Magnetically Recoverable N-Heterocyclic Carbene–Gold(I) Catalyst for Hydroamination of Terminal Alkynes

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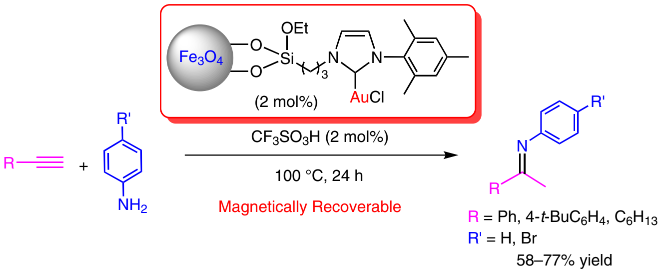

R = Ph, 4-*t*-BuC_6H_4, C_6H_{13}
R' = H, Br
58–77% yield

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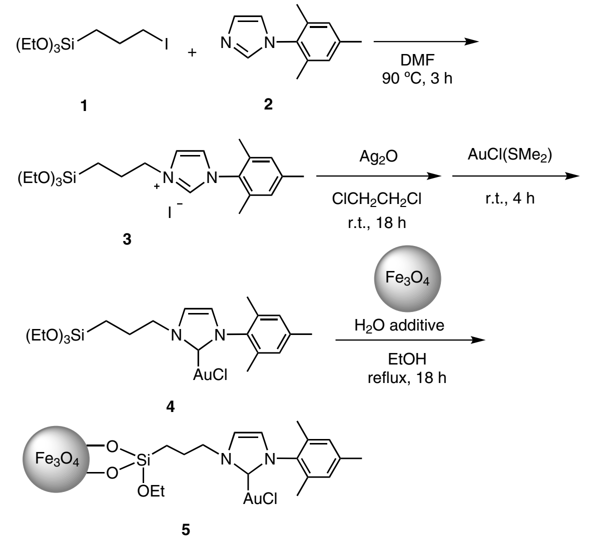
Abstract We prepared a magnetically recoverable gold(I) catalyst by immobilizing an N-heterocyclic carbene–gold(I) complex on magnetite and applied it to the hydroamination of alkynes. By employing 2 mol% of the magnetite-supported gold(I) catalyst, the hydroamination of terminal alkynes proceeded smoothly to provide the corresponding imine in a fair chemical yield. Moreover, after the reaction, the magnetic gold(I) catalyst was readily recovered by use of an external magnet and could be reused up to five times.

Key words amination, N-heterocyclic carbene complexes, catalysis, imines, supported catalysis

Gold catalysts have recently gained a great deal of attention as an emerging tool for a range of useful synthetic transformations.[1] In particular, gold(I) complexes have seen increased utility as catalysts for the activation of alkynes toward addition by a variety of nucleophiles.[1a] For example, the catalytic addition of an organic N–H bond to alkynes (hydroamination) to give nitrogen-containing molecules is of great interest to both the academic and industrial community.[2] Despite the widespread application of these types of reactions in organic synthesis, some obstacles stand in the way of their large-scale application to the pharmaceutical and fine-chemical industries, including high cost and the possibility of contamination with catalytic gold in the final product. One of the most promising solutions to these problems is the immobilization of the gold(I) complex as a catalyst on an insoluble support. Heterogenization of catalytic gold(I) by immobilization on various organic and inorganic supports has previously been successful, making it possible for the immobilized gold(I) catalyst to be recovered by filtration of the reaction mixture.[3]

Magnetic nanoparticles have emerged as smart and promising supports for immobilization of the catalytic metal, because magnetic nanoparticle-supported catalysts can be easily separated from the reaction medium by use of an external magnet, which provides a simple separation of the catalysts without filtration.[4] The magnetic separation circumvents time-consuming and laborious separation steps and allows for practical continuous catalysis. Besides the easy separation, an interesting feature of magnetic nanoparticles is their convenient surface modification, which provides a wide range of magnetic-functionalized catalysts showing identical and sometimes even higher activity than their homogeneous counterparts in organic transformations. Recently, magnetic nanoparticle-supported and magnetically recoverable transition-metal complexes such as palladium,[5] ruthenium,[6] and osmium[7] have been increasingly reported with a high level of catalytic activity. We report herein the synthesis of a magnetically recoverable gold(I) catalyst by the immobilization of an N-heterocyclic carbene (NHC)–gold(I) complex on magnetite[8,9] and its application to the hydroamination of alkynes. Moreover, this magnetite-supported NHC–gold(I) catalyst was clearly collected from the reaction mixture by use of an external magnet and could be reused repeatedly.

A magnetic nanoparticle-supported NHC–gold(I) complex **5** was synthesized as follows (Scheme 1). Magnetite (Fe_3O_4) was chosen for use as a magnetic support, since it could be readily prepared by a conventional coprecipitation method.[10] The silane coupling agent having an NHC–gold(I) complex **4** was prepared according to a modification of the synthetic scheme reported by Corma.[3e] Imidazolium iodide **3** was synthesized by stirring of an *N*,*N*-dimethylformamide (DMF) solution of (3-iodopropyl)triethoxysilane (**1**)[11] and 1-(2,4,6-trimethylphenyl)imidazole (**2**)[12] at 90 °C for 3 hours under an argon atmosphere. After the evaporation of DMF in vacuo, 1,2-dichloroethane and silver(I) oxide were added, and the reaction mixture was stirred at room temperature for 18 hours under an argon atmosphere. AuCl(SMe_2) was subsequently added, and the reaction mixture was stirred at room temperature for 4 hours under an argon atmosphere. After the Celite® filtration of the reaction mixture and the evaporation of the solvent, the silane coupling agent having an NHC–gold(I) complex **4** was obtained.[13] Finally, magnetite and **4** were refluxed in ethanol for 18 hours under an argon atmosphere to afford the magnetite-supported NHC–gold(I) complex **5**, which was separated by magnetic decantation using an external magnet. The loading of **5** was 0.17 mmol/g, which was determined by ICP-AES of gold.[14]

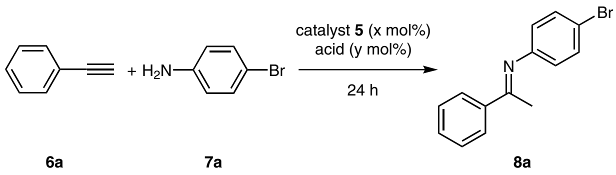


Scheme 1 Preparation of **5**

We then examined the catalytic activity of **5** by performing the hydroamination of alkenes (Table 1). The procedure employed here was a modification of Tanaka's synthetic sequence.[2f] By stirring a solution of ethynylbenzene (**6a**) and 4-bromoaniline (**7a**) with 1 mol% of the catalyst **5** at 80 °C for 24 hours under an argon atmosphere, the hydroamination of **6a** proceeded. The magnetite-supported gold(I) catalyst **5** was rapidly collected using an external magnet, and the reaction mixture was then transferred out of the reaction vessel.[15] The corresponding imine **8a** was obtained in a 37% chemical yield, and acetophenone was also obtained in a 7% chemical yield (Table 1, entry 1), probably due to decomposition of the imine **8a** by the small amount of water contained in the catalyst **5**.

We then performed the catalytic hydroamination of ethynylbenzene (**6a**) using an acidic promoter. The chemical yield of the imine **8a** was enhanced by using 1 mol% of an acid. In particular, by employing trifluoromethanesulfonic acid as an acidic promoter, the imine **8a** was obtained in a 62% chemical yield (Table 1, entry 3). It is supposed that the acid contributed to the activation of catalyst **5** by the formation of a cationic gold(I) moiety in situ.[2f,16] We next examined the catalytic amount and the reaction temperature when using trifluoromethanesulfonic acid as an acidic promoter. By carrying out the reaction using 2 mol% of the catalyst **5** at 100 °C, the imine **8a** was obtained in the highest chemical yield (77%; Table 1, entry 5). Needless to say, the use of an acidic promoter alone, without catalyst **5**, did not catalyze the hydroamination of **6a** (Table 1, entry 6).

Table 1 Hydroamination of Ethynylbenzene **6a** Catalyzed by **5**[a]

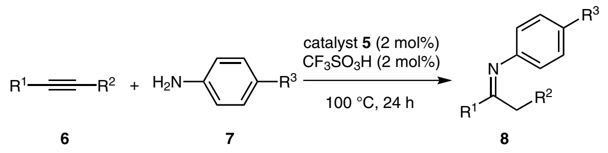


Entry	Catalyst **5** (x mol%)	Acid (y mol%)	Temp (°C)	Yield (%)[b,c]
1	1	none (0)	80	37 (7)
2	1	$12WO_3·H_3PO_4·nH_2O$ (1)	80	46 (22)
3	1	CF_3SO_3H (1)	80	62 (14)
4	2	CF_3SO_3H (2)	80	69 (17)
5	2	CF_3SO_3H (2)	100	77 (20)
6	0	CF_3SO_3H (2)	80	1 (1)

[a] Reaction conditions: Catalyst **5** (x mol%), acid (y mol%), **6a** (3 equiv), **7a** (1 equiv), carried out at the indicated temperature for 24 h under an argon atmosphere.
[b] Determined by the integration of ^1H NMR absorptions referring to an internal standard.
[c] The value in parentheses is the chemical yield of acetophenone.

Encouraged by these results, we subsequently performed the various hydroaminations of alkynes **6** by employing 2 mol% of the catalyst **5** and trifluoromethanesulfonic acid at 100 °C for 24 hours (Table 2). When hydroamination of ethynylbenzene (**6a**) was performed using aniline (**7b**) instead of 4-bromoaniline (**7a**), the corresponding imine **8b** was obtained (70%; Table 2, entry 2).[17] But the chemical yield of **8** in the case using aniline (**7b**) was lower than that in the case using 4-bromoaniline (**7a**). This tendency in the reactivity of **7** is similar to that previously reported, which arose from the introduction of an electron-withdrawing group to the phenyl group of aniline.[2f] Also in the case of the hydroamination of 4-*tert*-butyl-ethynylbenzene (**6b**), the difference in the reactivity between **7a** and **7b** was confirmed (Table 2, entries 3 and 4).[18] In addition, the hydroamination of 1-octyne (**6c**), which was an aliphatic terminal alkyne, also proceeded smoothly to provide the corresponding imine **8e** in a 75% chemical yield (Table 2, entry 5). However, the hydroamination of diphenylacetylene (**6d**), which was an internal alkyne, hardly proceeded (1%; Table 2, entry 6).[19]

Table 2 Various Hydroaminations of Alkynes **6**[a]

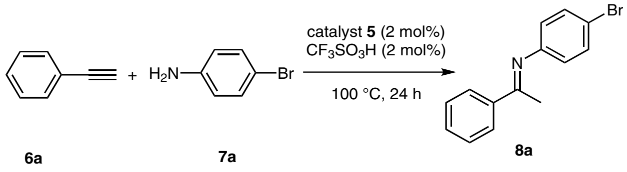


Entry	Alkyne			Amine		Product	Yield (%)[b,c]
	R^1	R^2	**6**	R^3	**7**		
1	Ph	H	**6a**	Br	**7a**	**8a**	77 (20)
2	Ph	H	**6a**	H	**7b**	**8b**	70 (16)
3	4-*t*-BuC_6H_4	H	**6b**	Br	**7a**	**8c**	72 (19)
4	4-*t*-BuC_6H_4	H	**6b**	H	**7b**	**8d**	58 (25)
5	C_6H_{13}	H	**6c**	Br	**7a**	**8e**	75[d] (21)
6[e]	Ph	Ph	**6d**	H	**7b**	**8f**	1 (1)

[a] The reaction conditions were the same as those indicated in Table 1.
[b] Determined by the integration of ^{1}H NMR absorptions referring to an internal standard.
[c] The value in parenthesis is the chemical yield of the corresponding ketone.
[d] *E*/*Z* = 75:25 (determined by integration of ^{1}H NMR absorptions).
[e] Conditions: 1 equiv of **6d** and 3 equiv of **7b** were used.

Finally, the reusability of the catalyst **5** was examined using ethynylbenzene (**6a**) and 4-bromoaniline (**7a**), as shown in Table 3.[20] In this experiment, it was found that the catalyst **5** was readily collected from the reaction mixture by use of an external magnet, and could be reused up to five times, and that the corresponding imine **8a** could be consistently obtained in a fair chemical yield. In addition, it was revealed that the formation of acetophenone was suppressed by the reaction after the second, probably due to the decrease in the small amount of water contained in the magnetite-supported catalyst **5**.

Table 3 Catalyst Recycling in Hydroamination of Ethynylbenzene **6a** Using 4-Bromoaniline (**7a**)[a]



Run	1st	2nd	3rd	4th	5th
Yield (%)[b,c]	73 (22)	83 (14)	84 (7)	85 (5)	86 (3)

[a] The reaction conditions were the same as those indicated in Table 1.
[b] Determined by the integration of ^{1}H NMR absorptions referring to an internal standard.
[c] The value in parenthesis is the chemical yield of acetophenone.

In summary, we prepared a novel magnetite-supported NHC–gold(I) complex. By employing 2 mol% of the magnetite-supported gold(I) complex as a catalyst, the hydroamination of terminal alkynes proceeded smoothly. Moreover, the magnetic gold(I) catalyst was readily recovered by use of an external magnet and could be reused up to five times.

Acknowledgment

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562134. Included are synthetic procedures for the preparations of **3**, **4**, and **5**, ^{1}H NMR and ^{13}C NMR data of **3** and **4**, and X-ray diffraction patterns of magnetite and **5**.

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(13) ^{1}H NMR and ^{13}C NMR data of **3** and **4** are shown in the Supporting Information.

(14) **Selected Data for Compound 5**
Black powder. IR (KBr): 3086, 2916, 1651, 1558, 1512, 1458, 1042, 949, 903, 856 cm^{-1}. Anal.; found (%): C, 2.29; H, 0.33; N, 0.22; Cl, 0.87; Au, 3.36. An X-ray diffraction pattern is shown in the Supporting Information.

(15) **General Procedure**
To a solution of the alkyne **6** (9 mmol) and the amine **7** (3 mmol) were successively added the indicated amounts of the magnetite-supported gold(I) catalyst **5** and an acid under an argon atmosphere. The reaction mixture was stirred at the indicated temperature for 24 h under an argon atmosphere. The magnetite-supported gold(I) catalyst **5** was separated by magnetic decantation using an external magnet, and the reaction mixture was then transferred out of the reaction vessel, followed by washing of the catalyst **5** with the alkyne **6** three times under argon atmosphere. The chemical yield of the imine **8** and the corresponding ketone were determined by integrating ^{1}H NMR absorptions referring to an internal standard [4-*tert*-butyltoluene (1 mmol)], which was added to the reaction mixture. Any organic solvents were not used for washing of the catalyst **5** in order to avoid the vaporization of products and an internal standard during the evaporation of organic solvents in vacuo. Also in the case of catalyst recycling as shown in Table 3, ethynylbenzene (**6a**), namely no organic solvents was used for washing of the catalyst **5** because this catalytic conversion was sequentially carried out without the evaporation of solvents in vacuo after the magnetic decantation.

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(17) NMR spectra of **8a**,[21] **8b**,[22] **8d**,[23] and **8f**[24] are in accordance with those reported in the literature.

(18) **Selected Data for New Compounds**
(*E*)-4-Bromo-*N*-{1-(4-*tert*-butylphenyl)ethylidene}aniline (8c)
White powder; yield: 72%; mp 138.0–138.6 °C. IR (KBr): 2963, 2901, 2866, 1628, 1601, 1474, 1296, 1211, 1007, 853, 841, 586 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.89 (d, J = 8.4 Hz, 2 H, ArH), 7.45 (t, J = 9.2 Hz, 4 H, ArH), 6.66 (d, J = 8.4 Hz, 2 H, ArH), 2.20 (s, 3 H, CH$_3$), 1.35 [s, 9 H, C(CH$_3$)$_3$]. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 166.0, 154.3, 151.0, 136.5, 132.0, 127.1, 125.5, 121.4, 116.1, 35.0, 31.3, 17.4. Anal. Calcd (%) for C$_{18}$H$_{20}$NBr: C, 65.46; H, 6.10; N, 4.24; Br, 24.19. Found (%): C, 65.53; H, 5.98; N, 4.28; Br, 24.11.
4-Bromo-*N*-(2-octylidene)aniline (8e)
Colorless oil; *E*/*Z* mixture; yield: 75%. IR (KBr): 2954, 2927, 2857, 1661, 1480, 1365, 1231, 1167, 1069, 1008, 842, 654 cm^{-1}. ^{1}H NMR and ^{13}C NMR resonances were presented as two signals (indicated as major and minor). ^{1}H NMR (400 MHz, THF-d_8): δ = 7.38–7.35 (m, 2 H, ArH), 6.56–6.52 (m, 2 H, ArH), 2.37 (t, J = 7.5 Hz, 2 H, CH$_2$, major), 2.11 (t, J = 7.9 Hz, 2 H, CH$_2$, minor), 2.08 (s, 3 H, CH$_3$, minor), 1.74 (s, 3 H, CH$_3$, major), 1.69–1.62 (m, 2 H, CH$_2$, major), 1.51–1.44 (m, 2 H, CH$_2$, minor), 1.42–1.32 (m, 6 H, (CH$_2$)$_3$, major), 1.26–1.17 (m, 6 H, (CH$_2$)$_3$, minor), 0.91 (t, J = 6.7 Hz, 3 H, CH$_3$, major), 0.85 (t, J = 7.0 Hz, 3 H, CH$_3$, minor). ^{13}C NMR (100 MHz, THF-d_8): δ (major) = 172.0, 152.2, 132.32, 121.85, 115.8, 41.8, 32.5, 29.7, 26.5, 23.3, 19.3, 14.3; δ (minor) = 172.4, 151.7, 132.27, 121.80, 115.6, 34.5, 32.2, 29.9, 27.5, 25.6, 23.1, 14.2. MS (EI): *m*/*z* calcd for C$_{14}$H$_{20}$NBr: 281.0779 [M$^+$]; found: 281.0780.

(19) In Table 2, entry 6, the magnetically recovered gold(I) catalyst **5** was washed with aniline (**7b**) after the hydroamination.

(20) The magnetically recovered gold(I) catalyst **5** was reused for the subsequent hydroamination of the alkyne **6a** by the addition of **6a**, **7a**, and trifluoromethanesulfonic acid to the reaction vessel.

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