

Oxidation of alcohols with copper(II) salts mediated by nitroxyl radicals immobilized on ultrafine silica and ferrite surface

Norio Tsubokawa ^{a,*}, Takuya Kimoto ^a, Takeshi Endo ^b

^a Department of Chemistry and Chemical Engineering, Faculty of Engineering, Niigata University, 8050, Ikarashi 2-nocho, Niigata 950-21, Japan

^b Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, Japan

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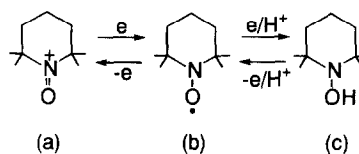
Abstract

The oxidations of alcohols with copper(II) salts mediated by 2,2,6,6-tetramethylpiperidinyloxy radical (TEMPO) moieties immobilized on ultrafine silica and ferrite surface were investigated. The immobilization of TEMPO structure on the silica and ferrite surface was achieved by the reaction of 4-hydroxyl TEMPO with acid anhydride groups on these surfaces, which were introduced by the treatment of surface carrying hydroxyl groups with 4-trimethoxysilyl-1,2,5,6-tetrahydrophthalic anhydride. The oxidations of primary alcohols, secondary alcohols, and diols with copper(II) salts scarcely proceeded in the absence of mediator. On the contrary, in the presence of TEMPO-supported silica and ferrite (Silica-TEMPO and Ferrite-TEMPO) as mediator, primary alcohols, secondary alcohols, and diols were oxidized with copper(II) salts to give the corresponding aldehydes, ketones, and lactones, respectively. Based on the above results, the oxidations of alcohols were considered to proceed as follows: alcohols are oxidized with oxoamminium moieties on silica and ferrite surface, which were formed by the reaction of surface TEMPO moieties with copper(II) salts, and oxoamminium moieties on the surface itself are reduced to the corresponding hydroxylamine moieties after the oxidation. Then the hydroxylamine moieties are oxidized with copper(II) salts to regenerate TEMPO moieties on the surface. For example, in the case of the oxidation of benzyl alcohol, Silica-TEMPO was recycled about 45 times. Silica-TEMPO and Ferrite-TEMPO were readily recovered from reaction mixture by centrifugation.

Keywords: Alcohols; Ferrite; Mediator; Nitroxyl radical; Oxidation; Silica

1. Introduction

2,2,6,6-Tetramethylpiperidinyloxy radical (TEMPO) is known as a stable radical and used as spin label and radical trapping agents of unstable radicals. The nitroxyl radical (b), TEMPO derivatives, is readily converted to oxoamminium salt (a) by one electron oxidation and to hydroxyl amine (c) by one electron reduction as shown in Scheme 1 [1,2].



Scheme 1.

It has been reported that oxoamminium salts act as oxidizing agent of alcohols and diols to the corresponding carbonyl compounds and lactones [3–6].

Furthermore, the oxidation of alcohols and diols by copper(II) salts has reported to be medi-

* Corresponding author. Fax. (+81-25)2633174.

ated by TEMPO [7–9]. In the oxidation using TEMPO as mediator, various copper(II) salts can oxidize primary alcohols, secondary alcohols, and aliphatic diols, to give the corresponding aldehydes, ketones, and lactones, respectively. During the reaction, these alcohols are oxidized with oxoammonium salt, which is formed easily by the reaction of TEMPO with copper(II) salts, and oxoammonium salt itself is reduced to hydroxylamine after the oxidation. Then the hydroxylamine is oxidized with copper(II) salts to regenerate TEMPO. Furthermore, Semmelheck et al. have reported the oxidation of alcohols with oxygen and copper(II) salts mediated by TEMPO [10].

On the other hand, the reaction by use of reagent-supported insoluble powders have several advantages: (1) product isolation is simplified, (2) expensive reagent is easily recovered and possibly reused, and (3) reagent-supported powders are non-toxic since it is insoluble and non-volatile.

In the present paper, the immobilization of TEMPO moieties on ultrafine silica and ferrite surface and the oxidation of alcohols with copper(II) salts mediated by TEMPO moieties immobilized on these surfaces are described.

2. Experimental

2.1. Materials and reagents

Ultrafine silica and ferrite used were Aerosil 200 obtained from Nippon Aerosil Co., Japan and ultrafine nickel–zinc ferrite ($\text{NiO ZnO Fe}_2\text{O}_3$) obtained from Sumitomo Cement Co. Ltd., Japan, respectively. The properties of these ultrafine particles were shown in Table 1. The content of hydroxyl groups was determined by measuring volumetrically the amount of ethane evolved by the reaction with triethylaluminum [11,12]. The silica and ferrite were washed with distilled water and dried at 110°C in vacuo before use.

4-Trimethoxysilyl-1,2,5,6-tetrahydrophthalic anhydride (TSPA) obtained from Nissan Chemical Ind. Ltd., Japan, was used without further

Table 1
Properties of ultrafine silica and ferrite

Ultrafine particle	BET surface area (m ² /g)	Particle size (nm)	OH group (mmol/g)
Silica ^a	200	16	1.37
Ferrite ^b	100	15	0.50

^a Aerosil 200 (Nippon Aerosil Co., Japan).

^b NiO ZnO Fe₂O₃ (Sumitomo Cement Co. Ltd., Japan).

purification. 4-Hydroxy-2,2,6,6-tetramethylpiperidinyloxy radical (4-Hydroxy TEMPO) obtained from Aldrich Chemical Co. was used without further purification.

Benzyl alcohol, n-octyl alcohol, n-butyl alcohol, ethyl alcohol, 2-hexanol, 3-hexanol, cyclohexanol, benzhydrol, 1,4-butanediol, and 1,5-pentanediol were used after ordinary purification. Guaranteed reagent grade copper(II) chloride, copper(II) nitrate, copper(II) hydroxide, and *N,N'*-dicyclohexylcarbodiimide (DCC) were used without purification.

Acetonitrile was dried over potassium hydroxide, and subsequently distilled under diphosphorous pentoxide. Dichloromethane was purified by distillation.

2.2. Immobilization of nitroxyl radicals onto silica and ferrite surface

The immobilization of nitroxyl radicals onto silica and ferrite surface was achieved by the reaction of 4-hydroxy TEMPO with these surfaces carrying acid anhydride groups using DCC as a catalyst.

The immobilization of acid anhydride moieties on silica and ferrite surface was achieved by the reaction of hydroxyl groups on silica and ferrite surface with TSPA in toluene. The procedures were described in detail in a preceding paper [13].

The reaction of acid anhydride moieties with 4-hydroxy TEMPO was carried out as follows. Into a 100 cm³ flask, 2.0 g of ultrafine silica (ferrite) having acid anhydride moieties, 0.30 g of 4-hydroxy TEMPO, 0.30 g of DCC, and 30.0 cm³ of toluene were charged and the reaction mixture was stirred at 70°C under nitrogen. After the reac-

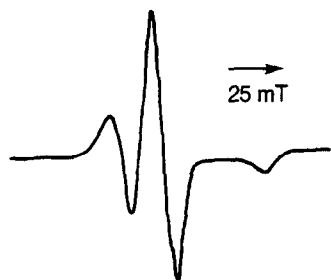
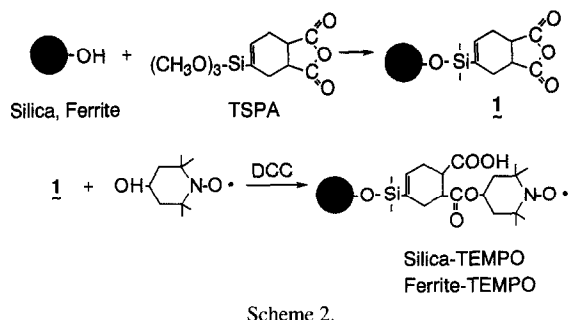


Fig. 1. ESR spectra of nitroxyl radical-supported silica (Silica-TEMPO).

Table 2
The amount of TEMPO groups on silica and ferrite

Ultrafine particle	Acid anhydride group (mmol/g)	TEMPO group (mmol/g)
Silica	0.96	0.20
Ferrite	0.30	0.09

tion for 8 h, the resulting silica (or ferrite) was washed with methanol repeatedly and dried at 110°C in vacuo.

Nitroxyl radical-supported silica and ferrite were abbreviated as Silica-TEMPO and Ferrite-TEMPO, respectively.

2.3. Oxidation of alcohols with Cu(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO

The oxidation with copper(II) salts mediated by TEMPO-supported silica and ferrite was carried out as follows. Into a 100 cm³ flask, 0.10 g of Silica-TEMPO (or Ferrite-TEMPO), 1.0 mmol of alcohol, 3 equiv. of copper(II) salt as oxidant, 2.0 cm³ of acetonitrile as a solvent, and one equivalent of copper(II) hydroxide were charged. The reaction mixture was stirred with a magnetic stir-

rer at 25°C. When Ferrite-TEMPO was used as mediator, the reaction was carried out in a sealed tube and the reaction mixture was shaken at 25°C.

After the reaction, Silica-TEMPO and Ferrite-TEMPO were removed from the reaction mixture by centrifugation. Ferrite-TEMPO is recovered by use of a magnet. Then the product was determined by GLC and the yield was calculated.

2.4. IR and ESR spectra

IR spectra of TEMPO-supported silica and ferrite were recorded on a Hitachi infrared spectrometer Model 730-30 using KBr pellets. ESR spectra were obtained at ambient temperature on a JEOL JES-FEIXG spectrometer. The sample silica for the ESR measurement was sealed in ESR tubes in vacuo.

3. Results and discussion

3.1. Immobilization of TEMPO on silica and ferrite surface

We chose ultrafine silica and ferrite as support of TEMPO, because the silica has high hydroxyl group content and ferrite can be removed from reaction mixture by a magnet. The immobilization of nitroxyl radicals on these surfaces was carried out by the reaction of 4-hydroxy TEMPO with surface acid anhydride groups, which were prepared by the treatment of hydroxyl groups with 4-trimethoxysilyl-1,2,5,6-tetrahydrophthalic anhydride (TSPA), in the presence of DCC as shown in Scheme 2.

Fig. 1 shows the ESR spectrum of the silica obtained from the above reaction. The spectrum was consistent with that of randomly oriented TEMPO in solid [14,15]. Therefore, it is clear that nitroxyl radicals are successfully immobilized on the silica surface. The amount of nitroxyl radicals immobilized on silica and ferrite surface was determined by elemental analysis as shown in Table 2. These results indicate that the reaction degree of acid anhydride moieties on silica and

Table 3
Oxidation of benzyl alcohol with Cu(II) salts under several conditions^a

Mediator	Oxidant	(equiv.)	Cu(OH) ₂ (equiv.)	Yield ^b (%)
None	CuCl ₂	3	1	0.5
Untreated silica	CuCl ₂	3	1	0.5
Silica-TEMPO	CuCl ₂	3	1	88.1
Silica-TEMPO	Cu-(NO ₃) ₂ ·3H ₂ O	3	2	90.1
Silica-TEMPO	- ^c	-	1	1.0
Untreated ferrite	CuCl ₂	3	1	0.5
Ferrite-TEMPO	CuCl ₂	3	1	33.7
Ferrite-TEMPO	Cu-(NO ₃) ₂ ·3H ₂ O	3	2	43.7
Ferrite-TEMPO	- ^c	-	1	0.7

^a Silica, 0.10 g (ferrite, 0.20 g); benzyl alcohol, 1.0 mmol; CH₃CN, 2.0 ml; 25°C; 48 h.

^b GLC yield based on the starting alcohol.

^c The reaction was carried out in vacuo in the dark.

ferrite surface reacted with 4-hydroxyl TEMPO was relatively small: only 20–30% of acid anhydride moieties on these surfaces reacted with 4-hydroxy TEMPO. This may be due to the fact that the reaction is subjected to steric hindrance when acid anhydride moieties are fixed on these solid surfaces.

3.2. Oxidation of benzyl alcohol with Cu(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO

The oxidation of benzyl alcohol with copper(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO was examined. The oxidations by use of Silica-TEMPO and Ferrite-TEMPO as mediator have several advantages: (1) product isolation is simplified, (2) Silica-TEMPO and Ferrite-TEMPO are easily recovered and possibly re-used, and (3) Silica-TEMPO and Ferrite-TEMPO is non-toxic since it is insoluble and non-volatile.

Table 3 shows the results of the oxidation of benzyl alcohol with copper(II) salts in the pres-

ence and in the absence of mediator. In the reaction, copper(II) hydroxide was used as acid trapping agent. Copper(II) salts alone have no ability to oxidize benzyl alcohol and in the presence of untreated silica and ferrite benzyl alcohol is not oxidized by copper(II) salt at all. In the absence of oxidant (in oxygen free atmosphere in the dark), the oxidation of benzyl alcohol was scarcely proceeded even in the presence of Silica-TEMPO. On the contrary, in the presence of Silica-TEMPO or Ferrite-TEMPO, the oxidation of benzyl alcohol with copper(II) salts, such as copper(II) chloride and copper(II) nitrate, proceeded to give benzaldehyde.

Based on the above results, it is concluded that Silica-TEMPO and Ferrite-TEMPO act as a mediator for the oxidation of benzyl alcohol with copper(II) salts. The oxidation of benzyl alcohol may be considered to proceed as follows (Scheme 3): benzyl alcohol is oxidized with oxoammonium moieties on silica surface, which are formed by the reaction of surface TEMPO moieties with copper(II) salts, and oxoammonium moieties on silica itself are reduced to hydroxylamine moieties after the oxidation. Then the hydroxylamine groups are again oxidized with copper(II) salt to regenerate Silica-TEMPO. For example, in the case of the oxidation of benzyl alcohol, Silica-TEMPO was recycled about 45 times.

3.3. Oxidation of various alcohols with Cu(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO

Table 4 shows the results of the oxidation of primary alcohols with copper(II) salts mediated

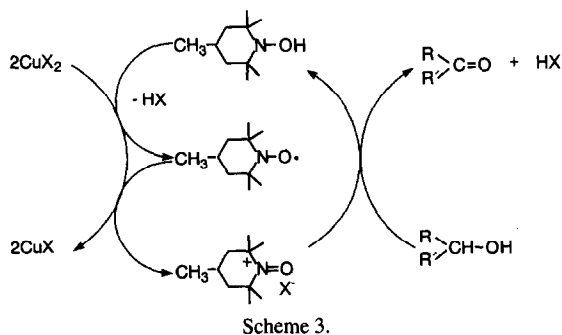


Table 4
Oxidation of primary alcohols with Cu(II) salts mediated by Silica-TEMPO^a

Alcohol	Oxidant	Yield (%) ^b
Ethyl alcohol	CuCl ₂	15.7
	Cu(NO ₃) ₂ ·3H ₂ O	17.8
n-Butyl alcohol	CuCl ₂	30.2
	Cu(NO ₃) ₂ ·3H ₂ O	32.1
n-Octyl alcohol	CuCl ₂	37.4
Benzyl alcohol	CuCl ₂	88.1

^a Silica-TEMPO, 0.10 g; alcohol, 1.0 mmol; oxidant, 3.0 mmol; Cu(OH)₂, 1.0 mmol; CH₃CN, 2.0 ml; 25°C: 48 h.

^b GLC yield based on the starting alcohol.

Table 5
Oxidation of secondary alcohols with Cu(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO^a

Alcohol	Mediator	Oxidant	Yield (%) ^b
2-Hexanol	Silica-TEMPO	CuCl ₂	42.6
	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	35.5
	Silica-TEMPO	— ^c	0.5
	Ferrite-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	12.3
3-Hexanol	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	40.2
Cyclohexanol	Silica-TEMPO	CuCl ₂	38.4
	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	70.8
Benzhydrol	Silica-TEMPO	CuCl ₂	55.9
	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	0.6
	Ferrite-TEMPO	CuCl ₂	30.3
	Ferrite-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	20.3

^a Alcohol, 0.05 mmol; Oxidant, 0.15 mmol; Cu(OH)₂, 0.1 mmol; CH₂Cl₂, 1.5 ml; 25°C: 24 h.

^b GLC yield based on the starting alcohol.

^c The reaction was carried out in vacuo in the dark.

Table 6
Oxidation of diols with Cu(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO^a

Diol	Mediator	Oxidant	Yield (%) ^b
1,4-Butanediol	Silica-TEMPO	CuCl ₂	65.8
	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	60.5
	Ferrite-TEMPO	CuCl ₂	33.1
	Ferrite-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	40.4
1,5-Pentanediol	Silica-TEMPO	Cu(NO ₃) ₂ ·3H ₂ O	10.2
	Silica-TEMPO	CuCl ₂	12.1

^a Mediator, 0.10 g; diol, 0.55 mmol; Oxidant, 1.65 mmol; Cu(OH)₂, 1.10 mmol; CH₂Cl₂, 1.5 ml; 25°C: 24 h.

^b GLC yield based on the starting diol.

by Silica-TEMPO. It became apparent that the oxidation of these primary alcohols proceeded to give the corresponding aldehydes [5,7].

Furthermore, the oxidation of secondary alcohols was examined. As shown in Table 5, these secondary alcohols were also oxidized with copper(II) salts using Silica-TEMPO and Ferrite-TEMPO as mediator to give the corresponding ketones [5,7]. The ability of Ferrite-TEMPO as mediator was considerably smaller than that of Silica-TEMPO. This may be due to lower TEMPO group content of ferrite surface.

Table 6 shows the results of the oxidation of diols with copper(II) salts mediated by Silica-TEMPO and Ferrite-TEMPO. It was found that diols are also oxidized with copper(II) salts using Silica-TEMPO and Ferrite-TEMPO as mediator to give the corresponding lactones [6,8].

4. Conclusions

The immobilization of TEMPO moieties on silica and ferrite surface was achieved by the reaction of 4-hydroxyl TEMPO with acid anhydride moieties previously introduced onto these surfaces. TEMPO-supported silica and ferrite has ability to mediate the oxidation of alcohols with copper(II) salts to give the corresponding aldehydes, ketones, and lactones. These TEMPO-supported powders were readily recovered from reaction mixture by centrifugation and especially TEMPO-supported ferrite was recovered by use of a magnet.

TEMPO-supported silica and ferrite are expected to be able to apply as a mediator for the oxidation of alcohols with oxygen and for the oxidation of terminal hydroxyl groups of polymers to produce functional polymers having terminal formyl groups.

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