

# Rhenium-Catalyzed Diastereoselective Synthesis of Aminoindanes via the Insertion of Allenes into a C–H Bond

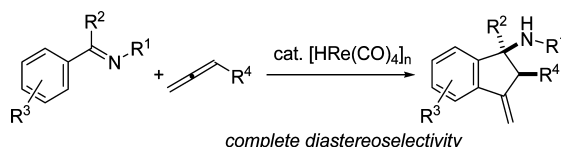
Yoichiro Kuninobu,\* Peng Yu, and Kazuhiko Takai\*

Division of Chemistry and Biochemistry, Okayama University, Tsushima, Kita-ku, Okayama 700-8530, Japan

kuninobu@cc.okayama-u.ac.jp; ktakai@cc.okayama-u.ac.jp

Received July 14, 2010

## ABSTRACT



Aminoindane derivatives were synthesized diastereoselectively by the treatment of aromatic imines with allenenes in the presence of a catalytic amount of a rhenium complex,  $[\text{HRe}(\text{CO})_4]_n$ . The allenenes inserted into the aromatic C–H bonds.

There have recently been many reports on transformations via C–H bond activation because such powerful and efficient transformations have the potential to replace previous methods.<sup>1</sup> Among them, diastereoselective transformation via C–H bond activation is a much desired reaction.<sup>2</sup> For example, the following research has been reported: chiral substrate-controlled intramolecular reactions,<sup>3</sup> chiral substrate-controlled intermolecular reactions,<sup>4</sup> and chiral rhodium-catalyzed C–H functionalizations

using diazo compounds.<sup>5</sup> However, examples of annulations with high diastereoselectivity are still rare. We report herein a highly diastereoselective rhenium-catalyzed formal [3 + 2] cycloaddition between achiral aromatic imines and achiral allenenes.

Treatment of aromatic ketimine **1a** with aliphatic allene **2a** in the presence of a catalytic amount of a rhenium complex,  $[\text{HRe}(\text{CO})_4]_n$ ,<sup>6–9</sup> without any solvents at 115 °C for 24 h gave aminoindane derivative **3a** in 88% yield as a

(1) There have been several reviews on transition-metal-catalyzed transformations via C–H bond activation. See: (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. (d) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (e) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (f) Mkhali, I. A.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890. (g) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147.

(2) For a review, see: Giri, R.; Shi, B.-F.; Engle, K. M.; Mangel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242.

(3) (a) Dangel, B. D.; Johnson, J. A.; Sames, D. *J. Am. Chem. Soc.* **2001**, *123*, 8149. (b) Wong, M.-K.; Chung, N.-W.; He, L.; Yang, D. *J. Am. Chem. Soc.* **2003**, *125*, 158. (c) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578. (d) Rech, J. C.; Yato, M.; Duckett, D.; Ember, B.; LoGrasso, P. V.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 490. (e) Fraunhoffer, K. J.; White, M. C. *J. Am. Chem. Soc.* **2007**, *129*, 7274. (f) McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc.* **2009**, *131*, 402. (g) Li, Q.; Yu, Z.-X. *J. Am. Chem. Soc.* **2010**, *132*, 4542.

(4) (a) Giri, R.; Chen, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 2112. (b) Pastine, S. J.; Gribkov, D. V.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128*, 14220. (c) Heumann, A.; Reglier, M.; Waegell, B. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 366.

(5) (a) Davies, H. M. L.; Venkataramani, C.; Hansen, T.; Hopper, D. W. *J. Am. Chem. Soc.* **2003**, *125*, 6462. (b) Davies, H. M. L.; Jin, Q. *J. Am. Chem. Soc.* **2004**, *126*, 10862.

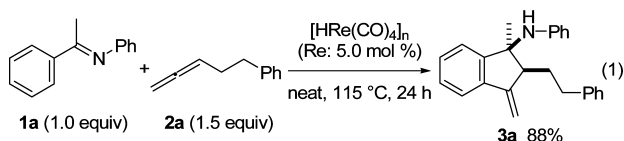
(6) Masciocchi, N.; Sironi, A. *J. Am. Chem. Soc.* **1990**, *112*, 9395.

(7) We have already reported several rhenium-catalyzed transformations via C–H bond activation. See: (a) Kuninobu, Y.; Tokunaga, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 202. (b) Kuninobu, Y.; Nishina, Y.; Shouho, M.; Takai, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2766. (c) Kuninobu, Y.; Nishina, Y.; Nakagawa, C.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 12376. (d) Kuninobu, Y.; Tokunaga, Y.; Takai, K. *Chem. Lett.* **2007**, *36*, 872. (e) Kuninobu, Y.; Nishina, Y.; Matsuki, T.; Takai, K. *J. Am. Chem. Soc.* **2008**, *130*, 14062. (f) Kuninobu, Y.; Nishina, Y.; Okaguchi, K.; Shouho, M.; Takai, K. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1393. (g) Kuninobu, Y.; Fujii, Y.; Matsuki, T.; Nishina, Y.; Takai, K. *Org. Lett.* **2009**, *11*, 2711. (h) Kuninobu, Y.; Matsuki, T.; Takai, K. *J. Am. Chem. Soc.* **2009**, *131*, 9914.

(8) Rhenium complexes  $[\text{ReBr}(\text{CO})_3(\text{thf})]_2$ ,  $\text{ReBr}(\text{CO})_5$ , and  $\text{Re}_2(\text{CO})_{10}$ , previously revealed to have catalytic activities in promoting transformations via C–H bond activation, did not give any products via the insertion of allene **2a** into the C–H bond of ketimine **1a**.

(9) Another group has also reported rhenium-catalyzed transformation via C–H bond activation. See: Chen, H. Y.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3391.

single product (eq 1).<sup>10–13</sup> In this reaction, a quaternary carbon center was constructed, and the two stereochemical centers of **3a** were defined completely.<sup>14</sup> In addition, the *exo*-methylene moiety of the product was not isomerized under the reaction conditions. There has been only one report on transition-metal-catalyzed insertion of an allene into a C–H bond of aromatic compounds.<sup>15</sup> In this reaction, the terminal carbon–carbon double bond of an allene inserts into an aromatic C–H bond. However, in our reaction, the insertion occurred at the internal carbon–carbon double bond of allene **2a**.



First, we investigated several aromatic and olefinic imines (Table 1). The corresponding aminoindane derivatives were

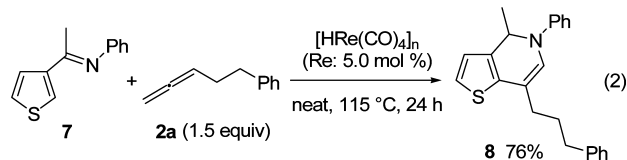
**Table 1.** Reactions between Several Imines **1** and Allene **2a**<sup>a</sup>

| entry            | R <sup>1</sup>    | R <sup>2</sup> | R <sup>3</sup>    | yield / %                                |
|------------------|-------------------|----------------|-------------------|------------------------------------------|
| 1 <sup>b,c</sup> | PhCH <sub>2</sub> | Me             | H                 | <b>1b</b> <b>3b</b> 81                   |
| 2                | Ph                | Et             | H                 | <b>1c</b> <b>3c</b> 82                   |
| 3                | Ph                | H              | H                 | <b>1d</b> <b>3d</b> 94                   |
| 4                | Ph                | Me             | 4-MeO             | <b>1e</b> <b>4a</b> 90                   |
| 5 <sup>b</sup>   | Ph                | Me             | 4-Me              | <b>1f</b> <b>3e</b> 86                   |
| 6 <sup>b</sup>   | Ph                | Me             | 4-CF <sub>3</sub> | <b>1g</b> <b>3f</b> 85                   |
| 7 <sup>b</sup>   | Ph                | Me             | 4-Br              | <b>1h</b> <b>3g</b> 87                   |
| 8 <sup>b</sup>   | Ph                | Me             | 3-Me              | <b>1i</b>                                |
|                  |                   |                |                   | <b>3h</b> <b>3h'</b> 84 [3h:3h' = 78:22] |
| 9 <sup>b</sup>   | Ph                | Me             | 2-Me              | <b>1j</b>                                |
|                  |                   |                |                   | <b>3i</b> 46 <b>4b</b> 24                |
| 10               |                   |                |                   | <b>5</b> <b>6</b> 32                     |

<sup>a</sup> **2a** (1.5 equiv). <sup>b</sup> 135 °C. <sup>c</sup> [HRe(CO)<sub>4</sub>]<sub>n</sub> (Re: 10 mol %).

formed completely diastereoselectively. The aromatic ketimine with a benzyl group at the nitrogen atom, **1b**, provided aminoindane derivative **3b** in 81% yield (entry 1). The corresponding aminoindane derivative **3c** was generated from the aromatic ketimine bearing an ethyl group at the R<sup>2</sup> position, **1c** (entry 2). Aromatic aldimine **1d** produced aminoindane **3d** quantitatively (entry 3). By using an aromatic ketimine having a methoxy group at the para position, **1e**, methylene indene **4a** was formed in 90% yield after the elimination of aniline from the corresponding aminoindane derivative (entry 4). Aromatic ketimines with a methyl or trifluoromethyl group at the para position, **1f** and **1g**, afforded aminoindanes **3e** and **3f** in 86% and 85% yields, respectively (entries 5 and 6). The reaction was not affected by a functional group, such as a bromine atom (entry 7). The corresponding aminoindane derivatives **3h** and **3h'** were obtained as a mixture of two regioisomers using an aromatic ketimine with a methyl group at the meta position of the imino group (entry 8). In the case of using an aromatic ketimine bearing a methyl group at the ortho position, **1j**, a mixture of aminoindane **3i** and methyleneindene **4b** was formed in 46% and 24% yields, respectively (entry 9). The allene **2a** also inserted into an olefinic C–H bond, and methylenecyclopentadiene **6** was afforded in 32% yield (entry 10).<sup>16</sup>

A heteroaromatic ketimine **7** also reacted with allene **2a** (eq 2). However, the desired reaction did not occur, and a bicyclic compound with sulfur and nitrogen atoms on the cyclic skeleton **8** was generated in 76% yield.<sup>17</sup>



Next, several allenes were investigated (Table 2). Allenes with a functional group, such as an ether, silyl ether, or ester,

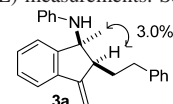
(10) Aminoindane derivative **3a** was not formed using the following transition-metal complexes: Mn<sub>2</sub>(CO)<sub>10</sub>, MnBr(CO)<sub>5</sub>, Ru<sub>3</sub>(CO)<sub>12</sub>, RuH<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>3</sub>, and RhCl(PPh<sub>3</sub>)<sub>3</sub>.

(11) Investigation of the amount of [ReH(CO)<sub>4</sub>]<sub>n</sub>: 1.0 mol %, 9%; 2.5 mol %, 72%; 10 mol %, 45%.

(12) Investigation of solvents: hexane, 67%; toluene, 55%; CH<sub>2</sub>ClCH<sub>2</sub>Cl, trace; THF, 34%; EtOH, 0%; DMF, 0%; CH<sub>3</sub>CN, 23%.

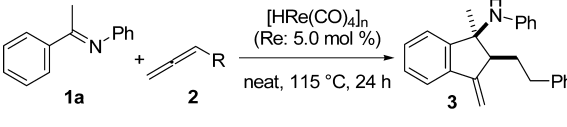
(13) Investigation of reaction time: 1 h, 10%; 3 h, 53%; 8 h, 68%; 24 h, 72%.

(14) The stereochemistry of **3a** was determined by differential nuclear Overhauser effect (difNOE) measurements. See the following structure:



(15) During our investigations, one example of iridium-catalyzed insertion of an allene into an aromatic C–H bond was reported. See: Zhang, Y. J.; Skucas, E.; Krische, M. J. *Org. Lett.* **2009**, *11*, 4248. However, the reaction point is quite different from our reaction. The reaction occurs at the terminal position (α-position) of an allene, whereas our reaction proceeded at the β-position of the allene.

(16) When 1-methyl-2-phenyl-1*H*-imidazole or 2-phenylpyridine was employed as a substrate, allene **2a** inserted into a C–H bond at the *ortho*-position of the aromatic substrates and alkenylated products was obtained in low yields (ca. 20%).

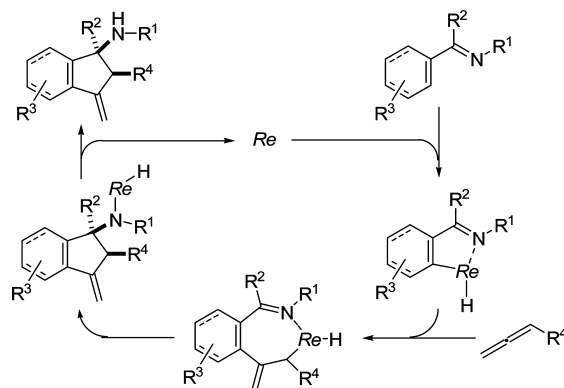
**Table 2.** Reactions between Ketimine **1a** and Allenes **2**<sup>a</sup>


| entry          | R  | yield / %                                   |
|----------------|----|---------------------------------------------|
| 1              |    | <b>2b</b> <b>3j</b> 95                      |
| 2              |    | <b>2c</b> <b>3k</b> 77                      |
| 3              |    | <b>2d</b> <b>3l</b> 92                      |
| 4              | Ph | <b>2e</b> <b>3m</b> 22                      |
| 5 <sup>b</sup> |    | <b>2f</b> <b>3n</b> 74 [67:33] <sup>c</sup> |

<sup>a</sup> **2a** (1.5 equiv). <sup>b</sup> **2f** (0.50 equiv) was added three times. <sup>c</sup> The ratios of *E* and *Z* isomers are given in square brackets.

gave the corresponding aminoindanes without losing the functional group (entries 1–3). When an allene bearing a phenyl group, **2e**, was employed, the yield of the corresponding aminoindane derivative **3m** decreased (entry 4). The corresponding aminoindane **3n** was formed as a mixture of *E* and *Z* isomers using internal allene **2f** (entry 5).<sup>18</sup> However, an aminoindane derivative was not formed using a geminal disubstituted allene (6-vinylideneundecane).

The proposed mechanism for the formation of aminoindanes is as follows (Scheme 1): (1) rhenium-catalyzed C–H

**Scheme 1.** Proposed Mechanism for the Formation of Aminoindanes **3** and Aminocyclopentene **5**

bond activation of aromatic compounds; (2) insertion of an allene into the formed Re–C bond; (3) intramolecular nucleophilic cyclization to give an aminoindane or aminocyclopentene derivative.<sup>7a,b</sup> During the intramolecular cyclization, steric repulsion between the R<sup>2</sup> and R<sup>4</sup> groups causes them to orient trans to each other on the five-membered ring after the cyclization.

In summary, we have succeeded in rhenium-catalyzed synthesis of aminoindane derivatives via the insertion of allenes into a C–H bond of aromatic compounds followed by successive intramolecular nucleophilic cyclization. Examples of the insertion of allenes into aromatic and olefinic C–H bonds are still rare. In addition, the stereochemistry of the two new carbon centers is defined completely. We hope that this reaction will become a useful method to synthesize aminoindane derivatives diastereoselectively.

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

**Supporting Information Available:** General experimental procedure and characterization data for aminoindanes **3**, methyleneindenes **4**, methylenecyclopentadiene **6**, and bicyclic compound **8**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL101627X

(17) We assume two possible pathways to explain the mechanism for the formation of bicyclic compound **8**. One possibility is that after the insertion of allene **2a** into a C–H bond of ketimine **7**, intramolecular nucleophilic cyclization did not occur, and instead, reductive elimination followed by electrocyclic reaction and isomerization of the olefin moieties proceeded. The other is that intermolecular aza-Diels–Alder reaction between allene **2a** and ketimine **7** and isomerization of the olefin occurred sequentially.

(18) In the case of using an allene with a chlorine, bromine, or iodine atom (6-halo-1,2-hexadienes), the desired aminoindanes were formed in trace amounts.