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# Aerobic oxidation of alcohols to aldehydes and ketones using ruthenium(III)/Et<sub>3</sub>N catalyst

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A simple, efficient method for oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones has been developed. Using RuCl<sub>3</sub>/Et<sub>3</sub>N as catalyst, the oxidation of benzyl alcohol with oxygen could be achieved with  $332 h^{-1}$  turnover frequency in the absence of solvent. The influence of versatile N-containing additives on the catalytic efficiency has been discussed. The presence of minor water would substantially promote the catalytic efficiency, and its role in catalysis has been investigated in detail. The insensitive Hammett correlations of the substituted benzyl alcohols, the normal substrate isotope effect ( $k_H/k_D = 3.5$  at 335 K), and the linear relationship between O<sub>2</sub> pressure and turnover frequency imply that the reoxidation of the Ru(III) hydride intermediate to the active species shares the rate-determining step with the hydride transfer in the catalytic cycle. Copyright © 2011 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: alcohol oxidation; ruthenium(III) chloride; triethylamine; mechanism

# Introduction

Selective oxidation of alcohols to their corresponding aldehydes and ketones is a significant process in organic synthesis and industrial manufacture. <sup>[1–5]</sup> These oxidations usually proceed by using stoichiometric oxidants like hypochlorite, dichromate, permanganate and chromate, which apparently cause serious heavy metal pollution and toxic by-products. <sup>[6–10]</sup> Developing clean processes for alcohol oxidations has been attracting attention for a long while in academic chemistry. For a typical alcohol oxidation, oxygen is the greenest oxidant, and water would be the sole byproduct if there is no further oxidation of the corresponding carbonyl compounds occurring in the oxidation process. However, such a green technology still remains a great challenge.

A number of catalytic methods using oxygen have been examined for selective oxidation of alcohols. <sup>[10–17]</sup> These methods include using simple redox transition metal salts and their complexes by homogeneous oxidation, supported transition metal ions by heterogeneous oxidation, or transition metal free oxidation using an organic catalyst like (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and/or their combinations with bromide or sodium nitrate. An early example of alcohol oxidation is Uemura's Pd(OAc)<sub>2</sub>/pyridine/MS3A system, in which various aromatic, alkenic and aliphatic alcohols could be successfully transformed to the corresponding carbonyl compounds. [18-20] Recent promising examples include Sheldon's aqueous Pd/PhenS system (turnover number 200-400), <sup>[21]</sup> Mizuno's heterogeneous Ru/Al<sub>2</sub>O<sub>3</sub> system (turnover number close to 1000 and turnover frequency up to 340 h<sup>-1</sup>), <sup>[22]</sup> and Hu's metal free TEMPO/HBr/NaNO<sub>2</sub> system (turnover number up to 16 000). <sup>[23,24]</sup> However, the challenges still remain for industrial-scale oxidation of alcohols. The substantial barriers inhibiting their industrialization include use of expensive ligands, toxic and corrosive co-catalysts like bromide and NaNO<sub>2</sub>, large amounts of solvent and additives like Na<sub>2</sub>CO<sub>3</sub>, NaOAc and molecular sieves, and low catalytic activity in most cases (1-5% catalyst loading).

In mechanistic studies of metal ion-mediated alcohol oxidations, <sup>[22,25–31]</sup> three key steps generally occur in the total catalytic cycle. They are (i) formation of the metal alcoholate intermediate by ligand exchange, (ii) hydride transfer from the C-H bond to the metal ion to generate the M<sup>n+</sup>-H intermediate and carbonyl product, and finally, (iii) regeneration of the active metal species through oxidation of the M<sup>n+</sup>-H intermediate. The linear Hammett plot of substitute effect with a negative slope generally supports that the hydride transferring to form the carbocation type intermediate serves as the rate-determining step in the catalytic cycle. [11,29,32,33] Formation of the M<sup>n+</sup>-H intermediate through hydride transfer has been directly proposed in Pd, Ru, and Au-catalyzed alcohol oxidations, and the oxygen insertion of Pd<sup>2+</sup>-H to generate Pd<sup>2+</sup>-OOH intermediate, and then regenerate the active  $Pd^{2+}$  species with release of  $H_2O_2$ , has also been proposed by Uemura.<sup>[20]</sup> The rate-determining step may also be tunable in these three steps depending on the reaction conditions.<sup>[34]</sup> Although much effort has been made to widely explore versatile catalysts and to understand their mechanisms, the detailed roles of each composition in catalysts are not fully understood in most cases. In this work, we report a simple catalyst composite of simple ruthenium(III) salt with triethylamine for alcohol oxidations. In the absence of solvent, the oxidation could proceed with a turnover frequency of  $332 h^{-1}$ . In particular, the roles of the N-containing bases, promotion of oxidation by minor water, and related mechanisms have been widely discussed, which provides a full account of the factors which control the oxidation in this RuCl<sub>3</sub>/Et<sub>3</sub>N system.

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# **Reagent Sources**

The *p*-substituted benzyl alcohols and (±)-1-phenylethanol were purchased from Alfa Aesar; benzyl- $\alpha$ , $\alpha$ -d<sub>2</sub> alcohol (99.5 atom% D) came from C/D/N lsotopes Inc., and other reagents came from a local company.

# General Procedure for Oxidation in the Absence of Solvent

To a 15 ml glass-lined reaction tube, RuCl<sub>3</sub>.*n*H<sub>2</sub>O catalyst (0.1 mmol, 0.0207 g), Et<sub>3</sub>N ligand (0.8 mmol, 0.11 ml), and benzyl alcohol (48 mmol, 5 ml) were added and stirred at room temperature until the catalyst was completely dissolved. The reaction tube was placed in a stainless reactor, and the resulting reactor was charged with O<sub>2</sub> (20 atm), heated at 371 K in an oil bath with stirring (1000 rpm) for 20 h. The conversion and selectivity were determined by gas chromatography (GC) using ethyl benzoate as the internal standard.

# **General Procedure for Versatile Alcohol Oxidation**

To a 15 ml glass-lined reaction tube, RuCl<sub>3</sub>.*n*H<sub>2</sub>O catalyst (0.1 mmol, 0.0207 g), Et<sub>3</sub>N ligand (0.8 mmol, 0.11 ml) and *t*-butyl alcohol (5 ml) were added and stirred at room temperature until the catalyst was completely dissolved. Then alcohol substrate (10 mmol) was added and the reaction tube was placed in a stainless reactor. The resulting reactor was charged with O<sub>2</sub> (20 atm), heated at 371 K in an oil bath with stirring (1000 rpm). The products were analyzed by GC or high-performance liquid chromatography (HPLC) with the internal standard method.

# General Procedure for Oxidation through Pretreatment with Silver Salt

To a 15 ml glass-lined reaction tube, RuCl<sub>3</sub>, $nH_2O$  catalyst (0.05 mmol, 0.0103 g), Et<sub>3</sub>N ligand (0.4 mmol, 0.056 ml), H<sub>2</sub>O (2.8 mmol, 0.05 ml), silver salt (0.15 mmol), and benzyl alcohol (48 mmol, 5 ml) were added and stirred at room temperature until the catalyst was completely dissolved. After removal of silver chloride through filtration, the filtrate in the reaction tube was placed in a stainless reactor. The resulting reactor was charged with O<sub>2</sub> (20 atm), heated at 358 K in an oil bath with stirring (1000 rpm). The products were analyzed by GC using ethyl benzoate as the internal standard.

# General Procedure for the Relationship between O<sub>2</sub> Pressure and Turnover Frequency

To a 15 ml glass-lined reaction tube,  $RuCl_3.nH_2O$  catalyst (0.1 mmol, 0.0207 g), Et<sub>3</sub>N ligand (0.8 mmol, 0.11 ml) and *t*-butyl alcohol (5 ml) were added and stirred at room temperature until the catalyst was completely dissolved; then, benzyl alcohol (9.6 mmol, 1 ml) was added. The reaction tube was placed in a reactor and charged with the required oxygen pressure, and heated at 360 K in an oil bath with stirring (1000 rpm). The products were analyzed by GC using ethyl benzoate as the internal standard.

# **General Procedure for Kinetic Reaction for Hammett Plot**

In a typical oxidation,  $RuCl_{3.n}H_2O$  catalyst (0.02 mmol, 0.0041 g),  $Et_3N$  ligand (0.16 mmol, 0.022 ml) and *t*-butyl alcohol (1 ml) were added to a 15 ml glass-lined reaction tube, and the resulting

reaction mixture was stirred at room temperature until the catalyst was completely dissolved. Then, *p*-substituted benzyl alcohol (2 mmol) was added, and the glass tube was placed in a 50 ml stainless reactor. The reactor was charged with  $O_2$  (20 atm) and heated at 316 K in an oil bath with stirring (1000 rpm). The products were analyzed by GC using ethyl benzoate as the internal standard.

# **Results and Discussion**

# Effect of Additives on Alcohol Oxidation

Using ruthenium(III) trichloride (RuCl<sub>3</sub>.*n*H<sub>2</sub>O) as catalyst, oxidation of benzyl alcohol was carried out in the absence of solvent with oxygen as the terminal oxidant. In order to investigate the modulation of the ligand on the catalytic activity of the Ru(III) cation, a list of simple N-containing base additives were examined and the results are summarized in Table 1. One may see that trimethylamine (Me<sub>3</sub>N) and its analogue, triethylamine (Et<sub>3</sub>N), afford a similar best efficiency for benzyl alcohol oxidation, that is, above 98% yield of benzaldehyde (entries 3 and 4), while other N-containing additives provide relatively lower efficiency. Imidazole provides 14% conversion with 3% yield, pyridine gives 10% conversion with 3% yield, pyrrole affords 31% conversion with 12% yield, and the conversion and yield are 28% and 13%, respectively, for piperidine.

Since trimethyl and triethylamine additives demonstrate a very similar high activity, the additional experiments were designed under gentler reaction conditions to obtain a relatively low conversion for distinguishing their activity difference. As shown in Table 2, when using 0.05 mmol RuCl<sub>3</sub>.*n*H<sub>2</sub>O catalyst with a catalyst/additive ratio of 1:8 at 371 K, triethylamine demonstrates a better activity than trimethylamine, that is, 65% vs. 50% for conversion, and 63% vs. 47% for selectivity. Because the commercially available trimethylamine contains a large content of water

Table 1. The effect of ligand on alcohol oxidation						
Entry	Ligand	р <i>К</i> а	Conversion (%)	Yield (%)		
1	Pyridine	5.17	10	3		
2	Imidazole	6.99	14	3		
3	Me <sub>3</sub> N (33% aq)	9.8	99	99		
4	Et <sub>3</sub> N	10.7	98	98		
5	Piperidine	11.24	28	13		
6	Pyrrolidine	11.3	31	12		

Conditions: benzyl alcohol (48 mmol, 5 ml),  $RuCl_{3.}nH_{2}O$  (0.1 mmol, 0.0207 g), catalyst: ligand =1:8, oil bath 371 K,  $O_2$  20 atm, 20 h.

Table 2. Comparison of trimethylamine and triethylamine <sup>a</sup>				
Entry	Ligand	Conversion (%)	Selectivity (%)	
1	Me <sub>3</sub> N (aq)	50	47	
2 <sup>b</sup>	Et₃N	65	63	
3 <sup>c</sup>	Et <sub>3</sub> N (aq)	96	93	

<sup>a</sup>Conditions: benzyl alcohol (48 mmol, 5 ml), RuCl<sub>3</sub>.nH<sub>2</sub>O (0.05 mmol, 0.0103 g), catalyst: ligand =1:8, oil bath 371 K, O<sub>2</sub> 20 atm, 14 h. <sup>b</sup>No additional water added.

 $^{\rm c}0.05$  ml (2.8 mmol) water added (as in trimethylamine 30% aqueous solution).

(33% aqueous solution), the extra 0.05 ml of water was added to the reaction mixture for triethylamine to mimic the reaction conditions of trimethylamine, and it generates even better results: 96% conversion with 93% selectivity. This leads to the conclusion that triethylamine demonstrates much better activity than does trimethylamine.

Generally, there could be at least two roles that the N-containing base additives may play in the alcohol oxidations. <sup>[35]</sup> One is to function as a ligand to modulate the redox properties of the metal ion to facilitate alcohol oxidation; the other is to serve as a base to assist the formation of the metal alcoholate. In the case of palladium catalyst, the third role is to inhibit the formation of palladium precipitate through coordination with the reduced palladium(0). The  $pK_a$  values of the investigated amines in the present study are listed in Table 1, and the correlation of  $pK_a$  with the catalytic activity of the ruthenium(III) catalyst is shown in Fig. 1.

In Fig. 1 one may see that modest bases, including trimethylamine  $(pK_a = 9.8)$  and triethylamine  $(pK_a = 10.7)$  provide the highest activity in catalytic oxidation of alcohol, whereas both weak bases like pyridine ( $pK_a = 5.17$ ) and strong bases like pyrrolidine ( $pK_a = 11.3$ ) afford lower efficiency. To examine whether the amine plays a bifunctional role, including serving as base to assist the formation of the metal alcoholate and coordinating with the Ru(III) ion as ligand to modulate its redox properties, sodium bicarbonate (NaHCO<sub>3</sub>), which is a poor ligand ( $pK_a$  value = 10.33), located between trimethylamine ( $pK_a = 9.8$ ) and triethylamine ( $pK_a = 10.7$ ), was added in place of triethylamine for alcohol oxidation, and it was found that both conversion (27%) and selectivity (74%) were much lower than those of trimethylamine and triethylamine, suggesting that the coordination of amine with the Ru(III) ion is critical for efficient catalytic oxidation. In the mass spectrum of RuCl<sub>3</sub>/Et<sub>3</sub>N in the catalytic solution, there is only one viable mass spectral peak, at m/z = 239.1 (see Fig. S7 in supporting information), which can be related to ruthenium cation, and it could be assignable to a [Ru<sup>III</sup>(H)(Et<sub>3</sub>N)(Cl)]<sup>+</sup> intermediate (the existence of only one chloride anion in the sphere of the Ru(III) ion is supported by its characteristic isotope peak). Apparently, there is also only one triethylamine ligated to the Ru(III) cation. The influence of the amount of triethylamine on catalytic activity is shown in Fig. 2. Without triethylamine, using RuCl<sub>3</sub> alone provides only 7% conversion under the described reaction conditions. Adding one equivalent of triethylamine could improve the yield sharply to 30%, and adding more triethylamine may further improve the catalytic efficiency. For example, with the ratio of RuCl<sub>3</sub>/Et<sub>3</sub>N at 1:8, the



**Figure 1.** Correlation of  $pK_a$  values of amine with catalytic efficiency. Conditions: benzyl alcohol (48 mmol, 5 ml), RuCl<sub>3</sub>.*n*H<sub>2</sub>O (0.1 mmol, 0.0207 g), catalyst:ligand =1:8, oil bath 371 K, O<sub>2</sub> 20 atm, 20 h.



**Figure 2.** Influence of RuCl<sub>3</sub>/Et<sub>3</sub>N ratio on reactivity. Conditions: benzyl alcohol (48 mmol, 5 ml), RuCl<sub>3</sub>.nH<sub>2</sub>O (0.05 mmol, 0.0103 g), catalyst:ligand =1:8, H<sub>2</sub>O (2.8 mmol, 0.05 ml), oil bath 358 K, O<sub>2</sub> 20 atm, 4 h.

yield could be improved up to 52%. Taken together, the results suggest that triethylamine may play two roles in oxidation: one equivalent of triethylamine may be essential for coordination with the Ru(III) cation to modulate its redox properties as demonstrated by the mass spectrum, the remainder serving as base to help the formation of the Ru(III) alcoholate.

## Effect of Water on Alcohol Oxidation

As stated above, the presence of little water could surprisingly improve the catalytic activity sharply (Table 2, entry 3). Although alcohol oxidation has been extensively investigated in aqueous solution or organic solvent/water solvent mixtures, <sup>[36–40]</sup> discussion of the acceleration of alcohol oxidation by water and its role in reaction is still very limited. Recently, Xu even reported a rare water-promoted alcohol oxidation when using a VOSO<sub>4</sub>/NaNO<sub>2</sub> catalyst system, and the role of water was interpreted to play a key role in the redox cycle between NO and O<sub>2</sub>, and also to assist the formation of HNO<sub>2</sub> at the beginning. <sup>[41]</sup> Apparently, such roles may not occur in the RuCl<sub>3</sub>/Et<sub>3</sub>N system reported here; thus the alternative roles of water need to be elucidated in the present study.

In the catalytic cycle of alcohol oxidation, the first step is the coordination of alcohol to the active metal cation center through ligand exchange to generate the metal alcoholate intermediate. [29,34,42] In the case of using RuCl<sub>3</sub>.nH<sub>2</sub>O as the catalyst, dissociation of chloride anion, a relatively strong donor, may accelerate the formation of the Ru(III) alcoholate intermediate and meanwhile modulate the redox properties of the Ru(III) cation to facilitate the alcohol oxidation. Importantly, as stated earlier, the mass spectrum of the RuCl<sub>3</sub>/Et<sub>3</sub>N in the catalytic solution revealed that only one chloride anion is attached to the Ru(III) cation. Reasonably, one may expect that adding minor water to the reaction mixture could help the dissociation of chloride anion from the coordination sphere of the Ru(III) cation, thus accelerating the metal alcoholate formation and improving the catalytic efficiency. The conductivity measurements of the catalytic solution provide direct evidence for the water-promoted chloride dissociation. The conductivity of pure benzyl alcohol is only 0.036 µS/cm (in the literature, it is 0.24 mS/cm with tetra-n-butylammonium perchlorate as supporting electrolyte). <sup>[43]</sup> The conductivity is 0.461  $\mu$ S/cm in benzyl alcohol containing 8 mM Et<sub>3</sub>N and 0.27 M water, and 1.60 µS/cm with 1 mM RuCl<sub>3</sub>. It increases to 4.44 µS/cm with 1 M RuCl<sub>3</sub> and 8 M Et<sub>3</sub>N (note: Et<sub>3</sub>N reagent contains trace water ( $\leq$ 0.2%). In the case of benzyl alcohol containing 1 mM RuCl<sub>3</sub>, 8 mM Et<sub>3</sub>N plus 0.27 M water – a similar condition of catalytic oxidation – the conductivity increases to 5.39 µS/cm. These results apparently support the addition of minor water in promoting the dissociation of chloride anion from RuCl<sub>3</sub>.

To further examine whether the dissociation of the chloride anion from the Ru(III) cation is helpful for efficient catalytic oxidation, silver salt was tested to forcefully precipitate the chloride anion from RuCl<sub>3</sub> in the reaction mixture prior to the oxidation reaction. After removal of silver chloride through filtration, the catalytic efficiency can be apparently improved. As shown in Table 3, without pretreatment with silver salt it takes 10 h to achieve 76% conversion with 63% selectivity (entry 1), whereas it can achieve 92% conversion with 99% selectivity in 10 h through pretreatment with silver salt. Apparently, removal of chloride may improve not only the catalytic efficiency, but also the selectivity (entry 2). Incidentally, catalytic oxidation of alcohol by silver(I) cation itself has been eliminated through using silver(I) salt alone as catalyst (entry 3).

Other evidence to suggest the acceleration of chloride dissociation through adding water comes from kinetic analysis of alcohol oxidation (Fig. 3). Without additional water added in the reaction mixture, an obvious induction period occurs in this RuCl<sub>3</sub>-catalyzed alcohol oxidation. During the induction period, water is accumulated gradually as the reaction proceeds, after which the oxidation rate speeds up. In contrast, no induction period was observed in the case of adding additional water to the reaction mixture, indicating the accelerated active intermediate formation by adding minor water. Therefore, the combined evidence strongly suggests that the role of water in the reaction is to promote the dissociation of chloride anion from the coordination sphere of the Ru(III) cation to facilitate metal alcoholate formation, and thus modulate the redox properties of the Ru(III) cation. Although oxidation can be accelerated by adding minor water, replacing the normal water with D<sub>2</sub>O does not reveal any solvent isotope effect, which indicates that water is not involved in the rate-determining step of the catalytic cycle, but may just participate in the dissociation of chloride initially. Under the optimized conditions, The RuCl<sub>3</sub>/Et<sub>3</sub>N system can achieve a turnover frequency of  $332 \, h^{-1}$  in the absence of solvent (equation (1)). To the best of our knowledge, this TOF value shows one of the highest efficiencies in metal ionmediated alcohol oxidations.





**Figure 3.** Kinetic process of alcohol oxidation with RuCl<sub>3</sub>.nH<sub>2</sub>O catalyst. Conditions: benzyl alcohol (48 mmol, 5 ml), RuCl<sub>3</sub>.nH<sub>2</sub>O (0.05 mmol, 0.0103 g), catalyst:ligand (Et<sub>3</sub>N) = 1:8, oil bath 358 K, O<sub>2</sub> 20 atm.

## Scope of RuCl<sub>3</sub>/Et<sub>3</sub>N-Mediated Alcohol Oxidation

The oxidations of versatile alcohols were investigated and the results are summarized in Table 4. Since most substituted benzyl alcohols are solid at room temperature, t-butanol was applied as the solvent in this part. As shown in Table 4, benzyl alcohol can be efficiently converted into benzyl aldehyde with or without solvent. Under the current conditions, while the derivatives of benzyl alcohol with electron-donating substituents could be smoothly oxidized to the corresponding aldehydes with both conversion and selectivity above 90%, the electron-withdrawing substituted benzyl alcohols could also be transformed to the corresponding aldehydes, but their selectivity is relatively low. In the oxidation of *p*-nitrobenzyl alcohol, the selectivity of aldehyde is only 42%, and o-hydroxobenzyl alcohol even provides selectivity as low as 35%. In other cases, oxidation of 1-phenylethanol needs 35 h to achieve 100% conversion with 87% selectivity, cinnamyl alcohol provides 100% conversion with 88% selectivity, and allyl alcohol gives only 72% conversion with 12% selectivity.

Interestingly, it was found that the catalytic activity of the RuCl<sub>3</sub>/Et<sub>3</sub>N system is insensitive to the electronic effect of the *p*-substituted benzyl alcohols. For example, under the identical conditions, oxidation could be accomplished in 4 h for all of *p*-CH<sub>3</sub>O-, CH<sub>3</sub>-, H-, Cl-, and CF<sub>3</sub>-substituted benzyl alcohols except *p*-NO<sub>2</sub>. Such a phenomenon was further supported by the kinetic Hammett plot for the oxidation of *p*-substituted benzyl alcohols. As shown in Fig. 4 (kinetic data see also Fig. S1-S6 and Table S1 in supporting information), neither the electron-donating substituents nor the electron-withdrawing substituents demonstrated any obvious influence on the reaction rate, and the Hammett plots of both substituent constant  $\sigma$  and  $\sigma^+$  provide an identical fit, suggesting that dehydrogenation may not be any more rate

Table 3. The effect of silver source <sup>a</sup>					
Entry	Additive	Amount (mmol)	Conversion (%)	Selectivity (%)	
1	_	_	76	63	
2	AgSbF <sub>6</sub>	0.15	92	99	
3 <sup>b</sup>	AgOAc	0.05	<1	100	

<sup>a</sup>Conditions: benzyl alcohol (48 mmol, 5 ml), RuCl<sub>3</sub>.*n*H<sub>2</sub>O (0.05 mmol, 0.0103 g), catalyst:ligand (Et<sub>3</sub>N) = 1:8, H<sub>2</sub>O (2.8 mmol, 0.05 ml), additive, oil bath 358 K, O<sub>2</sub> 20 atm, 10 h. <sup>b</sup>No RuCl<sub>3</sub>.*n*H<sub>2</sub>O added.

Table 4.         Substrate scope of RuCl <sub>3</sub> /Et <sub>3</sub> N-catalyzed alcohol oxidation <sup>a</sup>					
Entry	Substrate	Time (h)	Conversion(%)	Selectivity (%)	
1	Benzyl alcohol	0.7	97	99	
2 <sup>b</sup>	Benzyl alcohol	1	85	98	
3 <sup>c</sup>	Benzyl alcohol	4	96	99	
4 <sup>c</sup>	4-Methoxybenzyl alcohol	4	99	95	
5 <sup>c</sup>	4-Methylbenzyl alcohol	4	95	95	
6 <sup>c</sup>	4-Chlorobenzyl alcohol	3.5	99	75	
7 <sup>c</sup>	4-Trifluoromethylbenzyl alcohol	4	97	83	
8 <sup>d</sup>	4-Nitrobenzyl alcohol	12	99	41	
9 <sup>c</sup>	3,4-Dimethoxybenzyl alcohol	4	99	90	
10 <sup>c</sup>	4-Hydroxybenzyl alcohol	4	47	70	
11	Cinnamyl alcohol	5	100	88	
12	1-Phenylethanol	35	99	87	
13	Allyl alcohol	4	72	12	

<sup>a</sup>Conditions: alcohol (1 ml), RuCl<sub>3</sub>.nH<sub>2</sub>O (0.1 mmol, 0.0207 g), catalyst:ligand (Et<sub>3</sub>N) = 1:8, oil bath 371 K, O<sub>2</sub> 20 atm.

<sup>b</sup>Alcohol (10 mmol, 1.08 g), RuCl<sub>3-</sub>*n*H<sub>2</sub>O (0.025 mmol, 0.0051 g), catalyst:ligand (Et<sub>3</sub>N) = 1:8, H<sub>2</sub>O (1.4 mmol, 0.025 ml), oil bath 371 K, O<sub>2</sub> 20 atm.

<sup>c</sup>Alcohol (10 mmol), *t*-BuOH (5 ml).

<sup>d</sup>Alcohol (5 mmol), *t*-BuOH (5 ml).

limiting. These results are very rare in oxidation proceeding by a hydride transfer process. <sup>[34,42]</sup> Generally, a linear correlation was obtained with a negative  $\rho$  value, which is consistent with hydride transfer serving as the rate-determining step. <sup>[11,29,32,33]</sup> The insensitive substituent effect demonstrated here has implied that, in this RuCl<sub>3</sub>/Et<sub>3</sub>N-catalyzed alcohol oxidation, the rate-determining step possibly has shifted from the common hydride transfer to other steps such as formation of the Ru(III) alcoholate or reoxidation of the Ru(III) hydride intermediate.

Because the C=O group in benzaldehyde has a strong stretching frequency at ~1700 cm<sup>-1</sup>, it provides a chance to monitor benzaldehyde formation by IR technology during benzyl alcohol oxidation. It was found that, under atmospheric condition at room temperature, formation of benzaldehyde occurs immediately but no further formation occurs after 10 min (Fig. 5). GC analysis shows that benzyl alcohol substrate still remains dominant with only trace aldehyde formation, suggesting that formation of the Ru(III) alcoholate and further hydride transfer to form aldehyde may not be rate determining, but the reoxidation of the Ru(III) hydride intermediate would be slow. Consequently, oxygen pressure may have a significant influence on catalytic efficiency. As shown in Fig. 6, turnover frequency linearly increases with the increase in oxygen pressure, suggesting that the reoxidation of Ru(III) hydride by oxygen most probably serves as the rate-determining step in this RuCl<sub>3</sub>/Et<sub>3</sub>N system. However, the kinetic isotope effect provides the opposite information. The  $k_{\rm H}/k_{\rm D}$  value for oxidation of normal benzyl alcohol and benzyl alcohol- $\alpha$ - $\alpha$ - $d_2$  in a single run is 3.5 at 335 K, which is very similar to the findings for Ru/Al<sub>2</sub>O<sub>3</sub> ( $k_{\rm H}/k_{\rm D} = 4.2$  at 373 K), Ru<sup>IV</sup>(trpy)(bpy)O<sup>2+</sup> ( $k_{\rm H}/k_{\rm D} = 2.7$ at 298 K), but smaller than obtained in other ruthenium catalytic systems. [11,29,32,44–47] Importantly, the  $k_{\rm H}/k_{\rm D}$  value of 3.5 still supports that the hydride transfer step may be relatively slow in the catalytic cycle, even though the Hammett plot suggests the opposite conclusion. A plausible explanation is that the rates of hydride transfer and reoxidation of the Ru(III) hydride intermediate becomes comparable in this RuCl<sub>3</sub>/Et<sub>3</sub>N-catalyzed alcohol oxidation. Increasing the oxygen pressure would accelerate the reoxidation of the Ru(III) hydride intermediate, thus improving catalytic efficiency. A plausible mechanism has been proposed for this RuCl<sub>3</sub>/Et<sub>3</sub>N-catalyzed alcohol oxidation in which the reoxidation of the H-Ru(III) moiety shares the rate-determining step with the hydride transfer (Scheme 1).



**Figure 4.** Hammett plot for the oxidation of *p*-substituted benzyl alcohols catalyzed by RuCl<sub>3</sub>/Et<sub>3</sub>N.



 $\ensuremath{\textit{Figure 5.}}$  Time scan of the benzaldehyde formation monitored by IR instrument.



Figure 6. Relationship between  ${\rm O}_2$  pressure and turnover frequency (TOF).



 $\mbox{Scheme 1.}\ A$  plausible mechanism for the  $\mbox{RuCl}_3/\mbox{Et}_3\mbox{N-mediated}$  alcohol oxidation.

As stated early, the only viable Ru(III) species is the  $(Et_3N)Ru^{III}(CI)$ having one Et<sub>3</sub>N molecule and one chloride anion ligated to the Ru(III) cation under the reaction conditions (The net charge of the (Et<sub>3</sub>N)Ru<sup>III</sup>(CI) species has been ignored for convenience); thus the (Et<sub>3</sub>N)Ru<sup>III</sup>(CI) species has been proposed as one intermediate in the catalytic cycle. Through ligation of the alcohol substrate to the Ru(III) cation, the generated Ru(III) alcoholate intermediate further proceeds hydride transfer from the C-H bond of the alcoholate to the Ru(III) cation to generate aldehyde product with the Ru<sup>III</sup>(H)(Et<sub>3</sub>N)(CI) intermediate which could be oxidized by oxygen to regenerate the active (Et<sub>3</sub>N)Ru<sup>III</sup>(CI) species. In the literature, there exist at least two proposed mechanisms for the ruthenium-mediated alcohol oxidations. One is the H-Ru(III) intermediate involved oxidation, in which regeneration of the active Ru(III) species proceeds by O2 insertion of the H-Ru(III) bond followed by HO2 release;  $^{[29,30,32,34]}$  the other is the H-Ru(II) species involved dehydrogenation mechanism in which the hydrogen transfer may occur. [48-51] In our complementary experiments, the attempts to trap the H-Ru(II) intermediate by acetone to form isopropanol under pressured nitrogen or oxygen failed. Since there are no detectable Ru(II) species by mass spectrometry in the catalytic solution and no hydrogen transfer reaction observed, but a Ru(III) species, that is,  $[Ru^{III}(H)(Et_3N)(CI)]^+$  at m/z = 239.1, was detected by mass spectrometry in the catalytic solution, the H-Ru(III) intermediate involved mechanism has been proposed in this RuCl<sub>3</sub>/Et<sub>3</sub>N-mediated alcohol oxidation.

# Conclusion

A simple RuCl<sub>3</sub>/Et<sub>3</sub>N catalytic system has been reported for oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones. The N-containing additives may play two roles in reaction: one is to serve as ligand to modulate the redox properties of the Ru(III) cation; the other is to assist in the formation of the metal alcoholate in the catalytic cycle. Adding minor water to the catalytic system would substantially improve the catalytic efficiency, and the role of water has been proposed to accelerate the dissociation of the chloride anion from the coordination sphere of the Ru(III) cation, and thus to modulate the redox properties of the Ru(III) cation to facilitate oxidation. Under optimal conditions, a turnover frequency of benzyl alcohol oxidation of  $332 h^{-1}$  can be achieved. The insensitive substituent effect in the Hammett plot with a normal  $k_{\rm H}/k_{\rm D}$  value of 3.5, and the significant influence of oxygen pressure on catalytic efficiency, indicate that, in the catalytic cycle, the rates of hydride transfer and reoxidation of the Ru(III) hydride intermediate are possibly comparable, and may share the rate-determining step. The current study not only provides a rare example in which the roles of each catalytic composition have been clearly elucidated, but the information obtained here may also provide an approach for completely understanding the roles of each part in other catalysts, and these advances may help in the rational design of alcohol oxidation catalysts.

## SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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