Heterocycles

International Edition: DOI: 10.1002/anie.201700596
German Edition: DOI: 10.1002/ange.201700596

Yttrium-Catalyzed Intramolecular Hydroalkoxylation/Claisen Rearrangement Sequence: Efficient Synthesis of Medium-Sized Lactams

*Bo Zhou, Long Li, Xin-Qi Zhu, Juan-Zhu Yan, Yi-Lin Guo, and Long-Wu Ye**

Abstract: *An efficient yttrium-catalyzed intramolecular hydroalkoxylation/Claisen rearrangement sequence has been achieved, thus enabling facile access to a diverse array of valuable medium-sized lactams. Furthermore, a mechanistic rationale for this novel cascade reaction is well supported by a variety of control experiments.*

Medium-sized lactams (8- to 11-membered rings), especially the eight-membered lactams (benzazocinones), are important structural motifs which have been found in bioactive molecules and natural products (Figure 1).[1] However, such units are regarded as difficult structures to access because of entropic effects and transannular interactions,[2] and only very limited methods have been developed to date,[3–5] with intramolecular carbonylation[3] and ring-closing metathesis (RCM)[1e,4] being the most popular choices. Thus, new methods for the efficient construction of this type of skeleton are highly desired.

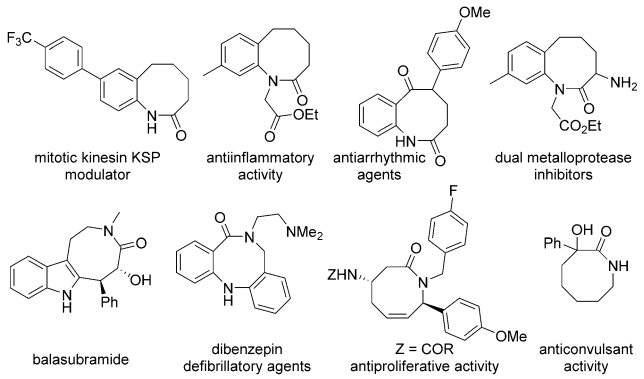
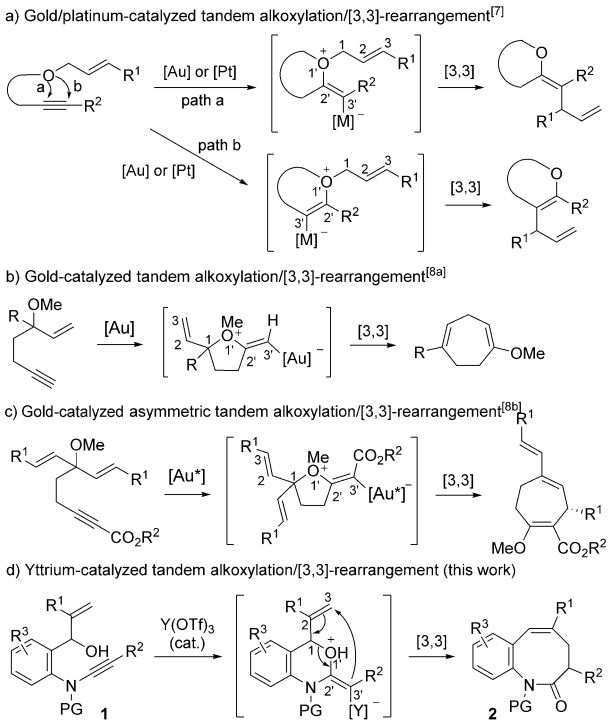


Figure 1. Benzazocinones in bioactive molecules and natural products.

Recently, transition-metal-catalyzed tandem intramolecular alkoxylation/Claisen rearrangement has attracted considerable interest in organic synthesis because of its high bond-forming efficiency and atom economy in the formation of functionalized cyclic compounds.[6–9] For example, gold- or platinum-catalyzed domino reactions involving alkoxylation and subsequent Claisen-type rearrangement for the preparation of five- and six-membered heterocycles has been well established by the groups of Hashmi, Liu, and others (Scheme 1 a).[7] In a related study, Rhee et al. reported an elegant protocol for the synthesis of various cycloheptane skeletons by gold-catalyzed alkoxylation of 3-alkoxy-1,6-enynes/Claisen rearrangement (Scheme 1 b).[8a] In 2015, Toste et al. disclosed its enantioselective version by asymmetric desymmetrization strategy (Scheme 1 c).[8b] Despite these remarkable achievements, these intramolecular cascade reactions have so far been limited to noble-metal catalysts. In addition, the construction of important medium-sized rings by this strategy has not been reported to date. Inspired by our recent study on ynamide chemistry,[10,11] we envisioned that



Scheme 1. Transition-metal-catalyzed tandem intramolecular alkoxylation/[3,3] rearrangement. PG = protecting group.

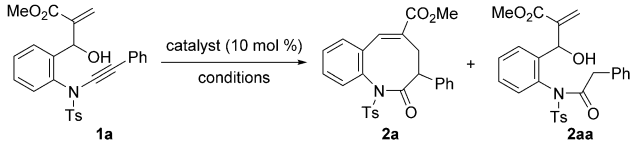
[*] B. Zhou, L. Li, X.-Q. Zhu, J.-Z. Yan, Y.-L. Guo, Prof. Dr. L.-W. Ye
Collaborative Innovation Center of Chemistry for Energy Material, State Key Laboratory of Physical Chemistry of Solid Surfaces, Key Laboratory for Chemical Biology of Fujian Province and College of Chemistry and Chemical Engineering, Xiamen University
Xiamen 361005 (China)
E-mail: 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)

Supporting information for this article can be found under: http://dx.doi.org/10.1002/anie.201700596.

the synthesis of eight-membered benzolactams (**2**) might be achieved by catalytic intramolecular hydroalkoxylation of ynamides (**1**) and subsequent Claisen rearrangement. Herein, we describe the realization of such an yttrium-catalyzed tandem intramolecular hydroalkoxylation/Claisen rearrangement, thus allowing the atom-economical synthesis of various synthetically useful benzazocinones (Scheme 1 d). In addition, this chemistry can be extended to the direct construction of other types of valuable medium-sized lactams. Moreover, the mechanistic rationale for this novel tandem sequence is well supported by a variety of control experiments.

Table 1 shows the realization of the cascade cyclization of the ynamide **1a** in the presence of various transition metals.[13] To our delight, typical gold catalysts such as IPrAuNTf$_2$ and

Table 1: Optimization of reaction conditions.[a]



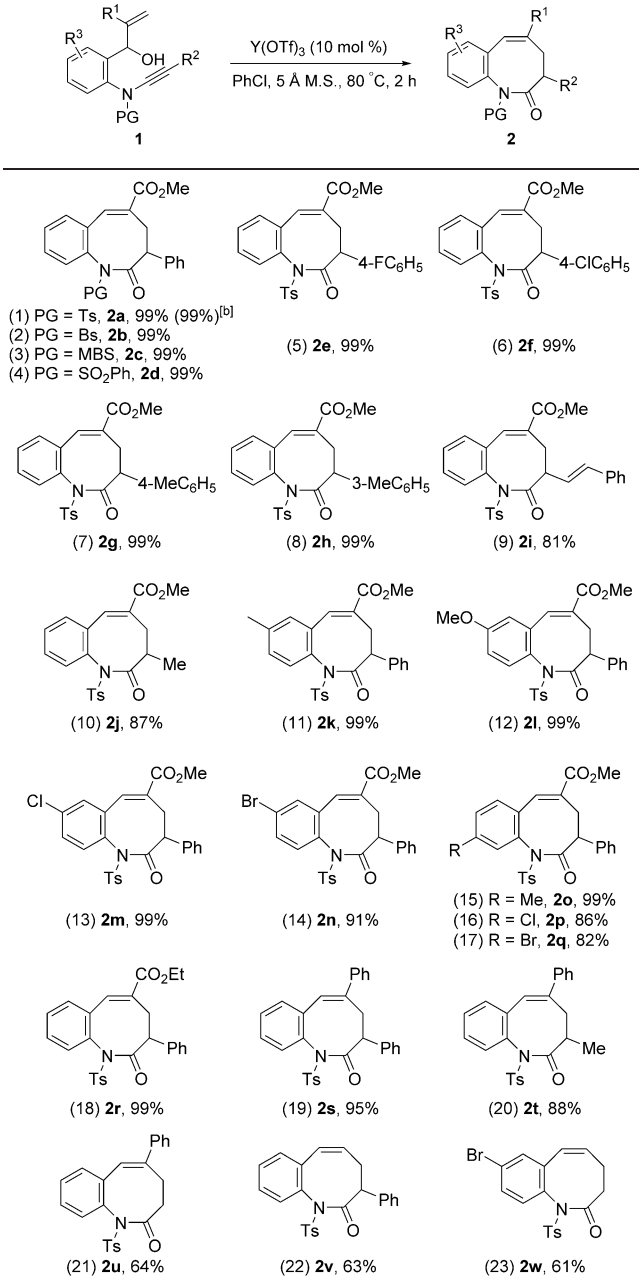
Entry	Catalyst	Reaction conditions	Yield [%][b]	
			2a	**2aa**
1	IPrAuNTf$_2$	PhCl, 80 °C, 2 h	76	< 2
2	Ph$_3$PAuNTf$_2$	PhCl, 80 °C, 2 h	55	< 2
3	AgOTf	PhCl, 80 °C, 2 h	84	10
4	Cu(OTf)$_2$	PhCl, 80 °C, 2 h	87	< 2
5	Zn(OTf)$_2$	PhCl, 80 °C, 2 h	86	4
6	In(OTf)$_3$	PhCl, 80 °C, 2 h	78	5
7	Yb(OTf)$_3$	PhCl, 80 °C, 2 h	88	< 2
8	Y(OTf)$_3$	PhCl, 80 °C, 2 h	91	3
9	TsOH	PhCl, 80 °C, 2 h	36	< 2
10	HOTf	PhCl, 80 °C, 2 h	18	45
11	Y(OTf)$_3$	toluene, 80 °C, 2 h	90	5
12	Y(OTf)$_3$	DCE, 80 °C, 2 h	87	5
13[c]	Y(OTf)$_3$	PhCl, 80 °C, 2 h	99	< 1

[a] Reaction conditions: [**1a**] = 0.05 M. [b] Measured by ^{1}H NMR spectroscopy using diethyl phthalate as internal standard. [c] Using 5 Å molecular sieves (M.S.; 30 mg/0.1 mmol) as an additive. DCE = 1,2-dichloroethane, Tf = trifluoromethanesulfonyl, Ts = 4-toluenesulfonyl.

Ph$_3$PAuNTf$_2$ could indeed catalyze the putative hydroalkoxylation/Claisen rearrangement reaction to produce the desired benzazocinone **2a** in 76 and 55 % yield, respectively (entries 1 and 2). Somewhat surprisingly, it was found that other non-noble metals could also be used to catalyze this tandem reaction (entries 3–8), with Y(OTf)$_3$ giving the best yield of the desired **2a** (entry 8). Notably, Brønsted acids[12] such as TsOH and HOTf were not effective in promoting this reaction (entries 9 and 10), and significant formation of hydration product **2aa** was observed in the latter case (entry 10). Further screening of solvents such as toluene and DCE led to a slightly decreased yield (entries 11 and 12). Gratifyingly, **2a** could be obtained in almost quantitative yield by using 5 Å molecular sieves as an additive (entry 13).

With the optimal reaction conditions in hand (Table 1, entry 13), the scope of the reaction was explored. As shown in Table 2, the reaction proceeded smoothly with different sulfonyl-protected ynamides, thus affording the desired

Table 2: Reaction scope for the formation of the benzazocinones **2**.[a]

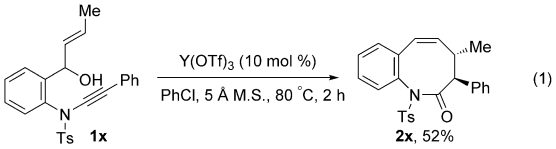


[a] Reactions run in vials; [**1**] = 0.05 M. Yields of isolataed products are reported. [b] The reaction was carried out on a 3.0 mmol scale with 5 mol % Y(OTf)$_3$; [**1a**] = 0.10 M.

benzazocinones **2a–d** in almost quantitative yields (entries 1–4; **2a** was confirmed by X-ray diffraction).[14] In addition, ynamides bearing different R^2 groups also worked very efficiently to produce the corresponding **2e–h** (entries 5–8). When R^2 was either a styryl or alkyl group, the desired product, **2i** or **2j**, respectively, was also formed in corresponding yields of 81 and 87 % yield (entries 9 and 10). Then, various aryl-substituted ynamides were screened and the reaction furnished the desired **2k–q** in 82–99 % yields (entries 11–17). The reaction was also extended to other R^1-substituted ynamides, allowing the assembly of the corre-

sponding **2r**–**w** in 61–99% yields (entries 18–23). Notably, terminal ynamides also worked well to deliver products with serviceable yields (entries 21 and 23). This cascade cyclization is easy to scale-up. A gram-scale reaction of 1.38 grams of **1a** was carried out in the presence of 5 mol% of $Y(OTf)_3$, thus furnishing 1.38 grams of the desired **2a** in 99% yield (entry 1). Thus, this protocol provides a highly efficient and practical route for the construction of benzazocinones.

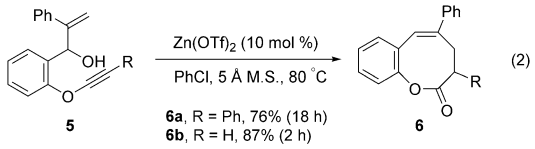
This reaction was also extended to the substrate **1x**, which does not contain a terminal alkene tethered to the ynamide. In this case, the corresponding benzazocinone **2x** was obtained as a single isomer with serviceable yield [Eq. (1)].



(1)

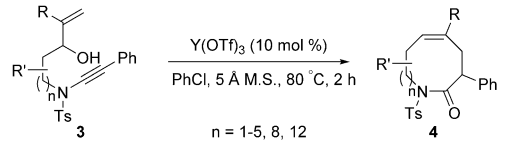
Besides the formation of benzazocinones, this tandem reaction was also viable for the construction of other valuable medium-sized lactams. As depicted in Table 3, the reaction worked efficiently with aliphatic ynamides, thus leading to the formation of the corresponding functionalized azocinones **4a**,**b** in excellent yields (entries 1 and 2). In addition, many 9- to 11-membered medium rings can also be synthesized in 52–97% yields (entries 3–9). Interestingly, this chemistry could also be extended to the preparation of the macrocycles **4j**–**l** in 58–74% yields (entries 10–12). Of note, low concentrations are necessary to circumvent the competing intermolecular reaction in the case of the substrates **3k** and **3l**, and a small amount of the 38-membered ring **4l′** was detected in the latter case (entry 12).[13] The molecular structures of **4c**, **4j**, **4l**, and **4l′** were confirmed by X-ray diffraction.[14]

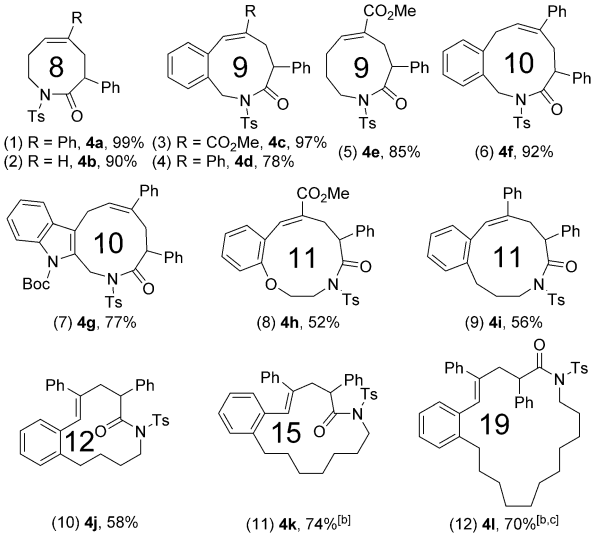
In addition to ynamides, this cascade cyclization also occurred efficiently with alkynyl ethers (**5**) by employing $Zn(OTf)_2$ as a catalyst, thus affording the desired eight-membered benzolactones (benzoxocinones) **6a**,**b** in high yields [Eq. (2)]. Of note, this heterocyclic moiety is found in a range of bioactive natural and non-natural products.[15]



(2)

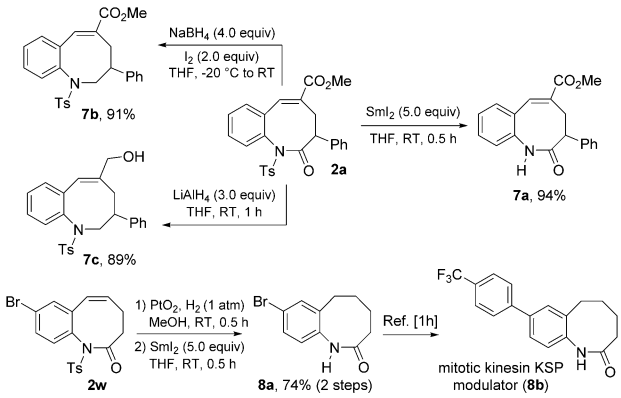
Table 3: Reaction scope for the formation of other medium and large ring lactams **4**.[a]





[a] Reactions run in vials; [**3**] = 0.05 M. Yields of isoalated products are reported. [b] [**3**] = 0.005 M, 12 h. [c] 38-membered ring **4l′** was formed in 8% yield. Boc = *tert*-butoxycarbonyl.

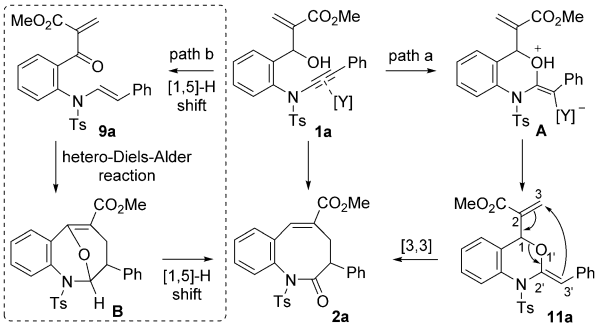
Further synthetic transformation of the as-synthesized lactams was also explored (Scheme 2). For example, the Ts group in the lactam **2a** was easily removed upon treatment with SmI_2 to give the corresponding **7a** in 94% yield. Interestingly, the use of $NaBH_4$ combined with I_2 led to the selective reduction of the amide group to deliver the benzazocine **7b** in 91% yield. In contrast, both the amide and ester groups of **2a** were reduced to afford the benzazocine **7c** in 89% yield upon exposure to $LiAlH_4$. Moreover, the formal synthesis of the bioactive molecule **8b** was achieved in 74% yield (2 steps) starting from the corresponding benzazocinone **2w** by a facile hydrogenation of the double bond and removal of the Ts group.



Scheme 2. Transformation of selected benzazocinones. THF = tetrahydrofuran.

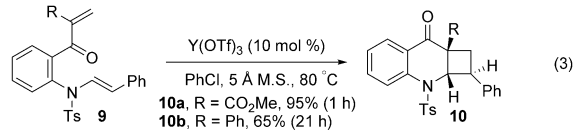
To probe the reaction mechanism, we first performed the reaction in the presence of 5 equivalents of $H_2{}^{18}O$ and found that no ^{18}O was incorporated into the product, thus indicating that the oxygen of the newly formed carbonyl group of product **2a** originates wholly from the hydroxy group of the substrate **1a**.[13] In addition, the product **2aa** could not be

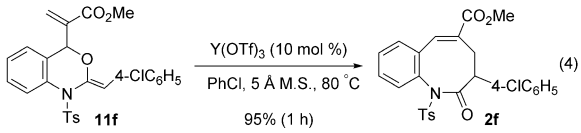
converted into **2a** under the relevant reaction conditions, and rules out **2aa** as an intermediate on the way to **2a**.[13,16] Moreover, we prepared[13] and subjected **9** to the optimal reaction conditions, and found that the reaction afforded the corresponding [2+2] adduct **10** but not **2** [Eq. (3)], thus indicating that the reaction pathway involving double [1,5] hydride shift is less likely (Scheme 3, path b).[17] In



Scheme 3. Plausible mechanism.

particular, it was found that the ketene aminal **11f**[13,18] could be readily converted into the corresponding **2f** when subjected to yttrium catalysis, thus strongly supporting that [3,3] rearrangement was presumably involved in such a tandem process [Eq. (4)].





On the basis of the above experimental observations, a plausible mechanism accounting for the formation of **2a** is illustrated in Scheme 3 (path a). Initially, the hydroxy group attacks the [Y]-activated ynamide **1a** to afford the vinyl-yttrium intermediate **A** via a keteniminium intermediate.[19] Subsequent proton transfer and [3,3] rearrangement, which may also be promoted by yttrium catalyst through coordination with the oxygen atom to facilitate the cleavage of C–O bond, allows the formation of the final **2a**.

In summary, we have developed a novel yttrium-catalyzed hydroalkoxylation/Claisen rearrangement sequence, thus leading to the highly efficient and atom-economical synthesis of various valuable medium, and even, large ring lactams from readily available ynamides. In addition, the construction of eight-membered benzolactones can also be achieved by a similar cascade cyclization of alkynyl ethers. Moreover, control experiments provide further evidence on the feasibility of the proposed mechanism.

Acknowledgements

We are grateful for financial support from the NNSFC (21622204, 21572186 and 21272191), the NSFFJ for Distinguished Young Scholars (2015J06003), the President Research Funds from Xiamen University (20720150045), and NFFTBS (No. J1310024). We also thank Prof. Dr. Xin Lu (Xiamen University) for valuable discussions.

Conflict of interest

The authors declare no conflict of interest.

Keywords: cyclization · heterocycles · homogeneous catalysis · rearrangements · yttrium

[1] For selected examples, see: a) S. Pathak, A. Pramanik, *Eur. J. Org. Chem.* **2013**, 4410; b) J. L. Kenwright, W. R. J. D. Galloway, L. Wortmann, D. R. Spring, *Synth. Commun.* **2013**, *43*, 1508; c) R. T. Yu, R. K. Friedman, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 13250; d) N. Brown, B. Xie, N. Markina, D. VanderVelde, J.-P. H. Perchellet, E. M. Perchellet, K. R. Crow, K. R. Buszek, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4876; e) H. Sun, Z. Nikolovska-Coleska, J. Lu, J. L. Meagher, C.-Y. Yang, S. Qiu, Y. Tomita, Y. Ueda, S. Jiang, K. Krajewski, P. P. Roller, J. A. Stuckey, S. Wang, *J. Am. Chem. Soc.* **2007**, *129*, 15279; f) M. Rössle, J. Christoffers, *Synlett* **2006**, 106; g) N. D. Adams, M. G. Darcy, D. Dhanak, K. J. Duffy, D. M. Fitch, S. D. Knight, K. A. Newlander, A. N. Shaw, PCT Int. Appl. WO 2006/113432A2, **2006**; h) V. Peesapati, S. Ponnuru, *Indian J. Chem. Sect. B* **2003**, *42*, 1975; i) W. J. Brouillette, G. B. Brown, T. M. DeLorey, S. S. Shirali, G. L. Grunewald, *J. Med. Chem.* **1988**, *31*, 2218; j) M. W. Winkley, J. L. Diebold, U.S. Patent 4755505A, **1988**.

[2] a) J. Chang, J. Reiner, J. Xie, *Chem. Rev.* **2005**, *105*, 4581; b) U. Nubbemeyer, *Top. Curr. Chem.* **2001**, *216*, 125; c) L. Yet, *Chem. Rev.* **2000**, *100*, 2963; d) G. A. Molander, *Acc. Chem. Res.* **1998**, *31*, 603; e) G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, *14*, 95; f) T. Iwai, H. Okochi, H. Ito, M. Sawamura, *Angew. Chem. Int. Ed.* **2013**, *52*, 4239; *Angew. Chem.* **2013**, *125*, 4333; g) W. Zhao, Z. Li, J. Sun, *J. Am. Chem. Soc.* **2013**, *135*, 4680; h) W. Zhao, Z. Wang, J. Sun, *Angew. Chem. Int. Ed.* **2012**, *51*, 6209; *Angew. Chem.* **2012**, *124*, 6313.

[3] For examples of palladium-catalyzed intramolecular carbonylation under CO atmosphere, see: a) R. Mancuso, D. S. Raut, N. Marino, G. De Luca, C. Giordano, S. Catalano, I. Barone, S. Andò, B. Gabriele, *Chem. Eur. J.* **2016**, *22*, 3053; b) S.-M. Lu, H. Alper, *J. Am. Chem. Soc.* **2008**, *130*, 6451; c) S.-M. Lu, H. Alper, *J. Am. Chem. Soc.* **2005**, *127*, 14776.

[4] For examples of RCM approaches, see: a) R. Kaul, S. Surprenant, W. D. Lubell, *J. Org. Chem.* **2005**, *70*, 3838; b) C. J. Creighton, G. C. Leo, Y. Du, A. B. Reitz, *Bioorg. Med. Chem.* **2004**, *12*, 4375; c) H. Bieräugel, T. P. Jansen, H. E. Schoemaker, H. Hiemstra, J. H. van Maarseveen, *Org. Lett.* **2002**, *4*, 2673.

[5] For other recent examples, see: a) W. Zhao, H. Qian, Z. Li, J. Sun, *Angew. Chem. Int. Ed.* **2015**, *54*, 10005; *Angew. Chem.* **2015**, *127*, 10143; b) S. Wu, R. Zeng, C. Fu, Y. Yu, X. Zhang, S. Ma,

Chem. Sci. **2015**, *6*, 2275; c) S. S. Scully, S.-L. Zheng, B. K. Wagner, S. L. Schreiber, *Org. Lett.* **2015**, *17*, 418; d) Q. Zhao, C. Li, *Org. Lett.* **2008**, *10*, 4037.

[6] For gold-catalyzed intermolecular hydroalkoxylation/Claisen rearrangement, see: a) J. Li, L. Lin, B. Hu, P. Zhou, T. Huang, X. Liu, X. Feng, *Angew. Chem. Int. Ed.* **2017**, *56*, 885; b) N. Li, T.-Y. Wang, L.-Z. Gong, L. Zhang, *Chem. Eur. J.* **2015**, *21*, 3585; c) A. Gómez-Suárez, D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo, S. P. Nolan, *ACS Catal.* **2014**, *4*, 2701; d) J. M. Ketcham, B. Biannic, A. Aponick, *Chem. Commun.* **2013**, *49*, 4157; e) Y. Wang, L. Liu, L. Zhang, *Chem. Sci.* **2013**, *4*, 739; f) A. Wetzel, F. Gagosz, *Angew. Chem. Int. Ed.* **2011**, *50*, 7354; *Angew. Chem.* **2011**, *123*, 7492; g) B. Lu, Y. Luo, L. Liu, L. Ye, Y. Wang, L. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 8358; *Angew. Chem.* **2011**, *123*, 8508; h) Y. Wang, L. Ye, L. Zhang, *Chem. Commun.* **2011**, *47*, 7815.

[7] For reviews, see: a) H. V. Adcock, P. W. Davies, *Synthesis* **2012**, 3401; b) X. Huang, S. Klimczyk, N. Maulide, *Synthesis* **2012**, 175; for recent selected examples, see: c) M. C. Blanco Jaimes, V. Weingand, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 12504; d) M. Ackermann, J. Bucher, M. Rappold, K. Graf, F. Rominger, A. S. K. Hashmi, *Chem. Asian J.* **2013**, *8*, 1786; e) C.-M. Ting, C.-D. Wang, R. Chaudhuri, R.-S. Liu, *Org. Lett.* **2011**, *13*, 1702; f) F. M. Istrate, F. Gagosz, *Beilstein J. Org. Chem.* **2011**, *7*, 878; g) M. Ueda, A. Sato, Y. Ikeda, T. Miyoshi, T. Naito, O. Miyata, *Org. Lett.* **2010**, *12*, 2594; for the relevant platinum-catalyzed alkoxylation reactions involving the allylic cation, see: h) A. Fürstner, P. W. Davies, *J. Am. Chem. Soc.* **2005**, *127*, 15024; i) A. Fürstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863.

[8] a) H. J. Bae, B. Baskar, S. E. An, J. Y. Cheong, D. T. Thangadurai, I. Hwang, Y. H. Rhee, *Angew. Chem. Int. Ed.* **2008**, *47*, 2263; *Angew. Chem.* **2008**, *120*, 2295; b) H. Wu, W. Zi, G. Li, H. Lu, F. D. Toste, *Angew. Chem. Int. Ed.* **2015**, *54*, 8529; *Angew. Chem.* **2015**, *127*, 8649.

[9] For the relevant platinum- or gold-catalyzed aza-Claisen rearrangement, see: a) V. Gobé, P. Retailleau, X. Guinchard, *Chem. Eur. J.* **2015**, *21*, 17587; b) K. Cariou, B. Ronan, S. Mignani, L. Fensterbank, M. Malacria, *Angew. Chem. Int. Ed.* **2007**, *46*, 1881; *Angew. Chem.* **2007**, *119*, 1913; c) F. M. Istrate, F. Gagosz, *Org. Lett.* **2007**, *9*, 3181; for the relevant Au-catalyzed redox reaction, see: d) B. Lu, Y. Li, Y. Wang, D. H. Aue, Y. Luo, L. Zhang, *J. Am. Chem. Soc.* **2013**, *135*, 8512.

[10] For recent 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.

[11] For selected examples, see: a) W.-B. Shen, X.-Y. Xiao, Q. Sun, B. Zhou, X.-Q. Zhu, J.-Z. Yan, X. Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2017**, *56*, 605; *Angew. Chem.* **2017**, *129*, 620; 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) 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; e) L. Li, C. Shu, B. Zhou, Y.-F. Yu, X.-Y. Xiao, L.-W. Ye, *Chem. Sci.* **2014**, *5*, 4057.

[12] For the relevant Brønsted acid or Lewis acid catalyzed Ficini–Claisen-tpye rearrangement by employing oxazolidinone-derived ynamides as substrates, see: a) N. P. Grimster, D. A. A. Wilton, L. K. M. Chan, C. R. A. Godfrey, C. Green, D. R. Owen, M. J. Gaunt, *Tetrahedron* **2010**, *66*, 6429; b) M. O. Frederick, R. P. Hsung, R. H. Lambeth, J. A. Mulder, M. R. Tracey, *Org. Lett.* **2003**, *5*, 2663; c) J. A. Mulder, R. P. Hsung, M. O. Frederick, M. R. Tracey, C. A. Zificsak, *Org. Lett.* **2002**, *4*, 1383.

[13] For details, see the Supporting Information.

[14] CCDC 1511125 (**2a**), 1519770 (**4c**), 1520377 (**4j**), 1525362 (**4l**) and 1525363 (**4l′**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[15] For selected reviews, see: a) A. Hussain, S. K. Yousuf, D. Mukherjee, *RSC Adv.* **2014**, *4*, 43241; b) I. Shiina, *Chem. Rev.* **2007**, *107*, 239; c) A. Parenty, X. Moreau, J.-M. Campagne, *Chem. Rev.* **2006**, *106*, 911; d) G. Rousseau, *Tetrahedron* **1995**, *51*, 2777.

[16] For a zinc-catalyzed hydrative aldol reaction, see: A. M. Jadhav, V. V. Pagar, D. B. Huple, R.-S. Liu, *Angew. Chem. Int. Ed.* **2015**, *54*, 3812; *Angew. Chem.* **2015**, *127*, 3883.

[17] For recent reviews on hydride transfer, see: a) M. C. Haibach, D. Seidel, *Angew. Chem. Int. Ed.* **2014**, *53*, 5010; *Angew. Chem.* **2014**, *126*, 5110; b) L. Wang, J. Xiao, *Adv. Synth. Catal.* **2014**, *356*, 1137; c) B. Peng, N. Maulide, *Chem. Eur. J.* **2013**, *19*, 13274.

[18] For the relevant Claisen rearrangement of the vinyl-substituted ketene aminals, see: a) P. A. Evans, A. B. Holmes, R. P. McGeary, A. Nadin, K. Russell, P. J. O'Hanlon, N. D. Pearson, *J. Chem. Soc. Perkin Trans. 1* **1996**, 123; b) P. A. Evans, A. B. Holmes, K. Russell, *Tetrahedron Lett.* **1992**, *33*, 6857.

[19] For Tf_2O-mediated [3,3] sigmatropic rearrangement involving keteniminium intermediates, see: a) B. Peng, D. Geerdink, N. Maulide, *J. Am. Chem. Soc.* **2013**, *135*, 14968; b) C. Madelaine, V. Valerio, N. Maulide, *Angew. Chem. Int. Ed.* **2010**, *49*, 1583; *Angew. Chem.* **2010**, *122*, 1628.

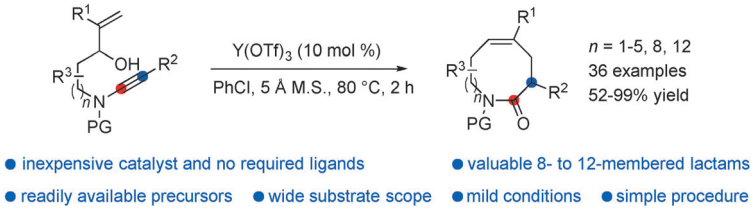
Manuscript received: January 17, 2017
Final Article published: ■■ ■■, ■■■■

Communications

Heterocycles

B. Zhou, L. Li, X.-Q. Zhu, J.-Z. Yan, Y.-L. Guo, L.-W. Ye* ——— ■■■■–■■■■

Yttrium-Catalyzed Intramolecular Hydroalkoxylation/Claisen Rearrangement Sequence: Efficient Synthesis of Medium-Sized Lactams



Ring maker: An efficient yttrium-catalyzed tandem intramolecular hydroxyalkylation/Claisen rearrangement has been achieved, enabling facile access to a diverse array of valuable medium-sized lactams. A mechanistic rationale for this novel reaction sequence is well supported by a variety of control experiments.