



## Solvent-free selective oxidation of primary and secondary alcohols catalyzed by ruthenium-bis(benzimidazole)pyridinedicarboxylate complex using hydrogen peroxide as an oxidant <sup>☆</sup>

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### ABSTRACT

A convenient and selective oxidation of alcohols with aqueous hydrogen peroxide to give the corresponding carbonyl compounds under solvent-free conditions has been developed. By applying ruthenium-bis(benzimidazole)pyridinedicarboxylate complex [Ru(bbp)(pydic)] as catalyst, primary, and secondary alcohols were oxidized to aldehydes and ketones in good yield and excellent selectivity under mild conditions.

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### Introduction

Oxidation of alcohols to corresponding carbonyl compounds is of great importance for both laboratory and synthetic industrial applications.<sup>1</sup> In traditional oxidation processes, large amounts of toxic and volatile organic solvents and metal oxidants were extensively used. The need for environmentally benign and clean oxidation reactions remains an important goal of chemical research.<sup>2</sup> Hence, developing green selective oxidation process of alcohols is still a challenging task in catalysis.<sup>3</sup> By comparing different oxidation methods, it is apparent that the oxidant used in the respective transformation defines the quality and applicability of the method. In addition to molecular oxygen, hydrogen peroxide is an environmentally benign oxidant, which theoretically generates only water as a by-product.<sup>4</sup> Therefore, the discovery of new protocol catalyst using H<sub>2</sub>O<sub>2</sub> is gathering much attention. In this content, variety of transition metal-based catalysts has been intensively investigated toward the oxidation of alcohols so far.<sup>5</sup>

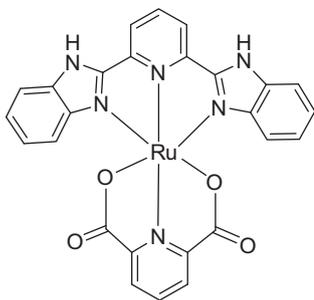
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Ruthenium complexes with nitrogen-based ligands have been intensively investigated in order to develop catalysts for organic oxidation processes.<sup>6</sup> We ever reported an efficient oxidation process of alcohols catalyzed ruthenium porphyrins in the presence of molecular oxygen.<sup>7</sup> Nishiyama first reported the asymmetric epoxidation by one kind of ruthenium complex based on bis(oxazolinyl)pyridine, that is, ruthenium-(pyridinebisoxazoline) (pyridinedicarboxylate) complex [Ru(pybox)(pydic)].<sup>8</sup> Through modification of Nishiyama's catalyst, Beller research group developed efficient asymmetric epoxidation processes with a greener oxidant such as *tert*-butylhydroperoxide (TBHP) or hydrogen peroxide in recent years.<sup>9</sup>

We looked for ruthenium complexes that should be efficient for the oxidation of alcohols. Inspired by the efficiency of Nishiyama's catalyst in the epoxidation, we adopted the introduction of 2,6-bis(benzimidazole)pyridine as the counterpart to synthesize new catalyst with dual closed meridional stereotopes around an active metal. Hence, based on 2,6-bis(benzimidazole)pyridine and pyridinedicarboxylate, the novel kind ruthenium complex [Ru(bbp)(pydic)] (Scheme 1) was successfully synthesized and was applied as catalyst in the oxidation reactions. Interestingly to find this ruthenium complex is efficient for the selective oxidation of alcohols to corresponding carbonyl compounds with hydrogen peroxide as oxidant. Meanwhile, the noteworthy feature for this catalytic system could be that the selective oxidation of alcohols can be achieved under solvent-free conditions.



Scheme 1. The structure of Ru(bbp)(pydic).

**Table 1**  
Oxidation of benzyl alcohol catalyzed by Ru(bbp)(pydic) with aqueous H<sub>2</sub>O<sub>2</sub><sup>a</sup>

Entry	Solvent	Conv. <sup>b</sup> (%)	Yield <sup>b</sup> (%)
1	Toluene	5	4
2	Ethyl acetate	12	10
3	CH <sub>3</sub> OH	66	63
4	CH <sub>3</sub> CN	78	74
5	Solvent free	97	96

<sup>a</sup> Reaction condition: benzyl alcohol (2 mmol), catalyst ( $2 \times 10^{-3}$  mmol), 30% H<sub>2</sub>O<sub>2</sub> (10 mmol), 60 °C, 60 min. solvent (2 mL).

<sup>b</sup> Determined by GC.

**Table 2**  
Optimization of reaction conditions under solvent free conditions<sup>a</sup>

Entry	Substrate: H <sub>2</sub> O <sub>2</sub> <sup>b</sup>	T (°C)	Conv. <sup>c</sup> (%)	Yield <sup>c</sup> (%)
1	1:5	40	37	35
2	1:5	80	>99	87
3	1:2	60	43	40
4	1:3	60	64	62
5	1:6	60	98	93
6 <sup>d</sup>	1:5	60	5	3
7 <sup>e</sup>	1:5	60	83	80
8 <sup>f</sup>	1:5	60	>99	92

<sup>a</sup> Reaction condition: benzyl alcohol (2 mmol), catalyst ( $2 \times 10^{-3}$  mmol), 60 min.

<sup>b</sup> Molar ratio.

<sup>c</sup> Determined by GC.

<sup>d</sup> In the absence of catalyst.

<sup>e</sup> Catalyst ( $2 \times 10^{-4}$  mmol).

<sup>f</sup> Catalyst ( $2 \times 10^{-2}$  mmol).

## Results and discussion

To explore the reactivity and selectivity of the Ru(bbp)(pydic) catalyst,<sup>10</sup> benzyl alcohol was used as a model substrate. Various solvents were examined in the presence of Ru(bbp)(pydic) catalyst and H<sub>2</sub>O<sub>2</sub> (Table 1, entries 1–8).<sup>11</sup> After much experimentation on optimizing solvent, it was found that the use of a less-polar solvent like toluene and ethyl acetate afforded benzaldehyde in low yields (entries 1 and 2). Higher yield of benzaldehyde was obtained using polar solvents like methanol and acetonitrile (entries 3 and 4). Gratifyingly, it was found under solvent free conditions, the catalyst gave excellent conversion to benzaldehyde with 96% yield (entry 5).

The effect of reaction parameters was examined by performing the reaction in solvent-free conditions, as listed in Table 2. Only 35% yield of benzaldehyde was obtained when the reaction was conducted at 40 °C, while the selectivity would become poor as further rising the temperature to 80 °C (entries 1 and 2). Therefore, the optimized temperature was proved to be 60 °C. The yield of benzaldehyde increased with increasing the molar ratio of H<sub>2</sub>O<sub>2</sub>/benzyl alcohol (entries 3 and 4). The large excess amount of H<sub>2</sub>O<sub>2</sub> could promote the over-oxidation of benzaldehyde, which resulted in the slight decreasing of selectivity toward benzaldehyde (entry 5). The reaction almost did not occur in the absence of catalyst (entry 6). Similarly, the yield of benzaldehyde increased with the rising amount of catalyst. And the excess amount of catalyst caused decrease of selectivity to benzaldehyde (entry 8).

To examine the scope of the alcohol reaction with H<sub>2</sub>O<sub>2</sub>–Ru(bbp)(pydic) system, we extended our studies to various primary alcohols. The results are summarized in Table 3.

It was found that most primary alcohols were smoothly converted to corresponding carbonyl compounds with high conversion rate and excellent selectivity. Compared with the electron-withdrawing groups at *para*-position for benzylic alcohols, the electron-donating groups seemed more favorable to the formation of carbonyl compounds (entries 1–4, Table 3). For basic substrates like 4-pyridinemethanol (entry 5, Table 3), additional amounts of catalyst are needed to improve reaction rates and to ensure good conversions. The catalytic system is also efficient for the oxidation of saturated primary aliphatic alcohols such as 2-phenylethanol and 1-octanol (entries 6 and 7, Table 3).

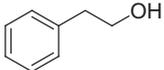
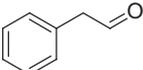
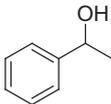
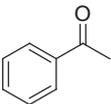
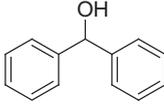
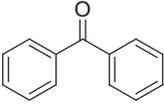
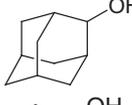
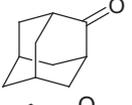
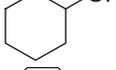
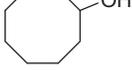
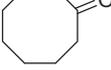
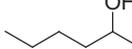
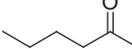
As shown in Table 3, the H<sub>2</sub>O<sub>2</sub>–Ru(bbp)(pydic) system was found to be selective, efficient for the oxidation of secondary

**Table 3**  
Oxidation of various alcohols with H<sub>2</sub>O<sub>2</sub> catalyzed by Ru(bbp)(pydic)<sup>a</sup>

Entry	Substrate	Product	Time (h)	Conv. <sup>b</sup> (%)	Yield <sup>b</sup> (%)
1			1	97	96
2			1	98	96
3			1	96	93
4			2	82	81
5 <sup>c</sup>			3	76	74

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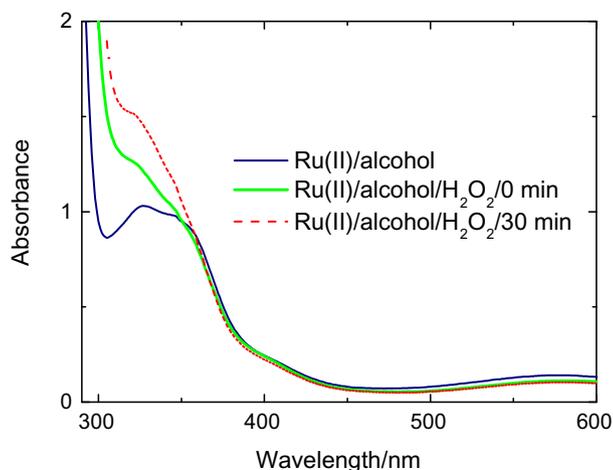
Table 3 (continued)

Entry	Substrate	Product	Time (h)	Conv. <sup>b</sup> (%)	Yield <sup>b</sup> (%)
6			1	95	92
7			1	98	94
8			1	92	92
9			3	82	82
10			3	78	76
11			1	94	93
12			1	89	87
13			1	97	95

<sup>a</sup> Reaction condition: substrate (2 mmol), catalyst ( $2 \times 10^{-3}$  mmol), 30%  $\text{H}_2\text{O}_2$  (10 mmol), 60 °C.

<sup>b</sup> Determined by GC.

<sup>c</sup> Catalyst ( $4 \times 10^{-3}$  mmol).



**Figure 1.** UV-vis spectra of Ru(bbp)(pydic) catalyst in the solution of benzyl alcohol oxidation in the presence of hydrogen peroxide, benzyl alcohol (2 mmol), catalyst ( $2 \times 10^{-3}$  mmol), 30%  $\text{H}_2\text{O}_2$  (10 mmol), 60 °C.

alcohols. The reaction works well with sterically hindered alcohols such as diphenylmethanol and 2-adamantanol (entries 9 and 10, Table 3). Many other secondary cyclic alcohols were efficiently oxidized in the catalytic system (entries 11 and 12, Table 3). The catalytic oxidation can also be successfully performed with aliphatic secondary alcohols (entry 13, Table 3).

Ru(bbp)(pydic) catalyst was monitored by in situ UV-vis spectroscopy during the reaction with  $\text{H}_2\text{O}_2$  (5 equiv) under solvent-free conditions. The in situ UV-vis spectroscopy was recorded on the AvaSpec-2048 $\times$ 14 with a fiber optic probe. As shown in Figure 1, the initial characteristic absorption peaks of Ru(bbp)(pydic) were

at 325 and 346 nm. Addition of  $\text{H}_2\text{O}_2$  resulted in the immediate conversion of the original spectrum containing the two characterized peaks into a new spectrum displaying absorption peak at 320 nm. This spectrum as well as the spectroscopic features supports the conclusion that the complex has been converted into a ruthenium(III) species.<sup>12</sup> As reported previously by Beller, ruthenium oxo complex was the active catalyst in the asymmetric epoxidation system.<sup>9d</sup> As to Ru(bbp)(pydic)-catalyzed alcohols oxidation, the reaction mechanism could also involve the participation of Ru-oxo species generated from the reaction between Ru(bbp)(pydic) and hydrogen peroxide. The formation of carbonyl compounds was attributed to the reaction of alcohols with Ru-oxo species, followed by the  $\beta$ -hydride elimination. Further mechanistic studies on the active species are under investigation.

In conclusion, the Ru(bbp)(pydic) catalyst system described herein is efficiently oxidizing alcohols in solvent free conditions when hydrogen peroxide is used as an oxidant. Both primary and secondary alcohols were oxidized into their corresponding carbonyl compounds in good yield. Further studies to improve the reaction rate through catalyst modifications and detailed mechanistic studies are ongoing.

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  - The synthesis routine for ruthenium complex catalyst was shown as following. First, the 2,6-bis(benzimidazolyl)pyridine was synthesized by the condensation reaction of 1,2-phenylenediamines and pyridine-2,6-dicarboxylic acid in the presence of polyphosphoric acid at 180 °C in 50% yield. Then, to a solution of ligand 2,6-bis(benzimidazolyl)pyridine (149 mg, 0.48 mmol) and [Ru(*p*-cymene)Cl<sub>2</sub>]<sub>2</sub> (150 mg, 0.24 mmol) in EtOH (8 mL), disodium pyridine-2,6-dicarboxylate (0.48 mmol) in EtOH/H<sub>2</sub>O (2:1, 10 mL) was added under argon atmosphere. The whole reaction mixture was heated at 80 °C for 1 h. It turns deep purple after stirring for 15 min at 80 °C. The dark violet precipitate was collected by filtration to give product (194 mg, 0.34 mmol) in 70% yield. Ru(bbp)(pydic): Calcd for C<sub>26</sub>H<sub>16</sub>N<sub>6</sub>O<sub>4</sub>Ru: C, 52.44; H, 3.05; N, 14.11. Found: C, 52.31; H, 3.02; N, 14.35%; IR (KBr)/cm<sup>-1</sup>: 3400, 3060, 1620, 1450, 1399, 1220, 1160, 1020, 913, 742, 688. <sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>): δ 14.04 (s, 2H), 11.00 (s, 3H), 9.96 (s, 3H), 7.10–7.37 (m, 4H), 7.43–8.06 (m, 4H). EI-MS: *m/z* 577.
  - The catalytic oxidation of alcohol was carried out in a magnetically stirred glass reaction tube fitted with a reflux condenser. A typical procedure was as follows using benzyl alcohol as model substrate: benzyl alcohol (2 mmol) and Ru(bbp)(pydic) (2 × 10<sup>-3</sup> mmol, 0.1 mol % based substrate) were added into a reaction tube. The reactor containing this mixture was heated to 60 °C in an oil bath under vigorous stirring, and then 30% H<sub>2</sub>O<sub>2</sub> (10 mmol) was slowly dropped in. The resulting system was stirred at 60 °C for 60 min. At the end of reaction, the resulting products and unreacted substrate were extracted by dichloromethane three times. The extracted liquid mixture was analyzed by GC and GC-MS. GC analyses were performed on a Shimadzu GC-2010 plus chromatography equipped with Rtx-5 capillary column (30 m × 0.25 mm × 0.25 μm). GC-MS analyses were recorded on a Shimadzu GCMS-QP2010 equipped with Rxi-5 ms capillary column (30 m × 0.25 mm × 0.25 μm).
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