

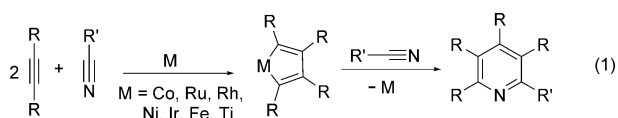
Synthetic Methods

Regiocontrolled Gold-Catalyzed [2+2+2] Cycloadditions of Ynamides with Two Discrete Nitriles to Construct 4-Aminopyrimidine Cores**

Somnath Narayan Karad and Rai-Shung Liu*

Abstract: Reported herein is the novel gold-catalyzed intermolecular [2+2+2] cycloaddition of ynamides with two discrete nitriles to form monomeric 4-aminopyrimidines, which are pharmaceutically important structural motifs. The utility of this new cycloaddition is demonstrated by the excellent regioselectivity obtained using a variety of ynamides and nitriles.

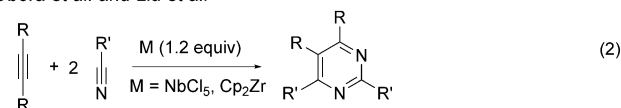
Metal-catalyzed [2+2+2] cycloadditions are powerful tools for constructing six-membered carbo- or heterocyclic frameworks with atom economy.^[1] Alkynes and nitriles are two common triple-bond motifs, and catalytic [2+2+2] cycloadditions between alkynes and nitriles have been extensively studied with many catalysts, including Co,^[2] Ru,^[3] Rh,^[4] Fe,^[5] Ni,^[6] Ir,^[7] and Ti.^[8] Such reactions were reported to afford pyridines nearly exclusively, thus involving two discrete alkynes and one nitrile as a result of the initial formation of metallocyclopentadienes [Eq. (1)]. In contrast, the construction of a monomeric pyrimidine core from one alkyne and two discrete nitriles still remains unprecedented even though such an azacycle is a pharmaceutically important structural motif.^[9]



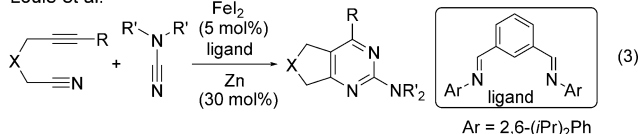
Obora et al.^[10a] and Liu et al.^[10b] reported the synthesis of pyrimidines from alkynes and aryl nitriles, but NbCl₅ (1.2 equiv) or [Cp₂Zr] (1.3 equiv) were used in large proportions to attain satisfactory yields [Eq. (2); Cp = cyclopentadiene]. Although Louie et al.^[10c] reported the synthesis of pyrimidines using FeI₂/Zn catalysts, the applicable substrates were limited to 5-cyano-1-ynes and cyanamides in a bimolecular process, and the reactions suffered from low product yields (< 50 %) in most instances [Eq. (3)].

This work reports the catalytic synthesis of monomeric 4-aminopyrimidines through gold-catalyzed regioselective

Obora et al. and Liu et al.



Louie et al.



[2+2+2] cycloadditions between various ynamides and nitriles [Eq. (4); EWG = electron-withdrawing group]. Ynamides are substrates widely used in numerous organic reactions because of their versatile reactivity.^[11] Such alkynes are potent nucleophiles but become reactive electrophiles upon coordination with gold catalysts.^[12] We searched for gold catalysts to implement a nucleophilic attack of nitriles onto gold π -alkyne species to initiate the reaction. Monomeric 4-aminopyrimidine cores are commonly found in many bioactive molecules including minoxidil (**I**),^[13a] thiamine (**II**),^[13b] pyrimethamine (**III**),^[13c] epiroprim (**IV**),^[13d] bacimethrin (**V**),^[13e] and sulfamethomidine (**VI**)^[13f] as depicted in Figure 1.

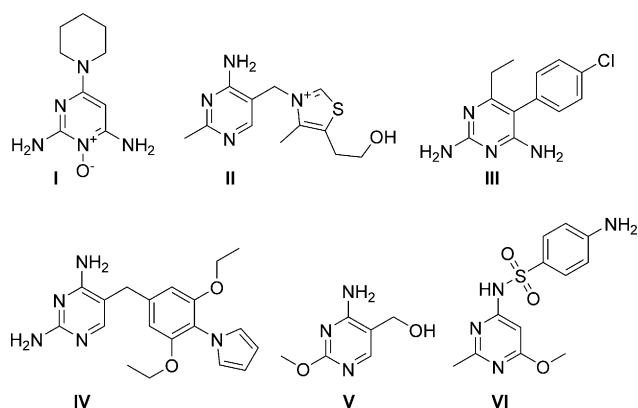
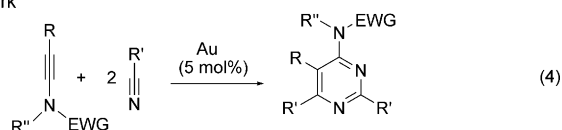


Figure 1. Representative bioactive molecules.

This work



[*] S. N. Karad, Prof. Dr. R.-S. Liu
Department of Chemistry, National Tsing Hua University
101, Sec. 2, Kuang-Fu Rd., Hsinchu, 30013 (Taiwan)
E-mail: rslu@mx.nthu.edu.tw
Homepage: <http://chem-en.web.nthu.edu.tw/files/13-1117-33454.php>

[**] We thank National Science Council, Taiwan, for financial support of this work.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201405312>.

Table 1: Catalytic reactions over gold catalysts.

Entry	Catalyst ^[a]	Solvent ^[b]	t [h]	Yields [%] ^[c] 1 a	3 a
1	AuCl ₃	DCE	12	65	20
2	[LAuCl]/AgNTf ₂	DCE	9	—	75
3	[IPrAuCl]/AgNTf ₂	DCE	10.5	—	73
4	[Ph ₃ PAuCl]/AgNTf ₂	DCE	4	—	95
5	[Ph ₃ PAuCl]/AgSbF ₆	DCE	4	—	89
6	[Ph ₃ PAuCl]/AgOTf	DCE	3.5	—	93
7	AgNTf ₂	DCE	12	75	—
8	[Ph ₃ PAuCl]/AgNTf ₂	toluene	7.5	—	84
9	[Ph ₃ PAuCl]/AgNTf ₂	C ₆ H ₅ Cl	2.5	—	86
10	[Ph ₃ PAuCl]/AgNTf ₂	1,4-dioxane	9	—	65

[a] **2a** (4 equiv). [b] [**1a**] = 0.20 M. [c] Product yields are reported after purification using a silica column. IPr = 1,3-bis(diisopropyl phenyl)-imidazol-2-ylidene, L = P(*t*Bu)₂(*o*-biphenyl), Ms = methanesulfonyl, Tf = trifluoromethanesulfonyl.

Table 1 shows the realization of a catalytic synthesis of the pyrimidine species **3a** using the ynamide **1a** and benzonitrile (**2a**; 4 equiv). We first tested the reaction with AuCl₃ (5 mol %) in hot 1,2-dichloroethane (DCE, 75 °C, 12 h), from which **3a** and unreacted **1a** were obtained in 20 and 65 %, respectively (entry 1). The cationic gold catalysts [P(*n*Bu)₂(*o*-biphenyl)AuCl]/AgNTf₂ and [IPrAuCl]/AgNTf₂ enabled complete consumption of **1a** in hot DCE (75 °C, 9–10.5 h) to afford **3a** in 75 and 73 % yield, respectively (entries 2 and 3). The yield of **3a** was greatly improved to 95 % with [PPh₃AuCl]/AgNTf₂ within a brief period (4 h, entry 4). Other anions in [PPh₃AuCl]/AgX (X = SbF₆ and OTf) maintained high yields (89–93 %) of **3a** (entries 5 and 6). AgNTf₂ alone was found to be inactive in hot DCE (75 °C) for a prolonged period (entry 7). With [PPh₃AuCl]/AgNTf₂ in other solvents, the yields of **3a** were 84 %, 86 %, and 65 %, respectively, in toluene, chlorobenzene, and 1,4-dioxane (entries 8–10). The molecular structure of **3a** was confirmed with X-ray diffraction.^[14]

We prepared additional ynamides (**1b–r**) to assess the substrate scope (Table 2). Most reactions were performed with [PPh₃AuNTf₂] (5 mol %), ynamides, and benzonitrile (4 equiv) in hot DCE (75 °C; **1b–m**) whereas in the cases of **1n–r** the reactions were run at 28 °C. For the ynamides **1b–d**, bearing various sulfonamide substituents (R' = *n*-butyl, phenyl, and benzyl), the corresponding pyrimidine products **3b–d** were obtained in 75–89 % yields. The cycloadditions were applicable also to the ynamides **1e** and **1f** comprising tosyl-substituted and cyclic sulfonamides, thus giving the desired **3e** (93 %) and **3f** (74 %), respectively. We tested the reactions on the ynamides **1g–i** in which the phenyl group bears different substituents (X = OMe, Cl and CO₂Me), thus yielding the desired **3g–i** in satisfactory yields. The reactions were compatible with 2- and 3-thienyl-substituted ynamides (**1j** and **1k**), thus yielding the corresponding pyrimidine derivatives **3j** (79 %) and **3k** (81 %), respectively. For other

Table 2: Catalytic cycloadditions with various ynamides.

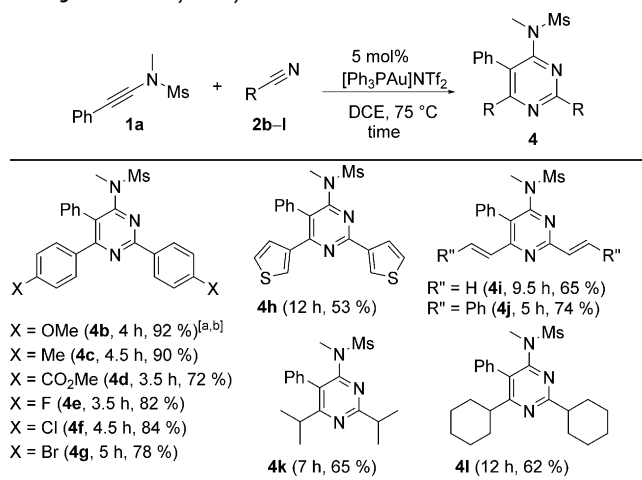
 R' = <i>n</i> Bu (3b , 4.5 h, 82 %)	 R' = Ph (3e , 6.5 h, 93 %)	 R' = Bn (3f , 3.5 h, 74 %)
 X = OMe (3g , 5.5 h, 86 %)	 X = Cl (3j , 4.5 h, 87 %)	 X = CO ₂ Me (3k , 5.5 h, 84 %)
 3l (4 h, 78 %)	 3m (4 h, 92 %)	 3n (10 h, 65 %)
 3o (12 h, 61 %)	 3p (2 h, 45 %)	 R ¹ = Ph (3r , 3.5 h, 46 %)
		 R ¹ = H (3s , 12 h, 62 %)

[a] [**1**] = 0.20 M, [PPh₃AuCl]/AgNTf₂ (5 mol %), benzonitrile (4.0 equiv).
[b] Product yields are reported after purification on a silica column.
[c] Reactions were carried out at 75 °C for **1b–m** and at 28 °C for **1n–r**.

heteroaryl-substituted ynamides, **1l** and **1m**, the corresponding cycloadducts **3l** and **3m** were produced efficiently. The alkyl-substituted ynamides **1n** and **1o** (R = cyclopropyl and *n*-butyl) were also amenable to this reaction at 28 °C, thus yielding pyrimidines **3n** and **3o** in 65 and 61 % yield, respectively. Such cycloadditions were extended to the alkenyl-substituted ynamides **1p–r**, thus giving compounds **3p–r** in reasonable yields.

Table 3 depicts the nitriles **2b–l** which are compatible with our catalytic cycloadditions. For the 4-substituted benzonitriles **2b,c**, bearing electron-donating groups (X = OMe and Me), the gold-catalyzed cycloadditions proceeded smoothly to yield the pyrimidine products **4b,c** in excellent yields. This synthetic method was also feasible for the electron-deficient benzonitriles **2d–g** (X = CO₂Me, F, Cl and Br), thus providing the desired **4d–g** in 72–84 % yields. For 3-thienylnitrile, the resulting product **4h** was obtained in 53 % yield. We also examined the reactions on two alkenylnitriles, **2i** and **2j** (R' = H and Ph), thus yielding the desired **4i** and **4j** in 65 and 74 % yield, respectively. To our delight, this method was also compatible with the aliphatic nitriles **2k** and **2l**, thus yielding the desired pyrimidine species **4k** and **4l**, respectively in 62–

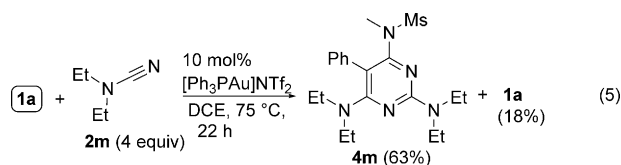
Table 3: Gold-catalyzed cycloadditions with various nitriles.



[a] [1a] = 0.20 M, [Ph₃PAuCl]/AgNTf₂ (5 mol %), nitrile (4.0 equiv).
[b] Product yields are reported after purification on a silica column.

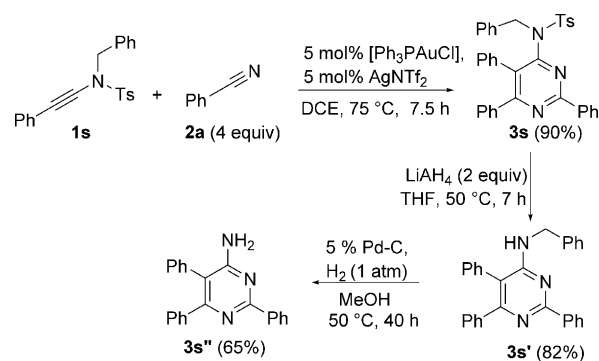
65 % yields. The molecular structure of the cycloadduct **4i** was determined by X-ray diffraction.^[14]

Inspired by the presence of triamino substituents as in minoxidil (see structure in Scheme 1), we undertook a gold-catalyzed cycloaddition between the ynamide **1a** and diethylaminonitrile (**2m**; 4 equiv) in hot DCE [75 °C, 22 h, Eq. (5)], thus providing the triamino-containing pyrimidine **4m** in 63 % yield, together with unreacted **1a** in 18 % yield. Such a highly electron-rich pyrimidine core did not inhibit the catalytic reaction, and further highlights the utility of this synthetic method.

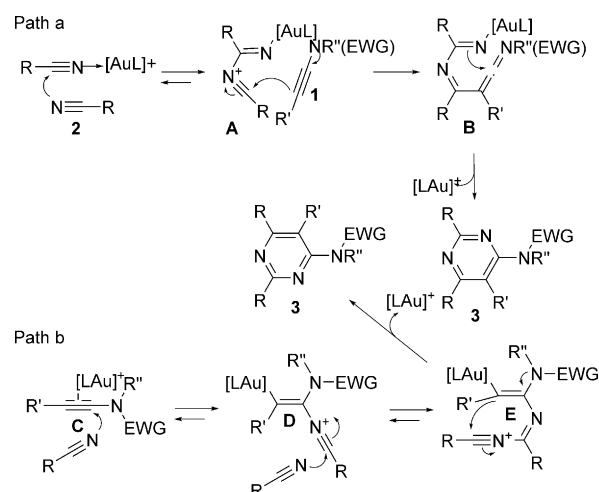


The sulfonamide group of the resulting pyrimidines can be transformed into an amine (NH₂) which is present in most bioactive molecules (Figure 1). Treatment of the ynamide **1s** with benzonitrile and [PPh₃AuNTf₂] (5 mol %) in hot DCE (75 °C, 7.5 h) gave the 4-aminopyrimidine **3s** in 90 % yield (Scheme 1). Subsequent reduction^[15] of **3s** with LiAlH₄ led to the removal of tosyl to yield the species **3s'** in 82 % yield. A subsequent reductive degradation of this 4-benzylaminopyrimidine with Pd/C and H₂ in MeOH afforded the amine-containing compound **3s''** in 65 % yield.

Shown in Scheme 2 are two postulated mechanisms to rationalize the formation of the 4-aminopyrimidines **3**. We envisage that a gold catalyst might catalyze dimerization of the nitrile **2** to form the intermediate **A**, which is subsequently attacked by **1** to yield the ketenimine species **B** (path a). A ring closure of **B** is expected to give the desired product **3**, a pathway postulated by Obora co-workers.^[10a] Alternatively, the nitrile might attack the gold π -alkyne species **C** to form



Scheme 1. Transformation of a sulfonamide into an amine. Ts = 4-toluenesulfonyl.



Scheme 2. Mechanisms for the synthesis of 4-aminopyrimidines.

the nitrilium species **D** which is highly electrophilic and induces a second attack by a nitrile to form another nitrilium species, **E**. A subsequent intramolecular cyclization of **E** forms the same product **3** (path b).

We envisage that path a will give stable trimers of nitriles if only the gold catalyst is present. Our control experiments revealed that [PPh₃AuNTf₂] failed to catalyze the trimerization of **2a** in hot DCE (75 °C) after 12 hours and the starting **2a** was recovered in 87%.^[16] According to literature reports, the trimerizations of nitriles are facilitated only with alkaline metals in PhM (M = Na, Li), or Mg⁰, Fe⁰, and Ni⁰ salts. Their dimers were postulated as intermediates.^[17] Although we were unable to obtain supportive data for path a involving initial dimerization of nitriles, this mechanism cannot be excluded completely. In contrast, path b indicates the feasibility of a gold π -alkyne inducing a dimerization of nitriles in a reversible process before it is trapped by a tethered nucleophile.

Before this work, metal-catalyzed intermolecular [2+2+2] cycloaddition reactions of alkynes with nitriles were mainly limited to the production of pyridines rather than pyrimidines. We herein report new gold-catalyzed [2+2+2] cycloadditions between ynamides and nitriles to afford monomeric 4-aminopyrimidines, which are commonly

found in many bioactive molecules. The practicability of such intermolecular cycloadditions^[18–20] is demonstrated by the wide scope with respect to both the ynamides and nitriles. We postulate that the reaction mechanism involves initial attack of a π -alkyne on two nitriles followed by a ring closure. Extension of this method to construct complicated pyrimidine frameworks is under current investigation.

Received: May 15, 2014

Published online: July 2, 2014

Keywords: cycloadditions · gold · heterocycles · homogeneous catalysis · synthetic methods

- [1] For selected reviews, see: a) J. A. Varela, C. Saá, *Chem. Rev.* **2003**, *103*, 3787–3801; b) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, *348*, 2307–2327; c) B. Heller, M. Hapke, *Chem. Soc. Rev.* **2007**, *36*, 1085–1094; d) M. R. Shaaban, R. El-Sayed, A. H. M. Elwahi, *Tetrahedron* **2011**, *67*, 6095–6130; e) G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev.* **2011**, *40*, 3430–3444; f) K. Tanaka, *Heterocycles* **2012**, *85*, 1017–1043.
- [2] For cobalt, see selected examples: a) P. Garcia, Y. Evanno, P. George, M. Sevrin, G. Ricci, M. Malacria, C. Aubert, V. Gandon, *Chem. Eur. J.* **2012**, *18*, 4337–4344; b) P. Garcia, Y. Evanno, P. George, M. Sevrin, G. Ricci, M. Malacria, C. Aubert, V. Gandon, *Org. Lett.* **2011**, *13*, 2030–2033; c) B. Heller, B. Sundermann, C. Fischer, J. You, W. Chen, H.-J. Drexler, P. Knochel, W. Bonrath, A. Gutnov, *J. Org. Chem.* **2003**, *68*, 9221–9225; d) K. Kase, A. Goswami, K. Ohtaki, E. Tanabe, N. Saino, S. Okamoto, *Org. Lett.* **2007**, *9*, 931–934; e) A. Gutnov, B. Heller, C. Fischer, H.-J. Drexler, A. Spannenberg, B. Sundermann, C. Sundermann, *Angew. Chem.* **2004**, *116*, 3883–3886; *Angew. Chem. Int. Ed.* **2004**, *43*, 3795–3797; f) J. A. Varela, L. Castedo, C. Saá, *Org. Lett.* **1999**, *1*, 2141–2143; g) H.-T. Chang, M. Jeganmohan, C.-H. Cheng, *Org. Lett.* **2007**, *9*, 505–508; h) B. L. Gray, X. Wang, W. C. Brown, L. Kuai, S. L. Schreiber, *Org. Lett.* **2008**, *10*, 2621–2624; i) L. V. R. Boñaga, H.-C. Zhang, A. F. Moretto, H. Ye, D. A. Gauthier, J. Li, G. C. Leo, B. E. Maryanoff, *J. Am. Chem. Soc.* **2005**, *127*, 3473–3485; j) C. Yuan, C.-T. Chang, A. Axelrod, D. Siegel, *J. Am. Chem. Soc.* **2010**, *132*, 5924–5925.
- [3] For ruthenium, see: a) Y. Yamamoto, R. Ogawa, K. Itoh, *J. Am. Chem. Soc.* **2001**, *123*, 6189–6190; b) Y. Yamamoto, S. Okuda, K. Itoh, *Chem. Commun.* **2001**, 1102–1103; c) Y. Yamamoto, K. Kinpara, T. Saigoku, H. Takagishi, S. Okuda, H. Nishiyama, K. Itoh, *J. Am. Chem. Soc.* **2005**, *127*, 605–613; d) J. A. Varela, L. Castedo, C. Saá, *J. Org. Chem.* **2003**, *68*, 8595–8598; e) Y. Yamamoto, K. Kinpara, R. Ogawa, H. Nishiyama, K. Itoh, *Chem. Eur. J.* **2006**, *12*, 5618–5631.
- [4] For rhodium, see: a) K. Tanaka, N. Suzuki, G. Nishida, *Eur. J. Org. Chem.* **2006**, 3917–3922; b) K. Tanaka, H. Hara, G. Nishida, M. Hirano, *Org. Lett.* **2007**, *9*, 1907–1910; c) A. Wada, K. Noguchi, M. Hirano, K. Tanaka, *Org. Lett.* **2007**, *9*, 1295–1298; d) Y. Komine, K. Tanaka, *Org. Lett.* **2010**, *12*, 1312–1315; e) T. Shibata, T. Uchiyama, K. Endo, *Org. Lett.* **2009**, *11*, 3906–3908.
- [5] For iron, see: a) C. Wang, X. Li, F. Wu, B. Wan, *Angew. Chem.* **2011**, *123*, 7300–7304; *Angew. Chem. Int. Ed.* **2011**, *50*, 7162–7166; b) C. Wang, D. Wang, F. Xu, B. Pan, B. Wan, *J. Org. Chem.* **2013**, *78*, 3065–3072; c) T. K. Lane, B. R. D'Souza, J. Louie, *J. Org. Chem.* **2012**, *77*, 7555–7563; d) B. R. D'Souza, T. K. Lane, J. Louie, *Org. Lett.* **2011**, *13*, 2936–2939.
- [6] For nickel, see: a) T. Takahashi, F.-Y. Tsai, Y. Li, H. Wang, Y. Kondo, M. Yamanaka, K. Nakajima, M. Kotora, *J. Am. Chem. Soc.* **2002**, *124*, 5059–5067; b) M. M. McCormick, H. A. Duong, G. Zuo, J. Louie, *J. Am. Chem. Soc.* **2005**, *127*, 5030–5031; c) P. Kumar, S. Prescher, J. Louie, *Angew. Chem.* **2011**, *123*, 10882–10886; *Angew. Chem. Int. Ed.* **2011**, *50*, 10694–10698; d) R. M. Stolley, H. A. Duong, D. R. Thomas, J. Louie, *J. Am. Chem. Soc.* **2012**, *134*, 15154–15162; e) R. M. Stolley, M. T. Maczka, J. Louie, *Eur. J. Org. Chem.* **2011**, 3815–3824; f) D. Dallinger, M. Irfan, A. Suljanovic, C. O. Kappe, *J. Org. Chem.* **2010**, *75*, 5278–5288.
- [7] For iridium, see: G. Onodera, Y. Shimizu, J.-N. Kimura, J. Kobayashi, Y. Ebihara, K. Kondo, K. Sakata, R. Takeuchi, *J. Am. Chem. Soc.* **2012**, *134*, 10515–10531.
- [8] For titanium, see: a) D. Suzuki, Y. Nobe, Y. Watai, R. Tanaka, Y. Takayama, F. Sato, H. Urabe, *J. Am. Chem. Soc.* **2005**, *127*, 7474–7479; b) D. Suzuki, R. Tanaka, H. Urabe, F. Sato, *J. Am. Chem. Soc.* **2002**, *124*, 3518–3519; c) R. Tanaka, A. Yuza, Y. Watai, D. Suzuki, Y. Takayama, F. Sato, H. Urabe, *J. Am. Chem. Soc.* **2005**, *127*, 7774–7780.
- [9] Reviews for the synthetic methods and biological functions of pyrimidines: a) M. D. Hill, M. Movassaghi, *Chem. Eur. J.* **2008**, *14*, 6836–6844; b) I. M. Lagoja, *Chem. Biodiversity* **2005**, *2*, 1–50; c) K. S. Jain, T. S. Chitre, P. B. Miniyaar, M. K. Kathiravan, V. S. Bendre, V. S. Veer, S. R. Shahane, C. J. Shishoo, *Curr. Sci.* **2006**, *90*, 793–803; d) S. R. Walker, E. J. Carter, B. C. Huff, J. C. Morris, *Chem. Rev.* **2009**, *109*, 3080–3098.
- [10] a) Y. Satoh, K. Yasuda, Y. Obora, *Organometallics* **2012**, *31*, 5235–5238; b) X. You, S. Yu, Y. Liu, *Organometallics* **2013**, *32*, 5273–5276; c) T. K. Lane, M. H. Nguyen, B. R. D'Souza, N. A. Spahn, J. Louie, *Chem. Commun.* **2013**, 49, 7735–7737.
- [11] Reviews for ynamides: 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*, 560–578; b) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064–5106; c) G. Evano, A. Coste, K. Jouvin, *Angew. Chem.* **2010**, *122*, 2902–2921; *Angew. Chem. Int. Ed.* **2010**, *49*, 2840–2859.
- [12] For gold-catalyzed reactions on ynamides, see selected examples: a) S. N. Karad, S. Bhunia, R.-S. Liu, *Angew. Chem.* **2012**, *124*, 8852–8856; *Angew. Chem. Int. Ed.* **2012**, *51*, 8722–8726; b) R. B. Dateer, B. S. Shaibu, R.-S. Liu, *Angew. Chem.* **2012**, *124*, 117–121; *Angew. Chem. Int. Ed.* **2012**, *51*, 113–117; 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) E. Rettenmeier, A. M. Schuster, M. Rudolph, F. Rominger, C. A. Gade, A. S. K. Hashmi, *Angew. Chem.* **2013**, *125*, 5993–5997; *Angew. Chem. Int. Ed.* **2013**, *52*, 5880–5884; e) S. Kramer, Y. Odabachian, J. Overgaard, M. Rottländer, F. Gagosz, T. Skrydstrup, *Angew. Chem.* **2011**, *123*, 5196–5200; *Angew. Chem. Int. Ed.* **2011**, *50*, 5090–5094; f) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem.* **2011**, *123*, 9093–9097; *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935.
- [13] a) P. Balakrishnan, S. Shanmugam, W. S. Lee, W. M. Lee, J. O. Kim, D. H. Oh, D.-D. Kim, J. S. Kim, B. K. Yoo, H.-G. Choi, J. S. Woo, C. S. Yong, *Int. J. Pharm.* **2009**, *377*, 1–8; b) M. E. Webb, A. Marquet, R. R. Mendel, F. Rébeillé, A. G. Smith, *Nat. Prod. Rep.* **2007**, *24*, 988–1008; c) A. S. Limpert, M. E. Mattmann, N. D. P. Cosford, *Beilstein J. Org. Chem.* **2013**, *9*, 717–732; d) A. Gangjee, A. Vasudevan, S. F. Queener, R. L. Kisliuk, *J. Med. Chem.* **1996**, *39*, 1438–1446; e) J. L. Zilles, L. R. Croal, D. M. Downs, *J. Bacteriol.* **2000**, *182*, 5606–5610; f) J. Huges, L. C. Roberts, A. J. Coppridge, *J. Urol.* **1975**, *114*, 912–914.
- [14] CCDC 1001397 (**3a**), 1001398 (**4i**) 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.
- [15] V. Coeffard, C. Thobie-Gautier, I. Beaudet, E. L. Grognet, J. P. Quintard, *Eur. J. Org. Chem.* **2008**, 383–391.
- [16] We have examined the ¹³C NMR study for an equimolar mixture of benzonitrile and [PPh₃AgCl]/AgSbF₆ in CD₂Cl₂. The ¹³C NMR signal of the nitrile appeared at δ = 119.2 ppm, close

of that of free nitrile ($\delta = 118.8$ ppm). This observation revealed that this gold catalyst had certain affinity toward nitrile.

- [17] a) J. I. Ogonor, *Tetrahedron* **1981**, 37, 2909–2910; b) R. N. Anker, A. H. Cook, *J. Chem. Soc.* **1941**, 323–331; c) S. Aharonovich, M. Botoshansky, R. M. Waymouth, M. S. Eisen, *Inorg. Chem.* **2010**, 49, 9217–9229; d) D. R. Armstrong, K. W. Henderson, M. MacGregor, R. E. Mulvey, M. J. Ross, W. Clegg, P. A. O’Neil, *J. Organomet. Chem.* **1995**, 486, 79–93; e) D. R. Armstrong, W. Clegg, M. MacGregor, R. E. Mulvey, P. A. O’Neil, *J. Chem. Soc. Chem. Commun.* **1993**, 608–610; f) P. Langer, M. Döring, D. Seyferth, *Chem. Commun.* **1998**, 1927–1928; g) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, 52, 3674–3680; h) J. J. Eisch, X. Ma, K. I. Han, J. N. Gitua, C. Krüger, *Eur. J. Inorg. Chem.* **2001**, 77–88.
- [18] For reviews of gold-catalyzed cycloaddition reactions, see: a) A. S. K. Hashmi, *Chem. Rev.* **2007**, 107, 3180–3211; b) F. López, J. L. Mascareñas, *Beilstein J. Org. Chem.* **2011**, 7, 1075–1094; c) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria, A. Simonneau, *Chem. Rev.* **2011**, 111, 1954–1993; d) D. Garayalde, C. Nevado, *ACS Catal.* **2012**, 2, 1462–1479.
- [19] Selected examples: a) J. Barluenga, M. Á. Fernández-Rodríguez, P. García-García, E. Aguilar, *J. Am. Chem. Soc.* **2008**, 130, 2764–2765; b) H. Faustino, F. López, L. Castedo, J. L. Mascareñas, *Chem. Sci.* **2011**, 2, 633–637; c) H. Faustino, I. Alonso, J. L. Mascareñas, F. López, *Angew. Chem.* **2013**, 125, 6654–6658; *Angew. Chem. Int. Ed.* **2013**, 52, 6526–6530.
- [20] These alkyne/nitrile cycloadditions did not proceed with either diphenylacetylene or phenylacetylene using $[PPh_3AuCl]/AgNTf_2$. The former was recovered in 76% yield whereas the latter gave complicated mixture of products.