DOI: 10.1002/ange.201101009

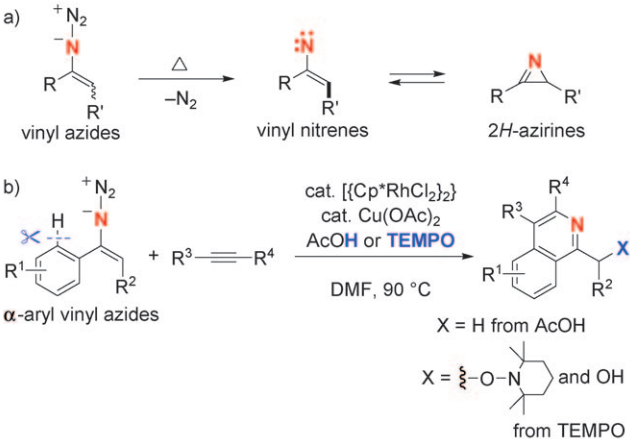
Synthetic Methods

Synthesis of Isoquinolines from α-Aryl Vinyl Azides and Internal Alkynes by Rh–Cu Bimetallic Cooperation**

*Yi-Feng Wang, Kah Kah Toh, Jian-Yuan Lee, and Shunsuke Chiba**

Multimetallic catalytic systems including their synergystic cooperation can potentially achieve chemical transformations that are unprecedented with monometallic catalysts. In spite of the recent and significant development of the multimetallic catalytic reactions in organic synthesis,[1,2] it is still a challenge to achieve the rational design of artificial multimetallic catalytic systems and their application to organic transformations that possess distinct functionality and are highly efficient. A hetero-bimetallic system that performs sequential reactions is of great interest, in which one catalyst achieves the initial step to give an intermediate that is relayed to another for the next transformation to produce the final product.[3]

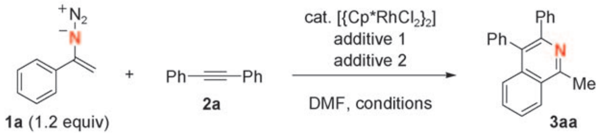
We have recently been interested in the application of vinyl azides for the synthesis of aza-heterocyles.[4] One of the intriguing chemical features of vinyl azides is their thermal decomposition into highly strained three-membered cyclic imines, 2*H*-azirines, which could be regarded as an equivalent of a vinyl nitrene (Scheme 1 a).[5] Our current study focuses on the use of these nitrogen atoms derived from α-aryl vinyl azides to direct a metal complex for *ortho* C–H metallation,[6] which might be followed by a C–C and C–N bond-formation sequence to construct aza-heterocyclic frameworks. Herein, we report the synthesis of highly substituted isoquinolines from readily available α-aryl vinyl azides and internal alkynes under a rhodium/copper bimetallic catalytic system (Scheme 1 b). A preliminary mechanistic investigation revealed that both the rhodium and copper are prerequisites for achieving the catalytic cycle, and play their particular roles with synergistically during the multistep sequence. The present transformation is carried out in the following steps: 1) Cu^I-mediated denitrogenative reductive formation of imine derivatives from α-aryl vinyl azides probably through the C–N bond cleavage of putative 2*H*-azirine intermediates, 2) formation of an iminyl rhodium(III) species and their *ortho* C–H rhodation, alkyne insertion, and C–N bond reductive elimination to afford isoquinolines.



Scheme 1. a) Thermal decomposition of vinyl azides into 2*H*-azirines. b) This work. $Cp^* = C_5Me_5$. TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxyl.

Davies and co-workers showed that the combined use of $[\{Cp^*RhCl_2\}_2]$ and NaOAc generates $[Cp^*Rh(OAc)_n]$ species and results in fission of certain C–H bonds with the aid of an intramolecular directing group such as the imino group to afford rhodacycle complexes.[7] This chemistry has been thoroughly investigated in terms of the reactivity of the rhodacycles as well as the reaction mechanism of the cyclometallation reported by Jones et al.[8] Recently, this method was successfully applied to various kinds of heterocycle syntheses involving the insertion of alkynes.[9,10] Based on

Table 1: Optimization of the reaction conditions.[a]



Entry	[{Cp*RhCl$_2$}$_2$] [mol %]	Additive 1 (mol %)	Additive 2 (mol %)	Conditions	**3aa** [%][b]
1	5	NaOAc (30)	–	110 °C, 12 h	0
2	5	CsOPiv (30)	–	110 °C, 12 h	0
3	5	$Cu(OAc)_2$ (20)	–	110 °C, 0.3 h	70
4	5	$Cu(OAc)_2$ (20)	H_2O (100)	90 °C, 1 h	67[c]
5	5	$Cu(OAc)_2$ (20)	AcOH (100)	90 °C, 0.6 h	80
6	2.5	$Cu(OAc)_2$ (20)	AcOH (100)	90 °C, 2 h	84
7	2.5	CuOAc (20)	AcOH (100)	90 °C, 0.5 h	84

[a] All reactions were carried out in the scale of 0.5 mmol of alkyne **2a** with 1.2 equiv of vinyl azide **1a** under a N_2 atmosphere. [b] Yields of isolated products are based on alkyne **2a**. [c] Yields as determined by NMR analysis of the crude reaction mixture.

---

[*] Y.-F. Wang, K. K. Toh, J.-Y. Lee, Dr. S. Chiba
Division of Chemistry and Biological Chemistry
School of Physical and Mathematical Sciences
Nanyang Technological University
Singapore 637371 (Singapore)
Fax: (+65) 6791-1961
E-mail: shunsuke@ntu.edu.sg

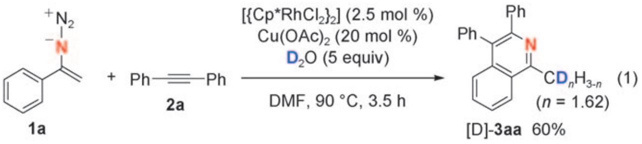
[**] This work was supported by funding from Nanyang Technological University and Singapore Ministry of Education (Academic Research Fund Tier 2: MOE2010-T2-1-009).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201101009.

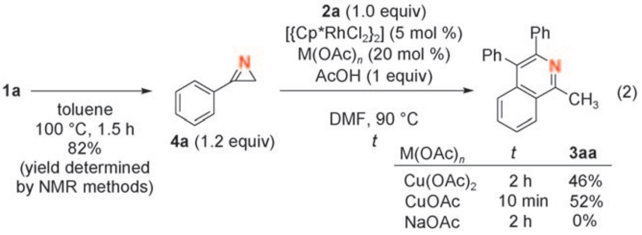
these studies, we embarked on our investigation of the reaction of α-azido styrene (**1a**) and diphenylacetylene (**2a**) using [{Cp*RhCl$_2$}$_2$] as a catalyst with carboxylate sources to target isoquinoline derivatives (Table 1). Although the utilization of NaOAc or CsOPiv (30 mol %) as carboxylate sources did not afford any *ortho* C−H functionalization products (entries 1 and 2), the reaction with Cu(OAc)$_2$ (20 mol %) at 110 °C in DMF gave 1-methyl-3,4-diphenylisoquinoline (**3aa**) in 70 % yield (entry 3). The addition of acetic acid (1 equiv) proved to be optimal for the isoquinoline formation, allowing the use of a lower temperature (90 °C) and a catalytic amount of [{Cp*RhCl$_2$}$_2$] (2.5 mol %; entries 5 and 6). Notably, an acceleration of the reaction rate was observed when utilizing CuOAc instead of Cu(OAc)$_2$ (entry 7).[11] It was also confirmed that the reaction with Cu(OAc)$_2$ in the absence of [{Cp*RhCl$_2$}$_2$] did not afford isoquiniline **3aa** at all.

By utilizing the [{Cp*RhCl$_2$}$_2$]/Cu(OAc)$_2$ (5/20 mol %) catalytic system,[12] we examined the generality of this catalytic method for the synthesis of substituted isoquinolines (Table 2). The present process showed wide substrate tolerance for internal alkynes (entries 1–8). Diarylacetylenes reacted smoothly with vinyl azide **1a**, giving isoquinolines **3** in good yields (entries 1–3). The reactions with dialkyl-substituted alkynes also proceeded smoothly (entries 4 and 5). Insertion of an unsymmetrical alkyne, 1-phenyl-1-propyne (**2g**), occurred regioselectively to provide 4-methyl-3-phenylisoquinoline (**3ag**) as a sole product (entry 6). Similarly, methyl 3-phenylpropiolate (**2h**) and thienylacetylene **2i** afforded isoquinoline **3ah** and **3ai**, respectively, in a regioselective manner albeit in moderate yields (entries 7 and 8). Electron-withdrawing groups could be installed as substituents on the benzene ring of vinyl azides **1**[13] to result in isoquinoline formation in good yields, although the vinyl azide **1c** bearing an electron-donating moiety (OMe: entry 10) as well as 1-naphthyl vinyl azide **1g** (entry 14) were sluggish. This process tolerated C−Br bonds (entries 3, 12, and 15). In the case of *meta*-substituted substrates, regioisomeric mixtures were obtained where the less sterically hindered C−H bond was preferentially cleaved (marked in blue) (entries 15 and 16). This method allowed the construction of γ-carboline and 1*H*-pyrrolo[2,3-*c*]pyridine structures (entries 17 and 18). Similarly, benzofuranyl and benzothiofuranyl vinyl azides **1l** and **1m** could be utilized for this transformation albeit in moderate yield in the case of benzofuranyl derivative **3la** (entries 19 and 20). At the β position of vinyl azides **1**, methyl, hydroxymethyl, and aminomethyl functional groups could be introduced, thus leading to the corresponding isoquinolines **3** in good to moderate yields (entries 21–26).

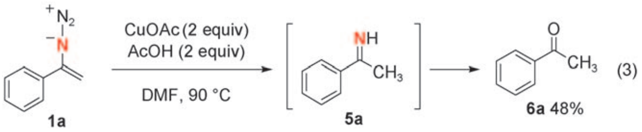
To probe the reaction mechanism especially with regard to the function of both catalysts in the present isoquinoline formation, a series of experiments were examined using vinyl azide **1a** and alkyne **2a**. The reaction in the presence of D$_2$O (5 equiv) led to incorporation of deuterium at the methyl group of isoquinoline [D]-**3aa** [Eq. (1); DMF = *N*,*N*-dimethylformamide], whereas the utilization of [D$_7$]DMF as a solvent did not provide deuterated isoquinoline at all.[14] These observations indicated that a hydrogen atom at the methyl moiety could be introduced not through a radical pathway but in an ionic manner.



Next, we thermally decomposed **1a** in toluene at 100 °C to prepare 2*H*-azirine **4a**, which was then subjected to the reaction with alkyne **2a** in the presence of [{Cp*RhCl$_2$}$_2$] and metal acetates as catalysts. The reaction with Cu(OAc)$_2$ or CuOAc as a metal acetate afforded isoquinoline **3aa**, whereas utilization of NaOAc did not form **3aa** [Eq. (2)]. The reaction with CuOAc was completed within 10 minutes whereas that of Cu(OAc)$_2$ needed 2 hours, which was consistent with the reactions of vinyl azides (Table 1, entries 6 and 7). The reaction of vinyl azide **1a** with 2 equivalents of CuOAc in the presence of AcOH provided acetophenone (**6a**) in 48 % yield, probably by the hydrolysis of the putative N−H imine intermediate **5a** [Eq. (3)]. Notably, the reaction with [{Cp*RhCl$_2$}$_2$]/Cu(OAc)$_2$ under an oxygen atmosphere did not afford isoquinoline **3aa** at all, whereas a CO atmosphere gave isoquinoline **3aa** in 82 % yield within 0.5 hours [Eq. (4)]. These results suggested that both rhodium and copper are required to induce *ortho*-C−H functionalization from 2*H*-azirine **4a**. Lower-valent copper(I) species might play an indispensable role of reductive ring opening of 2*H*-azirines to give imine derivatives[15] that could be used to initiate the Rh^{III}-catalyzed *ortho*-C−H rhodation with subsequent insertion of alkynes. The UV/Vis spectra for the treatment of Cu(OAc)$_2$ in DMF at 90 °C showed the disappearance of the band in the visible region corresponding to Cu(OAc)$_2$ (≈700 nm) within 30 minutes (see the Supporting Information), thereby implying that DMF might reduce Cu(OAc)$_2$ to form a Cu^I species.[16,17]



M(OAc)$_n$	t	3aa
Cu(OAc)$_2$	2 h	46%
CuOAc	10 min	52%
NaOAc	2 h	0%



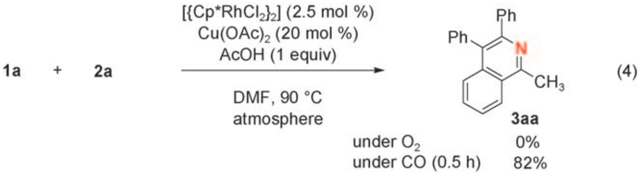
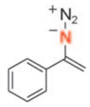
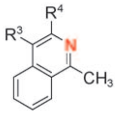
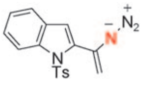
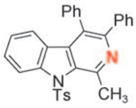
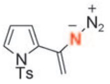
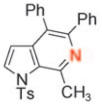
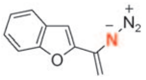
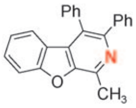
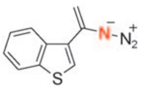
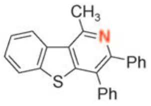
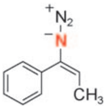
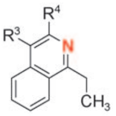
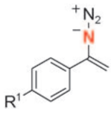
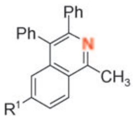
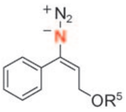
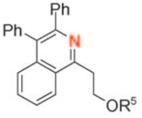
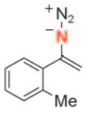
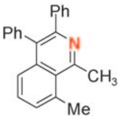
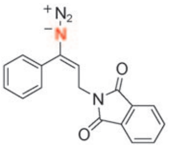
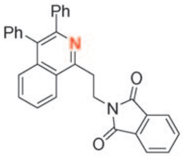
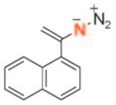
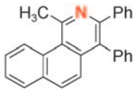
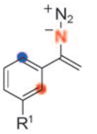
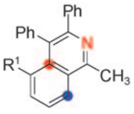
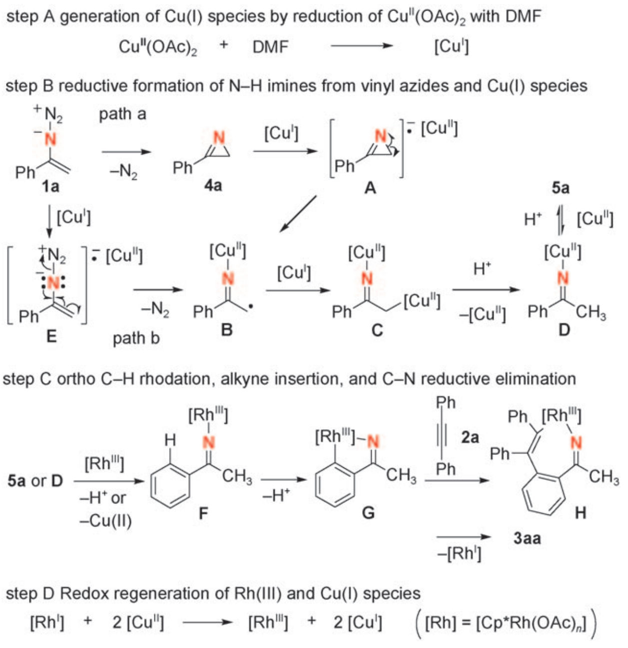


Table 2: Substrate scope.[a]

Entry	Vinyl azides **12**	Alkynes **2**	Yield	Entry	Vinyl azides **1**	Alkynes **2**	Yield
		$R^3-\equiv-R^4$		17			
1	**1a**	**2b** (R^3, R^4 = 4-MeOC$_6$H$_4$)	**3ab**: 77%		**1j**	**2a**	**3ja**: 82%
2	**1a**	**2c** (R^3, R^4 = 4-ClC$_6$H$_4$)	**3ac**: 70%	18			
3[c]	**1a**	**2d** (R^3, R^4 = 4-BrC$_6$H$_4$)	**3ad**: 83%		**1k**	**2a**	**3ka**: 77%
4	**1a**	**2e** (R^3, R^4 = *n*Pr)	**3ae**: 71%	19[f]			
5	**1a**	**2f** (R^3, R^4 = CH$_2$OTBS)	**3af**: 54%		**1l**	**2a**	**3la**: 45%
6	**1a**	**2g** (R^3 = CH$_3$, R^4 = Ph)	**3ag**: 82%				
7	**1a**	**2h** (R^3 = CO$_2$Me, R^4 = Ph)	**3ah**: 27%	20	**1m**	**2a**	**3ma**: 75%
8	**1a**	**2i** (R^3 = *n*-hexyl, R^4 = 2-thienyl)	**3ai**: 52%[d]				
		Ph—≡—Ph		21[e]	**1n**	**2a**	**3na**: 85%
9	**1b** (R^1 = Me)	**2a**	**3ba**: 80%	22[e]	**1n**	**2e**	**3ne**: 54%
10	**1c** (R^1 = OMe)	**2a**	**3ca**: 45%[d]	23[e]	**1n**	**2g**	**3 ng**: 80%
11[e]	**1d** (R^1 = CO$_2$Me)	**2a**	**3da**: 86%				
12	**1e** (R^1 = Br)	**2a**	**3ea**: 80%	24	**1o** (R^5 = TBDPS)	**2a**	**3oa**: 46%
				25	**1p** (R^5 = allyl)	**2a**	**3pa**: 40%
13	**1f**	**2a**	**3 fa**: 70%				
				26	**1q**	**2a**	**3qa**: 85%
14	**1g**	**2a**	**3ga**: 38%				
			 				
15	**1h** (R^1 = Br)	**2a**	**3ha**: 74% **3ha′**: 12%				
16	**1i** (R^1 = NO$_2$)	**2a**	**3ia**: 66% **3ia′**: 5%				

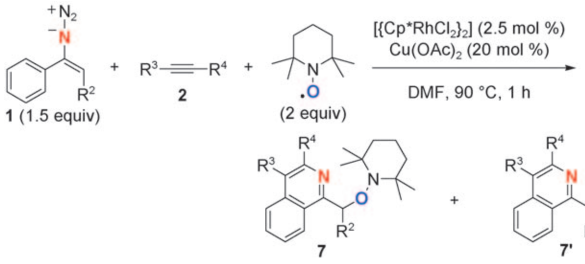
[a] The reactions were carried out by treatment of a mixture of vinyl azides **1** (1.2 equiv) and alkyne **2** (0.5 mmol) with $[\{Cp^*RhCl_2\}_2]$ (5 mol%) and Cu(OAc)$_2$ (20 mol%) in the presence of AcOH (1 equiv) in DMF (2.5 mL) at 90 °C under N$_2$ atmosphere for 1–2 h. [b] Yields of isolated products. [c] 1.5 equiv of vinyl azides **1a** was used. [d] NMR yields. [e] 2.5 mol% of $[\{Cp^*RhCl_2\}_2]$ was utilized. [f] 10 mol% of $[\{Cp^*RhCl_2\}_2]$ was utilized. TBS = *tert*-butyldimethylsilyl. TBDPS = *tert*-butyldiphenylsilyl. Ts = *p*-toluenesulfonyl.



Scheme 2. The proposed reaction pathway.

Based on these experimental data, a proposed mechanism for the reaction using the [{Cp*RhCl$_2$}$_2$]/Cu(OAc)$_2$ catalytic system was outlined in Scheme 2. First, Cu(OAc)$_2$ might be reduced by DMF to form a Cu^I species (step A). Thermal denitrogenative decomposition of the vinyl azide **1a** gave 2*H*-azirines **4a**, which could be reduced by the Cu^I species to afford the anion radical **A** (step B, path a). Consecutive C–N bond cleavage of **A** formed the iminyl copper(II) radical intermediate **B**, which could be additionally reduced with Cu^I and protonated to deriver N–H imine **5a** along with a Cu^{II} species. Alternatively, the direct reduction of the vinyl azide **1a** by a Cu^I species could also be proposed to form the putative radical intermediates **B** through a vinyl azide anion radical **E** (path b).[18] Formation of the rhodacycle **G** from **5a** or iminyl copper species such as **D** with Rh^{III} via iminyl rhodium **F**, subsequent insertion of alkyne **2a**, and C–N reductive elimination from **H** could provide isoquinoline **3aa** with generation of a Rh^I species (step C). Finally, a redox reaction between Rh^I and Cu^{II} species would lead to regeneration of Rh^{III} and Cu^I (step D).

Table 3: Reaction with TEMPO.[a]



Entry	Vinyl azides **1**	Alkynes **2**	Yield[b]	Yield[b]
1	**1n** ($R^2=CH_3$)	**2a** (R^3, R^4 = Ph)	**7na**: 68%	**7na'**: 15%
2	**1n** ($R^2=CH_3$)	**2e** (R^3, R^4 = *n*Pr)	**7ne**: 39%	**7ne'**: 42%
3	**1n** ($R^2=CH_3$)	**2g** ($R^3=CH_3$, R^4 = Ph)	**7ng**: 55%	**7ng'**: 18%
4[c]	**1q** ($R^2=CH_2NPI$)	**2a** (R^3, R^4 = Ph)	**7qa**: 48%	**7qa'**: 29%

[a] All reactions were carried out with alkyne **2** (0.5 mmol), vinyl azide **1** (1.5 equiv), and of TEMPO (2 equiv) in DMF (2.5 mL) under a N_2 atmosphere for 1 h. [b] Yields of isolated products based on alkynes **2**. [c] 5 mol% of [{Cp*RhCl$_2$}$_2$] was utilized. NPI = *N*-phthalimidoyl.

It could be speculated that the reductive formation of imine derivatives from vinyl azides proceeds by the protonation of the Cu^{II} aza-enolates such as **C** (Scheme 2, step B). We envisioned trapping such putative aza-enolates with the other electrophiles for further functionalization of isoquinoline derivatives. Recent literature precedents have shown that Cu^{II}/TEMPO complexes work as an ionic electrophile.[19] When TEMPO (2 equiv) was added instead of AcOH in the reaction of vinyl azides **1n** and **1q** with alkynes **2** under the [{Cp*RhCl$_2$}$_2$]/Cu(OAc)$_2$ catalytic system, isoquinoline/TEMPO adducts **7** and alcohols **7'** were isolated in good combined yields (Table 3).[20–23] From vinyl azide **1q**, the 1,2-aminoalcohol unit could be installed in the isoquinoline framework (entry 4).

In summary, we have developed a synthetic method to deliver highly substituted isoquinolines from readily available α-aryl vinyl azides and internal alkynes in the presence of a [{Cp*RhCl$_2$}$_2$]/Cu(OAc)$_2$ bimetallic catalyst system. Further exploitation of the other types of multimetallic cooperation, which achieve unprecedented organic transformations, is currently underway.

Received: February 9, 2011
Revised: March 24, 2011

Keywords: alkynes · azides · copper · heterocycles · rhodium

---

[1] For reviews, see: a) J. M. Lee, Y. Na, H. Han, S. Chang, *Chem. Soc. Rev.* **2004**, *33*, 302; b) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187; c) G. J. Rowlands, *Tetrahedron* **2001**, *57*, 1865; d) B. Bosnich, *Inorg. Chem.* **1999**, *38*, 2554; e) E. K. van den Beuken, B. L. Feringa, *Tetrahedron* **1998**, *54*, 12985.

[2] For selected reviews on biomimetic design inspired by multimetallic enzyme systems, see: a) S. Itoh, S. Fukuzumi, *Acc. Chem. Res.* **2007**, *40*, 592; b) E. A. Lewis, W. B. Tolman, *Chem. Rev.* **2004**, *104*, 1047; c) P. Molenveld, J. F. J. Engbersen, D. N. Reinhoudt, *Chem. Soc. Rev.* **2000**, *29*, 75; d) N. H. Williams, B. Takasaki, M. Wall, A. J. Chin, *Acc. Chem. Res.* **1999**, *32*, 485.

[3] For recent selected examples, see: a) L. J. Gooßen, F. Rudolphi, C. Oppel, N. Rodríguez, *Angew. Chem.* **2008**, *120*, 3085; *Angew. Chem. Int. Ed.* **2008**, *47*, 3043; b) S. Ko, B. Kang, S Chang, *Angew. Chem.* **2005**, *117*, 459; *Angew. Chem. Int. Ed.* **2005**, *44*, 455; c) S. Ko, C. Lee, M.-G. Choi, Y. Na, S. Chang, *J. Org. Chem.* **2003**, *68*, 1607; d) J. Cossy, F. Bargiggia, S. BouzBouz, *Org. Lett.* **2003**, *5*, 459; e) N. Jeong, S. D. Seo, J. Y. Shin, *J. Am. Chem. Soc.* **2000**, *122*, 10220.

[4] a) Y.-F. Wang, S. Chiba, *J. Am. Chem. Soc.* **2009**, *131*, 12570; b) Y.-F. Wang, K. K. Toh, S. Chiba, K. Narasaka, *Org. Lett.* **2008**, *10*, 5019; c) S. Chiba, Y.-F. Wang, G. Lapointe, K. Narasaka, *Org. Lett.* **2008**, *10*, 313.

[5] a) Å. S. Timén, E. Risberg, P. Somfai, *Tetrahedron Lett.* **2003**, *44*, 5339; b) B. C. G. Söderberg, *Curr. Org. Chem.* **2000**, *4*, 727; c) D. Knittel, *Synthesis* **1985**, 186.

[6] For recent reiews on C–H functionalization, see: a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; b) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; c) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 677; d) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem.* **2009**, *121*, 9976; *Angew. Chem. Int. Ed.* **2009**, *48*, 9792; e) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094; f) A. A. Kulkarni, O. Daugulis, *Synthesis* **2009**, 4087; g) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, 3013.

[7] D. L. Davies, O. Al-Duaij, J. Fawcett, M. Giardiello, S. T. Hilton, D. R. Russell, *Dalton Trans.* **2003**, 4132. For a review on carboxylate-assisted transition metal catalyzed C–H bond functionalizations, see: L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315.

[8] L. Li, W. W. Brennessel, W. D. Jones, *Organometallics* **2009**, *28*, 3492.

[9] For reports on Rh^{III}-catalyzed oxidative C–H bond functionalization/C–N bond formation with alkynes, see: a) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326; b) J. Chen, G. Song, C.-L. Pan, X. Li, *Org. Lett.* **2010**, *12*, 5426; c) Y. Su, M. Zhao, K. Han, G. Song, X. Li, *Org. Lett.* **2010**, *12*, 5462; d) T. K. Hyster, T. Rovis, *J. Am. Chem. Soc.* **2010**, *132*, 10565; e) S. Rakshit, F. W. Patureau, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 9585; f) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 2068; g) S. Mochida, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2010**, *39*, 744; h) N. Guimond, K. Fagnou, *J. Am. Chem. Soc.* **2009**, *131*, 12050; i) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Commun.* **2009**, 5141; j) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 16474.

[10] For a report on Rh^{III}-catalyzed redox-neutral synthesis of azaheterocycles from benzhydroxamic acid derivatives and O-acetyl oximes with alkynes, see: a) N. Guimond, C. Gouliaras, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 6908; b) P. C. Too, Y.-F. Wang, S. Chiba, *Org. Lett.* **2010**, *12*, 5688.

[11] The other solvents such as MeOH, DMSO, and toluene were not viable for this transformation. For the reactions in the presence of other Cu salts; see the Supporting Information.

[12] Cu(OAc)$_2$ was mainly utilized as the catalyst since CuOAc is very sensitive to moisture, air, and light.

[13] All vinyl azides **1** were prepared from the corresponding alkenes; see the Supporting Information.

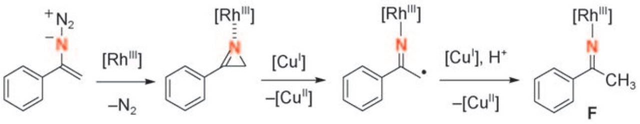
[14] For reports on utilization of DMF as a hydrogen radical source, see: a) I. Kamiya, H. Tsunoyama, T. Tsukuda, H. Sakurai, *Chem. Lett.* **2007**, *36*, 646; b) F. Minisci, A. Citterio, E. Vismara, C. Giordano, *Tetrahedron* **1985**, *41*, 4157; c) G. Palla, *Tetrahedron* **1981**, *37*, 2917..

[15] S. Auricchio, S. Grassi, L. Malpezzi, A. S. Sartori, A. M. Truscello, *Eur. J. Org. Chem.* **2001**, 1183.

[16] a) J. Kim, S. Chang, *J. Am. Chem. Soc.* **2010**, *132*, 10272; b) A. Y. S. Malkhasian, M. E. Finch, B. Nikolovski, A. Menon, B. E. Kucera, F. A. Chavez, *Inorg. Chem.* **2007**, *46*, 2950; c) J. J. Teo, Y. Chang, H. C. Zeng, *Langmuir* **2006**, *22*, 7369.

[17] The UV/Vis spectra for the treatment of $[\{Cp^*RhCl_2\}_2]$ in DMF at 90°C showed no change of the band in the visible region corresponding to $[\{Cp^*RhCl_2\}_2]$ at 410 nm; see the Supporting Information.

[18] Reduction of Rh^{III}/vinyl azides or Rh^{III}/2*H*-azirine complexes (as shown below) by Cu^{I} species is also speculated as another mechanistic possibility to form iminyl Rh^{III} intermediate **F** directly.



[19] a) J. F. Van Humbeck, S. P. Simonovich, R. R. Knowles, D. W. C. Macmillan, *J. Am. Chem. Soc.* **2010**, *132*, 10012; b) C. Michel, P. Belanzoni, P. Gamez, J. Reedjik, E. J. Baerends, *Inorg. Chem.* **2009**, *48*, 11909.

[20] It was confirmed that treatment of isoquinoline **3na** with TEMPO under the present catalytic reaction conditions does not form **7na** and **7na′** at all.

[21] The structure of **7ng** was confirmed by the X-ray crystallographic analysis. CCDC 805444 (**7ng**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See the Supporting Information.

[22] The formation of alcohols **7′** might occur through the reduction of the TEMPO adduct **7** with Cu^{I} species that is generated in situ.

[23] Oxidative and reductive cleavages of the N–O bond of **7** were examined; see the Supporting Information.