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Deep eutectic solvent supported TEMPO for oxidation of alcohols†

Yuecheng Zhang, Fenglian Lü, Xiaohui Cao and Jiquan Zhao*

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A novel deep eutectic solvent supported TEMPO (DES–TEMPO) composed of *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)dodecyl ammonium salt ([Quaternium-TEMPO]$^+$Br$^-$) and urea was prepared. An efficient catalytic system for the oxidation of alcohols with molecular oxygen as terminal oxidant has been developed from DES–TEMPO and $Fe(NO_3)_3 \cdot 9H_2O$. The DES–TEMPO/$Fe(NO_3)_3$ system showed good performances on the selective oxidation of various alcohols to the corresponding aldehydes and ketones under mild and solvent-free conditions. The DES could be recovered easily and recycled up to five times in the oxidation of benzyl alcohol without significant loss of catalytic activity.

1. Introduction

The oxidation of alcohols to the corresponding aldehydes and ketones is one of the most widely used reactions in organic chemistry, and the carbonyl compounds are used in production of bulk and fine chemicals such as perfumes, pharmaceuticals and organic intermediates.[1–3] Traditional methods to carry out this reaction involve the use of stoichiometric inorganic oxidants, such as chromium(VI) oxide,[1,4] MnO_2 or hypervalent iodine compounds,[5–9] which would generate large amount of by-products and cause pollution to the environment. From both economic and environmental viewpoints, the development of effective catalytic oxidation processes with molecular oxygen as the terminal oxidant is most attractive, because molecular oxygen is inexpensive and water is produced as the only by-product in principle. Many catalytic systems have been developed and showed high efficiency in the aerobic oxidation of alcohols to the corresponding aldehydes and ketones. Among all the systems the ones based on stable nitroxyl radical 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) in combination with metals as co-catalysts are the most reported.[10–19] Of particular interest are the catalytic systems involving iron as co-catalyst because iron is very cheap and readily available. Several TEMPO based catalytic systems involving iron as co-catalyst[15–20] have been found being effective in the aerobic oxidation of alcohols. Although these systems are successful for efficient aerobic oxidation of alcohols, the separation of TEMPO from reaction products remains a problem especially on a large scale production. Immobilization of TEMPO on some supports can be regarded as a good alternative. Therefore, TEMPO has been immobilized onto various inorganic[21–28] and organic supports or polymers,[29–32] affording diversified catalysts so as to realize the separation of TEMPO from the reaction mixture. However, the immobilization of TEMPO on solid supports generally results in decrease of activity or extending reaction time in some cases. For resolving this problem TEMPO has been also supported on several ionic liquids.[33–35] Due to their good mobility the ionic liquid-supported TEMPO showed performances similar to those of non-supported counterpart in terms of activity and selectivity.

Deep eutective solvents (DESs) as a novel class of ionic liquids have been receiving great attention.[36] DESs, which were first reported by Abbott and co-workers,[37] are generally obtained by the interfusion of quaternary ammonium salts and hydrogen bond donors (*e.g.* amides, amines, alcohols, and carboxylic acids). When the components are mixed the melting point is drastically decreased. The melting point depression, relative to the melting points of the individual components in the mixture, results from the charge delocalization of hydrogen bonding between the halide anion and the hydrogen donor moiety. DESs have their unique properties except those similar to ionic liquids, which make them excellent choices for the preparation of materials in different fields.[38–44] Their ionic nature and relatively high polarity show high solubility for many ionic species, such as metal salts. They also have some momentous advantages over other types of ionic liquids, especially their simple and easy preparation as pure phases from cheap and easily available components and their relative chemical stability towards atmospheric moisture and temperature.[36,37] Therefore, we attempt to immobilize TEMPO on a DES to obtain a novel TEMPO-based catalyst with advantages of easy separation and good mobility for the oxidation of alcohols. Encouragingly, a low catalytic amount of the DES supported TEMPO in conjugation with $Fe(NO_3)_3$ has shown excellent catalytic properties in

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School of Chemical Engineering and Technology, Hebei University of Technology, Tianjin 300130, People's Republic of China. E-mail: zhaojq@hebut.edu.cn; yczhang@hebut.edu.cn; Fax: +86 22 60202926; Tel: +86 22 60202926; +86 2260204279

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the aerobic oxidation of various alcohols under mild and solvent-free conditions. Herein, we report the preparation and catalytic performances of the DES supported TEMPO on the oxidation of alcohols with molecular oxygen as a terminal oxidant.

2. Results and discussion

2.1 Synthesis of *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)dodecyl ammonium salt ($[\text{Quaternium-TEMPO}]^+Br^-$)

With the aim of preparation of DES supported TEMPO, a precursor quaternary ammonium with a TEMPO moiety, which is *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl) dodecyl ammonium bromide ($[\text{Quaternium-TEMPO}]^+Br^-$) was synthesized in two steps as shown in Scheme 1. First, 4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl bromide was synthesized from 4-OH-TEMPO and 1,4-dibromobutane followed the standard procedure in literature.[45] Then quaternization of *N*,*N*-dimethyldodecylamine with 4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl) butyl bromide gave $[\text{Quaternium-TEMPO}]^+Br^-$ in 76% yield. The structure of $[\text{Quaternium-TEMPO}]^+Br^-$ was characterized by ^1H NMR, ^{13}C NMR and HR-MS (ESI). Due to the interference of the free radical present in the structure of $[\text{Quaternium-TEMPO}]^+Br^-$, the ^1H NMR and ^{13}C NMR were obtained from the sample of $[\text{Quaternium-TEMPO}]^+Br^-$ reduced by phenylhydrazine.

2.2 Preparation of DES supported TEMPO based on $[\text{Quaternium-TEMPO}]^+Br^-$ and urea

With the $[\text{Quaternium-TEMPO}]^+Br^-$ in hand, a series of DESs with a TEMPO moiety (DES supported TEMPO) were prepared by mixing $[\text{Quaternium-TEMPO}]^+Br^-$ with urea in different molar ratios. Here, urea acts as a hydrogen bond donor.[36] In the preparation process the two solids were mixed together firstly. The mixture was heated slowly and maintained at 60 °C to 80 °C for a period of time resulting in the formation of eutectic solvent with 100% atom economy. From Table 1 it can be seen that the melting points of the resulted DESs with a TEMPO moiety (DES–TEMPO) are dependent on the molar ratio of $[\text{Quaternium-TEMPO}]^+Br^-$ to urea. If the molar ratio of $[\text{Quaternium-TEMPO}]^+Br^-$ to urea was lower than 2 : 1, the melting points of DESs were always higher than 60 °C. With the increase of $[\text{Quaternium-TEMPO}]^+Br^-$, the melting points of the DESs decreased. When the molar ratio of $[\text{Quaternium-TEMPO}]^+Br^-$ to urea was 2 : 1, a DES with a melting point of 60 °C was received and the melting point maintained constant with further increase of $[\text{Quaternium-TEMPO}]^+Br^-$. It is conceivable that each amino group in the urea structure is combined with a $[\text{Quaternium-TEMPO}]^+Br^-$ through a hydrogen bond in this case (Scheme 2). Here, we can say that the TEMPO was supported on DES. This DES supported TEMPO ($[\text{Quaternium-TEMPO}]^+Br^-$–urea = 2 : 1), which is denoted as DES–TEMPO, is miscible with various alcohols and capable of dissolving $Fe(NO_3)_3$.

Table 1 Melting points and viscosities of DESs with different molar ratios of $[\text{Quaternium-TEMPO}]^+Br^-$ to urea

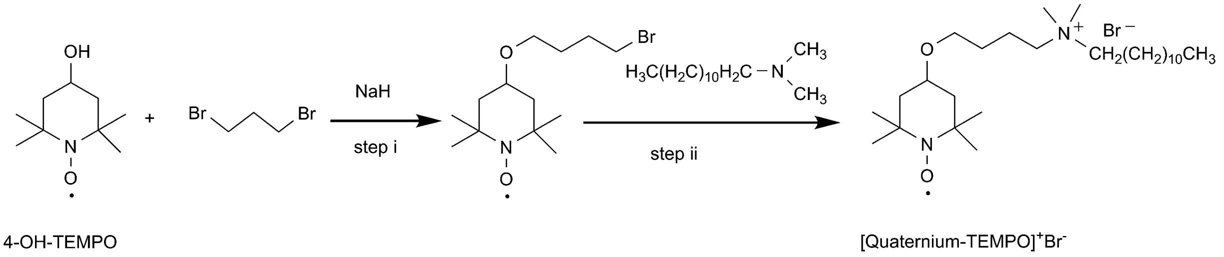
Entry	Urea: $[\text{Quaternium-TEMPO}]^+Br^{-a}$	T_f (°C)	Viscosities (cP)
1	1 : 0.5	80	221(80 °C)
2	1 : 1	70	329(70 °C)
3			635(60 °C)
4	1 : 2	60	355(70 °C)
5			262(80 °C)
6	1 : 3	60	660(60 °C)

[a] Molar ratio.

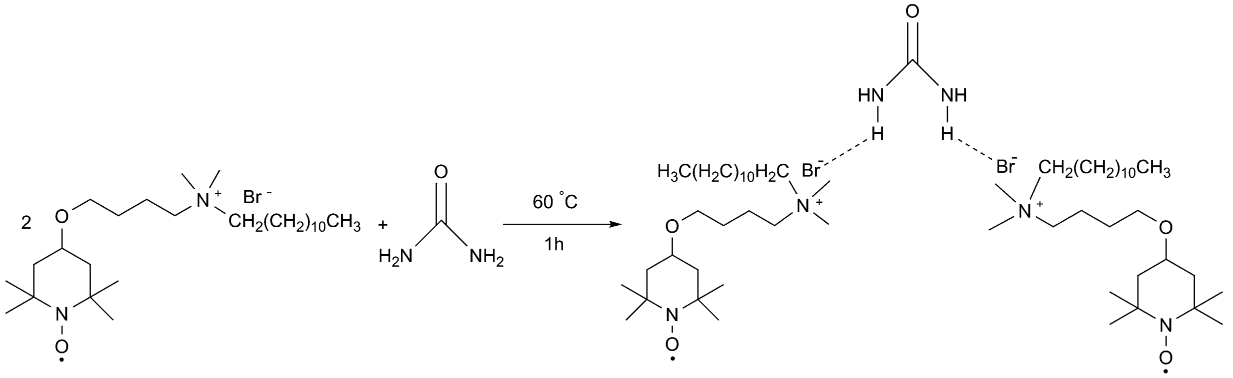
The viscosities of the DES–TEMPOs have also been listed in Table 1. It can be found that the viscosities of the DES–TEMPOs increased with the molar ratio of $[\text{Quaternium-TEMPO}]^+Br^-$ to urea. In addition, the viscosities of the DES–TEMPOs decreased with the increase of temperature.

2.3 Catalytic activity

The catalytic performance of the DES–TEMPO in combination with $Fe(NO_3)_3 \cdot 9H_2O$ as co-catalyst was evaluated for the aerobic oxidation of benzyl alcohol as a model substrate. The reaction was carried out under atmospheric O_2 pressure and solvent-free conditions at 60 °C—the melting point of DES–TEMPO. The benzyl alcohol (10 mmol) was completely converted to benzaldehyde with a selectivity of higher than 99% in 1.5 h in the presence of DES–TEMPO (1.25 mol%) and $Fe(NO_3)_3 \cdot 9H_2O$ (3 mol%) (Table 2, entry 4). This corresponds to a TOF of 26.4 h^{-1} which is an excellent result for an aerobic oxidation of alcohols involving a TEMPO catalyst. Decreasing the DES–TEMPO loading from 1.25 mol% to 1 mol% led to slow reaction, the reaction time required to finish the reaction increased from 1.5 h to 2.5 h (Table 2, entries 4 and 6). It is worth noting that



Scheme 1 General synthetic route for $[\text{Quaternium-TEMPO}]^+Br^-$.



Scheme 2 The preparation and structure of DES-supported TEMPO.

Table 2 Effect of each component in the DES–TEMPO/$Fe(NO_3)_3$ catalyst on the aerobic oxidation of benzyl alcohol[a]

Entry	DES–TEMPO (mol%)	$Fe(NO_3)_3$ (%)	Time (h)	Conv.[b] (%)	Select.[b] (%)	TON[c]	TOF[d] (h^{-1})
1	0	3	1	8.7	>99	0	0
2	1.25	0	1	0.4	>99	0.2	0.2
3	1.25	3	1	93	>99	37.2	37.2
4	1.25	3	1.5	>99	>99	39.6	26.4
5	1.25	2	4.5	>99	>99	39.6	8.8
6	1.00	3	2.5	>99	>99	49.5	19.8
7[e]	2.50	3	1.5	86	>99	34.4	23.0

[a] Reaction conditions: benzyl alcohol 10 mmol, reaction temperature 60 °C, atmospheric oxygen pressure. [b] Conversions and selectivity were determined by GC (area normalization method). [c] TON = moles of product/2(moles of DES–TEMPO). [d] TOF = TON/reaction time. [e] TEMPO was used instead of DES–TEMPO.

the use of TEMPO instead of DES–TEMPO resulted in a decrease of the conversion of benzyl alcohol under the same reaction conditions (Table 2, entry 7), confirming the favorable role of the DES moiety to the oxidation reaction. Either only use of DES–TEMPO without $Fe(NO_3)_3 \cdot 9H_2O$ as a co-catalyst or $Fe(NO_3)_3 \cdot 9H_2O$ in the absence of DES–TEMPO afforded very poor results, which indicated that both DES–TEMPO and $Fe(NO_3)_3$ were essential in the aerobic oxidation of benzyl alcohol (Table 2, entries 1 and 2). It can be concluded that 1.25 mol% of DES–TEMPO in combination with 3% $Fe(NO_3)_3 \cdot 9H_2O$ as catalytic system was very effective in the oxidation of benzyl alcohol to benzaldehyde with oxygen as an oxidant.

The reaction was also performed under different temperature. Generally, the reaction rate increased with the increase of reaction temperature. Detailed results can be found in ESI.†

Several metal nitrates and ferric chloride were also evaluated as co-catalyst in the oxidation of benzyl alcohol. As shown in Table 3, only $Fe(NO_3)_3 \cdot 9H_2O$ and $Cr(NO_3)_3 \cdot 9H_2O$ worked well and had similar efficiency (Table 3, entries 3 and7). The reaction catalyzed by co-catalysts such as $Cu(NO_3)_2 \cdot 3H_2O$ and $Co(NO_3)_2 \cdot 6H_2O$ produced unfavorable results (Table 3, entries 5 and 6). The common feature of Fe^{3+} and Cr^{3+} is that both of them have higher oxidation potentials than Cu^{2+} and Co^{2+}. $FeCl_3 \cdot 6H_2O$ itself as co-catalyst did not work too (Table 3, entry 1). However, the reaction proceeded in moderate efficiency when $NaNO_2$ was added (Table 3, entry 2). The results indicate that iron counterion is critical to the reaction, and NO_x is essential in the reaction. It should be mentioned that excess water retarded the reaction (Table 3, entry 4).

In order to evaluate the versatility of this novel catalytic system, the aerobic oxidation of various alcohols including secondary aliphatic alcohols, benzylic alcohols, heterocyclic alcohols and also primary alcohols to the corresponding carbonyl compounds was explored, and the results are shown in Table 4. It can be seen from Table 4 that various types of primary benzylic alcohols, including those bearing both electron-withdrawing and electron-donating groups, were selectively converted to their corresponding aromatic aldehydes in excellent yields under the optimal reaction conditions. However, the time required to finish the reaction was different (Table 4, entries 1, 2, 5, 6, 8), which is different from aerobic oxidation of alcohols catalyzed by a metal-free catalyst system.[46] These results demonstrated that electronic effects seem to have some effects on the reaction of substrate with a substituent para to the -hydroxymethyl. As observed in the case of non-supported 4-OH-TEMPO as a catalyst,[15] electron-donating groups were in favor of the reaction, whereas electron-withdrawing groups were unfavorable to the reaction. In addition, the position of the substituent on the benzene ring has certain effects on the reactivity of benzylic alcohols, too. The substrate with an *o*-substituent showed poor reactivity compared to that with an *m*- or *p*-substituent due to the steric hindrance (Table 4, entries

Table 3 DES–TEMPO catalyzed aerobic oxidation of benzyl alcohol with different metal salts as co-catalysts[a]

Entry	Metal salts	Time (h)	Conv.[b] (%)	Select.[b] (%)	TON[c]	TOF[d] (h^{-1})
1	$FeCl_3\cdot6H_2O$	1.5	3.1	>99	1.2	0.8
2	$FeCl_3\cdot6H_2O/NaNO_2$	2	79.2	>99	31.6	15.8
3	$Fe(NO_3)_3\cdot9H_2O$	1.5	>99	>99	39.6	26.4
4[e]	$Fe(NO_3)_3\cdot9H_2O$	1.5	5.3	>99	2.1	1.4
5	$Cu(NO_3)_2\cdot3H_2O$	17.5	24.0	>99	9.6	0.5
6	$Co(NO_3)_2\cdot6H_2O$	1.5	3.1	>99	1.2	0.8
7	$Cr(NO_3)_3\cdot9H_2O$	1.5	>99	>99	39.6	26.4

[a] Reaction conditions: benzyl alcohol 10 mmol, 1.25% DES–TEMPO, 3% salt(s), atmospheric oxygen pressure. [b] Conversions and selectivity were determined by GC (area normalization method). [c] TON = moles of product/2(moles of DES–TEMPO). [d] TOF = TON/reaction time. [e] 2 ml H_2O was added.

2–4, 8–9). Overall, the reaction rate was determined by the combination of the electronic and steric effects. This catalytic system also showed good tolerance for the heterocyclic substrates, and good to excellent yields of the corresponding aldehydes were received by increasing the loadings of DES–TEMPO and $Fe(NO_3)_3$ or (and) extending reaction time (Table 4, entries 12 and 13). 2-Thioylmethyl alcohol, which is usually regarded as a difficult substrate in the aerobic oxidation catalyzed by transition metals,[47] was smoothly converted into 2-thenaldehyde in high yield (Table 4, entry12); 2-pyridyl methanol was also converted to 2-pyridinecarboxaldehyde in a conversation of 81% and a selectivity of 98% when both the amounts of DES–TEMPO and $Fe(NO_3)_3$ were increased to 8 mol% (Table 4, entry13). Cinnamic alcohol, which is a representative of allylic alcohols, was totally converted to the corresponding aldehyde in 4 h when the loadings of DES–TEMPO and $Fe(NO_3)_3$ were 1.5 mol% and 5 mol%, respectively (Table 4, entry11). The increase of the loadings of DES–TEMPO and $Fe(NO_3)_3$ indicated that the oxidation of allylic alcohols was more difficult than that of benzylic alcohols. In the oxidation of 1-butanol longer reaction time was required to finish the reaction, and small amounts of over oxidation products butyric acid and butyl butyrate were detected by GC (Table 4, entry14). It is very important to note that this system is also effective in the aerobic oxidations of both secondary benzylic and aliphatic alcohols which are poor substrates in most of the transition-metal catalyst systems,[10–12,48,49] giving the respective ketones in good to excellent yield with slight modifications (Table 4, entries 15–21). Various types of secondary benzylic alcohols, including those bearing both electron-withdrawing and electron-donating groups, were selectively converted to the corresponding ketones in excellent yields under relative higher loadings of DES–TEMPO (2.5 mol%) and $Fe(NO_3)_3$ (5 mol%) (Table 4, entries 15–18). Secondary aliphatic alcohols were also oxidized to the corresponding ketones in good to excellent yields (Table 4, entries19 and 20). Even cyclohexanol, which is regarded as a difficult substrate for TEMPO-mediated oxidation,[50] was converted to cyclohexanone in a good yield of 86% when the loadings of DES–TEMPO and $Fe(NO_3)_3$ were increased to 4 mol% and 8 mol%, respectively (Table 4, entry19). These results demonstrate that the DES–TEMPO based catalyst system has broad applicability in the aerobic oxidations of alcohols.

To demonstrate practicality of this methodology, a multi-gram scale reaction was carried out with benzyl alcohol as substrate. Same results were received when the loading amount of benzyl alcohol was increased to 40 mmol (Table 4, entry 1).

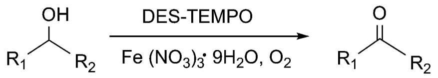
2.4 Recycling of DES–TEMPO

Finally, the recyclability of DES–TEMPO was investigated using benzyl alcohol as a model substrate. After each catalytic run the product benzaldehyde was distilled off in vacuum and the residue was used directly in subsequent runs. It is worth mentioning that fresh $Fe(NO_3)_3$ was required to add in each successive run. The results listed in Table 5 show that no decreases in the rate and selectivity were observed in the first 5 runs. However, the activity of the catalytic system gradually decreased with further recycling and the conversion of benzyl alcohol to benzaldehyde was only 27% in 1.5 h under the described conditions in the eighth run. The decrease of the activity of the catalytic system may be due to the accumulation of the solid substance derived from $Fe(NO_3)_3$ with recycling times.

2.5 Mechanistic aspect

The detailed mechanism for the aerobic oxidation of alcohols catalyzed by this catalytic system is not clear. However, it has been found from Table 3 that NO_3^- is essential in the reaction. Therefore, it is likely that NO_x derived from NO_3^- is playing a key role in this system and this has been suggested in the other Fe/TEMPO systems by others.[15,51] It has also been suggested that NO_2 can assist in the re-oxidation of Fe^{2+} to Fe^{3+}.[51] From Table 3 it has also been found that only the metal ions (Fe^{3+} and Cr^{3+}) with higher oxidation potentials can promote the aerobic oxidation of benzyl alcohol. Furthermore, it has been confirmed that Fe^{3+} can oxidize 4-OH-TEMPO to oxammonium cation (4-OH-TEMPO$^+$), a highly efficient oxidizing ingredient for alcohols, while itself was reduced to Fe^{2+}.[15] Based on the above facts, a possible overall mechanism of this catalytic oxidation can be described as a cascade of redox reactions involving three cycles in Scheme 3. Initially, Fe^{3+} oxidizes [Quaternium-TEMPO]$^+$Br$^-$ to oxammonium cation [Quaternium-TEMPO$^+$]$^+$Br$^-$. Then [Quaternium-TEMPO$^+$]$^+$Br$^-$ serves as an oxidant to transform alcohol to the corresponding carbonyl compound, while itself is reduced to [Quaternium-TEMPO]$^+$Br$^-$. The role of the NO_3^- is to

Table 4 Aerobic of alcohols to carbonyl compounds catalyzed by TEMPO-supported DES in combination of $Fe(NO_3)_3 \cdot 9H_2O$[a]



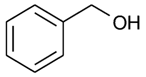
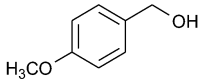
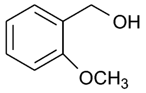
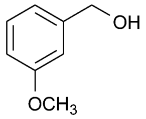
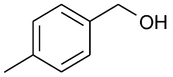
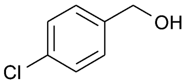
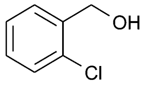
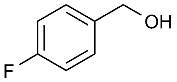
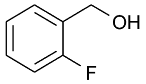
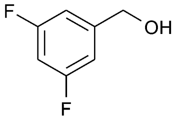
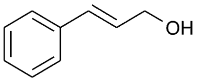
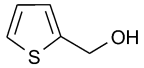
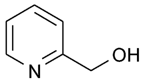
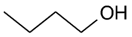
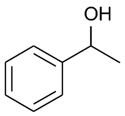
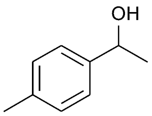
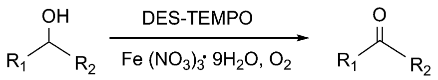
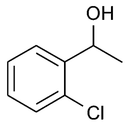
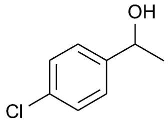
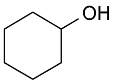
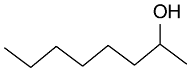
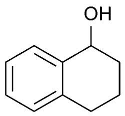
Entry	Substrate	Catalyst	t (h)	Conv.[b] (%)	Select.[b] (%)	TON[c]	TOF[d] (h^{-1})
1[e]		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	1.5	>99(93)	>99	39.6	26.4
2		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	0.75	>99	>99	39.6	52.8
3		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	2.5	>99	>99	39.6	15.8
4		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	1.5	>99(91)	>99	39.6	26.4
5		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	1.5	>99	>99	39.6	26.4
6[f]		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	2.5	>99(91)	>99	39.6	15.8
7[f]		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	2	>99(83)	>99	39.6	19.8
8		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	2	>99(92)	>99	39.6	19.8
9		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	4	>99(87)	>99	39.6	9.9
10		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	1.5	>99	>99	39.6	26.4
11		1.5% DES–TEMPO/5%Fe(NO_3)$_3$	4	>99(92)	>99	33.0	8.3
12		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	2.5	>99(94)	>98	39.6	15.8
13		4% DES–TEMPO/8%Fe(NO_3)$_3$	9	81	99	10.1	1.1
14[g]		1.25% DES–TEMPO/3%Fe(NO_3)$_3$	11	97	94	38.8	3.5
15		2.5% DES–TEMPO/5%Fe(NO_3)$_3$	1.5	>99(91)	>99	19.8	13.2
16		2.5% DES–TEMPO/5%Fe(NO_3)$_3$	0.5	>99	>99	19.8	39.6

Table 4 (*Contd.*)



Entry	Substrate	Catalyst	*t* (h)	Conv.^{b} (%)	Select.^{b} (%)	TON^c	TOF^d (h^{-1})
17		2.5% DES–TEMPO/5%$Fe(NO_3)_3$	2.5	>99	>99	19.8	7.9
18		2.5% DES–TEMPO/5%$Fe(NO_3)_3$	1	>99(83)	>99	19.8	19.8
19		4% DES–TEMPO/8%$Fe(NO_3)_3$	1	86	>99	10.8	10.8
20		2.5% DES–TEMPO/5%$Fe(NO_3)_3$	2	97(89)	>99	19.4	9.7
21		4% DES–TEMPO/8%$Fe(NO_3)_3$	9	80	>99	10.0	1.1

[a] Reaction conditions: alcohol 10 mmol, reaction temperature 60 °C, atmospheric oxygen pressure. [b] Conversions and selectivity were determined by GC (area normalization method); data in parentheses were isolated yields; all products were determined by ^{1}H NMR. [c] TON = moles of product/2(moles of DES–TEMPO). [d] TOF = TON/reaction time. [e] The loading amount of benzyl alcohol was 40 mmol. [f] The reaction temperature was kept on 70 °C until the substrates was melted, then resumed to 60 °C. [g] Acid (4.6%) and esters (2.4%) were detected.

Table 5 Recycling of DES–TEMPO in the aerobic oxidation of benzyl alcohol[a]

Run	Conversion^b (%)	Selectivity^b (%)	TON^c	TOF^d (h^{-1})
1	>99	>99	39.6	26.4
2	>99	>99	39.6	26.4
3	>99	>99	39.6	26.4
4	>99	>99	39.6	26.4
5	>99	>99	39.6	26.4
6	85	>99	34.0	22.7
7	66	>99	26.4	17.6
8	27	>99	10.8	7.2

[a] Reaction conditions: alcohol 10 mmol, reaction temperature 60 °C, atmospheric oxygen pressure. [b] Conversions and selectivity determined by GC (area normalization method). [c] TON = moles of product/2(moles of DES–TEMPO). [d] TOF = TON/reaction time.

be a source of NO_2,[52] which is responsible for the oxidation of Fe^{2+} to Fe^{3+} and NO_3^- is reduced to NO_2^-. Finally, NO_3^- can be easily regenerated by the oxidation of NO_2^- with molecular oxygen.[52]

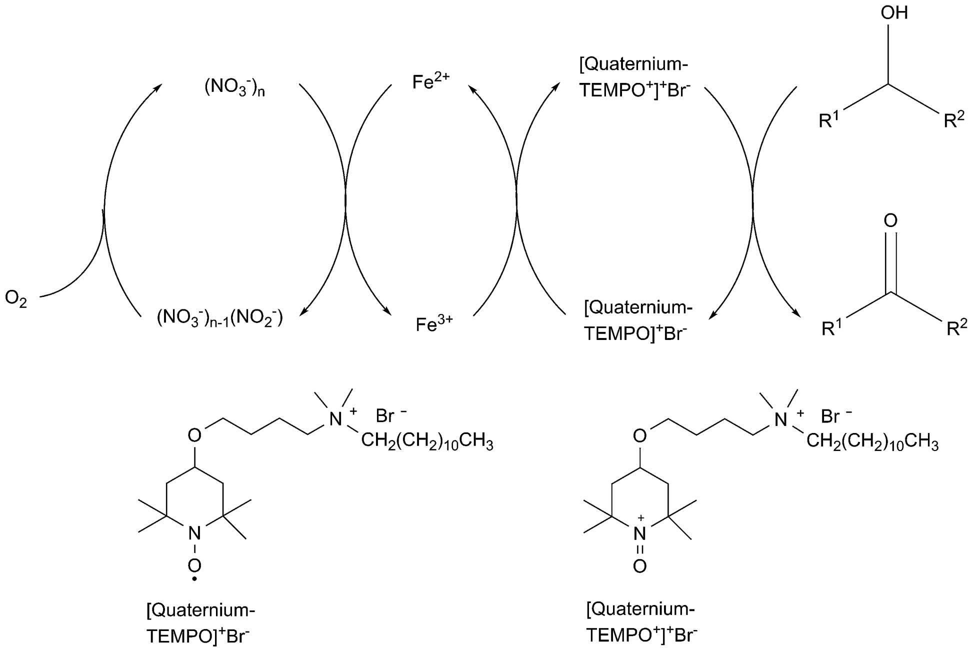
3. Conclusion

A quaternary ammonium grafted with a TEMPO moiety was synthesized. The quaternary ammonium mixed with urea in a molar ratio of 2 : 1 to give a DES supported TEMPO (DES–TEMPO) with a melting point of 60 °C. Catalytic amount of DES–TEMPO in combination with $Fe(NO_3)_3$ as co-catalyst showed excellent performances on the oxidation of various alcohols to their corresponding carbonyl compounds with molecular oxygen as oxidant under solvent-free conditions. The DES–TEMPO performed better than TEMPO under the same reaction conditions. The DES–TEMPO could be easily recovered from the reaction mixture in the oxidation of benzyl alcohol, and reused up to five times with no significant loss of catalytic activity. The novel catalyst system not only offers the advantages of simplified workup procedure and easy recycling generally associated with heterogenized TEMPO with inorganic and organic polymers, but also has high activity and selectivity due to its solubility in the substrate. This process thus represents a greener pathway for aerobic oxidation of alcohols into carbonyl compounds, which manifested in the aspects of recyclability of the catalyst, use of non-toxic and cheap $Fe(NO_3)_3$ as co-catalyst, and absence of solvent in reaction.

4. Experimental section

4.1 General remarks

4-OH-TEMPO was purchased from Energy Chemical. 1,4-Dibromobutane was obtained from Tianjin Keruisi Fine



Scheme 3 Proposed mechanism for the catalytic aerobic oxidation of alcohols.

Chemical Co., LTD. Alcohols were obtained from Alfa Aesar China (Tianjin) Co., Ltd. All the chemicals were used as received. Solvents were purified by standard methods and dried if necessary.

^{1}H MNR and ^{13}C MNR spectra were recorded with TMS as internal standard on a Bruker AC-P 400 spectrometer. ESI mass spectra were recorded on a LCQ Advanced high-resolution spectrometer. The viscosity was measured on a NDJ-79 rotary viscometer, Shanghai Changji Geological Instrument Co., LTD. Oxidation reaction samples were analyzed on a Shandong Lunan Ruihong Gas Chromatograph (SP-6800A) equipped with a FID detector and a SE 30 column (30 m × 0.5 μm). The conditions used in gas chromatography were temperature of the detector 280 °C, column temperature 130–220 °C (varying with alcohols), pressure of the carrier gas 0.05–0.07 MPa (varying with alcohols), split ratio of injection 10 : 1.

4.2 Synthesis of 4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl) butyl bromide

To a solution of 4-hydroxy-TEMPO (2.58 g, 0.015 mol) in anhydrous acetone (20 ml) was added NaH (0.6 g, 0.015 mol) and the resulting slurry was stirred at room temperature for 10 min. 1,4-Dibromobutane (4.86 g, 0.0225 mol) was then added and the mixture was stirred at room temperature for 3 h. After reaction acetone was removed under reduced pressure. Water (30 ml) was then added to dissolve the solid residue. The aqueous layer was extracted with methylene chloride (15 ml × 3). The combined organic extracts were dried over Na_2SO_4 and concentrated under vacuum. The resulting concentrated solution was separated by flash chromatography (10 : 1 (v/v), petroleum–ethyl acetate) to obtain red viscous liquid (1.15 g, 25% yield). The sample of the product was reduced by phenylhydrazine to record the ^{1}H NMR. ^{1}H NMR (400 MHz; $CDCl_3$; Me_4Si) δ: 1.14 (6H, s, piperidine-Me), 1.20 (6H, s, piperidine-Me), 1.42 (2H, t, $J = 11.6$ Hz, piperidine-C*H*H), 1.66–1.70 (2H, m, O–CH_2–$C\mathit{H}_2$–CH_2–CH_2–Br), 1.87–1.94 (4H, m, O–CH_2–CH_2–$C\mathit{H}_2$–CH_2–Br, piperidine-CH*H*), 3.42–3.47 (4H, m, OCH_2, $BrCH_2$), 3.50–3.57 (1H, m, piperidine-CH).

4.3 Synthesis of *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-opiperidoxylxyl-4-)butyl)dodecyl ammonium salt ([Quaternium-TEMPO]$^+$Br$^-$)

Under stirring, *N*,*N*-dimethyldodecylamine (2.15 g, 7 mmol) was slowly added to a solution of 4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl bromide (1.86 g, 8.4 mmol) in 20 ml of tetrahydrofuran. The mixture was then heated to reflux and stirred for 6 h. After cooling to room temperature, tetrahydrofuran was removed by reduced pressure. Then water (20 ml) was added to dissolve the quaternary ammonium salt and ethyl acetate (20 ml) was added to dissolve the un-reacted raw materials. The aqueous layer was extracted with ethyl acetate several times. Finally water was distilled by reduced pressure to give a red viscous liquid (2.66 g, 76.6% yield). The sample of the product was reduced by phenylhydrazine to record the ^{1}H NMR and ^{13}C NMR. ^{1}H NMR (400 MHz; $CDCl_3$; Me_4Si) δ: 0.88 (3H, t, $J = 6.8$ Hz, Me), 1.26 (12H, s, piperidine-Me), 1.28–1.48 (18H, m, N–CH_2–CH_2–$(C\mathit{H}_2)_9$–CH_3), 1.65–1.88 (8H, m, piperidine-CH_2, O–CH_2–$C\mathit{H}_2$–CH_2–CH_2–N, N–CH_2–$C\mathit{H}_2$–C_9H_{18}–CH_3), 2.00–2.13 (2H, m, O–CH_2–CH_2–$C\mathit{H}_2$–CH_2–N), 3.35 (6H,s, NMe), 3.43–3.47 (2H, m, N–$C\mathit{H}_2$–CH_2–C_9H_{18}–CH_3), 3.55 (2H, t, $J = 6$ Hz, O–CH_2–CH_2–CH_2–$C\mathit{H}_2$–N), 3.63–3.68 (2H, m, OCH_2), 3.71–3.76 (1H, m, piperidine-CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.11 (Me), 19.89 (O–CH_2–CH_2–$\mathit{C}H_2$–CH_2–N), 20.69 (N–CH_2–CH_2–C_8H_{16}–$\mathit{C}H_2$–CH_3), 22.64 (N–CH_2–$\mathit{C}H_2$–C_9H_{18}–CH_3), 22.66 (N–CH_2–CH_2–$\mathit{C}H_2$–C_8H_{16}–CH_3), 26.22 (O–CH_2–$\mathit{C}H_2$–CH_2–CH_2–N), 26.54 (piperidine-Me), 29.22, 29.28, 29.41, 29.46, 29.56, 31.85, 31.99

($N–CH_2–CH_2–CH_2–(CH_2)_7–CH_2–CH_3$), 44.60 (piperidine-$CH_2$), 51.26 (NMe), 59.29 (piperidine-C), 63.50 ($N–CH_2–CH_2–C_9H_{18}–CH_3$), 63.84 ($O–CH_2–CH_2–CH_2–CH_2–N$), 66.80 (piperidine-CH), 70.71 (OCH_2). HR-MS (ESI): *m*/*z* 440.4336. $C_{27}H_{56}N_2O_2$ calculated *m*/*z*: 440.4342.

4.4 Preparation of DES–TEMPO

Into a round-bottom flask equipped with a magnetic stirrer was added *N*,*N*-dimethyl-(4-(2,2,6, 6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)dodecyl ammonium salt (0.4 mmol, 0.2082 g) and urea (0.2 mmol, 0.015 g). The mixture was heated at 60 °C for a period of time until a clear liquid was appeared, which resulted in the formation of DES–TEMPO with 100% yield. The obtained DES–TEMPO was used without any further purification.

4.5 Representative procedure for the oxidation of alcohols

In a typical process, into a 5 ml two-necked, round-bottom flask equipped with a magnetic stirrer and an oxygen balloon was added DES–TEMPO (0.25 mmol, 0.1375 g). Then, benzyl alcohol (10 mmol) and $Fe(NO_3)_3·9H_2O$ (0.3 mmol, 0.1231 g) was added successively at 60 °C under stirring. The oxygen from the balloon was introduced and controlled through a triple valve. The reaction was monitored by GC equipped with a suitable column. The sample was diluted with acetonitrile before injection.

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