Effective Au(III)–$CuCl_2$-catalyzed addition of alcohols to alkenes†

Xin Zhang and Avelino Corma*

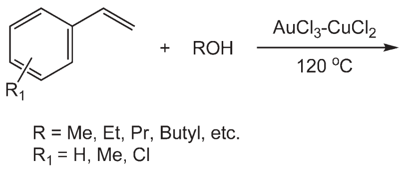
Received (in Cambridge, UK) 9th May 2007, Accepted 8th June 2007
First published as an Advance Article on the web 26th June 2007
DOI: 10.1039/b706961h

Alkenes can be activated by Au(III) catalysts, and the effective addition of alcohols to alkenes can be carried out under mild conditions with Au(III), provided that catalytic amounts of $CuCl_2$ are added, which significantly stabilize the cationic Au(III).

A catalytic 'gold rush' has been recently seen for homogeneous[1] as well as for heterogeneous catalysis.[2] Gold salts and organic complexes are able to activate C–C multiple bonds,[1,3] halogen-substituted aromatics and hydrogen,[4] enabling the synthesis of fine chemicals. The reactions of gold salts with alkynes and allenes have been the basis of the present 'gold rush' in organic chemistry.[1] Although a variety of functional groups are able to add to alkynes and allenes activated by gold,[1] there are very few examples of nucleophilic addition to alkenes catalyzed by gold.[5] Recently, Yao and Li[5a] reported that Au(III) catalyzes the addition of β-diketones to alkenes with Ag(I) as co-catalyst. An interesting Au(I)-mediated addition of phenols and carboxylic acids to alkenes has also been described.[5c] Since, in contrast to additions to alkynes, the use of alkenes opens up the possibility of stereoselective catalysis,[1b] the development of new procedures for the synthesis of fine chemicals by the activation of alkenes is highly desired. However, despite the success of the addition of alcohols to alkynes[6] and strained allenes,[5b] additions of alcohols to alkenes catalyzed by gold have been claimed to be unsuccessful.[1b]

We report here that alkenes can be activated by Au(III) catalysts (*e.g.*, $AuCl_3$, $HAuCl_4$), and the effective addition of various alcohols to alkenes can be realized by employing these Au(III) catalysts with the addition of catalytic amounts of $CuCl_2$ under mild conditions (see Supporting Information†). The role of $CuCl_2$ in these gold(III)–$CuCl_2$ catalysts (*e.g.*, $AuCl_3$–$CuCl_2$) is to stabilize the cationic Au(III).

The addition of methanol to styrene for the synthesis of (1-methoxyethyl)benzene (Scheme 1) over $AuCl_3$ at 80 °C gave a conversion and selectivity of 8.3 and 39.1%, respectively, whereas when the reaction temperature was increased to 120 °C, the conversion and selectivity sharply increased to 38.2 and 80.4%, respectively. The direct addition of methanol to styrene also occurs with $HAuCl_4$, AuCl, and $PdCl_2$ catalysts at 120 °C (Fig. 1A), giving styrene conversions of 45.8, 4.5 and 28.6%. A selectivity for (1-methoxyethyl)benzene of about 70% is found for all cationic Au catalysts (Fig. 1B). The main by-product is (2,2-dimethoxyethyl)-benzene, and the total selectivity for (1-methoxyethyl)benzene plus (2,2-dimethoxyethyl)benzene is up to 96% for all cationic gold and Pd(II) catalysts. Clearly, the catalytic activity of Au(III) is much higher than that of Au(I) or $PdCl_2$.



Scheme 1 Intermolecular addition of alcohols to alkenes.

It should be noted that the conversion of styrene increases with reaction time, reaching a maximum after 1.0, 2.5, 1.0, and 1.5 h for $AuCl_3$, $HAuCl_4$, AuCl, and $PdCl_2$ catalysts, respectively, and then remains constant for a longer time (Fig. 1A). This result indicates that all cationic gold and Pd(II) catalysts deactivate very quickly during the reaction. This is due to the reduction of cationic gold and Pd(II), since most of the gold and palladium were in the metal form when the catalytic activity stopped. It has been reported that cationic gold and Pd(II) are easily reduced, even at room temperature, and that alkynes, alkenes, alcohols, CO and phosphines present in the reaction media are the reducing agents.[1c,7] Although cationic gold has mainly been used to activate alkynes and allenes in homogeneous catalysis,[1] it is surprising that little attention has been given to catalyst deactivation due to the reduction of cationic gold during the reaction.

In our case, and in order to avoid (or at least to retard) the reduction of the cationic gold and Pd(II) species, we thought about stabilizing the Au(III) and Pd(II) by means of a coupled redox cycle involving $CuCl_2$. Although in a first approximation (taking into account the redox potentials[8a,9]), it would appear that the oxidation of Au(0) and Pd(0) by $CuCl_2$ would be difficult, it

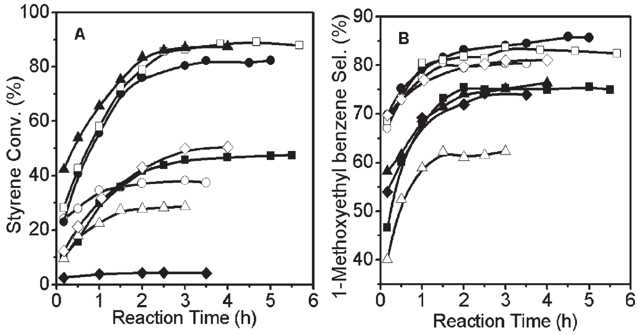


Fig. 1 Kinetic plots showing the conversion of styrene (A), and selectivity to (1-methoxyethyl)benzene (B) against reaction time for the addition of methanol to styrene over cationic Au and Pd(II) catalysts: (○) $AuCl_3$, (■) $HAuCl_4$, (◆) AuCl, (△) $PdCl_2$, (●) $AuCl_3$–$CuCl_2$, (□) $HAuCl_4$–$CuCl_2$, (◇) AuCl–$CuCl_2$, (▲) $PdCl_2$–$CuCl_2$.

Instituto de Tecnología Química, UPV-CSIC, Universidad Politécnica de Valencia, Avda. de los Naranjos s/n, 46022, Valencia, Spain.
E-mail: acorma@itq.upv.es; Fax: +34 9638 77809; Tel: +34 9638 77800

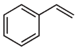
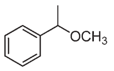
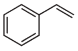
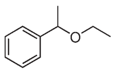
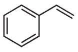
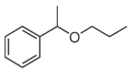
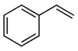
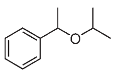
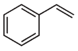
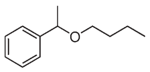
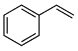
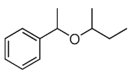
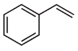
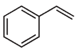
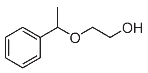
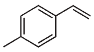
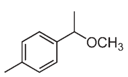
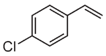
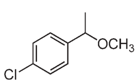
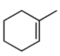
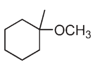
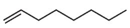
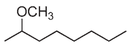
† Electronic supplementary information (ESI) available: Experimental details, MS and ^{1}H-NMR spectra. See DOI: 10.1039/b706961h

should be considered that cationic Au and Pd(II) species can be easily stabilized by complex formation in the presence of chloride ions,[1,8a] and the initially reduced metallic Au nanoparticles should have a lower redox potential.[10] Indeed, the oxidation of Pd(0) with Cu^{2+} ions is well established in the Wacker process.[8]

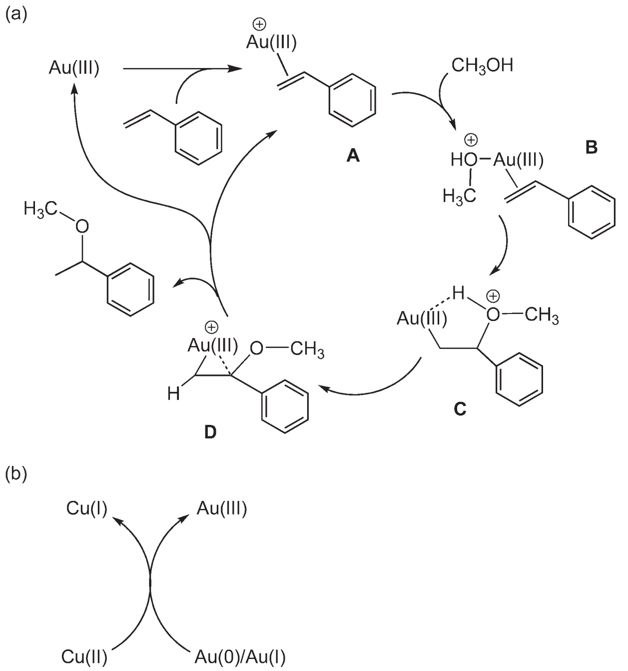
The results in Fig. 1 show that the addition of catalytic amounts of $CuCl_2$ to the above-mentioned Au(III), Au(I) and Pd(II) catalysts strongly increases their catalytic performance under the same reaction conditions. For example, addition of 2 equivalents (*i.e.* 0.2 mmol) of $CuCl_2$ to $AuCl_3$, $HAuCl_4$ or AuCl increases the conversions of styrene from 38.2, 45.8, and 4.5% to 82.2, 88.2, and 50.0%, respectively, and more than a two-fold increase in styrene conversion was found after the addition of 2 equivalents of $CuCl_2$ to $PdCl_2$ (Fig. 1A). The selectivity for (1-methoxyethyl)benzene also increases with all catalysts upon addition of $CuCl_2$ (Fig. 1B). It should be noted that the styrene conversion of $CuCl_2$ alone (using the same amount as for catalysis with cationic gold, *i.e.* 0.1 mmol) is only 1.0% after 2 h. The shape of the kinetic curves in Fig. 1A shows a slower catalyst deactivation in the presence of $CuCl_2$, which would be in agreement with a stabilization of the cationic gold and Pd(II), with a corresponding decrease in the rate of formation of the non-active metallic forms. Meanwhile, a green-tinged white precipitate was observed due to the reduction of $CuCl_2$ to CuCl when using cationic gold and Pd(II) catalysts.

The stabilizing effect was proven through the observation that $AuCl_3$ (0.1 mmol) in 1.0 mL of methanol at 120 °C starts to form metallic particles after 2 minutes, while in the presence of $CuCl_2$ (0.2 mmol), no metallic particles were observed in one hour. The same occurs in the case of $PdCl_2$. These result demonstrates that

Table 1 Addition of alcohols to alkene over $AuCl_3$–$CuCl_2$ catalyst[a]

Entry	Alkene	Alcohol	*T*/h	Alkene conv. (%)	Product (%)		
					Main product		Others[b]
1		Methanol	3.5	82.2		84.5	15.5
2		Ethanol	4.0	92.5		85.8	14.2
3		1-Propanol	4.0	94.8		83.7	16.3
4		2-Propanol	4.0	67.0		73.9	26.1
5		1-Butanol	4.0	95.0		86.7	13.3
6		2-Butanol	4.0	68.5		84.1	15.9
7		*tert*-Butyl alcohol	4.0	2.6	—		—
8		Glycol	5.7	88.1		80.7	19.3
9		Methanol	2.5	93.1		85.7	14.3
10		Methanol	8.0	74.6		79.3	20.7
11		Methanol	12	60.1		93.4	6.6
12[c]		Methanol	12	52.3		67.8	32.2

[a] Conducted with 1.5 mL mixtures of alcohols and alkenes (1.21 mmol) at 120 °C, using 8 mol% $AuCl_3$ and 16 mol% $CuCl_2$. [b] Other products are given in the Notes and references section. The side-reactions for addition of alcohols to alkenes over Au(III)–$CuCl_2$ are the chlorination of alkenes, the oxidation of alkenes in alcohols affording aldehyde acetals, and the hydration of alkenes due to a small amount of H_2O in the alcohols and $CuCl_2$. The intermolecular dehydration of alcohols, affording ethers, was also detected. The detailed distributions of the other products in Table 1 are given below. Entries 1–6: 4.0–15.0% (1,2-dichloroethyl)benzene, about 2.0–5.0% acetals and various other products. Entry 8: 8.9% 2-(1-phenylethyl)-1,3-dioxolane, and 4.2% (1,2-dichloroethyl)benzene. Entry 9: 5.4% of a mixture of 4-methyl-1-(2,2-dimethoxyethyl)benzene and 4-methyl-1-(1,2-dimethoxyethyl)benzene, and 6.9% 4-methyl-1-(1,2-dichloroethyl)benzene. Entry 10: 6.3% of a mixture of 4-chloro-1-(1,2-dimethoxyethyl)benzene and 4-chloro-1-(2,2-dimethoxyethyl)benzene, and 8.9% 4-chloro-1-(1,2-dichloroethyl)benzene. Entry 11: 1.9% 1-methylcyclohexanol and 1.0% 2-methylcyclohexanone. Entry 12: 6.8% of a mixture of 2-octene and 3-octene. [c] The reaction temperature was 150 °C.



Scheme 2 (a) Proposed catalytic mechanism and (b) a coupled redox cycle involving $CuCl_2$.

the rate of reduction of Au(III) and Pd(II) into the corresponding metals is strongly decreased in the presence of $CuCl_2$.

The $AuCl_3$–$CuCl_2$ catalytic system has been applied to the addition of various alcohols to alkenes, as summarized in Table 1. It is shown that the catalyst works very well for primary alcohols (entries 2, 3, 5), with styrene conversions in the order of ~95% and the selectivity for the ether ~85%. Secondary alcohols react more slowly than primary alcohols, while tertiary alcohols have very low reactivity (entries 4, 6, 7). Interestingly, addition of ethylene glycol is also effective, and gives 88.1% styrene conversion and 71.7% selectivity for 2-(1-phenylethoxy)ethanol (entry 8). The alcohols can also be added to other alkenes (entries 9–12), following Markovnikov's rule.

The nucleophilic additions to alkenes are also interesting because they provide the possibility of introducing chiral centers in the corresponding unsymmetrical products.[1b] In our case, a mixture of diastereoisomers in a 50 : 50 ratio is observed when reacting 2-propanol and 2-butanol (the products contain two chiral centers; entries 4 and 6, Table 1). In the case of primary alcohols, the ratio of the diastereomeric ethers changes significantly with reaction time. For instance, for ethanol, a 73 : 27 ratio is observed after 0.5 h, but epimerization results when the reaction time is increased further.

In the reaction mechanism for the addition of alcohols to alkenes over Au(III)–$CuCl_2$ (Scheme 2a), and by analogy with alkynes,[6a] Au(III) acts as a Lewis acid that activates the alkene to form the corresponding gold complex (**A**), which is then attacked by the alcohol to form the intermediate complex (**B**). Both **B** and the transition state (**C**) would be sterically quite crowded,[6a] and this could be the reason why secondary alcohols react more slowly than primary alcohols while tertiary alcohols fail in this reaction. A rearrangement of **C** to **D** affords the final product and regenerates the Au(III) catalyst. However, there is a parallel process in which Au(III) is reduced into the less active Au(I) and then into the non-active Au(0). This makes the reaction stop at low levels of conversion, unless the reduction process is slowed down by the redox cycle in the presence of $CuCl_2$ (Scheme 2b).

In summary, we have shown that Au(III) can be an effective catalyst for the intermolecular addition of alcohols to alkenes provided that catalytic amounts of $CuCl_2$ are introduced into the reaction medium. The process is then based on an $AuCl_3$–$CuCl_2$ catalytic system, in which Au(III) acts as a Lewis acid active site while $CuCl_2$ slows down the deactivation of the former.

We thank the Spanish government (Project MAT 2006-14274-C02-01) for financial support. X. Zhang thanks P. Serna and J. Gaona for kind help.

Notes and references

1 For most recent reviews, see: (*a*) A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896; (*b*) A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2005, **44**, 6990; (*c*) A. Hoffmann-Röder and N. Krause, *Org. Biomol. Chem.*, 2005, **3**, 387; (*d*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Commun.*, 2007, 333; (*e*) D. J. Gorin and F. D. Toste, *Nature*, 2007, **446**, 395.

2 For selected references, see: (*a*) G. C. Bond and D. T. Thompson, *Catal. Rev. Sci. Eng.*, 1999, **41**, 319; (*b*) G. J. Hutchings and M. Haruta, *Appl. Catal., A*, 2005, **291**, 2; (*c*) A. Corma and P. Serna, *Science*, 2006, **313**, 332; (*d*) X. Zhang, H. Shi and B.-Q. Xu, *Angew. Chem., Int. Ed.*, 2005, **44**, 7132; (*e*) X. Zhang, H. Wang and B.-Q. Xu, *J. Phys. Chem. B*, 2005, **109**, 9678.

3 For selected most recent examples, see: (*a*) G. Lemière, V. Gandon, N. Agenet, J.-P. Goddard, A. Kozak, C. Aubert, L. Fensterbank and M. Malacria, *Angew. Chem., Int. Ed.*, 2006, **45**, 7596; (*b*) A. S. K. Hashmi, M. C. Blanco, D. Fischer and J. W. Bats, *Eur. J. Org. Chem.*, 2006, 1387; (*c*) J. Barluenga, A. Diéguez, A. Fernández, F. Rodríguez and F. J. Fananás, *Angew. Chem., Int. Ed.*, 2006, **45**, 2091; (*d*) E. Genin, P. Y. Tullec, S. Antoniotti, C. Brancour, J.-P. Genêt and V. Michelet, *J. Am. Chem. Soc.*, 2006, **128**, 3112; (*e*) A. W. Sromek, M. Rubina and V. Gevorgyan, *J. Am. Chem. Soc.*, 2005, **127**, 10500; (*f*) J.-J. Lian and R.-S. Liu, *Chem. Commun.*, 2007, 1337.

4 (*a*) C. González-Arellano, A. Corma, M. Iglesias and F. Sanchez, *J. Catal.*, 2006, **238**, 497; (*b*) C. González-Arellano, A. Corma, M. Iglesias and F. Sanchez, *Chem. Commun.*, 2005, **27**, 3451; (*c*) C. González-Arellano, A. Abad, A. Corma, H. García, M. Iglesias and F. Sánchez, *Angew. Chem., Int. Ed.*, 2007, **46**, 1536.

5 (*a*) X. Yao and C.-J. Li, *J. Am. Chem. Soc.*, 2004, **126**, 6884 (*b*) A. S. K. Hashmi, L. Schwarz, J.-H. Choi and T. M. Frost, *Angew. Chem., Int. Ed.*, 2000, **39**, 2285; (*c*) C.-G. Yang and C. He, *J. Am. Chem. Soc.*, 2005, **127**, 6966; (*d*) J. Zhang, C.-G. Yang and C. He, *J. Am. Chem. Soc.*, 2006, **128**, 1798.

6 (*a*) J. H. Teles, S. Brode and M. Chabanas, *Angew. Chem., Int. Ed.*, 1998, **37**, 1415; (*b*) Y. Fukuda and K. Utimoto, *J. Org. Chem.*, 1991, **56**, 3729.

7 (*a*) *Handbook of Reagents for Organic Synthesis: Reagents, Auxiliaries, and Catalysts for C–C Bond Formation*, ed. R. M. Coates and S. E. Denmark, John Wiley & Sons, Chichester, UK, 1999, p. 566; (*b*) J. Guzman and B. C. Gates, *J. Am. Chem. Soc.*, 2004, **126**, 2672.

8 (*a*) J. Tsuji, *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*, John Wiley & Sons, Chichester, UK, 2000, p. 420 (*b*) J. E. Bäckvall, B. Åkermark and S. O. Ljunggren, *J. Am. Chem. Soc.*, 1979, **101**, 2411.

9 *Handbook of Chemistry and Physics* (80th edn), ed. D. R. Lide, CRC Press, Boca Raton, FL, USA, 1999, p. 8–21.

10 (*a*) S. Carrettin, J. Guzman and A. Corma, *Angew. Chem., Int. Ed.*, 2005, **44**, 2242; (*b*) L. D. Burke, A. J. Ahern and A. P. O'Mullane, *Gold Bull.*, 2002, 35.