ORGANIC LETTERS

2006
Vol. 8, No. 13
2891−2893

Sequential Ruthenium-Catalyzed Hydroamination and Rhenium-Catalyzed C–H Bond Activation Leading to Indene Derivatives

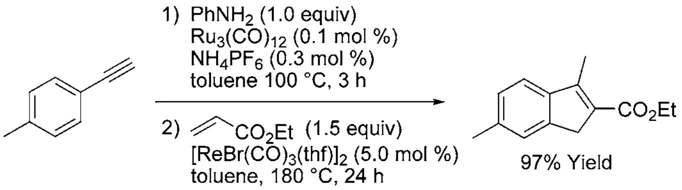
Yoichiro Kuninobu,* Yuta Nishina, and Kazuhiko Takai*

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

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

Received May 9, 2006

ABSTRACT



Formal [3+2] annulation of arylacetylenes and α,β-unsaturated carbonyl compounds is achieved in a one-pot reaction by successive treatment of the acetylenes with aniline and a catalytic amount of $Ru_3(CO)_{12}$ and NH_4PF_6 and C–H bond activation catalyzed by $[ReBr(CO)_3(thf)]_2$. The result suggests that the second rhenium-catalyzed indene formation is not disturbed by the first catalyst system.

Recently, one-pot sequential reactions using two or more metal catalysts have received considerable attention as efficient chemical transformations because they estimate a number of workup steps, which are bothersome and often cause a decrease in yields.[1] We have previously reported on the rhenium-catalyzed synthesis of indene derivatives, which are partial structures in functional materials,[2] medicines,[3] and organic compounds,[4] via C−H bond activation. We achieved this using aromatic ketimines or ketimines generated in situ by reactions between ketones and anilines.[5] The other route to prepare ketimines is hydroamination of aromatic acetylenes with amines (Figure 1).[6] In this study, we examined the successive hydroamination of aromatic acetylenes and rhenium-catalyzed C−H bond activation of the formed aromatic ketimines leading to indene derivatives.

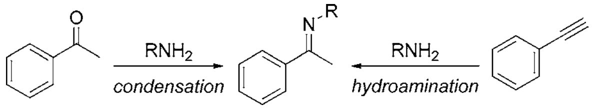


Figure 1. Preparation methods of aromatic ketimines.

Initially, we attempted to use Cp_2TiMe_2[7] and $AuCl_3$[8] for the hydroamination step. Although an aromatic ketimine was generated from phenylacetylene and aniline with the catalysts, the corresponding indene derivative was not obtained

---

[1] Shibasaki, M.; Yamamoto, Y., Eds. *Multimetallic Catalysts in Organic Synthesis*; Wiley-VCH: Weinheim, 2004.

[2] (a) Akbulut, U.; Khurshid, A.; Hacioglu, B.; Toppare, L. *Polymer* **1990**, *31*, 1343. (b) Barbera, J.; Rakitin, O. A.; Ros, M. B.; Torroba, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 296. (c) Yang, J.; Lakshmikanthan, M. V.; Cava, M. P. *J. Org. Chem.* **2000**, *65*, 6739.

[3] Korte, A.; Legros, J.; Bolm, C. *Synlett* **2004**, *13*, 2397 and references therein.

[4] Miller, R. B.; Frincke, J. M. *J. Org. Chem.* **1980**, *45*, 5312.

[5] Kuninobu, Y.; Nishina, Y.; Shouho, M.; Takai, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2766.

[6] (a) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, *32*, 104. (b) Bytschkov, I.; Doye, S. *Eur. J. Org. Chem.* **2003**, 935.

[7] For the titanium complex-catalyzed hydroamination of acetylene with aniline, see: Haak, E.; Bytschkov, I.; Doye, S. *Angew. Chem., Int. Ed.* **1999**, *38*, 3389.

[8] Luo, Y.; Li, Z.; Li, C.-J. *Org. Lett.* **2005**, *7*, 2675.

10.1021/ol0611292 CCC: $33.50

by successive treatment of the ketimine with a rhenium complex, $[ReBr(CO)_3(thf)]_2$, in toluene at 180 °C for 24 h. On the other hand, when a ruthenium complex, $Ru_3(CO)_{12}$,[9] was used as the catalyst for hydroamination, the sequential reactions proceeded as we expected. We report herein the ruthenium- and rhenium-catalyzed one-pot synthesis of indene derivatives by the reactions of aromatic acetylenes with aniline followed by treatment with α,β-unsaturated carbonyl compounds.

Treatment of phenylacetylene **1a** with aniline and a catalytic amount of $Ru_3(CO)_{12}$ and NH_4PF_6 at 100 °C in toluene generated an aromatic ketimine,[9,10] which was then treated with ethyl acrylate **2a** in the presence of $[ReBr(CO)_3(thf)]_2$, in toluene at 180 °C for 24 h. The indene derivative **3a** was obtained via ruthenium-catalyzed hydroamination and rhenium-catalyzed C−H bond activation in 82% yield (Table 1, entry 1).[11,12] This result indicates that the first-step conditions such as the choice of catalysts and solvents do not disturb the second reaction with the rhenium catalyst.

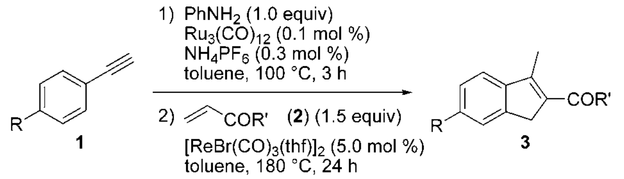
Acetylenes having electron-donating groups at the para position of the aromatic ring, **1b** and **1c**, gave the corresponding indene derivatives **3b** and **3c** in good to excellent yields, respectively (Table 1, entries 2 and 3). However, an indene derivative was not formed when using an acetylene bearing an electron-withdrawing group at the para position of the aromatic ring.[13] An acetylene having a methyl group at the ortho position of the aromatic ring gave the corresponding indene derivative **3d** in 26% yield (Table 1, entry 4). To investigate the selectivity, nonsymmetrical acetylene **1e** was used. As a result, indene derivatives **3e** and **4e** were obtained as a mixture of isomers (Table 1, entry 5). 2-Ethynylnaphthalene also gave a mixture of two isomers, **3f** and **4f**, in 81% combined yields (Table 1, entry 6).

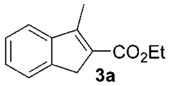
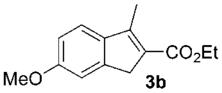
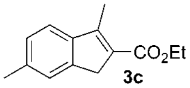
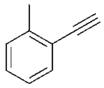
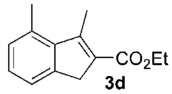
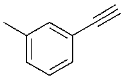
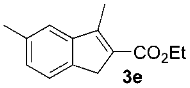
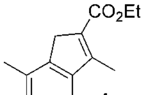
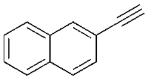
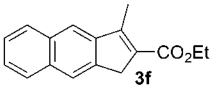
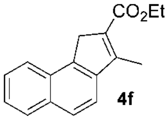
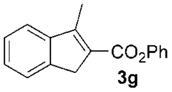
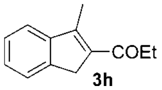
Next, we investigated the substituent of the α,β-unsaturated esters. By treatment of phenylacetylene **1a**, aniline, and phenyl acrylate **2b**, the corresponding indene derivative **3g** was formed in moderate yield (Table 1, entry 7). Vinyl ketone **2c** also generated an indene derivative **3h** in moderate yield (Table 1, entry 8), although the corresponding indene derivatives were not obtained when using styrene, acrylonitrile, and *tert*-butyl acrylate, due to polymerization.

Because phenyl acetylenes polymerize gradually with the rhenium complex, the yield of **3a** decreased to 21% when both ruthenium and rhenium catalysts were added with aniline at the same time.[14]

We consider the proposed reaction mechanism as follows:[15] (1) ruthenium-catalyzed hydroamination of an aromatic acetylene with aniline; (2) rhenium-catalyzed C−H bond activation at the ortho position of an aromatic ketimine;[5,16] (3) insertion of an α,β-unsaturated carbonyl compound into a carbon−rhenium bond; (4) intramolecular nucleophilic cyclization; (5) reductive elimination and the elimination of aniline (or vice versa) (Scheme 1).

Table 1. Reactions of Aromatic Acetylenes with α,β-Unsaturated Esters



entry	R	R'	product	% yield[a,b]
1	**1a** (R = H)	**2a** (R' = OEt)	 **3a**	82 (85)
2	**1b** (R = MeO)	**2a**	 **3b**	63 (75)
3	**1c** (R = Me)	**2a**	 **3c**	97 (>99)
4	 **1d**	**2a**	 **3d**	26 (32)
5	 **1e**	**2a**	 **3e**  **4e**	72 (80) [82:18]
6	 **1f**	**2a**	 **3f**  **4f**	81 (87) [77:23]
7	**1a**	**2b** (R' = OPh)	 **3g**	66 (72)
8	**1a**	**2c** (R' = Et)	 **3h**	49 (57)

[a] Isolated yield. The yield determined by ^1H NMR is reported in parentheses. [b] The ratio between **3** and **4** is reported in brackets.

---

(9) Tokunaga, M.; Eckert, M.; Wakatsuki, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3222.

(10) Because hydroamination of internal acetylenes does not proceed with $Ru_3(CO)_{12}$,[9] the procedure is applicable for terminal alkynes.

(11) The ^1H NMR yields were determined by using 1,1,2,2-tetrachloroethane as an internal standard.

(12) *p*-Anisidine gave indene derivative **3a** in almost the same yield as aniline. However, cyclohexylamine did not provide **3a** at all.

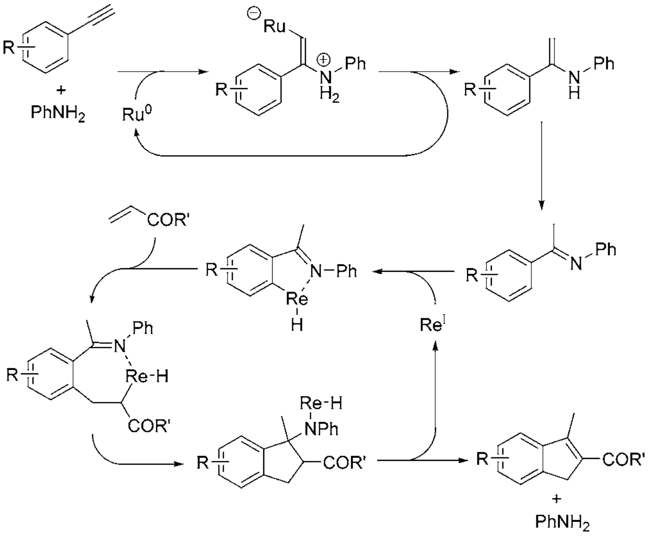
(13) The electron-withdrawing group decreased the reactivity in both the ruthenium-catalyzed hydroamination and the rhenium-catalyzed formation of indene frameworks. This might be the main reason an indene derivative was not formed by using 1-ethynyl-4-trifluoromethylbenzene.

(14) Treatment of a mixture of **1a** and **2a** with 50 mol % of aniline in the presence of $Ru_3(CO)_{12}$ (1.0 mol %), NH_4PF_6 (3.0 mol %), and $[ReBr(CO)_3(thf)]_2$ (3.0 mol %) at 180 °C for 24 h gave **3a** in 21% yield.

(15) (a) Neither the combination of the ruthenium complex, $Ru_3(CO)_{12}$, NH_4PF_6, and aniline nor the combination of the rhenium complex, $[ReBr(CO)_3(thf)]_2$, NH_4PF_6, and aniline gave indene derivatives.

(16) (a) Kuninobu, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2005**, *127*, 13498. (b) Kuninobu, Y.; Tokunaga, Y.; Kawata, A.; Takai, K. *J. Am. Chem. Soc.* **2006**, *128*, 202.

Scheme 1. Proposed Mechanism of the Formation of Indene Derivatives



In summary, we have succeeded in the synthesis of indene derivatives by the formal [3+2] annulation of aromatic terminal acetylenes with α,β-unsaturated carbonyl compounds. These reactions contain two important reaction steps: (1) ruthenium-catalyzed hydroamination of an aromatic acetylene with aniline; (2) rhenium-catalyzed reaction of the aromatic ketimine with an α,β-unsaturated carbonyl compound via C−H bond activation, conjugate addition, intramolecular nucleophilic cyclization, and the elimination of aniline.

Acknowledgment. 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.

Supporting Information Available: General experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra for indene derivatives (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL0611292