Asymmetric Catalysis

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

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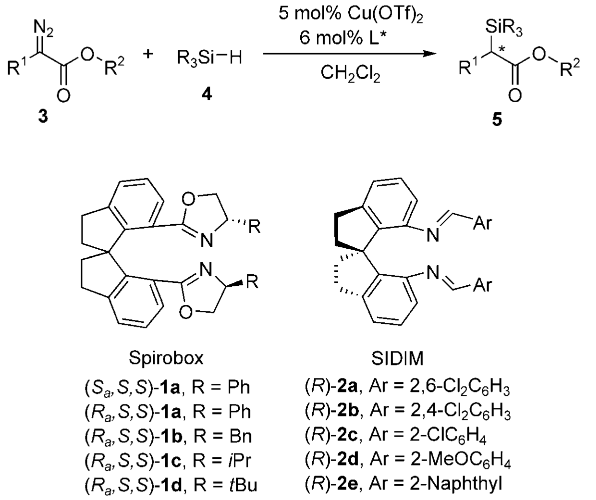
Chiral silanes are versatile intermediates for stereoselective transformations in organic synthesis.[1] Transition-metal-catalyzed carbenoid insertion into Si–H bonds provides a direct and efficient method for the synthesis of silane-containing compounds.[2] The most popular catalysts used in Si–H bond-insertion 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 α-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 rhodium(II) *N*-[*p*-(dodecylphenyl)-sulfonyl]prolinate. 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 copper-catalyzed 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 bond-insertion 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-complex-catalyzed asymmetric carbenoid insertion into the Si–H bond, with high yields and excellent enantioselectivities (up to 99% *ee*).



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 CH_2Cl_2 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-dimethylphenylsilyl-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*)-**1a** 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 **2a**–**e**, incorporating a chiral spirobiindane backbone. The chiral spiro diimines **2a**–**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 **2a**–**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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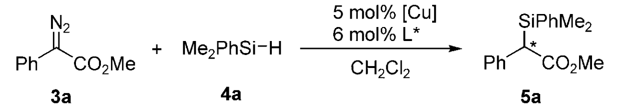
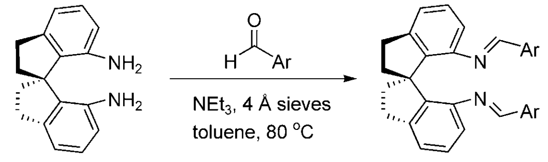
Table 1: Copper-catalyzed asymmetric Si−H insertion of methyl α-diazophenylacetate with dimethylphenylsilane: optimization of conditions.[a]



Entry	Ligand L*	[Cu]	T [°C]	t [h]	Yield[b] [%]	ee[c] [%]
1	(S_a,S,S)-**1a**	CuCl/NaBAr$_F$	25	2	92	21
2	(R_a,S,S)-**1a**	CuCl/NaBAr$_F$	25	2	95	81
3	(R_a,S,S)-**1b**	CuCl/NaBAr$_F$	25	2	95	35
4	(R_a,S,S)-**1c**	CuCl/NaBAr$_F$	25	2	96	71
5	(R_a,S,S)-**1d**	CuCl/NaBAr$_F$	25	10	90	37
6	(R)-**2a**	CuCl/NaBAr$_F$	0	1	95	93
7	(R)-**2b**	CuCl/NaBAr$_F$	0	1	95	83
8	(R)-**2c**	CuCl/NaBAr$_F$	0	10	93	78
9	(R)-**2d**	CuCl/NaBAr$_F$	0	1	93	50
10	(R)-**2e**	CuCl/NaBAr$_F$	0	10	92	69
11	(R)-**2a**	Cu(OTf)$_2$/NaBAr$_F$	0	1	95	93
12	(R)-**2a**	Cu(OTf)$_2$	0	1	93	93
13	(R)-**2a**	(CuOTf)$_2$ Tol	0	1	98	93
14	(R)-**2a**	CuPF$_6$(MeCN)$_4$	0	3	96	91
15	(R)-**2a**	Cu(OTf)$_2$	−40	5	95	97
16	(R)-**2a**	Cu(OTf)$_2$	−60	6	94	98
17[d]	(R)-**2a**	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 CH_2Cl_2 (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.



(*R*)-**6** (*R*)-**2**

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 copper-catalyzed 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 CuPF$_6$ 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 CH_2Cl_2 were also tested in this insertion reaction. However, none of them gave results superior to CH_2Cl_2 (data not shown).

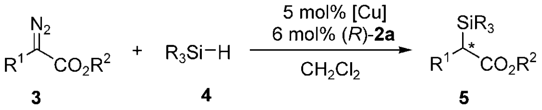
A variety of α-diazoesters were examined as substrates for the Si−H insertion reaction with dimethylphenylsilane, under the optimal reaction conditions. All substrates reacted to produce the corresponding α-silylesters in high yields and excellent enantioselectivities (90–99% *ee*), regardless of the 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-silylesters 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 $PhMe_2SiH$ and (*o*-Tol)-Me_2SiH 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 copper-catalyzed 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%)

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



Entry	R^1	R^2	Silane	*T* [°C]	Product	Yield [%]	*ee* [%]
1	Ph	Me	PhMe$_2$SiH	−60	**5a**	94	98
2	*o*-MeC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5b**	91	96
3	*o*-MeOC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5c**	89	90
4	*m*-MeC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5d**	95	99
5	*p*-MeC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5e**	97	97
6	*m*-MeOC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5f**	89	98
7	*p*-MeOC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5g**	93	95
8	*p*-PhC$_6$H$_4$	Me	PhMe$_2$SiH	−60	**5h**	95	96
9	*o*-ClC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5i**	91	97
10	*m*-ClC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5j**	88	98
11	*p*-ClC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5k**	95	99
12	*m*-BrC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5l**	87	97
13	*p*-BrC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5m**	86	98
14	*m*-FC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5n**	85	97
15	*p*-FC$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5o**	87	93
16	*m*-CF$_3$C$_6$H$_4$	Me	PhMe$_2$SiH	−40	**5p**	88	97
17	2-Naphthyl	Me	PhMe$_2$SiH	−60	**5q**	92	98
18	Ph	Et	PhMe$_2$SiH	−60	**5r**	92	98
19	Ph	*i*Pr	PhMe$_2$SiH	−60	**5s**	95	97
20	Ph	Me	Et$_3$SiH	−60	**5t**	94	96
21	Ph	Me	*n*Pr$_3$SiH	−60	**5u**	95	97
22	Ph	Me	Ph$_2$MeSiH	−60	**5v**	88	93
23	Ph	Me	*i*Pr$_3$SiH	0–25	–	NR[b]	–
24	PhCH=CH	Et	PhMe$_2$SiH	0–25	–	ND[c]	–
25	Me	Et	PhMe$_2$SiH	−40	**5w**	60	35
26	Me	Et	*o*-TolMe$_2$SiH	−40	**5x**	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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[1] I. Fleming, A. Barbero, D. Walter, *Chem. Rev.* **1997**, *97*, 2063.

[2] For reviews, see: a) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, **1998**; b) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911.

[3] For earlier examples of copper-catalyzed carbenoid insertions into Si–H bonds, see: a) F. Rijkens, M. J. Janssen, W. Drenth, G. J. M. van derKerk, *J. Organomet. Chem.* **1964**, *2*, 347; b) H. Watanabe, T. Nakano, K.-I. Araki, H. Matsumoto, Y. J. Nagai, *J. Organomet. Chem.* **1974**, *69*, 389; c) V. E. Baikov, L. P. Danilkina, K. A. Oglobin, *J. Gen. Chem.* **1981**, *51*, 1858. For earlier examples of rhodium-catalyzed carbenoid insertions into Si–H bonds, see: d) V. Bagheri, M. P. Doyle, J. Taunton, E. E. Claxton, *J. Org. Chem.* **1988**, *53*, 6158; e) O. Andrey, Y. Landai, D. Planchenault, *Tetrahedron Lett.* **1993**, *34*, 2977; f) Y. Landais, D. Planchenault, *Tetrahedron Lett.* **1994**, *35*, 9549; g) O. Andrey, Y. Landais, D. Planchenault, V. Weber, *Tetrahedron* **1995**, *51*, 12083.

[4] R. T. Buck, M. P. Doyle, M. J. Drysdale, L. Ferris, D. C. Forbes, D. Haigh, C. J. Moody, N. D. Pearson, Q.-L. Zhou, *Tetrahedron Lett.* **1996**, *37*, 7631.

[5] H. M. L. Davies, T. Hansen, J. Rutberg, P. R. Bruzinski, *Tetrahedron Lett.* **1997**, *38*, 1741.

[6] M. Ge, E. J. Corey, *Tetrahedron Lett.* **2006**, *47*, 2319.

[7] a) P. Bulugahapitiya, Y. Landais, L. Parra-Rapado, D. Planchenault, V. Weber, *J. Org. Chem.* **1997**, *62*, 1630; b) R. T. Buck, D. M. Coe, M. J. Drysdale, C. J. Moody, N. D. Pearson, *Tetrahedron Lett.* **1998**, *39*, 7181; c) S. Kitagaki, M. Kinoshita, M. Takeba, M. Anada, S. Hashimoto, *Tetrahedron: Asymmetry* **2000**, *11*, 3855; d) R. T. Buck, D. M. Coe, M. J. Drysdale, L. Ferris, D. Haigh, C. J. Moody, N. D. Pearson, J. B. Sanghera, *Tetrahedron: Asymmetry* **2003**, *14*, 791. For examples of diastereoselective Si–H bond insertion, see: e) Y. Landais, D. Planchenault, *Tetrahedron Lett.* **1994**, *35*, 4565; f) Y. Landais, D. Planchenault, V. Weber, *Tetrahedron Lett.* **1994**, *35*, 9549.

[8] a) L. A. Dakin, S. E. Schaus, E. N. Jacobsen, J. S. Panek, *Tetrahedron Lett.* **1998**, *39*, 8947; b) L. A. Dakin, P. C. Ong, J. S. Panek, R. J. Staples, P. Stavropoulos, *Organometallics* **2000**, *19*, 2896.

[9] B. Liu, S.-F. Zhu, W. Zhang, C. Chen, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, *129*, 5834.

[10] a) C. Chen, S.-F. Zhu, B. Liu, L.-X. Wang, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, *129*, 12616; b) S.-F. Zhu, C. Chen, Y. Cai, O.-L. Zhou, *Angew. Chem.* **2008**, *120*, 946; *Angew. Chem. Int. Ed.* **2008**, *47*, 932.

[11] C. Chen, S.-F. Zhu, X.-Y. Wu, Q.-L. Zhou, *Tetrahedron: Asymmetry* **2006**, *17*, 2761.