Molecular Catalysis 492 (2020) 111013

Contents lists available at ScienceDirect

Molecular Catalysis

journal homepage: www.elsevier.com/locate/mcat

Oxidative NHC catalysis for base-free synthesis of benzoxazinones and benzoazoles by thermal activated NHCs precursor ionic liquid catalyst using air as oxidant

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ARTICLE INFO

Keywords:
Ionic liquids
N-heterocyclic carbine
Oxidative NHC catalysis
Benzoxazinones
Benzoazoles

ABSTRACT

A reusable thermal activated NHC precursor ionic liquid catalyst ($[BMIm]_2[WO_4]$) has been prepared and developed for the synthesis of nitrogen-containing heterocycles such as benzoxazinones and benzoazoles through imines activation. $[BMIm]_2[WO_4]$ exhibited the good activity for the base-free condensation and oxidative NHC catalysis tandem under air atmosphere. The catalyst can be recovered and reused for at least five runs in gram scale synthesis without any decrease in catalytic activity. Furthermore, the control experiments demonstrated that the reaction involved formation of aromatic aldimines, NHC-catalyzed oxidative formation of imidoyl azoliums and intramolecular cyclization to generate the product.

1. Introduction

Benzo-fused nitrogen-containing heterocyclics such as benzoazoles (including benzothiazoles, benzoxazoles and benzimidazoles) and benzoxazinones are very attractive scaffolds in material science and drug discovery [1,2] As shown in Fig. 1 and 2-(stilben-4-yl)benzoxazole derivatives (BOXSB), as organic light-emitting diodes (OLED) materials, are used for electroluminescent (EL) devices [3]. 2-(2′-hydroxyphenyl) benzothiazole (HBT) are widely used as chemosensors for ion detection and bioimaging [4]. In addition, 2-substituted benzoxazinones, as the key building blocks in the synthesis of quinazolinone analogues, also exhibit a wide range of applications in biological and pharmaceutical researches [2,2]. Therefore, development of simple and practical protocols for construction of these benzo-fused nitrogen-containing heterocyclics has received great concern [5]. A popular synthetic route for synthesis of these kinds of *N*-heterocyclics is from aldehydes and 2-substituted aromatic amines involving cyclization and dehydrogenation oxidation [6]. Although many good catalytic systems for construction of benzoxazinones or benzoazoles have been achieved by using various catalysts [7], stoichiometric oxidants such as oxone are general required especially for the synthesis of benzoxazinone resulting in unexpected waste. Furthermore, few catalysts can be used for the synthesis of both benzoxazinones and benzoazoles. Therefore, in the view of the sustainable chemistry, exploration of new catalysts for synthesis of both benzoxazinones and benzoazoles using air as sole oxidant is a big challenge and very attractive.

N-heterocyclic carbene (NHC) has been proved to be very powerful catalyst for construction of complex molecules [8]. Usually, NHC can be used to promote transformation from aldehydes and Michael acceptors [9]. Recently, NHCs-catalyzed activation of aldimines to access to amides and nitrogen-containing heterocycles such as indoles [10] and quinolones [10] via aza-Breslow intermediates [10] have been reported. In addition, NHCs can also promote nucleophilic reaction in the normal way without polarity reversal with the generation of acyl azoliums under oxidative conditions [11]. In 2018, Biju and co-workers expanded oxidative NHC catalysis for synthesis of benzoxazoles through nucleophilic cyclization of activated aromatic aldimines [10]. However, due to the high activity and environmental sensitivity, NHCs are usually required to be formed in situ by adding excessive strong base [12], which requires extra procedures to deal with the excess organic or inorganic bases. Furthermore, NHCs precursors are quite difficult to recover and recycle because of the irreversible formation process of NHCs in the presence of oxidant and strong base. The base-free generation of NHC species from chloride salts has been reported by the groups of Bode [8] and Xiao [8], which provided another possibility to realize the activation of NHCs precursors.

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https://doi.org/10.1016/j.mcat.2020.111013
Received 25 March 2020; Received in revised form 7 May 2020; Accepted 11 May 2020
Available online 24 May 2020
2468-8231/

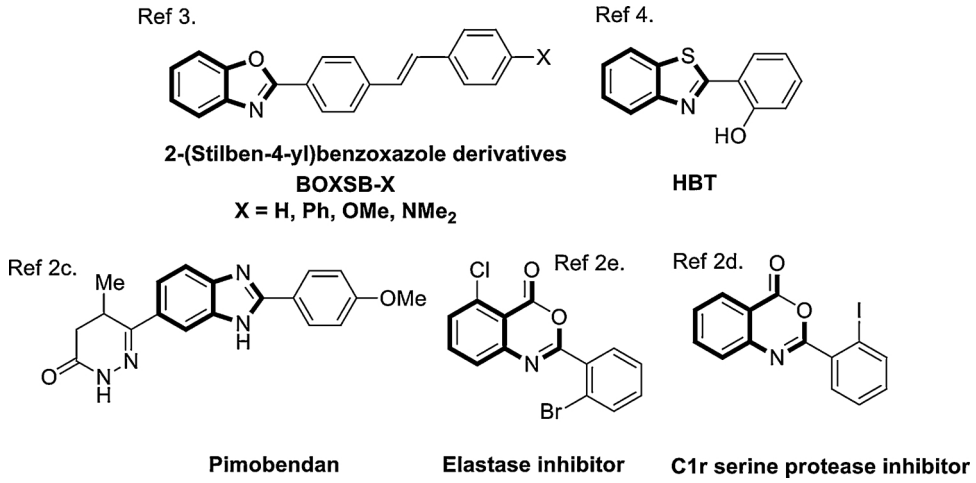


Fig. 1. Nitrogen-containing heterocyclics with biological activities and functional materials.

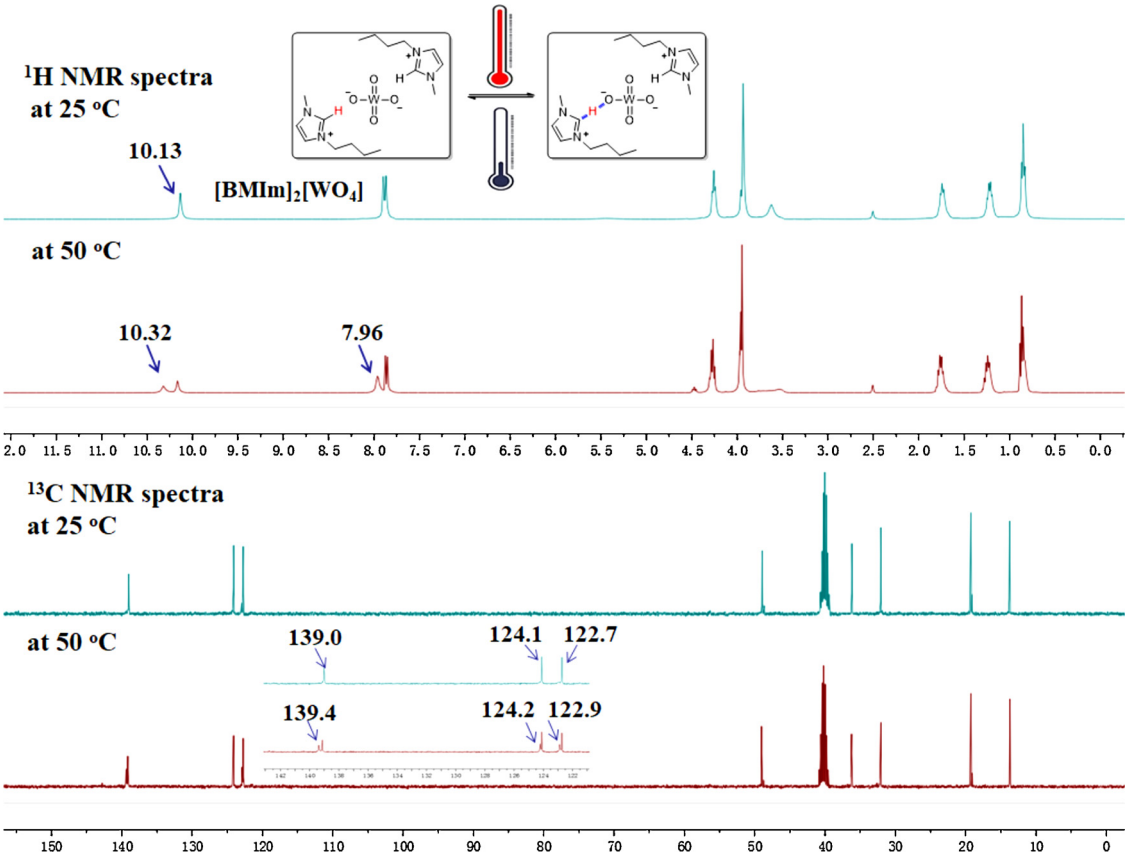


Fig. 2. Temperature-dependent ^{1}H and ^{13}C NMR spectra of $[BMIm]_2[WO_4]$ in DMSO-d_6 at 25 °C and 50 °C.

Ionic liquids (ILs) as green medium have been demonstrated to have unique properties in catalytic chemistry [13]. As catalysts, ILs also can promote many transformations including aerobic oxidation [14], condensation reaction [15], transesterification [16], etc. As an important class of ILs, imidazolium-based ILs with alkaline anions (i.e. acetate ion), providing NHCs related species [17], exhibited excellent performance in some NHC-catalyzed reactions. For instance, Chiarotto and co-workers reported oxidative esterification of aldehydes by using $BmimBF_4$ as NHC precursor and solvent [18]. Han and co-workers developed oxidative esterification of alcohols to esters using [EMIM]OAc as catalyst [18]. Hou and co-workers reported ionic liquid-catalyzed internal redox esterification of α,β-unsaturated aldehydes to saturated esters [19]. In addition, Chen and co-workers developed umpolung self-coupling reaction of biomass furaldehydes promoted by [EMIM]OAc [20]. On the other hand, in aerobic oxidation reactions, tungstate-based ILs and its support materials as recyclable catalysts for oxidation of cyclohexene, alcohols and sulfides using H_2O_2 as oxidant under acid conditions have been reported by the groups of Hashemi, Zohreh and Karimi [21]. However, few works have been reported using tungstate-based ILs for aerobic oxidation with molecular oxygen or air as sole oxidant under neutral or alkaline conditions. As our ongoing research in ILs-catalyzed reactions for green synthesis of heterocyclic compounds [22] and expanding the catalytic application of ILs in aldimines activation, we herein wish to report a tungstate-based imidazolium ILs catalyst as recyclable thermal activated NHC-precursor for the base-free synthesis of benzoazoles and benzothiazoles via aerobic oxidative NHC

catalysis using air as sole oxidant.

2. Experimental section

2.1. General methods

All chemical reagents are purchased from standard suppliers without further purification. Column chromatography was conducted with silica gel (mesh 200–300) from the Qingdao Ocean Chemicals. The ESI-MS spectra were recorded by a Finnigan 8230 instrument. High resolution mass spectrometry (HRMS) spectra analysis was performed by electrospray ionization (ESI-microTOF). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 spectrometer at 25 °C or 50 °C operating at 400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR by using $CDCl_3$ or DMSO-d_6 as solvents and TMS as an internal standard. FT-IR spectrum was recorded on Thermo Nicolet 870, and Raman spectra were recorded on LabRAM HR. Melting points of all products were uncorrected.

2.2. Preparation of ionic liquids catalysts

The solution of 1-butyl-3-methylimidazolium hydroxide ([BMIm]OH) in ethanol was prepared via ion exchange by using the anion-exchange resin. Then, half equivalent of H_2WO_4 was added to the ethanol solution of [BMIm]OH and stirred for 3 h. After complete neutralization, $[BMIm]_2[WO_4]$ was obtained under vacuum at 90 °C for 72 h to remove the solvent. The preparation procedure of tetrabutyl ammonium tungstate ($[N_{4444}]_2[WO_4]$) and [BMIm][OAc] are similar to the case of $[BMIm]_2[WO_4]$. The characterization results of NMR and FT-IR spectra for these two tungstate-based ILs were listed in the Supporting Information.

2.3. General procedure for synthesis of 2-arylbenzoxazoles 3

The mixture of *o*-aminophenols **1** (0.6 mmol, 1.2 equiv), aldehydes **2** (0.5 mmol, 1 equiv) in 1,4-dioxane (5 mL) was stirred at 100 °C with oil bath for 1 h. $[BMIm]_2[WO_4]$ (0.1 mmol, 53 mg, 0.2 equiv) was added to reaction mixture for further 4 h at 100 °C in the open air. The reaction was monitored by TLC. After completion of the reaction, the resulting solution was cooled to room temperature and pour it into the water (30 mL) followed by extraction with ethyl acetate (10 mL × 3). The combined organic phase was washed with water three times. The solvent was removed by vacuum evaporation. The pure products **3** were obtained by silica gel column chromatography.

2.4. General procedure for synthesis of 2-arylbenzothiazoles 5

The mixture of *o*-aminophenthiols **4a**, aldehydes **2** (0.5 mmol, 1 equiv) in 5 mL 1,4-dioxane was stirred at 100 °C with oil bath for 1 h. $[BMIm]_2[WO_4]$ (0.1 mmol, 53 mg, 0.2 equiv) was added to reaction mixture for further 4 h at 100 °C in the open air. The reaction was monitored by TLC. After completion of the reaction, the resulting solution was cooled to room temperature and pour it into the water (30 mL) followed by extraction with ethyl acetate (10 mL × 3). The combined organic phase was washed with water three times. The solvent was removed by vacuum evaporation. The pure products were obtained by silica gel column chromatography.

2.5. General procedure for synthesis of 2-arylbenzimidazoles 6

The mixture of *o*-phenylenediamines **4b** (0.6 mmol, 1.2 equiv), aldehydes **2** (0.5 mmol, 1 equiv) in 5 mL 1-butanol was stirred at 100 °C with oil bath for 1 h. $[BMIm]_2[WO_4]$ (0.1 mmol, 53 mg, 0.2 equiv) was added to reaction mixture for further 6 h at 100 °C in the open air. The following procedures are similar to the synthesis of 2-arylbenzothiazoles **5**. The pure products were obtained by silica gel column chromatography.

2.6. General procedure for synthesis of benzoxazinones *8*

The mixture of anthranilic acid **7** (0.5 mmol, 1 equiv), aldehydes **2** (1 mmol, 2 equiv) in toluene (5 mL) was stirred for 1 h with oil bath at 120 °C. After adding $[BMIm]_2[WO_4]$ (0.1 mmol, 53 mg, 0.2 equiv), the reaction mixture was further stirred for 35 h at 120 °C. After cooling to the room temperature, the reaction mixture was poured it into the water (30 mL) followed by extraction with ethyl acetate (10 mL × 3). The organic solution was evaporated under vacuum. The pure products were obtained by silica gel column chromatography.

2.7. Typical Procedure for the Synthesis of 2-(benzylideneamino)phenol (Schiff base I) [10]

The mixture of 2-aminophenol (1.06 g, 10 mmol), anhydrous $MgSO_4$ (3.0 g) and THF (10 mL) was stirred at 0 °C. Then benzaldehyde (1.06 g, 10 mmol) was added dropwise to the mixture. The reaction was stirred for 10 h at room temperature. After filtration, the filtrate was concentrated under vacuum. The product was obtained by recrystallization from cold EtOH (1.58 g, 80% yield).

2.8. General procedure for gram-scale synthesis of benzoxazinones, benzoxazoles and catalyst recovery

For benzoxazole **3a**, the mixture of 2-aminophenol o-aminophenol **1a** (12 mmol, 1.2 g, 1.2 equiv), benzaldehyde **2a** (10 mmol, 1.06 g, 1 equiv) in 1,4-dioxane (100 mL) was stirred at 100 °C for 1 h. Then $[BMIm]_2[WO_4]$ (2 mmol, 530 mg, 0.2 equiv) was added. The reaction mixture was further stirred for 4 h. After completion of the reaction, the mixture was poured into the water and extracted by ethyl acetate (35 mL × 3). The combined organic phase was washed with water three times. The solvent was removed by vacuum evaporation. The pure product of **3a** (1.56 g, 80% yield) were obtained by silica gel column chromatography (ethyl acetate/petroleum ether = 1/40).

For benzoxazinone **8f**, 2-amino-5-methylbenzoic acid **7f** (10 mmol, 1.51 g, 1 equiv) and benzaldehyde **2a** (20 mmol, 2.12 g, 2 equiv) in 100 mL toluene were allowed to stir for 1 h at 120 °C. After adding $[BMIm]_2[WO_4]$ (2 mmol, 530 mg, 0.2 equiv), the reaction mixture was further stirred for 35 h at 120 °C. After cooling to the room temperature, the reaction mixture was washed with water (40 mL × 3). The organic solution was evaporated under vacuum. The pure product of **8f** (1.42 g, 60% yield) were obtained by silica gel column chromatography (ethyl acetate/petroleum ether = 1/60).

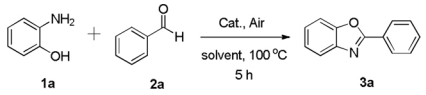
For recycling catalyst, the aqueous phase of reaction mixture was concentrated. The mixture was washed with anhydrous ether and dried vacuum at 90 °C to afford the reused catalyst.

3. Results and discussion

3.1. Synthesis and characterization of ionic liquids catalysts

The tungstate-based imidazolium ILs ($[BMIm]_2[WO_4]$) catalyst was prepared through neutralization reaction of tungstic acid and 1-butyl-3-methylimidazolium hydroxide from its bromide by anion-exchange process. The structure and physico-chemical properties of catalyst were subsequently characterized. Compared with Na_2WO_4, similar peaks were observed in the FT-IR and Raman spectrum of $[BMIm]_2[WO_4]$ (Figure S1 and S2). Furthermore, temperature-dependent NMR experiments were conducted. As shown in Fig. 2, a series of new peaks appeared in ^{1}H (δ = 10.32, 7.96) and ^{13}C NMR spectra at 50 °C (δ = 139.4, 124.2, 122.9), which indicated a possible enhancement of hydrogen bond interaction between the C-2 position of imidazolium and tungstate with temperature rising. Accordingly, heating would be a good choice to promote the possible proton transfer process at C-2

Table 1
Optimization of the reaction conditions for the synthesis of benzoxazole **3a**[a].



1a 2a 3a

Entry	Catalyst (mol%)	Solvent	Yield[b]
1	$[BMIm]_2[WO_4]$ (20)	Dimethyl sulfoxide	29%
2	$[BMIm]_2[WO_4]$ (20)	1-Butanol	32%
3	$[BMIm]_2[WO_4]$ (20)	Ethyl lactate	trace
4	$[BMIm]_2[WO_4]$ (20)	Toluene	50%
5	$[BMIm]_2[WO_4]$ (20)	*N*-methyl-2-pyrrolidone	34%
6	$[BMIm]_2[WO_4]$ (20)	*N,N*-Dimethylformamide	32%
7	$[BMIm]_2[WO_4]$ (20)	Cyclohexanol	36%
8	$[BMIm]_2[WO_4]$ (20)	Dichloroethane	38%
9	$[BMIm]_2[WO_4]$ (20)	Ethanol	trace
10	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	82%
11	None	1,4-Dioxane	NR
12	$[N_{4444}]_2[WO_4]$ (20)	1,4-Dioxane	22%
13	H_2WO_4 (20)	1,4-Dioxane	NR
14	$Na_2WO_4{\cdot}2H_2O$ (20)	1,4-Dioxane	NR
15	[BMIm][Br] (20)	1,4-Dioxane	NR
16	$Na_2WO_4{\cdot}2H_2O$ + 2[BMIm][Br] (20)	1,4-Dioxane	7%
17[c]	$Na_2WO_4{\cdot}2H_2O$ + 2[BMIm][Br] (20)	1,4-Dioxane	21%
18	$[BMIm]_2[WO_4]$ (5)	1,4-Dioxane	57%
19	$[BMIm]_2[WO_4]$ (10)	1,4-Dioxane	61%
20	$[BMIm]_2[WO_4]$ (15)	1,4-Dioxane	75%
21	$[BMIm]_2[WO_4]$ (25)	1,4-Dioxane	81%
22[d]	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	40%
23[e]	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	25%
24[f]	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	82%
25	[BMIm]OAc (20)	1,4-Dioxane	47%
26	DBU (20)	1,4-Dioxane	Trace
27	*t*-BuOK	1,4-Dioxane	< 5%
28[g]	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	77%
29[h]	$[BMIm]_2[WO_4]$ (20)	1,4-Dioxane	60%

[a] Reaction scale: 2-aminophenols 1a (0.6 mmol), benzaldehydes 2a (0.5 mmol), catalyst based on 2a.
[b] Isolated yield after flash column chromatography.
[c] With 0.4 eq. of 18-Crown-6.
[d] Reaction temperature at 80 °C.
[e] Reaction temperature at 60 °C.
[f] Reaction temperature at 120 °C.
[g] With 1 eq. of 1,1-diphenylethene.
[h] Reactants and catalyst were added at the same time. NR: no reaction. $[N_{4444}]_2[WO_4]$: Tetrabutylammonium tungstate.

position of $[BMIm]_2[WO_4]$.

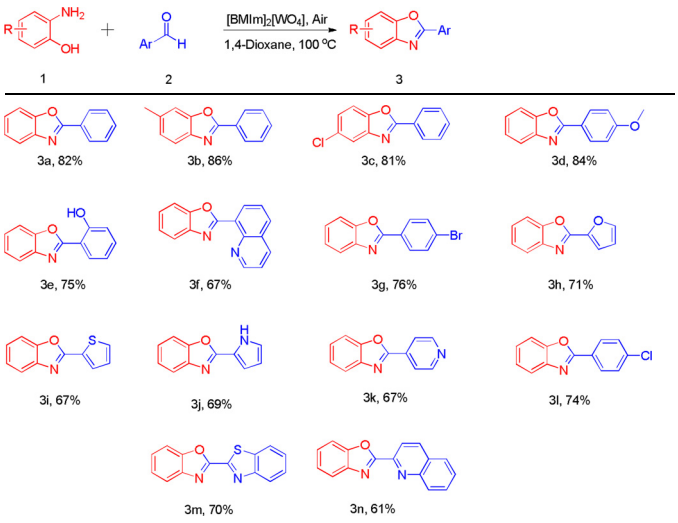
3.2. Synthesis of benzoxazole, benzothiazoles and benzimidazoles

Next, oxidative NHC catalysis for synthesis of benzoxazole **3a** by using $[BMIm]_2[WO_4]$ as thermal activated NHC precursor was investigated (Table 1). Initially, the model reaction of 2-aminophenol **1a** and benzaldehyde **2a** by treating with $[BMIm]_2[WO_4]$ in dimethyl sulfoxide (DMSO) at 100 °C under air atmosphere was conducted. As expected, the 2-phenyl benzoxazole **3a** was obtained with 29% isolated yield (Table 1, entry 1) in DMSO. After screening of some solvents (Table 1, entries 2–10), highly polar solvents such as alcohols, *N*-methyl-2-pyrrolidone (NMP) and dimethylformamide (DMF) (Table 1, entries 2, 3 and 5–9) are not good for the reaction, probably because the solvation effect of high polar solvents was unfavourable to proton transfer process between the imidazolium and tungstate. Toluene provided a medium yield (Table 1, entry 4). 1, 4-dioxane provided 82% isolated yield of **3a** (Table 1, entry 10). The yield of **3a** decreased from 82% to 57% with the catalyst loading reduced to 5 mol% (Table 1, entries 18–20). However, while the catalyst loading increased to 25 mol %, the yield was not significant improvement (Table 1, entry 21). The temperature has a great influence on the reaction. The yield of **3a** dropped down to 40% at 80 °C (Table 1, entry 22). When the temperature was lowered to 60 °C, the yield of product decreased to 25% (Table 1, entry 23). An increase in temperature to 120 °C, the yield did not increase significantly (Table 1, entry 24). These results indicated that the catalytic activity of $[BMIm]_2[WO_4]$ is affected by heat. Several catalysts in controlled experiments were then tested (Table 1, entries 11–17). No product of **3a** was detected without any catalysts (Table 1, entry 11). In addition, catalysts containing only tungstate such as H_2WO_4 and $Na_2WO_4{\cdot}2H_2O$ (Table 1, entries 13 and 14) or [BMIm][Br] (Table 1, entry 15) showed no catalytic activities under standard reaction conditions. A low yield of **3a** was obtained by tetrabutylammonium tungstate (Table 1, entry 12). This may be attributed to the weak alkaline and oxidation capacity of $[N_{4444}]_2[WO_4]$ via normal cyclization and subsequent oxidation [6]. It is worth noting that the combination of imidazolium and tungstate using Na_2WO_4 and [BMIm]Br provided only 7% isolated yield of **3a** (Table 1, entry 16). In addition, the yield of **3a** was improved by adding 18-crown-6 as cationic chelating agent (Table 1, entry 17). These controlled experiments indicated the importance of direct interaction between imidazolium and tungstate. Considering the possible free radical process in the alkaline condition with oxidant [7], some control experiments were conducted using 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) and potassium tert-butoxide (*t*-BuOK) as base in the absence of $[BMIm]_2[WO_4]$. The product of **3a** was trace (Table 1, entries 26 and 27). In addition, the yield of **3a** was almost no change by adding 1,1-diphenylethene as radical scavenger in the presence of $[BMIm]_2[WO_4]$ under standard conditions (Table 1 entry 28). Therefore, radical intermediates may not be formed in this reaction.

As the most common NHC precursor ionic liquid, [BMIm]OAc provided moderate yield of **3a** in standard reaction condition(Table 1, entry 25). Compared with $[BMIm]_2[WO_4]$, [BMIm]OAc showed less favorable for this aerobic oxidative NHC catalysis. It may be due to the instability of the [BMIm]OAc and the loss of acetic acid at such reaction temperature, resulting in the deactivation of the catalyst [23].

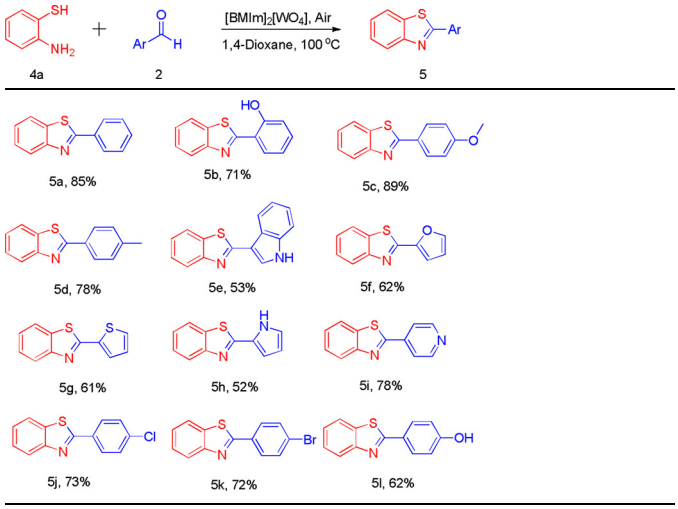
Subsequently, the substrate scope and generality of $[BMIm]_2[WO_4]$ catalyst for this oxidative NHC catalysis was examined. As shown in Table 2, various aryl aldehydes 2a-2 L including heteroaromatic aldehydes are relatively well tolerated in good yield at standard reaction conditions. The reaction of substituent on 2-aminophenol such as 2-amino-5-methylphenol (**2b**) or 2-amino-4-chlorophenol (**2c**) with benzaldehyde **2a** also reacted smoothly. The corresponding products of 3b

Table 2
Oxidative NHC catalysis for synthesis of benzoxazole.[a]



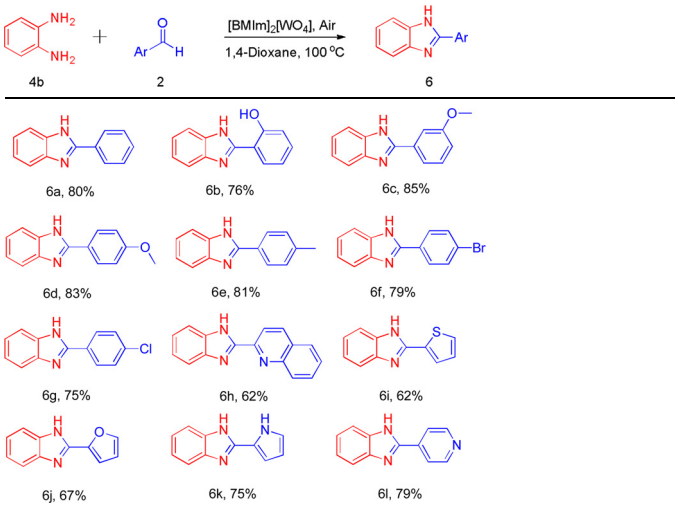
[a] Reaction conditions: 2-aminophenol 1 (0.5 mmol), benzaldehydes 2 (0.5 mmol), catalyst based on 1, 1,4-dioxane (5 mL), 5 h under air; Isolated yield.

Table 3
Synthesis of benzothiazoles [a]



[a] Reaction conditions: 2-aminobenzenethiol 4a (0.6 mmol), aldehydes 2 (0.5 mmol), catalyst (0.1 mmol) based on 2,1,4-dioxane (5 mL) for 5 h under air; Isolated yield.

Table 4
Synthesis of benzimidazoles[a].



[a] Reaction conditions: benzene-1,2-diamine 4b (0.6 mmol), aldehydes 2 (0.5 mmol), catalyst (0.1 mmol) based on 2,1-butanol (5 mL) for 7 h under air; Isolated yield.

and 3c were obtained in 86% and 81% yields respectively. Remarkably, the excited-state intramolecular proton transfer (ESIPT) emitter, 2-(2′-hydroxyphenyl)benzazole (HBX) (**3e**), can be directly obtained in 75% isolated yield without protecting hydroxyl group.

In view of the highly similar structure and synthesis pathway of benzoxazoles, benzimidazoles and benzothiazoles [6], we further investigated this oxidative NHC catalysis for the synthesis of benzothiazoles from 2-aminothiophenols, benzimidazoles from benzene-1,2-diamine with aldehydes. As shown in Table 3, a series of benzothiazoles could also be obtained in good yields under standard conditions from 2-aminothiophenol **4a** with various aromatic aldehydes **2**, which showed good compatibility. In addition, 2-(2′-hydroxyphenyl) benzothiazole (HBT, **5b**) can also be directly obtained in 71% isolated yield.

For the synthesis of benzimidazoles **6**, the reaction provided only 20% of 2-phenylbenzimidazole (**6a**) in 1,4-dioxane for 5 h from benzene-1,2-diamine **4b** and benzaldehydes **2** (Table S1). The reaction time was prolonged to 7 h, the yield of 2-phenylbenzimidazole (**6a**) was up to 28%. But the yield of **6a** was almost no increase when the reation time was up to 9 h. After screening solvents, 1-butanol was better for the synthesis of benzimidazoles **6**, probably due to the better solubility for the benzene-1,2-diamine **4b** (Table S1). Finally, 1-butanol was selected as solvent for the subsequent investigation on the generality and scope of oxidative NHC catalysis in synthesis of benzimidazoles **6**. As shown in Tables 2 and 4 arylbenzimidazoles **6** can be obtained with good yield (62%–85%) from benzene-1,2-diamine **4b** and the different of aromatic benzaldehydes, including aromatic heterocycle such as pyrrole, thiophene and quinoline.

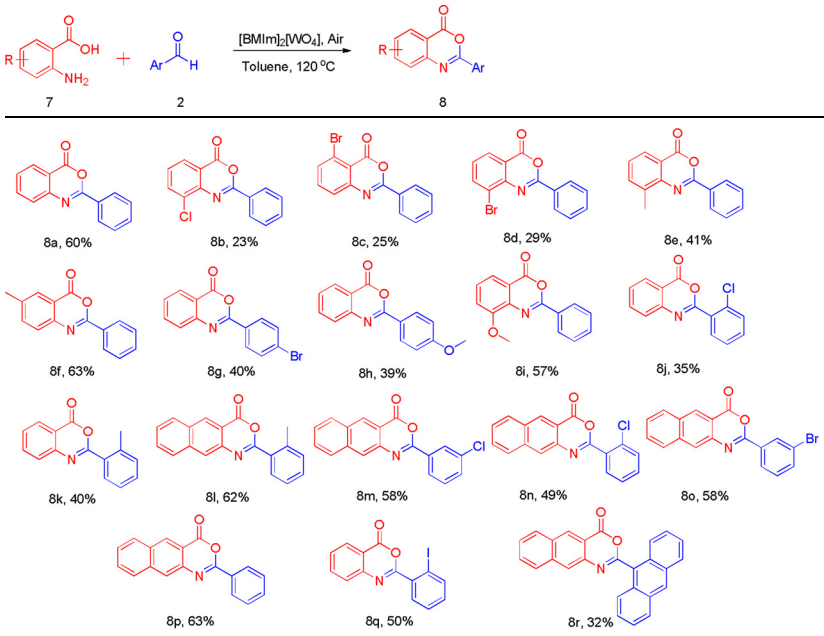
3.3. Synthesis of benzoxazinones

After getting the successful oxidative NHC catalysis for the synthesis of benzoazoles, we further tried to expand this protocol to the synthesis of benzoxazinones from anthranilic acid with aldehydes. In most cases, benzoxazinones is synthesized through the intramolecular cyclization from anthranilic acid and benzoyl chloride [24]. The direct cyclization of imines from anthranilic acid with aldehydes cannot proceed due to the weak nucleophilicity of carboxylic acid compared with –XH (X = O, S, NH). However, NHC as a strong nucleophile is expected to activate imines, which makes the intramolecular nucleophilic attack of imines from carboxylic acid more smoothly. Accordingly, the reaction of anthranilic acid with benzaldehyde was performed in 1, 4-dioxane at 100 °C. The only 15% isolated yield of benzoxazinone (**8a**) was obtained (Table S2, entry 5). The yield of benzoxazinone **8a** was improved to 25% after selection of solvents (Table S2, entries 1–10). When the reaction temperature was up to the 120 °C, the yield of benzoxazinone **8a** was increased to 60% (Table S2, entry 17). The yield of benzoxazinone **8a** was not increased with further raising raction temperature to 140 °C (Table S2, entry 18). As controlled experiments, no product was detected in the absence of catalyst (Table S2, entry 11) or in the presence of strong base such as DBU and *t*-BuOK (Table S2, entries 21 and 22). [BMIm]OAc provided low yield of benzoxazinone **8a** in such reaction conditions (Table S2, entry 13). The yield of benzoxazinone **8a** was dropped to 35% by increasing the amount of anthranilic acid **7a** (Table S2, entry 14), probably because the acidity of extra benzoxazinone **8a** was unfavourable to the catalyst. The yield of benzoxazinone **8a** was not good by using sodium 2-aminobenzoate compared with anthranilic acid **7a** as reactant due to the poor solubility of sodium 2-aminobenzoate in toluene (Table S2, entry 20). The reaction time was also investigated. The yield of **8a** was only 30% when the reaction time was 5 h (Table S2, entry 25). Prolonging the reaction time from 10 h to 36 h, the yield of **8a** was increased from 38% to 60% (Table S2, entries 26–28). The reaction time of synthesis of benzoxazinone **8a** was longer than benzoazoles, probable due to the weak nucleophilicity of carboxylic acid. Notably, $[N_{4444}]_2[WO_4]$ showed no catalytic activity for the synthesis of benzoxazinone **8a** (Table S2, entry 12), which suggested a possible activation of imines by NHC species promoted nucleophilic cyclization. Furthermore, the yield of benzoxazinone **8a** was almost no decreased in the presence of 1,1-diphenylethene as radical scavenger by using $[BMIm]_2[WO_4]$ as catalyst (Table S2 entry 23). With the optimized conditions in hand, the generality and scope of this protocol for the synthesis of benzoxazinones **8** was subsequently investigated. As shown in the Table 5, the reaction of substituted anthranilic acid or 3-amino-2-naphthoic acid with aromatic aldehydes **2** worked well in moderate yields.

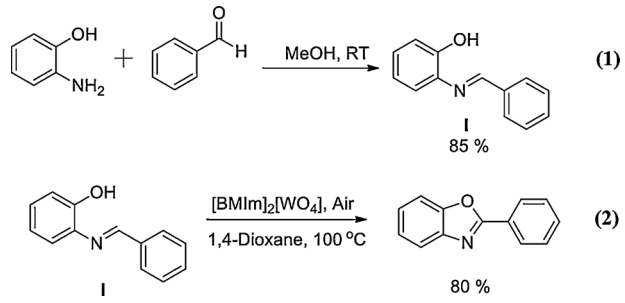
3.4. Possible mechanism of oxidative NHC catalysis by $[BMIm]_2[WO_4]$

In order to understand the role of $[BMIm]_2[WO_4]$ in reaction, additional experiments were conducted. While the reactants and $[BMIm]_2[WO_4]$ were added at the same time, the yields of the 2-phenyl benzoxazole **3a** and benzoxazinone (**8a**) were declined (Table 1, entry 29 and Table S2, entry 24). This indicated that the reaction may not be

Table 5
Synthesis of benzoxazinones[a].



[a] Reaction conditions: anthranilic acid 7 (0.5 mmol), aldehydes 2 (1 mmol), catalyst (0.1 mmol) based on 6, toluene (5 mL), 36 h under air; Isolated yield.



Scheme 1. Two-step synthesis of benzoxazole.

initiated by the activation of aldehydes by $[BMIm]_2[WO_4]$. Furthermore, the two-step synthesis of benzoxazole **3a** was perforemed (Scheme 1). The Schiff base (**I**) was purified and used as reactant under standard conditions. The desired **3a** was formed in 80% isolated yield. These results suggested a possible activation of imines by $[BMIm]_2[WO_4]$ promoted nucleophilic cyclization.

On the basis of literatures [6, 8, 10, 18] and our results, a possible mechanism of this oxidative NHC catalysis was proposed (Scheme 2). Initially, the Schiff base **I** was generated by condensation of corresponding amine with aromatic aldehydes. The NHC related species generated from $[BMIm]_2[WO_4]$ was subsequently activated aldimines through nucleophilic attack reaction to form intermediate **II** [8]. Then, the intermediate **II** transformed to intermediate **III** by oxidation under air conditions [8]. Finally, the product was generated through intramolecular nucleophilic addition and subsequent elimination of NHC related species.

3.5. Recovery and reuse of $[BMIm]_2[WO_4]$ catalyst

Due to the better recyclability of ionic liquids and the need for scale-up synthesis, the reusability of $[BMIm]_2[WO_4]$ catalyst in this oxidative NHC catalysis for gram-scale synthesis of benzoxazole (**3a**) and benzoxazinone (**8f**) have been checked. The $[BMIm]_2[WO_4]$ catalyst could be recycled and reused at least five times with no significant decline in isolated yield (Fig. 3). The recycled $[BMIm]_2[WO_4]$ catalyst was characterized by FT-IR (Figure S3). The characteristic peaks of recycled $[BMIm]_2[WO_4]$ were consistent with the fresh catalyst.

4. Conclusion

In summary, a reusable thermal activated NHC precursor ionic liquid catalyst ($[BMIm]_2[WO_4]$) has been developed for the synthesis of benzothiazoles, benzoxazoles, benzimidazoles and benzoxazinones. The temperature-dependent NMR results showed a possible proton transfer process between anions and cations and subsequent NHC production in $[BMIm]_2[WO_4]$ under thermal activation. This green oxidative NHC catalysis by using $[BMIm]_2[WO_4]$ catalyst provides several advantages such as base-free condition, using air as sole oxidant, broad scope for the synthesis of important *N*-containing heterocycles. After four recycles, the reused $[BMIm]_2[WO_4]$ catalyst still exhibited good catalytic activity in gram-scale synthesis. It is anticipated that this reusable thermal activated NHC precursor catalyst will be a good choice in NHC-catalyzed reaction.

Declaration of competing interest

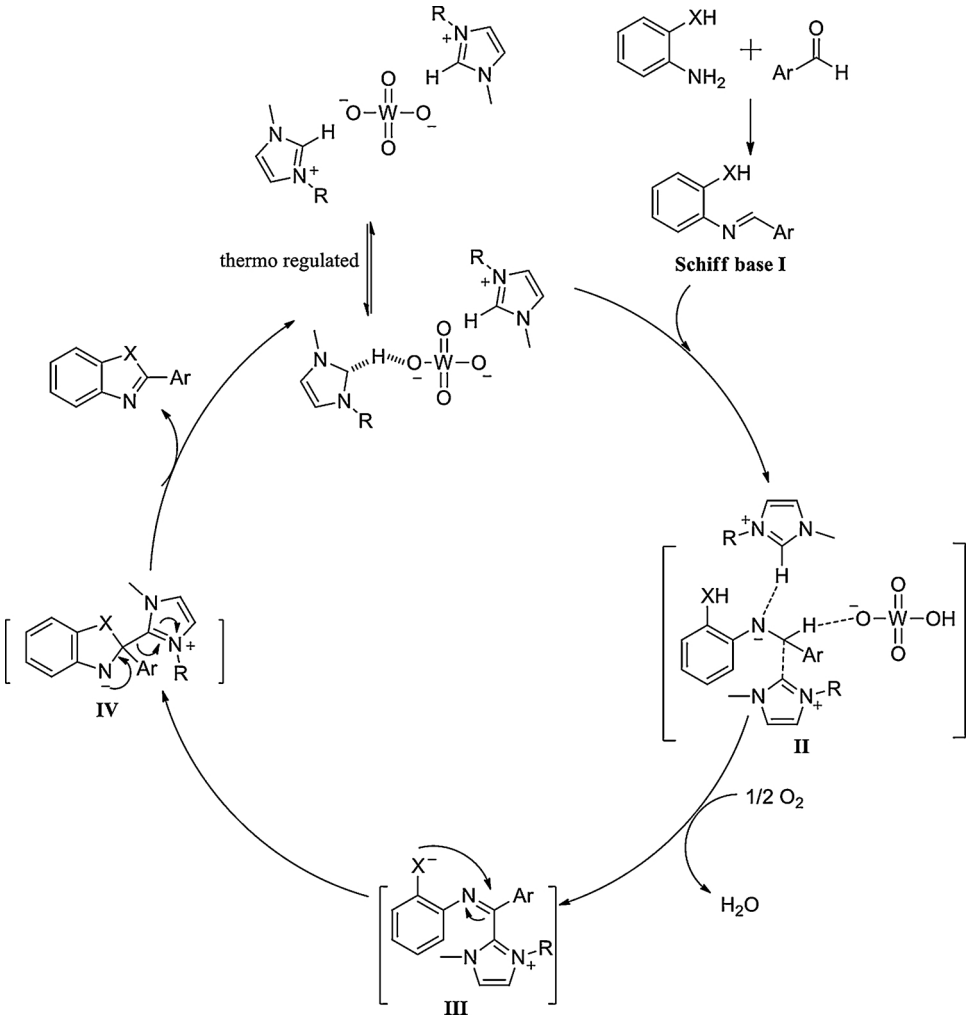
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Youkang Zhou: Writing - original draft. **Wei Liu:** . **Yuchen Liu:** . **Jiali Guan:** . **Jieying Yan:** . **Jian-Jun Yuan:** . **Duan-Jian Tao:** Writing - review & editing. **Zhibin Song:** Data curation, Writing - review & editing.

Acknowledgments

We thank the financial support by the National Natural Science Foundations of China (21606116, 21566011, 31570560), the Natural Science Foundations of Jiangxi Province (20161BAB213070, 20162BCB23026), and the Department of Education of Jiangxi



Scheme 2. Proposed mechanism of oxidative NHC catalysis by $[BMIm]_2[WO_4]$.

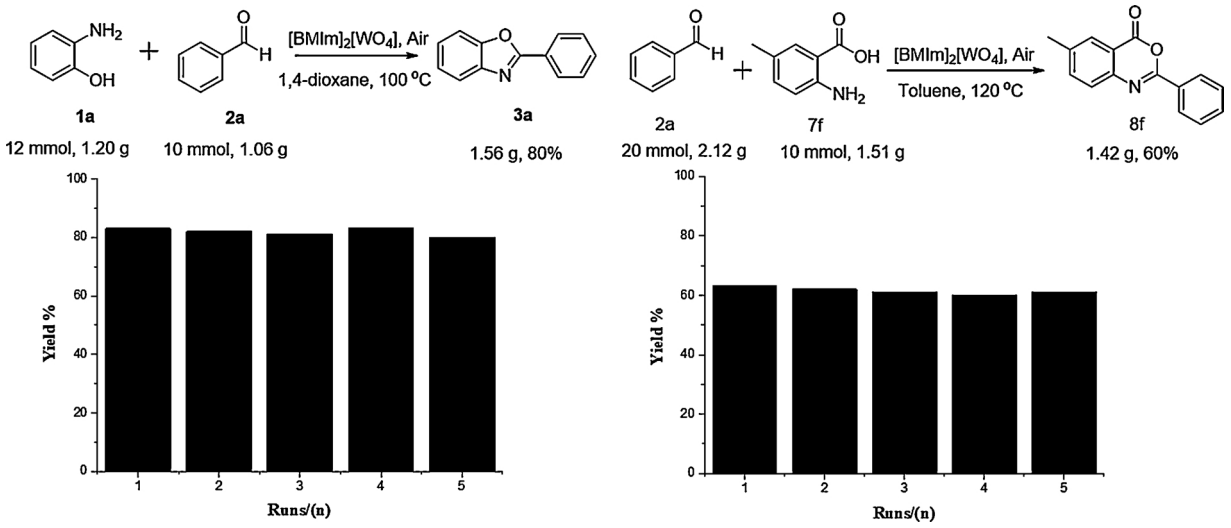


Fig. 3. Gram-scale synthesis of benzoxazole (**3a**) and benzoxazinone (**8f**) and recyclability of $[BMIm]_2[WO_4]$. Reaction condition for benzoxazole: 2-aminophenol (11 mmol), benzaldehyde (10 mmol), $[BMIm]_2[WO_4]$ (2 mmol) as the catalyst, and 1,4-dioxane (100 mL) as the solvent. Reaction condition for benzoxazinone (**8f**): 2-amino-5-methylbenzoic acid **7f** (10 mmol), benzaldehyde (20 mmol), $[BMIm]_2[WO_4]$ (2 mmol) as the catalyst, and toluene (100 mL) as the solvent.

Province (No. GJJ170176).

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.mcat.2020.111013.

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