A Heterogeneous Gold(I)-Catalyzed [2 + 2 + 1] Annulation of Terminal Alkynes, Nitriles, and Oxygen Atoms Leading to 2,5-Disubstituted Oxazoles

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Supporting Information

ABSTRACT: The first heterogeneous gold(I)-catalyzed [2 + 2 + 1] annulation of terminal alkynes, nitriles, and oxygen atoms has been achieved by using an MCM-41-immobilized phosphine-gold(I) complex as catalyst and 8-methylquinoline *N*-oxide as oxidant under mild conditions, yielding a variety of 2,5-disubstituted oxazoles in good to excellent yields with broad substrate scope. The new heterogeneous gold(I) catalyst can easily be recovered by simple filtration of the reaction solution and recycled for at least eight times without significant loss of activity.



Oxazoles with their 2 and 5 positions substituted with aryl or alkyl groups are privileged scaffolds found in many pharmacologically active synthetic molecules and natural products, which exhibit numerous significant biological activities and unique properties.¹ These oxazoles are also important synthetic intermediates in organic synthesis.² Subsequently, a variety of methods have been developed to form oxazoles, such as metal/ halogen-promoted intramolecular cyclization of acyclic precursors,³ transition-metal-catalyzed bimolecular annulation,⁴ oxidation of oxazolines,⁵ the C-C coupling of prefunctionalized oxazoles with various organometallic reagents,⁶ and other elegant protocols recently reported.⁷ However, most of these methods suffer from some drawbacks such as low atom efficiency, inaccessible starting materials, limited substrate scope and the use of stoichiometric amounts of sometimes toxic transition metal catalysts or oxidants. Hence, development of a more eco-friendly procedure for the synthesis of oxazole derivatives under mild conditions from readily available starting materials still represents a continuing challenge.

Homogeneous gold catalysis is among innovative projects of modern organic synthesis, and Au(I) or Au(III) complexes have evolved as mild Lewis acid catalysts for organic transformations requiring the activation of π bonds in the past two decades.⁸ Recently, gold(I) or gold(III)-catalyzed [3 + 2] cycloaddition⁹ and intramolecular cyclization of propargylic amides¹⁰ for the synthesis of oxazole derivatives under mild conditions have attracted considerable interest. The gold(I)-catalyzed one-pot heterocyclization of terminal alkynes with nitriles or cyanamides in the presence of an oxygen-delivering oxidant has provided a simple and efficient approach to 2,5-disubstituted oxazoles (Scheme 1a and 1b).¹¹ Li et al. described



Scheme 1. Homogeneous Gold(I)-Catalyzed Synthesis of Oxazoles

a. Gold(I)-catalyzed annulation of terminal alkynes with nitriles

$$R \longrightarrow \frac{Ph_{3}PAuNTf_{2} (5 \text{ mol}\%)}{N} \xrightarrow{R} \xrightarrow{Ph_{3}PAuNTf_{2} (5 \text{ mol}\%)} (1.3 \text{ equiv}), R^{1}-CN, 60 \text{ °C}$$

b. Gold(I)-catalyzed heterocyclization of terminal alkynes with cyanamides

$$R^{1} = + N = -N \begin{pmatrix} R^{2} & \frac{Ph_{3}PAuNTf_{2} (3 \text{ mol}\%)}{MeSO_{3}H (1.2 \text{ equiv})} \\ Me & N \end{pmatrix} \begin{pmatrix} R^{1} & N \end{pmatrix} \begin{pmatrix} R^{2} & N \end{pmatrix}$$

c. Gold(I)-catalyzed tandem reactions of amide-aldehyde-alkyne coupling and cyclization

d. Gold(I)-catalyzed annulation of a-diazo oxime ethers with nitriles



a gold(I)-catalyzed tandem reaction of amide–aldehyde– alkyne coupling and cyclization leading to 2,4,5-trisubstituted oxazoles (Scheme 1c).¹² Very recently, Park and co-workers

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reported a gold(I)-catalyzed annulation of α -diazo oxime ethers and nitriles, providing an alternative method for the synthesis of 2,4,5-trisubstituted oxazoles (Scheme 1d).¹³

Although these gold-catalyzed syntheses of oxazole derivatives are highly efficient, industrial applications of these homogeneous gold complexes remain a challenge because they are quite expensive, not recyclable, and difficult to separate from the product, which is a particularly significant drawback for their application in the pharmaceutical industry. Immobilization of homogeneous catalysts on various porous materials with high surface areas is usually the method of choice because the supported catalysts can be easily recovered by a simple filtration process after reactions.¹⁴ The discovery of mesoporous MCM-41 materials has provided a new possible candidate for an ideal support to immobilize homogeneous catalysts and given an enormous stimulus to research in heterogeneous transition-metal catalysis.¹⁵ The hexagonally ordered MCM-41 material possesses large and uniform pore size, ultrahigh surface area, big pore volume, and rich silanol groups in the inner walls.¹⁶ To date, some functionalized MCM-41-supported palladium,¹⁷ rhodium,¹⁸ molybdenum,¹⁹ gold,²⁰ and copper²¹ complexes have been successfully used as potentially green and sustainable catalysts in organic reactions. Recently, we reported the carbonylative cross-coupling reactions of aryl iodides with organostannanes,^{17d} arylboronic acids,^{17e} and triarylbismuths^{17f} catalyzed by immobilization of palladium in MCM-41 and the C-N and C-S bond formation reactions catalyzed by immobilization of copper in MCM-41²¹ with facile separation and recyclability of the catalysts. However, to the best of our knowledge, no example of a heterogeneous gold-catalyzed synthesis of oxazoles has been reported until now. In continuing our efforts to develop efficient heterogeneous transition-metal catalysts for organic synthesis,^{17d-f,21} herein we report the first synthesis of an MCM-41-immobilized phosphine gold(I) complex [MCM-41- PPh_3 -AuNTf₂] and its successful application to the [2 + 2 + 1] annulation of terminal alkynes, nitriles, and oxygen atoms from an oxidant leading to 2,5-disubstituted oxazoles (Scheme 2).

Scheme 2. Heterogeneous Gold(I)-Catalyzed Synthesis of 2,5-Disubstituted Oxazoles from Terminal Alkynes and Nitriles



The new heterogeneous gold(I) catalyst exhibits high catalytic activity in the reaction under mild reaction conditions and can easily be recovered from the reaction mixture by a simple filtration of the reaction solution, and its catalytic efficiency remains unaltered even after recycling eight times.

RESULTS AND DISCUSSION

The MCM-41-immobilized phosphine gold(I) complex [MCM-41–PPh₃–AuNTf₂] was synthesized according to the procedure summarized in Scheme 3. First, the mesoporous material MCM-41 reacted with 1-(4-(diphenylphosphino)-phenyl)-3-(3-(triethoxysilyl)propyl)urea²² in toluene at 100

Scheme 3. Synthesis of the MCM-41–PPh₃–AuNTf₂ Complex



°C for 24 h, followed by the silylation with Me₃SiCl in toluene at room temperature for 24 h to afford triphenylphosphinefunctionalized MCM-41 (MCM-41–PPh₃). The latter was subsequently treated with Me₂SAuCl and AgNTf₂ in dichloromethane (DCM) at room temperature to generate the MCM-41-immobilized phosphine gold(I) complex [MCM-41–PPh₃– AuNTf₂] as a gray powder, and the gold content of the complex was found to be 0.25 mmol g⁻¹ according to the ICP-AES measurements. The MCM-41–PPh₃–AuNTf₂ complex was characterized by small-angle X-ray powder diffraction (XRD) [Figure S1] and energy-dispersive X-ray spectroscopy (EDS) [Figure S2] [see Supporting Information].

The MCM-41-PPh₃-AuNTf₂ complex was then used as catalyst for the [2 + 2 + 1] annulation of terminal alkynes, nitriles, and oxygen atoms from an oxidant. Initial experiments with phenylacetylene (1a) and acetonitrile (2a) as both the reacting partner and the solvent were performed to optimize the reaction conditions, and the results are summarized in Table 1. At first, different N-oxides as oxidants were tested at 60 °C in the presence of 5 mol % MCM-41-PPh3-AuNTf2 complex (entries 1-6). Among the oxidants examined, pyridine N-oxide (A), 3,5-dichloropyridine N-oxide (B), 2,6-dibromopyridine N-oxide (C), and 2.4-dichloropyridine N-oxide (D) afforded a low to moderate yield (entries 1-4), both quinoline N-oxides (E and F) gave good results and 8-methylquinoline N-oxide (E) was the best choice (entries 5 and 6). When a homogeneous gold(I) complex was used as catalyst, the desired product 3a was isolated in 92% yield (entry 7), indicating that the catalytic activity of MCM-41-PPh₃-AuNTf₂ complex was comparable to that of Ph₃PAuNTf₂. The special catalytic role of gold(I) in this annulation was demonstrated by the inability of AgNTf₂ and HNTf₂ to catalyze this reaction (entries 8 and 9). In order to examine the effect of the support on the reaction, we prepared a magnetic nanoparticle-immobilized phosphine gold(I) complex (Fe₃O₄@SiO₂-PPh₃-AuNTf₂) by using a silica-coated Fe₃O₄ (Fe₃O₄@SiO₂) as the support instead of MCM-41 according to the procedure summarized in Scheme 3. However, when Fe₃O₄@SiO₂-PPh₃-AuNTf₂ was used as the catalyst, only a trace of the desired product 3a was formed (entry 10). The effect of the linker on the reaction was also examined by replacing 1-(4-(diphenylphosphino)phenyl)-3-(3-(triethoxysilyl)propyl)urea with a commercially available $(EtO)_3Si(CH_2)_2PPh_2$ in the procedure outlined in Scheme 3 to prepare another MCM-41-immobilized phosphine gold(I) complex [MCM-41-PPh₂-AuNTf₂]. The MCM-41-PPh₂-





entry	catalyst (mol %)	oxidant	temp (°C)	time (h)	yield (%) ^b
1	MCM-41–PPh ₃ –AuNTf ₂ (5)	Α	60	8	49
2	MCM-41– PPh_3 –AuNTf ₂ (5)	В	60	8	51
3	MCM-41– PPh_3 –AuNTf ₂ (5)	С	60	8	15
4	MCM-41– PPh_3 –AuNTf ₂ (5)	D	60	8	57
5	MCM-41– PPh_3 –AuNTf ₂ (5)	Ε	60	8	91 ^c
6	MCM-41–PPh ₃ –AuNTf ₂ (5)	F	60	8	77
7	$Ph_3PAuNTf_2$ (5)	Ε	60	4	92
8	$AgNTf_2$ (5)	Ε	60	24	0
9	$HNTf_2$ (5)	Ε	60	24	0
10	Fe_3O_4 @SiO_2-PPh_3-AuNTf_2(5)	Ε	60	24	trace
11	MCM-41– PPh_2 –AuNTf ₂ (5)	Ε	60	12	58
12	MCM-41–PPh ₃ –AuNTf ₂ (5)	Ε	25	24	0
13	MCM-41– PPh_3 –AuNTf ₂ (5)	Ε	40	24	11
14	MCM-41– PPh_3 –AuNTf ₂ (5)	Ε	80	8	85
15	MCM-41– PPh_3 –AuNTf ₂ (2.5)	Ε	60	24	79^d
16	MCM-41– PPh_3 –AuNTf ₂ (1.0)	Ε	60	48	42
17	MCM-41–PPh ₃ –AuNTf ₂ (10)	Ε	60	3	90
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^{*a*}Reaction conditions: 1a (0.3 mmol), oxidant (1.3 equiv) in MeCN (3 mL) under air. ^{*b*}Isolated yield. ^{*c*}TON and TOF was 18.2 and 2.3 h⁻¹, respectively. ^{*d*}TON and TOF was 31.6 and 1.3 h⁻¹, respectively.

AuNTf₂ complex could afford a moderate yield of 3a (entry 11). The effect of temperature on the model reaction was also investigated (Table 1, entries 5 and 12–14). The reaction did not work at room temperature, the reaction at 60 °C gave the best result, and other temperatures were substantially less effective. Reducing the amount of the catalyst to 2.5 mol % resulted in a lower yield, and a long reaction time was required (entry 15). When the amount of the catalyst was further decreased to 1.0 mol %, the reaction proceeded slowly and the desired product 3a was isolated in only 42% yield after 48 h (entry 16). Increasing the amount of the catalyst could shorten the reaction time but did not improve the yield (entry 17). Thus, the optimized conditions for this transformation are the MCM-41-PPh₃-AuNTf₂ (5 mol %), and 8-methylquinoline N-oxide (1.3 equiv) in acetonitrile as both the reacting partner and the solvent at 60 °C under air for 8 h (Table 1, entry 5).

With this promising result in hand, we started to investigate the scope of this heterogeneous gold(I)-catalyzed [2 + 2 + 1]annulation reaction under the optimized conditions, and the results are summarized in Table 2. First, various terminal alkynes were examined by using acetonitrile as the nitrile source. As shown in Table 2, a wide range of terminal arylacetylenes having different electronic and steric natures were allowed to react with acetonitrile. The electron-rich substituted phenylacetylenes 1b-e gave the desired products 3b-e in good to excellent yields. In contrast, the electrondeficient substituted phenylacetylenes 1f and 1g showed slightly lower reactivity and afforded the corresponding oxazoles 3f and 3g in 74 and 73% yield, respectively. A disubstituted phenylacetylene 1h and a biphenylacetylene 1i proved to be also good alkyne substrates and could react with acetonitrile effectively to give the desired products 3h and 3i in good yields. The reactions of sterically congested arylacetylenes such as 2-methylphenylacetylene 1j and 2-chlorophenylacetylene 1k were still serviceable even if ortho substitution did decrease the reaction yields due to steric hindrance. The bulky 1-naphthylacetylene could give the desired oxazole 31 in 72% yield. It is noteworthy that 1,4-diethynylbenzene 1m was selectively converted to an acetylene-containing oxazole 3m in 74% yield, which can be further functionalized. In addition to arylacetylenes, aliphatic terminal alkynes such as 1-hexyne 1n, 5-chloro-1-pentyne 10, and 5-phenyl-1-pentyne 1p underwent the annulation with acetonitrile smoothly to afford the corresponding products 3n-p in 71-88% yields. Cycloalkylacetylenes 1q and 1r were also suitable alkyne substrates and gave the desired oxazoles 3q and 3r in 76 and 84% yield, respectively. Interestingly, alkylacetylenes bearing a free carboxylic acid moiety or an acid-labile THP group 1s and 1t could react with acetonitrile effectively to furnish the expected oxazoles 3s and 3t in high yields. The scope of alkyne substrates can be expanded to heteroarylacetylenes. For example, the reaction of 3-ethynylthiophene 1u with acetonitrile gave the desired oxazole 3u in 78% yield. However, with propargyl alcohols and their derivatives as alkyne substrates, a complex mixture was formed due to the presence of intramolecular trapping of the α -oxo gold carbene intermediates as a major side reaction.²³ Similarly, propargyl amides and propargyl bromide were not good alkyne substrates.

This annulation reaction also permitted the use of other nitriles as both the reacting partner and the solvent. For example, isobutyronitrile 2b could react with phenylacetylene 1a and cyclopropylacetylene 1q smoothly to afford the desired oxazoles 3v and 3w in high yields. Phenylacetonitrile 2c underwent the annulation with phenylacetylene 1a effectively to give the expected oxazole 3x in 75% yield. Besides these three aliphatic nitriles, aromatic nitriles such as benzonitrile 2d and 4-methylbenzonitrile 2e were also good nitrile sources, and reactions with aryl- or alkylacetylenes proceeded smoothly,



"Reaction conditions: 1 (0.3 mmol), E (1.3 equiv) in R¹-CN (3 mL) at 60 °C under air for 8 h. ^bIsolated yield. ^cFor 24 h.

affording functionalized oxazoles 3y-3b' in good yields. In addition, a heterocyclic nitrile such as thiophene-2-carbonitrile 2f also proved to be a suitable nitrile source, and the reaction with 1d afforded the expected product 3c' in a moderate yield. Only when nitriles were used both as reagent and the reaction solvent did the annulation reaction proceed smoothly because nitriles could react with the gold carbene intermediate rapidly enough that some side reactions would be largely suppressed. So, when an expensive or not readily available nitrile was used as the substrate, the reaction must be carried out by using at least 3.0 equiv of the nitrile under solvent-free conditions; however, the solvent-free conditions were not suitable for heterogeneous catalysis. The present method provides a quite general, simple, and practical route for the synthesis of a variety of 2,5-disubstituted oxazoles from commercially available alkynes and nitriles. A range of functional groups were easily tolerated, including a free carboxylic acid moiety, an acid-labile THP group, an alkyl chloride, a cyclopropyl group, bulky 1naphthyl and tert-butyl groups, thienyl, and aryl groups having different electronic and steric natures.

To verify whether the observed catalysis was due to the heterogeneous catalyst MCM-41–PPh₃–AuNTf₂ or to a leached gold species in solution, we performed the hot filtration test.²⁴ For this, the reaction of phenylacetylene with acetonitrile was carried out until a conversion of 30%. Then the catalyst was removed from the solution at 60 °C by filtration, and the filtrate

was allowed to react further. In this case, no significant increase in conversion was observed, indicating that leached gold species from the catalyst (if any) are not responsible for the observed activity. It was also confirmed by ICP-AES analysis that no gold species could be detected in the filtrate. These results show that the gold(I) complex remains on the support at elevated temperatures during the reaction and the observed catalysis was intrinsically heterogeneous.

A plausible mechanism for heterogeneous gold(I)-catalyzed [2 + 2 + 1] annulation reaction of alkynes 1 and nitriles 2 with 8-methylquinoline *N*-oxide is illustrated in Scheme 4.²⁵ First, coordination of the MCM-41–PPh₃–AuNTf₂ complex to the C–C triple bond in terminal alkyne 1 gives an MCM-41-anchored phosphine–Au alkyne complex (A). The latter undergoes the reaction with an oxygen-delivering oxidant to produce an MCM-41-anchored phosphine-gold carbene intermediate (B) via an addition–elimination process. Then the nucleophilic attack by nitrile 2 on the gold carbene intermediate B affords the intermediate C. Finally, intermediate C can undergo the intramolecular cyclization to give the desired oxazole 3 and regenerate the MCM-41–PPh₃–AuNTf₂ complex.

For the practical application of a heterogeneous precious metal catalyst system, its ease of separation, stability, and reusability are important factors. The MCM-41–PPh₃–AuNTf₂ can be easily separated and recovered by a simple filtration of

Scheme 4. Proposed Catalytic Cycle



the reaction solution. We next examined the recycling of the catalyst by using the annulation reaction of phenylacetylene **1a** with acetonitrile. After carrying out the reaction, the catalyst was recovered by simple filtration and washed with ethyl acetate and diethyl ether. After being air-dried, it can be reused directly without further purification. The recovered gold catalyst was used in the next run, and almost consistent activity was observed for eight consecutive cycles (Figure 1). In



addition, the Au leaching in the supported catalyst was also determined by ICP-AES analysis. The gold content of the catalyst was found to be 0.24 mmol g^{-1} after eight consecutive runs, indicating that only 4% of gold had been lost from the MCM-41 support.

CONCLUSIONS

We have developed an efficient intermolecular reaction of α oxo gold carbenes generated via heterogeneous gold(I)catalyzed alkyne oxidation with nitriles leading to a variety of 2,5-disubstituted oxazoles in mostly good to excellent yields. This heterogeneous [2 + 2 + 1] annulation has many attractive features, such as (1) the substrate scope is broad, and a wide range of alkynes and nitriles are allowed, (2) the reaction conditions are exceptionally mild, (3) the reaction is tolerant of a range of functional groups including a free carboxylic acid moiety and an acid-labile THP group, and (4) this heterogeneous gold(I) catalyst can easily be prepared via a simple procedure from commercially readily available reagents, recovered by filtration of the reaction solution, and recycled for at least eight times without significant loss of activity.

EXPERIMENTAL SECTION

General Methods. All chemicals were reagent grade and used as purchased. The mesoporous MCM-41¹⁶ and 1-(4-(diphenylphosphino)phenyl)-3-(3-(triethoxysilyl)propyl)urea²² were prepared according to the literature methods. The silica-coated Fe₃O₄ (Fe₃O₄@ SiO_2) was prepared according to our previous procedure.²⁶ The products were purified by flash chromatography on silica gel. A mixture of EtOAc and light petroleum ether was generally used as eluent. All products were characterized by comparison of their spectra and physical data with those of authentic samples. IR spectra were recorded on an FT-IR spectrometer. ¹H and ¹³C NMR spectra were recorded at 400 or 100 MHz with CDCl₃ as the solvent and TMS as an internal standard. Chemical shifts are reported in δ (ppm) relative to TMS. HRMS spectra were recorded on a Q-Tof spectrometer with micromass MS software using electrospray ionization (ESI). Melting points are uncorrected. Gold content was determined with inductively coupled plasma atom emission spectrometry (ICP-AES). X-ray diffraction (XRD) measurements were carried out at room temperature using an X-ray powder diffractmeter. X-ray energy-dispersive spectroscopy (EDS) was performed using a microscope.

Preparation of MCM-41–PPh₃–AuNTf₂ and MCM-41–PPh₂–AuNTf₂ Complexes. 1-(4-(Diphenylphosphino)phenyl)-3-(3-(triethoxysilyl)propyl)urea (0.525 g, 1 mmol) was added to a suspension of 2.0 g of the MCM-41 in 100 mL of dry toluene. The mixture was stirred at 100 °C for 24 h under Ar. Then the solid was filtered, washed with CHCl₃ (2 × 20 mL), and dried in vacuum at 150 °C for 5 h. The dried white solid was then soaked in a solution of 2.5 g of Me₃SiCl in 80 mL of dry toluene at room temperature under stirring for 24 h. The solid product was filtered, washed with acetone (3 × 20 mL), and dried in vacuum at 120 °C for 5 h to obtain 2.367 g of hybrid material MCM-41-PPh₃. The phosphine content was found to be 0.36 mmol g⁻¹ by elemental analysis.

In a small Schlenk tube, 1.00 g of the above-functionalized MCM-41 (MCM-41–PPh₃) was mixed with Me₂SAuCl (83 mg, 0.28 mmol) in 30 mL of dry CH₂Cl₂. The mixture was stirred at room temperature for 8 h under an argon atmosphere. The precipitate was filtered off, washed with CH₂Cl₂, and then treated with AgNTf₂ (107 mg, 0.28 mmol) in CH₂Cl₂ (30 mL) at room temperature for 0.5 h. The solid product was filtered, washed with NH₃·H₂O (2 × 10 mL), distilled water, and EtOH, and dried under vacuum to give 1.039 g of a gray-gold complex (MCM-41–PPh₃–AuNTf₂). The gold content was found to be 0.25 mmol g⁻¹ by ICP-AES.

The MCM-41–PPh₂–AuNTf₂ complex was prepared by using $(EtO)_3Si(CH_2)_2PPh_2$ (0.377 g, 1 mmol) as the starting material in the same manner, the gold content was found to be 0.27 mmol g⁻¹ by ICP-AES.

Preparation of Fe₃O₄@SiO₂-PPh₃-AuNTf₂ Complex. To a suspension of 0.75 g of Fe₃O₄@SiO₂ in 30 mL of dry toluene was added a solution of 1-(4-(diphenylphosphino)phenyl)-3-(3-(triethoxysilyl)propyl)urea (0.263g, 0.5 mmol) in 10 mL of dry toluene. The mixture was stirred at 110 °C under argon atmosphere for 24 h. Then the resulting material was magnetically separated, washed repeatedly with toluene and CH₂Cl₂ to remove any unanchored species, and dried at 100 °C under vacuum for 5 h to afford 0.89 g of the triphenylphosphine-functionalized Fe₃O₄@SiO₂ (Fe₃O₄@SiO₂-PPh₃) as brown nanoparticles. The phosphine content was found to be 0.28 mmol g⁻¹ by elemental analysis.

In a small Schlenk tube, 0.5 g of Fe₃O₄@SiO₂-PPh₃ was mixed with Me₂SAuCl (42 mg, 0.14 mmol) in 15 mL of dry CH₂Cl₂. The mixture was stirred at room temperature for 8 h under an argon atmosphere. The solid material was magnetically separated, washed with CH₂Cl₂, and then treated with AgNTf₂ (53 mg, 0.14 mmol) in CH₂Cl₂ (15 mL) at room temperature for 0.5 h. The solid product was magnetically separated, washed with NH₃·H₂O (2 × 10 mL), distilled water, and EtOH, and dried under vacuum to give 0.519 g of Fe₃O₄@

 $SiO_2-PPh_3-AuNTf_2$ as brown nanoparticles. The gold content was found to be 0.21 mmol g^{-1} by ICP-AES.

General Procedure for the Heterogeneous Gold-Catalyzed Oxazole Formation. 8-Methylquinoline N-oxide (E, 62 mg, 0.39 mmol) and MCM-41–PPh₃–AuNTf₂ (60 mg, 0.015 mmol) were added to a solution of a terminal alkyne 1 (0.3 mmol) in nitrile 2 (3 mL) at 60 °C. The reaction mixture was stirred at 60 °C for 8–24 h. After being cooled to room temperature, the catalyst was separated by a simple filtration of the reaction solution, washed with ethyl acetate (2 × 5 mL) and diethyl ether (2 × 5 mL), and reused in the next run. The filtrate was concentrated under reduced pressure, and the residue was purified by chromatography on silica gel (eluent: light petroleum ether/ethyl acetate = 5:1) to afford the oxazole product 3.

2-Methyl-5-phenyloxazole (**3a**).²⁷ Light yellow solid (43.4 mg, 91%). Mp 58–59 °C. IR (KBr): 2925, 1696, 1558, 1451, 942, 766, 690 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.64–7.57 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.20 (s, 1H), 2.53 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.0, 151.1, 128.8, 128.2, 128.1, 123.9, 121.9, 14.1.

2-Methyl-5-(4-methylphenyl)oxazole (**3b**).²⁷ Light yellow solid (46.2 mg, 89%). Mp 57–58 °C. IR (KBr): 2923, 1646, 1596, 1554, 1060, 956, 824, 817 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 2.51 (s, 3H), 2.37 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.6, 151.3, 138.1, 129.5, 125.5, 123.9, 121.2, 21.3, 14.0.

5-(4-Butylphenyl)-2-methyloxazole (**3c**). Light yellow oil (55.5 mg, 86%). IR (neat): 2927, 1651, 1597, 1548, 1063, 954, 826 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.50 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.14 (s, 1H), 2.61 (t, J = 7.8 Hz, 2H), 2.50 (s, 3H), 1.65–1.55 (m, 2H), 1.41–1.30 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.7, 151.4, 143.1, 128.9, 125.7, 123.9, 121.2, 35.4, 33.5, 22.3, 14.0, 13.9. HRMS calcd for C₁₄H₁₇NO⁺ [M⁺]: 215.1310, found 215.1314.

5-(4-Methoxyphenyl)-2-methyloxazole (**3d**).²⁷ Light yellow solid (52.2 mg, 92%). Mp 89–90 °C. IR (KBr): 2962, 2837, 1585, 1506, 1028, 832, 814, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.51 (d, *J* = 8.8 Hz, 2H), 7.06 (s, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 2.49 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.3, 159.6, 151.1, 125.5, 121.1, 120.3, 114.3, 55.3, 14.0.

2-Methyl-5-(3-methylphenyl)oxazole (**3e**).²⁷ Light yellow oil (42.6 mg, 82%). IR (neat): 2925, 1643, 1587, 1546, 1083, 946, 816, 760 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.45–7.38 (m, 2H), 7.32–7.26 (m, 1H), 7.18 (s, 1H), 7.12 (d, J = 7.6 Hz, 1H), 2.52 (s, 3H), 2.39 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.9, 151.3, 138.5, 128.9, 128.8, 128.1, 124.6, 121.8, 121.1, 21.4, 14.0.

5-(4-Chlorophenyl)-2-methyloxazole (**3f**).²⁷ Light yellow solid (43.0 mg, 74%). Mp 84–85 °C. IR (KBr): 2924, 1641, 1599, 1442, 1059, 941, 812 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.56–7.51 (m, 2H), 7.41–7.34 (m, 2H), 7.19 (s, 1H), 2.52 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.3, 150.2, 133.9, 129.1, 126.7, 125.2, 122.3, 14.0.

5-(4-Bromophenyl)-2-methyloxazole (**3g**).²⁷ Light yellow solid (52.1 mg, 73%). Mp 82–83 °C. IR (KBr): 2922, 1664, 1574, 1550, 1360, 1077, 948, 817 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.53 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.21 (s, 1H), 2.52 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.3, 150.2, 132.0, 127.1, 125.4, 122.4, 121.9, 14.1.

5-(3-Chloro-4-methylphenyl)-2-methyloxazole (**3h**). Light yellow oil (48.6 mg, 78%). IR (neat): 2923, 1639, 1579, 1472, 1063, 931, 822 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.59 (d, *J* = 1.6 Hz, 1H), 7.40–7.35 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 2.52 (s, 3H), 2.39 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.2, 150.0, 135.9, 135.0, 131.4, 127.4, 124.5, 122.2, 122.1, 19.9, 14.1. HRMS calcd for C₁₁H₁₀ClNO⁺ [M⁺]: 207.0451, found 207.0446.

5-(4'-Ethylbiphenyl-4-yl)-2-methyloxazole (**3i**). White solid (66.4 mg, 84%). Mp 160–162 °C. IR (KBr): 2926, 1661, 1594, 1548, 1365, 1059, 942, 821 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.65 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.22 (s, 1H), 2.69 (q, *J* = 7.6 Hz, 2H), 2.53 (s, 3H), 1.27 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.1, 151.0,

143.8, 140.8, 137.7, 128.4, 127.3, 126.9, 126.8, 124.3, 121.9, 28.6, 15.6, 14.1. HRMS calcd for $C_{18}H_{17}NO^+$ [M⁺]: 263.1310, found 263.1322.

2-Methyl-5-(2-methylphenyl)oxazole (**3j**).^{11a} Light yellow oil (31.7 mg, 61%). IR (neat): 2927, 1648, 1585, 1557, 1142, 1092, 762 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.69–7.63 (m, 1H), 7.30–7.22 (m, 3H), 7.10 (s, 1H), 2.54 (s, 3H), 2.46 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.7, 150.5, 134.7, 131.1, 128.1, 127.5, 126.6, 126.1, 124.8, 21.8, 14.0.

5-(2-Chlorophenyl)-2-methyloxazole (**3k**). Brown oil (36.6 mg, 63%). IR (neat): 2924, 1645, 1575, 1448, 1061, 934, 760 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.77 (dd, J = 8.0, 1.6 Hz, 1H), 7.64 (s, 1H), 7.47–7.44 (m, 1H), 7.36–7.30 (m, 1H), 7.26–7.20 (m, 1H), 2.54 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.0, 147.7, 134.3, 130.6, 130.4, 128.6, 127.5, 127.1, 127.0, 14.0. HRMS calcd for C₁₀H₈CINO⁺ [M⁺]: 193.0294, found 193.0296.

2-Methyl-5-(naphthalen-1-yl)oxazole (**3**). Red brown oil (45.2 mg, 72%). IR (neat): 2923, 1639, 1592, 1578, 1345, 1083, 825, 746 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.26 (d, J = 8.0 Hz, 1H), 7.90–7.83 (m, 2H), 7.70 (d, J = 7.6 Hz, 1H), 7.57–7.47 (m, 3H), 7.29 (s, 1H), 2.59 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.3, 150.2, 133.9, 130.1, 129.3, 128.7, 126.9, 126.2, 126.1, 125.6, 125.3, 125.2, 124.9, 14.1. HRMS calcd for C₁₄H₁₁NO⁺ [M⁺]: 209.0841, found 209.0840.

5-(4-Ethynylphenyl)-2-methyloxazole (**3m**). Light yellow solid (40.7 mg, 74%). Mp 119–120 °C. IR (KBr): 3291, 2926, 2127, 1593, 1578, 1059, 949, 743 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.57–7.54 (m, 2H), 7.53–7.50 (m, 2H), 7.23 (s, 1H), 3.14 (s, 1H), 2.53 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.5, 150.4, 132.6, 128.4, 123.7, 122.9, 121.7, 83.3, 78.3, 14.1. HRMS calcd for C₁₂H₉NO⁺ [M⁺]: 183.0684, found 183.0678.

5-Butyl-2-methyloxazole (**3n**). Light yellow oil (29.6 mg, 71%). IR (neat): 2954, 1579, 1445, 1222, 1118, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.57 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.40 (s, 3H), 1.64–1.56 (m, 2H), 1.41–1.32 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.1, 152.7, 121.8, 29.7, 25.2, 22.1, 13.9, 13.7. HRMS calcd for C₈H₁₃NO⁺ [M⁺]: 139.0997, found 139.0989.

5-(3-Chloropropyl)-2-methyloxazole (**30**). Light yellow oil (39.3 mg, 82%). IR (neat): 2956, 1578, 1446, 1223, 1120, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.65 (s, 1H), 3.57 (t, *J* = 6.4 Hz, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 2.13–2.03 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 160.6, 150.7, 122.8, 43.7, 30.5, 22.7, 13.9. C₇H₁₀ClNO⁺ [M⁺]: 159.0451, found 159.0455.

2-Methyl-5-(3-phenylpropyl)oxazole (**3p**). Light yellow oil (53.1 mg, 88%). IR (neat): 2926, 1693, 1577, 1447, 1364, 1121, 751, 698 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.31–7.26 (m, 2H), 7.22–7.14 (m, 3H), 6.59 (s, 1H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.40 (s, 3H), 2.00–1.91 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 160.2, 152.2, 141.5, 128.5, 128.4, 126.0, 122.2, 35.1, 29.2, 24.9, 13.9. HRMS calcd for C₁₃H₁₅NO⁺ [M⁺]: 201.1154, found 201.1159.

5-Cyclopropyl-2-methyloxazole (**3q**). Light yellow oil (28.1 mg, 76%). IR (neat): 2972, 2359, 1614, 1569, 976, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.55 (s, 1H), 2.38 (s, 3H), 1.86–1.79 (m, 1H), 0.91–0.76 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): δ 159.7, 149.7, 121.0, 14.2, 13.9, 6.2. HRMS calcd for C₇H₉NO⁺ [M⁺]: 123.0684, found 123.0691.

5-Cyclohexyl-2-methyloxazole (**3r**).^{11a} Light yellow oil (41.6 mg, 84%). IR (neat): 2930, 2361, 1579, 1450, 1219, 754 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.54 (s, 1H), 2.65–2.54 (m, 1H), 2.39 (s, 3H), 2.02–1.95 (m, 2H), 1.81–1.67 (m, 3H), 1.42–1.29 (m, 5H). ¹³C NMR (100 MHz, CDCl₃): δ 159.8, 157.1, 120.2, 35.2, 31.1, 26.0, 25.7, 13.9.

5-(2-Methyloxazol-5-yl)pentanoic Acid (**3s**).^{11a} Light yellow solid (45.6 mg, 83%). Mp 76–77 °C. IR (KBr): 3115, 2942, 2358, 1696, 1262, 751 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.06 (br, 1H), 6.64 (s, 1H), 2.66–2.58 (m, 2H), 2.42 (s, 3H), 2.41–2.35 (m, 2H), 1.75–1.66 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): δ 177.6, 160.6, 152.2, 121.4, 33.8, 27.0, 25.2, 24.2, 13.7.

2-Methyl-5-[2-(tetrahydropyran-2-yloxy)ethyl]oxazole (**3t**).^{11a} Red brown oil (50.7 mg, 80%). IR (neat): 2942, 2873, 1579, 1384, 1123, 1035 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.68 (s, 1H), 4.62 (t, *J* = 3.4 Hz, 1H), 4.00–3.91 (m, 1H), 3.85–3.74 (m, 1H), 3.70– 3.59 (m, 1H), 3.55–3.44 (m, 1H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.41 (s, 3H), 1.85–1.76 (m, 1H), 1.74–1.66 (m, 1H), 1.61–1.47 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): δ 160.4, 149.7, 123.1, 98.7, 64.9, 62.2, 30.5, 26.5, 25.4, 19.4, 13.9.

2-Methyl-5-(thiophen-3-yl)oxazole (**3u**). Light yellow oil (38.7 mg, 78%). IR (neat): 2928, 2875, 1583, 1495, 1387, 1126, 1027 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.47–7.44 (m, 1H), 7.38–7.34 (m, 1H), 7.28–7.24 (m, 1H), 7.04 (s, 1H), 2.50 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 160.4, 148.0, 129.4, 126.7, 124.4, 121.4, 120.0, 14.0. HRMS calcd for C₈H₇NOS⁺ [M⁺]: 165.0248, found 165.0253.

2-Isopropyl-5-phenyloxazole (**3v**).²⁷ Light yellow oil (50.1 mg, 89%). IR (neat): 2974, 1569, 1456, 1276, 748, 699 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.61 (d, J = 7.6 Hz, 2H), 7.39 (t, J = 7.6 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 7.21 (s, 1H), 3.20–3.09 (m, 1H), 1.40 (d, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 168.7, 150.7, 128.8, 128.4, 128.1, 124.0, 121.6, 28.6, 20.5.

5-Cyclopropyl-2-isopropyloxazole (**3w**).^{11a} Light yellow oil (39.1 mg, 86%). IR (neat): 2973, 2359, 1612, 1569, 976, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.55 (s, 1H), 3.05–2.95 (m, 1H), 1.88–1.78 (m, 1H), 1.31 (d, *J* = 7.2 Hz, 6H), 0.92–0.88 (m, 2H), 0.77–0.70 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 167.4, 153.7, 120.7, 28.4, 20.4, 6.3, 6.2.

2-Benzyl-5-phenyloxazole (**3x**).²⁷ Light yellow solid (52.9 mg, 75%). Mp 50–52 °C. IR (KBr): 2925, 2359, 1565, 1453, 1106, 751, 697 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.62–7.57 (m, 2H), 7.43–7.24 (m, 9H), 4.18 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 162.6, 151.5, 135.5, 128.8, 128.7, 128.3, 128.2, 128.1, 127.1, 124.1, 122.0, 34.8.

2,5-Diphenyloxazole (**3y**).²⁷ White solid (47.8 mg, 72%). Mp 74–75 °C. IR (KBr): 2361, 1446, 1276, 1135, 762, 687 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.11 (dd, J = 7.4, 1.8 Hz, 2H), 7.74–7.71 (m, 2H), 7.51–7.41 (m, 6H), 7.34 (t, J = 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 161.2, 151.3, 130.3, 128.9, 128.8, 128.5, 128.1, 127.5, 126.3, 124.2, 123.5.

5-Butyl-2-phenyloxazole (**3z**). Light yellow oil (50.1 mg, 83%). IR (neat): 3028, 2926, 1597, 1454, 1120, 750, 712 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.48–7.38 (m, 3H), 6.83 (s, 1H), 2.72 (t, *J* = 7.4 Hz, 2H), 1.73–1.64 (m, 2H), 1.48–1.38 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 160.6, 153.3, 129.8, 128.7, 127.9, 126.0, 123.6, 29.8, 25.4, 22.2, 13.7. HRMS calcd for C₁₃H₁₅NO⁺ [M⁺]: 201.1154, found 201.1146.

5-tert-Butyl-2-phenyloxazole (**3a**'). Light yellow oil (37.4 mg, 62%). IR (neat): 2967, 2359, 1576, 1314, 955, 753 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.01 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.46–7.38 (m, 3H), 6.79 (s, 1H), 1.36 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 161.0, 160.4, 129.9, 128.7, 128.0, 126.0, 121.0, 31.6, 28.8. HRMS calcd for C₁₃H₁₅NO⁺ [M⁺]: 201.1154, found 201.1152.

2-(4-Methylphenyl)-5-phenyloxazole (**3b**'). White solid (49.4 mg, 70%). Mp 72–73 °C. IR (KBr): 2360, 1598, 1448, 1274, 1137, 764, 690 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.74–7.67 (m, 2H), 7.46–7.39 (m, 3H), 7.35–7.23 (m, 3H), 2.40 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 161.4, 150.9, 140.7, 129.6, 128.9, 128.3, 128.1, 126.3, 124.8, 124.2, 123.4, 21.6. HRMS calcd for C₁₆H₁₃NO⁺ [M⁺]: 235.0997, found 235.0992.

5-(4-Methoxyphenyl)-2-(thiophen-2-yl)oxazole (**3c**').²⁸ Light yellow solid (40.2 mg, 52%). Mp 91–92 °C. IR (KBr): 2965, 1574, 1503, 1496, 1025, 834, 817, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.70 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.62 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.43–7.39 (m, 1H), 7.26 (s, 1H), 7.14–7.09 (m, 1H), 6.96 (dd, *J* = 6.8, 2.0 Hz, 2H), 3.84 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 159.9, 156.8, 150.9, 130.2, 128.0, 127.9, 127.3, 125.7, 121.8, 120.6, 114.4, 55.4.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00386.

Copies of ¹H and ¹³C NMR spectra for the products (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

 (1) (a) Wipf, P. Chem. Rev. 1995, 95, 2115. (b) Hamada, Y.; Shioiri, T. Chem. Rev. 2005, 105, 4441. (c) Jin, Z. Nat. Prod. Rep. 2013, 30, 869. (d) Heng, S.; Gryncel, K. R.; Kantrowitz, E. R. Bioorg. Med. Chem. 2009, 17, 3916. (e) Davyt, D.; Serra, G. Mar. Drugs 2010, 8, 2755. (f) Walsh, C. T.; Malcolmson, S. J.; Young, T. S. ACS Chem. Biol. 2012, 7, 429. (g) Wilson, Z. E.; Fenner, S.; Ley, S. V. Angew. Chem., Int. Ed. 2015, 54, 1284.

(2) (a) Lipshutz, B. H. Chem. Rev. **1986**, 86, 795. (b) Clapham, B.; Sutherland, A. J. J. Org. Chem. **2001**, 66, 9033. (c) Chatani, N.; Fukuyama, T.; Tatamidani, H.; Kakiuchi, F.; Murai, S. J. Org. Chem. **2000**, 65, 4039. (d) Gissibl, A.; Finn, M. G.; Reiser, O. Org. Lett. **2005**, 7, 2325.

(3) For selected examples, see: (a) Merkul, E.; Muller, T. J. J. Chem. Commun. 2006, 4817. (b) Pan, Y.; Zheng, F.; Lin, H.; Zhan, Z. J. Org. Chem. 2009, 74, 3148. (c) Zheng, Y.; Li, X.; Ren, C.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. J. Org. Chem. 2012, 77, 10353. (d) Cheung, C. W.; Buchwald, S. L. J. Org. Chem. 2012, 77, 7526. (e) Wang, Y.-F.; Chen, H.; Zhu, X.; Chiba, S. J. Am. Chem. Soc. 2012, 134, 11980. (f) Senadi, G. C.; Hu, W.-P.; Hsiao, J.-S.; Vandavasi, J.-K.; Chen, C.-Y.; Wang, J.-J. Org. Lett. 2012, 14, 4478. (g) Hu, Y.; Yi, R.; Wang, C.; Xin, X.; Wu, F.; Wan, B. J. Org. Chem. 2014, 79, 3052.

(4) For selected examples, see: (a) Cano, I.; Alvarez, E.; Nicasio, M. C.; Perez, P. J. J. Am. Chem. Soc. 2011, 133, 191. (b) Wan, C.; Zhang, J.; Wang, S.; Fan, J.; Wang, Z. Org. Lett. 2010, 12, 2338. (c) Shi, B.; Blake, A. J.; Lewis, W.; Campbell, I. B.; Judkins, B. D.; Moody, C. J. J. Org. Chem. 2010, 75, 152. (d) Li, X.; Huang, L.; Chen, H.; Wu, W.; Huang, H.; Jiang, H. Chem. Sci. 2012, 3, 3463. (e) Odabachian, Y.; Tong, S.; Wang, Q.; Wang, M.; Zhu, J. Angew. Chem., Int. Ed. 2013, 52, 10878. (f) Xu, Z.; Zhang, C.; Jiao, N. Angew. Chem., Int. Ed. 2012, 51, 11367. (g) Zheng, J.; Zhang, M.; Huang, L.; Hu, X.; Wu, W.; Huang, H.; Jiang, H. Chem. 2014, 50, 3609. (h) Zhang, L.; Zhao, X. Org. Lett. 2015, 17, 184.

(5) For selected examples, see: (a) Meyers, A. I.; Tavares, F. X. J. Org. Chem. 1996, 61, 8207. (b) Phillips, A. J.; Uto, Y.; Wipf, P.; Reno, M. J.; Williams, D. R. Org. Lett. 2000, 2, 1165. (c) Williams, D. R.; Lowder, P. D.; Gu, Y.-G.; Brooks, D. A. Tetrahedron Lett. 1997, 38, 331. (d) Wang, Y.; Li, Z.; Huang, Y.; Tang, C.; Wu, X.; Xu, J.; Yao, H. Tetrahedron 2011, 67, 7406. (e) Huang, Y.; Ni, L.; Gan, F.; He, Y.; Xu, J.; Wu, X.; Yao, H. Tetrahedron 2011, 67, 2066. (f) Li, X.; Li, C.; Yin, B.; Liu, P.; Li, J.; Shi, Z.; Li, C. Chem. - Asian J. 2013, 8, 1408.

(6) (a) Alberico, D.; Scott, M. K.; Lautens, M. Chem. Rev. 2007, 107, 174.
(b) Flegeau, E. F.; Popkin, M. E.; Greaney, M. F. Org. Lett. 2006, 8, 2495.
(c) Lee, K.; Counceller, C. M.; Stambuli, J. P. Org. Lett. 2009, 11, 1457.
(d) Williams, D. R.; Fu, L. F. Org. Lett. 2010, 12, 808.
(e) Zhang, M. L.; Zhang, S. H.; Liu, M. C.; Cheng, J. Chem. Commun. 2011, 47, 11522.
(f) Shen, X.-B.; Zhang, Y.; Chen, W.-X.; Xiao, Z.-K.; Hu, T.-T.; Shao, L.-X. Org. Lett. 2014, 16, 1984.

(7) (a) Graham, T. H. Org. Lett. 2010, 12, 3614. (b) Saito, A.; Taniguchi, A.; Kambara, Y.; Hanzawa, Y. Org. Lett. 2013, 15, 2672.
(c) Selvi, T.; Srinivasan, K. Chem. Commun. 2014, 50, 10845. (d) Wang, B.; Chen, Y.; Zhou, L.; Wang, J.; Tung, C.-H.; Xu, Z. J. Org. Chem. **2015**, 80, 12718. (e) Zeng, T.-T.; Xuan, J.; Ding, W.; Wang, K.; Lu, L.-Q.; Xiao, W.-J. Org. Lett. **2015**, 17, 4070. (f) Chatterjee, T.; Cho, J. Y.; Cho, E. J. J. Org. Chem. **2016**, 81, 6995.

(8) For selected recent reviews of gold catalysis, see: (a) Gorin, D. J.; Toste, F. D. Nature 2007, 446, 395. (b) Hashmi, A. S. K. Chem. Rev. 2007, 107, 3180. (c) Gorin, D. J.; Sherry, B. D.; Toste, F. D. Chem. Rev. 2008, 108, 3351. (d) Wegner, H. A.; Auzias, M. Angew. Chem., Int. Ed. 2011, 50, 8236. (e) Corma, A.; Leyva-Perez, A.; Sabater, M. J. Chem. Rev. 2011, 111, 1657. (f) Obradors, C.; Echavarren, A. M. Acc. Chem. Res. 2014, 47, 902. (g) Dorel, R.; Echavarren, A. M. Chem. Rev. 2015, 115, 9028. (h) Huple, D. B.; Ghorpade, S.; Liu, R.-S. Adv. Synth. Catal. 2016, 358, 1348.

(9) (a) Davies, P. W.; Cremonesi, A.; Dumitrescu, L. Angew. Chem., Int. Ed. 2011, 50, 8931. (b) Luo, Y.; Ji, K.; Li, Y.; Zhang, L. J. Am. Chem. Soc. 2012, 134, 17412. (c) Chen, M.; Sun, N.; Chen, H.; Liu, Y. Chem. Commun. 2016, 52, 6324.

(10) (a) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. Org. Lett. 2004, 6, 4391. (b) Weyrauch, J. P.; Hashmi, A. S. K.; Schuster, A.; Hengst, T.; Schetter, S.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Bats, J. W. Chem. - Eur. J. 2010, 16, 956. (c) Hashmi, A. S. K.; Blanco Jaimes, M. C.; Schuster, A. M.; Rominger, F. J. Org. Chem. 2012, 77, 6394. (d) Peng, H.; Akhmedov, N. G.; Liang, Y.-F.; Jiao, N.; Shi, X. J. Am. Chem. Soc. 2015, 137, 8912. (11) (a) He, W.; Li, C.; Zhang, L. J. Am. Chem. Soc. 2011, 133, 8482. (b) Rassadin, V. A.; Boyarskiy, V. P.; Kukushkin, V. Y. Org. Lett. 2015, 17, 3502.

(12) Querard, P.; Girard, S. A.; Uhlig, N.; Li, C.-J. Chem. Sci. 2015, 6, 7332.

(13) Loy, N. S. Y.; Choi, S.; Kim, S.; Park, C.-M. Chem. Commun. 2016, 52, 7336.

(14) (a) Cole-Hamilton, D. J. Science 2003, 299, 1702. (b) Akiyama, R.; Kobayashi, S. Chem. Rev. 2009, 109, 594. (c) Climent, M. J.; Corma, A.; Iborra, S. Chem. Rev. 2011, 111, 1072. (d) Molnar, A. Chem. Rev. 2011, 111, 2251. (e) Yoon, M.; Srirambalaji, R.; Kim, K. Chem. Rev. 2012, 112, 1196.

(15) (a) Kresge, C. T.; Leonowicz, M. E.; Roth, W. J.; Vartuli, J. C.; Beck, J. S. Nature **1992**, 359, 710. (b) Maschmeyer, T.; Rey, F.; Sankar, G.; Thomas, J. M. Nature **1995**, 378, 159. (c) Zhou, W.; Thomas, J. M.; Shephard, D. S.; Johnson, B. F. G.; Ozkaya, D.; Maschmeyer, T.; Bell, R. G.; Ge, Q. Science **1998**, 280, 705. (d) Taguchi, A.; Schuth, F. *Microporous Mesoporous Mater.* **2005**, 77, 1. (e) Martin- Aranda, R. M.; Cejka, J. Top. Catal. **2010**, 53, 141.

(16) Beck, J. S.; Vartuli, J. C.; Roth, W. J.; Leonowicz, M. E.; Kresge, C. T.; Schmitt, K. D.; Chu, C. T.-W.; Olson, D. H.; Sheppard, E. W.; McCullen, S. B.; Higgins, J. B.; Schlenker, J. L. J. Am. Chem. Soc. **1992**, 114, 10834.

(17) For selected examples, see: (a) Mehnert, P. C.; Weaver, D. W.;
Ying, J. Y. J. Am. Chem. Soc. 1998, 120, 12289. (b) Mukhopadhyay, K.;
Sarkar, B. R.; Chaudhari, R. V. J. Am. Chem. Soc. 2002, 124, 9692.
(c) Baleizao, C.; Corma, A.; Garcia, H.; Leyva, A. J. Org. Chem. 2004, 69, 439. (d) Cai, M.; Zheng, G.; Ding, G. Green Chem. 2009, 11, 1687.
(e) Cai, M.; Peng, J.; Hao, W.; Ding, G. Green Chem. 2011, 13, 190.
(f) Hao, W.; Liu, H.; Yin, L.; Cai, M. J. Org. Chem. 2016, 81, 4244.
(18) Shyu, S.-G.; Cheng, S.-W.; Tzou, D.-L. Chem. Commun. 1999, 2337.

(19) (a) Jia, M.; Seifert, A.; Thiel, W. R. *Chem. Mater.* 2003, *15*, 2174.
(b) Nunes, C. D.; Valente, A. A.; Pillinger, M.; Fernandes, A. C.; Romao, C. C.; Rocha, J.; Goncalves, I. S. *J. Mater. Chem.* 2002, *12*, 1735.

(20) (a) Gonzalez-Arellano, C.; Corma, A.; Iglesias, M.; Sanchez, F. Adv. Synth. Catal. 2004, 346, 1758. (b) Corma, A.; Gutierrez-Puebla, E.; Iglesias, M.; Monge, A.; Perez-Ferreras, S.; Sanchez, F. Adv. Synth. Catal. 2006, 348, 1899. (c) Villaverde, G.; Corma, A.; Iglesias, M.; Sanchez, F. ACS Catal. 2012, 2, 399.

(21) (a) Xiao, R.; Zhao, H.; Cai, M. Tetrahedron 2013, 69, 5444.
(b) Zhao, H.; He, W.; Yao, R.; Cai, M. Adv. Synth. Catal. 2014, 356, 3092. (c) Cai, M.; Yao, R.; Chen, L.; Zhao, H. J. Mol. Catal. A: Chem.

2014, 395, 349. (d) Zhao, H.; He, W.; Wei, L.; Cai, M. Catal. Sci. Technol. **2016**, 6, 1488.

(22) Lindner, E.; Salesch, T.; Brugger, S.; Hoehn, F.; Wegner, P.; Mayer, H. A. J. Organomet. Chem. 2002, 641, 165.

(23) (a) Ye, L.; He, W.; Zhang, L. J. Am. Chem. Soc. 2010, 132, 8550.
(b) Ye, L.; He, W.; Zhang, L. Angew. Chem., Int. Ed. 2011, 50, 3236.

(24) Lempers, H. E. B.; Sheldon, R. A. J. Catal. 1998, 175, 62.

(25) (a) Li, G.; Zhang, L. Angew. Chem., Int. Ed. 2007, 46, 5156.

(b) Ye, L.; Cui, L.; Zhang, G.; Zhang, L. J. Am. Chem. Soc. 2010, 132,

3258. (c) Lu, B.; Li, C.; Zhang, L. J. Am. Chem. Soc. 2010, 132, 14070.
 (26) Yang, W.; Wei, L.; Yi, F.; Cai, M. Catal. Sci. Technol. 2016, 6,

4554.

(27) Ibata, T.; Sato, R. Bull. Chem. Soc. Jpn. 1979, 52, 3597.

(28) Pulici, M.; Quartieri, F.; Felder, E. R. J. Comb. Chem. 2005, 7, 463.