Lewis Acid Character of Zero-valent Gold Nanoclusters under Aerobic Conditions: Intramolecular Hydroalkoxylation of Alkenes

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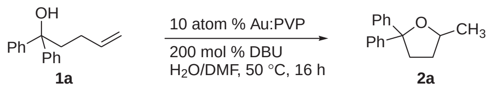
Gold nanoclusters stabilized by poly(*N*-vinyl-2-pyrrolidone) (**Au:PVP** NCs, $\phi = 1.3$ nm) behave as Lewis acid catalyst in aqueous media under aerobic conditions, to promote the intramolecular hydroalkoxylation of unactivated alkenes. Molecular oxygen generates a reaction center having the Lewis acidic character on the surface of Au NCs in which constituent gold atoms are formally in zero-valence state.

Oxidation reactions have been a central issue in the active research area of gold nanocluster (Au NC) catalysis since the landmark report by Haruta et al.[1,2] In a series of publications, we showed that Au NCs stabilized by poly(*N*-vinyl-2-pyrrolidone) (**Au:PVP** NCs) exhibit high catalytic activity for aerobic oxidation reactions such as oxidation of alcohols[3] and generation of hydrogen peroxide,[4] but only when the diameter is reduced to less than ca. 2 nm. It was proposed that a superoxo-like molecular oxygen species generated on the cluster surface plays a key role in these oxidation reactions. We also observed that Au:PVP NCs with an average diameter of 1.3 nm (**Au:PVP**(1.3))[5] catalyzed homocoupling reactions of arylboron compounds under aerobic conditions.[6] This result hints at the possibility that an electron-deficient site at the cluster surface, generated by adsorption of O_2, behaves as a formal Lewis acid and provides a site for transmetalation of aryl moieties. In order to test the idea that Au NCs in aqueous media under aerobic conditions act as a Lewis acid, we studied the activity of **Au:PVP**(1.3) in the intramolecular hydroalkoxylation of unactivated alkenes, which is conventionally promoted by Lewis acid catalysts.

Under aerobic oxidation conditions, γ-hydroxyalkenes generally undergo Wacker-type oxidation[7] or oxygenation (Scheme 1).[8] In contrast, when 1,1-diphenyl-4-penten-1-ol (**1a**) was treated with 10 atom % of **Au:PVP**(1.3) and 200 mol % of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) at 50 °C for 16 h in H_2O/DMF mixed solvent under air, **2a** was obtained in 87% yield without the formation of Wacker-type products **3**, **4**, or oxygenation product **5** (Entry 1, Table 1 and Scheme 1). Cyclization did not occur under carefully degassed conditions (Entry 2), or using a catalyst of greater cluster diameter (**Au:PVP**(9.5)); the latter showed no catalytic activity for aerobic oxidation (Entry 3).[3,4,6] These results indicate that O_2 does not act as an oxidant but plays an essential role in the present reaction. The catalytic behavior of **Au:PVP**(1.3) appears to be similar to that of Au^I/Au^{III} complexes, which are applied as Lewis acid catalyst particularly for activation of C–C multiple bonds.[9–11] It is thought that O_2 generates a reaction center with Lewis acid character on the Au NC surface; the constituent atoms of Au NCs are formally in a zero-valence state.

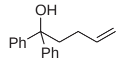
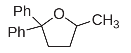
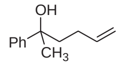
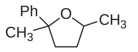
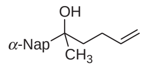
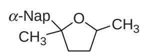
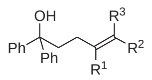
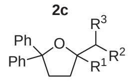
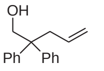
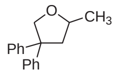
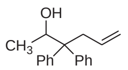
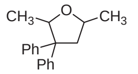
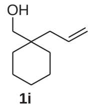
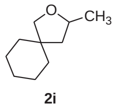
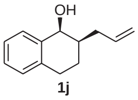
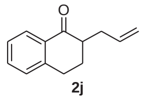
Table 1. The role of molecular oxygen in the cyclization of **1a**



Entry	Catalyst	Conditions	Yield/%
1	**Au:PVP**(1.3)	under air	87
2	**Au:PVP**(1.3)	under degassed conditions	0
3	**Au:PVP**(9.5)	under air	0

Representative results of hydroalkoxylation of alkenes catalyzed by **Au:PVP**(1.3) are summarized in Table 2. The reactivity of tertiary alcohols is dependent to a remarkable extent on the substituents at the α-position of the alcohols. Although the reaction of **1a** proceeds smoothly (Entry 1; also Table 1, Entry 1), no reaction occurs with the phenyl-methyl derivative **1b** (Entry 2). In contrast, cyclization does occur with the α-naphthyl-methyl derivative **1c** to afford **2c** in 62% yield (Entry 3). Although we

Table 2. Hydroalkoxylation of alkenes catalyzed by **Au:PVP**(1.3)[a]

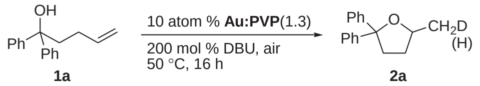
Entry	Alkene	Product	Yield/%[b]
1	 **1a**	 **2a**	87
2	 **1b**	 **2b**	0
3	 **1c**	 **2c**	62 (1.1:1)
			
4	**1d** $R^1 = CH_3$, $R^2 = H$, $R^3 = H$	**2d**	38
5	**1e** $R^1 = H$, $R^2 = CH_3$, $R^3 = H$	**2e**	8
6	**1f** $R^1 = H$, $R^2 = CH_3$, $R^3 = CH_3$	**2f**	0
7	 **1g**	 **2g**	93
8	 **1h**	 **2h**	93 (3.6:1)
9	 **1i**	 **2i**	33
10	 **1j**	 **2j**	77

[a]Reaction conditions:[12] **Au:PVP**(1.3) (10 atom %),[13] alkene (0.05 mmol), DBU (200 mol %), H_2O (10 mL), DMF (5 mL), 50 °C, 16–24 h. [b]Diastereomeric ratios are given in parentheses.

cannot provide a clear-cut explanation for such unprecedented reactivity (Entries 1–3) at this stage, these results suggest that the catalytic site is not a gold ionic species leached out from the cluster but the surface of the cluster. The larger size of the aromatic ring is expected to interact with the surface of the Au NCs stronger.[14] The efficiency of the hydroalkoxylation is also sensitive to subsititution at the alkene moiety. The introduction of other substituents at the internal and/or terminal alkenic carbon decreases the yields of the products (Entries 4–6), probably due to steric hindrance. Next, the reactions of primary/secondary alcohols are examined. It is anticipated that cyclization would compete with alcohol oxidation because the reaction is conducted under conditions similar to those for aerobic oxidation.[3] However, cyclization takes place predominantly for the aliphatic alcohols, giving **2** (Entries 7–9). It is noteworthy that substrates with aromatic rings gave better results in this type of reaction. In contrast, aerobic oxidation is preferred in the reaction of benzylic alcohols, giving the corresponding ketones selectively (Entry 10).

To elucidate the source of the hydrogen at the terminal carbon, the reaction was carried out in D_2O and/or DMF-d_7 (Table 3).[12] Compound **2a**-D was obtained only when DMF-d_7 was employed, which revealed that the hydrogen was introduced via a radical process. It should be pointed out that the use of either D_2O or DMF-d_7 diminished the reaction rate.

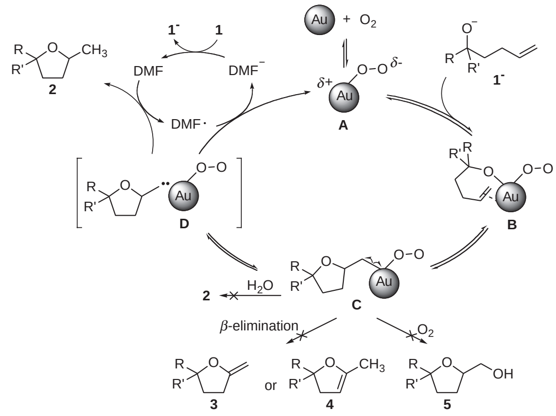
Table 3. Labeling experiment for hydroalkoxylation



Entry	Solvent	Yield/%		
		1a	**2a**-H	**2a**-D
1	H_2O/DMF	0	87	0
2	D_2O/DMF	3	80	0
3	H_2O/DMF-d_7	32	0	63
4	D_2O/DMF-d_7	50	0	42

A possible mechanism is shown in Scheme 1. As proposed in previous studies,[3,4,6] the reaction is initiated by the formation of key intermediate **A**, which possesses an electron-deficient site generated by adsorption of O_2 onto the surface of the Au NCs. **A** acts as a Lewis acid, activating both the alkoxide and alkene by adsorption onto the surface (**B**), and giving **C** by the insertion of an alkene into the O–Au bond. From **C**, neither β-elimination, O_2 insertion, nor protonation proceeds; only homolytic dissociation takes place, generating the radical intermediate **D**, which afforded **2** via hydrogen abstraction from DMF accompanied by the regeneration of free Au NCs. Judging from the decrease in the reaction rate in DMF-d_7, as shown in Table 3, all the steps between **A** and **D** may be in equilibrium.

In summary, we showed that **Au:PVP**(1.3) possesses a unique character as a formal Lewis acid catalyst, emerging only under aerobic conditions in basic aqueous media. Of special note is the unique character of the C–Au intermediate (**C**). That is, the C–Au bond is resistant to β-hydrogen elimination, insertion of O_2, and even protonation, but does undergo homolytic cleavage. On the basis of these phenomena, we consider that Au NCs containing organic ligands have potential as an efficient source of long-lived radicals; this has also been postulated based on a trapping reaction of organic radicals using Au NCs.[15] We hope that the present study represents the beginning of a new era of Au NC use in areas other than oxidation catalysis.



Scheme 1. A possible mechanism for **Au^0:PVP**-catalyzed hydroalkoxylation.

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