ChemPubSoc Europe

DOI: 10.1002/chem.201405965

CHEMISTRY
A European Journal
Communication

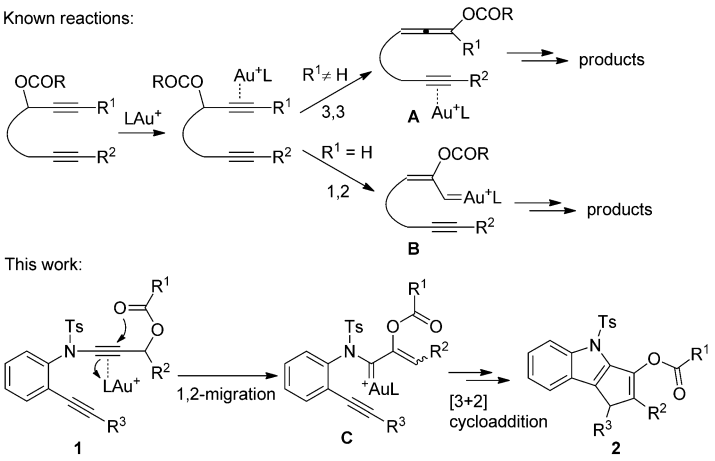
Synthetic Methods

Gold(I)-Catalyzed 1,2-Acyloxy Migration/[3+2] Cycloaddition of 1,6-Diynes with an Ynamide Propargyl Ester Moiety: Highly Efficient Synthesis of Functionalized Cyclopenta[*b*]indoles

Jun Liu,[a] Ming Chen,[a] Liangwei Zhang,[a, b] and Yuanhong Liu*[a]

Abstract: A gold-catalyzed cycloisomerization of 1,6-diynes containing an ynamide propargyl ester or carbonate moiety has been developed that provides an attractive route to a diverse-substituted 3-acyloxy-1,4-dihydrocyclopenta[*b*]indoles. Mechanistic studies indicate that the reaction likely proceeds through a competitive 1,2-OAc migration followed by [3+2] cycloaddition of the vinyl gold–carbenoid intermediate with the pendant triple bond. The synthetic utility of the obtained cyclopenta[*b*]indole products was demonstrated by their efficient transformations by deprotection or double-bond isomerization reactions.

In recent years, gold-catalyzed cycloisomerizations of 1,*n*-diynes have emerged as an important methodology in the construction of diversely functionalized polycyclic molecules.[1,2] A particularly attractive strategy is based on the cycloisomerizations of 1,*n*-diynes bearing a propargyl ester or carbonate moiety.[3] Generally, these reactions are initiated through the selective activation of the propargyl moiety by gold catalyst[4] to trigger an efficient generation of a gold-coordinated carboxyallene **A** through 3,3-rearrangement[3a–j] or vinyl gold–carbenoid **B** through 1,2-acyloxy migration,[3k–l] depending on the electronic or steric nature on either end of the propargyl moiety (Scheme 1). Both **A** and **B** show unique reactivities for further functionalizations by reactions with the pendant alkyne. Usually internal propargyl carboxylates undergo 3,3-rearrangement, whereas terminal propargyl carboxylates prefer 1,2-acyloxy migration. However, the reaction pathway may be altered by effects such as the structural factors of the substrates, catalysts, ligands, reaction conditions, or additives, etc. For example, it was reported that 1,7-diyne containing a propargyl benzoate and a terminal alkyne moiety underwent a concerted double cyclization initiated by nucleophilic attack of the aryl ring at the propargylic position.[3c] Recently, ynamides[5] have attracted considerable interest in π-acid transition-metal-catalyzed reactions[6] due to the enhanced electrophilicity arising from the polarized triple bond compared with the normal alkynes. During our ongoing project on gold-catalyzed cycloisomerizations of 1,*n*-diynes bearing a propargyl carbonate moiety,[3a,d] we envisioned that the presence of a heteroatom-tethered propargyl carboxylate such as an ynamide functionality in 1,*n*-diynes[7] may have an important impact on the reaction patterns, and may also allow efficient access to valuable nitrogen heterocycles. However, to the best of our knowledge, the effect of such heteroatom substituents has not been investigated.[8] Herein, we report the first example of gold-catalyzed cycloisomerization of 1,6-diyne **1** with an ynamide propargyl ester moiety, which provides a straightforward route to oxygenated 1,4-dihydrocyclopenta[*b*]indole **2**, a commonly occurring structural motif in pharmaceuticals and natural products,[9] with high efficiency (Scheme 1). Notably, the reaction likely proceeds by a competitive 1,2-acyloxy migration of an internal propargyl moiety to afford vinyl gold–carbenoid **C**, which serves as a three-atom building block for formal [3+2] cycloaddition with the pendant alkyne according to mechanistic studies.[10] Prior to this study, there are only few reports dealing



Scheme 1. Gold-catalyzed cycloisomerizations of diynes bearing a propargyl ester.

[a] *Dr. J. Liu, M. Chen, L. Zhang, Prof. Y. Liu*
State Key Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry
Chinese Academy of Sciences,
345 Lingling Lu, Shanghai 200032 (P. R. China)
E-mail: yhliu@mail.sioc.ac.cn

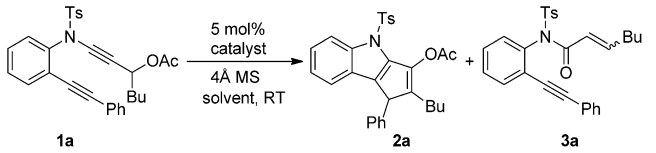
[b] *L. Zhang*
Center of Drug Discovery, College of Pharmacy
China Pharmaceutical University, 24 Tongjia Xiang Road
Nanjing 210009 (P. R. China)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201405965.

with the reactivity of the in-situ formed gold–carbenoid intermediates from 1,*n*-diynes, including cyclopropenation/Nazarov cyclization,[3l] gold–carbene transfer,[2a] and [2+2+1] cycloaddition with aldehydes.[3k]

Based on the superior catalytic activity of [Au(Johnphos)(MeCN)]SbF_6 (catalyst **A**) in various gold-catalyzed reactions, we first investigated the cycloisomerization of benzene-bridged 1,6-diynyl acetate **1a** in the presence of catalyst **A**. The results are shown in Table 1. We were pleased to see that treatment of **1a** with 5 mol% of catalyst **A** and 4 Å molecular sieves in dichloromethane at room temperature for 3 h enabled complete consumption of **1a** to afford 3-acyloxy-1,4-dihydrocyclopenta[*b*]indole **2a** in 68% yield (Table 1, entry 1). It was noticed that some amounts of colored byproducts were also formed during the process according to TLC analysis. We reasoned that the concentration of the substrates may have an effect on the reaction course. To our delight, decreasing the substrate concentration from 0.1 to 0.03 M improved the yield of **2a** to 75% (entry 2). Further decreasing the substrate concentration to 0.015 or 0.01 M resulted in the significant improvement of the product yield, as the same 83% yields of **2a** were obtained (entries 4–5). Performing the reaction in the absence of molecular sieves led to **2a** in 56% yield, along with 25% of undesired α,β-unsaturated imide **3a** formed by 3,3-rearrangement of the propargyl acetate moiety followed by hydrolysis with a trace amount of water (entry 6). The reaction could also proceed in 1,2-dichloroethane, with a slight lower yield of **2a** (76%, entry 7). However, switching the solvent to toluene did not give satisfactory results (entry 8). The frequently used gold(I) complexes such as [Au(IPr)]SbF_6, [Au(PPh_3)]SbF_6, or [Au(PPh_3)]NTf_2 were not effective for this transformation, and the diyne **1a** remained in 24–73% (entries 9–11). The results indicated that the nature of the ligand on gold catalyst played an important role in this cascade reaction. Interestingly, when a gold(III) complex, such as [$AuCl_2$(Pic)], was used as the catalyst, α-acyl-α,β-unsaturated **4a** was obtained exclusively in 88% yield with a *E* geometry of the double bond[11] (entry 12). The formation of **4a** can be rationalized by a gold-catalyzed tandem 3,3-rearrangement/oxocarbenium ion formation/acyl-migration process similar to that previously reported for gold(III)-catalyzed acyl migration of propargylic esters by Zhang et al.[12] Control experiments with $AgSbF_6$ alone could not afford the desired **2a** (entry 13). The structure of 1,4-dihydrocyclopenta[*b*]indole product **2** was confirmed by X-ray crystallographic analyses of **2a**, **2i**, and **2m**[13] (vide infra). Apparently, a formal 1,2-OAc migration took place during the reaction according to the structure of product **2**.

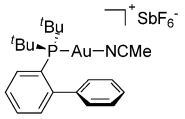
Table 1. Optimization studies for the formation of 1,4-dihydrocyclopenta[*b*]indole **2a**.



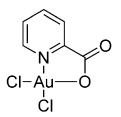
1a **2a** **3a**

Entry	Cat. (5 mol%)	[Substrate] [M]	Solvent	*t* [h]	Yield [%][a]		
					1a	**2a**	**3a**[b]
1	**A**	0.1	CH_2Cl_2	3	–	68	–
2	**A**	0.03	CH_2Cl_2	3	–	75	–
3	**A**	0.02	CH_2Cl_2	3	–	80	–
4	**A**	0.015	CH_2Cl_2	3	–	83	–
5	**A**	0.01	CH_2Cl_2	3	–	83	–
6[c]	**A**	0.015	CH_2Cl_2	3	–	56	25 (only *E*)
7	**A**	0.015	$ClCH_2CH_2Cl$	1	–	76	–
8[d]	**A**	0.015	toluene	3	9	–	58 (52:6)
9[d,e]	[AuCl(IPr)]/$AgSbF_6$	0.015	CH_2Cl_2	4	24	–	35 (only *E*)
10[d,f]	[AuCl(PPh_3)]/$AgSbF_6$	0.015	CH_2Cl_2	4	38	–	22 (19:3)
11	[Au(PPh_3)]NTf_2	0.015	CH_2Cl_2	5	73	–	–
12[g]	[$AuCl_2$(Pic)]	0.015	CH_2Cl_2	1	–	–	–
13[d]	$AgSbF_6$	0.015	CH_2Cl_2	4	76	–	7 (3:4)

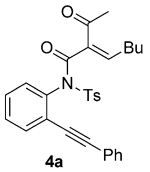
[a] Isolated yields. All the reactions were carried out on 0.3 mmol scale in the presence of 75 mg 4Å MS. [b] The ratio of *E*/*Z* isomers is shown in parentheses. [c] Without MS. [d] ^1H NMR spectroscopic yields using CH_2Br_2 as the internal standard. [e] 25% **4a** was also formed. [f] 4% **4a** was also formed. [g] **4a** was isolated in 88% yield. IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; Pic = 2-picolinate.



catalyst **A**



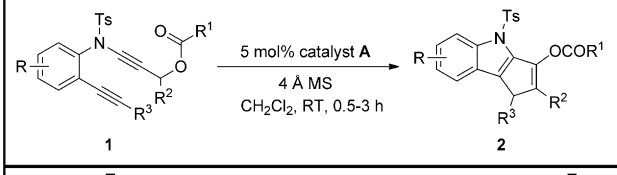
[$AuCl_2$(Pic)]



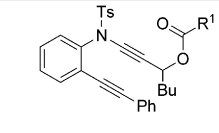
4a

We chose the reaction conditions shown in Table 1, entry 4 to examine the scope of this novel cascade reaction. The results are shown in Table 2. The effect of the protection groups was examined first. Ac and Piv, as well as Bz groups, could be well-accommodated in this reaction, leading to **2a–c** in 50–83% yields. The presence of a sterically demanding Piv group in **1b** gave **2b** in moderate yield of 50%, which indicated that the reaction is sensitive to the bulkiness of the migrating group. Propargyl carbonate **1d** also underwent the reaction smoothly to furnish **2d** in 79% yield. Next, we examined the effect of R^3 group on the alkyne terminus. The reaction applied to a wide variety of aryl-substituted alkynes, and the functionalities of Cl-, F-, Me-, MeO-, and 3,4,5-$(MeO)_3$ groups on aromatic rings were tolerated well during the reaction, affording the corresponding products **2e–i** and **2k** in good to high yields. Especially, sterically encumbered *o*-MeO-substituted substrate **1i** was smoothly converted into the corresponding **2i** in a good yield of 76%. A thienyl group could also be incorporated successfully into the sequence, providing **2j** in 86% yield. Substrate **1l** bearing a cyclohexenyl

Table 2. Gold-catalyzed cyclizations of 1,6-diynyl esters to cyclopenta[*b*]indoles.[a]



1 2

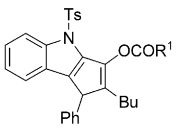


1a, R^1 = Me

1b, R^1 = *t*Bu

1c, R^1 = Ph

1d, R^1 = OMe

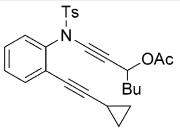


2a, 83%

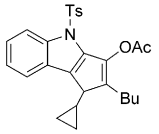
2b, 50%

2c, 80%

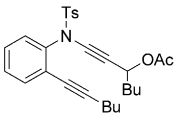
2d, 79%



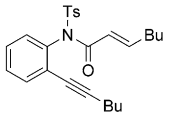
1m



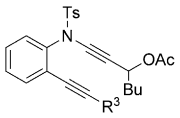
2m, 84%



1n



3n, 95%



1e, R^3 = *p*-ClC_6H_4

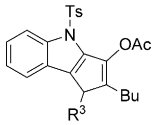
1f, R^3 = *p*-FC_6H_4

1g, R^3 = *p*-MeC_6H_4

1h, R^3 = *p*-$MeOC_6H_4$

1i, R^3 = *o*-$MeOC_6H_4$

1j, R^3 = 2-thienyl



2e, 66%

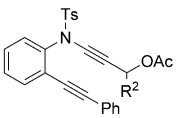
2f, 82%

2g, 92%

2h, 89%

2i, 76%

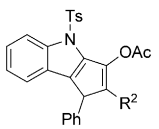
2j, 86%



1o, R^2 = Me

1p, R^2 = Et

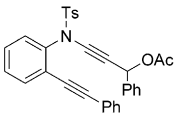
1q, R^2 = *i*Pr



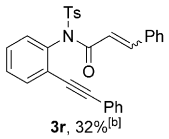
2o, 80%

2p, 81%

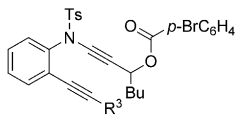
2q, 73%



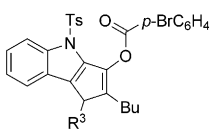
1r



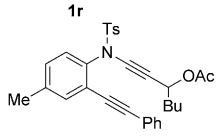
3r, 32%[b]



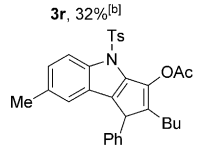
1k, R^3 = 3,4,5-$(MeO)_3C_6H_2$



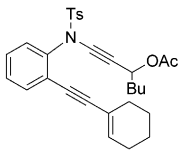
2k, 90%



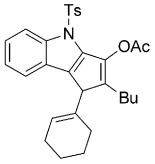
1s



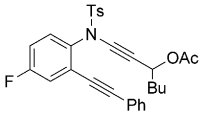
2s, 72%



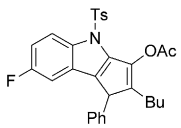
1l



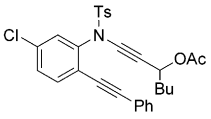
2l, 90%



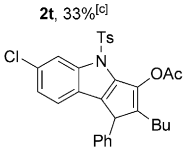
1t



2t, 33%[c]



1u



2u, 29%[d]

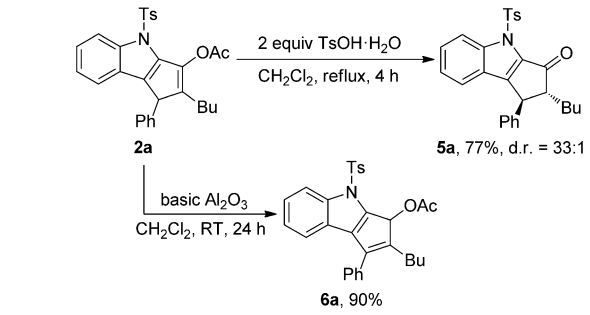
[a] Isolated yields. [b] *Z*/*E* = 1.1:1. [c] 50% of **3t** (*E*/*Z* = 1.3:1) was also isolated. [d] 43% of **3u** (*E*/*Z* = 1.4:1) was also isolated.

group converted into **2l** with a high isolated yield (90%). A cyclopropyl-substituted alkyne **1m** was efficiently transformed to **2m** in 84% yield. However, the use of a butyl-substituted alkyne **1n** did not deliver the desired cyclopenta[*b*]indole product; instead, alkene **3n** was formed in 95% yield with excellent *E* stereoselectivity. This result is likely due to the fast hydrolysis of the allenic intermediate formed by a competing 3,3-rearrangement. The substituent effect on propargylic position (R^2) was also investigated. Alkyl groups, such as Me, Et or more bulky *i*Pr groups as R^2 were all compatible, leading to **2o**–**q** in 73–81% yields. However, when R^2 is a phenyl group, only alkene product **3r** was obtained as a mixture of *Z*/*E* isomers. The electronic nature of the substituent on the parent phenyl ring also has a strong influence on the reaction course, for example, while electron-donating methyl-substituted **1s** worked efficiently to afford **2s** in a good yield of 72%, the electron-withdrawing F- or Cl-substituted **1t** or **1u** afforded the desired **2t** and **2u** only in low yields of 33 and 29%, respectively. The results may be due to the decreased nucleophilicity of the alkyne moiety, which cannot trap the gold–carbenoid intermediate in an efficient way.

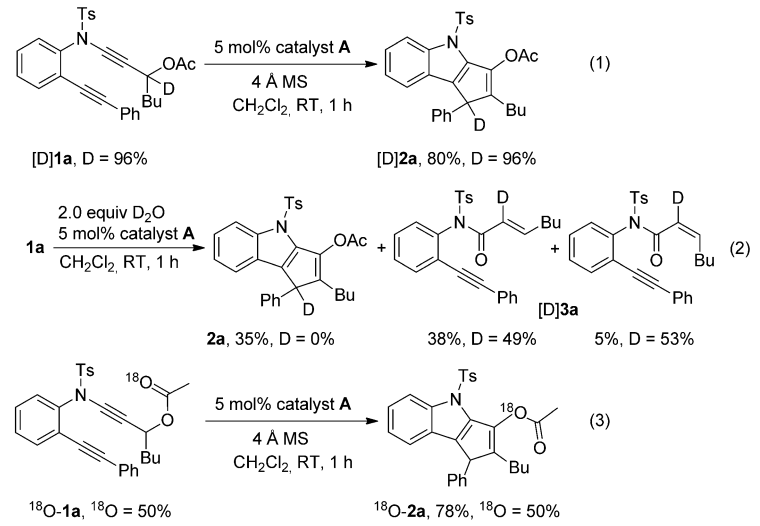
The utility of the cyclopenta[*b*]indole products **2** was demonstrated by transformation reactions of **2a** (Scheme 2). Deprotection of **2a** under acidic conditions afforded cyclopentenone **5a** with high stereoselectivity. To our surprise, stirring a CH_2Cl_2 solution of **2a** in the presence of basic Al_2O_3 afforded double-bond-isomerized product **6a** in 90% yield. The structure of **6a** was unambiguously confirmed by X-ray crystallography of its analogue **6k**.[13,14]

We also prepared the deuterium-labeled diynyl ester to probe the reaction mechanism. Full incorporation of deuterium at the alkyl carbon atom of the cyclopentadiene ring was observed upon cyclization of [D]**1a**. In addition, cyclization of **1a** in the presence of 2.0 equivalents of D_2O afforded **2a** in 35% yield without deuterium incorporation, along with 43% of [D]**3a** with moderate deuterium incorporation. These results implied that H-migration process might occur in a concerted way. To have a better understanding of the –OAc migration process and the subsequent transformations into heterocycles, we examined the cycloisomerization of carbonyl-labeled ^{18}O-**1a** under gold-catalyzed conditions. It was found that ^{18}O-**2a** was produced in 78% yield with the ^{18}O label located at the acyloxy position[14,15] (Scheme 3).

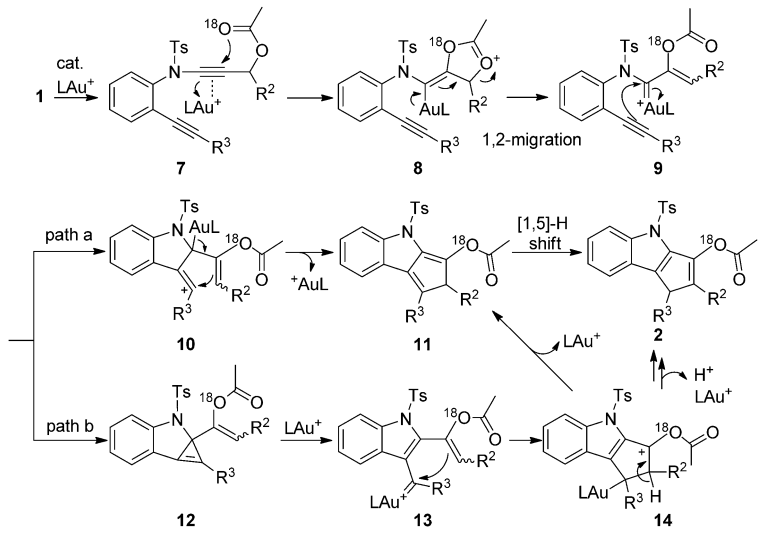
Based on the above observations, we propose the following mechanism for this transformation (Scheme 4). First, selective



Scheme 2. Transformation of OAc-substituted cyclopenta[*b*]indole **2a**.



Scheme 3. Isotopic-labeling experiments.



Scheme 4. Proposed reaction mechanism.

activation of the propargyl acetate moiety by gold results in the competitive formation of α-vinyl gold–carbenoid **9** by 1,2-acyloxy migration. Compound **9** might be stabilized by the adjacent nitrogen atom. Although 3,3-rearrangement through a 6-*endo*-dig cyclization could be favored in this step since the alkynyl carbon atom adjacent to nitrogen atom is more electrophilic due to the electronic polarization of the triple bond, this reaction pathway might be suppressed by fast transformation through a 1,2-migration-initiated cascade sequence. 3,3-Rearrangement might also be reversible with 1,2-acyloxy migration.[16] After that, two reaction pathways may be possible for the formation of cyclopenta[*b*]indole product **2**. In path a, attack of the remaining alkyne moiety to the gold carbenoid affords vinyl cationic species **10**. Subsequent nucleophilic attack of the alkene moiety to the vinyl cation followed by elimination of the gold catalyst leads to intermediate **11**, which undergoes 1,5-H shift to deliver the final product **2**. Trapping of the gold carbenoid by an alkyne followed by attack of the aryl ring to the vinyl cation has been recently reported by Davies et al.[17] Alternatively, transfer of the gold carbenoid moiety across the triple bond, possibly by ring opening of the cyclopropene intermediate[3l,10] **12**, affords the gold–carbenoid **13**. Cyclization of **13** results in the formation of cation **14**. Compound **14** might undergo direct deauration to give **11**, which isomerizes to **2**. It may also undergo deprotonation and protodeauration to provide the product **2**. However, this process is not supported by a deuterium-label experiment result, since no deuterium incorporation was found when the reaction was carried out in the presence of D_2O.

In summary, we have disclosed a new reaction pattern for gold-catalyzed cycloisomerizations of 1,6-diynes containing an ynamide propargyl ester moiety that provides an attractive route to a diverse-substituted 3-acyloxy-1,4-dihydrocyclopenta[*b*]indoles. Mechanistic studies indicate that the reaction likely proceeds through a competitive 1,2-OAc migration followed by [3+2] cycloaddition of the vinyl gold–carbenoid intermediate with the pendant triple bond. It is also noted that the reactions initiated through a 1,2-acyloxy migration of internal alkynes are quite rare in gold catalysis.[16a,18] Our results also indicated that the 1,2- versus 1,3-acyloxy migration can be affected by the nature of the catalysts and the alkyne substituents. Further exploration and applications of this chemistry are underway in our group.

Acknowledgements

We thank the National Natural Science Foundation of China (Grant Nos. 21125210, 21372244, 21121062), Chinese Academy of Science, and the Major State Basic Research Development Program (Grant No. 2011CB808700) for financial support.

Keywords: cycloaddition · gold · homogeneous catalysis · propargyl ester · ynamides

[1] For recent reviews on gold catalysis, see: a) *Modern Gold Catalyzed Synthesis* (Eds.: A. S. K. Hashmi, F. D. Toste), Wiley-VCH, Weinheim, **2012**; b) *Gold Catalysis: An Homogeneous Approach*, (Eds.: F. D. Toste, V. Michelet), Imperial College Press, London, **2014**.

[2] For gold-catalyzed cycloisomerization of 1,*n*-diynes, see: a) P. Nösel, L. N. Dos Santos Comprido, T. Lauterbach, M. Rudolph, F. Rominger, A. S. K. Hashmi, *J. Am. Chem. Soc.* **2013**, *135*, 15662; b) T. Lauterbach, S. Arndt, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.* **2013**, *355*, 1755; c) Y. Wang, A. Yepremyan, S. Ghorai, R. Todd, D. H. Aue, L. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7795; *Angew. Chem.* **2013**, *125*, 7949; d) L. Ye, Y. Wang, D. H. Aue, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 31; e) Q. Wang, S. Aparaj, N. G. Akhmedov, J. L. Petersen, X. Shi, *Org. Lett.* **2012**, *14*, 1334; f) Y. Odabachian, X. F. Le Goff, F. Gagosz, *Chem. Eur. J.* **2009**, *15*, 8966; g) J. J. Lian, R. S. Liu, *Chem. Commun.* **2007**, 1337; h) J. J. Lian, P. C. Chen, Y. P. Lin, H. C. Ting, R. S. Liu, *J. Am. Chem. Soc.* **2006**, *128*, 11372.

[3] For gold-catalyzed cycloisomerizations of 1,*n*-diynyl esters or carbonates, see: a) M. Chen, J. Liu, L. Wang, X. Zhou, Y. Liu, *Chem. Commun.* **2013**, *49*, 8650; b) C. H. Oh, J. H. Kim, B. K. Oh, J. R. Park, J. H. Lee, *Chem. Eur. J.* **2013**, *19*, 2592; c) W. Rao, M. J. Koh, P. Kothandaraman, P. W. H. Chan, *J. Am. Chem. Soc.* **2012**, *134*, 10811; d) Y. Chen, M. Chen, Y. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 6493; *Angew. Chem.* **2012**, *124*, 6599; e) D. Lebœuf, A. Simonneau, C. Aubert, M. Malacria, V. Gandon, L. Fensterbank, *Angew. Chem. Int. Ed.* **2011**, *50*, 6868; *Angew. Chem.* **2011**, *123*, 7000; f) D. H. Zhang, L. F. Yao, Y. Wei, M. Shi, *Angew. Chem. Int. Ed.* **2011**, *50*, 2583; *Angew. Chem.* **2011**, *123*, 2631; g) T. Luo, S. L. Schreiber, *J. Am. Chem. Soc.* **2009**, *131*, 5667; h) C. H. Oh, A. Kim, *New J. Chem.* **2007**, *31*, 1719; i) J. Zhao, C. O. Hughes, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 7436; j) C. H. Oh, A. Kim, W. Park, D. I. Park, N. Kim, *Synlett* **2006**, 2781; k) W. Rao, P. W. H. Chan, *Chem. Eur. J.* **2014**, *20*, 713; l) W. Rao, M. J. Koh, D. Li, H. Hirao, P. W. H. Chan, *J. Am. Chem. Soc.* **2013**, *135*, 7926.

[4] For reviews on gold-catalyzed reactions of propargyl carboxylates, see: a) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350; b) N. Marion, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 2750; *Angew. Chem.* **2007**, *119*, 2806; c) S. Wang, G. Zhang, L. Zhang, *Synlett* **2010**, 692.

[5] For reviews, see: a) 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; b) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840; *Angew. Chem.* **2010**, *122*, 2902; c) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064.

[6] For selected papers on gold-catalyzed reactions of ynamides, see: a) S. N. Karad, R. S. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 9072; *Angew. Chem.* **2014**, *126*, 9218; b) Z. Xin, S. Kramer, J. Overgaard, T. Skrydstrup, *Chem. Eur. J.* **2014**, *20*, 7926; c) H. V. Adcock, T. Langer, P. W. Davies, *Chem. Eur. J.* **2014**, *20*, 7262; d) Y. Tokimizu, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2014**, *16*, 3138; e) S. Couty, C. Meyer, J. Cossy, *Angew. Chem. Int. Ed.* **2006**, *45*, 6726; *Angew. Chem.* **2006**, *118*, 6878; f) M. C. Blanco Jaimes, V. Weingand, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 12504; g) R. B. Dateer, B. S. Shaibu, R. S. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 113; *Angew. Chem.* **2012**, *124*, 117; h) S. Kramer, Y. Odabachian, J. Overgaard, M. Rottländer, F. Gagosz, T. Skrydstrup, *Angew. Chem. Int. Ed.* **2011**, *50*, 5090; *Angew. Chem.* **2011**, *123*, 5196; i) D. Vasu, H. H. Hung, S. Bhunia, S. A. Gawade, A. Das, R. S. Liu, *Angew. Chem. Int. Ed.* **2011**, *50*, 6911; *Angew. Chem.* **2011**, *123*, 7043; j) A. S. K. Hashmi, S. Pankajakshan, M. Rudolph, E. Enns, T. Bander, F. Rominger, W. Frey, *Adv. Synth. Catal.* **2009**, *351*, 2855; k) S. Couty, C. Meyer, J. Cossy, *Tetrahedron* **2009**, *65*, 1809; l) A. S. K. Hashmi, M. Rudolph, J. W. Bats, W. Frey, F. Rominger, T. Oeser, *Chem. Eur. J.* **2008**, *14*, 6672.

[7] For gold-catalyzed reactions of 1,*n*-diynes bearing an ynamide moiety, see: N. Ghosh, S. Nayak, A. K. Sahoo, *Chem. Eur. J.* **2013**, *19*, 9428.

[8] For intermolecular reactions of ynamide propargyl esters with indoles, see: S. J. Heffernan, J. M. Beddoes, M. F. Mahon, A. J. Hennessy, D. R. Carbery, *Chem. Commun.* **2013**, *49*, 2314.

[9] a) Y.-C. Kong, K. F. Cheng, R. C. Cambie, P. G. Waterman, *J. Chem. Soc. Chem. Commun.* **1985**, 47; b) K. Stratmann, R. E. Moore, R. Bonjouklian, J. B. Deeter, G. M. L. Patterson, S. Shaffer, C. D. Smith, T. A. Smitka, *J. Am. Chem. Soc.* **1994**, *116*, 9935; c) J. M. Lopchuk, I. L. Green, J. C. Badenock, G. W. Gribble, *Org. Lett.* **2013**, *15*, 4485.

[10] For gold-catalyzed intermolecular cycloadditions of ynamides with propargylic carboxylates, see: E. Rettenmeier, A. M. Schuster, M. Rudolph, F. Rominger, C. A. Gade, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 5880; *Angew. Chem.* **2013**, *125*, 5993.

[11] For determination of the double-bond configuration, see the Supporting Information.

[12] S. Wang, L. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 8414.

[13] CCDC 1018150 (**2a**), 1018151 (**2i**), 1018152 (**2m**), 1018084 (*E*-**3u**) and 1018153 (**6k**) contain 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.

[14] See the Supporting Information.

[15] For a pioneering study on structural dependence of ^{18}O isotope shifts in ^{13}C NMR spectra, see: a) J. C. Vederas, *J. Am. Chem. Soc.* **1980**, *102*, 374; b) J. M. Risley, R. L. Van Etten, *J. Am. Chem. Soc.* **1979**, *101*, 252.

[16] For a discussion on the reversibility of the 3,3-rearrangement and 1,2-acyloxy migration, see: a) G. Li, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 3740; b) E. J. Cho, *Chem. Eur. J.* **2012**, *18*, 4495; c) W. Rao, X. Sally, S. N. Berry, P. W. H. Chan, *Chem. Eur. J.* **2014**, *20*, 13174.

[17] J. F. Briones, H. M. L. Davies, *J. Am. Chem. Soc.* **2012**, *134*, 11916.

[18] a) V. Mamane, T. Gress, H. Krause, A. Füstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654; b) X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 5802; c) C. H. M. Amijs, V. López-Carrillo, A. M. Echavarren, *Org. Lett.* **2007**, *9*, 4021; d) H. Zheng, X. Huo, C. Zhao, P. Jing, J. Yang, B. Fang, X. She, *Org. Lett.* **2011**, *13*, 6448.

Received: November 5, 2014
Published online on December 2, 2014