Organic LETTERS

Letter

pubs.acs.org/OrgLett

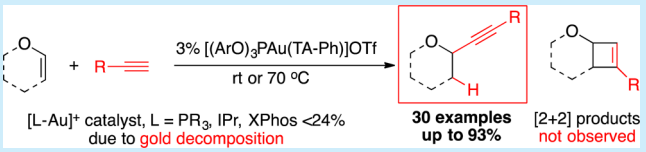
Gold-Catalyzed Vinyl Ether Hydroalkynylation: An Alternative Pathway for the Gold-Catalyzed Intermolecular Reaction of Alkenes and Alkynes

Seyedmorteza Hosseyni, Courtney A. Smith, and Xiaodong Shi*

The Department of Chemistry, University of South Florida, 4202 East Fowler Avenue, Tampa, Florida 33620, United States

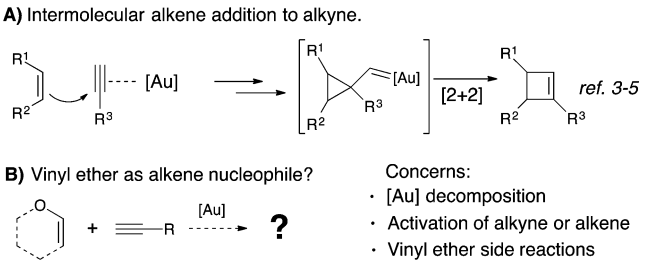
Supporting Information

ABSTRACT: In this report, the gold-catalyzed intermolecular reaction of vinyl ethers and terminal alkynes is investigated. Utilizing a triazole gold catalyst lessens gold decomposition in the presence of the vinyl ether and affords an alkynylation product instead of the [2 + 2] product. This protocol has been expanded to include glycal substrates, which undergo a one-pot alkynylation–Ferrier reaction to produce functionalized sugars in moderate to excellent yields with high diastereoselectivity.



Gold-catalyzed alkene and alkyne activation has greatly enriched synthetic research by providing new strategies of bond formation.[1] In general, Au(I) cations exhibit increased π-acid reactivity toward alkynes in comparison with alkenes. One illustration of this difference in reactivity is the gold-catalyzed enyne cycloisomerization, which is proven to be a powerful strategy for facile access to complex substrates.[2] In particular, the intermolecular enyne cycloisomerization of alkynes and alkenes, as reported by Echavarren and co-workers, produces diversified cyclobutenes.[3] This reaction commences with alkene nucleophilic addition to a gold-activated terminal alkyne (Scheme 1A).

Scheme 1. Au(I) Catalysis: Intermolecular Reactions of Alkenes and Alkynes



The final cyclobutene product is formed via ring expansion of a cyclopropane intermediate and subsequent elimination. This reaction is valuable because it enables straightforward access to the cyclobutene skeleton, which is challenging to synthesize using other methods. Moreover, this method has been successfully employed for macrocycle ring formation,[4] as well as for the total synthesis of natural products.[5] We wondered if using vinyl ethers as the alkene source would afford the analogous cyclobutene product.

Surprisingly, in sharp contrast to the previously reported [2 + 2] cycloaddition pathway, C-2-hydroalkynylation of the vinyl ether was obtained as the dominant product. Herein, we take advantage of the unique stability of TA-Au and report the TA-Au-catalyzed condensation of vinyl ethers and terminal alkynes.[6] This represents a divergent pathway of the gold-catalyzed intermolecular alkene–alkyne condensation reaction.

It is important to note that vinyl ethers have yet to be utilized as the alkene source in previous gold-catalyzed intermolecular alkene–alkyne condensations. Compared with regular alkenes, vinyl ethers bear a more electron-rich C=C double bond due to the donation of oxygen's electron density into the π system. This additional π-electron density may lead to decomposition (e.g., polymerization) of the vinyl ether substrate upon treatment with Lewis acids.[7] Furthermore, the high electron density of vinyl ethers may also accelerate $[L\text{-}Au]^+$ decomposition.

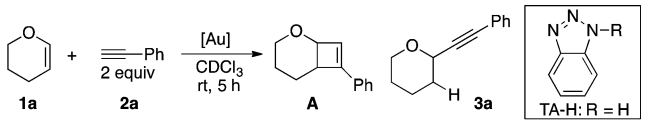
Our recent study involving the TA-Au-catalyzed enyne cycloisomerization of homopropargyl alcohols and terminal alkynes provides preliminary evidence in support of vinyl ether-promoted decomposition of Au. In this study, we demonstrated that the presence of vinyl ether leads to decomposition of $[L\text{-}Au]^+$. However, employing a triazole ligand, and thus a more stabilized gold complex, successfully prevented this catalyst decomposition.[8] Therefore, we postulated that the TA-Au catalyst may also be viable in our proposed transformation (Scheme 1B). To begin our investigation, we first evaluated the stability of PPh_3AuNTf_2 and $[PPh_3Au(TA\text{-}H)]OTf$ (TA-Au) in the presence of vinyl ether **1a** and 2 equiv of terminal alkyne **2a** (Scheme 2).

As shown in Scheme 2, monitoring the reaction with ^{31}P NMR confirmed the quantitative decomposition of PPh_3AuNTf_2 to form $(PPh_3)_2Au^+$ (eq 1).[9] Under identical conditions, less than 10% of $[PPh_3Au(TA\text{-}H)]OTf$ decomposed (eq 2), which highlights the improved stability of the TA-Au catalyst. Furthermore, reactions with either 5% PPh_3AuNTf_2 (eq 1) or 5% $[PPh_3Au(TA\text{-}H)]OTf$ (TA-Au) (eq 2) resulted in 100% conversion of the vinyl ether. However, no expected cyclobutene

Received: October 27, 2016

DOI: 10.1021/acs.orglett.6b03228
Org. Lett. XXXX, XXX, XXX–XXX

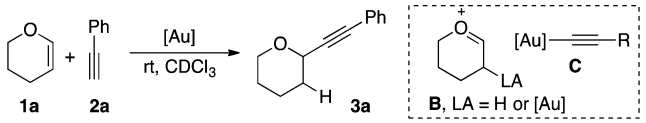
Scheme 2. Initial Evaluation of Propargyl Ether Synthesis



product **A** was observed. After careful analysis of the reaction mixture, the hydroalkynylation product **3a** was identified in both reactions as the only intermolecular condensation product incorporating both substrates.

Encouraged by these preliminary results, we conducted a detailed screening of the reaction conditions (Table 1).

Table 1. Optimization of the Reaction Conditions[a]



	catalyst	time (h)	conv (%)	yield[b] (%)
1	3% PPh_3AuNTf_2	2	100	24
2	3% $IPrAuNTf_2$	2	100	<10
3	3% $XPhosAuNTf_2$	2	100	16
4	3% $(ArO)_3PAuNTf_2$[c]	2	100	44
5	3% $(ArO)_3PAu$(TA-H)OTf[c]	4	100	54
6	3% $(ArO)_3PAu$(TA-Ph)OTf[c]	4	100	56
7	3% $(ArO)_3PAu$(TA-Ph)OTf[c] (**1a** was added slowly over 3 h)	6	100	78
8	other tested catalysts (5%): CuI, $Cu(OTf)_2$, $Ga(OTf)_3$, $ZnBr_2$, HOTf etc.	6	100	trace
9	other tested solvents: toluene, CH_3CN, THF, $MeNO_2$	6	100	<50

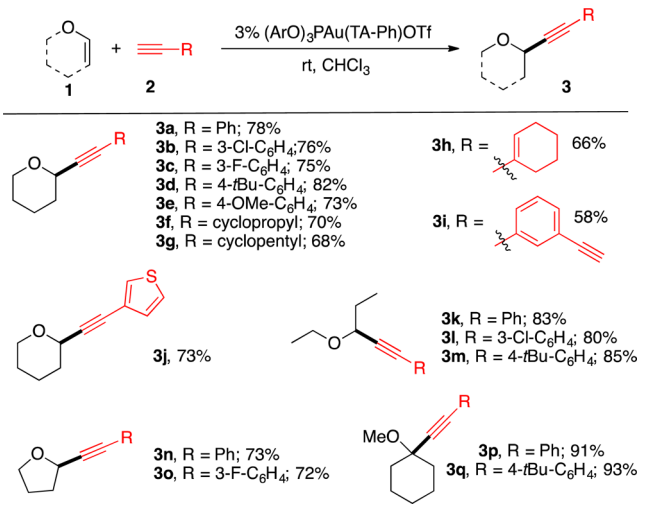
[a]Reaction conditions: Catalyst was added to a solution of **1a** (1 mmol) and **2a** (2 mmol) in $CDCl_3$ (1.33 mL) and the mixture stirred at room temperature. [b]^1H NMR yields were calculated using 1,3,5-trimethoxybenzene as an internal standard. [c]Ar = 2,4-di-*tert*-butylbenzene.

A small amount of the desired product was formed when PPh_3 was employed as the primary ligand (24%; entry 1). However, when an electron-rich, N-heterocyclic carbene ligand (10%; entry 2), or the bulky, electron-rich XPhos (2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl) ligand was used (16%; entry 3), the yield was diminished. Gratifyingly, switching to an electron-deficient phosphite ligand increased the yield to 44% (entry 4). This is likely due to the increased electrophilicity of its gold cation, which may favor the formation of gold acetylide **C**. The use of triazole−gold further increased the yields, reasonably attributed to the improved stability of the catalyst (entries 5 and 6). Monitoring the reaction via ^1H NMR indicated that the dihydropyran underwent self-condensation in the presence of gold. Theoretically, **1a** can attack intermediate **B** to produce undesired products. In support of this binding mode, Jones and co-workers have demonstrated that vinyl ethers can undergo complexation with gold to form η^1 or η^2 complexes.[10]

To provide evidence supporting the self-condensation of dihydropyran **1a** in the presence of gold, a control experiment was performed in which **1a** was reacted with TA-Au in the absence of **2a**. ^1H NMR monitoring indicated that vinyl ether **1a** converts to an uncharacterized dimerization product in the presence of gold. To avoid this self-condensation pathway, **1a** was added slowly to the reaction mixture over 3 h. Satisfyingly, this slow addition resulted in an increase in the yield to 78% (entry 7).

It is plausible that the formation of **3a** arises from alkyne addition to the oxocarbenium **B** that is formed in situ. Although an analogous metal-catalyzed hydroalkynylation of iminiums,[11] carbonyls,[12] and oxoniums[13] was previously reported, copper (I/II) salts were not able to promote the transformation. Other metal catalysts and acids also did not produce the desired product **3a** (entry 8). These results highlight the exceptional reactivity of the gold catalyst in promoting this challenging transformation. With the optimal conditions in hand, we investigated the scope of the reaction (Table 2).

Table 2. Substrate Scope of Propargyl Ether Synthesis[a,b]



[a]Reaction conditions: In a 2 mL vial, gold catalyst (0.03 mmol) was added to a solution of **2a** (2 mmol) in $CHCl_3$ (0.70 mL). The resulting reaction mixture was stirred, and **1a** (1 mmol) in 0.63 mL of $CHCl_3$ was added dropwise via syringe pump over 3 h. Isolated yields are reported. [b]Ar = 2,4-di-*tert*-butylbenzene.

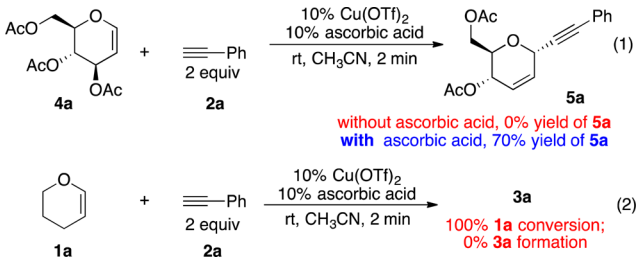
Fortunately, this reaction tolerates a wide range of vinyl ethers and alkynes. In evaluating the substrate scope of the alkyne, both electron-deficient (**3b,c,l,o**) and electron-rich (**3d,e,m**) aromatic alkynes produced good yields. Using *m*-diethynylbenzene yielded the monoalkynylation product **3i** in 58% yield. The conjugate enyne **3h** is also a viable substrate for this reaction, demonstrating the mildness of the conditions. Additionally, aliphatic alkynes bearing cyclopropyl (**3f**) and cyclopentyl (**3g**) substitutents can be used. A heteroaromatic-substituted alkyne was also tolerated, as the thiophene alkyne yielded 73% (**3j**). Concerning the reaction scope of vinyl ethers, both cyclic (**3a−j**; **3n,o**) and linear (**3k−m**) vinyl ethers afforded moderate yields of the desired product. However, monosubstituted vinyl ethers yielded the product in less than 30% yield, presumably due to their higher reactivity and relatively fast polymerization. Trisubstituted methyl vinyl ethers (**3p,q**) afforded the highest yield (91−93%) because of the aberrance of side products in comparison with di- and monosubstituted vinyl ethers. However, tetra-substituted vinyl ethers did not produce the desired product due to their low reactivity presumably from steric hindrance. In addition, using furan and benzofuran vinyl ether substrates resulted in low conversion due to the necessary disruption of aromaticity during the reaction. Overall, this reaction tolerated a wide range of alkynes and vinyl ethers.

DOI: 10.1021/acs.orglett.6b03228
Org. Lett. XXXX, XXX, XXX−XXX

After evaluating our new findings, we were keen to expand this chemistry to carbohydrate research. In recent years, gold catalysis has played a pivotal role in the development of glycosidation reactions.[14] We identified glycals, which contain a vinyl ether functional group, as an excellent substrate to expand our research.

It has been recently reported that a combination of ascorbic acid and $Cu(OTf)_2$ catalyzes the alkynylation and subsequent Ferrier-type elimination of glycal **4a** to produce **5a**.[15] We wondered whether this condition could be applied to unfunctionalized vinyl ethers. To demonstrate the difference in reactivity of **1a** and **5a**, we subjected **1a** and **2a** to this previously reported literature condition (Scheme 3). Surprisingly, no alkynylation product **3a** was observed under these conditions, and rapid decomposition of **1a** was detected via ^{1}H NMR.

Scheme 3. Copper-Catalyzed Reactions

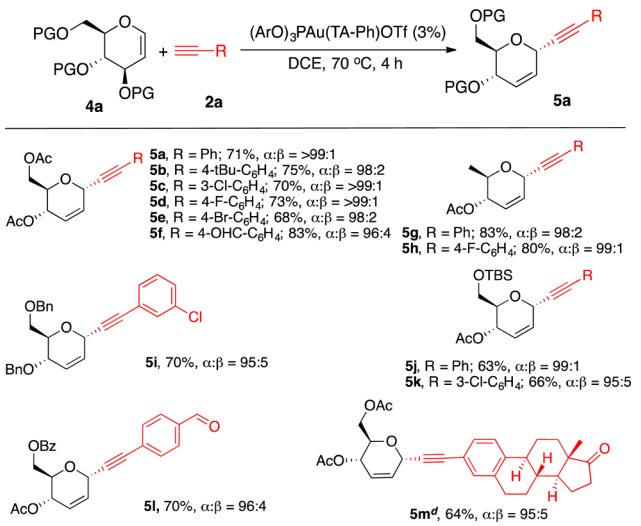


These results clearly highlight the enhanced reactivity of the gold catalytic method we have reported. Thus, to expand our reaction scope to include the Ferrier-type elimination of glycals, we subjected various glycal substrates to the optimized catalytic gold conditions. To ensure full conversion of the glycal, we increased the temperature to 70 °C. Rewardingly, moderate to excellent yields of the desired product **5a** were observed with only one diastereomer isolated for a majority of the substrates (Table 3). The diastereomeric ratio was determined via ^{1}H NMR, and the relative stereochemistry was assigned on the basis of previous literature reports.[16]

As with the reaction of simple vinyl ethers, a wide range of glycals could be used in the reaction. Glycals with −OAc (**5a**−**f**), −OBn (**5i**), or −OBz (**5l**) at the C-3 position were well tolerated. In addition, utilizing glycals bearing an OTBS substituent at the C-3 position of glycal could also afford the product in good yields (**5j**−**k**). Substrates with a methyl group at the C-6 position were used to investigate whether the presence of an OAc substituent at the C-6 position influenced the reaction yield or stereochemistry due to its proximity to the reaction center. The yield of these substrates bearing a C-6-methyl group did not vary considerably (**5g**,**h**). Notably, the cholesterol derivative **5m** was formed in moderate yield (64%), further illustrating the tolerance of the reaction. However, aliphatic alkynes were not compatible with the glycal transformation under the optimized reaction conditions.

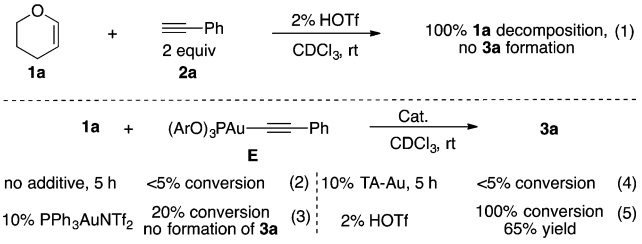
With the substrate scope of the transformation explored, we turned our attention to investigating the mechanism of the transformation. We synthesized gold acetylide **E** to test whether the intermediate could be used to form the desired product. Vinyl ether **1a** and gold acetylide **E** were subjected to a variety of conditions (Scheme 4). When **1a** and **2a** were treated with a catalytic amount of HOTf, **1a** underwent rapid decomposition and **3a** was not observed (eq 1). Treating **1a** with a stoichiometric amount (1 equiv) of gold acetylide **E** resulted in

Table 3. Substrate Scope of Glycosidation Reaction[a−c]



[a]Reaction conditions: In a 2 mL vial, gold catalyst (0.03 mmol) was added to a solution of **2a** (2 mmol) in 1,2-dichloroethane (1.33 mL), followed by addition of **4a** (1 mmol). The resulting mixture allowed stirring at 70 °C for 4 h. Isolated yields are reported unless otherwise stated. [b]Ar = 2,4-di-*tert*-butylbenzene. [c]Diastereomeric ratio determined via ^{1}H NMR. [d]^{1}H NMR yield was calculated using 1,3,5-trimethoxybenzene as an internal standard.

Scheme 4. Mechanistic Investigation



no conversion of the vinyl ether (eq 2). Adding 10% PPh_3AuNTf_2 and stoichiometric gold acetylide **E** to **1a** resulted in decomposition of both the gold catalyst and vinyl ether with no formation of the desired product (eq 3). Using the triazole gold catalyst $(ArO)_3PAu$(TA-Ph)OTf instead of PPh_3AuNTf_2 decreased the yield of the reaction due to the reduced reactivity of TA-Au (eq 4). Finally, treating **1a** with a combination of 2% HOTf and stoichiometric gold acetylide **E** afforded the desired product **3a** in 65% yield (eq 5).[17]

These results suggest that gold acetylide is the nucleophile for the observed hydroalkynylation reaction and that residual acid may promote the transformation. There are few instances of this reactivity mode of gold(I) found in the literature.[18] Furthermore, the main challenge of this class of reactions is avoiding vinyl ether promoted gold decomposition. This signifies the use of a triazole−gold catalyst, which is inherently more stable, in promoting this challenging transformation.

To conclude, herein we report the efficient reaction of vinyl ethers with terminal alkynes, producing a hydroalkynylation product. The previously reported [2 + 2] product was not observed in any of the studied cases, suggesting a new mechanistic route of this transformation. This reaction was performed under mild conditions and exhibits high functional group tolerance. A mechanistic investigation revealed the in situ generation of HOTf and gold acetylide as key components of the

DOI: 10.1021/acs.orglett.6b03228
Org. Lett. XXXX, XXX, XXX−XXX

reaction. An alkynylation−Ferrier reaction employing glycals was also realized, producing functionalized glycal derivatives with excellent diastereoselectivity.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03228.

Materials and methods, compound characterization, and NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xmshi@usf.edu.

ORCID

Xiaodong Shi: 0000-0002-3189-1315

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the NIH (1R01GM120240-01), NSF (CHE-1362057), and NSFC (21629201) for financial support.

■ REFERENCES

(1) For recent advances in gold catalysis, see: (a) Asiri, A. M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2016**, *45*, 4471−4503. (b) Zheng, Z.; Wang, Z.; Wang, Y.; Zhang, L. *Chem. Soc. Rev.* **2016**, *45*, 4448. (c) Pflästerer, S.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2016**, *45*, 1331−1367. (d) Khrakovsky, D. A.; Tao, C.; Johnson, M. W.; Thornbury, R. T.; Shevick, S. L.; Toste, F. D. *Angew. Chem., Int. Ed.* **2016**, *55*, 6079−6083. (e) Kawai, H.; Wolf, W. J.; DiPasquale, A. G.; Winston, M. S.; Toste, F. D. *J. Am. Chem. Soc.* **2016**, *138*, 587−593. (f) Ebule, R. E.; Malhotra, D.; Hammond, G. B.; Xu, B. *Adv. Synth. Catal.* **2016**, *358*, 1478−1481. (g) Johnson, J. S.; Chong, E.; Tu, K. N.; Blum, S. A. *Organometallics* **2016**, *35*, 655−659. (h) Gillie, A. D.; Reddy, R. J.; Davies, P. W. *Adv. Synth. Catal.* **2016**, *358*, 226−239. (i) Mokar, B. D.; Huple, D. B.; Liu, R.-S. *Angew. Chem., Int. Ed.* **2016**, *55*, 11892−11896. (j) McCallum, T.; Barriault, L. *Chem. Sci.* **2016**, *7*, 4754. (k) Pirovano, V.; Arpini, E.; Acqua, M. D.; Vicente, R.; Abbiati, G.; Rossi, E. *Adv. Synth. Catal.* **2016**, *358*, 403−409. (l) Lempke, L.; Ernst, A.; Kahl, F.; Weberskirch, R.; Krause, N. *Adv. Synth. Catal.* **2016**, *358*, 1491−1499. (m) Hosseyni, S.; Ding, S.; Su, Y.; Akhmedov, N. G.; Shi, X. *Chem. Commun.* **2016**, *52*, 296−299. (n) Jin, S.; Jiang, C.; Peng, X.; Shan, C.; Cui, S.; Niu, Y.; Liu, Y.; Lan, Y.; Liu, Y.; Cheng, M. *Org. Lett.* **2016**, *18*, 680−683. (o) Dorel, R.; Echavarren, A. M. *Chem. Rev.* **2015**, *115*, 9028−9072. (p) Lu, Z.; Han, J.; Hammond, G. B.; Xu, B. *Org. Lett.* **2015**, *17*, 4534−4537.

(2) For recent examples of enyne cycloisomerizations, see: (a) Chen, C.; Zou, Y.; Chen, X.; Zhang, X.; Rao, W.; Chan, P. W. H. *Org. Lett.* **2016**, *18*, 4730−4733. (b) Chen, G.-Q.; Fang, W.; Wei, Y.; Tang, X.-Y.; Shi, M. *Chem. Sci.* **2016**, *7*, 4318−4328. (c) Harris, R. J.; Widenhoefer, R. A. *Chem. Soc. Rev.* **2016**, *45*, 4533−4551. (d) Calleja, P.; Pablo, O.; Ranieri, B.; Gaydou, M.; Pitaval, A.; Moreno, M.; Raducan, M.; Echavarren, A. M. *Chem. - Eur. J.* **2016**, *22*, 13613−13618. (e) Asiri, A. M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2016**, *45*, 4471−4503. (f) Thummanapelli, S.; Hosseyni, S.; Su, Y.; Akhmedov, N.; Shi, X. *Chem. Commun.* **2016**, *52*, 7687−7690.

(3) For recent and original works on gold-catalyzed [2 + 2] reaction of alkyne and alkene, see: (a) de Orbe, E.; Echavarren, A. M. *Org. Synth.* **2016**, *93*, 115−126. (b) Obradors, C.; Echavarren, A. M. *Acc. Chem. Res.* **2014**, *47*, 902−912. (c) Homs, A.; Obradors, C.; Leboeuf, D.; Echavarren, A. M. *Adv. Synth. Catal.* **2014**, *356*, 221−228. (d) Muratore, M. E.; Homs, A.; Obradors, C.; Echavarren, A. M. *Chem. - Asian J.* **2014**, *9*, 3066−3082. (e) López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292−9294.

(4) Obradors, C.; Leboeuf, D.; Aydin, J.; Echavarren, A. M. *Org. Lett.* **2013**, *15*, 1576−1579.

(5) Ranieri, B.; Obradors, C.; Mato, M.; Echavarren, A. M. *Org. Lett.* **2016**, *18*, 1614−1617.

(6) Recent publications on TA-Au catalysis: (a) Motika, E. S.; Wang, Q.; Akhmedov, N. G.; Wojtas, L.; Shi, X. *Angew. Chem., Int. Ed.* **2016**, *55*, 11582−11586. (b) Yang, Y.; Qin, A.; Zhao, K.; Wang, D.; Shi, X. *Adv. Synth. Catal.* **2016**, *358*, 1433−1439. (c) Hosseyni, S.; Su, Y.; Shi, X. *Org. Lett.* **2015**, *17*, 6010−6013.

(7) (a) Aoshima, S.; Yoshida, T.; Kanazawa, A.; Kanaoka, S. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 1801−1813. (b) Hashmi, A. S. K.; Schäfer, S.; Göker, G.; Eisenbach, C. D.; Dirnberger, K.; Zhao-Karger, Z.; Crewdson, P. *Aust. J. Chem.* **2014**, *67*, 500−506. (c) Nzulu, F.; Telitel, S.; Stoffelbach, F.; Graff, B.; Morlet-Savary, F.; Lalevée, J.; Fensterbank, L.; Goddard, J. P.; Ollivier, C. *Polym. Chem.* **2015**, *6*, 4605−4611.

(8) Hosseyni, S.; Wojtas, L.; Li, M.; Shi, X. *J. Am. Chem. Soc.* **2016**, *138*, 3994−3997.

(9) Zhdanko, A.; Ströbele, M.; Maier, M. E. *Chem. - Eur. J.* **2012**, *18*, 14732−14744.

(10) (a) Sriram, M.; Zhu, Y.; Camp, A. M.; Day, C. S.; Jones, A. C. *Organometallics* **2014**, *33*, 4157−4164. (b) Zhu, Y.; Day, C. S.; Jones, A. C. *Organometallics* **2012**, *31*, 7332−7335. (c) Mazzone, G.; Russo, N.; Sicilia, E. *Organometallics* **2012**, *31*, 3074−3080. (d) Roithová, J.; Janková, S.; Jašíková, L.; Váňa, J.; Hybelbauerová, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 8378−8382.

(11) (a) Yin, L.; Otsuka, Y.; Takada, H.; Mouri, S.; Yazaki, R.; Kumagai, N.; Shibasaki, M. *Org. Lett.* **2013**, *15*, 698−701. (b) Han, J.; Xu, B.; Hammond, G. B. *J. Am. Chem. Soc.* **2010**, *132*, 916−917. (c) Gommermann, N.; Koradin, C.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 5763−5766.

(12) (a) Trost, B. M.; Bartlett, M. J.; Weiss, A. H.; Wangelin, A. J.; Chan, V. S. *Chem. - Eur. J.* **2012**, *18*, 16498−16509. (b) Trost, B. M.; Quintard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 6704−6708. (c) Takita, R.; Fukuta, Y.; Tsuji, R.; Ohshima, T.; Shibasaki, M. *Org. Lett.* **2005**, *7*, 1363−1366. (d) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806−1807. (e) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **1999**, *121*, 11245−11246.

(13) (a) Watson, M. P.; Maity, P. *Synlett* **2012**, *23*, 1705−1708. (b) Maity, M.; Srinivas, H. D.; Watson, M. P. *J. Am. Chem. Soc.* **2011**, *133*, 17142−17145.

(14) For gold catalyzed reactions in carbohydrate research see: (a) Zhu, Y.; Shen, Z.; Li, W.; Yu, B. *Org. Biomol. Chem.* **2016**, *14*, 1536−1539. (b) Shen, R.; Cao, X.; Laval, S.; Sun, J.; Yu, B. *J. Org. Chem.* **2016**, *81*, 10279−10294. (c) Liu, W.; Chen, Q.; Liang, J.; Du, Z.; Zhang, K.; Zheng, X.; O'Doherty, G. A. *Synlett* **2015**, *26*, 1683−1686. (d) Roy, R.; Rajasekaran, P.; Mallick, A.; Vankar, Y. D. *Eur. J. Org. Chem.* **2014**, *2014*, 5564−5573. (e) Adhikari, S.; Baryal, K. N.; Zhu, D.; Li, X.; Zhu, J. *ACS Catal.* **2013**, *3*, 57−60. (f) Tang, Y.; Li, J.; Zhu, Y.; Li, Y.; Yu, B. *J. Am. Chem. Soc.* **2013**, *135*, 18396−18405. (g) McKay, M. J.; Nguyen, H. M. *ACS Catal.* **2012**, *2*, 1563−1595. (h) Kayastha, A. K.; Hotha, S. *Chem. Commun.* **2012**, *48*, 7161−7163.

(15) (a) Kusunuru, A. K.; Tatina, M.; Yousuf, S. K.; Mukherjee, D. *Chem. Commun.* **2013**, *49*, 10154−10156. For additional examples of Cu/ascorbic acid catalysis, see: (b) Knöpfel, T. F.; Zarotti, P.; Ichikawa, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 9682−9683. (c) Knöpfel, T. F.; Carreira, E. M. *J. Am. Chem. Soc.* **2003**, *125*, 6054−6055.

(16) (a) Reddy, T. R.; Rao, D. S.; Kashyap, S. *RSC Adv.* **2015**, *5*, 28338−28343. (b) Tatina, M. B.; Kusunuru, A. K.; Yousuf, S. K.; Mukherjee, D. *Org. Biomol. Chem.* **2014**, *12*, 7900−7903. (c) Devari, S.; Kumar, M.; Deshidi, R.; Rizvi, M.; Shah, B. A. *Beilstein J. Org. Chem.* **2014**, *10*, 2649−2653. (d) Vieira, A. S.; Fiorante, P. F.; Hough, T. L. S.; Ferreira, F. P.; Lüdtke, D. S.; Stefani, H. A. *Org. Lett.* **2008**, *10*, 5215−5218.

(17) Grirrane, A.; Garcia, H.; Corma, A.; Álvarez, E. *ACS Catal.* **2011**, *1*, 1647−1653.

(18) Obradors, C.; Echavarren, A. M. *Chem. - Eur. J.* **2013**, *19*, 3547−3551.

DOI: 10.1021/acs.orglett.6b03228
Org. Lett. XXXX, XXX, XXX−XXX