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# Rhenium-Catalyzed Insertion of Nonpolar and Polar Unsaturated Molecules into an Olefinic C−H Bond

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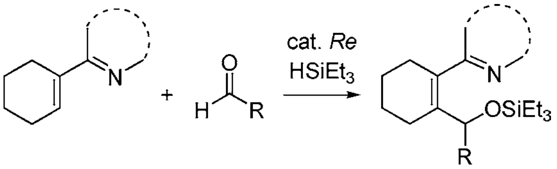
## ABSTRACT



**Treatment of olefins bearing a directing group with α,β-unsaturated carbonyl compounds, alkynes, or aldehydes in the presence of a catalytic amount of a rhenium complex, $[ReBr(CO)_3(thf)]_2$ gave γ,δ-unsaturated carbonyl compounds, dienes, and allyl silyl ethers, respectively. This reaction proceeds via C−H bond activation, insertion of unsaturated molecules into the formed rhenium−carbon bond, and then reductive elimination (or transmetalation in the case of aldehydes).**

Olefins are fundamental functional groups in organic compounds. Complex organic molecules can be constructed by functionalizing olefin moieties of substrates. For example, the Mizoroki−Heck reaction,[1] Fujiwara−Moritani reaction,[2] and olefin metathesis,[3] are well-known as preparative methods. Alternatively, multisubstituted olefins can be synthesized from alkenes in a direct and efficient manner via olefinic C−H bond activation. There have been several reports on such transformations: alkylation via intermolecular[4] and intramolecular[5] insertion of an alkene into a C−H bond, and acylation via successive insertion of carbon monoxide and alkene.[6] However, there have been fewer reports on olefin functionalizations via C−H bond activation compared with functionalizations of aromatic compounds.[7,8] In addition, it has been difficult to insert polar unsaturated molecules into an olefinic C−H bond. We report herein rhenium- and manganese-catalyzed insertion of nonpolar and polar unsaturated molecules into a C−H bond of olefins with a directing group.

Treatment of 2-(1-cyclohexenyl)pyridine (**1a**) with 2-ethylhexyl acrylate (**2a**) in the presence of a catalytic

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[1] Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066.

[2] Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992–1995.

[3] (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043. (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29.

[4] (a) Kakiuchi, F.; Tanaka, Y.; Sato, T.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 679–680. (b) Trost, B. M.; Imi, K.; Davies, I. W. *J. Am. Chem. Soc.* **1995**, *117*, 5371–5372. (c) Kakiuchi, F.; Sato, T.; Igi, K.; Chatani, N.; Murai, S. *Chem. Lett.* **2001**, 386–387. (d) Lim, Y.-G.; Kang, J.-B.; Lee, K.; Kim, Y. H. *Heteroatom Chem.* **2002**, *13*, 346–350.

[5] Fujii, N.; Kakiuchi, F.; Yamada, A.; Chatani, N.; Murai, S. *Chem. Lett.* **1997**, 425–426.

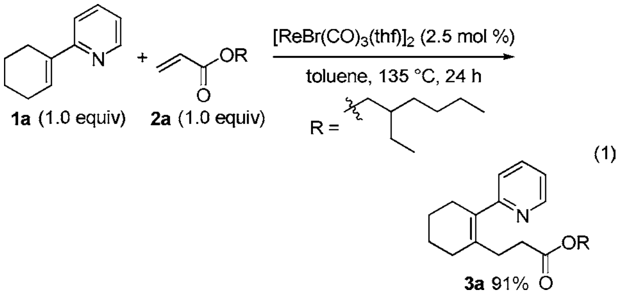
[6] Chatani, N.; Ishii, Y.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1998**, *63*, 5129–5136.

[7] There have been several reports on ruthenium- and rhodium-catalyzed transformations via C−H bond activation. (a) Kakiuchi, F.; Murai, S. *Top. Organomet. Chem.* **1999**, *3*, 47–79. (b) Guari, Y.; Sabo-Etienne, S.; Chaudret, B. *Eur. J. Inorg. Chem.* **1999**, 1047–1055. (c) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698–1712.

[8] We have reported on rhenium- and manganese-catalyzed transformations via C−H bond activation. (a) Kuninobu, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2005**, *127*, 13498–13499. (b) Kuninobu, Y.; Nishina, Y.; Shouho, M.; Takai, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2766–2768. (c) Kuninobu, Y.; Inoue, Y.; Takai, K. *Chem. Lett.* **2006**, *35*, 1376–1377. (d) Kuninobu, Y.; Kikuchi, K.; Takai, K. *Chem. Lett.* **2008**, *37*, 740–741. (e) Kuninobu, Y.; Nishina, Y.; Matsuki, T.; Takai, K. *J. Am. Chem. Soc.* **2008**, *130*, 14062–14063.

10.1021/ol900962v CCC: $40.75

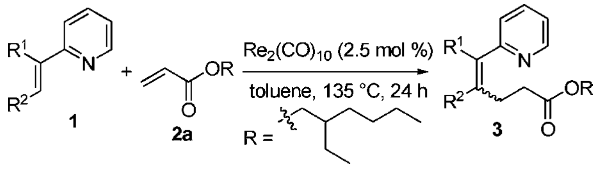
amount of a rhenium complex, [ReBr(CO)$_3$(thf)]$_2$, in toluene at 135 °C for 24 h promoted a conjugate addition-type reaction, and yielded $\gamma$,$\delta$-unsaturated ester **3a** in 91% yield (eq 1).[9,10] This result shows that the rhenium complex, [ReBr(CO)$_3$(thf)]$_2$, promoted the activation of the olefinic C−H bond.[8a−c]

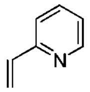
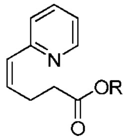
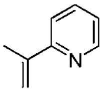
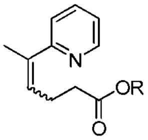
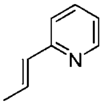
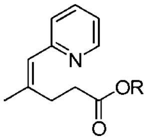


(1)

The reaction also proceeded when acyclic olefinic compounds were used as substrates (Table 1). In these investigations, a rhenium complex, Re$_2$(CO)$_{10}$, was employed as a catalyst because the olefinic substrates **1b**−**1d** were polymerized in the presence of a catalytic amount of [ReBr(CO)$_3$(thf)]$_2$. By the reaction of an olefinic compound with no substituents, **1b**, with acrylate **2a**, only *Z* isomer **3b** was formed in low yield (entry 1), and the polymerization of **1b** occurred. When olefinic substrates with a methyl group at the α- or $\beta$-position, **1c** and **1d**, were used, the reaction proceeded well, and $\beta$-alkylated products **3c** and **3d** were obtained in 76 and 77% yields (entries 2 and 3). In entry 2, **3c** was produced as a mixture of *Z* and *E* isomers.

**Table 1.** Investigation of Olefins **1**[a]

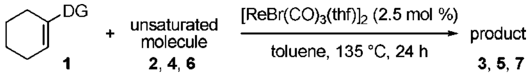


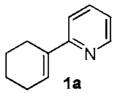
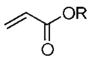
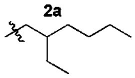
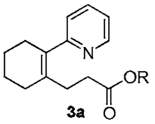
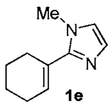
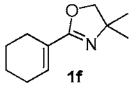
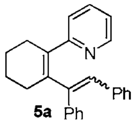
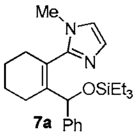
| entry | olefin | | product | | % yield[b,c] |
|---|---|---|---|---|---|
| 1 |  | **1b** |  | **3b** | 10 (12)<br>[99:1] |
| 2 |  | **1c** |  | **3c** | 76 (87)<br>[85:15] |
| 3 |  | **1d** |  | **3d** | 77 (85)<br>[99:1] |

[a] **2a** (1.0 equiv). [b] Isolated yield. Yield determined by $^1$H NMR is reported in parentheses. [c] The ratios of *Z* and *E* isomers are given in square brackets.

The selection of a directing group of olefinic substrates **1** is important to promote the reaction (Table 2). When acrylate **2a** or alkyne **4a** was employed as an unsaturated molecule, a pyridyl group was effective as a directing group; however, imidazolyl and oxazolinyl groups were ineffective (entries 1−6). On the other hand, an imidazolyl group promoted the reaction in the case of aldehyde **6a** (entry 8).[11] However,

**Table 2.** Investigation of Several Directing Groups[a]



| entry | olefin | unsaturated molecule | product | % yield[b,c] |
|---|---|---|---|---|
| 1 |  **1a** |  **2a**<br>R =  |  **3a** | 91 (96) |
| 2 |  **1e** | **2a** | — | 0 (0) |
| 3 |  **1f** | **2a** | — | 0 (0) |
| 4 | **1a** | Ph—≡—Ph<br>**4a** |  **5a** | 96 (97)<br>[88:12] |
| 5 | **1e** | **4a** | — | 0 (0) |
| 6 | **1f** | **4a** | — | 0 (0) |
| 7[d] | **1a** | PhCHO<br>**6a** | — | 0 (0) |
| 8[d] | **1e** | **6a** |  **7a** | 80 (90) |
| 9[d] | **1f** | **6a** | — | 0 (0) |

[a] **1** (1.0 equiv), **2**, **4** (1.0 equiv). [b] Isolated yield. Yield determined by $^1$H NMR is reported in parentheses. [c] The ratios of *E* and *Z* isomers are given in square brackets. [d] **6a** (1.0 equiv, 8 h) and HSiEt$_3$ (1.0 equiv, 8 h) were added three times, MS4A, 115 °C.

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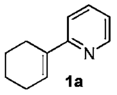
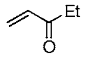
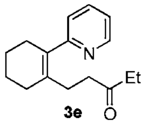
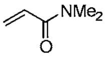
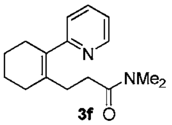
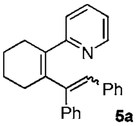
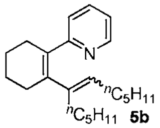
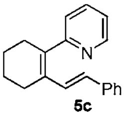
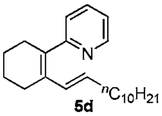
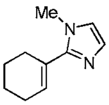
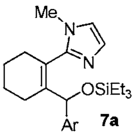
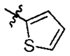
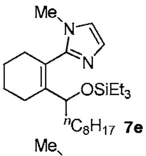
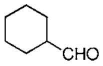
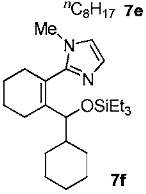
(9) This reaction also proceeded using a rhenium complex, Re$_2$(CO)$_{10}$ or ReBr(CO)$_5$, as a catalyst, and **3a** was formed in 73 and 81% yields, respectively. A rhodium complex, RhCl(PPh$_3$)$_3$, also produced **3a** in 50% yield. However, manganese complexes, Mn$_2$(CO)$_{10}$ and MnBr(CO)$_5$, and a ruthenium complex, RuH$_2$(CO)(PPh$_3$)$_3$, did not promote the reaction.

(10) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 5604–5605.

(11) Silyl ether **7a** was decomposed slightly during the isolation process. Therefore, the isolated yield was decreased compared with $^1$H NMR yield.

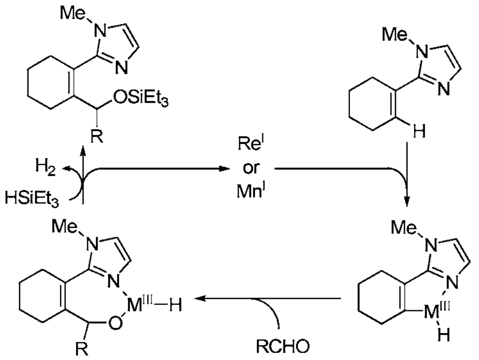
**Table 3.** Reactions between Olefins **1** and Unsaturated Molecules **2**, **4**, and **6**[a]

$$\underset{\mathbf{1}}{\text{olefin}} + \underset{\mathbf{2},\,\mathbf{4},\,\mathbf{6}}{\text{unsaturated molecule}} \xrightarrow[\text{toluene, 135 °C, 24 h}]{[\text{ReBr(CO)}_3(\text{thf})]_2\ (2.5\text{ mol \%})} \underset{\mathbf{3},\,\mathbf{5},\,\mathbf{7}}{\text{product}}$$

| entry | olefin | unsaturated molecule | product | % yield[b,c] |
|---|---|---|---|---|
| 1 |  **1a** |  **2b** |  **3e** | 91 (96) |
| 2[d] | **1a** |  **2c** |  **3f** | 47 (47) |
| 3 | **1a** | $Ph-\equiv-Ph$ **4a** |  **5a** | 96 (97)<br>[88:12] |
| 4[e] | **1a** | $^{n}C_5H_{11}-\equiv-{}^{n}C_5H_{11}$ **4b** |  **5b** | 54 (54)<br>[69:31] |
| 5[f,g] | **1a** | $\equiv-Ph$ **4c** |  **5c** | 96 (>99) |
| 6[f,g] | **1a** | $\equiv-{}^{n}C_{10}H_{21}$ **4d** |  **5d** | 96 (>99) |
| 7[h] |  **1e** | ArCHO<br>Ar = Ph **6a** |  **7a** | 80 (90) |
| 8[h,i] | **1e** | **6a** | **7a** | 46 (52) |
| 9[h] | **1e** | *p*-(MeO)$C_6H_4$ **6b** | **7b** | 81 (91) |
| 10[h] | **1e** | *p*-($CF_3$)$C_6H_4$ **6c** | **7c** | 87 (97) |
| 11[h] | **1e** |  **6d** | **7d** | 79 (86) |
| 12[j] | **1e** | $^{n}C_8H_{17}CHO$ **6e** |  **7e** | 65 (79) |
| 13[h] | **1e** |  **6f** |  **7f** | 52 (65) |

[a] **1** (1.0 equiv), **2**, **4**, **6** (1.0 equiv). [b] Isolated yield. Yield determined by $^1$H NMR is reported in parentheses. [c] The ratios of *E* and *Z* isomers are given in square brackets. [d] **2c** (1.2 equiv). [e] **4b** (1.5 equiv). [f] **4** (0.75 equiv, 12 h) was added two times. [g] $Re_2(CO)_{10}$ (5.0 mol %) was used as a catalyst. [h] **6** (1.0 equiv, 8 h) and $HSiEt_3$ (1.0 equiv, 8 h) were added three times, MS4A, 115 °C. [i] $MnBr(CO)_5$ (5.0 mol %) was used as a catalyst; 115 °C, 19 h. [j] **6e** (1.0 equiv, 16 h) and $HSiEt_3$ (1.0 equiv, 16 h) were added three times, MS4A, 115 °C.

**Scheme 1.** Proposed Mechanism for the Formation of Allyl Silyl Ethers



pyridyl and oxazolinyl groups had no promotion abilities (entries 7 and 9).

$\alpha,\beta$-Unsaturated ketone **2b** and $\alpha,\beta$-unsaturated amide **2c** also afforded the corresponding $\gamma,\delta$-unsaturated ketone **3e** and $\gamma,\delta$-unsaturated amide **3f** in 91 and 47% yields, respectively (Table 3, entries 1 and 2). Olefinic C−H functionalization also proceeded using alkynes (Table 3, entries 3−6). By the reaction of 2-(1-cyclohexenyl)pyridine (**1a**) with diphenylacetylene (**4a**), diene **5a** was provided in 96% yield (Table 3, entry 3). In this reaction, the product was obtained as a mixture of *E* and *Z* isomers. A rhodium complex, $RhCl(PPh_3)_3$, also promoted the insertion of alkyne **4a** into a C−H bond of olefin **1a**, and diene **5a** was obtained in 86% yield [*E*:*Z* = 88:12]. Dialkyl acetylene **4b** also gave the corresponding diene **5b**, however, the yield of **5b** was low (Table 3, entry 4).[12] Although there have been several examples of internal alkyne insertion into a C−H bond, only a few examples of terminal alkyne insertion has been reported.[10] As a result of investigating the insertion of terminal alkynes, we found the insertion of phenylacetylene (**4c**) and 1-dodecyne (**4d**) into a C−H bond of olefin **1a** produced tetrasubstituted dienes **5c** and **5d** in 96% yields, respectively (Table 3, entries 5 and 6). Next, we tried to insert polar unsaturated molecules, such as aldehydes.[13] Although benzaldehyde (**6a**) did not insert into a C−H bond of olefin **1a** at all, the insertion reaction proceeded when an imidazolyl group was used as a directing group (Table 3, entry 7). This reaction is a vinyl Grignard-type reaction, and generated an allyl silyl ether **7a** in 80% yield (Table 3, entry 7). A manganese catalyst, $MnBr(CO)_5$, also promoted the insertion of an aldehyde into an olefinic C−H bond. By the reaction of olefin **1e** with benzaldehyde (**6a**) and hydrosilane in the presence of a catalytic amount of a manganese complex, $MnBr(CO)_5$, provided the corresponding silyl ether **7a** in 46% yield (Table 3, entry 8).[14] Aryl aldehydes bearing

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(12) For the insertion of internal alkynes into an olefinic C−H bond, see: (a) Yotphan, S.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 2452–2453. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 3645–3651.

(13) For rhenium-catalyzed insertion of aldehydes into an aromatic C-H bond, see: (a) Kuninobu, Y.; Nishina, Y.; Nakagawa, C.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 12376–12377. (b) Kuninobu, Y.; Nishina, Y.; Takai, K. *Tetrahedron* **2007**, *63*, 8463–8468.

an electrodonating or withdrawing group, **6b** and **6c**, also yielded the corresponding silyl ethers **7b** and **7c** in 81 and 87% yields, respectively (Table 3, entries 9 and 10). A silyl ether **7d** was afforded in 79% yield using thiophene-2-carbaldehyde (**6d**) (Table 3, entry 11). Primary and secondary aliphatic aldehydes, **6e** and **6f**, also provided the corresponding silyl ethers, **7e** and **7f**, in 65 and 52% yields, respectively (Table 3, entries 12 and 13).

The proposed mechanism for the insertion of unsaturated molecules into an olefinic C−H bond is as follows (Scheme 1: represented by the reaction of aldehydes): (1) oxidative addition of an olefinic compound to a rhenium or manganese center (C−H bond activation); (2) insertion of an unsaturated molecule into the rhenium−carbon or manganese−carbon bond. At the next step, there are two pathways: (3-a) reductive elimination (in the case of acetylenes and $\alpha,\beta$-unsaturated carbonyl compounds) or (3-b) silyl protection via the formation of dihydrogen (in the case of aldehydes).

We have succeeded in rhenium-catalyzed functionalization of olefins via the insertion of unsaturated molecules into a C−H bond of an olefin moiety. In these transformations, $\alpha,\beta$-unsaturated carbonyl compounds, alkynes, and aldehydes can be employed as unsaturated molecules. As a result, $\gamma,\delta$-unsaturated carbonyl compounds, dienes, and allyl silyl ethers are obtained. We hope that this result will give a useful insight into synthetic organic chemistry.

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**Supporting Information Available:** General experimental procedure, characterization data for $\gamma,\delta$-unsaturated carbonyl compounds **3**, dienes **5**, and allyl sily ethers **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) For manganese-catalyzed insertion of aldehydes into an aromatic C-H bond, see: (a) Kuninobu, Y.; Nishina, Y.; Takeuchi, T.; Takai, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6518–6520.