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Hydrogenation

New Ruthenium Complexes Based on Tetradentate Bipyridine Ligands for Catalytic Hydrogenation of Esters

Fangyuan Wang,[a] Xuefeng Tan,[a] Hui Lv,*[a, b] and Xumu Zhang*[a, c]

Abstract: New bipyridinemethanamine-containing tetradentate ligands and their corresponding ruthenium complexes have been synthesized. The synthesized complexes performed well in the hydrogenation of a variety of esters with high efficiency (TON up to 9700) giving alcohols in good yields.

Ester reduction is one of the most important reactions and widely used in organic synthesis; however, this fundamental transformation is still a challenge both in the laboratory and industry. Generally, the ester reduction heavily relies on metal–hydride reagents (e.g., $LiAlH_4$ or $NaBH_4$),[1] which suffer from inherent drawbacks, such as use of stoichiometric amounts of the reagents, hazardous operations, tedious workup procedures, and high level of residual wastes.[2] In addition, the reduction of esters in industry mainly proceeds by heterogeneous catalysis under harsh conditions (200–300 °C, 200–300 atm).[3] Therefore, the development of efficient and environmentally friendly approaches is highly desirable.

In the past decades, homogenous catalytic hydrogenation of esters has been widely investigated, but significant progresses have only been made recently. In 2006, Milstein and co-workers reported their pioneer work in catalytic hydrogenation of esters with a PNN pincer-type ruthenium complex, in which an aromatization/dearomatization process was involved and exhibited good activities under relatively mild conditions (5 atm H_2, 115 °C).[4] Since then, catalytic hydrogenation of esters with homogenous catalysts have undergone a rapid development, and a series of efficient catalysts for ester reduction have been developed by Saudan,[5] Ikariya,[6] Kuriyamma,[7] Morris,[8] Gusev,[9] Pidko,[10] and others.[11] Very recently, Zhou[12] and our group[13] reported the bipyridyl-containing tetradentate ligands and a pyridin-2-ylmethanamine-containing tetradentate ligand, respectively, both of the ligands exhibited high catalytic activities in ester reduction under mild conditions and gave excellent results (Figure 1, TON up to 80 000 and TOF up to 10 000 h^{-1} for catalyst **I**, and TON up to 91 000 and TOF up to 1896 h^{-1} for catalyst **II**). Although great progresses have been made in the reduction of ester, developing more practical and efficient ligands in terms of ease of preparation and high turnover number (TON) is significant. Herein, we report a new type of bipyridinemethanamine-containing tetradentate ligands and their applications in catalytic hydrogenation of esters.

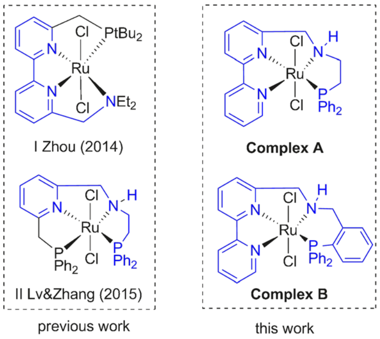

Figure 1. Efficient catalysts for ester hydrogenation.

Intrigued by the great success of catalyst **I** and catalyst **II** in ester reduction, we reasoned that the bipyridine fragment of catalyst **I** is critical to keep high activity due to the coordination capability and stability. For catalyst **II**, the pyridinemethanamine unit is very important to keep high acidity of the N–H group,[14] which is essential to activate the carbonyl group of esters. We envisioned that combination of the two key fragments in one molecule may exhibit high catalytic activity in ester reduction. With these thoughts in mind, we designed two bipyridinemethanamine-containing tetradentate ligands, which could be prepared by a concise synthetic route described in Scheme 1. Subsequently, their Ru complexes were prepared by the following procedure: $[RuCl_2(PPh_3)_3]$ was reacted with the ligands in toluene at 110 °C, and then the precipitation was washed by anhydrous ether. Ruthenium complexes **A** and **B** were obtained as air-stable (stable in air for at least

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[a] F. Wang, X. Tan, Prof. H. Lv, Prof. X. Zhang
Key Laboratory of Biomedical Polymers of Ministry of Education & College of Chemistry and Molecular Sciences
Wuhan University, Wuhan, Hubei 430072 (China)
E-mail: huilv@whu.edu.cn
xumu@whu.edu.cn

[b] Prof. H. Lv
Beijing National Laboratory for Molecular Sciences
CAS Key Laboratory of Molecular Recognition and Function
Institute of Chemistry, Chinese Academy of Sciences
100190 Beijing (China)

[c] Prof. X. Zhang
Department of Chemistry
South University of Science and Technology of China
Shenzhen, Guangdong, 518055 (China)

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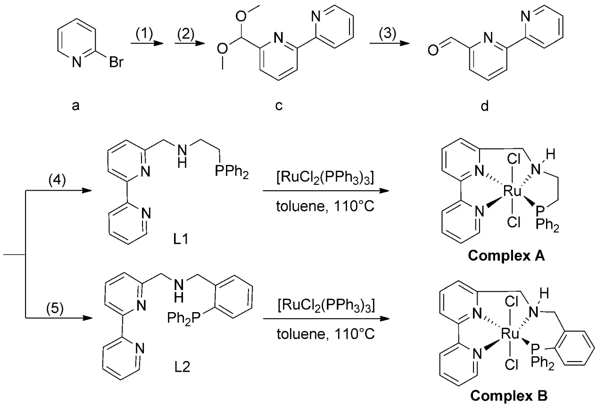


Scheme 1. The preparation of tetradentate bipyridine ligands and their corresponding ruthenium complexes. Reaction conditions: (1) *n*BuLi, $ZnCl_2 \cdot 2THF$, THF, −78 °C, 2 h. (2) [$Pd(PPh_3)_4$], 6-bromopyridine-2-carbaldehyde, THF, rt–50 °C, 36 h. (3) 37 % HCl (aq), THF, 60 °C, 4 h. (4) 2-(diphenylphosphino)ethanamine, $NaBH_4$, MeOH, rt, 8 h. (5) $NaBH_4$, MeOH, rt, 8 h, 2-(diphenylphosphino)benzenemethanamine.

3 months) deep red–violet solids in excellent yields. The ^{31}P NMR spectra of complexes **A** and **B** exhibited singlets at $\delta = 47.77$ and 49.68 ppm, respectively, demonstrating that the phosphorus atoms of the ligands were coordinated to the ruthenium atom. The geometry structure of complex B was established by X-ray diffraction analysis, which revealed that the catalyst was a hexacoordinate complex (Figure 2).

In order to evaluate the efficiency of complexes **A** and **B** in the reduction of esters, we chose methyl benzoate as a model substrate to optimize the reaction conditions. As shown in Table 1, when the reaction was carried out in toluene at 100 °C under 50 atm of H_2, complex **B** exhibited excellent activity in the presence of NaOMe (10 mol %), and methyl benzoate was reduced to alcohol with full conversion, whereas complex **A** just gave moderate yield under the same conditions (Table 1, entries 1–2). Thus, complex **B** was chosen as the catalyst for further optimization. On decreasing the catalyst loading to 0.01 mol %, the reaction proceeded smoothly and generated benzyl alcohol with 6500 TON (Table 1, entry 3). Subsequently, the screening of bases and solvents revealed that NaOEt and toluene were the best choice and afforded desired product with up to 9800 TON (Table 1, entries 4–13)

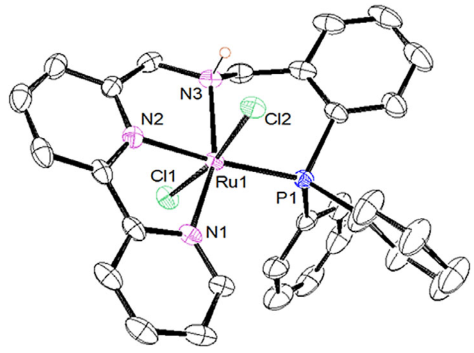
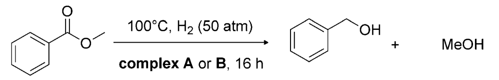


Figure 2. X-ray structure of complex **B**. Thermal ellipsoids set at 30 % probability. H atoms and disorders were omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru1–N1 2.077(3), Ru1–N2 2.007(3), Ru1–N3 2.101(3), Ru1–P1 2.2895(9), Ru1–Cl1 2.4167(9), Ru1–Cl2 2.4172(8), N2–Ru1–N1 78.59(12), N2–Ru1–N3 80.60(12), N1–Ru1–N3 158.81(12), N2–Ru1–P1 174.07(8), N1–Ru1–P1 107.34(9), N3–Ru1–P1 93.51(8), N2–Ru1–Cl1 85.29(8), N1–Ru1–Cl1 93.15(8), N3–Ru1–Cl1 89.05(8), P1–Ru1–Cl1 94.04(3), N2–Ru1–Cl2 86.42(8), N1–Ru1–Cl2 90.38(7), N3–Ru1–Cl2 84.38(8), P1–Ru1–Cl2 93.67(3), Cl1–Ru1–Cl2 170.17(3).

Table 1. Hydrogenation of methyl benzoate with ruthenium complexes **A** and **B**.[a]

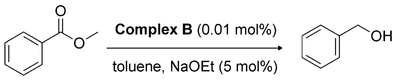


Entry	Cat (mol %)	Base (mol %)	Solvent	Yield [%][b]
1	A (0.02)	NaOMe (10)	toluene	40
2	B (0.02)	NaOMe (10)	toluene	99
3	B (0.01)	NaOMe (10)	toluene	65
4	B (0.01)	NaOMe (5)	toluene	94
5	B (0.01)	NaOEt (5)	toluene	98
6	B (0.01)	KO*t*Bu (5)	toluene	8
7	B (0.01)	NaOEt (5)	MeOH	8
8	B (0.01)	NaOEt (5)	EtOH	31
9	B (0.01)	NaOEt (5)	*i*PrOH	26
10	B (0.01)	NaOEt (5)	THF	16
12	B (0.01)	NaOEt (5)	dioxane	14
11	B (0.01)	NaOEt (5)	neat	5
13	B (0.01)	NaOEt (5)	DCM	0

[a] Reaction conditions: methyl benzoate (5 mmol), solvent (3 mL), H_2 (50 atm), 100 °C, 16 h. [b] Yield was determined by GC using *n*-tridecane as internal standard.

Also, the effects of temperature and pressure of hydrogen were investigated. The pressure of H_2 is critical to the reaction (Table 2, entries 1–4). Generally, a lower pressure gives inferior results for the reaction. The best turnover number was obtained, when the reaction was carried out at 50 atm of H_2. Further increasing the hydrogen pressure to 70 atm had no positive effects on the yield. The temperature also has a great influence on the reaction. Generally, increasing the temperature was beneficial for the turnover numbers, but when the temperature was higher than 80 °C, there was no further improvement of the yield (Table 2, entry 3 and entries 5-7)

Table 2. Optimization of the reaction temperature and pressure of H_2.[a]



Entry	*P* [atm][b]	*T* [°C][c]	Yield [%][d]
1	10	100	8
2	30	100	31
3	50	100	98
4	70	100	98
5	50	40	14
6	50	60	90
7	50	80	99

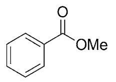
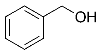
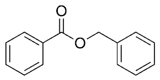
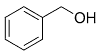
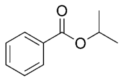
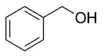
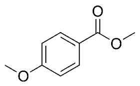
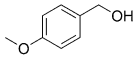
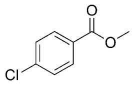
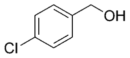
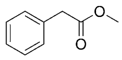
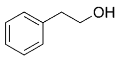
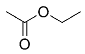
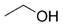
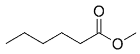
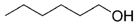
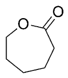
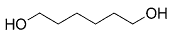
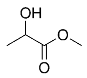
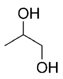
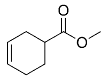
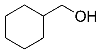
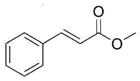
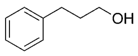
[a] Reaction conditions: methyl benzoate (5 mmol), NaOEt (0.25 mmol), toluene (3 mL), 16 h. [b] Pressure of H_2. [c] Temperature of the reaction. [d] Yield was determined by GC using *n*-tridecane as internal standard.

Consequently, the substrate scope of the hydrogenation of carboxylic esters was examined under optimal conditions (80 °C, 50 atm H_2, toluene). As shown in Table 3, all esters examined here can be reduced to the corresponding alcohols, although there were great differences in turnover numbers. Generally, unfunctionalized esters, such as simple aromatic esters and aliphatic esters, can be reduced with higher turnover numbers than functionalized esters. For aromatic esters, the steric and electronic effects have great influences on the results. Aromatic esters with high steric hindrance, such as isopropyl benzoate, gave the corresponding alcohols with a substantial reduction in TONs compared with methyl and benzyl benzoate (Table 3, entries 1–3). Substituent groups on the benzene ring, regardless of their electron-donating or -withdrawing nature, are inferior to the reaction, and the TON dropped dramatically. (Table 3, entries 4–5). Aliphatic esters performed well for this reaction and long chain aliphatic esters were converted to alcohols with relative low turnover numbers (Table 3, Entries 6–8). Cyclic aliphatic ester was also converted to 1, 6-Hexanediol smoothly with more than 1000 TONs (Table 3, Entry 9). Functionalized esters, such as dimethyl succinate typically challenging substrate for ester reduction were also tolerated for this reaction and generated corresponding alcohols with moderate TONs (Table 3, Entry 10). Unsaturated carboxylic esters were also evaluated, but they didn't exhibited chemoselectivity in the reaction, both alkene group and ester group were converted with moderate to high TONs (Table 3, Entries 11–12).

In conclusion, we have synthesized new bipyridinemethanamine-containing tetradentate ligands and their corresponding ruthenium complexes, which exhibited good catalytic activities in the reduction of esters (up to 9700 TON). The reaction displayed a wide substrate scope, giving alcohols in good to excellent yields. Development of new strategies and novel catalysts for the ester hydrogenation is ongoing in our group.

Table 3. Catalytic hydrogenation of esters in the presence of Complex **B**.[a]

$$\text{Ester} \xrightarrow[\text{toluene, } H_2\text{ (50 atm), 80°C, 16h}]{\textbf{Complex B}\text{, NaOEt (5 mol\%}} \text{Alcohol}$$

Entry	Substrate	Product	S/C	Yield [%][b]
1			10 000	99 (97)
2			10 000	97 (95)
3			2500	98 (93)
4			2500	91 (89)
5			2000	82 (80)
6			5000	71 (70)
7[c]			5000	95
8			2500	99 (95)
9			2500	48
10			200	99
11			1000	97 (90)
12			100	84 (80)

[a] Reaction conditions: substrate (5 mmol), NaOEt (0.25 mmol), toluene (3 mL), H_2 (50 atm), 80 °C, 16 h. [b] GC yield using *n*-tridecane as internal standard, and the value in parentheses is the isolated yield. [c] Substrate (10 mmol), NaOEt (0.5 mmol), H_2 (50 atm), 80 °C, 16 h.

Experimental Section

General procedure for the reduction of esters

In an argon glovebox, a 5 mL glass vial equipped with a magnetic stirring bar was added the required amount of complex **B** (0.01–0.5 mol%, or toluene solution of complex B, 1 mg mL^{-1}) and NaOEt (5 mol%) successively. In the mixture was added substrate (5 mmol) and toluene (3 mL in all), then the glass vial was placed in a 150 mL stainless-steel reactor (5 glass vials were used each time). The autoclave was carefully pressurized/depressurized with hydrogen (20 atm) gas three times before the reaction pressure of 50 atm was adjusted. The hydrogenation was performed at 80 °C for 16 h. The autoclave was depressurized carefully and the crude mixture was filtered through a plug of silica, and then was purified by column chromatography to obtain the desired product.

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Keywords: alcohols · esters · pyridine ligands · ruthenium · synthetic methods

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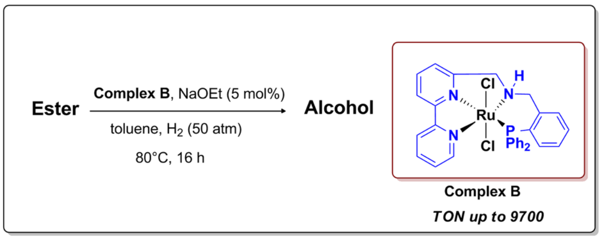
COMMUNICATION



A straightforward way to alcohols! New bipyridinemethanamine-containing tetradentate ligands and their corresponding ruthenium complexes have been synthesized. The synthesized complexes performed well in the hydrogenation of a variety of esters with high efficiency (TON up to 9700) giving alcohols in good yields (see scheme).

Hydrogenation

Fangyuan Wang, Xuefeng Tan, Hui Lv, Xumu Zhang**

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New Ruthenium Complexes Based on Tetradentate Bipyridine Ligands for Catalytic Hydrogenation of Esters