EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Gold-catalyzed post-Ugi cascade transformation for the synthesis of 2-pyridones

Authors: Xiaochen Du, Jiafeng Yu, Jing Gong, Manzoor Zaman, Olga Pereshivko, and Vsevolod A. Peshkov

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201900027

Link to VoR: http://dx.doi.org/10.1002/ejoc.201900027

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201900027

WILEY-VCH

COMMUNICATION

Gold-catalyzed post-Ugi cascade transformation for the synthesis of 2-pyridones

Xiaochen Du,[a] Jiafeng Yu,[a] Jing Gong,[a] Manzoor Zaman,[a] Olga P. Pereshivko,*[a] Vsevolod A. Peshkov*[a,b,c]

Abstract: A gold-catalyzed post-Ugi cascade transformation for the synthesis of 2-pyridones is described. The process involves furan-alkyne cyclization followed by furan ring-opening and cleavage of the isocyanide-originated fragment. The initially formed *cis* double bond can isomerize into a more stable *trans* double bond upon prolonged exposure to a strong Brønsted acid. Thus, the overall strategy provides a viable access towards two types of 2-pyridones.

Introduction

Multicomponent reactions (MCRs)[1] and cascade processes[2] involving creation and/or breakage of several bonds have become the key synthetic tools for the fast and convergent assembly of complex molecular and polymeric[3,4] structures. Combining four-component Ugi reaction with appropriate post-transformations is among the most popular strategies for the diversity-oriented synthesis (DOS) of various heterocyclic scaffolds.[5,6] A large sub-category of these processes involves intramolecular alkyne hydroarylations of propiolic-acid-derived Ugi adducts containing an electron-rich (hetero)aromatic group incorporated through an amine or an aldehyde component (Scheme 1a). This heteroaromatic group can be represented by an electron-rich benzene,[7] indole,[8] pyrrole,[9] thiophene or benzothiophene.[10] The simultaneous presence of a triple bond and an electron-rich hetero(aromatic) ring allows to cyclize such Ugi adducts in the presence of an appropriate Lewis or Brønsted acid. In some cases, the cyclization can be selectively diverted to either exo- or endo-mode by changing the applied catalytic system.[8d,9a,9c] With regard to (hetero)aromatic group, depending on the substitution pattern, two kinds of reaction pathways are possible. The first path involves cyclization onto an *ortho*-position of the (hetero)aromatic ring, leading to the formation of fused structures. Alternatively, the alkyne tether could undergo an ipso-attack involving dearomatization and the formation of spirocyclic motifs.[7a-d,8a-c]

When the electron-rich aromatic ring is represented by furan, the corresponding propiolic acid-derived Ugi adducts tend to display different type of reactivity engaging in an intramolecular Diels-Alder reaction of furan (IMDAF, Scheme 1b).[11] The resulting products featuring oxabicyclo[2.2.1]heptadiene moiety can undergo rearrangement into phenols imbedded into isoindolinone core (Scheme 1b).

In this paper, we report a novel gold-catalyzed post-Ugi cascade transformation for the synthesis of 2-pyridones (Scheme 1c). The process starts with a nucleophilic attack of a furan moiety onto the triple bond activated by a cationic gold catalyst. This follows by a furan ring-opening accompanied by cleavage[12] of the isocyanide-originated fragment (Scheme 1c). It should be noted that transition metal-catalyzed furan-alkyne transformations are well known and can proceed through various pathways that typically involve ring-opening of furan.[13] For example, gold-catalyzed furan-alkyne cyclization/ring-opening process converting furans into α,β-unsaturated carbonyl compounds has been advanced by the group of Liu.[13e-h] In addition, during preparation of this work, Jiang, Yin and coworkers reported a similar approach towards halogenated 2-pyridones by Pd-catalyzed furan-alkyne cyclization followed by furan ring-opening and halogen incorporation (Scheme 1d).[14]

Results and Discussion

We have started our study with preparation of a series of Ugi adducts **6** following the specifically designed two-step one-pot procedure (Scheme 2). Reacting furan-2-carbaldehydes **1** with anilines **2** at the elevated temperature of 50°C delivered imines **3**. Treating these preformed imines **3** with propiolic acids **4** and *tert*-butyl isocyanide (**5**) at decreased temperature of 15°C allowed to obtain desired Ugi adducts **6** in good to high yields ranging from 57% to 95%. Importantly, lowering the temperature at the final stage of the sequence was required to suppress an intramolecular furan Diels-Alder reaction of **6**.

Then, the Ugi adduct **6a** was selected as a model substrate to test its reactivity under the cationic gold(I) catalysis. Initially, the transformation of **6a** into 2-pyridones **7a** and **8a** was discovered when **6a** was treated with 5 mol% of $PPh_3AuCl/AgOTf$ using old chloroform as a solvent (Table 1, entry 1). However, these settings failed to deliver consistent results. Furthermore, we were unable to achieve a full conversion of **6a**. Importantly, the use of fresh chloroform as a solvent resulted in a complete shutdown of the transformation (Table 1, entry 2). Knowing that the prolonged storage of chloroform might lead to accumulation of some HCl,

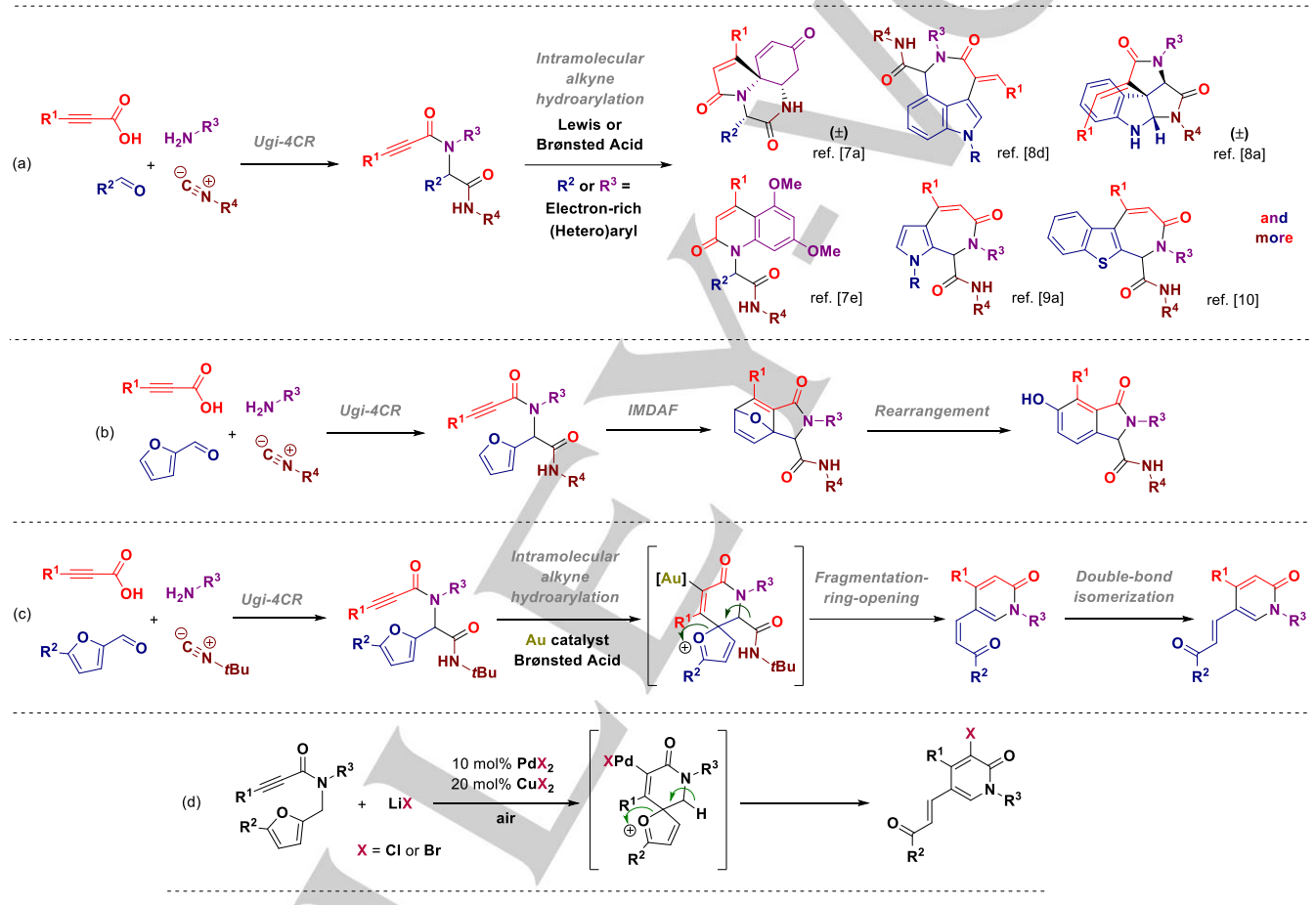
[a] X. Du, J. Yu, J. Gong, M. Zaman, Dr. O. P. Pereshivko, Dr. V. A. Peshkov
College of Chemistry, Chemical Engineering and Materials Science, Soochow University,
Dushu Lake Campus, Suzhou 215123, P. R. China
E-mails: olga@suda.edu.cn, vsevolod@suda.edu.cn
[b] Dr. V. A. Peshkov
Department of Chemistry, School of Science and Technology, Nazarbayev University,
53 Kabanbay Batyr Ave, Block 7, Astana 010000, Republic of Kazakhstan
E-mail: vsevolod.peshkov@nu.edu.kz
[b] Dr. V. A. Peshkov
The Environment and Resource Efficiency Cluster (EREC), Nazarbayev University,
Astana, Republic of Kazakhstan

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

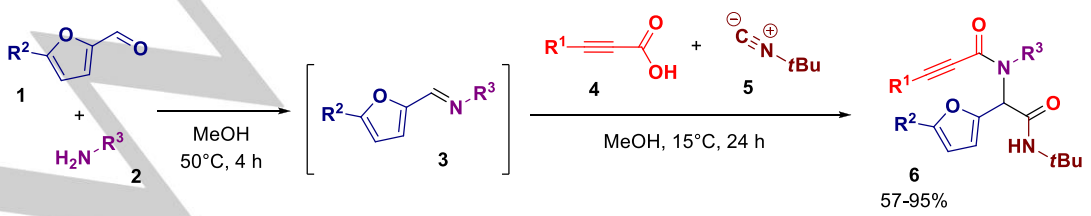
10.1002/ejoc.201900027

COMMUNICATION

we attributed this difference in reactivity to the absence of HCl in a fresh solvent. This result prompted us to realize that the presence of Brønsted acid is required for our process presumably to facilitate the protonolysis of vinyl gold species formed upon furan-alkyne cyclization step. Consequently, we setup two trial reactions in the presence of either trifluoroacetic or triflic acid (Table 1, entries 3 and 4). To our delight the use of triflic acid in a combination with 5 mol% of $PPh_3AuCl/AgOTf$ led to complete conversion of **6a** producing 2-pyridone **7a** in a 58% yield along with the minor amounts of 2-pyridone **8a** (Table 1, entry 4). Next, we have screened a number of in situ generated and preformed cationic gold(I) complexes featuring different ligands and counterions with the best result being obtained using 5 mol% of $PPh_3AuCl/AgPF_6$ (Table 1, entries 5-9). Tuning the catalyst ratio to 5 mol% of PPh_3AuCl and 10 mol% of $AgPF_6$ led to a further upgrade of the reaction outcome (Table 1, entry 10). Using 10 mol% of $AgPF_6$ in the presence of triflic acid or triflic acid in the absence of both silver and gold salts failed to deliver 2-pyridones **7a** and/or **8a** resulting in a degradation of substrate **6a** (Table 1, entries 11 and 12). Increasing the amount of triflic acid along with the use of prolonged reaction time fostered double bond isomerization producing 2-pyridone **8a** as a major product (Table 1, entry 13). Diluting the reaction mixture with EtOAc after complete conversion of **6a** was achieved led to a cleaner reaction and as a result an improved yield of **8a** (Table 1, entries 14-16).

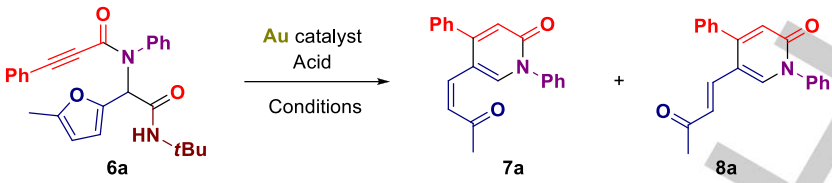


Scheme 1. a-c) Post-Ugi transformations of propiolic acid-derived Ugi adducts containing an electron-rich aromatic ring. d) Pd-catalyzed furan-alkyne cyclization followed by furan ring-opening and halogen incorporation leading to the formation of halogenated 2-pyridones.



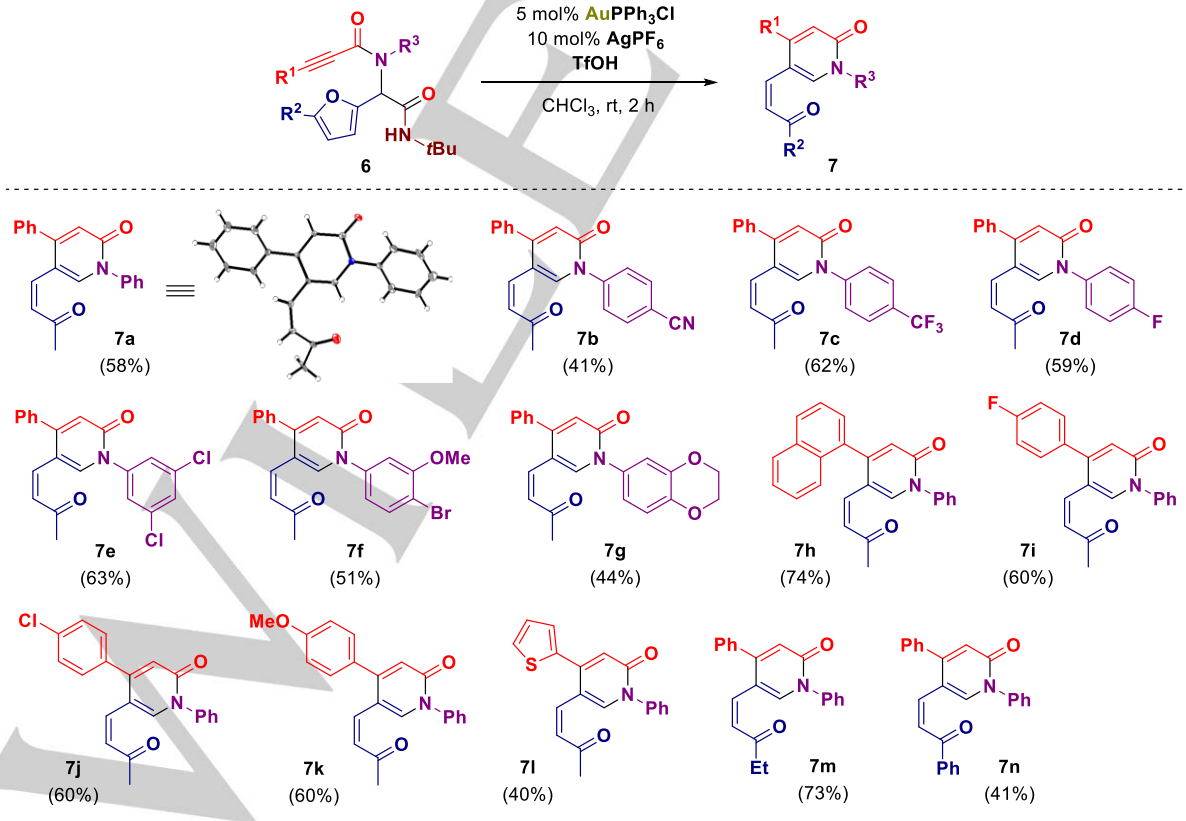
Scheme 2. Synthesis of Ugi adducts **6**.

Table 1. Optimization of the reaction conditions for the transformation of Ugi adduct **6a** into 2-pyridones **7a** and **8a**.[a]

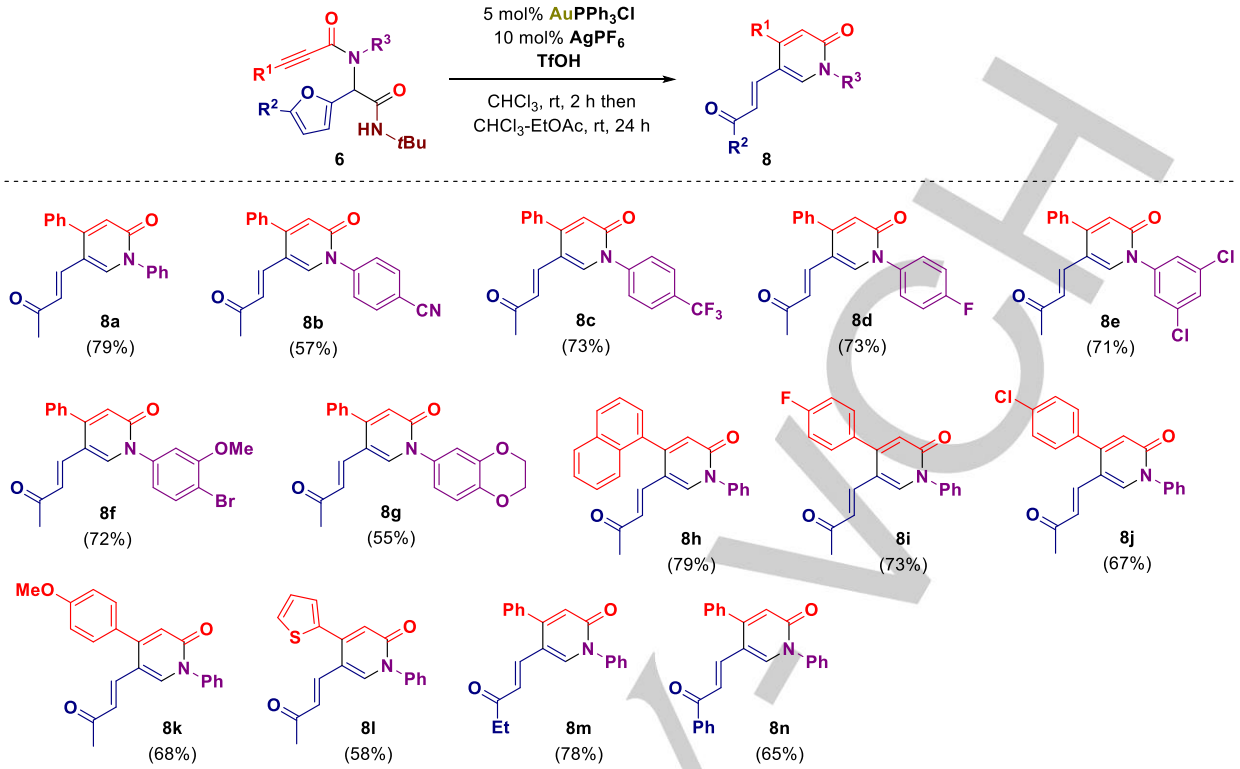


Entry	Catalyst	Acid additive[b]	Conditions	Conversion of **6a**[c]	Yield[c]	
					7a	**8a**
1	5 mol% $PPh_3AuCl/AgOTf$	-[d]	old $CHCl_3$, rt, 24 h	93-97	41-52	5-7
2	5 mol% $PPh_3AuCl/AgOTf$	-[d]	$CHCl_3$, rt, 2 h	0	-	-
3	5 mol% $PPh_3AuCl/AgOTf$	CF_3COOH	$CHCl_3$, rt, 24 h	85	45	6
4	5 mol% $PPh_3AuCl/AgOTf$	TfOH	$CHCl_3$, rt, 2 h	100	58	12
5	5 mol% $PPh_3AuCl/AgNTf_2$	TfOH	$CHCl_3$, rt, 2 h	100	59	13
6	5 mol% $PPh_3AuCl/AgNO_3$	TfOH	$CHCl_3$, rt, 2 h	92	45	11
7	5 mol% AuIPrCl/AgOTf	TfOH	$CHCl_3$, rt, 2 h	100	50	10
8	5 mol % [Au(JohnPhos)(MeCN)]SbF_6	TfOH	$CHCl_3$, rt, 6 h	96	62	10
9	5 mol% $PPh_3AuCl/AgPF_6$	TfOH	$CHCl_3$, rt, 2 h	100	64	12
10	5 mol% PPh_3AuCl/10 mol% $AgPF_6$	TfOH	$CHCl_3$, rt, 2 h	100	68 (58)[e]	19
11	10 mol% $AgPF_6$	TfOH	$CHCl_3$, rt, 3 h	60	-	-
12	-	TfOH[f]	$CHCl_3$, rt, 5 h	100	-	-
13	5 mol% PPh_3AuCl/10 mol% $AgPF_6$	TfOH[g]	$CHCl_3$, rt, 2 + 20 h	100	3	74
14[h]	5 mol% PPh_3AuCl/10 mol% $AgPF_6$	TfOH	$CHCl_3$, rt, 2 h then $CHCl_3$-EtOAc, rt, 40 h	100	25	60
15[h]	5 mol% PPh_3AuCl/10 mol% $AgPF_6$	TfOH[i]	$CHCl_3$, rt, 2 h then $CHCl_3$-EtOAc, rt, 40 h	100	10	76
16[h]	5 mol% PPh_3AuCl/10 mol% $AgPF_6$	TfOH[g]	$CHCl_3$, rt, 2 h then $CHCl_3$-EtOAc, rt, 20 h	100	3	82 (79)[e]

[a] Unless otherwise specified, all reactions were run on 0.3 mmol scale in 3 mL of solvent. [b] Unless otherwise specified, 7.5 µL of acid additive was used. [c] Determined by ^1H NMR using 3,4,5-trimethoxybenzaldehyde as an internal standard. [d] No acid additive was used. [e] Isolated yield is given in parenthesis. [f] 15 µL of TfOH was used. [g] Initially, 7.5 µL of TfOH was used, but after 2 h additional 15 µL was added. [h] For these entries, the reaction was initially conducted in 3 mL of $CHCl_3$ and then after 2 h it was diluted with 5 mL of EtOAc. [i] Initially, 7.5 µL of TfOH was used, but after 2 h additional 7.5 µL was added. JohnPhos = 2-(di-*tert*-butylphosphino)biphenyl; IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene.



Scheme 3. Scope of the gold-catalyzed cascade transformation of Ugi adducts **6** into 2-pyridones **7**.



Scheme 4. Scope of the gold-catalyzed cascade transformation of Ugi adducts **6** into 2-pyridones **8**.

Having these results in hand, we moved to evaluate the scope of this newly developed cationic gold(I)-catalyzed cascade process using initially prepared Ugi adducts **6**. Two modifications of the protocol were tested providing an access towards both initially formed 2-pyridones **7** and isomerized 2-pyridones **8** (Schemes 3 and 4). In general, the yields for 2-pyridones **7** were lower than those for the corresponding 2-pyridones **8** as the isomerization of **7** into **8** cannot be completely suppressed under the applied reaction settings. In most cases, separation of **7** from **8** was also rather difficult. Thus, the obtained samples of 2-pyridones **7** contained up to 15% of corresponding isomeric 2-pyridone **8**. Despite that in the reaction media 2-pyridones **7** tend to isomerize into 2-pyridones **8** featuring a more stable *trans* double bond, the samples of 2-pyridones **7** obtained after column chromatography were found to be relatively stable under the ambient conditions. Thus, the structure of representative 2-pyridone **7a** could be assured by the X-ray crystallographic analysis.[15] In contrast, 2-pyridones **8** were found to be prone to degradation making their isolation and characterization rather challenging. Thus, the isolated samples of these products should be stored in a fridge and all the operations under the ambient conditions should be done in a prompt manner.

Conclusions

In summary, we have found that Ugi adducts derived from propiolic acids and furan-2-carbaldehydes could undergo a gold-catalyzed cascade transformation providing an access towards two types of 2-pyridones that differ from each other by the configuration of the double bond formed after the ring opening of furan. The overall process involves furan-alkyne cyclization that triggers furan ring opening accompanied by the cleavage of the isocyanide-originated fragment. In this way, 2-pyridones containing *cis* double bond could be obtained in moderate yields, while 2-pyridones containing *trans* double bond are formed in moderate to good yields after prolonged exposure to a strong Brønsted acid.

Experimental Section

General procedure for the synthesis of Ugi adducts 6

Furan-2-carbaldehyde **1** (2.2 mmol) was dissolved in MeOH (5.0 mL) followed by the addition of aniline **2** (2 mmol). The reaction mixture was flashed with argon, sealed and stirred at 50°C for 4 h. Upon completion of this time, propiolic acid **4** (2.2 mmol), isocyanide **5** (2.8 mmol) and another portion of MeOH (5.0 mL) were added. The reaction mixture was flashed with argon, sealed and stirred at 15°C for 24 h. The resulting mixture was diluted with EtOAc and concentrated with silica. Column chromatography with petroleum ether/EtOAc (the ratio was adjusted according to TLC) as an eluent delivered desired Ugi adduct **6**.

General procedure for the synthesis of 2-pyridones 7

Ugi adduct **6** (0.3 mmol), $AgPF_6$ (7.6 mg, 0.03 mmol) and PPh_3AuCl (7.4 mg, 0.015 mmol) were placed in a crew cap vial followed by addition of dry $CHCl_3$ (3 mL) and CF_3SO_3H (7.5 µL). The reaction mixture was sealed and

stirred at 25°C for 2 h. The resulting mixture was diluted with EtOAc, washed with saturated aqueous solution of $NaHCO_3$ and concentrated under reduced pressure. The crude material was dissolved in a small amount of DCM and loaded on a silica gel column that was packed using petroleum ether. Column chromatography with petroleum ether/EtOAc (the ratio was adjusted according to TLC) as an eluent delivered 2-pyridone **7**.

General procedure for the synthesis of 2-pyridones 8

Ugi adduct **6** (0.3 mmol), $AgPF_6$ (7.6 mg, 0.03 mmol) and PPh_3AuCl (7.4 mg, 0.015 mmol) were placed in a crew cap vial followed by addition of dry $CHCl_3$ (3 mL) and CF_3SO_3H (7.5 µL). The reaction mixture was sealed and stirred at 25°C for 2 h. Upon completion of this time, EtOAc (5 mL) and another portion of CF_3SO_3H (15µL) were added. The reaction mixture was sealed and stirred at 25°C for 24 h. The resulting mixture was diluted with EtOAc, washed with saturated aqueous solution of $NaHCO_3$ and concentrated under reduced pressure. The crude material was dissolved in a small amount of DCM and loaded on a silica gel column that was packed using petroleum ether. Column chromatography with EtOAc/DCM (the ratio was adjusted according to TLC) as an eluent delivered 2-pyridone **8**.

Acknowledgements

This work was supported by the startup fund from Soochow University (grant Q410900714), National Natural Science Foundation of China (grant 21650110445), Natural Science Foundation of Jiangsu Province of China (grants BK20150317 and BK20160310), the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD) and the project of scientific and technologic infrastructure of Suzhou (grant SZS201708). M.Z. is grateful to Chinese Scholarship Council (CSC) for providing a doctoral scholarship.

Keywords: cascade transformations • gold catalysis • multicomponent reactions • 2-pyridones • Ugi reaction

[1] a) H. Bienaymé, C. Hulme, G. Oddon, P. Schmitt, *Chem. Eur. J.* **2000**, *6*, 3321–3329; b) J. Zhu, H. Bienaymé, *Multicomponent Reactions*, 1st ed., Wiley-VCH, Weinheim, **2005**; c) J. D. Sunderhaus, S. F. Martin, *Chem. Eur. J.* **2009**, *15*, 1300–1308; d) B. Ganem, *Acc. Chem. Res.* **2009**, *42*, 463−472. e) B. U. W. Maes, R. V. A. Orru, E. Ruijter, *Synthesis of Heterocycles via Multicomponent Reaction I & II*, Springer, Heidelberg, **2010**; f) B. Jiang, T. Rajale, W. Wever, S.-J. Tu, G. Li, *Chem. Asian J.* **2010**, *5*, 2318–2335; g) J. Zhu, Q. Wang, M. X. Wang, *Multicomponent Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2014**; h) L. Banfi, A. Basso, L. Moni, R. Riva, *Eur. J. Org. Chem.* **2014**, 2005–2015. i) L. Levia, T. J. J. Müller, *Chem. Soc. Rev.* **2016**, *45*, 2825–2846; j) M. V. Murlykina, A. D. Morozova, I. M. Zviagin, Y. I. Sakhno, S. M. Desenko, V. A. Chebanov, *Front. Chem.* **2018**, *6*, 527.

[2] a) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; b) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186; *Angew. Chem.* **2006**, *118*, 7292–7344; c) L. F. Tietze, G. Brasche, K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; d) H. Pellissier, *Chem. Rev.* **2013**, *113*, 442–524; e) H. Ohno, *Isr. J. Chem.* **2013**, *53*, 869–868; f) J. H. Kim, Y. O. Ko, J. Bouffard, S. Lee, *Chem. Soc. Rev.* **2015**, *44*, 2489–2507

[3] For review, see: R. Hu, W. Li, B. Z. Tang, *Macromol. Chem. Phys.* **2016**, *217*, 213–224.

[4] For selected examples, see: a) H. Kim, T.-L. Choi, *ACS Macro Lett.* **2014**, *3*, 791–794; b) L. Xu, R. Hu, B. Z. Tang, *Macromolecules* **2017**, 50, 6043–6053; c) H. Deng, E. Zhao, A. C. S. Leung, R. Hu, Y. Zhang, J. W. Y. Lam, B. Z. Tang, *Polym. Chem.* **2016**, *7*, 1836–1846; d) W. Fu, L. Dong, J. Shi, B. Tong, Z. Cai, J. Zhi, Y. Dong, *Macromolecules*, **2018**, *51*, 3254–3263.

[5] For reviews, see: a) L. Banfi, A. Basso, R. Riva, *Top. Heterocycl. Chem.* **2010**, *23*, 1–39; b) U. K. Sharma, N. Sharma, D. D. Vachhani, E. V. Van der Eycken, *Chem. Soc. Rev.* **2015**, *44*, 1836–1860; c) Z. Zhang, X. Zheng, C. Guo, *Chin. J. Org. Chem.* **2016**, *36*, 1241–1265; d) X. Li, X. Jia, L. Yin, *Chin. J. Org. Chem.* **2017**, *37*, 2237–2249; e) L. Banfi, A. Basso, C. Lambruschini, L. Moni, R. Riva, *Chem. Heterocycl. Comp.* **2017**, *53*, 382–408.

[6] For recent examples, see: a) T. Ramanivas, M. Parameshwar, G. Gayatri, J. B. Nanubolu, A. K. Srivastava, *Eur. J. Org. Chem.* **2017**, 2245–2257; b) J. Huang, X. Du, K. Van Hecke, E. V. Van der Eycken, O. P. Pereshivko, V. A. Peshkov, *Eur. J. Org. Chem.* **2017**, 4379–4388; c) H. Wei, G. Wang, Y. Wang, B. Li, J. Huang, S. Kashtanov, K. Van Hecke, O. P. Pereshivko, V. A. Peshkov, *Chem. Asian J.* **2017**, *12*, 825–829; d) S. Balalaie, R. R. Kejani, E. Ghabraie, F. Darvish, F. Rominger, F. Hamdan, H. R. Bijanzadeh, *J. Org. Chem.* **2017**, *82*, 12141−12152; e) P. Pertejo, P. Peña-Calleja, I. Carreira-Barral, R. Quesada, N. A. Cordero, F. J. Rodríguez, M. García-Valverde, *Org. Biomol. Chem.* **2017**, *15*, 7549–7557; f) Z.-L. Ren, P. He, W.-T. Lu, M. Sun, M.-W. Ding, *Org. Biomol. Chem.* **2018**, *16*, 6322–6331; g) X. Gao, C. Shan, Z. Chen, Y. Liu, X. Zhao, A. Zhang, P. Yu, H. Galons, Y. Lan, K. Lu, *Org. Biomol. Chem.* **2018**, *16*, 6096–6105; h) V. Srinivasulu, S. McN. Sieburth, R. El-Awady, N. M. Kariem, H. Tarazi, M. John O'Connor, T. H. Al-Tel, *Org. Lett.* **2018**, *20*, 836−839; i) C. Liu, G. Wang, Y. Wang, K. Van Hecke, O. P. Pereshivko, V. A. Peshkov, *Tetrahedron Lett.* **2018**, *59*, 1823–1827; j) Z. Li, L. Song, L. Van Meervelt, G. Tian, E. V. Van der Eycken, *ACS Catalysis* **2018**, 8, 6388-6393; k) R. Madhavachary, N. Naveen, Y. Wang, Q. Wang, M. Konstantinidou, A. Dömling, *Eur. J. Org. Chem.* **2018**, 3139−3143; l) M. Konstantinidou, K. Kurpiewska, J. Kalinowska-Tłuscik, A. Dömling, *Eur. J. Org. Chem.* **2018**, 6714−6719; l) Y.-M. Yan, H.-Y. Li, J. Ren, S. Wang, M.-W. Ding, *Synlett* **2018**, *29*, 1447−1450; m) J. Xiong, X. Wei, Y.-C. Wan, M.-W. Ding, *Tetrahedron* **2019**, *75*, 1072−1078.

[7] a) D. Yugandhar, S. Kuriakose, J. B. Nanubolu, A. K. Srivastava, *Org. Lett.* **2016**, *18*, 1040−1043; b) Y. He, Z. Li, G. Tian, L. Song, L. Van Meervelt, E. V. Van der Eycken, *Chem. Commun.* **2017**, *53*, 6413−6416; c) A. A. Nechaev, K. Van Hecke, M. Zaman, S. Kashtanov, L. Ungur, O. P. Pereshivko, V. A. Peshkov, E. V. Van der Eycken, *J. Org. Chem.* **2018**, *83*, 8170–8182; d) Y. He, Z. Li, K. Robeyns, L. Van Meervelt, E. V. Van der Eycken, *Angew. Chem. Int. Ed.* **2018**, *57*, 272–276; e) X. Du, J. Huang, A. A. Nechaev, R. Yao, J. Gong, E. V. Van der Eycken, O. P. Pereshivko, V. A. Peshkov, *Beilstein J. Org. Chem.* **2018**, *14*, 2572–2579.

[8] a) S. G. Modha, A. Kumar, D. D. Vachhani, J. Jacobs, S. K. Sharma, Parmar, V. S.; L. Van Meervelt, E. V. Van der Eycken, *Angew. Chem. Int. Ed.* **2012**, *51*, 9572–9575; b) F. Schröder, N. Erdmann, T. Noël, R. Luque, E. V. Van der Eycken, *Adv. Synth. Catal.* **2015**, *357*, 3141–3147; c) F. Schröder, U. K. Sharma, M. Mertens, F. Devred, D. P. Debecker, R. Luque, E. V. Van der Eycken, *ACS Catal.* **2016**, *6*, 8156−8161; d) A. Kumar, Z. Li, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Chem. Commun.* **2013**, *49*, 6803–6805; e) D. D. Vachhani, A. Kumar, S. G. Modha, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Synthesis* **2015**, *47*, 1337–1347.

[9] a) S. G. Modha, A. Kumar, D. D. Vachhani, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Chem. Commun.* **2012**, *48*, 10916–10918; b) Z. Li, A. Kumar, D. D. Vachhani, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Eur. J. Org. Chem.* **2014**, 2084–2091; c) Z. Li, A. Kumar, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Tetrahedron* **2015**, *71*, 3333–3342.

[10] A. Kumar, D. D. Vachhani, S. G. Modha, S. K. Sharma, V. S. Parmar, E. V. Van der Eycken, *Synthesis* **2013**, *45*, 2571–2582.

[11] a) D. L. Wright, C. V. Robotham, K. Aboud, *Tetrahedron Lett.* **2002**, *43*, 943–946; b) C. P. Gordon, K. A. Young, M. J. Robertson, T. A. Hill, A. McCluskey, *Tetrahedron* **2011** , *67*, 554–561.

[12] For the post-Ugi transformations involving cleavage of the isocyanide-originated fragment, see: a) V. Tyagi, S. Khan, P. M. S. Chauhan, *Tetrahedron Lett.* **2013**, *54*, 1279–1284; b) T. T. T. Trang, A. A. Peshkov, J. Jacobs, L. Van Meervelt, V. A. Peshkov, E. V. Van der Eycken, *Tetrahedron Lett.* **2015**, *56*, 2882–2886. In the above processes the cleavage is achieved under basic conditions, while in our process it is assumed that the cleavage is triggered by a furan ring-opening.

[13] a) B. Martín-Matute, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2001**, *40*, 4754–4757; b) B. Martín-Matute, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *J. Am. Chem. Soc.* **2003**, *125*, 5757–5766; c) H. Yamamoto, I. Sasaki, H. Imagawa, M. Nishizawa, *Org. Lett.* **2007**, *9*, 1399−1402; d) A. S. K. Hashmi, M. Rudolph, H.-U. Siehl, M. Tanaka, J. W. Bats, W. Frey, *Chem. Eur. J.* **2008**, *14*, 3703–3708; e) Y. Chen, Y. Lu, G. Li, Y. Liu, *Org. Lett.* **2009**, *11*, 3838–3841; f) Y. Chen, G. Li, Y. Liu, *Adv. Synth. Catal.* **2011**, *353*, 392–400; g) Y. Chen, Y. Liu, *J. Org. Chem.* **2011**, *76*, 5274–5282; h) C. Wang, Y. Chen, X. Xie, J. Liu, Y. Liu, *J. Org. Chem.* **2012**, *77*, 1915−1921; i) A. S. K. Hashmi, M. Ghanbari, M. Rudolph, F. Rominger, *Chem. Eur. J.* **2012**, *18*, 8113–8119.

[14] Y. Yang, C. Fei, K. Wang, B. Liu, D. Jiang, B. Yin, *Org. Lett.* **2018**, *20*, 2273−2277.

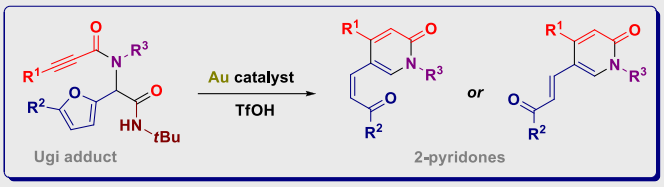
[15] CCDC 1889130 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

10.1002/ejoc.201900027

WILEY-VCH

Entry for the Table of Contents

COMMUNICATION



A gold-catalyzed post-Ugi cascade transformation for the synthesis of two types of 2-pyridones is described. The process involves furan-alkyne cyclization followed by a furan ring-opening and a cleavage of the isocyanide-originated fragment.

Cascade transformations

Xiaochen Du, Jiafeng Yu, Jing Gong, Manzoor Zaman, Olga P. Pereshivko, Vsevolod A. Peshkov**

Page No. – Page No.

Gold-catalyzed post-Ugi cascade transformation for the synthesis of 2-pyridones