A Facile and Efficient Catalytic System for the Oxidation of Alcohols with Gold(III) and Ionic Liquid Immobilized TEMPO under Solvent-Free Conditions

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Abstract: A facile and efficient protocol for the oxidation of alcohols with gold(III) and ionic liquid immobilized TEMPO is described. This catalytic system is highly selective for the oxidation of primary and secondary benzylic alcohols, heterocyclic alcohols, and allylic alcohols affording the respective carbonyl compounds in good to excellent yields.

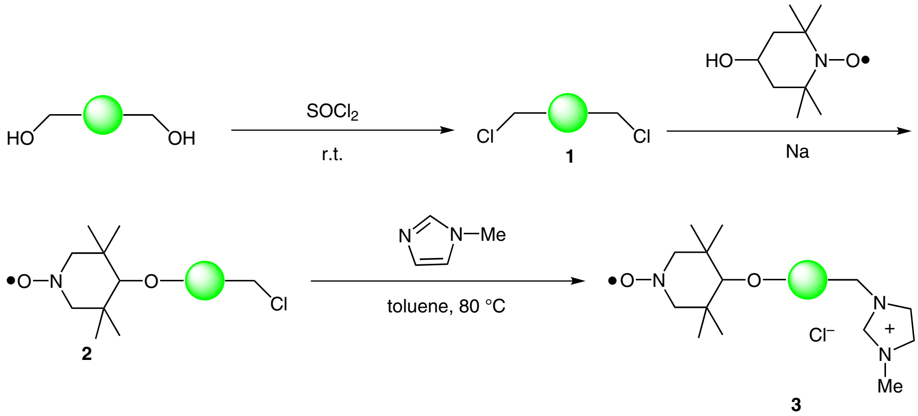
Key words: facile catalytic system, oxidation of alcohols, gold(III), ionic liquid immobilized TEMPO, solvent-free

Selective oxidation of alcohols into carbonyl compounds is one of the most important organic transformations.[1–3] Various chemical reagents have been used to accomplish this transformation efficiently and selectively.[4,5] Recent demand for eco-friendly chemical processes has encouraged the development of clean catalytic oxidations employing O_2 as the ultimate oxidant. These attractive catalytic systems display high atom economy and release only innocuous byproducts. Many transition-metal-supported catalysts such as the Pd/HAP,[6] Pd@resin,[7] Ru/Al_2O_3,[8,9] or salts have been utilized to catalyze this reaction.[10–17]

2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO), as a stable, free nitroxyl radical, has been proved to be a very effective catalyst for the aerobic oxidation of alcohols.[18–23] Immobilization of TEMPO has generated substantial interest. In 2008, Liu[24] et al. described a novel TEMPO-bearing ionic liquid (IL) and its catalytic activity for the selective oxidation of alcohols to their corresponding carbonyl compounds. The IL-supported TEMPO radical shows good catalyst properties in terms of activity and selectivity and can be easily recycled and reused. Wu[25] et al. also described an efficient synthesis of an IL-supported TEMPO which was used for the oxidation of alcohols to aldehydes and ketones. The predictable solubility of IL allows an easy separation of the oxidation products. Furthermore, the IL-supported TEMPO can be recycled and used several times without the loss of efficiency.

Gold is well-known as a very effective catalyst for the oxidation of alcohols; however, recent studies mainly focus on heterogeneous gold nano catalysts[26–28] and examples of gold(III)-catalyzed reactions are very limited.[29] As a result of our interest in developing green reaction protocols, we report herein a novel catalytic system with gold(III) and IL-immobilized TEMPO which has been shown to be an effective catalyst for the selective aerobic oxidation of alcohols into the corresponding aldehydes or ketones.

The synthesis of IL-immobilized TEMPO (Imim-PEG_{1000}-TEMPO) is shown in Scheme 1. Imim-PEG_{1000}-TEMPO was readily prepared in a three-step procedure (Scheme 1). PEG-1000 was treated with thionyl chloride in dry toluene at 0 °C under an inert gas for 24 hours to af-



Scheme 1 Synthesis of Imim-PEG_{1000}-TEMPO

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ford intermediate **1**. The intermediate **1** was then treated with the sodium salt of 4-hydroxy-TEMPO for 12 hours at room temperature to afford intermediate **2**. Then, intermediate **2** was subsequently added to *N*-methylimidazole in toluene at 80 °C for 20 hours to generate the corresponding IL-immobilized TEMPO (Scheme 1).

With benzyl alcohol as the model substrate, exploratory experiments were initiated to screen the catalyst system. The results are summarized in Table 1 and show that both $AuCl_3$ or TEMPO are essential for good performance (Table 1, entries 1–3). The exploratory experiments were then extended by screening metal salts in the catalyst system. It can be seen that, among the salts tested, $AuCl_3$ showed much higher catalytic activity than the other transition-metal salts for the aerobic oxidation of benzyl alcohol (Table 1, entries 3–7). The cobalt and manganese salts showed moderate catalytic activity (Table 1, entries 4 and 5), and nickel and iron salts showed no catalytic activity (Table 1, entries 6 and 7).

Table 1 Effects of Metal Salt on the Oxidation of Benzyl Alcohol[a]

Entry	Metal salt	TEMPO	Conv. (%)	Yield (%)
1	$AuCl_3$	–	–	–
2	–	Imim-PEG_{1000}-TEMPO	–	–
3	$AuCl_3$	Imim-PEG_{1000}-TEMPO	100	95
4	$CoCl_3$	Imim-PEG_{1000}-TEMPO	78	73
5	$MnCl_3$	Imim-PEG_{1000}-TEMPO	56	54
6	$NiCl_3$	Imim-PEG_{1000}-TEMPO	–	trace
7	$FeCl_3$	Imim-PEG_{1000}-TEMPO	–	trace

[a] Reaction conditions: benzyl alcohol (10 mmol), Imim-PEG_{1000}-TEMPO (0.5 mmol), metal salt (0.5 mmol), 60 °C.

Moreover, the effect of the amount of catalyst was evaluated. The reaction was operative in a range of the catalyst loading up to 20 mol% with the best performance in the presence of 5 mol% catalyst (Table 2, entries 1–5). Oxidation occurred most effectively at 60 °C, but the system showed some activity at room temperature (Table 2, entries 6–9). Control experiments were then carried out in other solvents including DMSO, MeCN, and toluene (Table 2, entries 10–12). As expected, toluene did not dissolve the catalyst and demonstrated poor performance under identical conditions, indicating that solubility of the catalyst is important. Imim-PEG_{1000}-TEMPO is superior to TEMPO in DMSO or MeCN. One explanation may be stabilization of the gold(III) species during the catalytic cycle caused by coordination of the chloride. Another reason may be that the formed gold(III) complex has higher activity than the gold(III) ion and could interact with the TEMPO molecule in a manner that is more favorable for the reaction.

Based on these results, the substrate scope of this methodology was examined by employing other alcohols, and the results are shown in Table 3. It is evident that the catalytic system is effective and highly selective for the oxidation of benzylic, heterocyclic, and allylic alcohols to their respective carbonyl compounds. The primary benzylic alcohols gave the best performance, and the electronic properties and steric hindrance of the substituents on the benzene ring not significantly affect reactivity (Table 3, entries 1–9). In the case of substrates containing double bonds, the double bond was not affected (Table 3, entry 10). Furthermore, secondary benzylic alcohols such as benzhydrol gave moderate conversions by prolonging the reaction time (Table 3, entries 11 and 12). Heterocyclic al-

Table 2 Reaction Conditions for the Oxidation of Benzyl Alcohol[a]

Entry	Catalyst (mol%)	Solvent	Temp (°C)	Conv. (%)	Yield (%)
1	–	–	60	–	–
2	Imim-PEG_{1000}-TEMPO (1)/$AuCl_3$ (1)	–	60	89	84
3	Imim-PEG_{1000}-TEMPO (5)/$AuCl_3$ (5)	–	60	100	95
4	Imim-PEG_{1000}-TEMPO (10)/$AuCl_3$ (10)	–	60	100	95
5	Imim-PEG_{1000}-TEMPO (20)/$AuCl_3$ (20)	–	60	100	94
6	Imim-PEG_{1000}-TEMPO (5)/$AuCl_3$ (5)	–	r.t.	54	50
7	Imim-PEG_{1000}-TEMPO (5)/$AuCl_3$ (5)	–	40	90	85
8	Imim-PEG_{1000}-TEMPO (5)/$AuCl_3$ (5)	–	80	100	90
9	Imim-PEG_{1000}-TEMPO (5)/$AuCl_3$ (5)	–	100	100	82
10	TEMPO (5)/$AuCl_3$ (5)	DMSO	60	70	69
11	TEMPO (5)/$AuCl_3$ (5)	MeCN	60	79	75
12	TEMPO (5)/$AuCl_3$ (5)	toluene	60	33	31

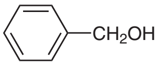
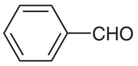
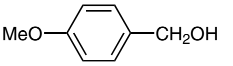
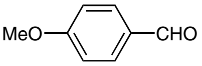
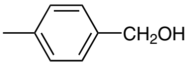
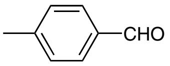
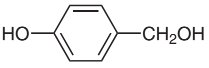
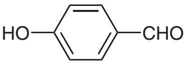
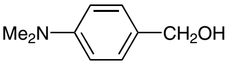
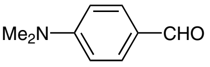
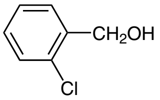
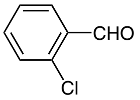
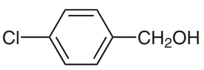
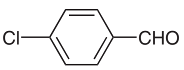
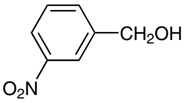
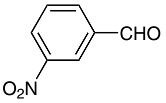
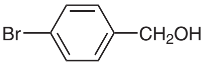
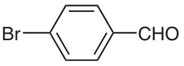
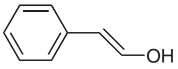
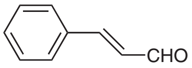
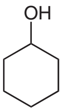
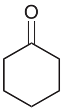
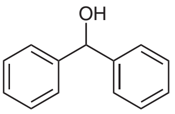
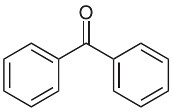
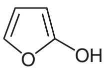
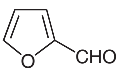
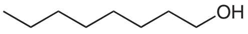
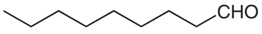
[a] Reaction conditions: benzyl alcohol (10 mmol), Imim-PEG_{1000}-TEMPO or TEMPO, $AuCl_3$, 60 °C.

cohols, such as furfuryl alcohol, were also suitable substrates (Table 3, entries 13). The aliphatic allylic alcohol, cinnamyl alcohol, gave a moderate yield (Table 3, entry 14).

According to the literature and our observations, taking benzyl alcohol as an example, a possible mechanism is proposed in Scheme 2. In this process, TEMPO is oxidized to *N*-oxopiperidinium with the help of gold(III) to initiate a series of electron- and proton-transfer steps that lead to formation of the carbonyl compound. The TEMPOH this generated is oxidized to TEMPO via one electron of the redox cycle with O_2.

In conclusion, we have developed an efficient and environment friendly method for the oxidation of alcohols catalyzed by gold(III) and ionic liquid immobilized TEMPO. Showing to the high activity and substrate compatibility, the catalytic system demonstrated a good catalytic performance. Further investigations of the application of this catalyst to other oxidation processes as well as to clarify the precise mechanism of this oxidation process are currently in progress.

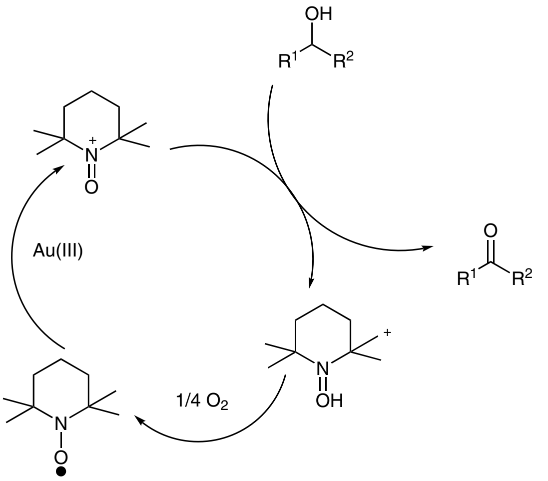
Table 3 Oxidation of Various Alcohols[a]

Entry	Substrate	Product	Time (h)	Conv. (%)[b]	Yield (%)[c]
1			6	100	95
2			5	100	96
3			8	99	95
4			6	>99	98
5			6	100	96
6			8	>99	98
7			8	100	95
8			9	99	93
9			8	99	88
10			6	91	84
11			10	93	92
12			10	90	89
13			8	90	85
14			16	80	74

[a] Reaction conditions: alcohol (10 mmol), Imim-PEG_{1000}-TEMPO (0.5 mmol), $AuCl_3$ (0.5 mmol), 60 °C.

[b] Determined by HPLC.

[c] Isolated yield.



Scheme 2 The mechanism of oxidation of alcohols

General Procedure for the Preparation of Imim-PEG$_{1000}$-TEMPO
To a solution of PEG-1000 (0.06 mol, 60 g) in toluene (150 mL) pyridine (0.12 mol, 9.6 mL) was added, followed by $SOCl_2$ (0.12 mol, 8.7 mL) over 30 min under N_2 atmosphere at 0 °C. The resulting slurry was stirred for 24 h at r.t. and filtered. Toluene was then removed by rotary evaporation under reduced pressure to give intermediate **1** as a gray viscous liquid. To a suspension of Na (1.15 g, 0.05 mol) in benzene (100 mL) 4-hydroxy-TEMPO (8.6 g, 0.05 mol) was added, and the resulting slurry was stirred for 8 h at r.t. under reflux. Intermediate **1** (0.025 mol) was then added and stirring resumed for 12 h at r.t. The suspension was then filtered, and the filtrate was concentrated under reduced pressure. This solution was then added to Et_2O, the mixture stirred vigorously, the precipitate collected by filtration, washed twice with Et_2O (50 mL), and dried under vacuum. The product **2** was obtained as orange-red viscous solid. To *N*-methylimidazole (2.05 g, 0.025 mol) dissolved in toluene, intermediate **2** (0.025 mol) was added, and the mixture was stirred at 80 °C for 20 h. The reaction progress was determined by HPLC and, when complete, the mixture was evaporated under reduced pressure to give Imim-PEG1000-TEMPO as an orange red oil with a yield of 98.%.

General Procedure for the Oxidation of Alcohols
To a 10 mL round-bottom flask, Imim-PEG$_{1000}$-TEMPO (0.5 mmol), $AuCl_3$ (0.5 mmol) and benzyl alcohol (10 mmol) were successively added with vigorous stiring. The reaction was allowed to proceed at 60 °C and monitored by TLC. Upon completion, the reaction mixture was cooled to r.t. and extracted three times by adding Et_2O. The organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure to give benzaldehyde (95% yield). All products had spectroscopic data consistent with the assigned structures.

Acknowledgment

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