The catalytic activity of a cyclometalated ruthenium(III) complex for aerobic oxidative dehydrogenation of benzylamines

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ABSTRACT

The ruthenium(III) complex bearing benzo[*h*]quinoline as a cyclometalated ligand was synthesized and characterized by ESI-MS, elemental analysis, cyclic voltammetry and crystallography. The complex serves as an efficient catalyst for the aerobic oxidative dehydrogenation of benzylamines to the corresponding benzonitriles under mild conditions.

Keywords: Cyclometalated compounds; Ruthenium(III); Dehydrogenation; Amine.

1. Introduction

Development of catalytic systems using molecular oxygen as an oxidant has attracted much attention from the consideration of green chemistry [1]. In particular, the aerobic oxidation of amines is a useful method to obtain nitriles which have a great utility in the synthesis of pharmaceutical compounds and industrial materials [2]. We previously reported that the aerobic oxidative dehydrogenation of imidazolines and benzylamines is catalyzed by a cyclometalated ruthenium complex, [RuCl(ppy)(tpy)][PF_6] (**1a**) (ppy = 2-phenylpyridine; tpy = 2,2':6',2''-terpyridine) [3]. In these reactions, the essential steps are the coordination of substrate to the ruthenium center and the aerobic oxidation of the ruthenium center. Therefore, the key feature of the catalyst **1a** is to have a Cl ligand and a cyclometalated ligand. Since the Cl ligand easily dissociates, a substrate can coordinate to the vacant position. The σ-donor character of the cyclometalated ppy ligand lowers the redox potential, which enables the aerobic oxidation of the ruthenium center. This concept is considered to differ from that of the common ruthenium-catalyzed dehydrogenation reaction which includes the formation of ruthenium hydride species [2a-g,4]. To investigate this aerobic dehydrogenation system, we focused on a ruthenium(III) complex bearing benzo[*h*]quinoline (bhq) as a cyclometalated ligand, [RuCl(bhq)(tpy)][PF_6] (**1b**), which can be considered to satisfy the above molecular design. Bhq is known to form readily cyclometalated transition metal complexes due to the stability of the five-membered heterometallacycle [5]. The Ru(III) complex **1b** has not been isolated, although the preparation of the corresponding Ru(II) complex, [RuCl(bhq)(tpy)], was reported [6]. We

report herein preparation and characterization of **1b**. The catalytic activity of **1b** for the aerobic oxidative dehydrogenation of benzylamines is also described.

2. Results and discussion

*2.1. Synthesis of Ru(III) complex **1b***

The cyclometalated ruthenium(III) complex, [RuCl(bhq)(tpy)][PF_6] (**1b**), was prepared by stirring [$RuCl_3$(tpy)] and bhq in 2-methoxyethanol at 70 °C in the presence of $AgPF_6$. After the removal of AgCl precipitation and the anion exchange with NH_4PF_6, **1b** was obtained as a green solid in 31% yield (Scheme 1). The ESI-MS spectrum of **1b** showed the parent peak at *m/z* = 548 as a monocation pattern.

Insert Scheme 1.

The structure of complex **1b** was confirmed by X-ray analysis. The ORTEP drawing of **1b** is shown in Fig.1 with selected bond lengths. Since the Ru-Cl bond length of **1b** (2.418(2) Å) is slightly shorter than that of **1a** (2.4431(13) Å) [7], it is considered that the *trans* influence of the cyclometalated bhq ligand is smaller than that of ppy ligand.

Insert Fig. 1

Cyclic voltammetry was performed on a DMF solution of **1b** with 0.1 M [^{n}Bu_4N][PF_6] as a supporting electrolyte. Three reversible redox waves were observed at $E_{1/2}$ = –0.16, –2.11, and –2.31 V *vs.* Fc^+/Fc. The former one is assigned to the Ru(III)/Ru(II) redox couple, and latter two are based on the redox processes of terpyridine and benzo[*h*]quinoline, respectively (Fig. 2). The redox potential of Ru(III)/(II) in **1b** ($E_{1/2}$ = +0.48 V *vs.* NHE) lies in a similar range observed for **1a** ($E_{1/2}$ = +0.46 V) [7], and is expected to be sufficiently low for the aerobic oxidation of the ruthenium center.

Insert Fig. 2

2.2. Application to aerobic oxidative dehydrogenation

First, oxidative dehydrogenation of 4-methylbenzylamine (**2a**) using **1b** as a catalyst was carried out in methanol under reflux in air. The reaction was monitored by ^{1}H NMR spectroscopy using mesitylene as an internal standard. The desired 4-methylbenzonitrile (**3a**) was obtained in good yield after 14 h (Table 1, entry 1). The reaction proceeded much faster using molecular oxygen (1 atm), the same reaction under a nitrogen atmosphere gave only a trace amount of product (entries 2 and 3). These results indicate that molecular oxygen participates as the oxidant in the catalytic reaction. The addition of bases accelerated the reaction, K_2CO_3 and Cs_2CO_3 were especially effective (entries 2, 4-7). It is considered that the base induces deprotonation of the NH group of the coordinated substrate. The reaction proceeded even at room temperature; **3a** was obtained in 80% yield (entry 8).

Insert Table 1

Next, the catalytic activity of **1b** for the aerobic oxidative dehydrogenation of various benzylamines **2a**-**2g** was investigated; the results are summarized in Table 2. The corresponding benzonitriles **3a**-**3g** were obtained in every case. When the substance has an electron-withdrawing group, the overreaction forming by-products such as 4-trifluoromethylbenzamide caused a decrease in the yield of the nitrile [8].

Insert Table 2

To probe the reaction pathway, similar ruthenium complexes, $[Ru(bhq)(bpy)_2][PF_6]$ **1c** (bpy = 2,2'-bipyridine) and $[RuCl(phen)(tpy)][PF_6]$ **1d** (phen = 1,10-phenanthroline), were employed. In both cases, negligible catalytic activities were observed (Table 3, entries 1 and 2). The inactivity of **1c** shows the coordination of **2a** to the metal center is indispensable. The inactivity of **1d** indicates that the redox potential of Ru(III)/Ru(II) ($E_{1/2}$ = +1.02 V *vs.* NHE [9]) is not enough low for the aerobic oxidation of the ruthenium center. These results show that the reaction is facilitated by the coordination of substrate to the metal center and the control of the redox potential at the metal center. Consequently, we conclude that the reaction pathway for **1b** is the same to **1a** (Scheme B1, see Appendix B) [3,10]. However the reaction using **1b** was slower than that of **1a** (Table 3, entries 3 and 4). This result is consistent with the data of X-ray analysis and cyclic voltammetry; the cyclometalated complex with a longer Ru-Cl bond length and a lower redox potential serves as a superior catalyst for this aerobic dehydrogenation system.

Insert Table 3

3. Conclusions

We have prepared a cyclometalated ruthenium(III) complex **1b** whose structure was confirmed by a single-crystal X-ray diffraction study. The complex **1b** was found to be an effective catalyst for the aerobic oxidative dehydrogenation of benzylamines. It was revealed that the catalytic activity correlates with the Ru-Cl bond length and the redox potential. The method outlined in this paper is expected to contribute to the design of catalysts for aerobic oxidative dehydrogenation. Further studies including an investigation of the reaction mechanism are in progress.

4. Experimental

4.1. General

2a, methanol-d_4 (Acros), $AgPF_6$, **2c**, **2d**, **2f**, **2g**, 1,8-diazabicyclo[5.4.0]undec-7-ene (Aldrich), K_2CO_3, Na_2CO_3, Cs_2CO_3, 2-methoxyethanol (Kanto Chemical), benzo[*h*]quinoline, **2b**, **2e**, and mesitylene (TCI) were commercially available and were used without any further purification. Complexes $[RuCl_3(tpy)]$ [11], **1a** [7], **1c** [5e], and **1d** [9] were prepared in accordance with the

previous literature methods. Column chromatography was carried out by using Aluminium oxide 90 active acidic (Merck).

Elemental analysis was carried out with a Perkin-Elmer 2400-CHN instrument. ESI-Mass spectrum was recorded on an Applied Biosystems QStar Pulsar *i* spectrometer. Cyclic voltammograms were recorded on a ALS/CH Instruments Electrochemical analyzer 1200A with a PFCE carbon working electrode, a Pt wire counter electrode and a 0.10 M $AgNO_3$/Ag reference electrode in a DMF solution containing 0.10 M [^{n}Bu$_4$N][PF_6] as a supporting electrolyte at room temperature. Fc^+/Fc = +0.060 V *vs.* 0.10 M $AgNO_3$/Ag, and +0.64 V *vs.* NHE. ^{1}H NMR spectra were measured on a JEOL EX-270, a JNM-ECS-400 and a Bruker AVANCE-400 NMR spectrometers.

4.2. Synthesis of Ru(III) complex ***1b***

[$RuCl_3$(tpy)] (200 mg, 0.45 mmol), bhq (163 mg, 0.91 mmol) and $AgPF_6$ (184 mg, 0.73 mmol) were dissolved in 2-methoxyethanol (55 mL) and stirred at 70 °C for 12 h. The solution was cooled to –20 °C for 1 h and then filtered through Celite to remove the AgCl precipitate. The filtrate was concentrated to ca. 1 mL. An aqueous NH_4PF_6 solution was added to the concentrate. The resulting precipitate was filtered off and purified by column chromatography (grade III alumina, acidic, toluene/acetonitrile = 2/1). The green band was collected and acetonitrile was evaporated. The precipitate was collected by filtration to give **1b** as a green solid (98 mg, 31%). ESI-MS: m/z = 548{M-PF_6}$^+$. Anal. Calcd. for [RuCl(bhq)(tpy)][PF_6]·2H_2O ($C_{28}H_{23}ClF_6N_6O_2PRu$): C, 46.13; H, 3.18; N, 7.69. Found C, 46.31; H, 3.52; N, 7.44.

4.3. X-ray crystal structure determination

$C_{29.5}H_{22}N_4F_6PClO_{0.5}Ru$, M = 722.01, monoclinic, space group *C*2/m (No. 12), a = 15.0252(8) Å, b = 24.2483(12) Å, c = 16.4057(9) Å, β = 97.9443(16)°, V = 5919.8(5) Å^3, T = 88(1) K, Z = 8, D_{calcd} = 1.620 g cm^{-3}, μ = 7.412 cm^{-1}, F(000) = 2888.00, crystal size 0.30×0.10×0.05 mm. 28552 reflections collected, 6900 unique (R_{int} = 0.175), $R_1(I > 2\sigma(I))$ = 0.1089, R (All reflections) = 0.1952, wR2 (All reflections) = 0.3525, Single crystals of **1b** were obtained by the slow diffusion of hexane into its solution in acetone. Intensity data were collected on a Rigaku R-AXIS Rapid diffractometer with Mo-Kα radiation. Crystals were mounted on a glass capillary tube. A full matrix least-squares refinement was used for non-hydrogen atoms except for PF_6^- with anisotropic thermal parameters method by SHELXL-97 program. Hydrogen atoms were refined using the riding model.

*4.4. Oxidative dehydrogenation of 4-methylbenzylamine (**2a**) to 4-methylbenzonitrile (**3a**) using **1b** as a catalyst (Table 1, entry 2).*

A mixture of **2a** (19 μL, 0.15 mmol), ruthenium complex **1b** (5.2 mg, 7.5 x 10^{-3} mmol), K_2CO_3 (21 mg, 0.15 mmol), and mesitylene (10 μL, 7.5 x 10^{-2} mmol) in CD_3OD (1 mL) was stirred

under O_2 (1 atm). After stirring under reflux for 1 h, the yield was determined by ^{1}H NMR using mesitylene as an internal standard (89%). The spectral data of the obtained **3a** were identical to the previous literature [12].

Acknowledgements

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Appendix A. Supplementary material

A complete set of X-ray crystallographic structural data for complex **1b** (CCDC no. 794566) is available at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ,UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.ac.uk) on request, quoting the deposition number.

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:

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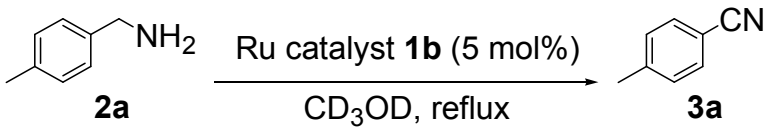
Table 1. Oxidative dehydrogenation of **2a** using **1b** as a catalyst[a]

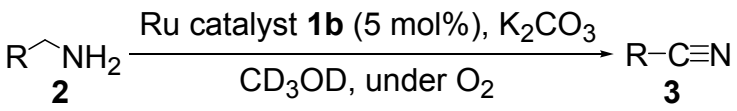


2a **3a**

Entry	Conditions		Time (h)	Yield (%)[b]
1	K_2CO_3	Air	14	78
2	K_2CO_3	O_2	1.5	89
3	K_2CO_3	N_2	1.5	trace
4	–	O_2	1.5	10
5	Na_2CO_3	O_2	1.5	23
6	Cs_2CO_3	O_2	1.5	88
7	DBU	O_2	1.5	31
8[c]	K_2CO_3	O_2	24	80

[a]The reaction was carried out in 1 mL CD_3OD with **2a** (0.15 mmol), **1b** (7.5×10^{-3} mmol) and a base (0.15 mmol).
[b]Determined by ^1H NMR spectroscopy using mesitylene as an internal standard.
[c]The reaction was performed at room temperature.

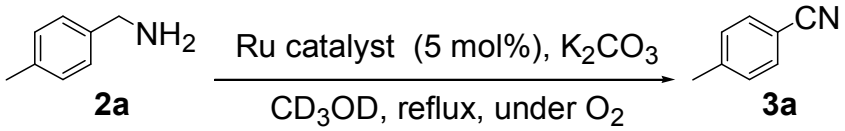
Table 2. Oxidative dehydrogenation of **2a-2g** using **1b** as a catalyst[a]



Entry	R		Temp. (°C)	Time (h)	Yield (%)[b]
1	*p*-MeC_6H_4	**a**	reflux	1.5	89
2	*m*-MeC_6H_4	**b**	reflux	1.5	76
3	*o*-MeC_6H_4	**c**	reflux	1.5	83
4	*p*-$MeOC_6H_4$	**d**	reflux	1.5	93
5	Ph	**e**	reflux	1.5	74
6	*p*-ClC_6H_4	**f**	30	24	72
7	*p*-$F_3CC_6H_4$	**g**	30	24	41

[a]The reaction was carried out in 1 mL CD_3OD with **2** (0.15 mmol), **1b** (7.5×10^{-3} mmol) and a base (0.15 mmol).
[b]Determined by ^1H NMR spectroscopy using mesitylene as an internal standard.

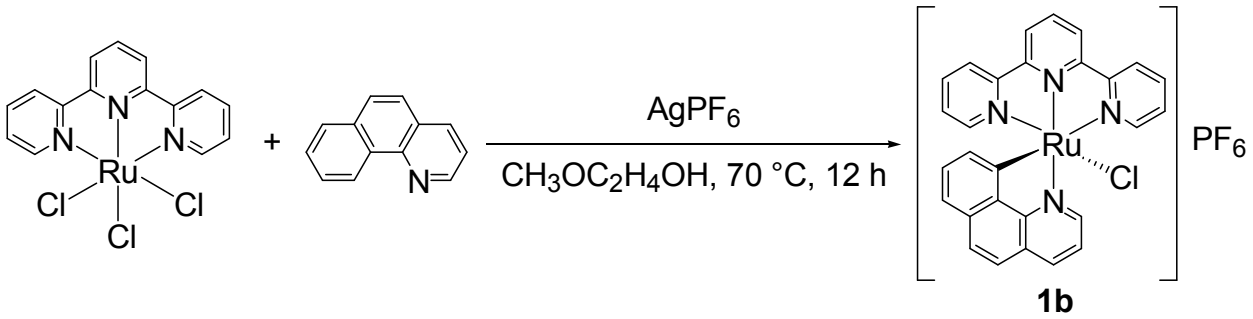
Table 3. Oxidative dehydrogenation of **2a** using **1a-1d** as a catalyst[a]



2a **3a**

Entry	Ru catalyst	Time (h)	Yield (%)[b]
1	**1c**	1.5	trace
2	**1d**	1.5	0
3[c]	**1a**	1	87
4	**1b**	1	77

[a]The reaction was carried out in 1 mL CD_3OD with **2a** (0.15 mmol), Ru catalyst (7.5×10^{-3} mmol) and a base (0.15 mmol).
[b]Determined by ^1H NMR spectroscopy using mesitylene as an internal standard.
[c]The data are originated from ref.[3b].



Scheme 1. Synthesis of Ru(III) complex **1b**.

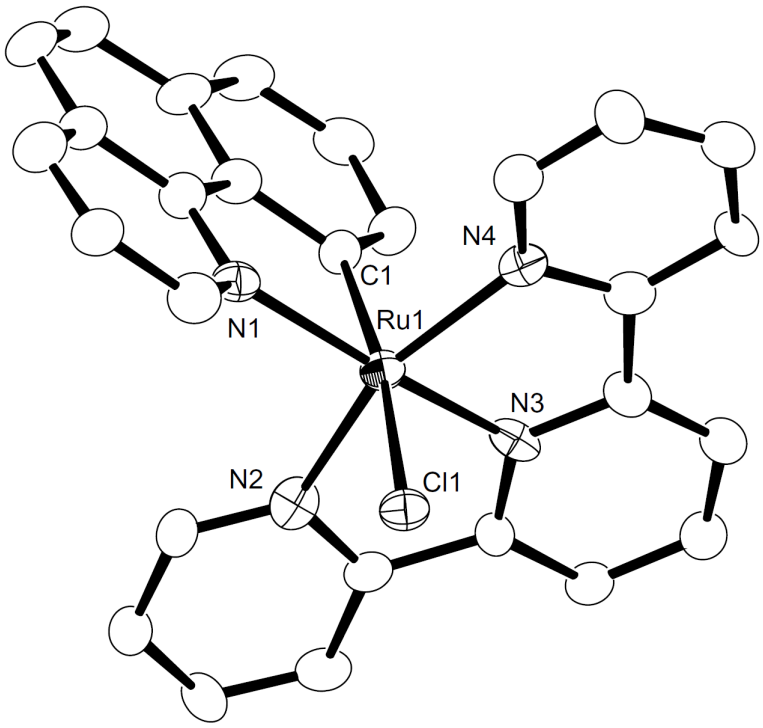


Fig. 1. ORTEP drawing of Ru complex **1b** at 30% ellipsoidal level. Hydrogen atoms, PF_6^- anion and solvated acetone molecules are omitted for simplicity. Selected bond lengths (Å): Ru(1)-C(1), 1.981(9); Ru(1)-N(1), 2.137(9); Ru(1)-N(2), 2.065(9); Ru(1)-N(3), 1.942(9); Ru(1)-N(4), 2.062(9); Ru(1)-Cl(1), 2.418(2).

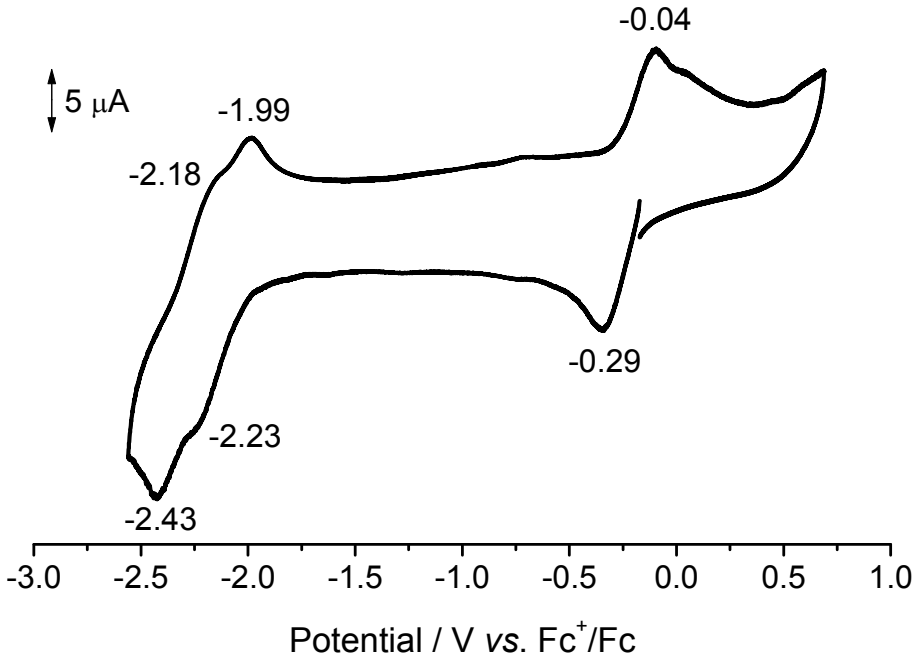


Fig. 2. Cyclic voltammogram of **1b** in DMF containing [^{n}Bu$_4$N][PF$_6$] (0.1 M). Sweep rate = 100 mV/s.