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Diruthenium complex catalyzed reduction of nitroarenes-investigation of reaction pathway

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ABSTRACT

A diruthenium complex, $[(\mathbf{L})Ru_2(\eta^6\text{-}C_6H_6)_2Cl_2](PF_6)_2$ (**1**) (**L** = 5-phenyl-2,8-di-2-pyridinylanthyridine), was prepared and characterized. This diruthenium complex **1** was found to be an efficient catalyst for the reduction of aromatic nitro compounds leading to the corresponding aniline derivatives with the use of hydrazine as the reducing agent at 80 °C in an ethanol solution. Catalytic activity of **1** towards various possible intermediates leading to anilines was investigated to understand the reaction pathway. These studies indicate that this reduction proceeds *via* a direct route as evidenced by hydroxylamines being observed as the major intermediate followed by the appearance of aniline under the catalytic conditions. Thus, the reaction pathway of this catalytic system is discussed.

1. Introduction

Anilines are important chemicals as the starting materials for organic synthesis, polymers, pharmaceuticals, and other aspects [1]. Generally, the catalytic reduction of nitroarenes is considered to be the most convenient way to prepare anilines and numerous catalysts accompanied with various reductants have been successfully employed. Despite these achievements, chemists are also interested in the reduction pathway operated under a specific catalytic condition. Reduction of nitroarenes generally comprises multi-step pathways and two routes are often discussed in the homogeneous catalysis (Scheme 1) [2]. The first step involves the reduction of nitro functionality into nitroso group, which is subsequently reduced to the hydroxyaminobenzene. This intermediate can undergo two competing routes to provide the final product: the direct reduction of hydroxyaminobenzene leading to aniline (Scheme 1, route A), and the condensation of nitroso- and hydroxyamino-benzene to generate azoxybenzene, which is further reduced to azobenzene, diphenylhydrazine and finally to aniline (Scheme 1, route B).

Pathway operating in a catalytic system really depends on the nature of catalyst and reaction conditions [2]. In a previous study, we found that reduction of nitroarenes catalyzed by a dipalladium complex (Fig. 1) undergoes the condensation pathway (route B) presumably due to the synergistic effect caused by the dinuclear catalyst to facilitate the condensation [3]. It is believed that metal ions in close proximity are expected to “cooperate” in promoting reactions. In this context, the use of binuclear complexes as catalysts in chemical transformation has received much attention [4]. Here, we report the preparation of a diruthenium complex containing an anthyridine-based ligand **L** and the catalytic activity of the complex on reduction of nitroarenes. Furthermore, the reaction pathway of this catalytic system is investigated.

2. Experimental section

2.1. General information

Chemicals and solvents were of analytical grade and were used without further purification. Nuclear magnetic resonance spectra were recorded on a 400 MHz spectrometer. Chemical shifts are given in parts per million relative to Me_4Si for ^1H and ^{13}C NMR. Ligand **L** and ruthenium complex [(bipy)Ru(η^6-C_6H_6)Cl]Cl (**2**) [bipy = 2,2′-bipyridine] were prepared according to the reported methods [5].

2.2. Preparation of Complex 1, $[(\mathbf{L})Ru_2(\eta^6\text{-}C_6H_6)_2Cl_2](PF_6)_2$

This complex was prepared according to Scheme 2. A mixture of **L** (70 mg, 0.17 mmol), $[Ru(\eta^6\text{-}C_6H_6)Cl_2]_2$ (90 mg, 0.18 mmol) and KPF_6 (60 mg, 0.34 mmol) in a 25 ml round-bottom flask was flashed with nitrogen. Anhydrous acetonitrile (5 mL) was syringed into the mixture and the resulting solution was heated under refluxing condition for 18 h. Upon cooling, the volume of the reaction mixture was reduced down to 1 ml and diethylether was added to precipitate out the desired

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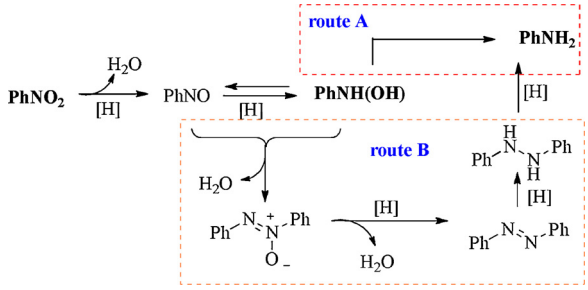


Scheme 1. Pathways for reduction of nitrobenzene.

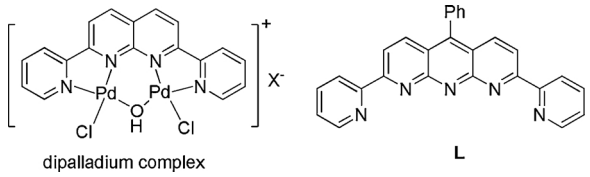
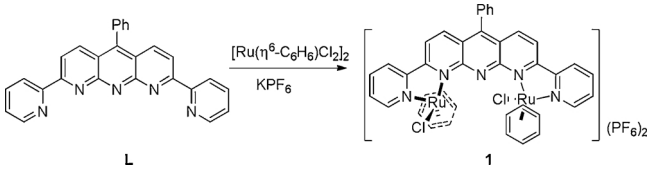


Fig. 1. Structures of dipalladium complex and ligand **L**.



Scheme 2. Preparation of complex **1**.

complex. The crude product was washed with water and then dried under vacuum to give **1** as dark purple solid (192.2 mg, 88%).^{1}H NMR (400 MHz, CD_3CN) δ = 9.57 (d, J = 5.2 Hz, 2 H), 8.68 (d, J = 8.1 Hz, 2 H), 8.62 (d, J = 9.0 Hz, 2 H), 8.51 (d, J = 9.0 Hz, 2 H), 8.36 (t, J = 7.8 Hz, 2 H), 7.94 (t, J = 6.5 Hz, 2 H), 7.86 (m, 3 H), 7.66 (m, 2 H), 6.19 (s, 12 H); ^{13}C NMR (100 MHz, CD_3CN) δ = 165.2, 158.5, 157.7, 156.8, 155.9, 142.2, 141.3, 133.7, 132.2, 131.8, 130.5, 130.4, 128.3, 124.4, 121.7, 88.7 ppm. UV–vis: λ_{max} (ε, $10^3 M^{-1} cm^{-1}$) : 505 (1.7), 415 (8.2), 377 (7.8), 294 (10.8), 252 (12.6), 227 (12.7) nm; HRMS (ESI-TOF): m/z [M-2·(PF_6)]$^{2+}$ calcd. for $C_{39}H_{29}Cl_2N_5Ru_2$, 420.4943; found 420.4932.

2.3. Catalytic-reduction of nitroarenes

A mixture of nitro compound (0.6 mmol) and complex **1** (1.5×10^{-3} mmol) in ethanol (2 mL) was placed in a reaction tube. The reaction vessel was flushed with nitrogen gas and a solution of $N_2H_4 \cdot H_2O$ (1.2 mmol) in ethanol was added. The mixture was stirred at 80 °C for a period of time as indicated in the tables. After the reaction, ethanol was removed under reduced pressure. The residue was analyzed by NMR spectroscopy. For the purification, chromatography on silica gels provided the desired compound in the pure form. The spectral data of the organic products are essentially identical to those reported ones.

2.4. Kinetic studies

A mixture of nitro compound (0.6 mmol) and complex (1.5×10^{-3} mmol) in a reaction tube with a stirring bar. The reaction vessel was flushed with nitrogen gas and a solution of $N_2H_4 \cdot H_2O$ (1.2 mmol) was added. The mixture was stirred at 80 °C for a period of time (from 3 to 7 h). At appropriate time intervals, 0.1 ml aliquots were removed using a syringe and quickly passed through Celite to remove the metal complexes with elution of diethylether. The filtrate was then concentrated under reduced pressure and analyzed by ^{1}H NMR spectroscopy.

2.5. Crystallography

Crystal suitable for X-ray determination was obtained for **1**·$(DMF)_2$. Cell parameters were determined either by a Siemens SMART CCD diffractometer. The structure was solved using the SHELXS-97 program [6] and refined using the SHELXL-97 program [7] by full-matrix least-squares on F2 values. Crystal data of **1**$(DMF)_2$: $C_{45}H_{43}Cl_2F_{12}N_7O_2P_2Ru_2$, Mw = 1276.84, Orthorhombic, space group P2(1)2(1)2(1); a = 14.6196(3) Å, b = 14.9766(3) Å, c = 21.6427(4) Å, α = 90°, β = 90°, γ = 90°; V = 4738.71(16) Å^3; Z = 4; $\rho_{calcd.}$ = 1.790 Mg m^{-3}; F(000) = 2552; Crystal size: 0.20 × 0.15 × 0.10 mm^3; reflections collected: 25,765; independent reflections: 10,133 [R(int) = 0.0541]; θ range 2.71–27.50°; goodness-of-fit on F_2 1.012; Final R indices [I > 2sigma(I)]R1 = 0.0461, wR2 = 0.0862; R indices (all data) R1 = 0.0674, wR2 = 0.0977. CCDC 1,864,735. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336,033.

3. Results and discussion

3.1. Preparation and characterization of complex 1

The ligand **L** used for preparation of the diruthenium complex was prepared by the previously reported method [5a]. Complexation of **L** with an equimolar amount of $[Ru(\eta^6\text{-}C_6H_6)Cl_2]_2$ in the presence potassium hexafluorophosphate in a refluxing acetonitrile solution gave the desired di-ruthenium complex as dark purple solids in 88% yield (Scheme 2). ^{1}H NMR spectrum of **1** reveals that the anthyridine protons of the ligand **L** are split into two set of doublets, clearly suggesting the symmetrical nature of the proposed structure. It is noticed that the signal for the η^6-benzene ring protons shows as a singlet at δ 6.19 with the integration of 12H at room temperature. ESI-HRMS of **1** in CH_3CN matrix shows a peak at m/z = 420.4943, which is matched with the theoretical value of 420.4932 of $[\mathbf{1} - 2(PF_6)]^{2+}$, supporting a dinuclear nature of the complex.

In addition to the spectroscopic characterization, the detail structural formulation of **1** was confirmed by a single-crystal X-ray study. ORTEP plot (Fig. 2) of cationic portion of **1** shows a pair of ruthenium atoms surrounded by **L**. Each metal ion is in an octahedral environment, as expected, with the coordination sphere formed by the bipyridine moiety of **L**, a η^6-benzene and a chloride. It is noticed that two benzene rings are opposite along the anthyridine rings, avoiding the steric interaction. Selected bond distances and bond angles are collected in

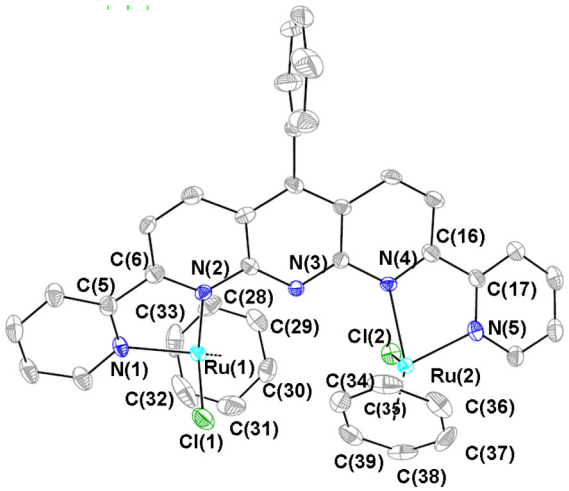


Fig. 2. ORTEP plot of cationic portion of **1** (30% probability level; label of some aromatic carbons are omitted for clarity).

Table 1
selected bond distances (Å) and angles (deg).

Ru(1)-N(1)	2.075(4)	Ru(2)-N(5)	2.068(4)
Ru(1)-N(2)	2.137(4)	Ru(2)-N(4)	2.120(4)
Ru(1)-Cl(1)	2.383(1)	Ru(2)-Cl(2)	2.390(1)
N(2)-Ru(1)-N(1)	77.5(2)	N(4)-Ru(2)-N(5)	77.5(2)
Cl(1)-Ru(1)-N(2)	88.2(1)	Cl(2)-Ru(2)-N(4)	88.1(1)
Cl(1)-Ru(1)-N(1)	83.6(1)	Cl(2)-Ru(2)-N(5)	80.1(1)

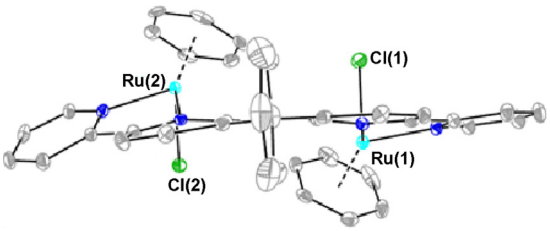


Fig. 3. Side view of cationic portion of **1** (30% probability level).

Table 1. All Ru-N bond lengths are quite similar, at 2.07–2.13 Å, which are in agreement with those of the reported bipyridine ruthenium complexes. Both angles of N(1)-Ru(1)-N(2) [77.5(2)°] and N(4)-Ru(2)-N(5) [77.5(2)°], deviated from 90°, are comparable to those of [(bipyridine)RuCl(L)] presumably due to the geometrical constrain of donors. The average Ru-$C_{(benzene)}$ distances (2.183(5) Å) are in the normal range of η^6 coordination modes. The distance of Ru(1)···Ru(2) is 5.4170(5) Å, indicating that two metal centers are far away from each other. No significant discrepancies in other bond lengths and angles are noticed in complex **1**. An interesting observation is the ligand itself is not seated in a plane of this crystal structure, as illustrated in Fig. 3. The chelating ring with Ru(2) is twisted and the metal center is above the coordination plane. The torsional angles of N(4)-C(16)-C(17)-N(5) is -17.1°, which is larger than that of N(1)-C(5)-C(6)-N(2) [- 4.5°]. Presumably, this is due to the steric congestion caused by the coordinating ligands.

3.2. Reduction of nitro-compounds

It is well-documented that transition metal complexes are frequently used as catalysts for reduction of nitroarenes [8]. Accordingly, the activity of the diruthenium complex **1** on reduction of nitroarenes with hydrazine as the reductant was investigated [9]. For the optimization, we chose the reduction of *p*-nitrotoluene as the model reaction with **1** as the pre-catalyst. A control experiment clearly showed the essentiality of a metal complex playing the role of catalysis (Table 2, entry 1). After several trials, it appears that a full conversion was achieved by carrying out the reaction using excess of hydrazine in the presence of 0.25 mol% of catalyst in an ethanol solution at 80 °C (Table 2, entry 2). Various solvents were screened and alcohols were found to be the best choice (Table 2, entries 2–8). Other solvents gave poor results. It is noticed that *N*-hydroxy-*p*-toluidine and 4,4′-azoxytoluene were produced in an acetonitrile solution (Table 2, entry 4). By lowering the ratio of hydrazine/nitrotoluene to 2:1, we were still able to obtain the full reduction product quantitatively even with a shorter period of time (7 h) (Table 2, entry 9). By comparison to the outcome of entry 11, the catalyst loading of 0.25 mol% appeared to be the best choice. By running the reaction under O_2 atmosphere, the product yield diminished by about 50%. Furthermore, the catalysis proceeded smoothly even with the addition of mercury during the reaction, indicating that the catalytic system is a homogeneous metal-catalyzed reaction. Two ruthenium complexes, [Ru(η^6-benzene)Cl]$_2$ and [(bipy)Ru(η^6-benzene)Cl]Cl (**2**), were also tested for comparison. However, these two complexes showed poor activity in this catalytic reduction. (Table 2, entries 14–16). By carrying out the reaction in air, the aniline product was obtained in poor yields accompanied with other intermediates even with the use of excess of hydrazine (Table 2, entries 17–18).

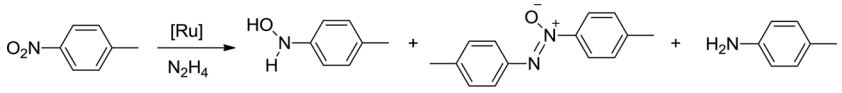
In order to understand more about the pathway of the catalytic process, we set up few experiments to study the nature of the catalyst and possible intermediates operated in the catalysis. First, the kinetics of the resultant reaction profile for the reduction of *p*-nitroulene catalyzed by **1** was performed (Fig. 4). It appears that there is a very short induction period for this catalytic system. *p*-Tolylhydroxylamine, a key intermidate, is generated at the beginning of the catalysis, and it remains as a constant concentration in the first two hours. After that, this species decreases slowly and eventually converted into the product at the end the reaction. The amount of *p*-toluidine cumulates gradually from the beginning and reaches to a full conversion at the end. It is noticed that *p,p′*-azoxytoluene appears after 1.5 h and remains as a very low concentration along the reaction and diminishes finally. From these observations, it seems that the reduction of *p*-nitrotoluene catalyzed by **1** proceeds *via* pathway A (Scheme 1). However, we are not able to exclude the possibility of pathway B due to the appearance of trace *p,p′*-azoxytoluene. Thus, we carried out a series of testing to find out the reactivity of catalytic system toward various possible intermediates under the optimized conditions.

The product distribution under the optimal catalytic conditions was examined with *p*-nitrosotoluene as the substrate (Table 3, entry a). Within 2 h, this substrate was fully converted into a mixture of *p,p′*-azoxytoluene, toluidine, *p,p'*-azotoluene and 1,2-di-*p*-tolylhydrazine with the major portion (61%) of azoxytoluene. For a longer period (20 h), the final reduction product (toluidine) did not increase much, whereas the amount of *p,p'*-azotoluene, which is the reduction product of azoxytoluene, increased slightly. On starting with *p,p′*-azoxytoluene, minor portion of reduction products were obtained, while more than 75% of substrate remained un-reacted (Table 3, entry b), indicating that the activity of **1** on reduction of azoxybenzenes is poor. Meanwhile, treatment of azotoluene under the catalytic conditions provided the 1,2-di-*p*-tolylhydrazine as the major reduction product accompanied with trace amount of toluidine (Table 3, entry c). Similarly, the diruthenium complex **1** showed a poor activity on the conversion of 1,2-di-*p*-tolylhydrazine into the desired product toluidine (Table 3, entry d). On the contrary, on using *p*-hydroxyaminotoluene as the substrate, complex **1** granted a full conversion of the substrate to *p*-toluidine (Table 3, entry e). Unlike nitrosotoluene as the substrate (entry a), the reduction of *p*-hydroxyaminotoluene under the optimal conditions did not give any accumulation of *p,p′*-azoxytoluene, a condensation of nitrosotoluene with *p*-hydroxyaminotoluene, indicating that the hydroxylamine is directly reduced to the final product [10–13].

Some generalizations can be made from the above control reactions. The catalytic process by complex **1** with N_2H_4 in the reduction of nitroarene undergoes preferentially *via* the direct reduction of hydroxyaminoarene. The catalytic system has poor activity on reduction of azoxy- and azo-arenes as compared to hydroxyaminoarenes, *i.e.* the activity of complex **1** is quite poor on the reductive cleavage of N—N bonds. Furthermore, once the nitrosoarene species appears in the reaction medium, the formation of azoxy species cannot be avoided, *i.e.* the rate of condensation of hydroxyaminoarene with nitrosoarene is comparable to the reduction steps. To our surprise, the catalyst showed a poor activity toward nitrosotoluene, which is generally known to be the key intermediate of this reduction (Scheme 1).

For further understanding the reduction pathway whether involving nitrosotoluene intermediate, we carried out another experiment by adding nitroso compound into the catalytic reaction. After a standard reaction of the reduction of nitrotoluene proceeded for 1 h, a quantity of 30 mol% *p*-nitrosotoluene was syringed into the reaction mixture. This reaction mixture was then monitored by ^{1}H NMR. In this reaction medium, a mixture of nitrotoluene, *p*-hydroxyaminotoluene, *p,p′*-azoxytoluene, *p,p′*-azotoluene and toluidine was identified, *i.e.* production of azoxy species appeared immediately. For a longer period, both *p,p′*-azoxytoluene and *p,p′*-azotoluene still remained, which is consistent with the results of experiments in Table 3 (entries a–d). Clearly, the appearance of nitroso intermediate in the catalytic process would

Table 2
Optimization for the reduction of *p*-nitrotoluene.[a]



I II III

entry	cat. (mol%)	N_2H_4 (mmol)	solvent	conv.[b]	yield (%)[b]		
					I	II	III
1	–	1.8	EtOH	0	0	0	0
2	**1** (0.25 mol%)	1.8	EtOH	100%	0	0	100
3	**1** (0.25 mol%)	1.8	MeOH	100%	0	0	99
4	**1** (0.25 mol%)	1.8	CH_3CN	46%	trace	6	35
5	**1** (0.25 mol%)	1.8	DCE	9%	0	0	7
6	**1** (0.25 mol%)	1.8	toluene	50%	0	0	48
7	**1** (0.25 mol%)	1.8	dioxane	12%	0	trace	6
8	**1** (0.25 mol%)	1.8	H_2O	32%	trace	0	22
9[c]	**1** (0.25 mol%)	1.2	EtOH	100%	0	0	99
10[c]	**1** (0.25 mol%)	0.6	EtOH	53%	trace	0	48
11	**1** (0.13 mol%)	1.2	EtOH	97%	7	6	83
12[c,d]	**1** (0.25 mol%)	1.2	EtOH	52%	0	trace	49
13[e]	**1** (0.25 mol%)	1.8	EtOH	100%	0	0	98
14	$[Ru(C_6H_6)Cl]_2$ (0.25 mol%)	1.2	EtOH	6%	trace	0	trace
15[c]	**2** (0.5 mol%)	1.2	EtOH	6%	trace	0	trace
16[c]	**2** (0.25 mol%)	1.2	EtOH	5%	trace	0	trace
17[f]	**1** (0.25 mol%)	1.2	EtOH	56%	18%	6%	30%
18[f]	**1** (0.25 mol%)	3.0	EtOH	96%	52%	9%	35%

[a] Reaction conditions: *p*-nitrotoluene (0.6 mmol), $N_2H_4{\cdot}H_2O$ and catalyst in solvent (1 mL) at 80 °C for 10 h, unless noted.
[b] Determined by ^1H NMR with 1,3,5-trimethoxybenzene as the internal standard.
[c] 7 h.
[d] O_2 (1 atm).
[e] Addition of mercury (0.24 g, 1.2 mmol) after the reaction proceeded.
[f] In air.

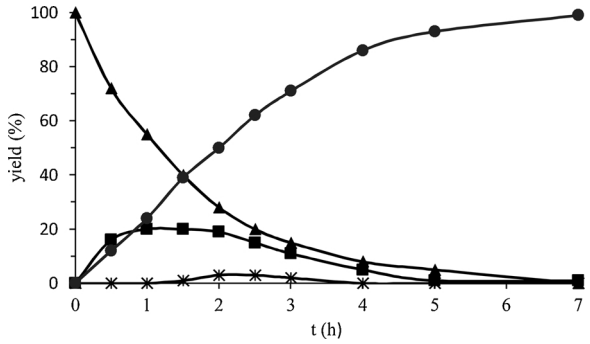


Fig. 4. Reaction profile of reduction of *p*-nitrotoulene (0.6 mmol) catalyzed by **1** (0.25 mol%) in EtOH at 80 °C with $N_2H_4{\cdot}H_2O$ (1.2 mmol) as reductant. *p*-nitrotoluene (▲); *p*-toluidine (●); *p*-hydroxyaminotoluene ( ); *p,p'*-azoxytoluene (*).

readily undergo the condensation with *p*-hydroxyaminotoluene to yield *p,p'*-azoxytoluene, thus inhibiting the reduction leading to anilines. These observations clearly indicate that the reduction pathway by catalyst **1** does not go through nitroso species. In other word, under this catalytic condition, nitroarenes is directly reduced to hydroxyaminoarenes, which undergoes a further reduction step to the final product [12].

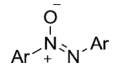
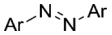
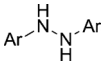
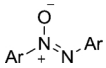
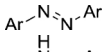
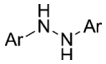
In order to rationalize the appearance of trace amount of *p,p'*-azoxytoluene during the reduction of nitrotoluene (Fig. 4), control experiments using nitrotoluene and related intermediates as substrates without complex **1** were performed, and results are listed in Scheme 3. It appears that the nitro compound cannot be reduced by N_2H_4 in ethanol at 80 °C (Scheme 3A), implying the necessity of catalyst. However, when nitrosotoluene was treated with hydrazine, even in the absence of complex **1**, the substrate was fully converted into *p,p'*-azoxytoluene (56%) and toluidine (38%) (Scheme 3B). Additionally, when *p*-hydroxyaminotoluene was treated with hydrazine in the absence of **1**, only minor portion of the substrate was transformed into *p,p'*-azoxytoluene (13%) and toluidine (6%) (Scheme 3C). Apparently, hydrazine is able to react with hydroxylamine and nitroso compounds directly without the assistance of metal catalysts, which may rationalize the presence of trace *p,p'*-azoxytoluene during the reduction of nitroarenes under this catalytic study, *i.e.* the species is generated from the direct reaction of *p*-hydroxyaminotoluene with hydrazine.

At this point, we believe that a direct route from nitrobenzene to phenylhydroxylamine contributes to the production of aniline under the complex **1** catalyzed condition, *i.e.* a pathway without going through the nitosoarene intermediates (Scheme 4). Such a reaction route has been proposed in few heterogeneous catalysis, but not homogeneous systems. To the best of our knowledge, no direct formation of hydroxylamines from nitroarenes catalyzed by a metal complex homogeneously has been described [10–12].

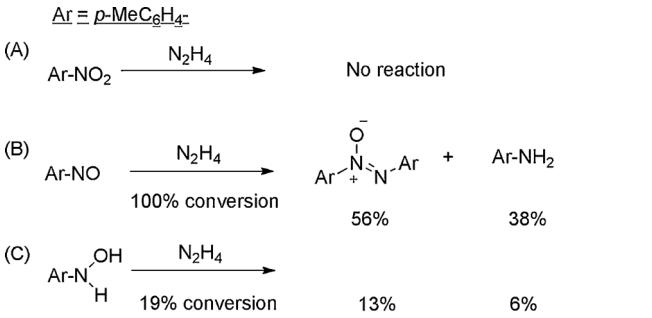
3.3. Mononuclear versus dinuclear ruthenium complexes

For comparison, the catalytic activities of the mono-nuclear complex $[(bipy)RuCl(\eta^6\text{-}C_6H_6)]Cl$ (**2**) under the above optimized reduction conditions was examined. Table 4 summarizes results of a series of reactions catalyzed by **2**. It appears that the catalytic activity of **2** in reduction of nitroarene is much less active than that of **1**, even for 24 h only 14% of conversion with 12% of amine product (Table 4, entry a). On starting with *p*-nitrosotoluene (entry b), *p,p'*-azoxytoluene and toluidine were the observed products. However, it is noticed that the ratio of these two products is similar to that of the control reaction mentioned above (Scheme 3B), revealing that complex **2** might not have any catalytic activity in this reaction. As for *p*-hydroxyaminotoluene, complex **2** did show catalytic activity on its reduction. However, the

Table 3
Catalytic activity of **1** toward various intermediates.[a]

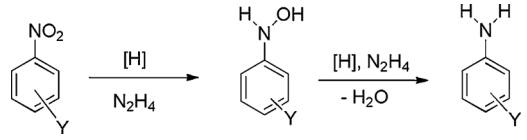
entry	substrate[b]	time	conv.				Ar-NH_2
a	Ar-NO	2 h	100%	61%	trace	trace	23%
		20 h	100%	49%	17%	trace	27%
b		7 h	22%	———	11%	trace	9%
		24 h	25%	———	10%	trace	14%
c		7 h	59%	———	———	55%	trace
d		7 h	10%	———	trace	———	6%
e		7h	100%	0%	0%	0%	100%

[a] Substrate (0.6 mmol), $N_2H_4{\cdot}H_2O$ (1.2 mmol) and **1** (0.25 mol%) in EtOH at 80 °C.
[b] Ar = *p*-MeC_6H_4-.



[a] Substrate (0.6 mmol) and $N_2H_4{\cdot}H_2O$ (1.2 mmol) in EtOH at 80 °C for 7 h.

Scheme 3. Reductions of nitrotoluene by N_2H_4 *without* metal catalyst **1**[a].



Scheme 4. Reduction pathway of nitroarenes catalyzed by **1**.

production of toluidine only reached 60% even for 24 h period (Table 4, entry c). Not surprisingly, a poor activity of **2** toward azoxytoluene was observed (Table 4, entry d). All of these investigations summarize that the catalytic activity of the dinuclear complex **1** is superior to that of the mono-nuclear complex **2**.

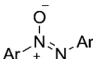
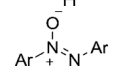
Diruthenium complex **1** appears to exert an excellent catalytic activity with a distinct pathway in this reduction and shows a higher efficiency relative to its mononuclear analogues. Structure-wise, complex **1** can be viewed as a linkage of two molecules of **2**. However, the catalytic activity of **1** shows a higher efficiency relative to its mononuclear analogues, suggesting a possible cooperative effect between two metal centers within **1**, which is absent in a mononuclear system. Thus, the cooperativity index (α) for a polymetallic catalyst with n centers (Eq. (1)), previously proposed by Jones and James [14], was used in this work to estimate the degree of cooperativity of complex **1**. Since the complex investigated here is a dinuclear species, the equation is simplified as shown in Eq. (2). In this equation, A_o stands for the activity of **1**; A_p is the predicted total activity of the dinuclear complex, which is summation of the measured activity of two molecules of complex **2**; and $A_{ave} = A_p/2$. Base on the conversions of the reaction catalyzed by **1** and **2** (Table 2, entries 9 and 16), the cooperativity index (α) for **1** is estimated to be 19, which is far larger than unity. This result implies that complex **1** readily benefits from the cooperative effect during the reaction course of this reduction. It would be interesting to know how the cooperative effect operates. However, we have attempted to reveal the possible intermediates of metal complexes, but not succeed, even by monitoring a sample with NMR or mass spectrometers.

$$\alpha = \frac{A_o - A_p}{A_{ave}} \quad \begin{array}{l} A_o\text{:activity of the polymetallic catalyst with n centers} \\ A_p\text{:predicted total activity of the polymetallic catalyst} \\ A_{ave}\text{: } A_p/n \end{array} \tag{1}$$

$$\alpha = \frac{A_{(complex\ 1)} - 2x\,[A_{(complex\ 2)}]}{[2x(A_{(complex\ 2)})]/2} \tag{2}$$

We were expected to isolate some catalytic intermediates coordinating to metal ions due to the suitable distance between Ru ions in **1**, but in vain. Nevertheless, the experimental data do show a possible synergistic

Table 4
Catalytic activity of **2** towards *p*-nitrotoluene and various intermediates.[a]

entry	substrate[b]	time	conv.				Ar-NH_2
a	Ar-NO_2	7 h	6%	< 3%	ND[c]	ND	< 5%
		24 h	14%	ND	< 3%	ND	12%
b	Ar-NO	2 h	100%	ND	55%	ND	38%
c		7 h	32%	———	< 5%	ND	30%
		24 h	90%	———	18%	8%	64%
d		24 h	20%	———	———	6%	12%

[a] Substrate (0.6 mmol), $N_2H_4{\cdot}H_2O$ (1.2 mmol) and **2** (0.5 mol%) in EtOH at 80 °C.
[b] Ar = *p*-MeC_6H_4-.
[c] ND = not detected.

Table 5
Reduction of substituted nitroarenes catalyzed by **1**.[a]

entry	substrate	$N_2H_4{\cdot}H_2O$	time	product (yield)
1	*p*-$MeC_6H_4NO_2$	1.2 mmol	7 h	*p*-$MeC_6H_4NH_2$ (95%)
2	*p*-$ClC_6H_4NO_2$	1.2 mmol	14 h	*p*-$ClC_6H_4NH_2$ (93%)
3	*p*-$BrC_6H_4NO_2$	1.2 mmol	7 h	*p*-$BrC_6H_4NH_2$ (94%)
4	*p*-$IC_6H_4NO_2$	1.2 mmol	10 h	*p*-$IC_6H_4NH_2$ (95%)
5	$C_6H_5NO_2$	1.2 mmol	7 h	$C_6H_4NH_2$ (91%)
6[b]	*p*-$CH_3OC_6H_4NO_2$	2.4 mmol	14 h	*p*-$MeOC_6H_4NH_2$ (92%)
7[b]	*p*-$CH_3COC_6H_4NO_2$	1.8 mmol	36 h	*p*-$CH_3C(=N\text{-}NH_2)C_6H_4NH_2$ (73%)
8[b]	*p*-$HCOC_6H_4NO_2$	2.4 mmol	24 h	*p*-$HC(=N\text{-}NH_2)C_6H_4NH_2$ (72%)
9[b]	*p*-$MeOOCC_6H_4NO_2$	2.4 mmol	30 h	*p*-$MeOOCC_6H_4NH_2$ (42%)
10[b]	*p*-$HOOCC_6H_4NO_2$	3.6 mmol	30 h	*p*-$HOOCC_6H_4NH_2$ (96%)
11[b]	*p*-$H_2NC_6H_4NO_2$	3.6 mmol	30 h	*p*-$H_2NC_6H_4NH_2$ (61%)[c]
12[b]	*p*-$HOC_6H_4NO_2$	3.6 mmol	30 h	*p*-$HOC_6H_4NH_2$ (40%)[c]
13.	*p*-$H_2NCOC_6H_4NO_2$	1.2 mmol	7 h	*p*-$H_2NCOC_6H_4NH_2$ (59%)[d]

[a] Reaction conditions: nitroarene (0.6 mmol), complex **1** (0.25 mmol%) and $N_2H_4{\cdot}H_2O$ (1.2 mmol) in ethanol (1 mL) at 80 °C; isolated yield.
[b] Complex **1** (0.5 mmol%).
[c] No isolation; NMR yields.
[d] Accompanied with *p*- $H_2NCOC_6H_4N(OH)H$ (40%).

interaction to promote the reduction.

3.4. Substrate scope of the reduction

With the above optimized conditions, a study to explore the reduction of various nitroarenes catalyzed by **1** was investigated (Table 5). Most aromatic nitro compounds were found to undergo the reduction to afford the respective anilines in good to excellent yields. In particular, the halo-substituted nitrobenzenes were reduced to yield the corresponding halo-anilines (Table 5, entries 2–4). In most cases, the reduction of halo-substituted nitrobenzenes always accompanies with the reduction of halogen, but this catalytic system offers an efficient way in this regard. In order to reach good yields, it is required to use excess of hydrazine for the reduction of acetyl or formyl substituted nitrobenzene, because of the consumption of hydrazine in the formation of hydrazone functionality [15]. Reduction of methyl *p*-nitrobenzoate provided the desired product methyl *p*-aminobenzoate in 42% yield with unidentified products due to the reaction of hydrazine with the ester functionality (Table 5, entry 9). However, the use of *p*-nitrobenzoic acid as substrate gave *p*-aminobenzoic acid in 96% yield (Table 5, entry 10). Reductions of *p*-nitro-aniline and *p*-nitrophenol proceeded similarly, but we had troublesome on the purification of the products (Table 5, entries 11–12). From these results, it appears that the developed procedure is applicable to nitroarenes containing both electron withdrawing and electron donating substituents. Substrates with electron withdrawing substituents require a longer time and excess of hydrazine. However, we found that the reaction of *p*-$H_2NCOC_6H_4NO_2$ under the standard condition gave the corresponding aniline in 59% accompanied with the hydroxyamine intermediate (Table 5, entry 13), indicating that the reduction of hydroxylamine is presumably to be the limiting step.

However, when using 1-nitrocyclexene and 2-phenyl-1-nitroethane, the corresponding reduced amine product was not obtained under the catalytic conditions. These reactions provided a mixture of complex substance. Apparently, this catalysis is only applicable to the aromatic nitro compounds.

4. Summary

In this work, a diruthenium complex **1** hosted by an anthyridine-based ligand has been prepared and structurally characterized. Notably, this complex appears to be an excellent pre-catalyst for reduction of nitroarenes with the use of hydrazine as the reducing agent. From the analysis of the activity of **1** towards various intermediates, the reaction pathway of this reduction catalyzed by **1** involves the direct reduction of nitro compound to form hydroxylaminearene, which is subsequently reduced to the final product, without going through nitrosoarene as the intermedaite. Such a direct reduction is quite rare in a homogeneous system. In addition, various substrates with other reducible functionality such as halo functionality were unaffected during the reduction, but carbonyl functionality may lead to the formation hydrazones during the reductions. However, the mechanism in detail on the direct formation of the hydroxyaminoarenes by the diruthenium complex remains unclear in current stage.

Acknowledgments

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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.2019.01.005.

References

[1] A.M. Tafesh, J. Weiguny, A review of the selective catalytic reduction of aromatic nitro compounds into aromatic amines, isocyanates, carbamates, and ureas using CO, Chem. Rev. 96 (1996) 2035–2052.
[2] (a) R.V. Jagadeesh, G. Wienhöfer, F.A. Westerhaus, A.-E. Surkus, H. Junge, K. Junge, M. Beller, A convenient and general ruthenium-catalyzed transfer hydrogenation of nitro- and azobenzenes, Chem. Eur. J. 17 (2011) 14375–14379;
(b) S.P. Annen, H. Grützmacher, Nitrosobenzene as a hydrogen acceptor in rhodium catalyzed dehydrogenation reactions of alcohols: synthesis of aldehydes and azoxybenzenes, Dalton Trans. 41 (2012) 14137–14145;
(c) G. Wienhoefer, M. Baseda-Krueger, C. Ziebart, F.A. Westerhaus, W. Baumann, R. Jackstell, K. Junge, M. Beller, Hydrogenation of nitroarenes using defined iron-phosphine catalysts, Chem. Commun. 49 (2013) 9089–9091;
(d) S. Hohloch, L. Suntrup, B. Sarkar, Arene–ruthenium(II) and −iridium(III) complexes with "click"-based pyridyl-triazoles, bis-triazoles, and chelating abnormal carbenes: applications in catalytic transfer hydrogenation of nitrobenzene, Organometallics 32 (2013) 7376–7385;
(e) S. Chen, G. Lu, C. Cai, Iridium-catalyzed transfer hydrogenation of nitroarenes to anilines, New J. Chem. 39 (2015) 5360–5365 and references therein.
[3] S.-T. Yang, P. Shen, B.-S. Liao, Y.-H. Liu, S.-M. Peng, S.-T. Liu, Catalytic reduction of nitroarenes by dipalladium complexes: synergistic effect, Organometallics 36 (2017) 3110–3116.
[4] (a) Z. Bian, S. Das, M.H. Wai, P. Hongmanorom, S. Kawi, A review on bimetallic nickel-based batalysts for CO_2 reforming of methane, ChemPhysChem 18 (2017) 3117–3134;
(b) Y.-B. Huang, J. Liang, X.-S. Wang, R. Cao, Multifunctional metal–organic framework catalysts: synergistic catalysis and tandem reactions, Chem. Soc. Rev. 46 (2017) 126–157;
(c) J. Fu, X. Huo, B. Li, W. Zhang, Cooperative bimetallic catalysis in asymmetric allylic substitution, Org. Biomol. Chem. 15 (2017) 9747–9759;
(d) J. Serrano-Plana, I. Garcia-Bosch, A. Company, M. Costas, Structural and reactivity models for copper oxygenases: cooperative effects and novel reactivities, Acc. Chem. Res. 48 (2015) 2397–2406 and references therein.
[5] (a) Y.-H. Lo, Y.-H. Liu, S.-M. Peng, S.-T. Liu, Ruthenium complexes with an anthyridine-based ligand. Synthesis, characterization and catalytic activity, J. Chin. Chem. Soc. 60 (2013) 839–845;
(b) D.A. Freedman, J.K. Evju, M.K. Pomije, K.R. Mann, Convenient synthesis of tris-heteroleptic ruthenium(II) polypyridyl complexes, Inorg. Chem. 40 (2001) 5711–5715.
[6] G.M. Sheldrick, SHELXS-97, Acta Crystallogr. Sect. A Found. Crystallogr. 46 (1990) 467–473.
[7] G.M. Sheldrick, SHELXL-97, University of Göttingen, Göttingen, Germany, 1997.
[8] N. Ono, The Nitro Group in Organic Synthesis, Wiley-VCH, New York, 2001.
[9] Z. Zhao, H. Yang, Y. Li, X. Guo, Cobalt-modified molybdenum carbide as an efficient catalyst for chemoselective reduction of aromatic nitro compounds, Green Chem. 16 (2014) 1274–1281.
[10] E.A. Gelder, S.D. Jackson, C.M. Lok, The hydrogenation of nitrobenzene to aniline: a new mechanism, Chem. Commun. (2005) 522–524.
[11] A. Corma, P. Concepción, P. Serna, A different reaction pathway for the reduction of aromatic nitro compounds on gold catalysts, Angew. Chem. Int. Ed. 46 (2007) 7266–7269.
[12] P.L. Gkizis, M. Stratakis, I.N. Lykakis, Catalytic activation of hydrazine hydrate by gold nanoparticles: chemoselective reduction of nitro compounds into amines, Catal. Commun. 36 (2013) 48–51.
[13] S. Wu, G. Wen, X. Liu, B. Zhong, D.S. Su, Model molecules with oxygenated groups catalyze the reduction of nitrobenzene: insight into carbocatalysis, ChemCatChem 6 (2014) 1558–1561.
[14] N.D. Jones, B.R. James, Homo- and heterobimetallic precursor catalysts for the Heck reaction, and a proposal for a general catalytic cooperativity index, Adv. Synth. Catal. 344 (2002) 1126–1134.
[15] U. Sharma, P. Kumar, N. Kumar, V. Kumar, B. Singh, Highly chemo- and regioselective reduction of aromatic nitro compounds catalyzed by recyclable copper(II) as well as cobalt(II) phthalocyanines, Adv. Synth. Catal. 352 (2002) 1834–1840.