Heterogeneous Gold-Catalyzed Selective Semireduction of Alkynes using Formic Acid as Hydrogen Source

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Abstract: A convenient and robust protocol for the selective transfer semireduction of alkynes was developed, using bio-renewable formic acid as the hydrogen source and easily handled supported gold nanoparticles as the catalyst. The catalytic system showed several attractive features such as high activity and selectivity, recyclability, scalability and adaptability to continuous operation under mild reaction conditions, thus providing a practical alternative to current methods for alkyne semireduction.

Keywords: alkynes; continuous operation; formic acid; semireduction; supported gold nanoparticles

Olefinic compounds constitute one of the largest classes of industrially synthesized organic chemicals and are important intermediates for a broad spectrum of products varying from petrochemicals to fine chemicals.^[1] Semireduction of alkynes is arguably the simplest and most straightforward approach to construct the olefinic linkage.^[2] The metal-catalyzed transfer semireduction (TSR)^[3-5] is attracting much attention because of its critical advantage over the conventional semihydrogenation method,^[6] which suffers from problems with over-reduction as well as safety concerns.^[7] Of special interest in this regard is the use of bio-renewable formic acid (FA) as safe and convenient hydrogen source, essentially owing to its inherent hydrogen donating capabilities as compared to most other TSR agents.^[8] In this context, TSR of alkynes in the presence of FA represents an area of growing importance and a variety of homogeneous metal-based TSR systems have been developed.^[5a-f] Despite their usefulness, the recovery of the costly and potentially toxic transition metals remains as a critical issue toward the development of a greener and more sustainable chemical synthesis. Therefore,

there is a pressing need to develop new recoverable and reusable catalysts that can enable rapid, ligandfree and chemoselective TSR of alkynes.

Heterogeneous catalysis by gold is a key emerging area with promise to enable the development of innovative methods for chemo- and regiocontrolled reductions.^[9] As a continuation of our efforts to exploit the potential of Au-catalyzed reductions,^[10] we recently discovered the outstanding catalytic ability of supported Au nanoparticles (NPs) for the reduction of nitroaromatics to anilines^[10f] as well as quinoline derivatives to their corresponding 1,2,3,4-tetrahydroquinolines^[10g] using FA as a terminal reductant. Given the clear benefits of adopting the Au-based transfer reduction protocols, we became attracted to the possibility of utilizing the Au-FA combination to develop new catalytic processes that enable selective alkyne semireduction under mild and heterogeneous conditions. Herein, we report an efficient, versatile, and scalable approach to the FA-mediated reductive transformation of alkyne compounds using a simple supported gold catalyst system under mild and clean conditions. The present Au-catalyzed, FA-mediated alkyne TSR system has the following noteworthy features: (i) unprecedented high catalytic efficiency toward alkene production under very mild and ligand-free conditions, (ii) high selectivity over very sensitive competing groups, and (iii) robust durability and easy compatibility with continuous flow systems.

At the outset of our studies we choose the reduction of phenylacetylene (**1a**) as the reaction model. We initially applied the procedures elaborated for the base-free transfer reduction of nitro compounds^[10f] to anilines at 60 °C in the presence of 5 equiv. of FA using Au deposited on single-phase rutile titania (Au/ TiO₂-R, see details in the Supporting Information) as a benchmark system. However, the reduction hardly occurred and no trace of styrene (**2a**) could be detected (Table 1, entry 1), despite an effort to optimize these screening assays by extending the reaction time Table 1. Semireduction of phenylacetylene (1a) to styrene (2a) using various catalysts.^[a]



Entry	Catalysts ^[b]	Hydrogen Source ^[c]	Temperature [°C]	Time [h]	Conversion ^[d] [%]	Selectivity ^[d] [%]
1	0.5% Au/TiO ₂ -R	FA	60	0.5	trace	_
2	0.5% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	56	>99
3	0.3% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	77	>99
4 ^[e]	0.3% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	75	>99
5	0.3% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.7	99	>99
6 ^[f]	0.3% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	25	2	99	>99
7 ^[g]	0.3% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	20	98	>99
8	0.8% Au/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	52	>99
9	0.1% Au/TiO ₂ -R	FA/NEt_3 (3:2)	60	0.5	76	>99
10 ^[h]	0.5% Au/TiO ₂ -R	H ₂	60	0.5	12	94
11	0.5% Au/TiO ₂ -R	H_3PO_2	60	0.5	trace	_
12	0.5% Au/TiO ₂ -R	2-propanol	60	0.5	trace	_
13	0.5% Au/TiO ₂ -A	FA/NEt_{3} (3:2)	60	0.5	28	>99
14	0.5% Au/TiO ₂ -P25	FA/NEt_3 (3:2)	60	0.5	47	>99
15	0.5% Au/ZrO ₂	FA/NEt ₃ (3:2)	60	0.5	11	>99
16	0.5% Au/CeO ₂	FA/NEt_3 (3:2)	60	0.5	5	>99
17	0.5% Au/Al ₂ O ₃	FA/NEt ₃ (3:2)	60	0.5	8	>99
18	0.5% Au/SiO ₂	FA/NEt_3 (3:2)	60	0.5	trace	_
19	AuNPore	FA/NEt ₃ (3:2)	60	0.5	trace	_
20	0.5% Pd/TiO ₂ -R	FA/NEt_3 (3:2)	60	0.5	trace	_
21	0.5% Pt/TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	trace	_
22	0.5% Ru/TiO ₂ -R	FA/NEt_3 (3:2)	60	0.5	trace	_
23	TiO ₂ -R	FA/NEt ₃ (3:2)	60	0.5	n.r.	_

^[a] *Reaction conditions:* **1a** (0.5 mmol), metal (0.5 mol%), hydrogen source (5 equiv.), acetone (2 mL).

^[b] The values given before the catalysts represent the weight content of the active metal deposited on solid supports.

^[c] Ratio of FA/NEt₃ is based on molar ratio.

^[d] Conversion and selectivity determined by GC using *p*-xylene as an internal standard. n.r. = no reaction.

^[e] Fifth run.

^[f] Catalyst (Au: 1 mol%), FA (15 equiv.).

^[g] **1a** (10 mmol), catalyst (Au: 0.05 mol%), FA (5 equiv.), acetone (10 mL).

^[h] H_2 introduced by bubbling.

or elevating the reaction temperature (Supporting Information, Table S1, entries 1–3). Alternative approaches by adding a small amount of base additives were investigated, and while a modest improvement was observed with triethanolamine or diethanolamine, NEt₃ was identified as a particularly effective base promoter (Supporting Information, Table S1, entries 4-7). Subsequent investigation focused on the influence of the NEt₃ concentration and led to the discovery of a 3:2 FA/NEt₃ mixture is capable of affording by far the most efficient conversion of 1a to 2a (Supporting Information, Table S1, entries 7–12). Among the solvents tested, acetone was found to be the most suitable medium for desired TSR (Supporting Information, Table S2). Importantly, no conversion was observed in the absence of the Au NPs (Table 1, entry 23).

These results prompted us to further optimize the Au/TiO₂-R system by altering the Au content during

the preparation procedure, which has proven quite influential for supported Au catalysts.^[10e,h] Finally, the optimized Au/TiO₂-R with a gold content of 0.3 wt% was carefully prepared by using a modified deposition-precipitation (DP) with NaOH procedure, designated as 0.3% Au/TiO₂-R. With this catalyst, it is possible to accomplish quantitative 1a-to-2a conversion within only 0.7 h at 60 °C (Table 1, entry 5). Notably, the selective transformation of **1a** to **2a** can still proceed smoothly to the end at temperatures as low as 25°C (entry 6). More relevant is that with this particular Au/TiO₂-R-FA combination the reaction was operative even upon decreasing the Au loading to 0.05 mol% (entry 7). Thus, in a gram-scale reaction of 1a (20-fold scale-up) for 20 h, a 98% yield of 2a was obtained (Supporting Information, Figure S1). In this case, remarkable values of the turnover number (TON = 1960) and initial turnover frequency (TOF = $300 h^{-1}$) were calculated. Already, these results represent the best catalyst productivities ever reported for previous FA-mediated TSR systems (Supporting Information, Table S3).^[5]

Besides TiO_2 -R, other polymorphic forms of TiO_2 as well as ZrO₂, Al₂O₃, CeO₂ and SiO₂ were also tested as supporting substrates for the TSR reaction. Whereas single-phase anatase TiO₂ supported Au gave quite a low yield of 2a (Table 1, entry 13), gold NPs loaded on commercial P25 (anatase/rutile=4/1) showed only moderate activity (Table 1, entry 14). Meanwhile, the performances of other supported Au catalysts were very poor under identical conditions (entries 15-18), showing that the coupling of rutile TiO₂ with Au NPs is essential for achieving a high TSR activity. Note that the use of the nanoporous Au catalyst without a support resulted in only a trace of 1a conversion (entry 19), further confirming the importance of the support in this efficient TSR system. After the reaction, the optimized 0.3% Au/TiO₂-R was readily separated from the reaction mixture by simple filtration and could be reused without loss of its activity or selectivity (entries 3 and 4). Inductively coupled plasma (ICP-AES) analysis showed the absence of Au species in the filtrate after the reaction (detection limit of 0.1 ppm), confirming that no leaching occurred during the reaction. Transmission electron microscopy (TEM) and X-ray photoelectron spectroscopy (XPS) measurements of 0.3% Au/TiO₂-R after the reuse revealed almost no change in the Au dispersion or metallic state of Au before and after reuse, corroborating the durability of 0.3% Au/TiO₂-R in the recycling experiments (Supporting Information, Figures S2–S5).

We confirmed in separate experiments that FA conversion in the presence of alkyne was much higher than the corresponding conversion in the absence of alkyne over 0.3% Au/TiO₂-R (Supporting Information, Table S4). Moreover, when replacing FA with H₂, much lower yields of 2a were achieved under otherwise identical reaction conditions and a certain amount of the over-reduced product is generated at such low **1a** conversion levels (Table 1, entry 10). Meanwhile, variation of the hydrogen source revealed that FA is the most effective (entries 11 and 12). Overall these results show that the present FA-mediated reaction is a TSR process and mechanisms entailing semihydrogenation utilizing H₂ gas in situ generated from the FA decomposition are not likely operating. To further understand the reaction pathways involved in the present Au/TiO₂-R-catalyzed semireduction, the kinetic isotope effect (KIE) was measured (Supporting Information, Table S5). When the substrate was allowed to react with HCOOD, the transformation of **1a** at low conversion levels (< 15%), with respect to that with HCOOH, gives $k_{\rm HCOOH}/k_{\rm HCOOD} = 1.04$. Meanwhile, the use of DCOOH or DCOOD instead of HCOOH in the semireduction of **1a** led to the observation of normal primary KIEs $(k_{\text{HCOOH}}/k_{\text{DCOOH}}=4.13, k_{\text{HCOOH}}/k_{\text{DCOOD}}=4.22)$. Taken together, these results indicate that the FA dissociation with the C–H bond cleavage at the catalyst surface is the rate-determining step of the present alkyne semireduction reaction.

Consistent with the case identified for catalytic reduction of nitroarenes to anilines using FA,^[10f] we found that gold is uniquely active for TSR of alkynes with FA compared with other noble metals (Table 1, entries 20-22). To gain an insight into the origin of the enhanced TSR activity achieved by using rutile TiO_2 as support, the decomposition of FA in the absence of 1a has been investigated for Au NPs deposited on different supports (Supporting Information, Figure S6). It is revealed that the lower performances observed with Au/TiO₂-A, Au/Al₂O₃, Au/CeO₂ and Au/SiO₂ are due to the fact that the FA decomposition rate catalyzed by these catalysts is significantly lower than that over the Au/TiO₂-R sample. This scenario is reinforced by another set of control assays showing that the FA decomposition over 0.3% Au/ TiO₂-R also occurred with much higher rates than that over other Au/TiO2-R-based materials with higher Au loadings. At this juncture, it is interesting to note that Au/ZrO₂ can only afford very limited TSR activity under otherwise identical conditions, despite the effectiveness of this material for FA dehvdrogenation.^[11] This could be rationalized by the fact that although a high FA activation activity is a prerequisite for TSR performance, the competitive pathway that favors unproductive FA decomposition should be minimized.

On the basis of the above observations and the known chemistry regarding the Au-mediated reaction of alkynes,^[12] we propose a catalytic cycle involving an unusual alkyne-assisted activation of the FA molecules over the supported Au NPs (Scheme 1). Although the precise way by which the hydrogen transfers from HCOOH to alkyne remains to be clarified at this stage, it is important to emphasize that an initial fast adsorption of alkynes onto Au NPs (Step 1) can be established based on the kinetic studies (Supporting Information, Figure S7, an unusual broken order concentration dependency of alkynes).^[8c,13] Subsequent adsorption of FA leads to the formation of Au-H⁺NEt₃ and Au-formate species, which are believed to be the key intermediates for the transfer reduction (Step 2). Eventually, the two hydrogen atoms from these two different species were rapidly consumed by the chemisorbed alkyne species generated in the first step, together with a final formation of the alkene products (Step 3). In the overall reaction, the unique alkynophilicity of small Au NPs (Supporting Information, Figure S3, data for XPS) attached to TiO₂-R thus may be one key aspect in leading to



Scheme 1. A proposed mechanism for the heterogeneous gold-catalyzed FA-mediated TSR of alkynes.

a facile Au-formate decarboxylation for the highly selective alkyne semireduction.

Building upon these results, we then extended our studies to various kinds of alkynes to establish the scope of this Au-FA-based TSR system. As depicted in Table 2, various structurally diverse terminal alkynes, including activated, inactivated, and heterocyclic ones, can be transformed into the corresponding alkenes in excellent yields without any over-reduced products being detected. These results are remarkable as the terminal alkynes are generally too active to stay in the partially reduced state in most conventional procedures.^[5] More significantly, a wide variety of synthetically useful functional groups, both electronwithdrawing and electron-donating, were not affected in the semireduction (entries 2-9). For example, halogen-substituted phenylacetylenes are selectivity transformed into the corresponding chloro- or fluorostyrenes with no observation of dehalogenation (Table 2, entries 3 and 4), which quite often occurs in the cases of other metal catalysts. Other reducible functional moieties are also tolerated, including ester, ether and ketone substituents (entries 5-9). Moreover, this Au-FA-mediated TSR process is not limited to arylalkynes, the semireduction of aliphatic alkynes can also be readily and efficiently achieved under the standard reaction conditions (Table 2, entry 10). The reaction was also adaptable to the semireduction of substrates bearing unprotected hydroxy groups to synthetically useful allyl alcohols (entry 11).

Furthermore, the Au-FA protocol also shows excellent promise for the semireduction of internal alkynes. It should be stressed that this transformation is generally more difficult than that of terminal alkynes owing to the steric hindrance of these molecules, and controlling the stereoselectivity of the reaction presents a further challenge.^[14] In line with the syn-addition manner as prevailing in heterogeneous semireduction processes,^[6] (Z)-alkenes are mostly formed from a wide range of simple and functionalized internal alkynes (Table 2, entries 12-16, 18-20). Interestingly, it turns out to be an exception for 4-phenyl-3-butyn-2one that an exclusive E-stereoselectivity is achieved (entry 17), which might result from the low activation energy of thee *cis-trans* isomerism for such α,β -ethylenic ketone structures. Notably, the semireductions of non-polar internal alkynes such as diphenylacetylene and 1-phenyl-1-propyne proceed quite smoothly under mild conditions in the present Au-FA system (entries 12 and 13), in contrast to the case with our previous Au-CO/H₂O system wherein elevated temperature and relatively long reaction time are required to facilitate the reduction kinetics.^[10d] Moreover, (Z)-3-hexen-1-ol (leaf alcohol), which is a commercially important fragrance material, can also be readily obtained as a sole product in 86% isolated yield (Table 2, entry 20).

Given the recognized merits of continuous processing,^[15] a flow system was implemented for 1a semireduction using the present Au-mediated TSR protocol (reaction conditions: 200 mg 0.3% Au/TiO₂-R, $0.25 \text{ mol } L^{-1}$ **1a**, $1.25 \text{ mol } L^{-1}$ FA, $0.83 \text{ mol } L^{-1}$ NEt₃, acetone as solvent, see the Supporting Information for details). At 60 °C with a flow rate of 4.5 mLh^{-1} , the reaction proceeded smoothly to afford the product quantitatively, corresponding to a space-time yield of 1.9 mol_{2a} $h^{-1}g_{Au}^{-1}$. Note that this value is considerably higher than that obtained for the batch-type reaction under identical conditions (*ca.* 1.4 mol_{2a} $h^{-1}g_{Au}^{-1}$, see Table 1, entry 5), underscoring the potential of the continuous method for intensified processing. It was shown that the exclusive selectivity toward 2a formation can be retained during the continuous operation, albeit with a progressive decrease in 1a conversions from 99% to 85% after 180 min on stream. It was noteworthy, however, that the activity of the spent catalyst could be recovered after the treatment in acetone (0.5 mLmin⁻¹ for 30 min),^[16] without significant loss of 2a yields after the regeneration (Figure 1, see the Supportinbg Information for details). As such, the turnover number (TON) after 9 h under these conditions approached 3,200, a notably higher number as compared with typical batch-type FA-based TSR systems.^[5] These results, while preliminary, suggest that this Au-FA-based continuous-flow TSR procedure holds great promise to develop more efficient yet substantially safer means for target-specific transformation of alkynes to the corresponding alkenes.

In summary, we have developed a practical and convenient protocol for selective semireduction of alkynes using green and bio-renewable FA as the terminal reductant. Driven by a simple and robust hetero-



		R ²	0.3% Au/TiO ₂ -R		R ¹	
		R ¹ 3:2 FA/N	NEt ₃ (5 equiv.), acetone	e (2 mL), 60 °C	R^2	
		1 : 0.5 mmol			2	
Entry	Substrate 1	Product 2		Entry	Substrate 1	Product 2
1		R = H 2a : 0.7	h 99%			
2		R = 3-M 2b : 0.7	le h 99%	13		
3		R = 3-C 2c: 0.5	l h 99%		1m	2m : 3 h 95% (85%), Z-sel. = 97%
4	Ř 1a−f	R R = 4-F 2a-f 2d: 0.5	h 99%	14		
5		R = 4-0 2e : 0.9 l	Me n 99%	0		
6		R = 4-C 2f : 0.5 h	OMe 1 99%		1n	96% (87%), Z-sel. = 99% Br
7				15		Br
	1g	2g : 0.5 h 99%		Br	10	2o : 2 h Br 98% (95%) Z-sel > 99%
8	0, s, 0	0, 0 , 5, 0 , 5, 0 , 0		16 O		
	1h	2h : 0.5 h 99% (85%)			0 1p	Ö 2p : 2 h 96% (82%), <i>Z</i> -sel. = 98%
9	N 1i	2i: 6 h		17		0 2q: 1 h
		98%	_		O	99% (89%), <i>E</i> -sel. > 99%
10 >	1j	2j : 3 h 96%		18		0 2r: 1 h
11	ОН	OH		19	ОН	98% (85%), Z-sel. > 99%
	1k	2k : 1h 96%			1s	2s : 1 h 99% (88%), Z-sel. > 99%
12	11	21: 3h	10/	20	HO	HO 2t: 2h
		93%, ∠-sei. > 99	770		- •	93% (86%), Z-sel. > 99%

^[a] Yield and selectivity determined by GC; numbers in parenthesis refer to isolated yield.

geneous gold catalyst, which enables the transfer semireduction by a remarkably facile and controlled alkyne-assisted FA activation, the protocol is efficient, operationally simple, scalable and readily adapted to a continuous-flow procedure, providing a valuable alternative to currently used methods for the transformation of alkynes to the corresponding alkenes.



Figure 1. Recycling experiments of the continuous-flow FAmediated TSR of **1a** over 0.3% Au/TiO₂-R. *Reaction conditions:* 200 mg catalyst, 0.25 mol L⁻¹ **1a**, 1.25 mol L⁻¹ FA, 0.83 mol L⁻¹ NEt₃, flow rate = 4.5 mL h^{-1} , 60 °C.

Experimental Section

General Procedure for the Transfer Semireduction of Alkynes with Formic Acid

The mixture of substrate (0.5 mmol), catalyst (metal: 0.5 mol%), formic acid (5 equiv.) as a FA/NEt₃ (3:2) mixture, acetone (2 mL) was added to a flask (10 mL) equipped with a reflux condenser. The resulting mixture was allowed to reflux with vigorous stirring (800 rpm) at 60 °C. After completion of the reaction, the reaction mixture was filtered and the filtrate was washed with water and extracted by ethyl acetate. The mixture was concentrated and dried under reduced pressure to give the crude product, which was purified by silica gel chromatography eluting with petroleum ether (60–90 °C)/ethyl acetate mixture. The conversion and selectivity were determined by GC-FID using *p*xylene as an internal standard.

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- [16] Consistent with the batch-type cases (Supporting Information, Figure S2), we confirmed that the Au leaching and the increase in Au particle size did not occur after the regeneration treatment. Thus, the decrease in 1a conversion with time-on-stream may arise from accumulation of olefinic oligomers on the active sites of the 0.3% Au/TiO₂-R material. Further investigation of the associated catalyst deactivation is ongoing in our laboratory.