Rhenium-catalyzed Addition of Trimethylsilylacetylene to Aldimines

Yoichiro Kuninobu,* Yuichi Inoue, and Kazuhiko Takai*

Division of Chemistry and Biochemistry, Graduate School of Natural Science and Technology, Okayama University, Tsushima, Okayama 700-8530

(Received September 6, 2006; CL-061030; E-mail: kuninobu@cc.okayama-u.ac.jp, ktakai@cc.okayama-u.ac.jp)

A rhenium complex, [ReBr(CO)₃(thf)]₂, catalyzes reactions of aldimines with trimethylsilylacetylene to give propargylamines in excellent yields. The reactions proceed at room temperature under solvent-free conditions.

Propargylamines are important intermediates and building blocks for organic synthesis, especially of biologically active compounds.¹ Although there have been many methods for synthesizing propargylamines, most of these need the activation of starting materials. Some well- known methods are the nucleophilic attack of alkynylides to imines,² alkynylzinc additions to acyl iminiums,³ and the addition of terminal alkynes to nitrones.^{4,5} There have recently been some reports on the transition metal-catalyzed synthesis of propargylamines without activating starting materials.⁶ These reactions do not need any bases and/or activation of imines to promote the reactions. However, in most cases, they need a solvent and/or harsh reaction conditions. In addition, the yields of propargylamines are sometimes decreased when imines having functional groups, such as methoxy, chloro,⁷ or bromo^{6a} groups, are used. We report herein that a rhenium catalyst⁸ promoted the reactions between aldimines and trimethylsilylacetylene under mild and solvent-free conditions, and gave propargylamines efficiently.

By the treatment of aldimine 1a (0.50 mmol) with trimethylsilylacetylene (2a) (0.55 mmol) in the presence of a rhenium catalyst, $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$ (2.5 mol%), in toluene (0.20 mL) at 25 °C for 24 h, the addition of the terminal acetylene to the imine moiety of the aldimine occurred, and propargylamine 3a was obtained in 56% yield. To improve the yield of 3a, several solvents were investigated. The yield of 3a decreased to 21% in hexane, a nonpolar solvent. When the rather polar solvents dichloromethane and THF were used, the yields were improved and propargylamine 3a was formed in 62% and 57% yields, respectively. However, more polar N,N-dimethylformamide provided 3a in only 7% yield. Interestingly, 3a was obtained in 89% yield by performing the reaction of 1a with 2a under solvent-free conditions (Table 1, Entry 1).^{9,10} The fact that this reaction proceeded without any solvent and even at room temperature (25 °C) deserves special mention. However, the addition reactions did not proceed at higher temperatures by using other terminal acetylenes, such as phenylacetylene, 1-ethynylcyclohexene, 1-octyne, and ethyl propiolate. Aldimines 1b and 1c bearing a benzyl or phenyl group on the nitrogen atom of the imine moiety, also gave the corresponding propargylamines in quantitative yields (Entries 2 and 3). In particular, aldimine 1c has high reactivity and the reaction completed within 3 h. However, an aldimine having a tosyl group on the nitrogen atom of the imine moiety did not provide the corresponding propargylamine, even though the imine moiety must be activated by the tosyl group. The reactions between aldimines and acetylene 2a proceeded smoothly by using both aldimines having an electron-donating and an electron-withdrawing group at the para-position of the aromatic ring of aldimines **1d** and **1e** (Entries 4 and 5). Aldimine **1f** gave the corresponding propargylamine **3f** quantitatively without losing a bromo group (Entry 6). This result is in contrast to a report that an aldimine having a bromo group gave the corresponding propargylamine in moderate yield.^{6a} Alkenyl aldimine **1g** afforded enyne **3g** in 80% yield (Entry 7). Similar to aromatic aldimines, aliphatic aldimines **1h**, **1i**, and **1j** also provided propargylamine **3h**, **3i**, and **3j**, in good to quantitative yields (Entries 8–10). A hetero-aromatic aldimine, furyl aldimine **1k**, also gave the corresponding propargylamine **3k** in 46% yield (Entry 11).

Next, we investigated the role of the rhenium complex. One of the possible functions of the rhenium catalyst is the activation of acetylene **2a** by coordination. As a result, the deprotonation of **2a** by aldimines or propargylamines might be promoted and the nucleophilicity of **2a** would be increased. However, the propargylamines were not formed by using platinum dichloride or gallium trichloride, which are well known as reagents that coordinate to acetylenes and increase the acidity of the alkynes. Another possibility is that the rhenium catalyst acted as a Lewis acid and activated the aldimines. However, other Lewis acids, scandium triflate, lanthanum triflate, ytterbium triflate, and indium triflate, did not promote the reaction.¹¹ These results indicate that

 Table 1. Reactions of several aldimines with trimethylsilylacetylene^a



^a**2a** (1.1 equiv.) ^bIsolated yield. The yield determined by ¹H NMR is reported in parentheses. ^cDichloromethane was used as a solvent. ^d $[ReBr(CO)_3(thf)]_2$ (5.0 mol %), **2a** (3.0 equiv.).



Scheme 1. Proposed mechanism of the formation of propargylamines.

the role of the rhenium catalyst is not only as a Lewis acid.

The proposed reaction mechanism is as follows (Scheme 1):¹² (1) Oxidative addition of trimethylsilylacetylene to a rhenium(I) center;¹³ (2) nucleophilic addition of an alkynyl-rhenium(III) species to an aldimine; (3) reductive elimination. As a result, a propargylamine is formed and the rhenium(I) catalyst is regenerated.

Although a reaction between phenylacetylene (**2b**) and aldimine **1c** did not occur with $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$, the reaction proceeded to give the corresponding adduct **4** quantitatively by using both the rhenium complex and copper(I) chloride (eq 1).¹⁴

$$Ph \underbrace{H}_{h} + \underbrace{Ph}_{h} + \underbrace{Ph}_{h} \underbrace{Ph}_{h} + \underbrace{Ph}_{h} \underbrace{Ph}_$$

Next, we investigated three-component coupling reactions. Initially, the reaction of benzaldehyde, aniline, and trimethylsilylacetylene was carried out. However, the corresponding propargylamine was not obtained, regardless of the quantitative formation of an aldimine, which was derived from benzaldehyde and aniline. Addition of molecular sieves to remove water did not produce the propargylamine but still the aldimine was obtained. Therefore, we carried out the reaction in two steps to avoid the influence of aniline on the rhenium-catalyzed addition of trimethylsilylacetylene (2a) to aldimine 1c. Treatment of benzaldehyde with aniline in the presence of molecular sieves at 25 °C for 3 h, followed by the addition of a catalytic amount of the rhenium complex, [ReBr(CO)3(thf)]2, and trimethylsilylacetylene (2a) gave the desired three-component coupling product, propargylamine 3c, in 95% yield (eq 2). In this reaction, aromatic aldimine 1c was formed in situ by the reaction of benzaldehyde with aniline, followed by the addition of trimethylsilylacetylene to 1c in a similar way to the reaction in Table 1, Entry 3.

$$\begin{array}{c} 0\\ Ph \\ H\\ (1.1 \ equiv.) \end{array} + \begin{array}{c} Ph \\ Ph \\ H\\ (1.1 \ equiv.) \end{array} (1.0 \ equiv.) \end{array} \begin{array}{c} 1) \ \text{molecular sieves (4A)} \\ \hline 2) \ [Re Br(CO)_3(thf)]_2 \ (2.5 \ mol \ \%) \end{array} \\ = \\ SiMe_3 \ (2a, \ 1.1 \ equiv.) \\ meat, \ 50 \ ^\circ C, \ 24 \ h \end{array} \begin{array}{c} HN \\ Ph \\ \hline 3c \\ 95\% \end{array} \begin{array}{c} Ph \\ SiMe_3 \end{array} (2)$$

In summary, we have succeeded in the rhenium-catalyzed synthesis of propargylamines by the reactions of aromatic aldimines with trimethylsilylacetylene in excellent yields under mild reaction conditions. Another merit of these reactions is that they proceed in the absence of a solvent. A propargylamine could also be obtained quantitatively by the stepwise treatment of benzaldehyde with aniline, and trimethylsilylacetylene, and the rhenium catalyst. Financial support by a Grant-in-Aid for Scientific Research on Priority Areas (No. 18037049, "Advanced Molecular Transformations of Carbon Resources"), and for Young Scientists (B) (No. 18750088) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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- 12 The reaction did not proceed in the presence of triethylamine or *N*-methylaniline instead of a rhenium complex, [ReBr-(CO)₃(thf)]₂. The result indicates that aldimines or propargyl amines did not increase the nucleophilicity of trimethylsilylacetylene (**2a**) by deprotonation.
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