Pyrrole Synthesis Hot Paper

DOI: 10.1002/anie.201405215

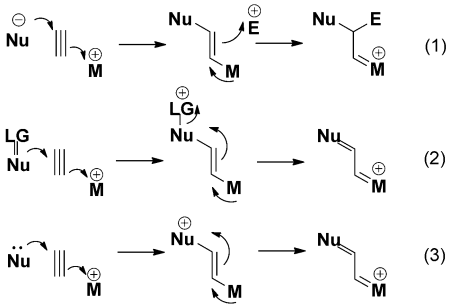
Catalyst-Dependent Divergent Synthesis of Pyrroles from 3-Alkynyl Imine Derivatives: A Noncarbonylative and Carbonylative Approach**

Gen-Qiang Chen, Xiao-Nan Zhang, Yin Wei, Xiang-Ying Tang, and Min Shi**

Abstract: *A novel Ru^0- and Rh^I-catalyzed noncarbonylative and carbonylative cycloisomerization of readily available 3-alkynyl imine derivatives has been developed to provide 3,4-fused or nonfused pyrrole derivatives efficiently in moderate to excellent yields. The key steps involve the formation of a ruthenium carbenoid intermediate or a rhodacycle intermediate, respectively. In these reactions, CO can serve as a ligand or a reagent.*

Of all the nitrogen-containing heterocycles, pyrroles are among the most important motifs in organic chemistry. The pyrrole nucleus is found prevalently in many bioactive natural products,[1] pharmaceutically important compounds,[2] and organic materials[3] including the blockbuster drug Atorvastatin Calcium.[2a] For this reason, the development of a general, simple, and efficient synthetic method to generate these structures has drawn the interest of many organic chemists, and various synthetic methods have been developed.[1,4] In addition to the traditional methods, such as the Knorr pyrrole synthesis, transition-metal-catalyzed approaches have also been developed.[5] However, new and practically useful synthetic methods are still highly desirable.

Over the last few decades, transition metals, especially the alkynophilic ones, have been extensively examined. It is well known that metal carbenoids[6] can be generated from alkynes in the following three ways (Scheme 1): 1) nucleophilic attack of an alkyne activated by metals and subsequent trapping of the vinyl–metal species by an electrophile;[7] 2) attack of the activated alkyne by a nucleophile bearing a leaving group (LG), thereby generating α-oxo-, α-imino-, or α-vinyl-metal carbenoids;[8] 3) the use of an uncharged element containing a lone pair of electrons as the nucleophile, which provides α-ylide-type metal carbenoids.[9] The first two modes are very common in the literature, but, the third is relatively rare.



Scheme 1. Three modes for the generation of metal carbenoids from alkynes.

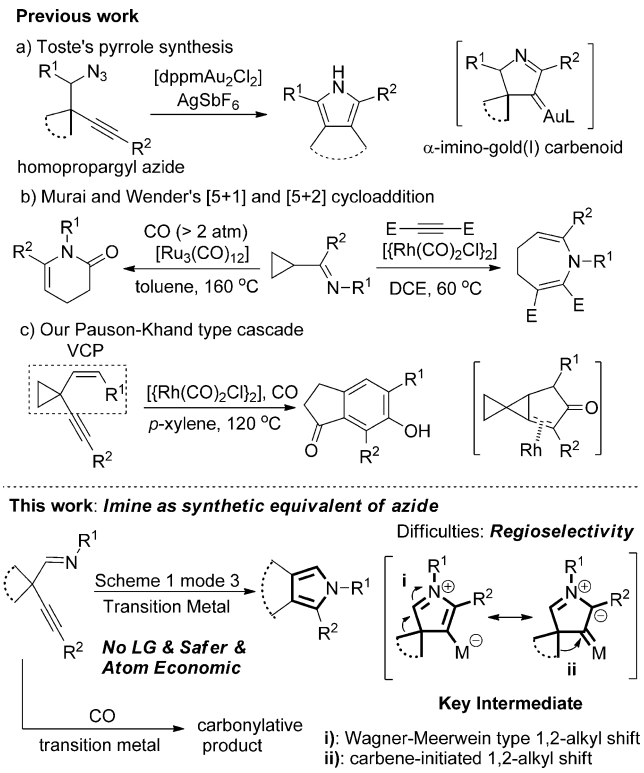
In 2005, Toste and co-workers[5e] reported an interesting gold-catalyzed synthesis of pyrroles from a homopropargyl azide (Scheme 2a). The key steps involved the generation of an α-imino-gold(I) carbenoid through nucleophilic attack on a gold(I)-activated alkyne and the subsequent gold(I)-assisted extrusion of N_2. The research groups of Zhang[8f] and Gagosz[8g] later reported similar reactions that led to indole derivatives. Inspired by the study of Toste and co-workers, we assumed that if the azide group was replaced by an imino functionality, an α-(azomethineylide)-metal carbenoid could be generated through the third mode shown in Scheme 1, and this would provide an atom-economic and safer route to multisubstituted pyrroles. The difficulties mainly lie in the regioselectivity[10] (Scheme 2, this work). On the other hand, cyclopropylimines[11] are very useful five-atom synthons in organic chemistry and their reactivities are quite similar to vinylcyclopropanes (VCPs).[12] In 2000 and 2002, Murai and co-workers[11a] and Wender et al.[11b] independently reported the [5+1] and [5+2] cycloaddition of cyclopropylimines (Scheme 2b). In 2013, we also disclosed an interesting tandem Pauson–Khand-type reaction of a cyclopropane-tethered 1,4-enyne[13] in the presence of rhodium(I) catalyst (Scheme 2c).[14] Based on these previous findings, we reasoned that carbonylative products could be obtained if the alkynyl unit was incorporated into the cyclopropylimine functionality (Scheme 2, this work). Herein, we report the novel Ru^0- and Rh^I-catalyzed noncarbonylative and carbonylative synthesis of substituted pyrroles from readily available 3-alkynyl imine derivatives.

We first utilized cyclopropyl-tethered 3-alkynyl imine **1a**[15,16] as the substrate and carried out the reaction in the

[*] G.-Q. Chen, X.-N. Zhang, Y. Wei, Dr. X.-Y. Tang, Dr. M. Shi
State Key Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry
Chinese Academy of Sciences
345 Linglin Lu, Shanghai 200032 (China)
E-mail: siocxiangying@mail.sioc.ac.cn
mshi@mail.sioc.ac.cn

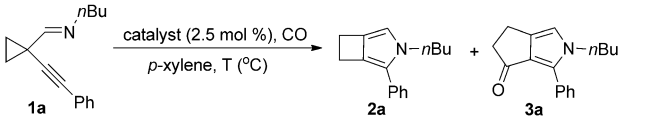
[**] We are grateful for financial support from the Shanghai Municipal Committee of Science and Technology (11JC1402600), the National Basic Research Program of China (973)-010CB833302, and the National Natural Science Foundation of China (20472096, 21372241, 21361140350, 20672127, 21102166, 21121062, 21302203, and 20732008).

Supporting information for this article (spectroscopic data of the compounds shown in Tables 1–3 and Scheme 3, the detailed descriptions of experimental procedures, and the crystal structures of **2k** and **3b**) is available on the WWW under http://dx.doi.org/10.1002/anie.201405215.



Scheme 2. Previous work and this work. dppm = bis(diphenylphosphino)methane, DCE = 1,2-dichloroethane.

Table 1: Optimization of the reaction conditions.



Entry[a]	Catalyst	*t* [h]	Solvent	*p* (1 atm)	*T* [°C]	Yield [%][b]	
						2a	**3a**
1	**[{Rh(CO)$_2$Cl}$_2$]**	**10**	**p-xylene**	**CO**	**100**	**11**	**81**[c]
2	[Rh(PPh$_3$)$_3$Cl]	10	*p*-xylene	CO	100	46	0
3	[Rh$_6$(CO)$_{16}$]	10	*p*-xylene	CO	100	34	0
4	[{Rh(cod)Cl}$_2$]	10	*p*-xylene	CO	100	19	44
5[c]	[Rh(dppp)(CO)Cl]	10	*p*-xylene	CO	100	18	47
6	[Rh(PPh$_3$)(CO)Cl]	10	*p*-xylene	CO	100	50	44
7	**[Ru$_3$(CO)$_{12}$]**	**10**	**toluene**	**CO or Ar**	**100**	**99**[c]	**n.d.**
8[d]	[Ru(cod)Cl$_2$]$_n$	10	*p*-xylene	Ar	100	31	n.d.
9	[Re$_2$(CO)$_{10}$]	10	*p*-xylene	Ar	100	67	n.d.
10[d]	[(*S*)-PhosAu-(CH$_3$CN)SbF$_6$]	12	DCM	Ar	RT	n.d.	n.d.

[a] The reaction was performed in a 25 mL flame- and vacuum-dried Schlenk tube. **1** (0.2 mmol) and the catalyst (2.5 mol%) was added and then the tube was evacuated and backfilled with CO or Ar five times. Solvent was then added and the reaction mixture stirred in an oil bath at the indicated temperature. [b] NMR spectroscopic yield. [c] Yield of isolated product. [d] ^{1}H NMR spectroscopic analysis of the crude product indicates that the product contains **1a** and **4a**. cod = 1,5-cyclooctadiene, dppp = 1,3-bis(diphenylphosphino)propane.

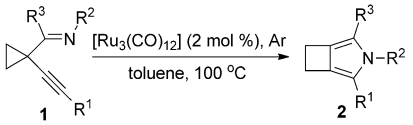
presence of [{Rh(CO)$_2$Cl}$_2$] in a CO atmosphere. Compounds **2a** and **3a** were obtained in 11% and 81% yields, respectively (Table 1, entry 1; for details see Scheme S7 in the Supporting Information). Next, we turned our attention to find the optimized reaction conditions for the current reaction by screening various rhodium catalysts such as the Wilkinson catalyst, [Rh$_6$(CO)$_{16}$], [{Rh(cod)Cl}$_2$], [Rh(dppp)(CO)Cl] and [Rh(PPh$_3$)$_2$(CO)Cl] (Table 1, entries 1–6). [{Rh(CO)$_2$Cl}$_2$] was found to be the best catalyst for the carbonylative synthesis of pyrroles. To our delight, when [Ru$_3$(CO)$_{12}$][16a,17,18] was used as the catalyst, the noncarbonylative product **2a** was obtained in almost quantitative yield without formation of **3a** (Table 1, entry 7). [Ru(cod)Cl$_2$]$_n$ produced **2a** in 31% yield (Table 1, entry 8), and [Re$_2$(CO)$_{10}$] gave **2a** in 67% yield (Table 1, entry 9). The cationic gold catalyst [(*S*)-PhosAu-(CH$_3$CN)SbF$_6$] did not afford the desired product (Table 1, entry 10).

The substrate scope of the ruthenium(0)-catalyzed reaction was next evaluated. Changing the R^2 substituent from a simple alkyl group to a benzyl, PMB, or 2-phenylethyl group afforded the desired products in excellent yields (Table 2, entries 1–7). The substituent on the alkyne functionality could be the substituted phenyl groups thienyl or Bn, which gave the desired products in moderate to excellent yields (Table 2, entries 7–16). The ketimine **1r** also afforded the desired product in excellent yield (Table 2, entry 17). However, the oxime ether[19] **1s** did not produce the desired product under the optimized conditions, probably because of the low nucleophilicity of the nitrogen atom in the oxime ether (Table 2, entry 18). The structure of **2** was further confirmed by X-ray diffraction analysis of product **2k** (see the Supporting Information for the ORTEP drawing and the CIF data).[20]

The substrate generality of the carbonylative pyrrole synthesis was also examined. The reactions proceeded smoothly when the R^2 substituent was changed from a simple alkyl group to a benzyl, PMB, or 2-phenylethyl group to afford the desired products in moderate to good yields (Table 3, entries 1–5). The substituent on the alkyne functionality could also tolerate a substituted phenyl group or thienyl, which provided the desired products in yields ranging from moderate to good (Table 3, entries 6–11). In this reaction, irrespective of whether an electron-donating group or electron-withdrawing group was introduced on the phenyl ring, the corresponding product was obtained in a relatively low yield. Ketimine **1r** could also afford the desired product **3r** in good yield (Table 3, entry 12). The oxime ether **1s** afforded the desired product **3s** in 31% yield under the optimized conditions (Table 3, entry 13). The structure of **3** was further determined by X-ray diffraction analysis of product **3b** (see the Supporting Information for the ORTEP drawing and the CIF data).[21]

Imines other than the cyclopropane-tethered ones (**1t** and **1u**) were also synthesized and subjected to the standard

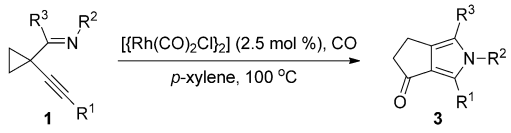
Table 2: Substrate generality of the ruthenium(0)-catalyzed noncarbonylative reaction.



Entry	R^1, R^2, R^3	Yield [%][a]
1	**1b**, R^1 = Ph, R^2 = *n*Pr, R^3 = H	**2b**, 97
2	**1c**, R^1 = Ph, R^2 = *i*Pr, R^3 = H	**2c**, 83
3	**1d**, R^1 = Ph, R^2 = *i*Bu, R^3 = H	**2d**, 95
4	**1e**, R^1 = Ph, R^2 = Bn, R^3 = H	**2e**, 91
5	**1f**, R^1 = Ph, R^2 = PMB, R^3 = H	**2f**, 94
6	**1g**, R^1 = Ph, R^2 = 2-Ph-Et, R^3 = H	**2g**, 89
7	**1h**, R^1 = *p*-Ph-Ph, R^2 = PMB, R^3 = H	**2h**, 94
8	**1i**, R^1 = *p*-Me-Ph, R^2 = *n*Bu, R^3 = H	**2i**, 97
9	**1j**, R^1 = 3,5-di-Me-Ph, R^2 = *n*Bu, R^3 = H	**2j**, 96
10	**1k**, R^1 = *p*-Cl-Ph, R^2 = *n*Pr, R^3 = H	**2k**, 93
11	**1l**, R^1 = *p*-F-Ph, R^2 = *n*Pr, R^3 = H	**2l**, 85
12	**1m**, R^1 = *p*-NO_2-Ph, R^2 = *n*Pr, R^3 = H	**2m**, 67
13	**1n**, R^1 = *p*-MeO-Ph, R^2 = *n*Pr, R^3 = H	**2n**, 93
14	**1o**, R^1 = 1-naphthyl, R^2 = *n*Pr, R^3 = H	**2o**, 98
15	**1p**, R^1 = 2-thienyl, R^2 = *n*Pr, R^3 = H	**2p**, 80
16	**1q**, R^1 = Bn, R^2 = *n*Pr, R^3 = H	**2q**, 84
17	**1r**, R^1 = Ph, R^2 = *n*Pr, R^3 = Me	**2r**, 93[b]
18[c]	**1s**, R^1 = Ph, R^2 = MeO, R^3 = Me	**2s**, –

[a] Yield of isolated product. [b] This product was not stable enough for column chromatography, and the yield was determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [c] **1s** was recovered quantitatively. Bn = benzyl, PMB = *p*-methoxybenzyl.

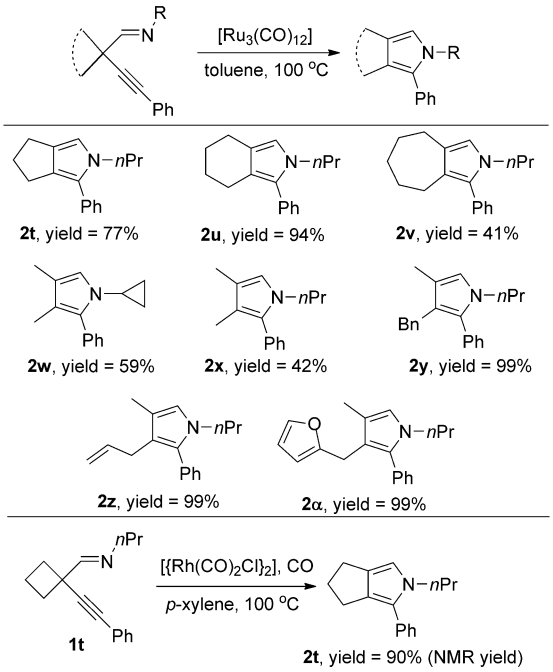
Table 3: Substrate generality of the rhodium(I)-catalyzed carbonylative reaction.



Entry[a]	R^1, R^2, R^3	Yield [%][b]
1	**1b**, R^1 = Ph, R^2 = *n*Pr, R^3 = H	**2b**, 83
2	**1c**, R^1 = Ph, R^2 = *i*Pr, R^3 = H	**2c**, 58
3	**1e**, R^1 = Ph, R^2 = Bn, R^3 = H	**2e**, 61
4	**1f**, R^1 = Ph, R^2 = PMB, R^3 = H	**2f**, 51
5	**1g**, R^1 = Ph, R^2 = 2-Ph-Et, R^3 = H	**2g**, 61
6	**1i**, R^1 = *p*-Me-Ph, R^2 = *n*Bu, R^3 = H	**2i**, 77
7	**1j**, R^1 = 3,5-di-Me-Ph, R^2 = *n*Bu, R^3 = H	**2j**, 75
8	**1k**, R^1 = *p*-Cl-Ph, R^2 = *n*Pr, R^3 = H	**2k**, 42
9	**1l**, R^1 = *p*-F-Ph, R^2 = *n*Pr, R^3 = H	**2l**, 54
10	**1n**, R^1 = *p*-MeO-Ph, R^2 = *n*Pr, R^3 = H	**2n**, 50
11	**1p**, R^1 = 2-thienyl, R^2 = *n*Pr, R^3 = H	**2p**, 49
12	**1r**, R^1 = Ph, R^2 = *n*Pr, R^3 = Me	**2r**, 84
13	**1s**, R^1 = Ph, R^2 = MeO, R^3 = Me	**2s**, 31

[a] The reaction was conducted on a 0.2 mmol scale. **2** was formed as minor product in all cases. [b] Yield of isolated product.

conditions. In the presence of $[Ru_3(CO)_{12}]$, the cyclobutane- or cyclopentane-tethered imine **1t** or **1u** could undergo the reaction smoothly to give the expected ring-expansion product **2t** or **2u** in good yield (Scheme 3). In the case of

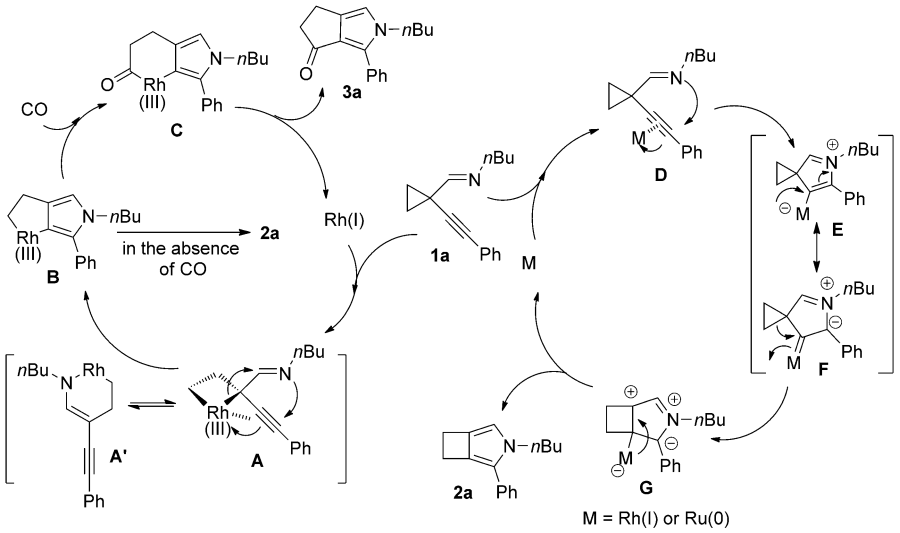


Scheme 3. Reactions of imines other than the cyclopropane-tethered ones.

the cyclohexane-tethered imine **1v**, the desired product **2v** was obtained in 41% yield (Scheme 3). In the cases of noncyclic symmetrical imines **1w** and **1x**, the corresponding pyrroles **2w** and **2x** could be also formed in moderate yields. Furthermore, the unsymmetrical substrates **1y**, **1z**, and **1α**, afforded the corresponding pyrroles **2y**, **2z**, and **2α** in almost quantitative yields as single regioisomers.[22] No enyne cyclization product was observed, thus indicating that $[Ru_3(CO)_{12}]$ is a very mild π acid. In the presence of $[\{Rh(CO)_2Cl\}_2]$ as the catalyst under CO, **1t** afforded **2t** in 90% yield rather than the carbonylative product, which suggests that CO insertion is only suitable for the cyclopropane-tethered substrate under Rh^I catalysis (Scheme 3).

An NMR monitoring experiment was conducted using **1a** as a model substrate to gain further insight into the reaction. **2a** was formed quantitatively in less than 5 min in the presence of $[Ru_3(CO)_{12}]$ in an ambient atmosphere. The use of $[\{Rh(CO)_2Cl\}_2]$ as the catalyst in an ambient atmosphere led to product **3a** in less than 10% yield after a few minutes, and product **2a** formed only slowly. It is quite clear that $[Ru_3(CO)_{12}]$ and $[\{Rh(CO)_2Cl\}_2]$ show completely different catalytic abilities (see Figure S1 in the Supporting Information).

On the basis of the NMR monitoring experiment and a control experiment (see Scheme S7 in the Supporting Information), a plausible reaction mechanism was proposed with **1a** used as a model substrate. For the formation of product **3a**:[23] oxidative addition of Rh^I to **1a** forms a rhodacyclobutane intermediate **A**, which is in equilibrium with **A′** through 1,3-migration.[11] Intramolecular nucleophilic attack of the imine on the activated alkyne and the subsequent rearrangement forms rhodium-containing pyrrole intermediate **B**.[24] Carbonylation of intermediate **B** gives **C**,



Scheme 4. A plausible reaction mechanism.

which undergoes reductive elimination to afford product **3a** and regenerates the Rh^I species. For the formation of product **2a**: the coordination of ruthenium(0) to the alkyne moiety of **1a** generates intermediate **D**, which undergoes intramolecular nucleophilic attack by the imine to form the vinyl-metal intermediate **E** and its resonance structure **F**. Ring expansion of the cyclopropane ring to cyclobutane and release of the metal catalyst produces **2a** and regenerates the catalytic species (Scheme 4). The reaction takes place by a completely different pathway when $[\{Rh(CO)_2Cl\}_2]$ or $[Ru_3(CO)_{12}]$ is used as the catalyst, probably because of the following reasons: 1) oxidative addition of $[\{Rh(CO)_2Cl\}_2]$ (60 °C) to the cyclopropylimine is easier than with $[Ru_3(CO)_{12}]$ (160 °C) (Scheme 2b);[11] 2) as for $[\{Rh(CO)_2Cl\}_2]$, the oxidative addition to cyclopropane takes place faster than its π-activation process.

In conclusion, an interesting noncarbonylative and carbonylative approach to substituted pyrrole derivatives catalyzed by Ru^0 and Rh^I in a highly chemoselective and safe manner have been developed. With this method, 3-azabicyclo[3.2.0]hepta-1,4-diene and 5,6-dihydrocyclopenta[*c*]pyrrol-4(2*H*)-one derivatives can be synthesized divergently from readily available cyclopropane tethered 3-alkynyl imine derivatives. This reaction can also be extended to other cyclic or acyclic 3-alkynyl imines. A plausible mechanism has also been proposed. Further efforts are in progress to develop the application of this method in the synthesis of biologically active molecules.

Received: May 13, 2014
Published online: ■■ ■■, ■■■■

Keywords: C–C bond activation · pyrrole synthesis · rhodium · ring expansion · ruthenium

[1] a) *Pyrroles, Part I, The Synthesis And The Physical And Chemical Aspects of the Pyrrole Ring* (Eds.: R. A. Jones), Wiley, New York, **1990**; b) *Pyrroles, Part II, The Synthesis Reactivity, and Physical Properties of Substituted Pyrroles* (Eds.: R. A. Jones), Wiley, New York, **1992**.

[2] a) R. B. Thompson, *FASEB J.* **2001**, *15*, 1671–1676; b) A. Fürstner, H. Szillat, B. Gabor, R. J. Mynott, *J. Am. Chem. Soc.* **1998**, 120, 8305–8314.

[3] *Handbook of Conducting Polymers*, 2ednd ed(Eds.: T. A. Skotheim, R. L. Elsenbaumer, J. R. Reynolds), Marcel Dekker, New York, **1998**.

[4] For reviews on pyrrole synthesis, see a) G. Balme, *Angew. Chem.* **2004**, *116*, 6396–6399; *Angew. Chem. Int. Ed.* **2004**, *43*, 6238–6241; b) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2198.

[5] For transition-metal-catalyzed pyrrole synthesis, see a) Y. Lu, B. A. Arndtsen, *Angew. Chem.* **2008**, *120*, 5510–5513; *Angew. Chem. Int. Ed.* **2008**, *47*, 5430–5433; b) R. Martín, M. R. Rivero, S. L. Buchwald, *Angew. Chem.* **2006**, *118*, 7237–7240; *Angew. Chem. Int. Ed.* **2006**, *45*, 7079–7082; c) R. Dhawan, B. A. Arndtsen, *J. Am. Chem. Soc.* **2004**, *126*, 468–469; d) S. Kamijo, C. Kanazawa, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 9260–9266; e) D. J. Gorin, N. R. Davis, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 11260–11261; f) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 2074–2075; g) D. J. St. Cyr, B. A. Arndtsen, *J. Am. Chem. Soc.* **2007**, *129*, 12366–12367; h) B. Gabriele, G. Salerno, A. Fazio, *J. Org. Chem.* **2003**, *68*, 7853–7861; i) S. Maiti, S. Biswas, U. Jana, *J. Org. Chem.* **2010**, *75*, 1674–1683; j) L. Lu, G. Chen, S. Ma, *Org. Lett.* **2006**, *8*, 835–838; k) J. T. Binder, S. F. Kirsch, *Org. Lett.* **2006**, *8*, 2151–2153; l) M. L. Crawley, I. Goljer, D. J. Jenkins, J. F. Mehlmann, L. Nogle, R. Dooley, P. E. Mahaney, *Org. Lett.* **2006**, *8*, 5837–5840; m) F. Chen, T. Shen, Y. Cui, N. Jiao, *Org. Lett.* **2012**, *14*, 4926–4929; n) B. Li, N. Wang, Y. Liang, S. Xu, B. Wang, *Org. Lett.* **2013**, *15*, 136–139.

[6] The three modes do not include a vinylidene-metal carbenoid that can be generated from terminal alkynes, see a) J. Bucher, T. Wurm, K. S. Nalivela, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem.* **2014**, *126*, 3934–3939; *Angew. Chem. Int. Ed.* **2014**, *53*, 3854–3858; for reviews or monographs on metal carbenoids, see b) *Metal Carbenes in Organic Synthesis* (Ed.: K. H. Dötz), Springer, Berlin, **2004**; c) *Metal Carbenes in Organic Synthesis* (Ed.: F. Z. Dörwald), Wiley-VCH, Weinheim, **1999**; d) M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919–939.

[7] For metal carbenoids generated in this manner, see a) D. Vasu, A. Das, R.-S. Liu, *Chem. Commun.* **2010**, *46*, 4115–4117; b) C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem.* **2004**, *116*, 2456–2460; *Angew. Chem. Int. Ed.* **2004**, *43*, 2402–2406; c) C. Nevado, C. Ferrer, A. M. Echavarren, *Org. Lett.* **2004**, *6*, 3191–3194.

[8] For α-oxo-metal carbenoids, see a) J. Xiao, X. Li, *Angew. Chem.* **2011**, *123*, 7364–7375; *Angew. Chem. Int. Ed.* **2011**, *50*, 7226–7236; b) X. Li, C. D. Incarvito, T. Vogel, R. H. Crabtree, *Organometallics* **2005**, *24*, 3066–3073; c) R. Liu, G. N. Winston-McPherson, Z.-Y. Yang, X. Zhou, W. Song, I. A. Guzei, X. Xu, W. Tang, *J. Am. Chem. Soc.* **2013**, *135*, 8201–8204; for α-imino-metal carbenoids, see d) Y. Xiao, L. Zhang, *Org. Lett.*

2012, *14*, 4662 – 4665; e) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738 – 1741; f) B. Lu, Y. Luo, L. Liu, L. Ye, Y. Wang, L. Zhang, *Angew. Chem.* **2011**, *123*, 8508 – 8512; *Angew. Chem. Int. Ed.* **2011**, *50*, 8358 – 8362; g) A. Wetzel, F. Gagosz, *Angew. Chem.* **2011**, *123*, 7492 – 7496; *Angew. Chem. Int. Ed.* **2011**, *50*, 7354 – 7358; for α-vinyl-metal carbenoids, see h) S. Kramer, T. Skrydstrup, *Angew. Chem.* **2012**, *124*, 4759 – 4762; *Angew. Chem. Int. Ed.* **2012**, *51*, 4681 – 4684.

[9] For metal-containing azomethine ylides, see a) N. Iwasawa, M. Shido, H. Kusama, *J. Am. Chem. Soc.* **2001**, *123*, 5814 – 5815; b) H. Kusama, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2002**, *124*, 11592 – 11593; c) H. Kusama, Y. Miyashita, J. Takaya, N. Iwasawa, *Org. Lett.* **2006**, *8*, 289 – 292; d) J. Takaya, Y. Miyashita, H. Kusama, N. Iwasawa, *Tetrahedron* **2011**, *67*, 4455 – 4466; for metal containing carbonyl ylide, see e) N. Asao, *Synlett* **2006**, 1645 – 1656; f) H. Kusama, N. Iwasawa, *Chem. Lett.* **2006**, *35*, 1082 – 1087; g) J.-R. Chen, X.-Q. Hu, W.-J. Xiao, *Angew. Chem.* **2014**, *126*, 4118 – 4120; *Angew. Chem. Int. Ed.* **2014**, *53*, 4038 – 4040.

[10] For the site selectivity of the 1,2-alkyl shift, see Z. Zhang, X. Tang, Q. Xu, M. Shi, *Chem. Eur. J.* **2013**, *19*, 10625 – 10631.

[11] For the reactions of cyclopropylimines, see a) A. Kamitani, N. Chatani, T. Morimoto, S. Murai, *J. Org. Chem.* **2000**, *65*, 9230 – 9233; b) P. A. Wender, T. M. Pedersen, M. J. C. Scanio, *J. Am. Chem. Soc.* **2002**, *124*, 15154 – 15155.

[12] For reactions that involve VCPs, see a) P. A. Wender, H. Takahashi, B. Witulski, *J. Am. Chem. Soc.* **1995**, *117*, 4720 – 4721; b) P. A. Wender, Z.-X. Yu, K. N. Houk, *J. Am. Chem. Soc.* **2004**, *126*, 9154 – 9155; c) P. A. Wender, G. G. Gamber, R. D. Hubbard, S. M. Pham, L. Zhang, *J. Am. Chem. Soc.* **2005**, *127*, 2836 – 2837; d) H. A. Wegner, A. de Meijere, P. A. Wender, *J. Am. Chem. Soc.* **2005**, *127*, 6530 – 6531; e) P. A. Wender, L. O. Haustedt, J. Lim, J. A. Love, T. J. Williams, J.-Y. Yoon, *J. Am. Chem. Soc.* **2006**, *128*, 6302 – 6303; f) P. A. Wender, R. T. Stemmler, L. E. Sirois, *J. Am. Chem. Soc.* **2010**, *132*, 2532 – 2533; g) P. A. Wender, L. E. Sirois, R. T. Stemmler, T. J. Williams, *Org. Lett.* **2010**, *12*, 1604 – 1607; h) P. A. Wender, A. B. Lesser, L. E. Sirois, *Angew. Chem.* **2012**, *124*, 2790 – 2794; *Angew. Chem. Int. Ed.* **2012**, *51*, 2736 – 2740; i) L. Jiao, Z.-X. Yu, *J. Org. Chem.* **2013**, *78*, 6842 – 6848; j) G.-J. Jiang, X.-F. Fu, Q. Li, Z.-X. Yu, *Org. Lett.* **2012**, *14*, 692 – 695; k) P. Liu, P. H.-Y. Cheong, Z.-X. Yu, P. A. Wender, K. N. Houk, *Angew. Chem.* **2008**, *120*, 4003 – 4005; *Angew. Chem. Int. Ed.* **2008**, *47*, 3939 – 3941; l) Y. Liang, X. Jiang, Z.-X. Yu, *Chem. Commun.* **2011**, *47*, 6659 – 6661; m) Z.-X. Yu, P. H.-Y. Cheong, P. Liu, C. Y. Legault, P. A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2008**, *130*, 2378 – 2379; n) P. Liu, L. E. Sirois, P. H.-Y. Cheong, Z.-X. Yu, I. V. Hartung, H. Rieck, P. A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2010**, *132*, 10127 – 10135; o) L. Jiao, M. Lin, Z.-X. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 447 – 461; p) M. Lin, F. Li, L. Jiao, Z.-X. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 1690 – 1693; q) M. Lin, G.-Y. Kang, Y.-A. Guo, Z.-X. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 398 – 405; r) L. Jiao, C. Yuan, Z.-X. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 4421 – 4430; s) L. Jiao, S. Ye, Z.-X. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 7178 – 7179.

[13] G.-Q. Chen, M. Shi, *Chem. Commun.* **2013**, *49*, 698 – 700.

[14] For transition-metal-catalyzed cyclizations of 1,4-enynes, see a) X. Shu, C. M. Schienebeck, W. Song, I. A. Guzei, W. Tang, *Angew. Chem.* **2013**, *125*, 13846 – 13850; *Angew. Chem. Int. Ed.* **2013**, *52*, 13601 – 13605; b) C. M. Schienebeck, P. J. Robichaux, X. Li, L. Chen, W. Tang, *Chem. Commun.* **2013**, *49*, 2616 – 2618; c) X. Li, S. Huang, C. M. Schienebeck, D. Shu, W. Tang, *Org. Lett.* **2012**, *14*, 1584 – 1587; d) X. Li, W. Song, W. Tang, *J. Am. Chem. Soc.* **2013**, *135*, 16797 – 16800; e) X. Xu, P. Liu, X. Shu, W. Tang, K. N. Houk, *J. Am. Chem. Soc.* **2013**, *135*, 9271 – 9274; f) X. Shu, X. Li, D. Shu, S. Huang, C. M. Schienebeck, X. Zhou, P. J. Robichaux, W. Tang, *J. Am. Chem. Soc.* **2012**, *134*, 5211 – 5221; g) X. Shu, S. Huang, D. Shu, I. A. Guzei, W. Tang, *Angew. Chem.* **2011**, *123*, 8303 – 8306; *Angew. Chem. Int. Ed.* **2011**, *50*, 8153 – 8156; h) X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 5802 – 5803; i) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**, *128*, 12614 – 12615; j) N. Marion, S. Díez-González, P. de Frémont, A. R. Noble, S. P. Nolan, *Angew. Chem.* **2006**, *118*, 3729 – 3732; *Angew. Chem. Int. Ed.* **2006**, *45*, 3647 – 3650.

[15] Compound **1a** was synthesized from 1-(1-phenylethynyl)cyclopropyl aldehyde **4a** (see Scheme S5 in the Supporting Information). For reactions of aldehydes, see a) G. Zhang, X. Huang, G. Li, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 1814 – 1815; b) G. Li, X. Huang, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 6944 – 6945; c) Y. Zhang, Z. Chen, Y. Xiao, J. Zhang, *Chem. Eur. J.* **2009**, *15*, 5208 – 5211; d) Y. Zhang, F. Liu, J. Zhang, *Chem. Eur. J.* **2010**, *16*, 6146 – 6150; e) J. Zhang, H. G. Schmalz, *Angew. Chem.* **2006**, *118*, 6856 – 6859; *Angew. Chem. Int. Ed.* **2006**, *45*, 6704 – 6707.

[16] We expected that the pyridinone derivatives could be afforded through a hetero-Pauson–Khand cascade under Rh^{I} catalysis (see Scheme S8 in the Supporting Information). For hetero-Pauson–Khand reactions, see a) N. Chatani, *Chem. Rec.* **2008**, *8*, 201 – 212; b) T. Iwata, F. Inagaki, C. Mukai, *Angew. Chem.* **2013**, *125*, 11344 – 11348; *Angew. Chem. Int. Ed.* **2013**, *52*, 11138 – 11142; c) N. M. Kablaoui, F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1997**, *119*, 4424 – 4431; d) N. Chatani, M. Tobisu, T. Asaumi, Y. Fukumoto, S. Murai, *J. Am. Chem. Soc.* **1999**, *121*, 7160 – 7161; e) M. Tobisu, N. Chatani, T. Asaumi, K. Amako, Y. Ie, Y. Fukumoto, S. Murai, *J. Am. Chem. Soc.* **2000**, *122*, 12663 – 12674.

[17] Some zero-valent metal-carbonyl complexes such as $[W(CO)_5]\cdot THF$ can serve as π acids to activate alkynes. For examples of the activation of alkynes by metal-carbonyl complexes, see a) H. Kusama, H. Yamabe, Y. Onizawa, T. Hoshino, N. Iwasawa, *Angew. Chem.* **2005**, *117*, 472 – 474; *Angew. Chem. Int. Ed.* **2005**, *44*, 468 – 470; b) T. Miura, N. Iwasawa, *J. Am. Chem. Soc.* **2002**, *124*, 518 – 519; c) K. Maeyama, N. Iwasawa, *J. Am. Chem. Soc.* **1998**, *120*, 1928 – 1929; d) N. Iwasawa, K. Maeyama, H. Kusama, *Org. Lett.* **2001**, *3*, 3871 – 3873; e) H. Kusama, H. Yamabe, N. Iwasawa, *Org. Lett.* **2002**, *4*, 2569 – 2571.

[18] Similar to Ru^{II}, $[Ru_3(CO)_{12}]$ can also serve as a π acceptor to activate alkynes, see a) M. Nishiumi, H. Miura, K. Wada, S. Hosokawa, M. Inoue, *Adv. Synth. Catal.* **2010**, *352*, 3045 – 3052; for the activation of alkynes by Ru^{II}, see b) N. Chatani, T. Morimoto, T. Muto, S. Murai, *J. Am. Chem. Soc.* **1994**, *116*, 6049 – 6050; $[Ru_3(CO)_{12}]$ is also commonly used in hydroformation and carbonylation etc; for recent examples of reactions catalyzed by $[Ru_3(CO)_{12}]$, see c) L. Wu, I. Fleischer, R. Jackstell, M. Beller, *J. Am. Chem. Soc.* **2013**, *135*, 3989 – 3996; d) L. M. Geary, B. W. Glasspoole, M. M. Kim, M. J. Krische, *J. Am. Chem. Soc.* **2013**, *135*, 3796 – 3799; e) N. Armanino, E. M. Carreira, *J. Am. Chem. Soc.* **2013**, *135*, 6814 – 6817; f) B. Y. Park, T. P. Montgomery, V. J. Garza, M. J. Krische, *J. Am. Chem. Soc.* **2013**, *135*, 16320 – 16323; g) N. Hasegawa, V. Charra, S. Inoue, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 8070 – 8073; h) S. Inoue, H. Shiota, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2009**, *131*, 6898 – 6899.

[19] a) Y. Zhang, J. Zhang, *Adv. Synth. Catal.* **2012**, *354*, 2556 – 2560; b) Y. Zhang, J. Zhang, *Synlett* **2012**, 1389 – 1393.

[20] CCDC 967860 (**2k**) 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.

[21] CCDC 973556 (**3b**) contains the supplementary crystallographic data for this paper.

[22] Our preliminary calculation indicated that the high regioselectivity observed was due to the weak interactions between the π system (benzyl, allyl, furan-2-ylmethyl) and the Ru center (see Figure S2 in the Supporting Information).

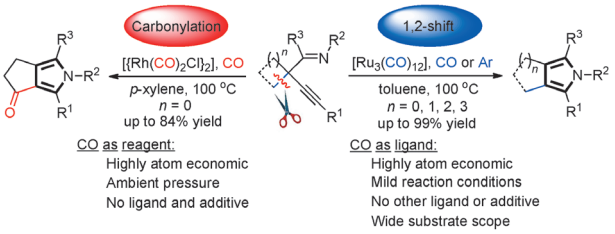
[23] In the absence of CO, product **2a** can be formed by reductive elimination from intermediate **B**; see M. Murakami, H. Amii, Y. Ito, *Nature* **1994**, *370*, 540 – 541.
[24] Carbonylation of intermediate **A′** to form a lactam was quite difficult, instead dehydrogenation may occur preferentially (see Ref. [11a]). Alternatively, another mechanism can also explain the formation of product **3a**, however, this mechanism involves the formation of a very strained intermediate, which makes this mechanism seem less possible (Scheme S9 in the Supporting Information).

Communications

Pyrrole Synthesis

G.-Q. Chen, X.-N. Zhang, Y. Wei, X.-Y. Tang,* M. Shi* _____ ■■■■–■■■■

Catalyst-Dependent Divergent Synthesis of Pyrroles from 3-Alkynyl Imine Derivatives: A Noncarbonylative and Carbonylative Approach



Carbonylation or not: A novel Ru^0- and Rh^I-catalyzed noncarbonylative and carbonylative synthesis of multisubstituted pyrroles from readily available 3-alkynyl imine derivatives has been developed. The key steps involve an oxidative addition and a 1,2-alkyl shift, respectively.