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COMMUNICATION

Free radical reaction promoted by ionic liquid : a route for metal-free oxidation depolymerization of lignin model compound and lignin

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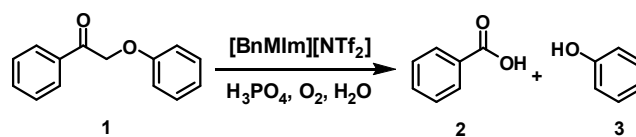
Ionic liquid 1-Benzyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([BnMIm][NTf₂]) can promote the generation of ·OOH free radical, and thereby efficiently transformed the β-O-4 lignin model compound 2-phenoxyacetophenone into benzoic acid and phenol using O₂ as the oxidant. Furthermore, the IL-based metal-free catalytic system can also depolymerize other lignin model compounds and organosolv lignin effectively.

Lignocellulosic biomass, a promising alternative to fossil resource, has attracted much attention in recent years.¹ As a main component of lignocellulosic biomass, lignin is considered to be the unique renewable aromatic resource² and can be used to produce useful aromatic compounds.³ Due to the structural complexity and variability, model compounds with β-O-4 linkage, which represents the most common substructure in lignin, are often adopted to disclose the chemical issues in lignin valorization.⁴ The transformations of lignin model compounds involve catalytic cracking,⁵ hydrolysis,⁶ reduction⁷ and oxidation.⁸ Catalysts used in these reactions involve homogenous or heterogeneous nickel catalysts,⁹ vanadium complex,¹⁰ ruthenium complex¹¹ and so on.¹² As one of the important transformations, oxidation process is usually catalyzed by different transition-metal-based catalysts.⁸ Although many metal-catalyzed methods are effective, the reserves of metal catalysts are limited in the earth and these catalysts also generate harmful metal waste leading to increased cost and energy consumption in the post-treatment. Obviously, it is highly desirable to explore metal-free routes using O₂ or H₂O₂ as the oxidant in lignin valorization. Recently, a metal-free oxidation of benzylic ketone to produce veratric acid and guaiacol was reported.¹³ The reaction was conducted in organic solvent using H₂O₂ as the oxidant in the presence of NaOH. Inorganic acid was used to neutralize the NaOH after reaction to recover the products.

In the reported transformations of lignin model compounds, volatile organic solvents are often used as reaction media.^{10a, 14} Recently, ionic liquids (ILs) with low volatility have received much interest in various fields such as in organic synthesis,¹⁵ catalysis,¹⁶ separation,¹⁷ and biology.¹⁸ Especially, using ILs as

reaction media to substitute volatile organic solvents is very promising.¹⁹ The transformation of lignin or lignin model compounds in ILs has become an interesting topic.^{4, 19-20} Moreover, ILs have some obvious advantages for lignin valorization because their functions can be designed,²¹ and they are excellent solvents for gases,²⁸ liquids, and lignin.

In this work, we report the first example that IL can promote the generation of OOH free radicals during the transformation of lignin, and this activation mode leads to producing benzoic acid and phenol very efficiently from β-O-4 lignin model compound 2-phenoxyacetophenone(1) under metal-free condition using O₂ as the oxidant with catalytic amount of H₃PO₄ (Scheme 1). The IL-based catalytic system could also depolymerize other lignin model compounds and organosolv lignin. Besides metal-free catalysis, this new route has some other attractive advantages. For example, the use of base and volatile organic solvent is avoided; high yields of the products can be isolated easily without tedious post-treatment; the IL used can be recycled and reused without loss of the yields of the products.



Scheme 1. Oxidation depolymerization of lignin model compound 1

We investigated the impacts of various ILs on the reaction shown in Scheme 1, and analytic results by high performance liquid chromatography (HPLC) are presented in Table 1. The structures of ILs are given in Scheme S1. We found that [BnMIm][NTf₂] + H₃PO₄ was very effective for the oxidation of lignin model compound 1 to produce benzoic acid and phenol in high yields. According to Table 1, the neutral IL-[BnMIm][NTf₂] could promote the reaction (entry 1). Interestingly, addition of minor amounts of phosphoric acid could increase yields of the products significantly (entry 2), suggesting that the acid is favorable to the reaction. Therefore, we studied the efficiency of acidic ILs 1-butyl-3-methylimidazolium hydrosulfate ([BMIm][HSO₄]) and 1-hexyl-3-methylimidazolium dihydrophosphate ([HMIm][H₂PO₄]). But the yields of the

products were low (entries 3 to 4), indicating that the anion of [BnMIm][NTf₂] played a decisive role in the oxidation reaction. To verify this argument, 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([BMIm][NTf₂]) and 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([EMIm][NTf₂]), which also have [NTf₂]⁻ anion, were used for the reaction (entry 5 and 6). High yields of benzoic acid and phenol were also obtained. For comparison, the common neutral IL 1-butyl-3-methylimidazolium chloride ([BMIm][Cl]) and organic solvent toluene were also tested in the presence of H₃PO₄ (entry 7 and 8), and very poor conversion and yields were obtained. The results demonstrate that H₃PO₄ cannot induce the occurrence of the reaction but play the cooperative roles with [NTf₂]⁻IL pushing the proceeding of the reaction

Table 1. Oxidation of lignin model compound **1** with different ILs^a

entry	Solvent	Conversion(%)	Y(2)(%) ^c	Y(3)(%) ^d
1 ^b	[BnMIm][NTf ₂]	40	29	7
2	[BnMIm][NTf ₂]	100	89	84
3	[BMIm][H ₂ SO ₄]	<1	<1	<1
4	[HMIm][H ₂ PO ₄]	30	4.8	3
5	[BMIm][NTf ₂]	100	84	68
6	[EMIm][NTf ₂]	100	78	65
7	[BMIm][Cl]	50	2.6	2
8	Toluene	20	<1	<1

^a reaction conditions: reactant **1** 0.212 g, IL 1 g, 85% H₃PO₄ 16 μ L, H₂O 46 μ L, O₂ 1.0 MPa, temperature, 403 K, reaction time 3 hours. ^b without H₃PO₄; ^c Y(2) = Yield of benzoic acid; ^d Y(3) = Yield of phenol.

Various inorganic and organic acids were tested (Table S1) in the reaction. The results showed that strong acids such as hydrochloric acid and sulfuric acid accelerated the conversion of **1**, but the selectivity for phenol and benzoic acid was low. On the other hand, weak acids like acetic acid and tungstic acid had low activity for the reaction. As a result, phosphoric acid showed best performance for the reaction. Just as reported,^{6b} acids are often used to catalyze lignin model compounds to produce useful chemicals through the protonation, nucleophilic attack and cracking reaction steps. Strong acids tend to cause more side reactions, while weak acids show very low activity. Therefore, the catalytic system with phosphoric acid was further studied.

The effects of various reaction parameters were studied in [BnMIm][NTf₂] and the results are presented in Figure 1, together with those to test the reusability of the IL. Figure 1a demonstrates the variation of the conversion and yields with the amount of phosphoric acid. It can be known from the figure that small amount of phosphoric acid could enhance the reaction very effectively. The conversion increased continuously with the amounts of the acid. The yields of benzoic acid and phenol increased firstly, and then decreased as the amount of phosphoric acid was more than 16 μ L. At the same time, the side reactions, such as esterification of benzoic acid and phenol as well as further oxidation of the products, were also be accelerated, resulting in lower yields of the desired products at higher phosphoric acid concentration. The dependence of amount of water on the reaction was illustrated in Figure 1b. With increasing amount of water, the conversion of the reactant and the yields of the products increased at the beginning. But with more

added water, the system was diluted, resulting in lower conversion and yields. Little products were generated without adding water because phosphoric acid (85%) contained a small amount of water. The results above reveal that water is necessary in the reaction. The dependence of the conversion of **1** and the yields of products on the pressure of oxygen is shown in Figure 1c. The reaction cannot proceed in the nitrogen atmosphere without oxygen, which means that oxygen is crucial for the reaction. The conversion increased rapidly as the oxygen pressure increased. The yields of benzoic acid and phenol reached a plateau when the oxygen pressure reached 1.0 MPa. After that, the yields dropped evidently. The main reason is that the side reactions occurred more considerably at higher oxygen pressure. The reusability of [BnMIm][NTf₂] was tested and the results are illustrated in Figure 1d. Obviously, the loss of the yields of benzoic acid and phenol was not notable in the four cycles, showing the excellent stability of the IL in the reaction system.

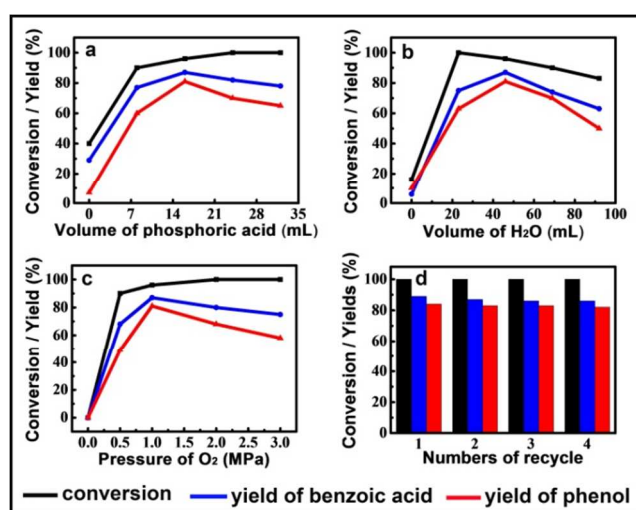


Figure 1. Effects of reaction parameters on the conversion and yields with the typical reaction condition: 0.212 g reactant **1**, 1 g IL, variational amounts of 85% H₃PO₄ aqueous solution (a), water (b) and oxygen (c) temperature, 403 K. (d) The reuse of [BnMIm][NTf₂] at the condition in Entry 2 of Table 1.

It is interesting to study the activation process of oxygen and the role of the [BnMIm][NTf₂] in the reaction. It was reported that ethers can be oxidized and form contact charge transfer complexes (CCTCs) through heating without light and any additional initiator.²⁵ UV-Vis spectroscopy can be used to study the formation of CCTCs by the change of the maximum absorption wavelength (λ_{\max}) of functional groups with and without oxygen.²⁵ We carried out the UV-vis experiments and the results are shown in Figure 2A. With nitrogen of 1.0 MPa at 353 K for 12 hours, the λ_{\max} of 2-phenoxyacetophenone was 243 nm. But with oxygen of 1.0 MPa under the same condition, the λ_{\max} moved to 282 nm. The red shift of the wavelength can be ascribed to that 2-phenoxyacetophenone(**1**) formed CTC with oxygen via Van der Waals' force.²⁶ The interaction increases delocalization of electrons of the complex, and eventually reduces the energy between the ground state and the excited state of the CTC.²⁵ As we know from literature, after formation of the CTC, the complex is not stable and tends to dissociate into oxygen free radical with partial negative charge, and the adjacent

-CH₂ group can transfer hydrogen to the negative oxygen radical to form OOH free radical. There are two benzene rings in **1**, and it can be deduced that the oxygen would interact with the one conjugated with carbonyl group.²⁷ To further verify the speculation, we studied the oxidation of other two lignin model compounds (Scheme S2) diphenyl ether (without -CH₂ group) and benzyl phenyl ether (with -CH₂ group). At the condition shown in entry 2 of Table 1, no reaction occurred for diphenyl ether, but benzyl phenyl ether was completely converted. The results also provide the information about the activation mode of O₂ in our reaction system (Scheme 1). Due to the strong electronegativity of heteroatoms contained in [NTf₂]⁻, the anion is beneficial to the delocalization of electron pairs, which accelerates the formation of OOH free radicals. Eventually, the oxidation depolymerization reaction is promoted significantly.

As we know, electron paramagnetic resonance (EPR) is the most direct and effective way to detect the existence of free radicals. Riboflavin is often chosen to generate OOH free radicals under the irradiation of ultraviolet light.²⁹ In our experiment, firstly, a standard system was used to generate and trap free radical consisting of 1 mM riboflavin in [BnMIm][NTf₂] with DMPO (dimethyl pyridine N-oxide) as the spin trap, and the spectra was obtained as depicted in Figure S1a. Then the EPR detection of our reaction system was conducted using [BnMIm][NTf₂] as the reaction medium with DMPO added to the reactor before the reaction, and it gave rise to identical spectrum with the above experiment ($g=2.01\pm 0.002$) (Figure 2B), which proved the generation of OOH free radicals in our reaction process. For comparison, another EPR detection was made using [BMIm][HSO₄] as the reaction medium at the same condition, but no signal was detected (Figure S1b). The results show that no free radicals was generated in [BMIm][HSO₄], which also reveals that inorganic acids in the reaction system cannot promote the generation of free radicals in [BMIm][HSO₄]. In addition, Table 1 shows that no reaction occurred in this IL (entry 3), suggesting that formation of free radicals is crucial for the reaction.

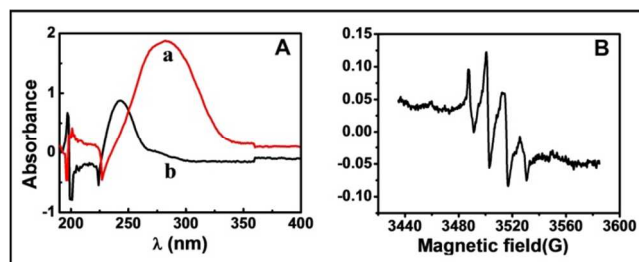


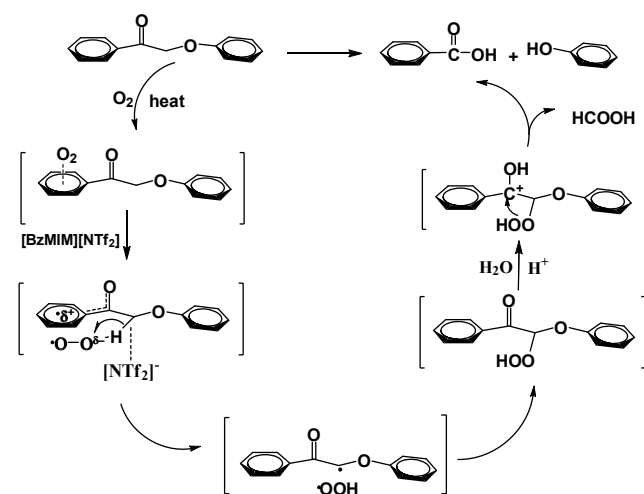
Figure 2. A) UV-vis absorption spectra of 2-phenoxyacetophenone with N₂(b) and O₂(a). B) EPR spectrum of OOH free radical trapped by DMPO in the reaction.

It can be known from Scheme 1 that a carbon atom of the reactant **1** lost in the reaction to produce benzoic acid and phenol. The gas chromatography (GC) analysis of the collected gases vented from the reactor after the reaction showed that the vented gases consisted of carbon dioxide, hydrogen and carbon monoxide. Figure S2 gives the GC spectra of the gaseous products in the reaction shown in entry 2 of Table 1. Considering that formic acid can be decomposed into carbon monoxide and water or into carbon dioxide and hydrogen under heating,²² we speculated that the lost carbon formed formic acid firstly in the

reaction, which further decomposed into these gases. The speculation was also confirmed by the detection of trace amount of formic acid by high performance liquid chromatography (HPLC) (Figure S3).

Based on the above experimental results and the knowledge in literature, we proposed a plausible mechanism of the reaction which is schematically shown in Scheme 2, and is discussed in the following. Firstly, 2-phenoxyacetophenone(**1**) forms CCTC with oxygen by the interaction between oxygen and the benzene ring conjugated with carbonyl group. Then, the CCTC can be oxidized into ROOH transition state, which is the key step in the oxidation process. After the dissociation of CCTC into oxygen free radical with partial negative charge and **1** with partial positive charge, the C-H bond adjacent to ether-oxygen atom is activated. On one hand, the lone pair electrons of oxygen atom in oxygen free radical can activate the hydrogen atom by forming hydrogen bond. On the other hand, the strong electronegativity of [NTf₂]⁻ is also in favour of the delocalization of electrons between C-H bond, thus promoting the cleavage of C-H bond. As a result, the dissociated hydrogen atom combines with O₂⁻ to form OOH free radical, and ROOH transition state is obtained. Finally, under the cooperation attack of H⁺ and water, the intermediate was transformed, releasing formic acid and producing benzoic acid and phenol.

To verify the application of the reaction system, another common lignin model compound, 2-phenoxy-1-phenylethanol was tested at 443 K with other conditions same as that in Entry 2 of Table 1. It was converted completely after four hours, and the yield of benzoic acid reached to 75%, phenol, benzaldehyde and other products were also obtained. We also studied the oxidation of organosolv lignin employing the IL-based system. After reaction of 20 hours, an orange oil fraction(75 wt%) was obtained. The oil can be easily dissolved in organic solvents and analysed by HPLC and GC-MS. The products contained benzoic acid (43 wt%), benzaldehyde, and some other compounds. The above results indicate that the IL-based system is also very effective to the depolymerization of organosolv lignin.



Scheme 2. Possible mechanism of oxidation of lignin model compound **1**.

In conclusion, we found that IL [BnMIm][NTf₂] combined with a small amount of H₃PO₄ is an excellent catalytic system and

medium for transformation of lignin model compound (**1**) into benzoic acid and phenol. A plausible mechanism is proposed based on the analysis of UV-Vis spectroscopy and electron paramagnetic resonance (EPR). Firstly, 2-phenoxyacetophenone(**1**) forms CCTC with oxygen by the interaction between oxygen and the benzene ring conjugated with carbonyl group. Then, with the promotion of [BnMIm][NTf₂], OOH free radicals can be generated and CCTC can be oxidized into ROOH. Finally, under the cooperation attack of H⁺ and water, the intermediate was transformed, releasing formic acid and producing benzoic acid and phenol. The results demonstrate for the first time that ionic liquid can promote the generation of OOH free radicals thereby accelerating the reactions. This metal-free route can also be applied for other lignin model compounds and organosolv lignin. This new protocol to cleave the C-C/C-O bonds in lignin has obvious advantages, such as metal free, highly efficient, avoiding the use of base and volatile organic solvent, and the IL can be easily recycled and reused. We believe that the route of free radical reaction promoted by an IL opens a promising way to design metal-free catalytic systems.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [GC analysis spectra of gases collected after the reaction; structures of the ILs used; oxidation of lignin model compound **1** with different acids; UV-vis absorption study; structures of other lignin model compounds studied in the work; EPR experiments and spectra; reuse of [BnMIm][NTf₂].]. See DOI:

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