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Synthesis and Catalytic Hydrogen Transfer Reaction of Ruthenium(II) Complex

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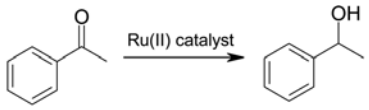
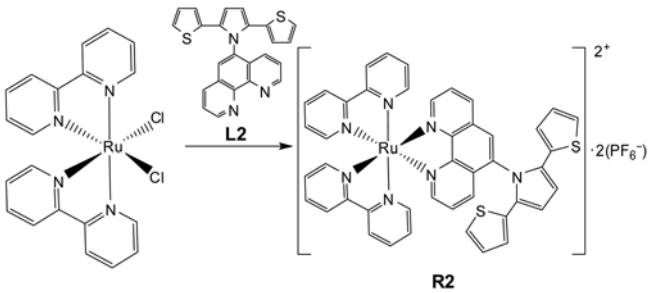
The catalytic hydrogenation of a ketone is a basic and critical process for making many types of alcohols used as the final products and precursors in the pharmaceutical, agrochemical, flavor, fragrance, materials, and fine chemicals industries.[1] The catalytic hydrogenation process developed by Noyori is a very attractive process. Formic acid and 2-propanol have been used extensively as hydrogenation sources. The advantage of using 2-propanol as a hydrogen source is that the only side product will be acetone, which can be removed easily during the workup process.[2] Hydrogen transfer (HT) catalysis, which generates alcohols through the reduction of ketones, is an attractive protocol that is used widely. Ruthenium(II) complexes are the most useful catalysts for the hydrogen transfer (HT) of ketones.[3] In this method, a highly active catalytic system employs a transition metal as a catalyst to synthesize alcohols, and is a replacement for the hydrogen-using hydrogenation process. The most active system is based on Ru, Rh and Ir, which includes a nitrogen ligand that facilitates the formation of a catalytically active hydride and phosphorus.[4]

Accordingly, this paper reports the best results for the hydrogen transfer reaction using novel Ru(II) complexes. Research examining the effectiveness of the catalysts employed acetophenone as the benchmark substrate (Scheme 1).

A suspension of $RuCl_3 \cdot 3H_2O$ (0.331 g, 1.6 mmol) and 2,2'-bipyridine (0.5 g, 3.2 mmol) in DMF (3.0 mL) was heated under reflux for 12 hours. [PhenTPy] dissolved in 100 mL of hot ethanol was added to 0.50 g (0.96 mmol) of *cis*-Ru-$(bpy)_2Cl_2$,[4e] dissolved in 50 mL of hot H_2O. The solution was deaerated with argon for 20 minutes and heated under reflux for three hours in an argon atmosphere (Scheme 2).



Scheme 1



Scheme 2. Preparation of Ruthenium(II) complex [Ru(bpy)$_2$-(PhenTPy)].

As shown in Figure 1 (**R1**, black line), a well-defined redox couple (II/II') was observed at +0.13/+0.22 V, corresponding to the Ru^{III}/Ru^{II} reaction.[4f] The Ru complex exhibits a redox peak because dimethylsulfoxide (DMSO) is an ambidentate ligand known for linkage isomerization that is dependent on the presence of O-bound or S-bound DMSO moieties. The redox couple appearing at the lower potential indicates that ruthenium interacts with the O-bound DMSO ligand.[4g] The redox peaks of the ligand, however, appeared at (I/I') and (III/III'). These were assigned to the redox reaction of the phenanthroline moiety of the PhenTPy ligand

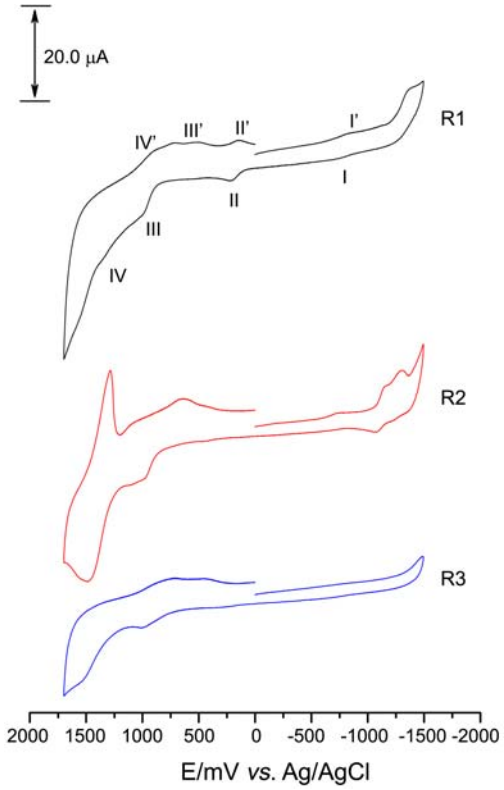
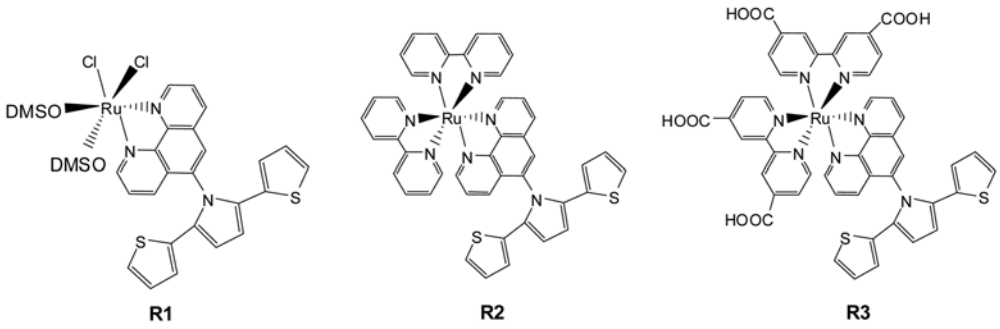


Figure 1. Cyclic voltammograms of 1.0 mM monomer Ruthenium complexes **R1** (black line), **R2** (red line) and **R3** (blue line) in 0.1 M TBAP/CH_2Cl_2 solution, scan rate of 100.0 mV/s.



itself[4h] and the oxidation of the thiophen background to be polymerized, respectively.[4i] In this case, the reversibility of the redox peaks of the Ru(II) complex was better than that of the ligand and a "prewave" was also observed at the positive foot of the PhenTPy ligand-based reduction.[4h] In addition, the redox peak of (IV/IV') observed at +1.32/+0.94 V corresponded to the Ru^{III}/Ru^{IV} reaction.[4j] Figure 1 shows the cyclic voltammetry behavior of R2 (red line) in a 0.1 M TBAP/CH_2Cl_2 solution. Two oxidation peaks at +1.32 and +0.97 V were assigned to Ru^{III}/Ru^{IV} and PhenTPy oxidation. A bpy ligand showed two irreversible redox processes at −1.01/−1.17 V and −1.25/−1.32 V. Two redox waves related the Ru ion were observed at +0.82/+0.43 V and +1.0/+0.72 V, as shown in Figure 1 (**R3**, blue line).

As shown in Table 1, experiments on the hydrogen transfer reactions of acetophenone with 2-propanol were conducted to yield the expected 1-phenylethanol with the Ru(II) complexes. 2-Propanol was used as the solvent. The **R1**, **R2** and **R3** catalysts (0.5 mol %) were used under reflux conditions. The **R2** catalyst showed the best results, 41%. Using **R2**, an additional experiment was conducted to determine the optimum reaction conditions. The conversion was improved by increasing quantity of the catalyst to 1.0 mol % or the reaction temperature to 150 °C. The quantity of the catalyst could be reduced to 0.1 mol % by increasing the reaction temperature to 150 °C using a stainless steel reactor. Under the conditions of 0.01 and 0.05 mol %, the level of conversion was 38 and 54%, respectively, which was unsatisfactory. For the reaction at high temperatures, **R1** and **R3** showed > 90% conversion. All the experiments were conducted for three hours. The conversion was 61% when the reaction time was decreased to 30 minutes, despite the quantity of the catalyst being increased to 1.0 mol %. A selection of substrates was made for further investigation. The reactions were carried out with various ketones using catalyst **R2** at 150 °C. A series of aromatic carbonyl compounds were reduced successfully to the corresponding alcohols in the presence of isopropanol, reaching high conversion. benzophenone, and 1-(naphthalen-2-yl)ethanone gave the expected adducts of diphenylmethanol, and 1-(naphthalen-2-yl)ethanol as the sole product in good to high yield (76%, and 99%). Aliphatic rings, such as cyclohexanone, received hydrogen atoms from isopropanol without byproducts in 80% yield.

Table 1. Results of transfer hydrogenation of acetophenone by 2-propanol catalyzed Ru-complexes

Entry	Cat (mol %)	Temp (°C)	Time (h)	Conv (%)[a]
1	**R1** (0.5)	reflux	3	18
2	**R2** (0.5)	reflux	3	41
3	**R3** (0.5)	reflux	3	21
4	**R2** (1.0)	reflux	3	90
5	**R2** (1.0)	150[b]	0.5	61
6	**R2** (0.5)	150[b]	3	100
7	**R2** (0.1)	150[b]	3	100
8	**R2** (0.01)	150[b]	3	38
9	**R2** (0.05)	150[b]	3	54
10	**R1** (0.1)	150[b]	3	94
11	**R3** (0.1)	150[b]	3	91

[a]determined by ^{1}H-NMR. [b]autocleave used.

In conclusion, the ruthenium(II) complex [Ru(bpy)$_2$-(PhenTPy)] was synthesized, and used for the transfer hydrogenation of ketones and the desired products were obtained in good yield. Based on the presented results, transition-metal complexes can be used as catalysts for a wide range of organic transformations. The relationship between the electro-reduction current density and temperature are being examined in this laboratory. Attempts to improve the catalytic activity and determine the transfer hydrogenation mechanism are currently in progress.

Experimental Section

Synthesis and Characterization of Ru(II) Complex (R1). The detail synthetic procedure and characterizations were presented in an earlier publication.[4f] Synthesis of characterization Ligand (**L2**): A round-bottom flask equipped with a nitrogen inlet and a agnetic stirrer was charged with 1,4-di(2-thienyl)-1,4-butanedione (5 mM, 1.25 g), 5-amino-1,10-phenanthroline (2 mM, 0.40 g), *p*-toluenesulfonic acid (PTSA) (5.4 mM, 1.03 g) and toluene (15 mL). The result mixture was stirred and refluxed for 32 h under nitrogen. Evaporation of the toluene, followed by flash column chromatography (SiO_2, dichloromethane), afforded the desired compound as a brown solid (85%); mp 130 °C, ^{1}H-NMR: (300 MHz; $CDCl_3$) 6.51 (m, 2H), 6.65 (m, 2H), 6.72 (s, 2H), 6.88 (dd, J = 5.1 Hz, 2H), 7.52 (m, 1H), 7.69 (m, 2H), 8.00 (s, 1H), 8.27 (d, J = 1.72 Hz, 1H), 9.17 (dd, J = 4.3 Hz, 1H), 9.28 (dd, J = 4.3 Hz, 1H); ^{13}C-NMR: (300

MHz; $CDCl_3$) 102.87, 112.90, 116.88, 118.95, 121.52, 122.24, 127.60, 128.00, 128.58, 130.41, 132.28, 133.59, 136.43, 139.90, 149.86, 154.69. MS 409 (M^+, 100%), Exact MS Caled for $C_{24}H_{15}N_3S_2$: 409.0707. Found: 409.0620.

Synthesis and Characterization of Ru(II) Complex (R2). 10% molar excess of PhenTPy (0.44 g, 1.08 mmol) dissolved in 100 mL of hot ethanol was added to 0.500 g (0.96 mmol) of *cis*-Ru-$(bpy)_2Cl_2{\cdot}2H_2O$[4e] dissolved in 50 mL of hot H_2O. The solution was deaerated with argon for 20 min and then heated at reflux for 3h under argon. Most of the ethanol was removed by rotary evaporation, and a 5-fold molar excess of NH_4PF_6 (0.98 g, 4.8 mmol) dissolved in H_2O was added to produce an orangish precipitate. The product was collected by suction filtration and purified by elution chromatography on an alumina column with a 2:1 toluene:acetonitrile solution. After elution and evaporation, the product was redissolved in a minimum amount of acetonitrile (< 5 mL) and dropped into 350 mL of rapidly stirred diethyl ether. The orangish powder was collected by suction filtration, washed with diethyl ether, and dried overnight under vacuum: Yield; 75%. HRMS (FAB) *m/z* calcd for ($C_{44}H_{31}NRuS_2$) 823.1124.

Synthesis and Characterization of Compound *cis*-Dichlorobis(4,4'-dicarboxy-2,2'-bipyridine)ruthenium. Under nitrogen atmosphere, in a 500 mL three-necked flask were placed commercially available $RuCl_3{\cdot}3H_2O$ (2.53 g, 9.68 mmol), 2,2'-Bipyridine-4,4'-dicarboxylic acid (4.50 g, 18.4 mmol) and 300 mL of *N,N*-dimethylformamide, and the mixture was refluxed for 24 h. After cooling down, the mixture was filtered, and the resulting filtrate was evaporated under vacuum to dryness. The resulting residue was washed with acetone/diethyl ether (1:4), 300 mL of 2 M HCl was added, and the mixture was stirred with ultrasonic for twenty minutes and then stirred for two hours without ultrasonic. After stirring, an insoluble material was collected by filtration and washed with 2.0 M HCl, acetone/diethyl ether (1:4) and diethyl ether. After drying under vacuum, 5.75 g of compound **3** was obtained. Yield: 85%. *Anal. Calc.* for $RuC_{24}H_{16}N_4Cl_2O_8$: C, 41.38; H, 2.87; N, 8.05; Cl, 10.20. Found: C, 41.52; H, 2.92; N, 8.17; Cl, 10.23%. ^{1}H NMR (D_2O/NaOD) δ ppm: 9.66 (4H, d), 8.87 (4H, s), 8.11 (4H, d).

Synthesis and Characterization of Ru(II) Complex (R3). *cis*-Dichlorobis(4,4'-dicarboxy-2,2'-bipyridine)ruthenium (180 mg, 0.27 mmol) and PhenTPy (225 mg, 0.55 mmol) were dissolved in ethylene glycol (30 mL), and the reaction mixture was heated to 170 °C under argon for 2 h. Then tetrabutyl ammonium hydroxide (1.1 g, 1.37 mmol) was added to the reaction mixture and further heated to 170 °C under argon for 2 h. After evaporating the solvent, the resulting solid was dissolved in water (15 mL) and was titrated with 0.2 M HNO_3. The reaction mixture was kept in a refrigerator overnight and allowed to warm to 25 °C. The resulting precipitation was collected on a sintered glass crucible by suction filtration. Yield: 35%. HRMS (FAB) *m/z* calcd for ($C_{48}H_{31}N_7O_8RuS_2$) 1001.0724.

A Typical Procedure for Hydrogen-transfer Reactions. In the standard reaction condition, Ru(II) complex (**R2**) (1.0 mg, 0.1 mol % with respect to the substrate concentration), acetophenone (0.13 mL, 1.1 mol), isopropanol (7.0 mL), and NaOH (4 mg, 0.1 mmol) were placed in a 25 mL stainless steel reactor. The reactor was tightly closed, and the mixture was stirred at 150 °C for 3 h. The catalysts were separated from the clean supernatant by centrifugation. The reaction products were analyzed by ^{1}H-NMR.

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