Catal Lett
DOI 10.1007/s10562-015-1634-0

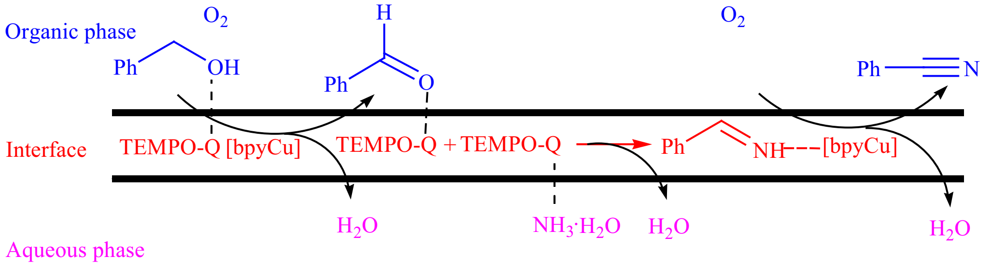
Solvent-Free Aerobic Oxidation of Alcohols to Nitriles Catalyzed by Copper Iodide in Combination with a Quaternary Ammonium Modified TEMPO

Yuecheng Zhang[1] · **Rong Huang**[1] · **Baosheng Gao**[1] · **Jiquan Zhao**[1]

Received: 15 July 2015 / Accepted: 25 September 2015

Abstract A catalytic system consisting of *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)dodecyl ammonium bromide (TEMPO-Q), CuI and 2,2′-bipyridine was established. This catalytic system (CuI/bpy/TEMPO-Q) showed high activity and good to excellent selectivity in the oxidative conversion of various alcohols to the corresponding nitriles with molecular oxygen as terminal oxidant and aqueous ammonia as nitrogen source under solvent-free conditions. Besides, the catalytic system also offers the advantages of simplified workup procedure. This protocol thus represents a greener pathway for the synthesis of nitriles from alcohols.

Graphical Abstract TEMPO-Q, a compound with both a TEMPO and a quaternary ammonium moieties, in combination with copper iodide and 2,2′-bipyridine as a catalytic system performed well in the oxidation of alcohols to nitriles with molecular oxygen as terminal oxidant in aqueous ammonia under solvent-free conditions. The catalytic system not only offers the advantages of simplified workup procedure, but also has high activity and selectivity due to the phase transfer catalysis of TEMPO-Q



Keywords *N*,*N*-Dimethyl-(4-(2,2,6, 6-tetramethyl-1-oxyl-4-piperidoxyl)butyl) · Dodecyl ammonium bromide · Copper iodide · Alcohol · Nitrile · Solvent-free · Aerobic oxidation

1 Introduction

Nitriles are a very important class of compounds in chemistry because they serve as versatile synthetic precursors and intermediates in pharmaceuticals, material, and fine chemicals [1–7]. Traditionally, nitriles were synthesized through

---

Electronic supplementary material The online version of this article (doi:10.1007/s10562-015-1634-0) contains supplementary material, which is available to authorized users.

✉ Jiquan Zhao
zhaojq@hebut.edu.cn

[1] School of Chemical Engineering and Technology, Hebei University of Technology, Tianjin 300130, People's Republic of China

the nucleophilic displacement of various leaving groups, such as halogen compounds, aryl sulfonates, alcohols, esters, ethers, nitro or amino compounds and diazonium salts with inorganic cyanide ions [8, 9]. However, the use of toxic solvents and stoichiometric amounts of reagents along with the production of large amounts of inorganic waste and tedious work-up procedures limits their application from a viewpoint of green chemistry. Therefore, the development of environmentally friendly procedures for nitrile synthesis is a very important subject in modern organic synthesis. As a consequence, many novel methods including use of DMF as the CN source for C-H functionalization of arenes [10–12], oxidative dehydrogenation of benzylic alcohols or methylarenes in the presence of various nitrogen sources [13–19], and dehydrogenation or oxidative dehydrogenation of primary amines [20–23] have been developed. Among all of them, the ones based on the aerobic oxidation of alcohols to nitriles in the presence of aqueous ammonia or its surrogate are the most attractive due to easy availability of molecular oxygen and H_2O as the only by-product in principle. Several strategies for this transformation have been accomplished either under the promotion of heterogeneous or homogeneous catalysts. $Ru(OH)_x/Al_2O_3$ [24], MnO_2 or MnO_2-supported on graphite [25, 26] and nitrogen-doped graphene-layered cobalt or iron oxides [27] as heterogeneous catalysts have been proved to be effective in the reaction. However, high temperature and pressure are generally required in these cases. Amongst homogeneous catalysts, Cu/TEMPO and Fe/TEMPO which have been demonstrated earlier to oxidize alcohols to aldehydes under aerobic conditions at ambient temperature also showed good performances in the aerobic oxidation of alcohols to nitriles in the presence of aqueous ammonia. For instances, Tao et al. [28] employed $Cu(NO_3)_2$/TEMPO in DMSO whereas Huang et al. [29] used CuI/TEMPO/bipyridine in ethanol or acetonitrile in the presence of oxygen to prepare nitriles from alcohols; Muldoon et al. [30] and Batra et al. [31] respectively used $Cu(OTf)_2$/TEMPO/bipyridine and $Fe(NO_3)_3$/TEMPO in acetonitrile in the presence of air instead of pure oxygen to achieve the conversion of alcohols to nitriles. These homogeneous systems have been found being effective in the aerobic oxidative conversion of alcohols to nitriles. However, a solvent is generally required in the homogeneous catalytic systems mentioned above, and the separation of TEMPO from reaction products remains a problem especially on a large scale production due to its volatility at distillation temperature of products. Therefore, there is a need for developing a catalytic system which can avoid the disadvantages described above.

Recently, we synthesized a quaternary ammonium with a TEMPO moiety known as *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)dodecyl ammonium bromide (TEMPO-Q). A catalytic system from this compound in combination with urea and $Fe(NO_3)_3·9H_2O$ showed good performances in the selective oxidation of various alcohols to the corresponding aldehydes and ketones under mild and solvent-free conditions with molecular oxygen as terminal oxidant. Moreover, TEMPO-Q is stable and non-volatile, thus, could be recovered easily and recycled up to five times in the oxidation of benzyl alcohol without significant loss of catalytic activity. When we employed TEMPO-Q in the oxidative conversion of alcohols to nitriles in aqueous ammonia under solvent-free conditions, good results were also received and TEMPO-Q could be easily separated from the mixture and recycled, too. Herein, we report the catalytic performances of TEMPO-Q in combination with a copper iodide (CuI) in the oxidative conversion of alcohols to nitriles with molecular oxygen as a terminal oxidant.

2 Experimental

2.1 Materials and Apparatus

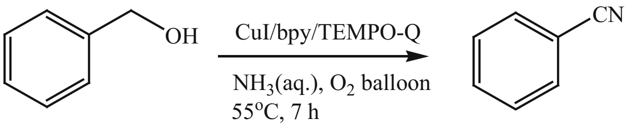
Aqueous ammonia (25 %), copper iodide (CuI), 2,2′-bipyridine and other reagents were obtained from Tianjin Fuchen Chemical Reagent Factory, China. All reagents were used as received without further purification. The secondary alcohols were obtained from Alfa Aesar China (Tianjin) Co., Ltd. The *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-opiperidoxylxyl-4-)butyl)dodecyl ammonium bromide (TEMPO-Q) was prepared as described in the literature [32] reported by us.

^1H MNR spectra of nitriles were recorded with TMS as internal standard on a Bruker AC-P 400 spectrometer. 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).

2.2 Catalytic Oxidation

In a typical process, into a 5 ml two-necked, round-bottom flask equipped with a magnetic stirrer and an oxygen balloon were added TEMPO-Q (0.25 mmol, 130 mg), CuI (0.25 mmol, 47.5 mg), 2,2′-bipyridine (0.25 mmol, 39 mg) and aqueous ammonia (0.75 mL) successively. After which the mixture was heated to 55 °C under strrring to reach a clear solution. Then, oxygen from the balloon was introduced and controlled through a triple valve to replace the air. Finally, benzyl alcohol or other substrate (5 mmol) was introduced through syringe. The reaction was run at 55 °C under strong strrring. The final reaction conversion and selectivity towards the corresponding nitrile were obtained by adding the sample into 1.0 mL of ethyl alcohol to get a homogeneous solution, then analyzing by GC.

Table 1 Effect of each component in the CuI/bpy/TEMPO-Q catalytic system on the conversion of benzyl alcohol to benzonitrile

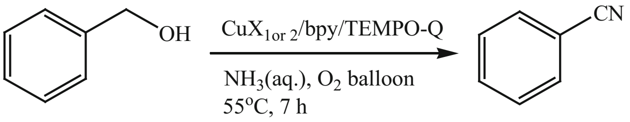


Entry	Bpy (mol%)	TEMPO-Q (mol%)	CuI (mol%)	Conversion (%)	Selectivity (%)		
					Nitrile	Aldehyde	Acid
1	5	5	5	99.8	93.9	2.9	3.1
2	–	5	5	97.6	80.7	19.2	0.1
3	5	–	5	5.9	71.2	28.8	0
4	5	5	–	7.3	17.1	82.9	0

Reaction conditions 5 mmol of benzyl alcohol, 5 mol% bpy, 5 mol% TEMPO-Q, 5 mol% CuI, 0.75 mL $NH_3 \cdot H_2O$, reaction temperature 55 °C, reaction time 7 h, O_2 pressure 0.1 MPa

The results were determined by GC

Table 2 Effect of the copper salt on the aerobic oxidative conversion of benzyl alcohol to benzonitrile



Entry	Cu salt	Conversion (%)	Selectivity (%)		
			Benzonitrile	Benzaldehyde	Benzoic acid
1	$CuBr_2$	60.4	16.7	83.1	0.1
2	$CuCl_2$	70.4	61.9	37.6	0.4
3	CuCl	72.6	45.7	51.2	3.1
4	$Cu(OAc)_2$	80.8	32.9	65.2	1.9
5	$Cu(OTf)_2$	78.4	76.4	23.6	0
6	$Cu(NO_3)_2$	97.6	78.3	21.7	0
7	CuI	99.8	93.9	2.9	3.1

Reaction conditions 5 mmol of benzyl alcohol, 5 mol% bpy, 5 mol% TEMPO-Q, 5 mol% Cu salt, 0.75 mL $NH_3 \cdot H_2O$, reaction time 7 h, reaction temperature 55 °C, O_2 pressure 0.1 MPa

The results were determined by GC

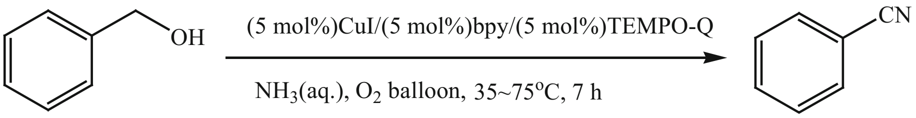
After reaction the product was extracted with EtOAc and the extract was distilled at atmospheric pressure to remove EtOAc. For the reaction with high conversion and selectivity the product was obtained by direct distillation under vacuum from the residue; otherwise, the product was received by column chromatography of the residue on silica gel using hexanes/EtOAc (95:5) as eluent.

3 Results and Discussion

3.1 Catalysis of the Novel Catalytic System

Huang et al. [29] first reported the aerobic oxidative conversion of alcohols to nitriles using CuI/bpy/TEMPO as catalytic system in acetonitrile. Therefore, the catalytic performance of the TEMPO-Q in combination with CuI and bpy was evaluated for the aerobic oxidative conversion of benzyl alcohol to benzonitrile. Initially, the reaction was carried out in 2.5 equiv of aqueous ammonia under atmospheric O_2 pressure and solvent-free conditions at 55 °C in 7 h in the presence of TEMPO-Q (5 mol%), CuI (5 mol%) and bpy (5 mol%). Encouragingly, the expected product was obtained in a yield of higher than 90 %. Then, the necessity of each component of the catalytic system was screened and the results are shown in Table 1. As observed in the table, either only use of TEMPO-Q without CuI as a co-catalyst or CuI in the absence of TEMPO-Q afforded very poor results, which indicated that both TEMPO-Q and CuI were essential in the aerobic oxidative conversion of

Table 3 The effect of the reaction temperature on the reaction



Entry	Temperature (°C)	Conversion (%)	Selectivity (%)		
			Benzonitrile	Benzaldehyde	Benzoic acid
1	35	64.7	66.9	33.1	0
2	45	94.1	78.7	21.2	0.1
3	55	>99.0	95.8	1.9	2.2
4	65	>99.0	87.8	1.5	10.6
5	75	>99.0	75.0	1.1	23.8

Reaction conditions 5 mmol of benzyl alcohol, 5 mol% bpy, 6 mol% TEMPO-Q, 5 mol% CuI, 0.75 mL $NH_3 \cdot H_2O$, reaction time 7 h, O_2 pressure 0.1 MPa

The results were determined by GC

benzyl alcohol to benzonitrile (Table 1, entries 3, 4). The presence of 2,2′-bipyridine is also important. Though the conversion of benzyl alcohol in the absence of 2,2′-bipyridine was compared to that in the presence of all the components, the selectivity towards benzonitrile was decreased to 80.7 % from 93.9 % (Table 1, entries 1, 2).

Next, several other copper salts including copper (I) and copper (II) salts were also evaluated as co-catalyst in the aerobic oxidative conversion of benzyl alcohol to benzonitrile in excessive aqueous ammonia. As shown in Table 2, only CuI gave excellent yield of benzonitrile (Table 2, entry 7). Though high conversion of benzyl alcohol was received in the case of $Cu(NO_3)_2$ as co-catalyst, the selectivity towards benzonitrile was only 78.4 % (Table 2, entry 6). Both $CuCl_2$ and $Cu(OTf)_2$ only exhibited moderate conversion of benzyl alcohol and selectivity towards benzonitrile under the same reaction conditions (Table 2, entries 2, 5). Meantime, the other copper salts led to unfavorable results due to either low activity or bad selectivity towards benzonitrile (Table 2, entries 1, 3, 4).

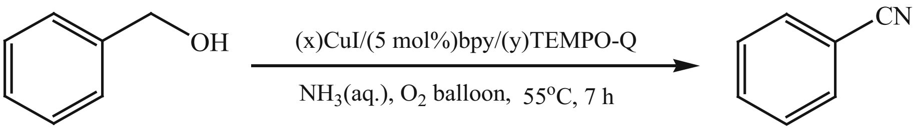
For obtaining the optimal reaction conditions, the reaction temperature was examined and the results are listed in Table 3. It can be seen that the conversion of benzyl alcohol increased with the increase of temperature; the selectivity towards benzonitrile increased in the beginning and reached its maximum at 55 °C (Table 3, entry 3), and then decreased with further increase of reaction temperature. We speculated that the decrease of the selectivity towards benzonitrile was due to the low solubility of ammonia in solution at higher temperature, leading to the deep oxidation of benzyl alcohol to benzoic acid (Table 3, entries 3–5).

The amount of CuI was optimized at 55 °C keeping the other parameters constant. The results are listed in Table 4, from which it can be learned that the time to finish the reaction shortened with the increase of CuI loading, and the selectivity towards benzonitrile increased in the beginning and reached its maximum (93.9 %) at 5 % mole of CuI (Table 4, entry 3), and then decreased with further increase of the CuI loading due to the deep oxidation of benzyl alcohol to benzoic acid (Table 4, entries 4 and 5).

The effect of TEMPO-Q loading on the reaction was also examined under the same conditions, and the results are also listed in Table 4. As can be seen from Table 4, increasing the TEMPO-Q loading from 3 to 7 mol% led to fast reaction, and the increase of the selectivity towards benzonitrile (Table 4, entries 3 and 6–9). When the TEMPO-Q loading was higher than 6 mol%, both the reaction time required to finish the reaction and the selectivity towards benzonitrile did not changed obviously (Table 4, entries 8 and 9).

After receiving the above results, TEMPO-Q and TEMPO were compared as catalysts in the oxidative conversion of benzyl alcohol to benzonitrile in various solvent to screen the advantage of TEMPO-Q over TEMPO and the results are given in Table 5. From the table we can find that the use of TEMPO instead of TEMPO-Q resulted in sharp decreases of both the conversion of benzyl alcohol and the selectivity towards benzonitrile in water, toluene and the absence of solvent under the same reaction conditions (Table 5, entries 1–4 and 7, 8); and though TEMPO-Q and TEMPO showed almost identical catalytic activity in acetonitrile, the selectivity towards benzonitrile is higher in the case of TEMPO-Q as catalyst (Table 5, entries 5, 6). These results confirmed the favorable role of the quaternary ammonium moiety to the oxidation reaction. It is believed that TEMPO-Q acted as both a role of TEMPO and a phase transfer catalyst in the reaction. Besides, almost same results were obtained in water compared to those in the absence of solvent (Table 5, entries 1–4).

Table 4 Effect of CuI or TEMPO-Q loading on the oxidative conversion of benzyl alcohol to benzonitrile

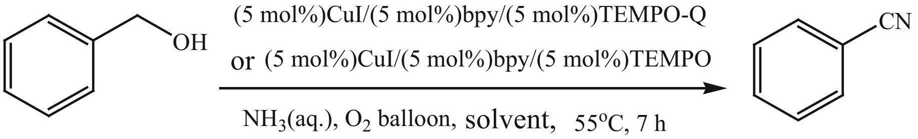


Entry	CuI (mol%)	TEMPO-Q (mol%)	Time (h)	Selectivity (%)		
				Benzonitrile	Benzaldehyde	Benzoic acid
1	3	5	13.5	66.3	21.4	12.2
2	4	5	9.5	86.2	7.2	6.5
3	5	5	7.0	93.9	2.9	3.1
4	6	5	6.5	82.3	6.5	11.1
5	7	5	5.0	73.0	7.8	19.1
6	5	3	7.5	67.8	28.4	3.7
7	5	4	7.0	89.3	7.4	3.2
8	5	6	7.0	95.8	1.9	2.2
9	5	7	7.0	96.1	1.9	1.9

Reaction conditions 5 mmol of benzyl alcohol, 5 mol% bpy, 0.75 mL $NH_3{\cdot}H_2O$, reaction temperature 55 °C, O_2 pressure 0.1 MPa

The results were determined by GC, conversion of benzyl alcohol always higher than 99 %

Table 5 The oxidative conversion of benzyl alcohol to benzonitrile catalyzed by TEMPO-Q and TEMPO in various solvents



Entry	Solvent	Time (h)	Catalyst	Conversion (%)	Selectivity (%)		
					Nitrile	Aldehyde	Acid
1	–	7	TEMPO-Q	99.9	95.8	1.9	2.2
2			TEMPO	57.3	75.2	24.8	0
3	H_2O	7	TEMPO-Q	99.9	95.8	2.3	1.9
4			TEMPO	65.0	72.9	27.1	0
5	MeCN	5	TEMPO-Q	99.9	95.5	2.7	1.8
6			TEMPO	99.9	80.4	19.6	0
7	Toluene	7	TEMPO-Q	99.9	94.7	5.1	0.1
8			TEMPO	80.2	51.7	48.3	0

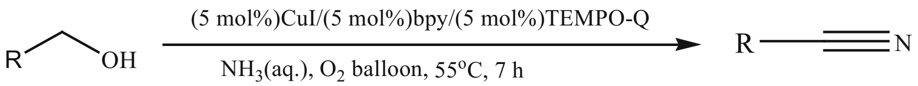
Reaction conditions 5 mmol of benzyl alcohol, 5 mol% bpy, 6 mol% Cat, 5 mol% CuI, 0.75 mL $NH_3{\cdot}H_2O$, 1.0 mL solvent, reaction temperature 55 °C, O_2 pressure 0.1 MPa

The results were determined by GC

From above experimental results we concluded the optimal reaction conditions which are benzyl alcohol 5 mmol, 2,2′-bipyridine 5 mol%, CuI 5 mol%, TEMPO-Q 6 mol%, $NH_3{\cdot}H_2O$ 0.75 mL, reaction temperature 55 °C, O_2 pressure 0.1 Mpa. Under the optimal reaction conditions the benzyl alcohol was converted to benzonitrile in a yield near 95.8 % (isolated yield 89.0 %) in 7 h in the absence of solvent.

Having obtained the optimal conditions for the reaction, we then evaluated the generality of the methodology employing various alcohols including benzylic alcohols, heterocyclic alcohols, cinnamic alcohol, geraniol, and representatives of aliphatic alcohols as substrates. The results are shown in Table 6. It can be seen from Table 6 that various types of primary benzylic alcohols, including those bearing both electron-withdrawing and electron-donating groups, were converted to their corresponding nitriles in good to excellent yields under the optimal reaction conditions. However, the time required to finish the reaction was different (Table 6, entries 1–5). It seems that the catalytic system is more efficient for the substrate with an electron-withdrawing substituent (Table 6, entries 2–5, 6 and 7, 8 and 9), which is different from the catalytic system reported by Huang et al. [29], but same as the one reported by Batra et al. [31]. These results are in contradiction with those in the aerobic oxidation of alcohols to the corresponding aldehydes catalyzed by the TEMPO-based catalytic systems, in which the electron-donating substituents generally can accelerate the reaction though not very strongly [33–36]. From the mechanism

Table 6 Oxidative conversion of various alcohols to nitriles



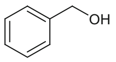
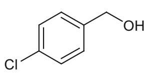
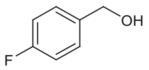
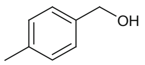
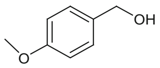
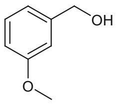
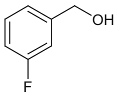
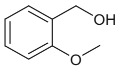
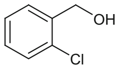
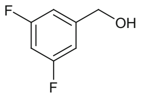
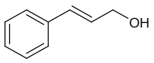
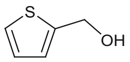
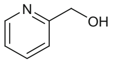
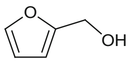
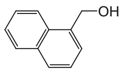
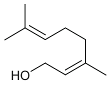
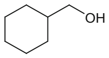
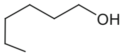
Entry	Substrate	Time (h)	Conversion[a] (%)	Selectivity[a] (%)			Yield[b] (%)
				Nitrile	Aldehyde	Acid	
1		7	99.9	95.8	1.9	2.2	95.7 (89.0)
2		6.5	93.8	91.9	8.0	0.1	86.2 (79.5)
3		6.5	99.7	87.2	12.6	0.2	86.9 (80.6)
4		8.0	99.9	89.7	6.2	4.1	89.6 (82.2)
5		8.5	85.7	86.7	10.5	2.8	74.3 (67.5)
6		8.0	82.9	72.9	27.0	0.1	60.4 (49.5)
7		7.0	86.4	97.1	2.8	0.1	83.9 (78.2)
8		10.5	73.2	77.5	20.4	2.0	56.7 (45.4)
9		9.0	86.2	88.8	11.2	0	76.5 (61.6)
10		2.5	99.1	99.9	0	0	99.0 (90.1)
11		8.0	83.6	87.0	12.9	0	72.7 (66.3)
12		9.0	99.9	85.3	14.7	0	85.2 (77.9)
13		10.0	94.0	75.5	24.0	0.5	71.0 (63.1)
14		12.0	93.1	87.2	12.8	0.1	81.2 (73.3)
15[c, d]		10.0	–	–	–	–	(72.1)
16			0.0	–	–	–	0.0

Table 6 continued

Entry	Substrate	Time (h)	Conversion[a] (%)	Selectivity[a] (%)			Yield[b] (%)
				Nitrile	Aldehyde	Acid	
17			0.0	–	–	–	0.0
18			0.0	–	–	–	0.0

Reaction conditions 5 mmol substrate, 0.75 mL $NH_3{\cdot}H_2O$, 6 mol% TEMPO-Q, 5 mol% CuI, 5 mol% bpy, reaction temperature 55 °C, O_2 pressure 0.1 MPa

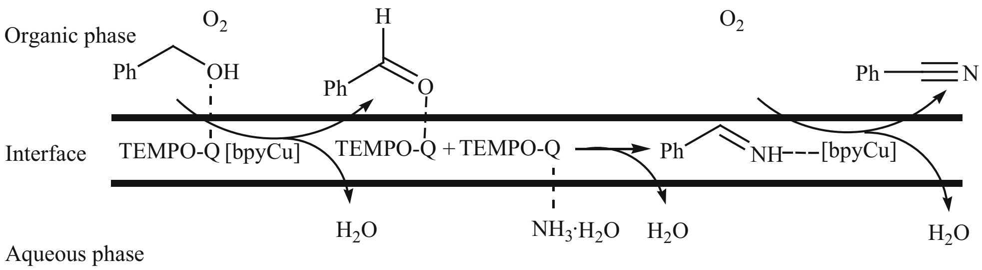
[a] Conversions and selectivity were determined by GC (area normalization method); all products were determined by ^{1}H NMR

[b] The data in the parentheses is the isolated yields

[c] Reation carried out in MeCN

[d] Using *N*,*N*-dimethyl-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)benzyl ammonium bromide (TEMPO-Q’) instead of TEMPO-Q gave same result

Fig. 1 TEMPO-Q promoted oxidative conversion of alcohol to nitrile in two-phase system



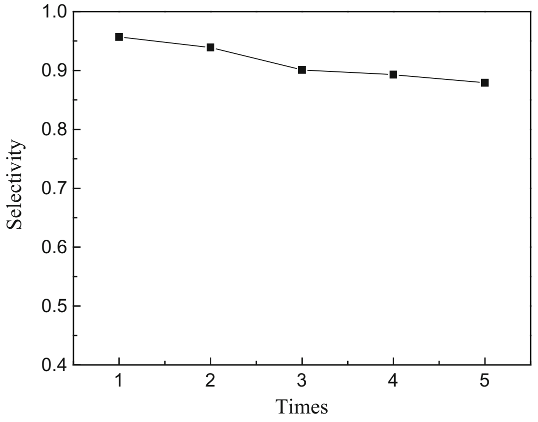


Fig. 2 Recycling of TEMPO-Q in the aerobic oxidation of benzyl alcohol to benzonitrile

proposed by Huang et al. [29] it can be concluded that aldehyde-to-nitrile transformation is a rate limiting step in the conversation of alcohol to nitrile by this protocol, which is in contrast to that in the presence of solvent. In the aldehyde-to-nitrile transformation process, the strong electron-withdrawing groups may enhance the reaction rate due to the increase in electrophilicity of the carbonyl carbon of the aldehydes generated from the alcohols, which is supported by the fact that 3,5-difluorobenzyl alcohol with two strong electron-withdrawing fluorines in the structure was almost quantitatively converted to its corresponding nitrile in only 2.5 h (Table 6, entry 10). In addition, the position of the substituent on the benzene ring has strong effects on the reactivity of benzylic alcohols. The substrate with an *o*-substituent showed poor reactivity compared to the ones with an *m*- and a *p*-substituent due to the steric hindrance (Table 6, entries 2 and 9, 5, 6 and 8) present in both the alcoholate-copper and imine-copper intermediates [29]. It is worth noting that the reaction must be carried out in acetonitrile in the case of α-naphthalenemethanol as substrate due to its higher melting point preventing it in a liquid state under the reaction temperature (Table 6, entry 15).

This catalytic system also showed good tolerance for the heterocyclic substrates, and good to excellent yields of the corresponding nitriles were received (Table 6, entries 12–14). 2-Thioylmethyl alcohol, which is usually regarded as a difficult substrate in the aerobic oxidation to its corresponding aldehyde catalyzed by transition metals [37], was smoothly converted into thiophene-2-carbonitrile in high yield (Table 6, entry 12); 2-pyridyl methanol was also converted to 2-pyridinecarbonitrile in a conversation of 94.0 % and a selectivity of 75.5 % under the same reaction conditions in 10 h (Table 6, entry 13). Cinnamic alcohol, which is a representative of aromatic allylic alcohols, was converted to its corresponding nitrile in a conversation of 83.6 % and a selectivity of 87.0 % in 8 h (Table 6, entry 11).

Same as the copper/TEMPO-based catalytic systems [28, 29, 38], but in contrast to the Iron Nitrate/TEMPO system [31], this catalytic system failed to afford the corresponding nitriles with aliphatic alcohols including geraniol (Table 6, entry 16–18). This is unambiguously attributed to the inefficiency of the copper/TEMPO-based catalytic systems in aerobic oxidation of aliphatic alcohols to aldehydes being intermediates in the oxidative conversion of alcohols to nitriles [39–41].

Control experiments indicated that use of TEMPO instead of TEMPO-Q resulted in a sharp decrease of conversion of benzyl alcohol to benzonitrile (Table 5, entries 1–4). In addition, the alcohol to nitrile conversion rate in this case is much higher than the ones catalyzed by the copper/TEMPO-based catalytic systems in the presence of various solvents [28–30]. On the basis of our investigation and the reports in literature it can be concluded that the attachment of a quaternary ammonium to TEMPO plays central roles in the aerobic oxidative conversion of alcohols to nitriles. Herein, due to the absence of solvent the reaction system was consisting of aqueous ammonia and alcohol (or aldehyde) two phases. In principle the oxidative conversion of alcohol to nitrile is consisting of three fundamental steps, which are the aerobic oxidation of alcohol to aldehyde, the condensation of aldehyde with ammonia to intermediate imine, and the aerobic oxidation of imine to nitrile [19, 29]. From both the structures of the bpy-Cu^+ generated in situ and TEMPO-Q, it is convincible that they will mainly exist in the interface between alcohol and aqueous ammonia. Thus, all the three fundamental steps mainly take place in the interface. Except for acting as a role of TEMPO, TEMPO-Q also acting as a phase transfer catalyst helped to transfer alcohol, aldehyde and ammonia into the interface in the reaction process, which accelerated the whole reaction (Fig. 1).

3.2 Recycling of TEMPO-Q

Finally, the recyclability of TEMPO-Q was investigated using benzyl alcohol as a model substrate. After each catalytic run the product benzonitrile was distilled off under vacuum and the residue was used directly in subsequent runs. However, fresh CuI was required to add in each successive run. It was found that the conversion was always higher than 99 %. The selectivity towards benzonitrile slightly decreased with recycling, and about 8.5 % of the total decrease of the selectivity towards benzonitrile was observed after five times recycling (Fig. 2). The results indicated that TEMPO-Q was stable and non-volatile and easily separated from the product, which could overcome the disadvantages of TEMPO in the same catalytic reaction.

4 Conclusions

In summary, we have established an efficient catalytic system (CuI/bpy/TEMPO-Q) for the aerobic oxidative conversion of benzylic and allylic alcohols to their corresponding nitriles by using aqueous ammonia as the nitrogen source. TEMPO-Q with both a TEMPO and a quaternary ammonium moiety acted as both a role of TEMPO and a phase transfer catalyst, which allowed the reaction proceeding smoothly under the solvent- and additive-free reaction conditions. The novel catalytic system not only offers the advantages of simplified workup procedure, but also has high activity and selectivity due to the phase transfer catalysis of TEMPO-Q. This protocol thus represents a greener pathway for aerobic oxidation of alcohols into their corresponding nitriles, which manifested in the aspects of use of aqueous ammonia as nitrogen source, absence of solvent in reaction.

Acknowledgments The authors are grateful for financial supports from the National Natural Science Foundation of China (No. 21276061), Natural Science Foundation of Hebei Province, China (No. B2013202158), and Research Fund for the Doctoral Program of Higher Education of China (No. 20121317110010).

References

1. Fatiadi AJ (1983) In: Patai S, Rappaport Z (eds) Preparation and synthetic applications of cyano compounds. Wiley, New York
2. Kleemann A, Engel J, Kutscher B, Reichert D (2001) Pharmaceutical substance: synthesis patents, applications, 4th edn. Georg Thieme, Stuttgart
3. Miller JS, Manson JL (2001) Acc Chem Res 34:563
4. Fleming FF, Wang Q (2003) Chem Rev 103:2035
5. Fleming FF, Yao L, Funk L, Shook BC (2010) J Med Chem 53:7902
6. Frizler M, Stirnberg M, Gutschow M (2010) Curr Top Med Chem 10:294
7. Berteotti A, Vacondio F, Lodola A, Bassi M, Silva C, Mor M, Cavalli A (2014) ACS Med Chem Lett 5:501
8. Friedrick K, Wallensfels K (1970) In: Rappoport Z (ed) The chemistry of the Cyano Group. Wiley, New York
9. Kornblum N, Smiley RA, Iffland DC (1955) J Am Chem Soc 77:6269
10. Ding S, Jiao N (2011) J Am Chem Soc 133:12374
11. Chen X, Hao XS, Goodhue CE, Yu JQ (2006) J Am Chem Soc 128:6790
12. Kim J, Chang S (2010) J Am Chem Soc 132:10272

13. Iida S, Togo H (2007) Tetrahedron 63:8274
14. Oishi T, Yamaguchi K, Mizuno N (2009) Angew Chem Int Ed 48:6286
15. Yamaguchi K, Kobayashi H, Mizuno N (2012) Angew Chem Int Ed 51:544
16. Reddy KR, Maheswari CU, Venkateshwar M, Prashanthi S, Kantam ML (2009) Tetrahedron Lett 50:2050
17. Zhou W, Zhang L, Jiao N (2009) Angew Chem Int Ed 48:7094
18. Wang T, Jiao N (2014) Acc Chem Res 47:1137
19. Yadav DKT, Bhanage BM (2013) Eur J Org Chem 2013:5106
20. Dandu D, Racha A, Pravin RL (2014) Adv Synth Catal 356:189
21. Kotani M, Koike T, Yamaguchi K, Mizuno N (2006) Green Chem 8:735
22. Mori K, Yamaguchi K, Mizugaki T, Kaneda K (2001) Chem Commun 461
23. Kim J, Stahl SS (2013) ACS Catal 3:1652
24. Oishi T, Kazuya Y, Mizuno N (2009) Angew Chem Int Ed 48:6286
25. Ishida T, Watanabe H, Takei T, Hamasaki A, Tokunaga M, Haruta M (2012) Appl Catal A 425:85–90
26. Nie R, Shi J, Xia S, Shen L, Chen P, Xiao FS (2012) J Mater Chem 22:18115
27. Jagadeesh RV, Junge H, Beller M (2014) Nat Commun 5:4123
28. Tao CZ, Liu F, Zhu YM, Liu WW, Cao ZL (2013) Org Biomol Chem 11:3349
29. Yin W, Wang C, Huang Y (2013) Org Lett 15:1850
30. Dornan LM, Cao Q, Flanagan JCA, Crawford JJ, Cook MJ, Muldoon MJ (2013) Chem Commun 49:6030
31. Dighe SU, Chowdhury D, Batra S (2014) Adv Synth Catal 356:3892
32. Zhang YC, Lü FL, Cao XH, Zhao JQ (2014) RSC Adv 4:40161
33. Wang NW, Liu RH, Chen JP, Liang XM (2005) Chem Commun 5322
34. Hoover JM, Stahl SS (2011) J Am Chem Soc 133:16901
35. Liu R, Dong C, Liang X, Wang XJ, Hu XQ (2005) J Org Chem 70:729–731
36. Hu ZZ, Kerton FM (2012) Appl Catal A 413–414:332
37. Hara T, Sawada J, Nakamura Y, Shimazu S (2011) Catal Sci Technol 1:1376
38. Yadav DKT, Bhanage BM (2013) Eur J Org Chem 23:5106
39. Gamez P, Arends IWCE, Reedijk J, Sheldon RA (2003) Chem Commun 2414
40. Gamez P, Arends IWCE, Reedijk J (2004) Adv Synth Catal 346:805
41. Figiel PJ, Leskelä M, Repo T (2007) Adv Synth Catal 349:1173