2. Preparation of spiro-diimine ligand 2

(Table 1, entry 6). Other SIDIM ligands (2b-e), with different steric and electronic properties, however, had lower enantioselectivities in the Si-H insertion reaction (Table 1, entries 7-10). In our previous studies on the copper-catalyzed N-H and O-H bond-insertion reactions using spirobox ligands 1a-d, the additive $NaBAr_F$ (NaBAr_F = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate) played a crucial role for obtaining high reactivity and enantioselectivity.^[9,10] However, in the present case, NaBAr_F was found to be unnecessary in the coppercatalyzed Si-H insertion reaction with SIDIM ligand (R)-2a if an ionic catalyst-precursor was used. For example, the reactions catalyzed by $Cu(OTf)_2/(R)$ -2a took place smoothly with or without NaBAr_F and gave essentially identical results (Table 1, entries 11 and 12). In addition to $Cu(OTf)_2$, other copper salts such as CuOTf and CuPF₆ were also suitable catalyst precursors for this Si-H insertion reaction (Table 1, entries 13 and 14). By decreasing the reaction temperature to -40 °C or -60 °C, the enantioselectivity was further enhanced to 97% *ee* and 98% *ee*, respectively, albeit with a longer reaction time needed for full conversion (Table 1, entries 15 and 16). On reducing the catalyst loading to 1 mol%, the Si-H insertion product was obtained in 85% yield with a slightly lower enantioselectivity (93% *ee*, Table 1, entry 17). Solvents other than CH₂Cl₂ were also tested in this insertion reaction. However, none of them gave results superior to CH₂Cl₂ (data not shown).

A variety of α -diazoesters were examined as substrates for the Si-H insertion reaction with dimethylphenylsilane, under the optimal reaction conditions. All substrates reacted to produce the corresponding a-silylesters in high yields and excellent enantioselectivities (90-99% ee), regardless of the nature and the position of substituents on the phenyl ring of the diazoesters (Table 2, entries 1-22). However, the reactivity of the substrate was influenced by the electronic properties of substituents on the phenyl ring of the α -diazophenylacetates. α -Diazophenylacetates containing an electron-withdrawing group had lower reactivities and needed a higher reaction temperature (-40°C) for complete conversion (Table 2, entries 9-16). With the exception of triisopropylsilane, which was too sterically bulky to undergo Si-H insertion, other silanes, including triethylsilane, tripropylsilane, and diphenylmethylsilane, can be applied as a silane source in the reaction with α -diazoesters to afford the desired α -silvlesters in very high yields and enantiopurities. The α -aryl group in the diazoester substrate is vital for obtaining high yield and enantioselectivity. For example, the reactions of methyl α-diazopropionate with PhMe₂SiH and (o-Tol)-Me₂SiH gave the Si-H insertion products in very low yields and ee values (Table 2, entries 25 and 26). Similarly, the substrate α -allyldiazoacetate afforded a complicated mixture of products in the Si-H insertion reaction (Table 2, entry 24).

In summary, we have developed a highly efficient coppercatalyzed asymmetric carbenoid insertion into Si–H bonds. By using chiral spirodiimine ligands, a wide range of α -silylesters were produced in excellent yields and enantioselectivities. The results achieved in this study represented, to our knowledge, the highest level of enantiocontrol for a catalytic Si–H bond-insertion reaction and indicated high potential for wide-ranging applications of these novel diimine ligands in other carbenoid-insertion reactions.

Experimental Section

Typical procedure: In a Schlenk tube, under an argon atmosphere, $Cu(OTf)_2$ (3.6 mg, 0.01 mmol) and (*R*)-**2a** (6.8 mg, 0.012 mmol) dissolved in CH_2Cl_2 (2.0 mL). The mixture was stirred at room temperature for 2 h, and then cooled to -60 °C. Dimethylphenylsilane (28 mg, 0.2 mmol) and α -diazophenylacetate (35 mg, 0.2 mmol) were added sequentially and the mixture was stirred at -60 °C for approximately 6 h, until the diazo compound was consumed completely. The mixture was concentrated under reduced pressure without further workup and purified by chromatography on silica gel with petroleum ether/ethyl acetate (20:1, v/v). The product **5a** was isolated in 94 % yield as a colorless oil. Enantiomeric excess (98%)

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Table 2: Asymmetric catalytic carbenoid insertion into Si-H Bonds of silanes.^[a]

	$R^{1} CO_{2}R^{2} + 3$		6	5 mol% [Cu] 6 mol% (<i>R</i>)- 2a	SiR₃		
			+ R ₃ Si-H	CH ₂ Cl ₂		$_{2}R^{2}$	
			4		5		
Entry	R ¹	R ²	Silane	T [°C]	Product	Yield [%]	ee [%]
1	Ph	Me	PhMe₂SiH	-60	5 a	94	98
2	o-MeC ₆ H₄	Me	PhMe₂SiH	-60	5 b	91	96
3	o-MeOC ₆ H₄	Me	PhMe₂SiH	-60	5 c	89	90
4	m-MeC ₆ H ₄	Me	PhMe₂SiH	-60	5 d	95	99
5	p-MeC ₆ H ₄	Me	PhMe₂SiH	-60	5 e	97	97
6	m-MeOC ₆ H₄	Me	PhMe₂SiH	-60	5 f	89	98
7	p-MeOC ₆ H ₄	Me	PhMe₂SiH	-60	5 g	93	95
8	p-PhC ₆ H ₄	Me	PhMe₂SiH	-60	5 h	95	96
9	o-CIC ₆ H ₄	Me	PhMe₂SiH	-40	5 i	91	97
10	m-ClC ₆ H ₄	Me	PhMe₂SiH	-40	5 j	88	98
11	p-ClC ₆ H ₄	Me	PhMe₂SiH	-40	5 k	95	99
12	m-BrC ₆ H ₄	Me	PhMe₂SiH	-40	51	87	97
13	p-BrC ₆ H ₄	Me	PhMe₂SiH	-40	5 m	86	98
14	m-FC ₆ H ₄	Me	PhMe₂SiH	-40	5 n	85	97
15	p-FC ₆ H ₄	Me	PhMe₂SiH	-40	5 o	87	93
16	m-CF ₃ C ₆ H ₄	Me	PhMe₂SiH	-40	5 p	88	97
17	2-Naphthyl	Me	PhMe₂SiH	-60	5 q	92	98
18	Ph	Et	PhMe₂SiH	-60	5 r	92	98
19	Ph	<i>i</i> Pr	PhMe₂SiH	-60	5 s	95	97
20	Ph	Me	Et₃SiH	-60	5t	94	96
21	Ph	Me	<i>n</i> Pr₃SiH	-60	5 u	95	97
22	Ph	Me	Ph₂MeSiH	-60	5 v	88	93
23	Ph	Me	<i>i</i> Pr₃SiH	0–25	-	NR ^[b]	-
24	PhCH=CH	Et	PhMe₂SiH	0–25	_	ND ^[c]	-
25	Me	Et	PhMe₂SiH	-40	5 w	60	35
26	Me	Et	o-TolMe₂SiH	-40	5 x	14	12

[a] Reaction conditions were the same as those in Table 1, entry 16; $[Cu] = Cu(OTf)_2$. The reactions were run to completion in times of 2–12 h. For the characterization and analyses of *ee* values of Si–H insertion products, see the Supporting Information. [b] NR = no reaction. [c] ND = not determined.

was determined by chiral HPLC analysis using a Daicel Chiralcel OD-H column.

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