

## Iridium(III)-Catalyzed Enantioselective Si–H Bond Insertion and Formation of an Enantioenriched Silicon Center

Yoichi Yasutomi, Hidehiro Suematsu, and Tsutomu Katsuki\*

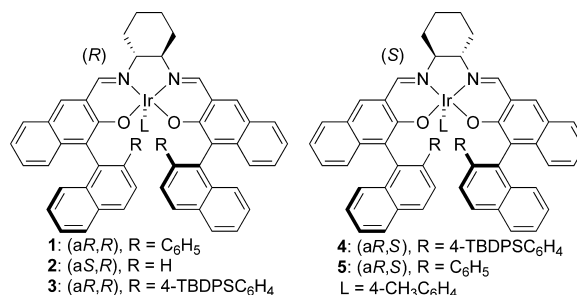
Department of Chemistry, Faculty of Science, Graduate School, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

Received October 14, 2009; E-mail: katsuscc@chem.kyushu-univ.jp

Recently, synthetic application of the compounds possessing silyl group(s) has been rapidly increasing,<sup>1</sup> and the development of their efficient synthesis is a topic of interest. Although various methods are available for the preparation of silyl compounds, asymmetric Si–H functionalization is a direct method for the preparation of chiral compounds possessing silyl group(s). In particular, asymmetric Si–H insertion of a metal carbenoid derived from  $\alpha$ -diazocarbonyl compounds is a potentially attractive route to produce chiral  $\alpha$ -silylcarbonyl compounds.<sup>2</sup> To date, copper(I) and rhodium(II) complexes have been widely used as the catalyst for this type of reaction. In 1996, Doyle and Moody reported a seminal study on enantioselective Si–H bond insertion with chiral dirhodium(II) catalysts in the presence of  $\alpha$ -phenyl- $\alpha$ -diazacetate, albeit with moderate selectivity.<sup>3,4</sup> Subsequent to this, Davies and co-workers reported that Si–H insertion of  $\alpha$ -alkenyl- $\alpha$ -diazacetate catalyzed by the rhodium(II) (*S*)-*N*-[*p*-(dodecylphenyl)sulfonyl]proline complex proceeded with good to high enantioselectivity (77–95% ee).<sup>5</sup> Panek and Jacobsen reported that a chiral copper-Schiff base complex catalyzed Si–H insertion using  $\alpha$ -phenyl- $\alpha$ -diazacetate with moderate to good yield and enantioselectivity (up to 88% ee).<sup>6</sup> Ge and Corey reported that a *N*-nonafluorobutane-sulfonylproline rhodium(II) complex was a good catalyst for Si–H insertion using  $\alpha$ -diazocyclohexenone derivatives.<sup>7</sup> Moreover, Zhou and co-workers reported that a copper/chiral spiro-diimine catalyst showed high enantioselectivity (93–99% ee) in the Si–H insertion using  $\text{ArC}(\text{N}_2)\text{CO}_2\text{Me}$ , while the reaction with  $\text{MeC}(\text{N}_2)\text{CO}_2\text{Et}$  had modest enantioselectivity and a moderate yield.<sup>8</sup> Still, the reaction using  $\text{RC}(\text{N}_2)\text{CO}_2\text{Et}$  (*R* = acyclic alkyl group) that readily undergoes  $\beta$ -hydride elimination<sup>2a,9</sup> is a challenging research target.<sup>8,10</sup>

We have recently discovered that iridium(III)-salen complexes (Figure 1) show potent carbene-transfer catalysis. The iridium-salen complex **1** catalyzes cyclopropanation of a variety of olefins using an  $\alpha$ -diazacetate with high *cis*- and enantioselectivity,<sup>11a,b</sup> while the reactions using a vinyl diazylactone show high *trans*- and enantioselectivity.<sup>11c</sup> Moreover, complexes **1** and **2** catalyze highly enantioselective C–H insertion using either  $\alpha$ -aryl- or  $\alpha$ -methyl-substituted  $\alpha$ -diazacetates.<sup>12</sup> These results suggested that an appropriate iridium-salen complex could regulate the conformation of the carbenoid intermediate, so as to prevent the competitive  $\beta$ -hydride elimination. Herein, we communicate the first iridium catalyzed asymmetric carbenoid insertion into a Si–H bond and the formation of a highly enantioenriched silicon center.

We initially examined the reaction of dimethylphenylsilane and ethyl  $\alpha$ -diazopropionate in the presence of complex **1** at 0 °C in dichloromethane (Table 1). The desired Si–H insertion occurred preferentially, and elimination proceeded slowly under the conditions (entry 1). The undesired  $\beta$ -hydride elimination was significantly suppressed at lower temperature, but the enantioselectivity was not much improved (entries 2 and 3). Considering the difference



in bond length and bond energy between C–H and Si–H bonds,<sup>1d</sup> we expected that the complexes having a higher molecular recognition ability would serve as an efficient catalyst for this reaction. Thus, we further examined the reaction at –78 °C with iridium complexes (**3** and **4**) that bear a concave-shaped salen ligand.<sup>13</sup> While the enantioselectivity was moderately increased by using **3** (entry 4), significant improvement to 97% ee was achieved by using **4** (entry 5). The reaction of *tert*-butyl  $\alpha$ -diazopropionate proceeded with high enantioselectivity in a good yield (entry 6). The insertion to *o*-tolyl dimethylsilane also proceeded equally efficiently (entry 7). Moreover, the reaction of *tert*-butyl  $\alpha$ -diazobutanoate proceeded with a high enantioselectivity of 97%, though the yield was moderate because of the formation of *tert*-butyl (*Z*)-2-butenate (entry 8).<sup>14</sup>

**Table 1.** Asymmetric Si–H Insertion with  $\alpha$ -Alkyl- $\alpha$ -Diazacetate<sup>a</sup>

$\text{ArMe}_2\text{Si-H} + \text{R}^1\text{C}(\text{CO}_2\text{R}^2)=\text{N}_2 \xrightarrow[\text{CH}_2\text{Cl}_2, \text{MS 4A, -78}^\circ\text{C, 24 h}]{\text{Ir(salen) (2.0 mol\%)}} \text{ArMe}_2\text{Si}(\text{H})\text{C}(\text{R}^1)\text{CO}_2\text{R}^2$ <b>6a-d</b>								
entry	cat.	prod.	Ar	R <sup>1</sup>	R <sup>2</sup>	% yield <sup>b</sup>	% ee <sup>c</sup>	
1 <sup>d</sup>	<b>1</b>	<b>6a</b>	Ph	Me	Et	71(86)	41 <sup>e</sup>	
2 <sup>f</sup>	<b>1</b>	<b>6a</b>	Ph	Me	Et	83(96)	37 <sup>e</sup>	
3	<b>1</b>	<b>6a</b>	Ph	Me	Et	89(98)	51 <sup>e</sup>	
4	<b>3</b>	<b>6a</b>	Ph	Me	Et	85	73 <sup>e</sup>	
5	<b>4</b>	<b>6a</b>	Ph	Me	Et	85	97	
6	<b>4</b>	<b>6b</b>	Ph	Me	<i>t</i> Bu	88	97	
7	<b>4</b>	<b>6c</b>	<i>o</i> -tol	Me	Et	85	98	
8	<b>4</b>	<b>6d</b>	Ph	Et	<i>t</i> Bu	47	97	

<sup>a</sup> Reaction was carried out on a 0.3 mmol scale. <sup>b</sup> Isolated yield. The value in the parentheses is the yield determined by <sup>1</sup>H NMR analysis with 1-bromonaphthalene as an internal standard. <sup>c</sup> Determined by HPLC analysis. <sup>d</sup> Run at 0 °C. <sup>e</sup> The major product is an enantiomer of the major product obtained with **4** as catalyst. <sup>f</sup> Run at –30 °C.

Although Si–H insertion reactions shown in Table 1 proceeded with excellent enantioselectivity, chirality was induced only on the carbon atom of the resultant Si–C bond. However, if the silane compound is prochiral, chirality should be induced also on the silicon atom<sup>15</sup> and provide a pair of diastereomers. To explore this possibility, we examined the reaction between prochiral (1-

**Table 2.** Construction of Chiral Silicon Atom<sup>a</sup>

$\text{Ph-Si-H} + \text{Me-CO}_2^t\text{Bu} \xrightarrow[\text{CH}_2\text{Cl}_2, \text{MS 4A}, -78^\circ\text{C}, 24 \text{ h}]{\text{Ir(salen)} (2.0 \text{ mol}\%), \text{N}_2} \text{Ph-Si-H-CO}_2^t\text{Bu} \quad \mathbf{6e-h}$						
(3.0 equiv.)	(1.0 equiv.)					
entry	cat.	prod.	R	% yield <sup>b</sup>	% de <sup>c</sup>	% ee <sup>d</sup>
1	<b>4</b>	<b>6e</b>	1-Np	73	85	94
2	<b>5</b>	<b>6e</b>	1-Np	86	92	99
3	<b>5</b>	<b>6f</b>	2,6-Xy	69	99	>99
4	<b>5</b>	<b>6g</b>	iPr	83	84	94
5	<b>5</b>	<b>6h</b>	Cy	74	86	95

<sup>a</sup> Reaction was carried on a 0.3 mmol scale. <sup>b</sup> Isolated yield. <sup>c</sup> Determined by <sup>1</sup>H NMR analysis. <sup>d</sup> Determined by HPLC analysis. 1-Np = 1-Naphthyl; 2,6-Xy = 2,6-Xylyl; Cy = Cyclohexyl.

**Table 3.** Asymmetric Si–H Insertion with  $\alpha$ -Aryl- $\alpha$ -Diazoacetates<sup>a</sup>

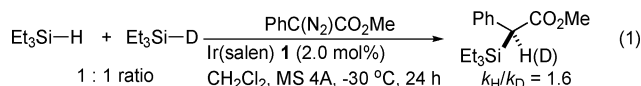
$\text{R}^1\text{Si-H} + \text{R}^2\text{-CO}_2\text{Me} \xrightarrow[\text{CH}_2\text{Cl}_2, \text{MS 4A}, -30^\circ\text{C}, 24 \text{ h}]{\text{Ir(salen)} (2.0 \text{ mol}\%), \text{N}_2} \text{R}^1\text{Si-H-CO}_2\text{Me} \quad \mathbf{6i-o}$						
(1.2 equiv.)	(1.0 equiv.)					
entry	cat.	prod.	R <sup>1</sup>	R <sup>2</sup>	% yield <sup>b,c</sup>	% ee <sup>d</sup>
1	<b>1</b>	<b>6i</b>	PhMe <sub>2</sub>	Ph	93	>99
2	<b>5</b>	<b>6i</b>	PhMe <sub>2</sub>	Ph	91	50 <sup>e</sup>
3	<b>1</b>	<b>6j</b>	Et <sub>3</sub>	2-MeOC <sub>6</sub> H <sub>4</sub>	92	99
4	<b>1</b>	<b>6k</b>	Et <sub>3</sub>	2-ClC <sub>6</sub> H <sub>4</sub>	95	>99
5	<b>1</b>	<b>6l</b>	Et <sub>3</sub>	3-MeOC <sub>6</sub> H <sub>4</sub>	95	>99
6	<b>1</b>	<b>6m</b>	Et <sub>3</sub>	3-ClC <sub>6</sub> H <sub>4</sub>	97	>99
7 <sup>f</sup>	<b>1</b>	<b>6n</b>	Et <sub>3</sub>	4-MeOC <sub>6</sub> H <sub>4</sub>	94	>99
8	<b>1</b>	<b>6o</b>	Et <sub>3</sub>	4-ClC <sub>6</sub> H <sub>4</sub>	97	>99

<sup>a</sup> Reaction was carried on a 0.3 mmol scale. <sup>b</sup> Isolated yield. <sup>c</sup> Formation of a trace amount carbene dimer (<5%) was detected by <sup>1</sup>H NMR analysis. <sup>d</sup> Determined by HPLC analysis. <sup>e</sup> The major product obtained with **5** is an enantiomer of the major product obtained with **1** as catalyst. <sup>f</sup> 3 equiv of silane were used.

naphthyl)phenylsilane and *tert*-butyl  $\alpha$ -diazopropionate (Table 2, entry 1). The reaction using **4** as catalyst proceeded with good diastereo- and enantioselectivity.<sup>16</sup> To our delight and surprise, superior selectivity was obtained when the complex **5** was used as the catalyst, and one of four possible diastereomers was produced exclusively (entry 2).<sup>17</sup> The reactions between other prochiral silanes including alkyl aryl silanes also proceeded with high diastereo- and enantioselectivity (entries 3–5).<sup>18</sup>

As discussed in the beginning of this article, several highly enantioselective Si–H insertions into trisubstituted silanes with  $\alpha$ -aryl- $\alpha$ -diazoacetates have been reported.<sup>5–8</sup> We also examined the insertion reactions between trisubstituted silanes and  $\alpha$ -aryl- $\alpha$ -diazoacetates using complex **1** or **5** as catalyst (Table 3). Since  $\beta$ -hydride elimination cannot occur in these reactions, the reactions were carried out at  $-30^\circ\text{C}$  with 1.2 equiv of the silanes. While the reaction with **5** as the catalyst was modestly enantioselective (entry 2), all the reactions with **1** were found to proceed with almost complete enantioselectivity ( $\geq 99\%$ ) and good yields. The formation of a trace amount of the carbene dimer (<5%) was observed under the conditions.

The kinetic isotope effect for the present reaction between triethylsilane and methyl  $\alpha$ -phenyl- $\alpha$ -diazoacetate was determined to be 1.6 in a competitive experiment. This value is consistent with the reported value ( $k_{\text{H}}/k_{\text{D}} = 1.5$ ) for rhodium-carbenoid Si–H insertion of dimethylphenylsilane<sup>19</sup> and supports the notion that the present reaction is a carbenoid Si–H insertion.



In conclusion, we were able to develop a highly enantioselective Si–H carbenoid insertion reaction into trisubstituted silanes using  $\alpha$ -alkyl- $\alpha$ -diazoacetates ( $\geq 97\%$  ee) or  $\alpha$ -aryl- $\alpha$ -diazoacetates ( $\geq 99\%$ ) in the presence of an appropriate iridium complex as catalyst. To our knowledge, this is the first example of highly enantioselective Si–H insertion reactions using  $\alpha$ -alkyl- $\alpha$ -diazoacetates. Moreover, Si–H insertion into a prochiral silane that provides a new direct method for forming a stereogenic silicon center was for the first time achieved with high enantioselectivity.

**Acknowledgment.** Financial support from Specially Promoted Research 18002011 and the Global COE Program, ‘Science for Future Molecular Systems’ from MEXT, Japan is gratefully acknowledged. H.S. is grateful for the JSPS Research Fellowships for Young Scientists.

**Supporting Information Available:** Experimental procedures, spectral data for Si–H insertion products, and HPLC conditions. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (1) (a) Denmark, S. E.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1560. (b) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: New York, 2000; Chapter 12. (c) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (d) *The Chemistry of organic Silicon Compounds*; Patai, S., Rappaport, Z., Eds.; John Wiley & Sons: 1989; Part 1, Part 2.
- (2) (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998; p 151. (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.
- (3) Buck, R.; Doyle, M. P.; Drysdale, M. J.; Ferris, L.; Forbes, D. C.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Zhou, Q.-L. *Tetrahedron Lett.* **1996**, *37*, 7631.
- (4) Landais, Y.; Planchenault, D. *Tetrahedron Lett.* **1994**, *35*, 4565.
- (5) Davies, H. M. L.; Hansen, T.; Rutberg, J.; Bruzinski, P. R. *Tetrahedron Lett.* **1997**, *38*, 1741.
- (6) Dakin, L. A.; Schaus, S. E.; Jacobsen, E. N.; Panek, J. S. *Tetrahedron Lett.* **1998**, *39*, 8947.
- (7) Ge, M.; Corey, E. J. *Tetrahedron Lett.* **2006**, *47*, 2319.
- (8) Zhang, Y.-Z.; Zhu, S.-F.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2008**, *47*, 8496.
- (9) (a) Taber, D. F.; Herr, R. J.; Pack, S. K.; Geremia, J. M. *J. Org. Chem.* **1996**, *61*, 2908. (b) Ikota, N.; Takamura, N.; Young, S. D.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4163.
- (10) For an example of asymmetric cyclopropanation using  $\alpha$ -alkyl- $\alpha$ -diazoesters, see: DeAngelis, A.; Dmitrenko, O.; Yap, G. P. A.; Fox, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 7230.
- (11) (a) Kanchiku, S.; Suematsu, H.; Matsumoto, K.; Uchida, T.; Katsuki, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 3889. (b) Suematsu, H.; Kanchiku, S.; Uchida, T.; Katsuki, T. *J. Am. Chem. Soc.* **2008**, *130*, 10327. (c) Ichinose, M.; Suematsu, H.; Katsuki, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 3121.
- (12) Suematsu, H.; Katsuki, T. *J. Am. Chem. Soc.* **2009**, *131*, 14218.
- (13) Hamada, T.; Irie, R.; Mihara, J.; Hamachi, K.; Katsuki, T. *Tetrahedron* **1998**, *54*, 10017.
- (14) The yield of *tert*-butyl (Z)-2-butenolate was determined to be 35% by <sup>1</sup>H NMR analysis with 1-bromonaphthalene as an internal standard, and its stereochemistry was assigned to be Z based on the coupling constant ( $J = 11.5 \text{ Hz}$ ) [the coupling constant of the *E*-isomer ( $J = 15.5 \text{ Hz}$ )].
- (15) For an example of enantiotopic selective alcoholysis of prochiral dihydrosilane with a chiral alcohol, see: Schmidt, D. R.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 1190.
- (16) For the determination of stereoselectivity of the reaction, see the Supporting Information.
- (17) The reaction with **1** was modestly stereoselective (10% de, 79% ee).
- (18) The reaction with PhC(N<sub>2</sub>)CO<sub>2</sub>Me did not give the desired product because it decomposed on chromatography to give PhCH<sub>2</sub>CO<sub>2</sub>Me.
- (19) A concerted electrophilic metal-carbenoid insertion mechanism has been proposed based on kinetic studies: Landais, Y.; Parra-Rapado, L.; Planchenault, D.; Weber, V. *Tetrahedron Lett.* **1997**, *38*, 229. (b) A similar value ( $k_{\text{H}}/k_{\text{D}} = 1.29$ , at  $0^\circ\text{C}$ ) has been reported: Dakin, L. A.; Ong, J. S.; Panek, P. C.; Staples, R. J.; Stavropoulos, P. *Organometallics* **2000**, *19*, 2896.

JA100833H