

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

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Received date

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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.¹ 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.² In some of these reactions, intramolecular nucleophilic cyclization occurs after the insertion of unsaturated molecules into a formed C(sp²)-Re bond.² 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)),³ and the second strategy is based on insertion of alkynes into a C-H bond of aromatic compounds (Figure 1(b)).⁴ The third process is oxidative-dehydrogenative alkenylation of C-H bonds using stoichiometric amount of an oxidant (Figure 1(c)).⁵ 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)).⁶

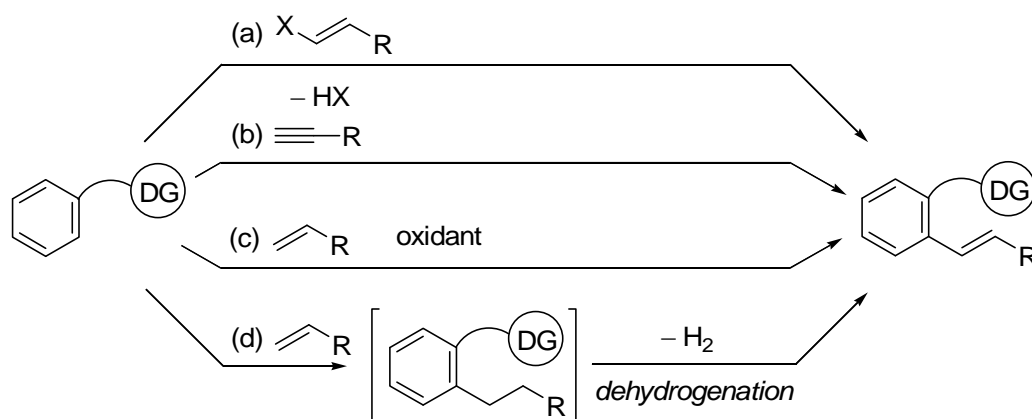
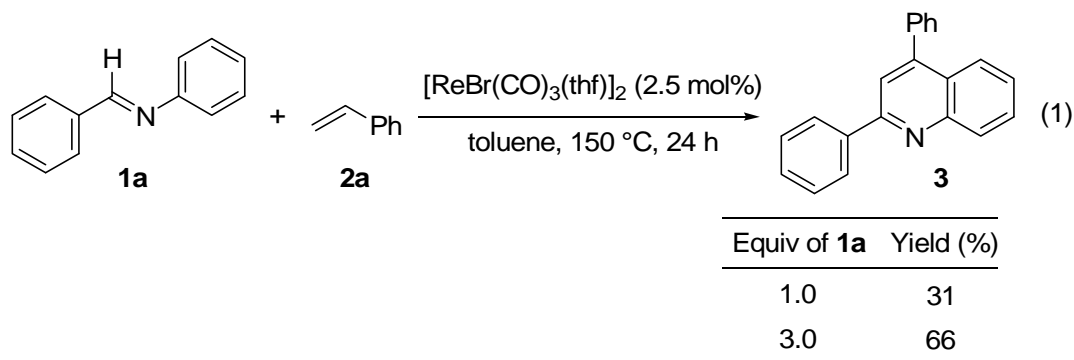


Figure 1. Four Methods for Alkenylation of Aromatic C-H Bonds.

2. Results and Discussion

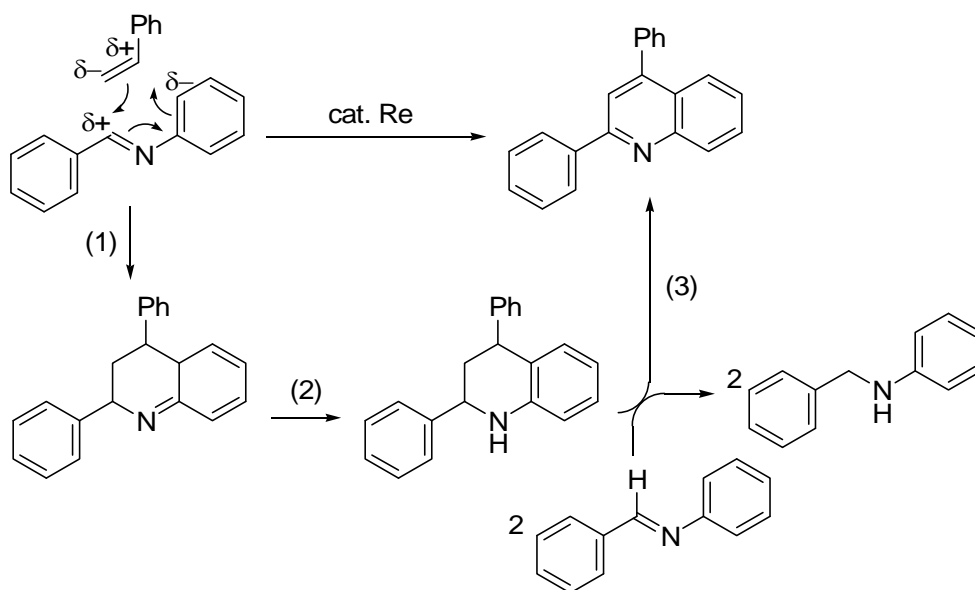
First, we investigated the reaction between aromatic aldimine **1a** and styrene (**2a**) using the rhenium complex, [ReBr(CO)₃(thf)]₂, as the catalyst. Quinoline derivative **3** was formed in 31% yield (eq 1).⁷ In this reaction, the rhenium complex worked as a Lewis acid and promoted a regioselective aza-Diels-Alder reaction.⁸

N-Benzyldaniline 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).

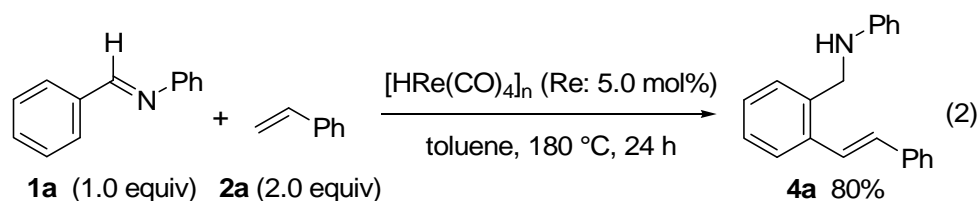


Since a rhenium complex, $[\text{ReBr}(\text{CO})_3(\text{thf})_2]$, has a higher Lewis acidity than $[\text{HRe}(\text{CO})_4]_n$, $[\text{ReBr}(\text{CO})_3(\text{thf})_2]$ promoted aza-Diels-Alder reaction without promoting C-H transformation. The possible mechanism for the formation of a quinoline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

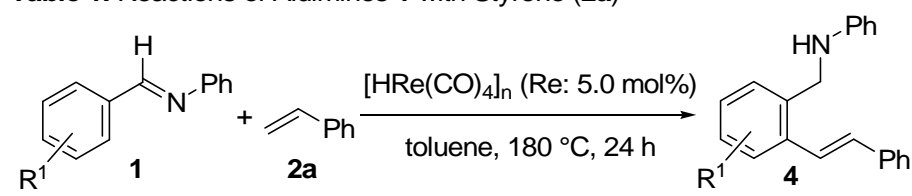
Scheme 1. Proposed Mechanism for the Formation of Quinoline Derivative **3**.

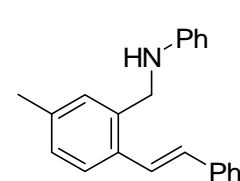
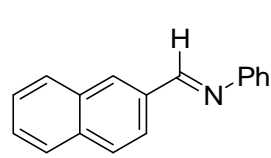
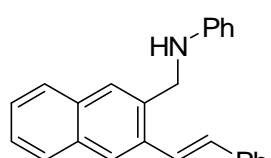


By changing the rhenium catalyst, $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$, to $[\text{HRe}(\text{CO})_4]_n$, the product of the reaction between aromatic aldimine **1a** and styrene (**2a**) changed dramatically. Treatment of **1a** with **2a** in the presence of a catalytic amount of the rhenium-hydride complex, $[\text{HRe}(\text{CO})_4]_n$, gave *N*-(2-styrylbenzyl)benzenamine (**4a**) in 80% yield (eq 2).⁹⁻¹² The catalytic activity for the formation of **4a** is much higher than that of other rhenium complexes that we have previously reported as being effective in C-H bond transformations.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.¹⁴ In this reaction, the loss of the imino group **1a** 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.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, **1b** and **1c**, produced 2-alkenylbenzylamines **4b** and **4c** in 70% and 76% yields, respectively (entries 1 and 2). The corresponding 2-alkenylbenzylamine **4d** was generated in 82% yield when aromatic aldimine bearing an electron-withdrawing group, **1d**, was employed. In the case of the aromatic aldimine with a methyl group at the *meta*-position, **1e**, only one isomer **4e** 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 **4f** was produced in 80% yield when aromatic aldimine **1f** with a methyl group at the *ortho*-position was employed (entry 5). Only one product **4g** was obtained with (*E*)-*N*-((naphthalen-2-yl)methylene)benzenamine (**1g**), which has two possible reaction points (entry 6). However, reaction between the aromatic ketimine *N*-(1-phenylethylidene)benzenamine and styrene (**2a**) did not provide the corresponding alkenylated product, but produced alkylated aromatic ketimine [*E*]-*N*-(1-(2-phenethylphenyl)ethylidene)benzenamine] in 7% yield.

Table 1. Reactions of Aldimines **1** with Styrene (**2a**)^a

Entry	R ¹	Yield (%) ^b
1 ^c	4-MeO 1b	4b 70 (73)
2	4-Me 1c	4c 76 (78)
3	4-CF ₃ 1d	4d 82 (87)
4	3-Me 1e	 4e 75 (79)
5 ^c	2-Me 1f	4f 80 (84)
6 ^d	 1g	 4g 78 (79)

^a **2a** (2.0 equiv).

^b Isolated yield. Yield determined by ¹H NMR is reported in parentheses.

^c 30 h.

^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.

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).¹⁶ 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.¹⁷

Table 2. Reactions of Aldimine **1a** with Alkenes **2**^a

Entry	R	Yield (%) ^b
1 ^c	4-MeC ₆ H ₄ 2b	4h 90 (91)
2	4-FC ₆ H ₄ 2c	4i 66 (76)
3	2d	4j 63 (66)
4 ^d	ⁿ C ₈ H ₁₇ 2e	4k + 4k' + 4k'' 4k + 4k' + 4k'' 85 (86) [77:11:12] ^e

^a **2** (2.0 equiv).

^b Isolated yield. Yield determined by ¹H NMR is reported in parentheses.

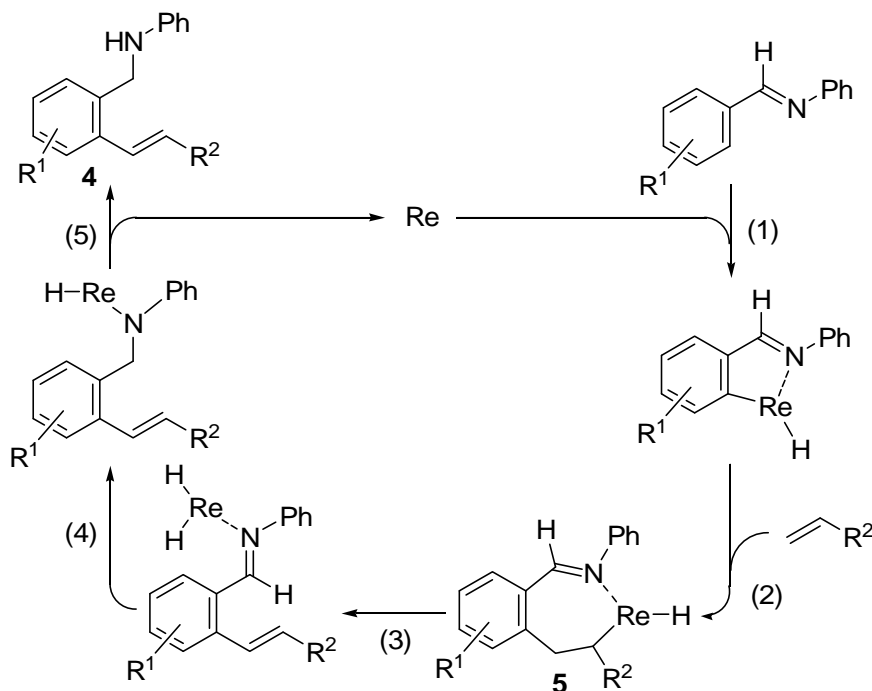
^c **2** (4.0 equiv).

^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

Scheme 2. Proposed Mechanism for the Formation of 2-alkenylbenzylamines **4**.



3. Summary

We have succeeded in developing the rhenium complex $[\text{HRe}(\text{CO})_4]_n$, 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, β -hydride elimination and hydrogenation of the imino group of the aromatic aldimine. The β -hydride elimination and hydrogenation steps are rare examples in transformations that proceed via aromatic C-H bond activation. By changing the rhenium catalyst to $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$, 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.

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 - (c) G. Dyker, *Angew. Chem. Int. Ed.* 38 (1999) 1698;
 - (d) F. Kakiuchi, T. Kochi, *Synthesis* (2008) 3013.
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- [7] Investigation of several rhenium catalysts and temperatures: $\text{Re}_2(\text{CO})_{10}$ at 180 °C, 0%; $\text{ReBr}(\text{CO})_5$ at 150 °C, 28% and at 180 °C, 30%; $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$ at 150 °C, 31% and at 180 °C, 28%; $[\text{HRe}(\text{CO})_4]_n$ at 150 °C, 0% and at 180 °C, 0%.
- [8] Iron-promoted and rhodium-catalyzed synthesis of quinoline derivatives via an aza-Diels-Alder reaction between *N*-aryl aldimines and styrenes has been reported.

- See: (a) R. Leardini, D. Nanni, A. Tundo, G. Zanardi, F. Ruggieri, *J. Org. Chem.* 57 (1992) 1842. (b) M. Beller, O. R. Thiel, H. Trauthwein, C. G. Hartung, *Chem. Eur. J.* 6 (2000) 2513.
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- [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.
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- [15] There has been a report on palladium-catalyzed oxidative *ortho*-olefination of *N*-substituted benzylamines using alkenes in the presence of a stoichiometric amount of an oxidant. See: G. Cai, Y. Fu, Y. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* 129 (2007) 7666.
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- [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).
- [18] For an example of the insertion of a carbon-nitrogen double bond into a rhenium-hydrogen bond, see: X.-Y. Liu, K. Venkatesan, H. W. Schmalle, H. Berke, *Organometallics* 23 (2004) 3153.