

Aerobic Oxidation of Secondary Alcohols to Ketones Catalyzed by Ionic Liquid Functionalized TEMPO

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Abstract

Protocols of aerobic oxidation of secondary alcohols to ketones by using TEMPO modified by bi-functionalized imidazolium-based ionic liquids have been developed. [Imim-TEMPO][X] (X= FeCl₄, CuCl₂) has been proved to be efficient and recyclable catalysts with modest or excellent yields and selectivity. Therefore, relevant literatures are summarized herein.

Keywords: aerobic oxidation, ionic liquids, secondary alcohols, TEMPO

The oxidation of secondary alcohols into the corresponding ketones is a transformation of fundamental importance in modern organic chemistry.^[1,2] Current emphases on economical and green chemistry^[3] have attracted many efforts to employ O₂ (or air) instead of other toxic, hazardous oxidants as the ultimate oxidants in catalytic oxidations.^[4-10] Recently, the stable nitroxyl radical, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) has been proved as an appealing metal-free catalyst in aerobic oxidation of alcohols.^[11-13] However, TEMPO itself is too weak to oxidize secondary alcohols^[14] and also is rather expensive due to its highly desirable renewability. The ideal conversion of secondary alcohols and controllable selectivity of corresponding ketones under the scope of green standards are still challenging. Therefore, developing efficient and recyclable catalytic systems for the selective transformations is an urgent research hot spot at present and in future. Recently, the ionic liquids supported TEMPO, combining the advantages of homogeneous catalysis with heterogeneous process technology, have been demonstrated to be efficient and recyclable

catalysts and also the environmentally benign reaction media.^[15-21]

Miao *et al.*^[20] have developed a TEMPO-based bimagnetic ionic liquid ([Imim-TEMPO][FeCl₄]) as a highly effective catalyst for secondary aromatic alcohols with yields up to 99% and selectivity of over 96% under mild conditions (Figure 1). It can be re-used for at least 5 reaction runs without significant loss of either activity or confined IL. They found that FeCl₃/NaNO₂, [Imim-TEMPO][Cl] or [Imim][FeCl₄] alone shows no activity in the reaction. The mechanism of the whole catalytic system remains unexplored.

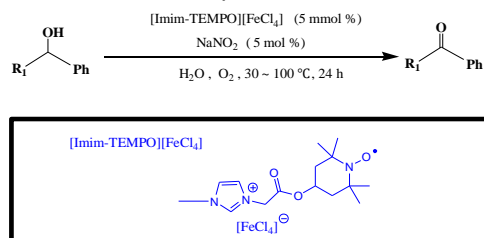


Figure 1. Aerobic oxidation of secondary alcohol catalyzed by [Imim-TEMPO][FeCl₄]/NaNO₂

In 2014, Zhao *et al.*^[21] have synthesized a bi-functionalized PEG₁₀₀₀ ionic liquid supported

TEMPO ([Imim-PEG₁₀₀₀-TEMPO] [CuCl₂]) to oxidize the same secondary alcohols, such as 1-phenylethanol or diphenylmethanol. Within less time than before, the catalytic system shows a great high efficiency and good compatibility for alcohol oxidation in the recycling process of 5 times. The author screened the impact of different metal salts in the catalytic system to the conversion and yields (Figure 2). Compared to DMSO, DMF and toluene as solvents, [Imim-PEG₁₀₀₀-TEMPO][CuCl₂] performs better due to its capability of forming homogeneous systems to enhance the reaction. In their paper, they assumed that the TEMPO moiety might be a hydrogen acceptor during the catalytic cycle. The TEMPO-mediated oxidation transfer Cu(I) to Cu(II) species. The transfer of β -hydrogen to TEMPO and intramolecular one-electron transfer leads to the ketone, TEMPOH and Cu(I) species.

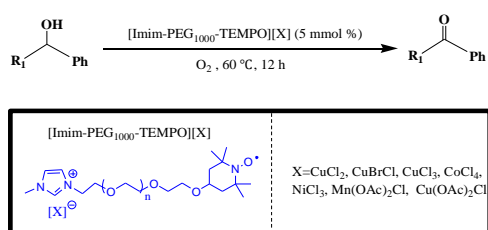


Figure 2. Aerobic oxidation of secondary alcohols catalyzed by [Imim-PEG₁₀₀₀-TEMPO][CuCl₂]

Several Imim-TEMPO moieties modified with other anionic functional groups have also been reported, such as tetrafluoroborate^[16], methanesulfonate^[18], and iodoarene moieties^[19], which can be applied for environmentally benign catalytic oxidation of secondary alcohols (Figure 3). The catalytic potential of bi-functionalized Imim-TEMPO is better than that of TEMPO itself. Homogeneous catalytic systems of IIs functionalized TEMPO allow a facile separation

of oxidation products^[22] and multiple times of recycling without the loss of catalytic efficiency. The results are summarized in Table 1.

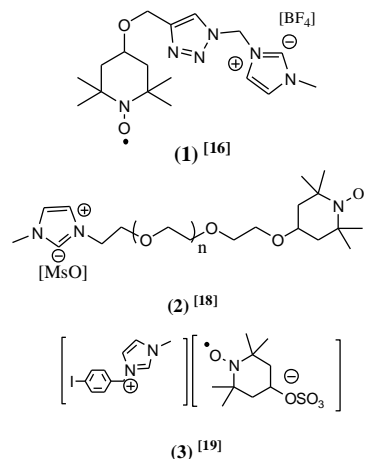


Figure 3. Bi-functionalized Imim-TEMPO radicals

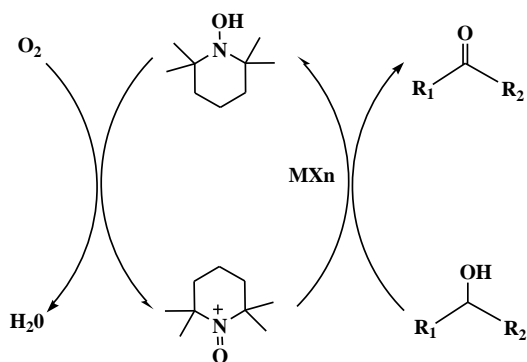
TEMPO+ recycling process (Figure 4) is a popularly recognized mechanism.^[21,23] Nevertheless, several successful examples of radical-based route have been reported.^[24,25] Bi-functionalized Imim-TEMPO, known as an efficient catalyst for aerobic oxidation of alcohols to their corresponding ketones with good selectivity and high recyclability, is a promising catalyst in the present and future. More anionic functional groups such as [AlX₄]⁻^[24], Cu(II)X₃⁻^[26], Ru(II)X₃⁻^[27], Mn(II)X₃⁻, CoX₃⁻^[28] (X = Cl, Br) should be developed to enhance Imim-TEMPO's catalytic activity towards the secondary aromatic alcohols, or even aliphatic alcohols. It also needs more research to prove whether it will be an efficient promoter for aerobic oxidation of C-H bonds,^[24,29] as we recently have found that TEMPO can promote the oxidation of β -isophorone.^[29]

Table 1. The catalytic performance of ILs functionalized TEMPO in the aerobic oxidation of the secondary alcohols to the corresponding ketones

Catalysts	Substrates	Conv. (%)	Yield (%)	Recycled times	Reference
[Imim-TEMPO][FeCl ₄]	PhCH(OH)CH ₃	100	>99	5	[20]
[Imim-PEG ₁₀₀₀ -TEMPO][CuCl ₂]	cyclohexanol	83	80	5	[21]
[Imim-TEMPO][BF ₄]	PhCH(OH)CH ₃	no	90	5	[16]
[Imim-PEG ₆₀₀ -TEMPO][OMS]	PhCH(OH)CH ₃	64	63	5	[18]
[Imim][TEMPO-OSO ₃]	cyclohexanol	no	88	5	[19]

Reaction conditions: Catalyst (5 mmol%); NaNO₂ (5 mol%); Temperature (30~100°C); Time (8~24 h); O₂.

The internal mechanism goes an ionic-based reaction or radical-based reaction or trapping reaction for the efficient catalytic oxidation should be further studied to make it clear and sure.

**Figure 4.** TEMPO+ recycling process of aerobic oxidation of alcohols

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