Advanced Synthesis & Catalysis

Accepted Article

Title: Gold-Catalyzed Oxidative Cyclization of Tryptamine Derived Enynamides: A Stereoselective Approach to Tetracyclic Spiroindolines

Authors: Meijun Lin, Lei Zhu, Jiajin Xia, Yinghua Yu, Jianxin Chen, Zhifeng Mao, and Xueliang Huang

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201800001

Link to VoR: http://dx.doi.org/10.1002/adsc.201800001

10.1002/adsc.201800001

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Gold-Catalyzed Oxidative Cyclization of Tryptamine Derived Enynamides: A Stereoselective Approach to Tetracyclic Spiroindolines

Meijun Lin[a,b],Lei Zhu[a,c], Jiajin Xia[a,c], Yinghua Yu[a], Jianxin Chen,*[b] Zhifeng Mao*[a] and Xueliang Huang*[a,c]

[a] Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou, Fujian 350002, China. E-mail: maozf@fjirsm.ac.cn; huangxl@fjirsm.ac.cn.
[b] College of Chemistry and Chemical Engineering, Fujian Normal University, Fuzhou, Fujian 350007, China. E-mail: jxchen@fjnu.edu.cn
[c] University of Chinese Academy of Sciences, Beijing 100049, China.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. In this work, we describe a new gold-catalyzed oxidative cascade cyclization of conjugated enynamides. The reaction could be carried out under relatively mild condition. In presence of a cationic gold catalyst bearing an *N*-heterocyclic carbene ligand, enynamides derived from tryptamine react with pyridine *N*-oxide, leading to the formation of a variety of tetracyclic spiroindolines in a stereoselective manner.

Keywords: gold catalyst; enynamide; tetracyclic spiroindolines; gold carbene; stereoselective

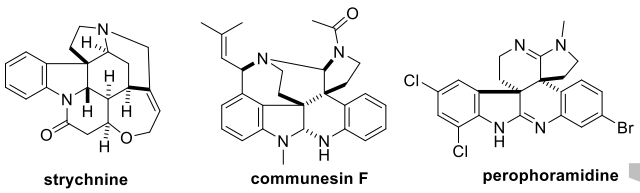
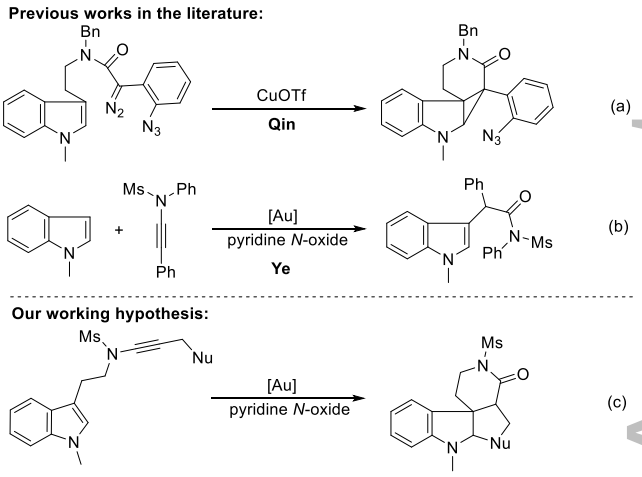


Figure 1. Naturally occurring polycyclic spiroindolines.



Scheme 1. Trapping metal-carbene intermediates by indole derivatives.

Transition metal carbene is a reactive intermediate that has found great potential in the synthetic community.[1] Diazo compounds are easily accessible, possessing tuneable reactivity. Thus they are frequently used as precursors for the generation of metal carbene species.[2] However, in view of their hazardous and potentially explosive nature, the development of an alternative carbene precursor has been a longstanding goal for the organic chemists. Pioneered by Toste[3] and Zhang,[4] and later was further exploited by others,[5] the strategy involving oxidative addition of alkynes in presence of a proper gold catalyst to produce α-oxo gold carbene has received considerable attention.[6,7]

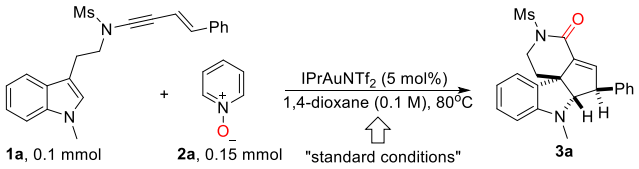
Polycyclic spiroindolines are prevalent structural motifs that embedded in a number of alkaloid natural products and pharmaceutical molecules with potent biological activities (Figure 1).[8] Among all the synthetic approaches to construct these frameworks, the methods based on catalytic dearomatization of the existing indole ring are of particular interests, regarding the availability of the starting materials and the high efficiency on the fused ring formation.[9]

Recently, Qin and co-workers have reported transition-metal catalyzed cyclopropanation of diazo compounds with indole derivatives (Scheme 1a),[10] which was further applied to the total synthesis of (±)-Communesin F,[10d] (±)-Vincorine[10e] and Kopsia indole alkaloids.[10f] More recently, Ye and co-

10.1002/adsc.201800001

workers reported an intermolecular trapping of α-oxo-gold carbene intermediate by indoles and anilines (Scheme 1b).[11] Inspired by these advances and our recent research interests in transition metal carbene chemistry,[12,13] we envisioned that a gold-catalyzed oxidative intramolecular annulation of tryptamine derived ynamide in presence of pyridine *N*-oxide might offer a direct approach to tetracyclic spiroindolines (Scheme 1c). Given the well-known procedure for the preparation of ynamides,[14,15] and the nondiazo feature, we believe that the successful implementation of our hypothesis might have the potential for the rapid and large scale synthesis complex molecules.

At the outset, we chose enynamide **1a** as the model substrate to react with pyridine *N*-oxide **2a** to test our hypothesis. Pleasingly, after brief examination of the reaction conditions,[16] we found that the reaction of **1a** and **2a** catalyzed by a cationic gold catalyst $IPrAuNTf_2$ (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene) in 1,4-dioxane could proceed smoothly at 80°C, and the target tetracyclic spiroindoline **3a** was isolated in nearly quantitative yield. Control experiments further highlight the critical role of the cationic nature for the gold catalyst, and Brønsted acid $HNTf_2$[5j] was not efficient as well (Scheme 2).



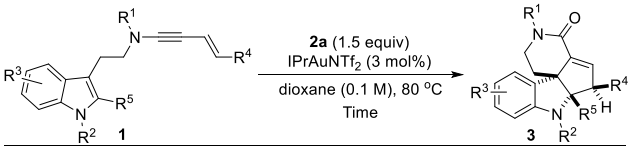
"variation from standard conditions"	time/h	yield/%
none	1.5	99
IPrAuCl was used as catalyst	12	99
$AgNTf_2$ was used as catalyst	2	16
$HNTf_2$ was used as catalyst	2	-

Scheme 2. Gold-catalyzed oxidative annulation of **1a** in presence of pyridine *N*-oxide **2a**.

After establishing a set of effective reaction conditions for **3a**. The reaction scope and limitation were further investigated and the results are compiled in Table 1. As depicted, the effects of protecting groups in amide moiety were firstly evaluated. The enynamides bearing Ms-, Ts-, Bs-, Ns-groups are all compatible with current transformation, giving the products in good to excellent yields (cf. **3a-3d**, 70-99%). Replacement of the methyl group with a benzyl group on the nitrogen atom of the indole moiety led to a slightly decrease of the reaction yield (cf. **3e**). When protecting group on the indole nitrogen moiety was switch to a carbamate group (e.g. Boc), a major product α-ketoamide resulting from over oxidation was obtained (results not shown). Introducing a variety of substituents on to the indole-ring has no strong influence on the reaction outcomes, regardless of the electronic or steric nature (cf. **3f-3l**).

Remarkably, tetracyclic spiroindoline **3u** containing two contiguous tetrasubstituted carbon stereocenters was isolated in excellent yield as a single diastereoisomer. Aryl/heteroaryl goups at the terminal position of the double bond with different

Table 1. Reaction scope for the synthesis of spiroindolines **3**.[a)]



Entry	Substrate	Product	Time, yield
1	**1a**, R = Ms	**3a**, R = Ms	1.5 h, 99%
2	**1b**, R = Ts	**3b**, R = Ts	2 h, 99%
3	**1c**, R = Bs	**3c**, R = Bs	2 h, 88%
4	**1d**, R = Ns	**3d**, R = Ns	2 h, 70%
5	**1e**	**3e**	1.5 h, 77%
6	**1f**, R = 5-F	**3f**, R = 5-F	1 h, 75%
7	**1g**, R = 5-Cl	**3g**, R = 5-Cl	2 h, 94%
8	**1h**, R = 5-OMe	**3h**, R = 5-OMe	2 h, 78%
9	**1i**, R = 4-Cl	**3i**, R = 4-Cl	2 h, 82%
10	**1j**, R = 4-Me	**3j**, R = 4-Me	4 h, 73%
11	**1k**, R = 6-Me	**3k**, R = 6-Me	4 h, 73%
12	**1l**, R= 7-Me	**3l**, R= 7-Me	2 h, 88%
13	**1m**, R = 4-OMe	**3m**, R = 4-OMe	1.5 h, 96%
14	**1n**, R = 4-Me	**3n**, R = 4-Me	2 h, 75%
15	**1o**, R = 4-Br	**3o**, R = 4-Br	1 h, 97%
16	**1p**, R = 4-Cl	**3p**, R = 4-Cl	2 h, 90%
17	**1q**, R = 4-F	**3q**, R = 4-F	1.5 h, 89%
18	**1r**, R = 3-Cl	**3r**, R = 3-Cl	1.5 h, 77%
19	**1s**, R= 2-Cl	**3s**, R= 2-Cl	2 h, 75%
20	**3t**, 1.5 h, 68%		
21	**3u**, 2 h, 89%		
22	**3v**, 17 h, 27%		
23	**3w**, 18 h, 44%		
24	**1x**	conditions	**SI-2**, 2 h, 72%

a) The reaction was carried out under an atmosphere of argon, in 0.3 mmol scale. Yields reported are for pure, isolated compounds.

electronic or steric characters were tolerated under current conditions, giving the corresponding products in good to excellent yields (cf. **3m**-**3s**, **3u**). Because of the over oxidation, the reactions of ynamides derived from phenylacetylene or 2-ethynylnaphthalene gave the spiroindoline **3v** or **3w** in 27% and 44% yields, respectively. It is worthwhile to mention that replacing the aryl group (R^4) with an alkyl group led to negligible formation of corresponding spiroindoline (results not shown). Interestingly, the reaction of Yang's indole-ynamide **1x**[17] under standard conditions gave a tosyl protected tryptamide **SI-2** in 72% yield. The structural configuration of the products and diastereoselectivity of current reaction in presence of **2a** were further confirmed by X-ray crystal analysis of **3a** (Figure 2).[18]

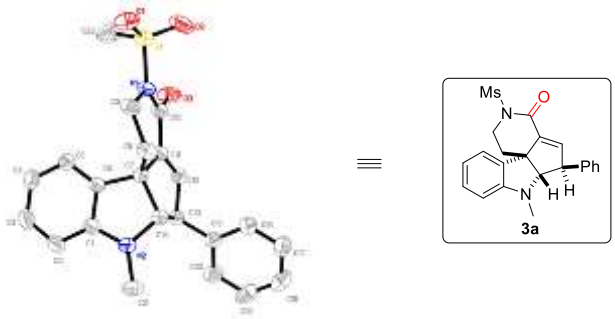
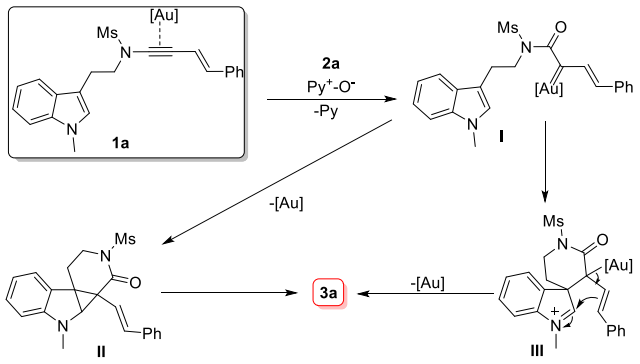


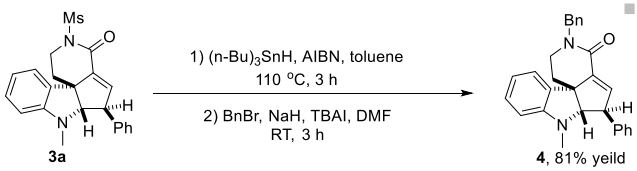
Figure 2. Crystal structure of spiroindoline **3a**. The thermal ellipsoids are drawn at 50% probability; hydrogen atoms are omitted for clarity.



Scheme 3. Plausible mechanism for gold-catalyzed oxidative annulation of enynamide **1a**.

According to the results obtained and previous reports on gold-catalyzed oxidative functionalization of alkynes, plausible reaction pathways leading to tetracyclic spiroindolines **3** were proposed in Scheme 3. The reaction was initiated by the coordination of the cationic gold catalyst with C-C triple bond. The oxidation of **1a** by pyridine *N*-oxide **2a** probably generates α-oxo-gold carbene intermediate **I**.[6] At this stage, an intramolecular cyclopropanation of the carbene intermediate takes place giving **II**.[10,11] Ring expansion of the fused cyclopropane ring would eventually furnish **3a**. Alternatively, the reaction may proceed via a stepwise cyclization pathway. Nucleophilic addition of 3-position of the indole-ring to the gold carbene carbon center would build up the spiro framework **III**. Intramolecular trapping of the iminium ion intermediate by tethered stryrene moiety would also furnish **3a**.

Under standard conditions, a gram-scale reaction was also carried out, and **3a** was obtained in 91% yield. Subsequently, preliminary manipulation of the tetracyclic spiroindoline **3a** was sought (Scheme 4). The methylsulfonyl group could be removed following a radical pathway. The resulting crude product was used without purification for the next step. Spiroindoline **4** was obtained in 81% overall yield.



Scheme 4. Synthetic manipulation on tetracyclic spiroindoline **3a**.

In conclusion, we have developed an efficient gold-catalyzed oxidative annulation of tryptamine derived enynamides. Based on our own results and previous reports, catalytic cycle involving α-oxo-gold carbene intermediate was proposed. In this event, a number of tetracyclic spiroindolines bearing three continuous carbon centers were obtained with high stereoselectivity. Furthermore, considering the well-established procedure for the preparation of ynamides, the method on modular synthesis of spiroindolines reported here may be helpful to build up a library of molecules with different structural complexities. Studies to extend the substrate scope and further applications on the synthesis of pharmaceutical relevant compounds are on-going in our laboratory.

Experimental Section

General procedure:

An oven-dried 10 mL schlenk tube equipped with a magnetic stirring bar was charged with enynamide **1a** (0.30 mmol, 113.5 mg), pyridine *N*-oxide **2a** (0.45 mmol, 42.8 mg), $IPrAuNTf_2$ (3 mol%, 7.8 mg) and 3 mL anhydrous 1,4-dioxane. The tube was then capped and the mixture stirred at 80 °C under an atmosphere of argon until the reaction was complete, then the mixture was cooled to room temperature and the solvent was removed under reduced pressure. The resulting residual was purified by column chromatography (petroleum ether/ethyl acetate) on silica gel to afford tetracyclic spiroindolines **3a**.

Acknowledgements

We are grateful for the financial support by NSFC (Grant No. 21402197, 21502190), NSF of Fujian (Grant No. 2015J05043, 2017J01031), Hundred-Talent Program and the Strategic Priority Research Program of the Chinese Academy of Sciences (Grant No. XDB20000000).

References

[1] For selected reviews: a) Doyle, M. P. *Chem. Rev.* **1980**, *66*, 919-939; b) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223-269; c) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911-935; d) M. S. Baird, *Chem. Rev.* **2003**, *103*, 1271-1294; e) H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev.* **2003**, *103*, 2861-2903; f) M. P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, *Chem. Rev.* **2010**, *110*, 704-724.

[2] For selected reviews: a) T. Ye, M. A. McKervey, *Chem. Rev.* **1994**, *94*, 1091-1160. b) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*, John Wiley & Sons, Inc., New York, NY, **1998**. c) Z. Zhang, J. Wang, *Tetrahedron* **2008**, *64*, 6577-6605. d) Y. Zhang, J. Wang, *Chem. Commun.* **2009**, *45*, 5350-5361. e) S.-F. Zhu, Q.-L. Zhou, *Acc. Chem. Res.* **2012**, *45*, 1365-1377. f) X. Guo, W. Hu, *Acc. Chem. Res.* **2013**, *46*, 2427-2440. g) A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire, M. A. McKervey, *Chem. Rev*. **2015**, *115*, 9981-10080.

[3] N. D. Shapiro, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 4160-4161.

[4] a) L. Ye, L. Cui, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 3258-3259; b) L. Ye, W. He, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 8550-8551; c) L. Ye, W. He, L. Zhang, *Angew. Chem.* **2011**, *123*, 3294-3297; *Angew. Chem. Int. Ed.* **2011**, *50*, 3236-3239; d) K. Ji, Z. Zheng, Z. Wang, L. Zhang, *Angew. Chem.* **2015**, *127*, 1261-1265; *Angew. Chem. Int. Ed.* **2015**, *54*, 1245-1249.

[5] For selected examples: a) H.-S. Yeom, J.-E. Lee, S. Shin, *Angew. Chem.* **2008**, *120*, 7148-7150; *Angew. Chem. Int. Ed.* **2008**, *47*, 7.40-7043; b) S. Bhunia, S. Ghorpade, D. B. Huple, R.-S. Liu, *Angew. Chem.* **2011**, *123*, 2993-2996; *Angew. Chem. Int. Ed*. **2011**, *50*, 2939-2942; c) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem.* **2011**, *123*, 7043-7046; *Angew. Chem. Int. Ed.* **2011**, *50*, 6911-6914; d) D. Qiana, J. Zhang, *Chem. Commun.* **2011**, *47*, 11152-11154; e) S. K. Pawar, C.-D. Wang, S. Bhunia, A. Mahadev Jadhav, R.-S. Liu, *Angew. Chem.* **2013**, *125*, 7707-7711; *Angew. Chem. Int. Ed.* **2013**, *52*, 7559-7563; f) L. Wang, X. Xie, Y. Liu, *Angew. Chem.* **2013**, *125*, 13544-13548; *Angew. Chem. Int. Ed.* **2013**, *52*, 13302-13306; g) S. N. Karad, R.-S. Liu, *Angew. Chem.* **2014**, *126*, 5548-5562; *Angew. Chem. Int. Ed.* **2014**, *53*, 5444-5448; h) D. Qian, H. Hu, F. Liu, B. Tang, W. Ye, Y. Wang, J. Zhang, *Angew. Chem.* **2014**, *126*, 13971-13975; *Angew. Chem. Int. Ed.* **2014**, *53*, 13751-13755; i) M. Chen, Y. Chen, N. Sun, J. Zhao, Y. Liu, Y. Li, *Angew. Chem.* **2015**, *127*, 1216-1220; *Angew. Chem. Int. Ed.* **2015**, *54*, 1200-1204; j) D. V. Patil, S. WooKim, Q. H. Nguyen, H. Kim, S. Wang, T. Hoang, S. Shin, *Angew. Chem.* **2017**, *129*, 3724-3728; *Angew. Chem. Int. Ed*. **2017**, *56*, 3670-3674.

[6] For selected reviews on α-oxo gold carbenes in catalysis: a) J. Xiao, X. Li, *Angew. Chem.* **2011**, *123*, 7364-7375; *Angew. Chem. Int. Ed.* **2011**, *50*, 7226-7236; b) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877-888; c) H.-S. Yeom, S. Shin, *Acc. Chem. Res.* **2014**, *47*, 966-977; e) Z. Zheng, Z. Wang, Y. Wang, L. Zhang, *Chem. Soc. Rev*. **2016**, *45*, 4448-4458.

[7] For selected reviews on gold catalysis: a) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478-3519; *Angew. Chem. Int. Ed*. **2007**, *46*, 3410-3449; b) A. S. K. Hashmi, *Chem. Rev*. **2007**, *107*, 3180-3211; c) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev*. **2008**, *108*, 3351-3378; d) C. M. Friend, A. S. K. Hashmi, *Acc. Chem. Res.* **2014**, *47*, 864-876; e) D. Qian, J. Zhang, *Chem. Soc. Rev*. **2015**, *44*, 677-698; f) R. Dorel, A. M. Echavarren, *Chem. Rev*. **2015**, *115*, 9028-9072; g) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506-516; h) W. Zi, F. D. Toste, *Chem. Soc. Rev.* **2016**, *45*, 4567-4589; i) A. M. Echavarren, A. S. K. Hashmi, F. D. Toste, *Adv. Synth. Catal.* **2016**, *358*, 1347; j) Y. Wei, M. Shi, *ACS Catal.* **2016**, *6*, 2515-2524.

[8] a) U. Beifuss, *Angew. Chem. Int. Ed Engl.* **1994**, *33*, 1144-1149; b) J. Bonjoch, D. Solé, *Chem. Rev.* **2000**, *100*, 3455-3482; c) A. Steven, L. E. Overman, *Angew. Chem. Int. Ed.* **2007**, *46*, 5488-5508; d) A. A. Patchett, R. P. Nargund, J. R. Tata, M. H. Chen, K. J. Barakat, D. B. Johnston, K. Cheng, W. W. Chan, B. Butler, G. Hickey, T. Jacks, K. Schleim, S.-S. Pong, L.-Y. P. Chaung, H. Y. Chen, E. Frazier, K. H. Leung, S.-H. L. Chiu and R. G. Smith, *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 7001-7005; e) S. M. Verbitski, C. L. Mayne, R. A. Davis, G. P. Concepcion, C. M. Ireland, *J. Org. Chem.* **2002**, *67*, 7124-7126; f) R. Jadulco, R. A. Edrada, R. Ebel, A. Berg, K. Schaumann, V. Wray, K. Steube, P. Proksch, *J. Nat. Prod.* **2004**, *67*, 78-81; g) S. E. O′Connor, J. J. Maresh, *Nat. Prod. Rep.* **2006**, *23*, 532-547; h) T. Feng, Y. Li, X.-H. Cai, X. Gong, Y.-P. Liu, R.-T. Zhang, X.-Y. Zhang, Q.-G. Tan, X.-D. Luo, *J. Nat. Prod.* **2009**, *72*, 1836-1841; i) K. Koyama, Y. Hirasawa, A. E. Nugroho, T. Hosoya, T. C. Hoe, K.-L. Chan, H. Morita, *Org. Lett.* **2010**, *12*, 4188-4191; j) Y.-P. Liu, Y.-L. Zhao, T. Feng, G.-G. Cheng, B.-H. Zhang, Y. Li, X.-H. Cai, X.-D. Luo, *J Nat. Prod*. **2013**, *76*, 2322-2329; k) K. D. Schleicher, Y. Sasaki, A. Tam, D. Kato, K. K. Duncan, D. L. Boger, *J. Med. Chem.* **2013**, *56*, 483−495; l) D. P. Zlotos, C. Tränkle, U. Holzgrabe, D. Gündisch, A. A. Jensen, *J. Nat. Prod.* **2014**, *77*, 2006-2013.

[9] For selected reviews: a) P. Siengalewicz, T. Gaich, J. Mulzer, *Angew. Chem.* **2008**, *120*, 8290-8296; *Angew. Chem. Int. Ed.* **2008**, *47*, 8170-8176; b) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003-3025; c) J. S. Cannon, L. E. Overman, *Angew. Chem.* **2012**, *124*, 4362-4386; *Angew. Chem. Int. Ed.* **2012**, *51*, 4288-

4311; d) S. P. Roche, J.-J. Youte Tendoung, B. Tréguier, *Tetrahedron* **2015**, *71*, 3549-3591; e) W. Zi, Z. Zuo, D. Ma, *Acc. Chem. Res.* **2015**, *48*, 702-711; f) C. Zheng, S.-L. You, *Chem.* **2016**, *1*, 830-857; g) W.-T. Wu, L. Zhang, S.-L. You, *Acta Chimica Sinica*, **2017**, *75*, 419-438;

[10] a) D. Zhang, H. Song, Y. Qin, *Acc. Chem. Res.* **2011**, *44*, 447-457; b) J. Yang, H. Song, X. Xiao, J. Wang, Y. Qin, *Org. Lett.* **2006**, *8*, 2187-2189; c) H. Song, J. Yang, W. Chen, Y. Qin, *Org. Lett.* **2006**, *8*, 6011-6014; d) J. Yang, H. Wu, L. Shen, Y. Qin, *J. Am. Chem. Soc.* **2007**, *129*, 13794-13795; e) M. Zhang, X. Huang, L. Shen, Y. Qin, *J. Am. Chem. Soc.* **2009**, *131*, 6013-6020; f) L. Leng, X. Zhou, Q. Liao, F. Wang, H. Song, D. Zhang, X.-Y. Liu, Y. Qin, *Angew. Chem.* **2017**, *129*, 3757-3761; *Angew. Chem. Int. Ed.* **2017**, *56*,3703-3707; For a recent asymmetric intramolecular cyclopropanation: g) H. Xu, Y.-P. Li, Y. Cai, G.-P. Wang, S.-F. Zhu, Q.-L. Zhou *J. Am. Chem. Soc.* **2017**, *139*, 7697-7700.

[11] a) L. Li, C. Shu, B. Zhou, Y.-F. Yu, X.-Y. Xiao, L.-W. Ye, *Chem. Sci.* **2014**, *5*, 4057-4064; b) C.-H. Shen, L. Li, W. Zhang, S. Liu, C. Shu, Y.-E. Xie, Y.-F. Yu. L.-W. Ye, *J. Org. Chem.* **2014**, *79*, 9313-9318; c) 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*, 6055-6062.

[12] a) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30-33; b) Y. Wu, L. Zhu, Y. Yu, X. Luo, X. Huang, *J. Org. Chem.* **2015**, *80*, 11407-11416; c) Y. Yu, G. Chen, L. Zhu, Y. Liao, Y. Wu, X. Huang, *J. Org. Chem.* **2016**, *81*, 8142-8154; d) X. Cheng, L. Zhu, M. Lin, J. Chen, X. Huang, *Chem. Commun.* **2017**, *53*, 3745-3748; e) Y. Liao, Q. Lu, G. Chen, Y, Yu, C, Li, X. Huang, *ACS Catal.* **2017**, *7*, 7529-7534; f) Y. Liao, L. Zhu, Y. Yu, G. Chen, X. Huang, *Chin. J. Org. Chem.* **2017**, *37*, 2785-2799.

[13] a) G. Chen, J. Song, Y. Yu, X. Luo, C. Li, X. Huang, *Chem. Sci.* **2016**, *7*, 1786-1790; b) X. Luo, G. Chen, L. He, X. Huang, *J. Org. Chem.* **2016**, *81*, 2943-2949; c) Y. Yu, Q. Lu, G. Chen, C. Li, X. Huang, *Angew. Chem.* **2018**, *130*, 325-329; *Angew. Chem. Int. Ed.* **2018**, *57*, 319-323.

[14] a) C. A. Zificsak, J. A. Mulder, R. P. Hsung, C. Rameshkumar, L.-L. Wei, *Tetrahedron* **2001**, *57*, 7575-7606; b) T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833-835; c) A. Coste, G. Karthikeyan, F. Couty, G. Evano, *Angew. Chem.* **2009**, *121*, 4445-4449; *Angew. Chem. Int. Ed.* **2009**, *48*, 4381-4385; d) B. Yao, Z. Liang, T. Niu, Y. Zhang, *J. Org. Chem.* **2009**, *74*, 4630-4633.

[15] For representative reviews of ynamides: a) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064-5106; b) G. Evano, A. Coste, K. Jouvin, *Angew. Chem.* **2010**, *122*, 2902-2921; *Angew. Chem. Int. Ed.* **2010**, *49*, 2840-2859; c) G. Evano, K. Jouvin, A. Coste, *Synthesis* **2013**, *45*, 17-26; d) 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*, 560-578; e) G. Evano, C. Theunissen, M. Lecomte, *Aldrichimica Acta* **2015**, *48*, 59-70; f) F. Pan, C. Shu, L.-W. Ye, *Org. Biomol. Chem.* **2016**, *14*, 9456-9465.

[16] See the Supporting Information for details.

[17] N. Zheng, Y.-Y. Chang, L.-J. Zhang, J.-X. Gong, Z. Yang, *Chem. Asian J.* **2016**, *11*, 371-375.

[18] CCDC 1582447 (**3a**) 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/.

10.1002/adsc.201800001

COMMUNICATION

Gold-Catalyzed Oxidative Cyclization of Tryptamine Derived Enynamides: A Stereoselective Approach to Tetracyclic Spiroindolines

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Meijun Lin[a,b],Lei Zhu[a,c], Jiajin Xia[a,c], Yinghua Yu[a], Jianxin Chen,*[b] Zhifeng Mao*[a] and Xueliang Huang*[a,c]