Rhenium-Catalyzed Insertion of Terminal Alkenes into a C(sp²)-H Bond and Successive Transfer Hydrogenation

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Abstract

Treatment of aromatic aldimines with terminal alkenes in the presence of a rhenium catalyst, [HRe(CO)₄]ₙ, gives 2-alkenylbenzylamines in good to excellent yields. This reaction proceeds via the insertion of the alkene into a C-H bond at the ortho-position of the imino group of the aromatic aldimine followed by sequential β-hydride elimination from the formed alkyl rhenium intermediate and then by hydrogenation of the imino group of the aldimine.

Keywords

Rhenium
Insertion
Hydrogen Transfer
Aldimine
Alkene

1. Introduction
C-H functionalization is one of the most efficient and direct methods in synthetic organic chemistry. There have, therefore, recently been many efforts to develop new transformations via C-H bond activation. In such transformations, insertion of unsaturated molecules into a C-H bond is well known, and the reactions usually stop at the insertion step. Our group has also reported on transformations via C-H bond activation using rhenium complexes as catalysts. In some of these reactions, intramolecular nucleophilic cyclization occurs after the insertion of unsaturated molecules into a formed C(sp²)-Re bond. During investigations of rhenium-catalyzed C-H transformations, we discovered the alkenylation reaction of aromatic compounds.

There have been several reports of alkenylation reactions of aromatic C-H bonds. The first approach involves the cross coupling reaction between aromatic compounds and alkenyl halides (Figure 1(a)), and the second strategy is based on insertion of alkynes into a C-H bond of aromatic compounds (Figure 1(b)). The third process is oxidative-dehydrogenative alkenylation of C-H bonds using stoichiometric amount of an oxidant (Figure 1(c)). The fourth route, which we also report herein, is the insertion of alkenes into a C-H bond of aromatic compounds followed by dehydrogenation of the formed alkylated aromatic compounds (Figure 1(d)).

![Figure 1. Four Methods for Alkenylation of Aromatic C-H Bonds.](image)

2. Results and Discussion

First, we investigated the reaction between aromatic aldimine 1a and styrene (2a) using the rhenium complex, [ReBr(CO)₃(thf)]₂, as the catalyst. Quinoline derivative 3 was formed in 31% yield (eq 1). In this reaction, the rhenium complex worked as a Lewis acid and promoted a regioselective aza-Diels-Alder reaction.
N-Benzylaniline was also formed as a side product. This result indicated that aldimine 1a also worked as a hydrogen acceptor to produce quinoline 3 from tetrahydroquinoline, which is part of an aza-Diels-Alder adduct between 1a and 2a. Therefore, by increasing the amount of 1a (3.0 equiv), the yield of 3 was improved to 66% (eq 1).

![Chemical structure](image_url)

Since a rhenium complex, [ReBr(CO)$_3$(thf)]$_2$, has a higher Lewis acidity than [HRe(CO)$_4$]$_n$, [ReBr(CO)$_3$(thf)]$_2$ promoted aza-Diels-Alder reaction without promoting C-H transformation. The possible mechanism for the formation of a quinoline derivative is shown in Scheme 1: (1) Aza-Diels-Alder reaction between an N-arylaldimine and styrene; (2) tautomerization; (3) transfer dehydrogenation of the formed tetrahydroquinoline with two equivalents of N-arylaldimine. In this mechanism, the regioselectivity must be determined by electron densities of N-arylaldimine and styrene.

**Scheme 1. Proposed Mechanism for the Formation of Quinoline Derivative 3.**
By changing the rhenium catalyst, [ReBr(CO)\textsubscript{3}(thf)]\textsubscript{2}, to [HRe(CO)\textsubscript{4}]n, the product of the reaction between aromatic aldimine 1\textsubscript{a} and styrene (2\textsubscript{a}) changed dramatically. Treatment of 1\textsubscript{a} with 2\textsubscript{a} in the presence of a catalytic amount of the rhenium-hydride complex, [HRe(CO)\textsubscript{4}]n, gave N-(2-styrylbenzyl)benzenamine (4\textsubscript{a}) in 80% yield (eq 2).\textsuperscript{9-12} The catalytic activity for the formation of 4\textsubscript{a} is much higher than that of other rhenium complexes that we have previously reported as being effective in C-H bond transformations.\textsuperscript{13} There have been several reports of the transition metal-catalyzed insertion of styrene (or other alkenes) into an aromatic C-H bond; however, transfer of dihydrogen did not occur after the insertion step.\textsuperscript{14} In this reaction, the loss of the imino group 1\textsubscript{a} may be disadvantage. However, it must be valuable to synthesize N-(2-alkenylbenzyl)benzenamines from aldimines and alkenes because the synthesis can be achieved without addition of any oxidant or hydrogen acceptor.\textsuperscript{15}

We next investigated the scope and limitations of the reaction, specifically evaluating the imines that are suitable for the transformation (Table 1). Aromatic aldimines with an electron-donating group, 1\textsubscript{b} and 1\textsubscript{c}, produced 2-alkenylbenzylamines 4\textsubscript{b} and 4\textsubscript{c} in 70% and 76% yields, respectively (entries 1 and 2). The corresponding 2-alkenylbenzylamine 4\textsubscript{d} was generated in 82% yield when aromatic aldimine bearing an electron-withdrawing group, 1\textsubscript{d}, was employed. In the case of the aromatic aldimine with a methyl group at the meta-position, 1\textsubscript{e}, only one isomer 4\textsubscript{e} was formed regioselectively in 75% yield (entry 4). Furthermore, the reaction was not inhibited by steric hindrance at the ortho-position; the corresponding 2-alkenylbenzylamine 4\textsubscript{f} was produced in 80% yield when aromatic aldimine 1\textsubscript{f} with a methyl group at the ortho-position was employed (entry 5). Only one product 4\textsubscript{g} was obtained with (E)-N-((naphthalen-2-yl)methylene)benzenamine (1\textsubscript{g}), which has two possible reaction points (entry 6). However, reaction between the aromatic ketimine N-(1-phenylethylidene)benzenamine and styrene (2\textsubscript{a}) did not provide the corresponding alkenylated product, but produced alkylated aromatic ketimine [(E)-N-(1-(2-phenethylphenyl)ethylidene)benzenamine] in 7% yield.
Next, we investigated the reactivity of several alkenes (Table 2). Styrene with an electron-donating group, 2b, gave 2-alkenylbenzylamine 4h in 90% yield (entry 1).

The corresponding 2-alkenylbenzylamine 4i was obtained using styrene bearing a fluorine atom at the para-position, 2c (entry 2). 2-Vinylnaphthalene (2d) also afforded 2-alkenylbenzylamine 4j in 63% yield (entry 3). A mixture of 2-alkenylbenzylamines 4k, 4k’ and 4k” was formed in 85% total yield when aliphatic alkene 2e was used as an olefinic substrate (entry 4). By investigating the ratios between 4k (trans-form) and 4k’ (cis-form) during the reaction, it was clarified that 4k’ should be formed from 4k by isomerization.
Table 2. Reactions of Aldimine 1a with Alkenes 2

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1c</td>
<td>4-MeC₆H₄</td>
<td>4h 90 (91)</td>
</tr>
<tr>
<td>2</td>
<td>4-FC₆H₄</td>
<td>4i 66 (76)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>4j 63 (66)</td>
</tr>
<tr>
<td>4d</td>
<td></td>
<td>4k + 4k' + 4k'' 85 (86) [77:11:12]e</td>
</tr>
</tbody>
</table>

a 2 (2.0 equiv).
b Isolated yield. Yield determined by ¹H NMR is reported in parentheses.
c 2 (4.0 equiv).
d After 24 h, [HRe(CO)₄]ₙ (Re: 5.0 mol%) and 2a (2.0 equiv) were added, and the reaction mixture was stirred at 180 °C for 24 h.
e The ratios between 4k, 4k' and 4k'' are reported in square brackets.

The proposed mechanism for reaction is as follows (Scheme 2): (1) oxidative addition of an aromatic aldimine to a rhenium center (C-H bond activation);2 (2) insertion of an alkene into the formed rhenium-carbon bond; (3) β-hydride elimination,6 (4) insertion of a carbon-nitrogen double bond of the imino group into a rhenium-hydrogen bond;18 (5) and reductive elimination to give 2-alkenylbenzylamines 4 and regenerate the rhenium catalyst. It is interesting to note that β-elimination from 5 proceeds preferentially instead of intramolecular nucleophilic cyclization, which occurs in previously reported rhenium-catalyzed C-H transformations.2

3. Summary

We have succeeded in developing the rhenium complex \([\text{HRe(CO)}_6]_n\), which catalyzes the synthesis of 2-alkenylbenzylamines from aromatic aldimines and alkenes. This reaction proceeds via aromatic C-H bond activation, insertion of the alkene into a C-H bond of the aromatic compound, \(\beta\)-hydride elimination and hydrogenation of the imino group of the aromatic aldimine. The \(\beta\)-hydride elimination and hydrogenation steps are rare examples in transformations that proceed via aromatic C-H bond activation. By changing the rhenium catalyst to \([\text{ReBr(CO)}_3(\text{thf})]_2\), a quinoline derivative was produced from an aromatic aldimine and styrene via an aza-Diels-Alder reaction.

Acknowledgment. This work was partially supported by the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

References

[1] There have been several reviews on transition metal-catalyzed transformations via C-H bond activation. See:
We have already reported several rhenium-catalyzed transformations that occur via C-H bond activation. See:

For examples, see:
(c) Y. Kuninobu, K. Kikuchi, Y. Tokunaga, Y. Nishina, K. Takai, Tetrahedron 64 (2008) 5974;

There have been a few reports of β-hydride elimination following the insertion of an alkene into an aromatic C-H bond. See:
(a) P. Hong, H. Yamazaki, Chem. Lett. (1979) 1335;

Investigation of several rhenium catalysts and temperatures: Re$_2$(CO)$_{10}$ at 180 °C, 0%; ReBr(CO)$_5$ at 150 °C, 28% and at 180 °C, 30%; [ReBr(CO)$_3$(thf)$_2$] at 150 °C, 31% and at 180 °C, 28%; [HRe(CO)$_4$] at 150 °C, 0% and at 180 °C, 0%.

Iron-promoted and rhodium-catalyzed synthesis of quinoline derivatives via an aza-Diels-Alder reaction between N-aryl aldimines and styrenes has been reported.

[9] The reaction did not proceed using the following transition metal complexes: Mn$_2$(CO)$_{10}$, MnBr(CO)$_5$, RuH$_2$(CO)(PPh$_3$)$_3$, Ru$_3$(CO)$_{12}$, RhCl(PPh$_3$)$_3$ and Ir$_4$(CO)$_{12}$.

[10] Investigation of catalytic amounts: 0.50 mol%, 7%; 1.0 mol%, 9%; 2.5 mol%, 22%.

[11] Investigation of several solvents: Neat, 7%; octane, trace; toluene, 80%; 1,2-dichloroethane, trace; n-hexanenitrile, 10%.

[12] Following the reviewer’s suggestion, we have examined the reactions between aldimine 1a and styrene (2a) using 5.0 equivalents of a hydrogen acceptor, such as norbornene or 3,3-dimethyl-1-butene, under the reaction conditions shown in eq 2. As a result, alkenylated product 4a was obtained in 4% and 64% yields, respectively.

[13] The reaction did not proceed using Re$_2$(CO)$_{10}$, ReBr(CO)$_5$ or [ReBr(CO)$_3$(thf)]$_2$.


[16] One possible reason for the formation of 4k’ (cis-form) is that 4k (trans-form) is isomerized to 4k’ under the reaction conditions. In fact, the ratios between 4k and 4k’ changed during the reaction. That is, at the beginning of the reaction, the ratio of 4k is high; however, the ratio of 4k decreased and that of 4k’ increased as the reaction proceeded.

[17] Yields of 4k and 4k’ (the ratios between 4k and 4k’): 1 h, 3%, 0% (100:0); 3 h, 16%, trace (>99:1); 8 h, 32%, 4% (89:11); 24 h, 63%, 10% (86:14).