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Rhodium-Catalyzed Reaction of Terminal Alkynes with Allylamine Leading to (*E*)-3-Alkylidene *N*-Heterocycles

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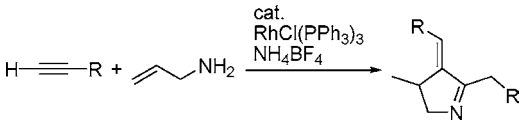
ABSTRACT



Terminal alkynes react with allylamine in the presence of a $RhCl(PPh_3)_3$ catalyst to give (*E*)-3-alkylidene-3,4-dihydro-2*H*-pyrroles. The products consist of two molecules of alkyne and one molecule of allylamine. Although dimers, trimers, and oligomers of alkynes are also obtained as byproducts, the addition of various ammonium salts to the reaction suppresses such oligomerization, resulting in an increase in product.

Vinylidene metal complexes,[1] which are readily generated by the reaction of a variety of transition-metal complexes with terminal alkynes under mild reaction conditions, are known to serve as catalyst precursors of metathesis polymerizations[2] or as key intermediates in several catalytic reactions.[3] The reactions include the regioselective addition of various oxygen-containing compounds to the terminal carbon atom of alkynes, via the nucleophilic attack of an oxygen atom on the α-carbon atom of the vinylidene metal species in the catalytic cycles.[4,5] However, corresponding reactions with nitrogen nucleophiles are relatively rare. The first reported example was the $(Et_3N)Mo(CO)_5$-catalyzed intramolecular endo cyclization of 2-alkynylanilines to indoles.[6] We previously reported that $TpRuCl(PPh_3)_2$ catalyzes the conversion of terminal alkynes to nitriles via the use of hydrazines as a nitrogen source.[7] Jun demonstrated that the hydrative dimerization of terminal alkynes gives α,β-unsaturated enones in a $RhCl(PPh_3)_3$/2-amino-3-picoline/benzoic acid catalyst system, in which α,β-unsaturated imines were formed as primary products and subsequently undergo hydration in situ.[8] We wish to report herein on a novel cyclization of terminal alkynes with allylamine catalyzed by $RhCl(PPh_3)_3$ leading to the formation of five-membered *N*-heterocyclic compounds (Scheme 1).

The reaction of 1-hexyne (**1a**, 1 mmol) with allylamine (1 mmol) in the presence of $RhCl(PPh_3)_3$ (0.05 mmol) in THF (2 mL) at 70 °C for 24 h in a 10 mL Schlenk tube gave a five-membered *N*-heterocyclic compound **2a** in 50% yield. Two terminal alkyne carbons were incorporated into

(1) For general reviews, see: (a) Bruce, M. I.; Swincer, A. *G. Adv. Organomet. Chem*. **1983**, *22*, 59. (b) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. (c) Cadierno, V.; Gamasa, M. P.; Gimeno, J. *Eur. J. Inorg. Chem.* **2001**, 571. (d) Selegue, J. P. *Coord. Chem. Rev.* **2004**, *248*, 1543.

(2) For a review on metathesis polymerization catalyzed by vinylideneruthenium complexes, see: Katayama, H.; Ozawa, F. *Coord. Chem. Rev.* **2004**, *248*, 1703.

(3) For reviews on catalytic reactions that proceeded via vinylidene metal intermediates, see: (a) Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1997**, 507. (b) Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311. (c) Bruneau, C. In *Topics in Organometallic Chemistry*; Bruneau, C., Dixneuf, P. H., Eds.; Springer: Berlin, 2004; Vol. 11 (*Ruthenium Catalysts and Fine Chemistry*), p 125. (d) Fishmeister, C.; Bruneau, C.; Dixneuf, P. H. In *Ruthenium in Organic Synthesis*; Murahashi, S.-I., Ed.; Wiley-VCH: Weinhelm, 2004, p 189. (e) Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed*. **2006**, *45*, 2176.

(4) For recent examples, see: (a) Davidson, M. H.; McDonald, F. E. *Org. Lett*. **2004**, *6*, 1601. (b) Grotjahn, D. B.; Lev, D. A. *J. Am. Chem. Soc*. **2004**, *126*, 12232.

(5) For reviews on transition-metal-catalyzed addition of heteroatom−hydrogen bonds to alkynes, see: (a) Togni, A., Grützmacher, H., Eds. *Catalytic Heterofunctionalization*; Wiley-VCH: Weinhelm, 2001. (b) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368. (c) Alonso, F.; Beletskaya, I.; Yus, P. M. *Chem. Rev.* **2004**, *104*, 3079.

(6) McDonald, F. K.; Chatterjee, A. K. *Tetrahedron Lett.* **1997**, *38*, 7687.

(7) Fukumoto, Y.; Dohi, T.; Masaoka, H.; Chatani, N.; Murai, S. *Organometallics* **2002**, *21*, 3845.

(8) Park, Y. J.; Kwon, B.-I.; Ahn, J.-A.; Lee, H.; Jun, C.-H. *J. Am. Chem. Soc*. **2004**, *126*, 13892.

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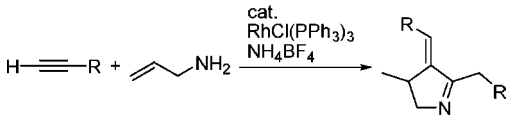
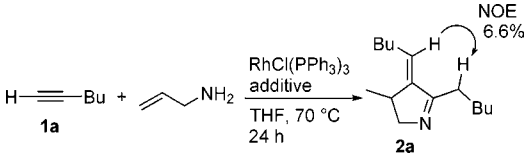
Scheme 1. $RhCl(PPh_3)_3$-Catalyzed Cyclization of Terminal Alkynes with Allylamine



the heterocycle. Interestingly, **2a** was obtained as a single regioisomer and the regiochemistry was established by ^1H NMR as well as NOE experiments. Dimers (10%) and trimers (15%) of 1-hexyne were also produced as byproducts, as $RhCl(PPh_3)_3$ is known to catalyze the oligomerization of terminal alkynes.[9] The addition of dimers in place of 1-hexyne in the present reaction system resulted in their quantitative recovery, indicating that dimers were not the initial products. Other complexes such as $[RhCl(cod)]_2$, $RhCl(CO)(PPh_3)_2$, $TpRh(PPh_3)_2$, $CpRuCl(PPh)_2/NH_4BF_4$, $[IrCl(cod)]_2/PPh_3$, and $IrCl(CO)(PPh_3)_2$ exhibited either poor or no catalytic activity at all.

The effects of additives on the $RhCl(PPh_3)_3$-catalyzed cyclization of **1a** with allylamine are shown in Table 1. The

Table 1. Effect of Additives on the $RhCl(PPh_3)_3$-Catalyzed Cyclization of **1a** with Allylamine[a]



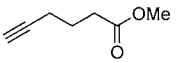
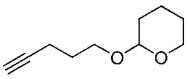
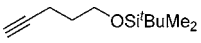
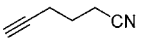
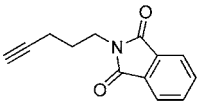
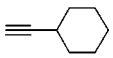
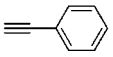
entry	additive	yield (%)[b]	entry	additive	yield (%)[b]
1	none	50	7	NH_4BF_4	78 (7)[c]
2	DBU	46	8		85[e,f]
3	$AgBF_4$	48 (32)[c]	9	NH_4PF_6	75 (10)[c]
4		66 (7)[c,d]	10		74[e]
5	$NaBF_4$	73	11	NH_4OTf	71 (11)[c]
6	NBu_4BF_4	66	12	NH_4Cl	71 (4)[c]

[a] Reaction carried out with **1a** (1.0 mmol) and allylamine (1.0 mmol) in THF (2 mL) in the presence of $RhCl(PPh_3)_3$ (0.05 mmol) and additive (0.06 mmol) at 70 °C for 24 h. [b] GC yield. [c] Recoveries of **1a** are in parentheses. [d] 48 h. [e] 30 h. [f] Isolated yield was 77%.

addition of various tetrafluoroborate salts suppressed the formation of oligomers and increased the yield of **2a** (entries 3−8). Among such salts, NH_4BF_4 gave the best result, an 85% yield (entry 8). Other ammonium salts, even NH_4Cl, were also effective as additives (entries 9−12).

Table 2 summarizes the results for the reactions of alkynes. Functional groups such as ester **1b**, THP **1c**, siloxy **1d**, nitrile **1e**, and imide **1f** were compatible with the reaction (entries 1−5). Although the reaction of ethynylcyclohexane (**1g**) afforded **2g** as product in 58% yield as listed in entry 6, the

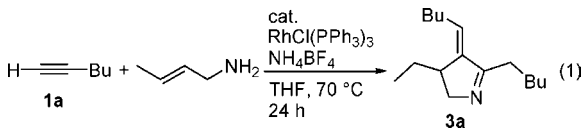
Table 2. $RhCl(PPh_3)_3/NH_4BF_4$-Catalyzed Cyclization of Terminal Alkynes with Allylamine[a]

entry	alkyne		product	yield (%)[b]
1		**1b**	**2b**	70
2		**1c**	**2c**	64
3		**1d**	**2d**	66
4		**1e**	**2e**	71
5		**1f**	**2f**	73
6		**1g**	**2g**	58
7		**1h**	**2h**	10
8		**1i**	**2i**	61[c]

[a] Reaction conditions: alkyne (1.0 mmol), allylamine (1.0 mmol) in THF (2 mL) in the presence of $RhCl(PPh_3)_3$ (0.05 mmol) and NH_4BF_4 (0.06 mmol) at 70 °C for 30 h. [b] Isolated yield. [c] **1i** was added to the mixture of allylamine and $RhCl(PPh_3)_3$ in THF at 70 °C over 2 h and then stirred at the same temperature for 2 h.

use of *tert*-butylacetylene (**1h**) gave **2h** in only 10% yield, with a large amount of unreacted **1h** (entry 7). Treatment of phenylacetylene (**1i**) with allylamine yielded **2i** in 30% yield along with dimers (10%) and some unidentified products; however, the slow addition of **1i** to the reaction mixture at 70 °C over 2 h improved the yield of **2i** to 61% (entry 8).

Although the reaction of **1a** with crotylamine also led to the formation of the 4-ethyl-substituted *N*-heterocycle **3a** in 40% yield (eq 1), the use of other alkenylamines, such as cinnamylamine and 3-butenylamine, resulted in no cyclization products.



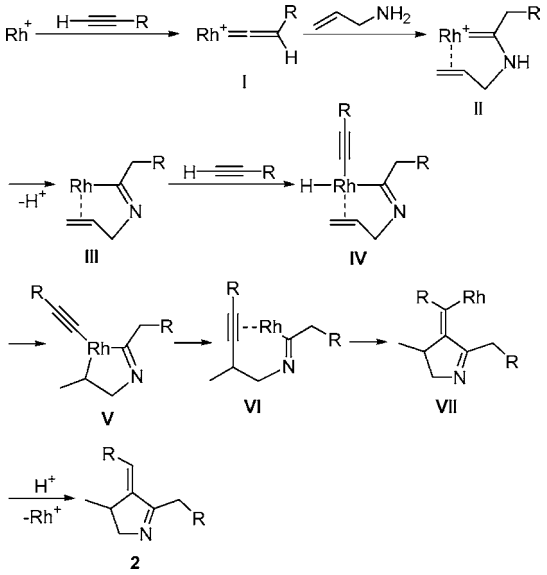
Although details of the reaction mechanism are unclear, a proposed mechanism for the present reaction via the formation of the vinylidene−rhodium complex[10] as the key intermediate is shown in Scheme 2. A cationic rhodium complex, generated from the in situ reaction of $RhCl(PPh_3)_3$ with NH_4BF_4, reacts with a terminal alkyne to form a vinylidene complex **I**.[11,12] Nucleophilic attack of the nitrogen

(9) (a) Shinger, H.; Wilkinson, G. *J. Chem. Soc. (A)* **1968**, 849. (b) Yoshikawa, S.; Kiji, J.; Furukawa, *J. Makromol. Chem.* **1977**, *178*, 1077. (c) Carlton, L.; Read, G. *J. Chem. Soc., Perkin 1* **1978**, 1631.

(10) For a review on vinylidene−rhodium complexes, see: Werner, H. *Coord. Chem. Rev.* **2004**, *248*, 1693.

(11) A cationic rhodium complex $[Rh(cod)_2]BF_4/PPh_3$ gave **2a** in 69% yield for 48 h.

Scheme 2. Proposed Mechanism



of the allylamine on the α-carbon of the vinylidene ligand provides an aminocarbene **II**, which undergoes deprotonation to afford an imino complex **III**. The oxidative addition of the second molecule of the terminal alkyne to **III** gives **IV**.[13] The metallacycle **V** is formed by the addition of an H−Rh bond to a C=C bond. Reductive elimination from **V** gives **VI**, which undergoes the cis addition of a C−Rh bond to a C≡C bond to afford **VII**. Finally, the protonolysis of **VII** furnishes **2**, with regeneration of the cationic rhodium species. Although the role of the NH_4 cation is unclear, protons would accelerate the formation of the vinylidene−rhodium complex **I** via the intermolecular protonation of the alkynyl ligand[14] and/or the protonolysis of **VII**.[15]

In summary, we reported herein the $RhCl(PPh_3)_3/NH_4BF_4$-catalyzed cyclization of terminal alkynes with allylamines to give (*E*)-3-alkylidene-3,4-dihydro-2*H*-pyrroles. The addition of various ammonium salts suppressed the oligomerization of the terminal alkynes, resulting in an increase in product yield. The scope, detailed mechanism, and synthetic application of this reaction are currently under investigation.

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Supporting Information Available: Experimental procedures and characterization of all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL0619415

(12) For an example of the cationic vinylidene−rhodium complex, see: Windmüller, B. B.; Nürnberg, O.; Wolf, J.; Werner, H. *Eur. J. Inorg. Chem.* **1999**, 613.

(13) Wolf, J.; Werner, H.; Serhadli, O.; Ziegler, M. L. *Angew. Chem., Int. Ed.* **1983**, *22*, 414.

(14) Bianchini, C.; Meli, A.; Peruzini, M.; Zanobini, F. *Organometallics* **1990**, *9*, 241.

(15) An alternative mechanism involves the formation of another vinylidene−rhodium complex **X** from **II** via **VIII** and **IX**.