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

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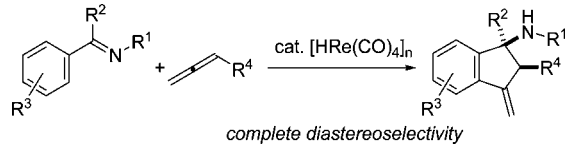
ABSTRACT



Aminoindane derivatives were synthesized diastereoselectively by the treatment of aromatic imines with allenes in the presence of a catalytic amount of a rhenium complex, $[HRe(CO)_4]_n$. The allenes 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.[1] Among them, diastereoselective transformation via C−H bond activation is a much desired reaction.[2] For example, the following research has been reported: chiral substrate-controlled intramolecular reactions,[3] chiral substrate-controlled intermolecular reactions,[4] and chiral rhodium-catalyzed C−H functionalizations using diazo compounds.[5] 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 allenes.

Treatment of aromatic ketimine **1a** with aliphatic allene **2a** in the presence of a catalytic amount of a rhenium complex, $[HRe(CO)_4]_n$,[6−9] 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) Mkhalid, 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.; Maugel, 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 $[ReBr(CO)_3(thf)]_2$, $ReBr(CO)_5$, and $Re_2(CO)_{10}$, 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.

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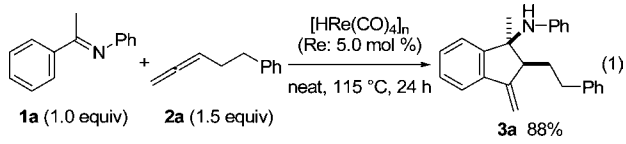
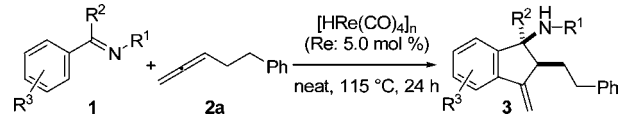
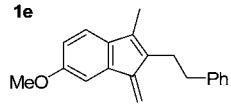
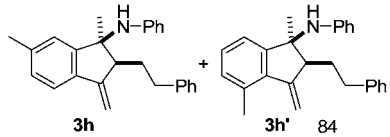
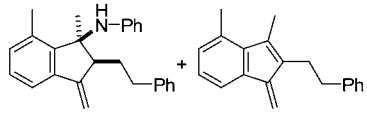
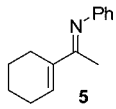
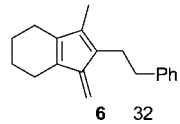
single product (eq 1).[10−13] In this reaction, a quaternary carbon center was constructed, and the two stereochemical centers of **3a** were defined completely.[14] In addition, the *exo*-methylene moiety of the product was not isomerized under the reaction conditions. There has been only one report on transition-metal-catalyzed insertion of an allene into a C−H bond of aromatic compounds.[15] 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 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^2 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).[16]

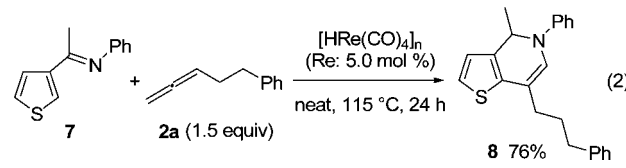
Table 1. Reactions between Several Imines **1** and Allene **2a**[a]



entry	R^1	R^2	R^3		yield / %
1[b,c]	$PhCH_2$	Me	H	**1b**	**3b** 81
2	Ph	Et	H	**1c**	**3c** 82
3	Ph	H	H	**1d**	**3d** 94
4	Ph	Me	4-MeO	**1e**	 **4a** 90
5[b]	Ph	Me	4-Me	**1f**	**3e** 86
6[b]	Ph	Me	4-CF_3	**1g**	**3f** 85
7[b]	Ph	Me	4-Br	**1h**	**3g** 87
8[b]	Ph	Me	3-Me	**1i**	 **3h** **3h'** 84 [**3h**:**3h'** = 78:22]
9[b]	Ph	Me	2-Me	**1j**	 **3i** 46 **4b** 24
10	 **5**				 **6** 32

[a] **2a** (1.5 equiv). [b] 135 °C. [c] $[HRe(CO)_4]_n$ (Re: 10 mol %).

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.[17]



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

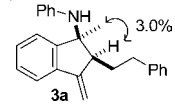
(10) Aminoindane derivative **3a** was not formed using the following transition-metal complexes: $Mn_2(CO)_{10}$, $MnBr(CO)_5$, $Ru_3(CO)_{12}$, $RuH_2(CO)(PPh_3)_3$, and $RhCl(PPh_3)_3$.

(11) Investigation of the amount of $[ReH(CO)_4]_n$: 1.0 mol %, 9%; 2.5 mol %, 72%; 10 mol %, 45%.

(12) Investigation of solvents: hexane, 67%; toluene, 55%; CH_2ClCH_2Cl, trace; THF, 34%; EtOH, 0%; DMF, 0%; CH_3CN, 23%.

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

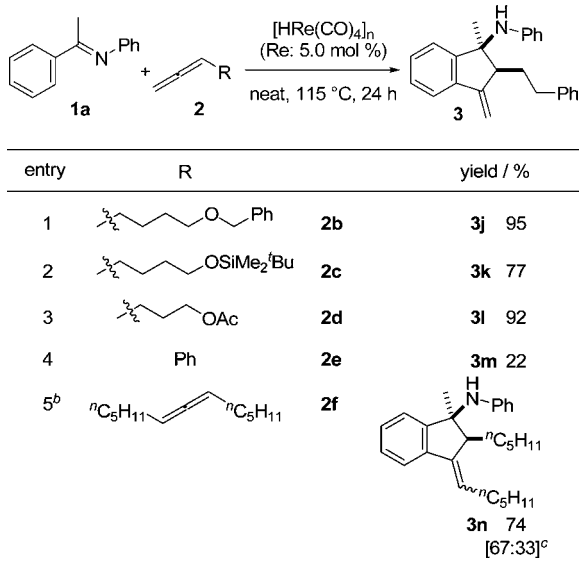
(14) The stereochemistry of **3a** was determined by differential nuclear Overhauser effect (difNOE) measurements. See the following structure:



(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**[a]

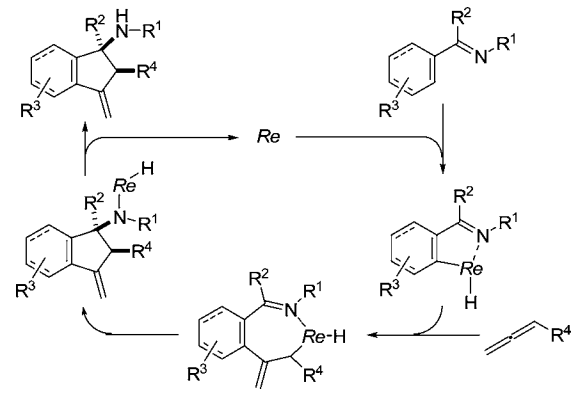


[a] **2a** (1.5 equiv). [b] **2f** (0.50 equiv) was added three times. [c] The ratios of *E* and *Z* isomers are given in square brackets.

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).[18] 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 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.[7a,b] During the intramolecular cyclization, steric repulsion between the R^2 and R^4 groups causes them to orient trans to each other on the five-membered ring after the cyclization.

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



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.

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(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.