Iron-Catalyzed Carbene Insertion Reactions of α-Diazoesters into Si–H Bonds†

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ABSTRACT: An efficient iron-catalyzed carbene insertion reaction of α-diazo carbonyl compounds into the Si–H bond was developed. A wide range of α-silylesters was obtained in high yields (up to 99%) from α-diazoesters using a simple iron(II) salt as catalyst.

Metal catalysts are fundamental tools in organic chemistry. Iron is a very abundant element; its low cost and environmentally benign character make it attractive. New catalytic methods taking advantage of Fe are in high demand. Compared to rare metals, Fe still needs to be developed for industrial applications. The chemistry of Fe is thus among the most promising fields to develop. Transition metal-catalyzed reactions of diazo compounds generate metal carbene or metal carbene species that can undergo diverse transformations, such as X–H (X = C, N, O, Si, S, etc) bond insertion reactions. The various oxidation states of Fe make it appealing as catalyst in diazo chemistry. Various Fe catalysts have been disclosed for N–H, O–H, and S–H bond insertion reactions. The only Fe-catalyzed enantioselective insertion reaction reported is an O–H bond insertion reaction using water or alcohols. To date, Rh/Rh(I), Cu/Cu(I), Ir(I), Ag(I), and Ru(I) complexes have been utilized as catalysts for Si–H bond insertion reactions. The insertion of carbene species into the Si–H bond was first reported in the reaction of diazoalkanes with silanes. Watanabe developed the reaction of various silanes with methyl α-diazoacetate using Cu powder. The Rh(III)-catalyzed reaction of α-diazoesters and α-diazoacetates with silanes was first reported by Doyle. Landais disclosed the synthesis of α-alkoxysilylacetic esters by Si–H bond insertion reaction of carbones, generated by Rh(III)-catalyzed decomposition of α-diazoacetate esters. Insertion reactions of diazo compounds into the Si–H bond were subsequently disclosed using Rh(I) catalysts, including enantioselective versions. A Rh(I)-catalyzed enantioselective Si–H bond insertion reaction of α-diazoesters and α-diazoacetates has been developed. Chiral Ir(III) complexes have also proven to be efficient catalysts for enantioselective Si–H bond insertion reaction. Cu(I)-catalyzed Si–H bond insertion was reported for the first time by Panek. Zhou also developed a Cu(I)-catalyzed highly asymmetric Si–H bond insertion reaction using spiro diimine ligands. Recent insertion reactions of diazo carbonyl compounds into the Si–H bond using Cu(I) catalysts have been reported, including from our group. Insertion of Si–H bonds using Ag(I) as catalyst was also demonstrated. Fe(II) being above Ru(I) in the periodic table, a cationic Ru(I) oxazoline catalyst appears to be an important precedent for efficient enantioselective insertion reaction into the Si–H bond.

In this article we report the insertion reactions of diazo compounds into Si–H bonds and demonstrate the scope and applicability of the reaction using highly practical conditions. Given that most of the catalyzed X–H bond insertion reactions involve Rh complexes, we focused here on an efficient and green metal catalytic system to probe the reactivity of diazo compounds into Si–H bonds. Diazo compounds were prepared from commercially available esters and ketones according to known procedures.† The reaction of methyl α-phenyl-α-diazoacetate 1a and EtSiH(II) in CH₂Cl₂ was first examined using Fe(OOTf)₃ as catalyst. The reaction was complete within 1 h and the corresponding α-silylester (2a) was obtained in 97% yield (Table 1, entry 1). Interestingly, this compound cannot be easily prepared using other synthetic methods, but diazo insertion reaction into the Si–H bond. Useful applications of these α-silylesters have been demonstrated. Using the same conditions, various Fe₈ sources (Table 1, entries 2–7) and Fe(II) (Table 1, entries 8–12) were tested but none of them afforded the same reactivity as Fe(OOTf)₃ (Table 1, entry 1). No conversion was obtained using Fe(OAc)₃ (Table 1, entry 4) and FeCl₃, as shown to be an efficient catalyst leading to 81% yield (Table 1, entry 5). Only traces of the product were observed when using FeBr₃ and Fe(acac)₃ as catalysts (Table 1, entries 11 and 12). Optimization studies indicated that Fe(OOTf)₃ was superior to the other Fe₈/Fe(II) sources for Si–H bond insertion reaction in CH₂Cl₂. Fe(OOTf)₃ has indeed been demonstrated as a superior catalyst in various transformations. It was consequently selected as the Fe₈ source for further studies.

Table 1. Screening of Iron Sources for Si–H Bond Insertion of Methyl α-Phenyl-α-diazoacetate 1a

![Table 1](image-url)
A catalyst loading of 5 mol % was effective using 2 equiv of Et₃SiH, whereas the product was formed in higher yield and decreased reaction time when the quantity of Et₃SiH was increased to 4 equiv (Table 2, entries 1 and 2). A catalyst loading of 2 mol % was tested, but the product was formed in lower yields in longer reaction times (Table 2, entries 3–4). A 5 mol % quantity of Fe(OTf)₃ together with 4 equiv of Et₃SiH, was selected for further studies.

**Table 2. Screening of Catalyst Loading for Si–H Bond Insertion Reaction of 1a***

<table>
<thead>
<tr>
<th>entry</th>
<th>Fe(OTf)₃ (x mol %)</th>
<th>Et₃SiH (y equiv)</th>
<th>time (h)</th>
<th>yield 2a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
<td>24</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>4</td>
<td>18</td>
<td>96</td>
</tr>
</tbody>
</table>

<sup>a</sup>Conditions: Fe(OTf)₃: (x mol %), Et₃SiH (y mmol), 1a (0.25 mmol), slow addition (1 h) of 1a.  
<sup>b</sup>Yield of isolated product.

The use of various solvents was studied in the insertion reaction of α-silylesteryl. Chloroform, 1,2-dichloroethane, diethyl ether, and toluene were all suitable solvents and very good to high yields were obtained (Table 3, entries 1–4). Hexane afforded a low yield (Table 3, entry 5). When the reaction was run in polar, coordinating solvents, such as MeCN and THF, the conversion was low and low yields were obtained (Table 3, entries 6 and 7). However, none of these solvents gave results superior to CH₂Cl₂, which was consequently chosen in further studies.

**Table 3. Screening of Solvents for Si–H Bond Insertion Reaction of Methyl α-Phenyl-α-diazoacetate 1a***

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>time (h)</th>
<th>yield 2a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHCl₃</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>DCE</td>
<td>3</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>Et₂O</td>
<td>12</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>12</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td>hexane</td>
<td>48</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>MeCN</td>
<td>48</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>18</td>
<td>48</td>
</tr>
</tbody>
</table>

<sup>a</sup>Conditions: Fe(OTf)₃: (5 mol %), silane (1 mmol), 1a (0.25 mmol), 40 °C, slow addition (1 h) of 1a.  
<sup>b</sup>Yield of isolated product.

A variety of α-diazoesters were examined to expand the scope of the substrates used for the Si–H bond insertion reaction with Et₃SiH, which was run under the optimal reaction conditions. All substrates reacted to produce the corresponding α-silylesteryl in good to excellent yields (Scheme 1, 2b–m, 65–99%), regardless of the nature and position of the substituents on the aromatic ring of the α-diazoesters (Scheme 1, 2b–m). However, the reactivity of the substrate was influenced by the electronic properties of the substituents on the aromatic ring of the α-aryl-α-diazoacetate. α-Aryl-α-diazoacetates containing electron-donating groups, such as methyl and methoxy groups (Scheme 1, 2b–c) required shorter reaction times to reach complete conversions. In contrast, α-aryl-α-diazoacetates containing electron-withdrawing groups, such as F, Cl, Br (Scheme 1, 2d–j), required longer reaction times to obtain desired α-silylesteryl in moderate to excellent yields (65–99%).

**Scheme 1. Fe<sup>III</sup>-Catalyzed Si–H Bond Insertion Reaction of α-Aryl-α-diazoacetates**

Next, the scope of silanes was evaluated. Different silanes, such as diphenylmethylsilane (Ph₂MeSiH), triphenylsilane (Ph₃SiH), phenylmethylsilane (PhMeSiH) were also successfully used in this transformation, affording the desired α-silylesteryl in moderate to high yields (Scheme 2, 3aa–n).
Scheme 3. Fe\textsuperscript{II}-Catalyzed Si–H Bond Insertion Reaction of \(\alpha\)- Aryl-\(\alpha\)-diazoacetates 1a–m with Various Silanes

\[
\begin{align*}
\text{N}_2 & \quad \text{R}\text{SiH} & \quad \text{Fe(OTf)}_2 (5 \text{ mol \%}) \\
4 \text{ a–e} & \quad \text{4 equiv} & \quad \text{C}_2 \text{H}_2 \text{N}_{2} & \quad \text{4 a–e} & \quad \text{4 equiv} & \quad \text{C}_2 \text{H}_2 \text{N}_{2}
\end{align*}
\]

\[\text{Scheme 3. Fe}^{\text{II}}\text{-Catalyzed Si–H Bond Insertion Reaction of Various Diazo Compounds}^\text{a}\]

\[
\begin{align*}
\text{N}_2 & \quad \text{R}\text{SiH} & \quad \text{Fe(OTf)}_2 (5 \text{ mol \%}) \\
4 \text{ a–e} & \quad \text{4 equiv} & \quad \text{C}_2 \text{H}_2 \text{N}_{2} & \quad \text{4 a–e} & \quad \text{4 equiv} & \quad \text{C}_2 \text{H}_2 \text{N}_{2}
\end{align*}
\]

\[\text{Scheme 4. Kinetic Isotope Effect experiment for Diaz o Insertion into Si–H and Si–D Bonds}^\text{d}\]

In order to get some insight into the mechanism of the reaction, the kinetic isotope effect (KIE) was investigated for the metal carbene insertion reaction of \(\alpha\)-diazoester, by running the competition study illustrated in Scheme 4.\textsuperscript{146, 147, 150} The reaction of 1a–c with a mixture of Et\textsubscript{3}SiH (2 equiv) and Et\textsubscript{3}SiD (2 equiv) was examined in CH\textsubscript{2}Cl\textsubscript{2} at 40 °C using Fe(OTf)\textsubscript{2} as catalyst. The desired \(\alpha\)-silylesters 2a–c and 2a’–c’ were formed in a 3:2.6 ratio (Scheme 4, KIE of 1.1). Based on the obtained KIE and the results obtained by Landais using Rh\textsubscript{2}(OAc)\textsubscript{4} no significant kinetic isotope effect was observed (k\textsubscript{H}/k\textsubscript{D} = 1.1) suggesting that the Si–H activation step may not be rate determining.

The following mechanism can be proposed (Figure 1). The diazo decomposition catalyzed by the iron complex occurs through the complexation of the negatively polarized carbon of the diazo substrate to the Fe\textsuperscript{II} catalyst. Afterwards, the Fe\textsuperscript{II} carbene is generated via an irreversible N\textsubscript{2} elimination. The metal carbene formation appears to be dependent on the electronic effects borne by the diazo compound, as demonstrated by the lower yields obtained with the electron-withdrawing groups substituting the aryl moiety. An electrophilic iron-carbene center through the illustrated transition state, together with a three-centered transition state, could be envisioned. The overall mechanism involves iron-mediated extrusion of N\textsubscript{2} in the slow step to form a metal carbene complex followed by insertion of the carbene fragment between a Si–H bond to regenerate the active catalyst.\textsuperscript{22}

Figure 1. Proposed Mechanism for the Fe(OTf)\textsubscript{2} catalyzed Insertion of \(\alpha\)-Diazoesters with Et\textsubscript{3}SiH

To sum up, we have successfully developed an efficient iron-catalyzed protocol for the metal carbene insertion reaction of \(\alpha\)-diazoesters into the Si–H bond. A wide range of \(\alpha\)-silylesters was synthesized in good to excellent yields using Fe(OTf)\textsubscript{2} in low catalytic loadings, i.e., 5 mol %. Moreover, this catalyst has been shown to be efficient for the metal carbene insertion reaction of \(\alpha\)-alkyl-\(\alpha\)-diazoesters and 4-(1-diazo-2,2, trifluoroethyl)-1,1\textsuperscript{b}biphenyl into the Si–H bond in good yields.
ASSOCIATED CONTENT

Supporting Information. Experimental details, characterization details, and spectral data are available in the Supporting information part. This material is available free of charge via the Internet at http://pubs.acs.org.

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