Heterocycles

International Edition: DOI: 10.1002/anie.201610042
German Edition: DOI: 10.1002/ange.201610042

Highly Site Selective Formal [5+2] and [4+2] Annulations of Isoxazoles with Heterosubstituted Alkynes by Platinum Catalysis: Rapid Access to Functionalized 1,3-Oxazepines and 2,5-Dihydropyridines

Wen-Bo Shen[+], Xin-Yu Xiao[+], Qing Sun, Bo Zhou, Xin-Qi Zhu, Juan-Zhu Yan, Xin Lu, and Long-Wu Ye**

Abstract: *Platinum-catalyzed formal [5+2] and [4+2] annulations of isoxazoles with heterosubstituted alkynes enabled the atom-economical synthesis of valuable 1,3-oxazepines and 2,5-dihydropyridines, respectively. Importantly, this Pt catalysis not only led to unique reactivity dramatically divergent from that observed under Au catalysis, but also proceeded via unprecedented α-imino platinum carbene intermediates.*

Catalytic transformations involving metal carbenes are among the most important aspects of homogeneous transition-metal catalysis. Recently, the generation of metal carbenes directly from readily available alkynes has attracted much attention, and various synthetic methods have been developed.[1] However, the generation of Pt carbenes has been explored relatively seldom as compared with the related Au carbenes,[1] and most studies have focused on vinyl Pt carbenes.[2] To the best of our knowledge, the generation of α-oxo or α-imino Pt carbenes has been unsucessful to date.[3,4] Hence, access to novel Pt carbenes is highly desirable, not only for the enrichment of platinum chemistry, but also because it may result in a selectivity switch for the construction of diverse intricate scaffolds.[5]

During the course of our recent studies on transition-metal-catalyzed tandem reactions based on ynamides,[6,7] we disclosed a novel and atom-economical route to the generation of α-imino Au carbenes through a gold-catalyzed formal [3+2] annulation between ynamides and isoxazoles, thus providing ready access to various 2-aminopyrroles (Scheme 1a).[8] Very recently, Hashmi and co-workers reported an elegant protocol for the synthesis of unprotected 7-acyl indoles through the gold-catalyzed C–H annulation of anthranils with ynamides by a similar strategy (Scheme 1b).[9] Notably, nonpolarized alkynes also underwent this transformation when MsOH (10 mol%) was used as an additive. This chemistry has also been aptly exploited in the synthesis of 3-aminopyrroles through the rhodium-catalyzed formal [3+2] annulation of 1,2,3-triazoles with isoxazoles by Tang and co-workers.[10]

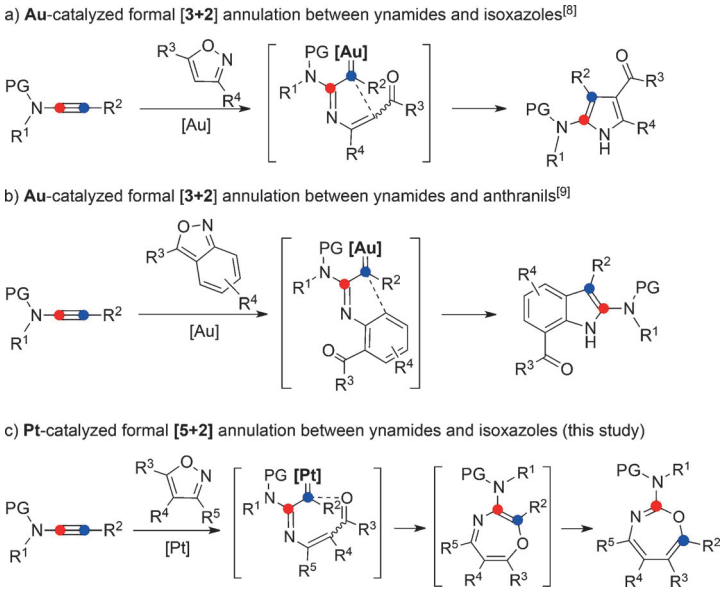
Herein, we report an unprecedented platinum-catalyzed formal [5+2] annulation between ynamides and isoxazoles through pathway presumably involving an α-imino Pt carbene (Scheme 1c), in sharp contrast to the above-reported [3+2] annulations. This Pt catalysis led to the unexpected formation of various polysubstituted 1,3-oxazepines, which are structural motifs commonly found in natural products and bioactive molecules.[11] This chemistry could also be extended to the site-selective synthesis of 2,5-dihydropyridines through a platinum-catalyzed formal [4+2] annulation between alkynyl ethers and isoxazoles. Furthermore, our proposed mechanistic rationale for this novel cascade reaction is strongly supported by theoretical calculations.

Considering that the formation of a bulky α-imino metal carbene intermediate may increase the chance of 1,7-cyclization, ynamide **1a** and fully substituted isoxazole **2a** were chosen as model substrates for our initial study. Typical gold catalysts, such as [IPrAuNTf$_2$] and [Ph$_3$PAuNTf$_2$], only afforded the 1,5-cyclization product **3aa**, as in our previously reported study (Table 1, entries 1–3).[8b] However, the desired 1,7-cyclization product was produced in 30% yield with [BrettPhosAuNTf$_2$] as the catalyst, and importantly, no formation of **3aa** was observed (entry 5). Interesting, the structure of this cyclized product was assigned by X-ray diffraction[12] as 1,3-oxazepine **3a** rather than the expected 1,4-oxazepine. Compounds **3a** and **3aa** could not be converted into one another under the relevant reaction conditions.[13] Product **3a** was formed exclusively with Pt catalysts, but with low efficiency even when the catalyst loading was increased to 10 mol% (entries 7–9). Gratifyingly, further studies revealed that the efficiency of the above PtCl$_2$-catalyzed reaction was substantially improved in toluene under a CO (1 atm) atmosphere,[14] under which conditions **3a** was formed in 86% yield (Table 1, entry 11). Brønsted acids and other (non-noble) metals did not catalyze this reaction.[13]

We explored the scope of the reaction under the optimized reaction conditions. Ynamides with different N-protecting groups were first investigated, and it was found

[*] W.-B. Shen,[+] X.-Y. Xiao,[+] Q. Sun, B. Zhou, X.-Q. Zhu, J.-Z. Yan, Prof. Dr. X. Lu, Prof. Dr. L.-W. Ye
Collaborative Innovation Center of Chemistry for Energy Materials
State Key Laboratory of Physical Chemistry of Solid Surfaces
Key Laboratory for Chemical Biology of Fujian Province
College of Chemistry and Chemical Engineering, Xiamen University
Xiamen 361005 (China)
E-mail: xinlu@xmu.edu.cn
longwuye@xmu.edu.cn
Prof. Dr. L.-W. Ye
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
Shanghai 200032 (China)
[+] These authors contributed equally.

Supporting information for this article can be found under: http://dx.doi.org/10.1002/anie.201610042.

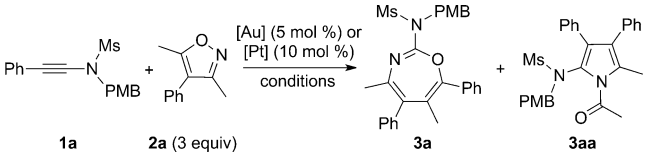


Scheme 1. Formal [3+2] versus [5+2] annulation via α-imino metal carbenes. PG = protecting group.

into the corresponding product **3l** in 74% yield (Table 2, entry 12). Attempts to extend the reaction to alkyl-substituted or terminal ynamides only gave a complex mixture of products.[13] To test the practicality of the current catalytic system, the reaction was carried out on a gram scale (4.0 mmol, 1.26 g) in the presence of $PtCl_2$ (5 mol%), and the desired product **3a** was obtained in 80% yield (1.56 g), thus highlighting the synthetic utility of this transformation (Table 2, entry 1).

We next extended the reaction to a variety of fully substituted isoxazoles **2** (Table 3). To our satisfaction, various aryl-substituted isoxazoles (R^2 = Ar) were compatible with this transformation, which gave the corresponding 1,3-oxazepines **3m–t** in 72–87% yield (entries 1–8). Interestingly, the reaction proceeded well to convert the corresponding styryl-substituted isoxazole into the desired product **3u** in 65% yield (entry 9). Finally, it was found that isoxazoles with other R^1 or R^3 substituents also reacted smoothly, thus allowing the assembly of the corresponding products **3v–y** in good yields (Table 3, entries 10–13). Thus, this

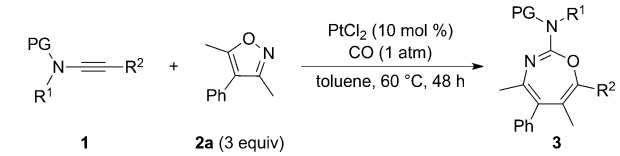
Table 1: Optimization of the reaction conditions.[a]

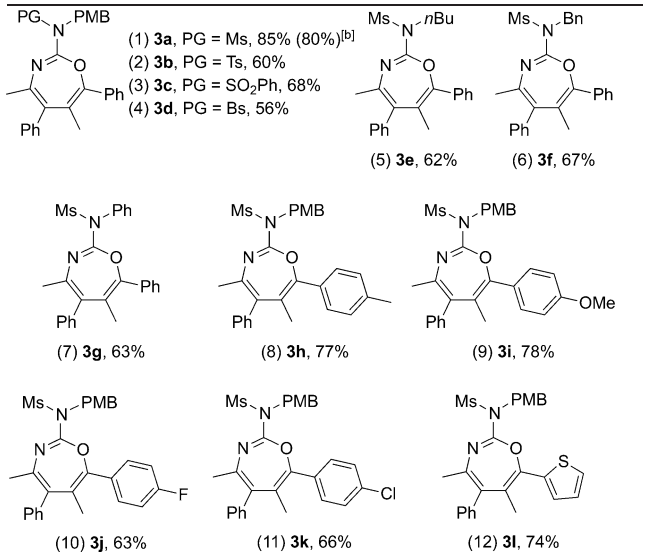


Entry	Metal catalyst	Reaction conditions	Yield [%][b] 3a	3aa	1a
1	$[(ArO)_3PAu]NTf_2$[c]	DCE, 80 °C, 14 h	<1	51	<1
2	$[IPrAu]NTf_2$	DCE, 80 °C, 14 h	<1	73	<1
3	$[Ph_3PAu]NTf_2$	DCE, 80 °C, 14 h	<1	59	<1
4	$[(CyJohnPhos)Au]NTf_2$	DCE, 80 °C, 14 h	10	54	<1
5	$[BrettPhosAu]NTf_2$	DCE, 80 °C, 14 h	30	<1	13
6	$[BrettPhosAu]NTf_2$	DCE, 60 °C, 48 h	36	<1	10
7	$PtCl_2$	DCE, 60 °C, 48 h	22	<1	71
8	$[Pt(C_2H_4)_2Cl_2]$	DCE, 60 °C, 48 h	11	<1	<1
9	$[Pt(MeCN)_2Cl_2]$	DCE, 60 °C, 48 h	26	<1	<1
10	$PtCl_2$	toluene, 60 °C, 48 h	45	<1	47
11	$PtCl_2$	toluene, CO, 60 °C, 48 h	86	<1	<1

[a] [**1a**] = 0.05 M. [b] The yield was determined by ^{1}H NMR spectroscopy with diethyl phthalate as the internal standard. [c] **Ar** = 2,4-di-*tert*-butylphenyl. BrettPhos = 2-(dicyclohexylphosphanyl)-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl, CyJohnPhos = 2-(dicyclohexylphosphanyl)biphenyl, DCE = 1,2-dichloroethane, IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, Ms = methanesulfonyl, PMB = *p*-methoxybenzyl, Tf = trifluoromethanesulfonyl.

Table 2: Reaction scope with different ynamides **1**.[a]



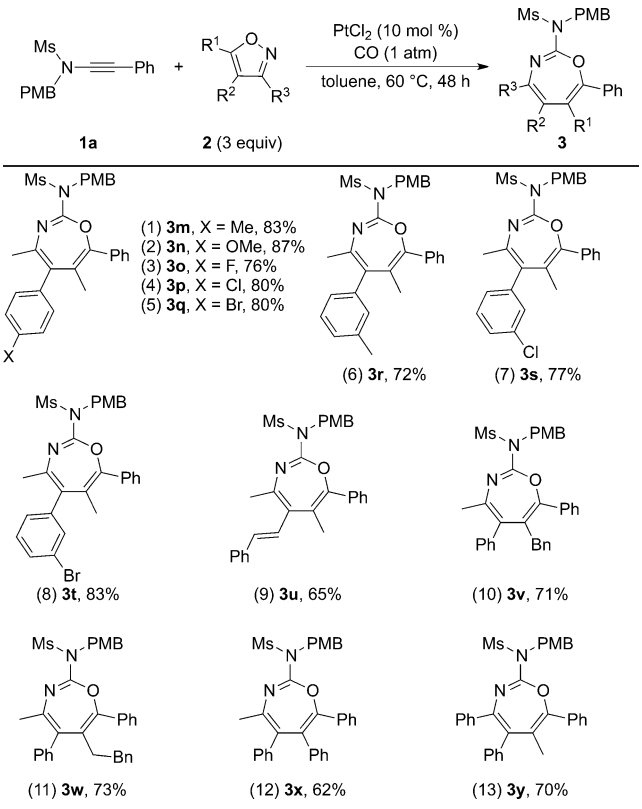


[a] Reactions were carried out in vials under a CO atmosphere (1 atm); [**1**] = 0.05 M; reported yields are for the isolated product. [b] The reaction was carried out on a 4.0 mmol scale with 5 mol% $PtCl_2$; [**1a**] = 0.10 M. Bn = benzyl, Bs = 4-bromobenzenesulfonyl.

that the methanesulfonyl-protected ynamide **1a** gave the best yield (Table 2, entries 1–4). Ynamides bearing different R^1 groups were also suitable substrates and were converted into the corresponding fully substituted 1,3-oxazepines **3e–g** in 62–67% yield (entries 5–7). Various aryl-substituted ynamides (R^2 = Ar) were screened, and the reaction furnished the desired products **3h–k** in moderate to good yields (entries 8–11). This new reaction was also extended to a heteroaryl-substituted ynamide, which was transformed

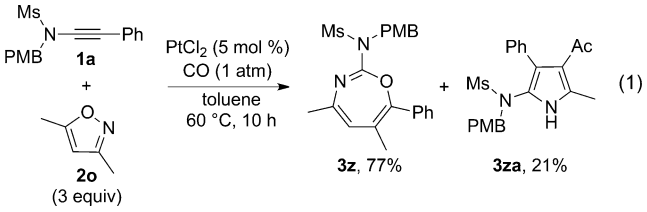
protocol provides a general and efficient way to prepare synthetically important 1,3-oxazepines, which are not readily accessible by known methods.[11,15] Our attempts to extend the platinum-catalyzed reaction to anthranil substrates only resulted in the formation of 7-formylindoles.[9a,13]

Table 3: Reaction scope with different isoxazoles **2**.[a]



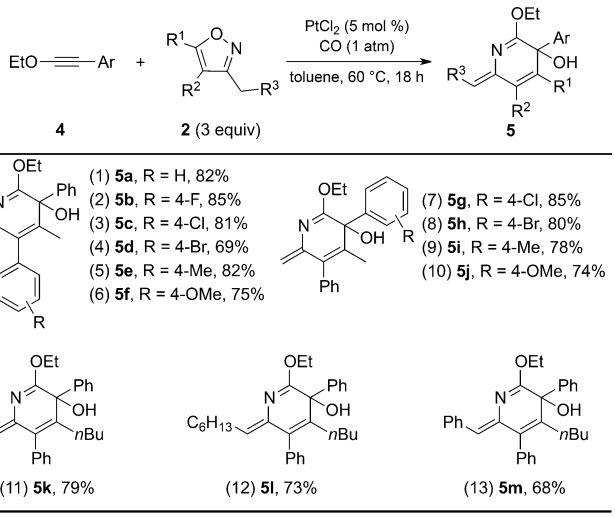
[a] Reactions were carried out in vials under a CO atmosphere (1 atm); [**1a**] = 0.05 M; reported yields are for the isolated product.

When the scope of this Pt catalysis was extended to 3,5-disubstituted isoxazoles, the formation of 2-aminopyrroles was observed to a significant extent. As shown in Equation (1), the treatment of ynamide **1a** with isoxazole **2o** in the presence of $PtCl_2$ (5 mol%) under CO (1 atm) afforded the corresponding 1,3-oxazepine **3z** in 77% yield along with 2-aminopyrrole **3za** in 21% yield. We speculate that the side 1,5-cyclization may arise from the decreased steric hindrance of the generated enone partner.



Besides ynamides, the reaction also proceeded well with alkynyl ethers to furnish unexpected 2,5-dihydropyridines through a formal [4+2] annulation. Thus, the treatment of isoxazoles **2** with alkynyl ethers **4** in the presence of $PtCl_2$ (5 mol%) under CO (1 atm) afforded the corresponding 2,5-dihydropyridines **5a–m** in 68–85% yield (Table 4). The reaction presumably involves a platinum-catalyzed amination-initiated 1,7-cyclization/6π electrocyclization/epoxide-opening cascade, and the formation of 2,5-dihydropyridines

Table 4: Formal [4+2] annulation of alkynyl ethers and isoxazoles to give 2,5-dihydropyridines.[a]

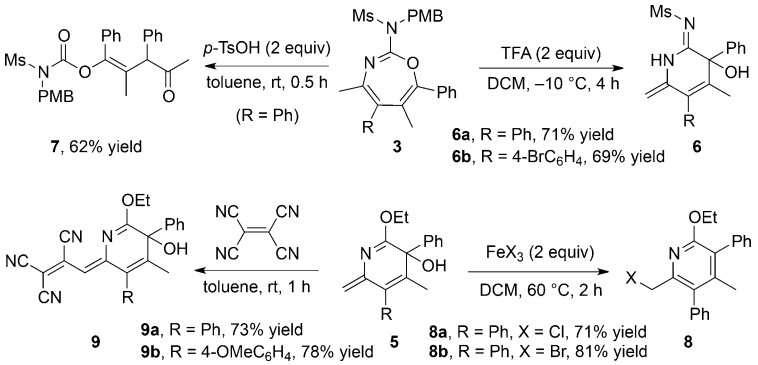


[a] Reactions were carried out in vials under a CO atmosphere (1 atm); [**4**] = 0.05 M; reported yields are for the isolated product.

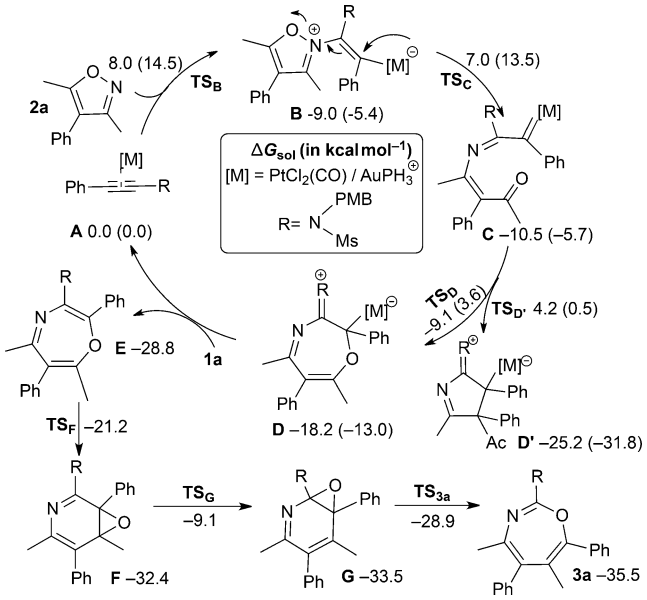
instead of the previous 1,3-oxazepines is attributed to thermodynamic factors.[13] Once again, only the 1,5-cyclization product was obtained when an isoxazole reacted with an alkynyl ether under gold catalysis.[13] Attempts to extend the reaction to nonpolarized alkynes, such as 1-octyne and phenylacetylene, only gave a complex mixture of products, and no desired seven-membered heterocycles were obtained.[13]

The further synthetic transformation of the as-synthesized products was also explored (Scheme 2).[13] Interestingly, the treatment of 1,3-oxazepine **3a** with trifluoroacetic acid (TFA) led to the formation of **6a** in 71% yield, whereas carbamate **7** was obtained in 62% yield by treatment with *p*-toluenesulfonic acid (*p*-TsOH). Furthermore, 2,5-dihydropyridines **5** could be converted into the corresponding 2-ethoxypyridines **8** in good yields. Notably, the reaction of **5** with tetracyanoethylene resulted in the formation of **9** in 73–78% yield. The molecular structures of **6b** and **9b** were confirmed by X-ray diffraction.[12]

On the basis of the above experimental observations and density functional theory (DFT) computations,[13] we propose that the platinum- and gold-catalyzed annulations between isoxazoles and ynamides proceed by the following mechanism (Scheme 3): Initially, nucleophilic attack of isoxazole **2a** on the [M]-ligated ynamide **A** forms a vinyl metal intermediate **B**,[13,14] which upon cleavage of the isoxazole N–O bond can isomerize to an α-imino metal carbene intermediate **C**. In the case of Pt catalysis, the platinum(II) carbene **C** favors kinetically 1,7-cyclization (via $\mathbf{TS_D}$) to afford eventually the formal [5+2] annulation product, that is, 1,3-oxazepine **3a**, through electrocyclization[16] and ring rearrangements.[17,18] On the contrary, in the case of Au catalysis,[8] the Au^I carbene **C** prefers 1,5-cyclization (via $\mathbf{TS_{D'}}$), which leads eventually to the formal [3+2] annulation product. Note that in the key metal carbene **C**, the carbenoid carbon atom bound to the tetracoordinated Pt^{II} center is more positively charged[13] (i.e., less selective in terms of the nucleophilicity of attacking sites),



Scheme 2. Transformation of the products. DCM = dichloromethane.



Scheme 3. Plausible mechanism accounting for the different chemoselectivity of platinum- and gold-catalyzed annulations of isoxazoles with ynamides. Relative free energies of key intermediates and transition states were computed at the SMD-M06/6-31G(d,p)/SDD level of theory in a solvent (toluene for Pt catalysis and DCE for Au catalysis) at 298 K. Data for Au catalysis are given in parentheses.

but more sterically hindered, than that bound to the linearly aligned dicoordinated Au^I center. Thus, the regioselectivity of intramolecular cyclization within the key metal carbene intermediate **C** is dominated by steric effects (i.e., favoring the sterically less hindered carbonyl oxygen atom) in the case of Pt catalysis, but depends mostly on the relative nucleophilicity of the attacking sites in the case of Au catalysis.

In summary, we have developed a novel platinum-catalyzed formal [5+2] annulation of ynamides with isoxazoles. Besides the efficient and atom-economical formation of valuable 1,3-oxazepine frameworks, the reactivity is dramatically divergent from that observed under Au catalysis. Moreover, a computational study provided further evidence for the feasibility of the proposed mechanism. Importantly, this protocol provides the first example of the generation of α-imino platinum carbenes. Furthermore, this Pt catalysis is also applicable to the site-selective synthesis of 2,5-dihydropyridines through the platinum-catalyzed formal [4+2] annulation of alkynyl ethers with isoxazoles.

Acknowledgements

We are grateful for financial support from the NNSFC (21272191, 21273177, 21572186, 91545105, and 21622204), the NSFFJ for Distinguished Young Scholars (2015J06003) and NFFTBS (No. J1310024).

Conflict of interest

The authors declare no conflict of interest.

Keywords: annulation · heterocycles · homogeneous catalysis · platinum · ynamides

[1] For selected recent reviews, see: a) W. Zi, F. D. Toste, *Chem. Soc. Rev.* **2016**, *45*, 4567; b) R. J. Harris, R. A. Widenhoefer, *Chem. Soc. Rev.* **2016**, *45*, 4533; c) D. B. Huple, S. Ghorpade, R.-S. Liu, *Adv. Synth. Catal.* **2016**, *358*, 1348; d) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028; e) Y. Wang, M. E. Muratore, A. M. Echavarren, *Chem. Eur. J.* **2015**, *21*, 7332; f) D. Qian, J. Zhang, *Chem. Soc. Rev.* **2015**, *44*, 677; g) L. Fensterbank, M. Malacria, *Acc. Chem. Res.* **2014**, *47*, 953; h) C. Obradors, A. M. Echavarren, *Acc. Chem. Res.* **2014**, *47*, 902; i) Y.-M. Wang, A.-D. Lackner, F. D. Toste, *Acc. Chem. Res.* **2014**, *47*, 889; j) A. S. K. Hashmi, *Acc. Chem. Res.* **2014**, *47*, 864; k) C. Obradors, A. M. Echavarren, *Chem. Commun.* **2014**, *50*, 16.

[2] For reviews, see: a) A. Fürstner, *Acc. Chem. Res.* **2014**, *47*, 925; b) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208; c) S. M. Abu Sohel, R.-S. Liu, *Chem. Soc. Rev.* **2009**, *38*, 2269; d) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem. Int. Ed.* **2008**, *47*, 4268; *Angew. Chem.* **2008**, *120*, 4338; e) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410; *Angew. Chem.* **2007**, *119*, 3478; for recent selected examples, see: f) P. A. Allegretti, K. Huynh, T. J. Ozumerzifon, E. M. Ferreira, *Org. Lett.* **2016**, *18*, 64; g) Y. Kwon, I. Kim, S. Kim, *Org. Lett.* **2014**, *16*, 4936; h) S. M. Stevenson, E. T. Newcomb, E. M. Ferreira, *Chem. Commun.* **2014**, *50*, 5239; i) D. Shu, W. Song, X. Li, W. Tang, *Angew. Chem. Int. Ed.* **2013**, *52*, 3237; *Angew. Chem.* **2013**, *125*, 3319; j) P. A. Allegretti, E. M. Ferreira, *Chem. Sci.* **2013**, *4*, 1053; k) W. Yang, T. Wang, Y. Yu, S. Shi, T. Zhang, A. S. K. Hashmi, *Adv. Synth. Catal.* **2013**, *355*, 1523; l) K. Saito, H. Sogou, T. Suga, H. Kusama, N. Iwasawa, *J. Am. Chem. Soc.* **2011**, *133*, 689; m) P. A. Allegretti, E. M. Ferreira, *Org. Lett.* **2011**, *13*, 5924.

[3] For reviews on the generation of α-oxo or α-imino Au carbenes, see: a) Z. Zheng, Z. Wang, Y. Wang, L. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 4448; b) P. W. Davies, M. Garzón, *Asian J. Org. Chem.* **2015**, *4*, 694; c) H.-S. Yeom, S. Shin, *Acc. Chem. Res.* **2014**, *47*, 966; d) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877; e) J. Xiao, X. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 7226; *Angew. Chem.* **2011**, *123*, 7364.

[4] For the generation of an iminium-bound Pt carbene, see: I. Nakamura, Y. Sato, M. Terada, *J. Am. Chem. Soc.* **2009**, *131*, 4198.

[5] For examples of a selectivity switch involving carbene intermediates, see: a) P. A. Allegretti, E. M. Ferreira, *J. Am. Chem.*

Soc. **2013**, *135*, 17266; b) G. Zhang, V. J. Catalano, L. Zhang, *J. Am. Chem. Soc.* **2007**, *129*, 11358; for other examples, see: c) Y. Qiu, D. Ma, W. Kong, C. Fu, S. Ma, *Org. Chem. Front.* **2014**, *1*, 62; d) S. G. Modha, A. Kumar, D. D. Vachhani, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Chem. Commun.* **2012**, *48*, 10916; e) A. Das, H.-K. Chang, C.-H. Yang, R.-S. Liu, *Org. Lett.* **2008**, *10*, 4061; f) A. S. K. Hashmi, E. Kurpejovic, W. Frey, J. W. Bats, *Tetrahedron* **2007**, *63*, 5879.

[6] For reviews on ynamide reactivity, see: a) G. Evano, C. Theunissen, M. Lecomte, *Aldrichimica Acta* **2015**, *48*, 59; b) X.-N. Wang, H.-S. Yeom, L.-C. Fang, S. He, Z.-X. Ma, B. L. Kedrowski, R. P. Hsung, *Acc. Chem. Res.* **2014**, *47*, 560; c) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064; d) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840; *Angew. Chem.* **2010**, *122*, 2902.

[7] For recent examples, see: a) F. Pan, X.-L. Li, X.-M. Chen, C. Shu, P.-P. Ruan, C.-H. Shen, X. Lu, L.-W. Ye, *ACS Catal.* **2016**, *6*, 6055; b) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567; c) L. Li, B. Zhou, Y.-H. Wang, C. Shu, Y.-F. Pan, X. Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2015**, *54*, 8245; *Angew. Chem.* **2015**, *127*, 8363; d) L. Li, C. Shu, B. Zhou, Y.-F. Yu, X.-Y. Xiao, L.-W. Ye, *Chem. Sci.* **2014**, *5*, 4057.

[8] a) A.-H. Zhou, Q. He, C. Shu, Y.-F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu, L.-W. Ye, *Chem. Sci.* **2015**, *6*, 1265; b) X.-Y. Xiao, A.-H. Zhou, C. Shu, F. Pan, T. Li, L.-W. Ye, *Chem. Asian J.* **2015**, *10*, 1854.

[9] a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794; *Angew. Chem.* **2016**, *128*, 804; during the preparation of our manuscript, a beautiful study on the annulation of propargylic silyl ethers with anthranils was reported: b) M. S. H. Jin, M. S. B. Tian, M. S. X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688; *Angew. Chem.* **2016**, *128*, 12880.

[10] X. Lei, L. Li, Y.-P. He, Y. Tang, *Org. Lett.* **2015**, *17*, 5224.

[11] For selected examples, see: a) C. F. Martinez-Farina, D. L. Jakeman, *Chem. Commun.* **2015**, *51*, 14617; b) W. R. Martínez, G. C. G. Militão, T. G. da Silva, R. O. Silva, P. H. Menezes, *RSC Adv.* **2014**, *4*, 14715; c) F. Shah, P. Mukherjee, J. Gut, J. Legac, P. J. Rosenthal, B. L. Tekwani, M. A. Avery, *J. Chem. Inf. Model.* **2011**, *51*, 852; d) R. Mueller, A. L. Rodriguez, E. S. Dawson, M. Butkiewicz, T. T. Nguyen, S. Oleszkiewicz, A. Bleckmann, C. D. Weaver, C. W. Lindsley, P. J. Conn, J. Meiler, *ACS Chem. Neurosci.* **2010**, *1*, 288; e) A. A. Abdel-Hafez, B. A. Abdel-Wahab, *Bioorg. Med. Chem.* **2008**, *16*, 7983; f) L. Galam, M. K. Hadden, Z. Ma, Q. Z. Ye, B. G. Yun, B. S. Blagg, R. L. Matts, *Bioorg. Med. Chem.* **2007**, *15*, 1939; g) A. Cul, A. Chihab-Eddine, A. Pesquet, Š. Marchalín, A. Daïch, *J. Heterocycl. Chem.* **2003**, *40*, 499.

[12] CCDC 1478424 (**3a**), 1478425 (**6b**), and 1504743 (**9b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[13] For details, see the Supporting Information.

[14] For the initial work on the acceleration of $PtCl_2$ catalysis by CO, see: A. Fürstner, P. W. Davies, T. Gress, *J. Am. Chem. Soc.* **2005**, *127*, 8244.

[15] a) A. Macé, S. Touchet, P. Andres, F. Cossío, V. Dorcet, F. Carreaux, B. Carboni, *Angew. Chem. Int. Ed.* **2016**, *55*, 1025; *Angew. Chem.* **2016**, *128*, 1037; b) S. Shang, D.-Z. Negrerie, Y. Du, K. Zhao, *Angew. Chem. Int. Ed.* **2014**, *53*, 6216; *Angew. Chem.* **2014**, *126*, 6330; c) V. Sridharan, S. Maiti, J. C. Menéndez, *J. Org. Chem.* **2009**, *74*, 9365; d) C. Ma, S.-J. Liu, L. Xin, J. R. Falck, D.-S. Shin, *Tetrahedron* **2006**, *62*, 9002; e) B. Bauvois, M.-L. Puiffe, J.-B. Bongui, S. Paillat, C. Monneret, D. Dauzonne, *J. Med. Chem.* **2003**, *46*, 3900.

[16] Owing to the rigid tetracoordinated structure around the Pt^{II} center and the electron deficiency at both the Pt^{II} carbenoid carbon and carbonyl carbon sites, the hypothetical [2+2] cycloaddition as a shortcut for the formation of **F** from **C** is quite unlikely; see: a) B. Martín-Matute, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2001**, *40*, 4754; *Angew. Chem.* **2001**, *113*, 4890; b) B. Martín-Matute, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *J. Am. Chem. Soc.* **2003**, *125*, 5757.

[17] a) A. S. K. Hashmi, M. Rudolph, J. P. Weyrauch, M. Wölfle, W. Frey, J. W. Bats, *Angew. Chem. Int. Ed.* **2005**, *44*, 2798; *Angew. Chem.* **2005**, *117*, 2858; b) J. Kurita, K. Iwata, T. Tsuchiya, *J. Chem. Soc. Chem. Commun.* **1986**, 1188.

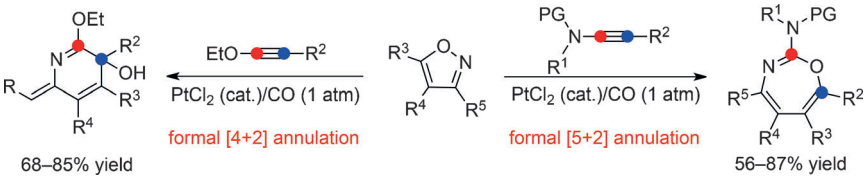
[18] For selected examples of the relevant C–C bond cleavage of epoxides, see: a) J. Zhang, Z. Chen, H.-H. Wu, J. Zhang, *Chem. Commun.* **2012**, *48*, 1817; b) T. Wang, C.-H. Wang, J. Zhang, *Chem. Commun.* **2011**, *47*, 5578; c) T. Wang, J. Zhang, *Chem. Eur. J.* **2011**, *17*, 86; d) Z. Chen, L. Wei, J. Zhang, *Org. Lett.* **2011**, *13*, 1170.

Manuscript received: October 13, 2016
Final Article published: ■■ ■■, ■■■■

Communications

Heterocycles

W.-B. Shen, X.-Y. Xiao, Q. Sun, B. Zhou, X.-Q. Zhu, J.-Z. Yan, X. Lu,* L.-W. Ye* _____ ■■■■–■■■■



Highly Site Selective Formal [5+2] and [4+2] Annulations of Isoxazoles with Heterosubstituted Alkynes by Platinum Catalysis: Rapid Access to Functionalized 1,3-Oxazepines and 2,5-Dihydropyridines

Gold's deviant relative: Platinum-catalyzed formal [5+2] and [4+2] annulations of isoxazoles and heterosubstituted alkynes provided valuable 1,3-oxazepines and 2,5-dihydropyridines (see scheme). This reactivity deviates dramatically from that observed under gold catalysis and involves the generation of an α-imino platinum carbene. A computational study provided evidence for the proposed mechanism of this unusual tandem sequence.

