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Ruthenium Complexes with *N*-Functionalized Secondary Amino Ligands: A New Class of Catalysts toward Efficient Hydrogenation of Esters‡

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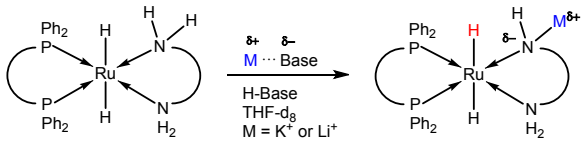
A series of ruthenium complexes (*o*-$PPh_2C_6H_4NHR)_2RuCl_2$ (R = Me, 3; Et, 4; CH_2Ph, 5) and (*o*-$PPh_2C_6H_4NH_2)[(CH_2NHR)_2]RuCl_2$ (R = Me, 7; Et, 8; *i*Pr, 9) modulated with mono-*N*-functionalized secondary amino ligand were synthesized and demonstrated as efficient catalysts in hydrogenation of esters into alcohols. The catalytic performances of these new complexes are much better than their corresponding primary amino ligand constituted complexes (*o*-$PPh_2C_6H_4NH_2)_2RuCl_2$ (2) and (*o*-$PPh_2C_6H_4NH_2)[(CH_2NH_2)_2]RuCl_2$ (6). The significant improvement is attributed to the increased electron density of the secondary amino ligand in comparison with that of the primary amino ligand.

Catalytic hydrogenation of esters into alcohols is one of the most important chemical processes in organic synthesis, and has been attracting extensive attentions.[1] Typically, Metal-NH ligand bifunctional catalysis in homogeneous hydrogenation has achieved significant progress,[2] since the discovery reported by Noyori and co-workers in 1995.[3] The authors discovered that the catalytic activity of phosphine-Ru(II) in aromatic ketones hydrogenation was significantly improved with the addition of 1 equiv. of 1,2-diamino ligand into the system, which they owed to the interaction between amino hydrogen and metal hydride. Recently, we reported that the *o*-$PPh_2C_6H_4NH_2$ ligand coordinated ruthenium complexes $[(PPh_3)(o\text{-}PPh_2C_6H_4NH_2)RuCl_2]_2$ (**1**) and (*o*-$PPh_2C_6H_4NH_2)_2RuCl_2$ (**2**) could effectively catalyze the selective hydrogenation of dimethyl oxalate (DMO) into methyl glycolate (MG).[4] The mechanistic and dynamic studies indicate that the cooperation between the ruthenium hydride and the amino hydrogen is responsible for the improved hydrogenation activity.[5]



Scheme 1 Substitution of amino hydrogen by alkali metal cation.

In 2013, Bergens et al. proposed that the amino hydrogen was substituted by alkali metal cation to form the intermediate of catalyst *trans*-[((*R*)-BINAP)((*R*,*R*)-dpen)RuH_2] in hydrogenation of amide and imide carbonyls at low temperatures (Scheme 1).[6] The metal hydride in the in-situ formed active intermediate has higher nucleophilicity to activate the C=O bond of carbonyl derivatives, resulting in promoting the catalytic activity. Recent mechanistic studies also indicated the positive correlation between the catalytic activity of metal-NH catalyst and the nucleophilicity of the metal hydride.[5a,e,7] The nucleophilicity of the metal hydride can be strengthened by increasing the electron density of the central metal, which has been well demonstrated in systems of Ru-MACHO complex $[NH(CH_2CH_2PPh_2)_2]RuHCl(CO)$ and bipyridine-based pincer complex (6-$CH_2P^tBu_2$-bipy)RuHCl(CO). When the CO ligand is replaced with more electron-rich monodentate *N*-heterocyclic carbene and hemilable Et_2N group, respectively, these complexes behaves much more active in catalysis.[8]

Inspired by these, we synthesize Ru-H catalysts coordinated with *N*-functionalized secondary amino ligand, aiming to enhance the nulecophilicity by introducing electron donating substituent on proximal N atoms. Herein, bis(aminophosphine)-ruthenium complexes containing secondary amino groups were designed based on our previous work. In addition, *N*,*N*'-substituted 1,2-diamino ligand was also introduced in this system, since diamino ligands were well known in Noyori-type catalysts.[9] Although 1,2-diamino ligand constituted ruthenium catalysts have been widely used in the catalytic hydrogenation of ketones and aldehydes, but the application in esters hydrogenation is rarely studied, with the

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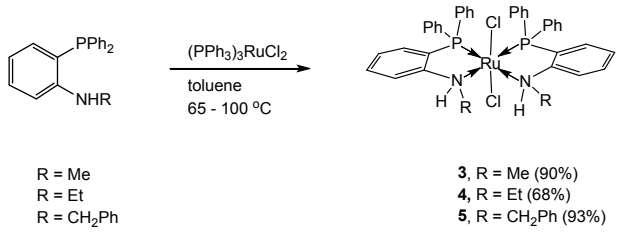
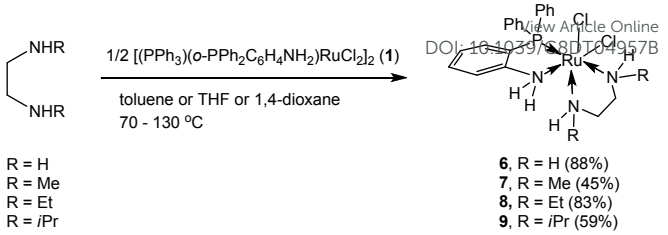
‡ Electronic Supplementary Information (ESI) available: Synthesis, crystallographic details, activity test, and NMR data. CCDC 1884111 & 1884112. For ESI and crystallographic data in CIF see DOI: 10.1039/x0xx00000x



Scheme 2 Synthesis of ruthenium complexes **3**-**5**.



Scheme 3 Synthesis of ruthenium complexes **6**-**9**.

only example reported by Kuriyama et al. in hydrogenation of optically active esters into alcohols.[10] Delightedly, these new species exhibit excellent activity in hydrogenation of esters.

The preparation of secondary amino ligand constituted complexes **3**-**5** and **6**-**9** is outlined in Schemes 2 and 3, respectively. Similar to the preparation of **2**,[4] complexes **3**-**5** were successfully isolated by reaction of $RuCl_2(PPh_3)_3$ with two equivalents of *o*-$PPh_2C_6H_4NHR$ in toluene at 65 to 100 °C. The $^{31}P\{^1H\}$ NMR spectra of **3**, **4**, and **5** exhibit two singlets at 57.61, 61.86; 56.67, 60.03; and 57.66, 59.30 ppm, respectively, revealing that there are two conformational isomers in solution state for each species, and the two *o*-$PPh_2C_6H_4NHR$ ligands bear same chemical environments. This is different from the corresponding primary amine complex **2**, which exhibits only one configuration in solution. Interestingly, the solid state ^{31}P NMR spectrum of **3** merely exhibits one broad peak (Fig. S7‡), suggesting that this complex transformed into one configuration during precipitation. Similar phenomena were also observed in **4** and **5**. Complex **3** has been crystallographically characterized and the molecular structure is presented in Fig. 1.

The ruthenium complexes **6**-**9**, in which the metal centers were simultaneously coordinated with a *o*-$PPh_2C_6H_4NH_2$ ligand and a 1,2-diamino ligand, were prepared by using complex **1** as synthetic precursor. As shown in Scheme 3, the reaction of **1** with two equivalents of $(CH_2NHR)_2$ (R = H, Me, Et, *i*Pr) produced complexes **6**-**9** with yields of 45-88%, respectively. The $^{31}P\{^1H\}$ NMR spectra of **7**, **8**, and **9** exhibit singlets at 71.35, 70.75, and 66.45 ppm, respectively, demonstrating that no PPh_3 ligands coordinated to the ruthenium center. Due to the insolubility of **6**, solid state ^{31}P NMR was measured and only one peak at 69.41 ppm was observed, suggesting the similar structure with **7** (or **8**, **9**). The geometry structure of **8** was established by X-ray diffraction analysis, which reveals the coordination interaction between diamino ligand and the ruthenium center (Fig. 1b). In addition, the two Cl atoms are located in a *cis*-configuration.

To study the catalytic activity of these ruthenium species armed with different secondary amino ligands, we evaluated the performance of complexes **2**-**9** in hydrogenation of DMO into MG under 100 °C with 0.05 mol% ruthenium catalyst, 0.5 mol% NaOMe, and 50 bar H_2 for 1 h. As shown in Fig. 2, to various extents, the activities of complexes **3**-**5** were improved in comparison with **2**, among which **3** gave the best result with a DMO conversion of 77%. The corresponding turnover frequency (TOF) value is 1520 h^{-1}, much higher than that of **2** (160 h^{-1}). In addition, complexes **4** and **5** also showed better activities than **2**, while worse than **3** under the same reaction conditions, which realized DMO conversions of 27% (TOF = 540 h^{-1}) and 24% (TOF = 480 h^{-1}), respectively.

Interestingly, the diamino ligand constituted complexes performed differently in DMO hydrogenation. Complex **6** binding to ethylenediamine showed no catalytic activity. In contrast, *N*,*N*'-dimethyl-1,2-ethanediamine and *N*,*N*'-diethyl-1,2-ethanediamine coordinated complexes **7** and **8** behaved distinctly different activities, which achieved DMO conversions of 36% and 100%, respectively. In addition, small amount of ethylene glycol (EG) (1% yield) was concomitantly produced over **8**. Actually, almost quantitive conversion of DMO has been realized by **8** within 0.5 h (*vide infra*, entry 2, Table 1), and the TOF value is 3920 h^{-1}. This value is nearly 27 and 24 times higher than those of **1** and **2**, respectively. To the best of our knowledge, this is the best result in selective hydrogenation of DMO into MG so far. Because of the relatively lower electron-donating ability of methyl group in comparison with ethyl group, the activity of **7** is inferior to **8**. According to the catalytic activities of **6**-**8**, a positive correlation between the hydrogenation activity of

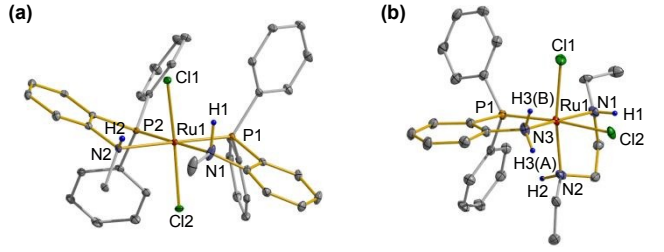


Fig. 1 X-ray crystal structures of (a) **3** and (b) **8** with thermal ellipsoids at 30% probability level. Most hydrogen atoms have been omitted for clarity.

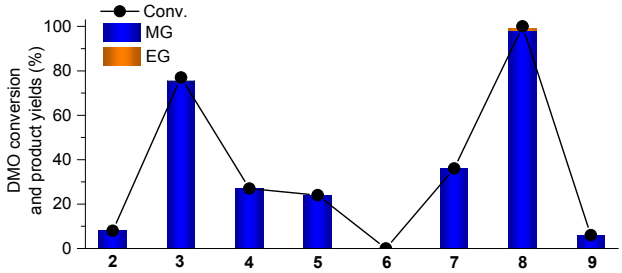


Fig. 2 Catalytic performance of complexes **2**-**9** for hydrogenation of DMO into MG (and/or EG). Reaction condition: 11.35 mmol DMO, 0.05 mol% ruthenium, 0.5 mol% NaOMe, 10 mL THF, 50 bar H_2, 100 °C, 1 h. The conversion of DMO and yield of alcohols were analyzed by gas chromatograph (GC) using *p*-xylene as an internal standard.

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Table 1 Hydrogenation of DMO into MG (and/or EG) by **8** under different reaction conditions.

Entry	Ru (%)	NaOMe /Ru[a]	T (°C)	$p(H_2)$ (bar)	time (h)	Conv. (%)[b]	Yield of MG (%)[b]	Yield of EG (%)[b]	TOF (h^{-1})
1	0.05	5	100	50	1	87	86	0	1720
2	0.05	10	100	50	0.5	99	98	0	3920
3	0.05	10	100	50	1	100	98	1	2000
4	0.05	15	100	50	1	87	86	0	1720
5	0.05	20	100	50	1	68	67	0	1340
6	0.2	10	100	10	1.5	100	99	0	330
7	0.2	10	RT	50	20	96	95	0	24
8	0.2	10	40	50	2	100	99	0	247
9	0.2	10	40	10	16	95	94	0	29
10	0.2	10	100	50	4	100	83	16	144
11	0.2	10	120	50	4	100	0	97	242
12	0.5	10	100	50	1	100	25	75	350
13	0.5	10	100	50	4	100	0	99	99

[a] Molar ratio. [b] Analyzed by GC using *p*-xylene as an internal standard.

ruthenium-NH catalyst and the electron density of the amino ligand was provided. Surprisingly, although isopropyl group has better electron-donating ability than methyl and ethyl groups, the activity of *N*,*N*'-diisopropyl-1,2-ethanediamine coordinated complex **9** is significantly lower than **7** and **8**, merely completed a DMO conversion of 6%, which is probably attributed to the steric hindrance.

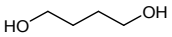
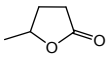
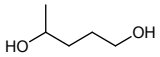
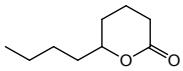
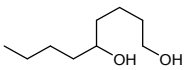
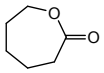
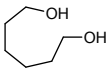
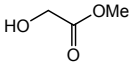
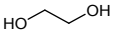
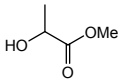
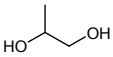
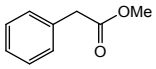
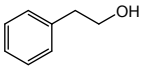
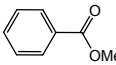
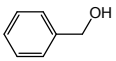
Obviously, the prominent catalytic performances of **3** and **8** in DMO hydrogenation verify the feasibility of improving the activity of ruthenium-NH catalyst through replacing the primary amine with a more electron-donating secondary amine. We also evaluated the catalytic performances of **2**-**9** in hydrogenation of acetophenone into 1-phenylethanol and benzaldehyde into benzyl alcohol, which are the typical examples of ketone and aldehyde. As shown in Fig. S3‡ and S4 ‡, the activity trend is similar to that in DMO hydrogenation, indicating that suitable alkyl group substitution could remarkably improve the catalytic efficiency. These results clearly show the significant role of the electronic effect in determining the catalytic efficiency. In addition, the steric effect can also inflict the catalytic activity.[11] Recently, we have systemically elaborated this effect in determining the hydrogenation activity of **2** in terms of density functional theory calculations and molecular dynamic simulations.[12] Similarly, in this work, due to the steric hindrance of the two isopropyl groups, complex **9** exhibited poor performances in DMO catalytic hydrogenation (Fig. 2). To some extent, it can also explain the difference between the activities of **3** and **4** (or **5**).

Furthermore, the most prominent complex **8** was employed to investigate the effect of reaction conditions in the DMO hydrogenation, and representative results were tabulated in Table 1. According to the amount of base, the reaction efficiency evolved in a volcanic trend (entries 1-5), passing through the summit by 10 equivalent of NaOMe over **8**. Although this trend is comparable with the reported catalyst systems,[7b,13] but the required amount of base for satisfactory result was significantly decreased.[9d,14] In a general trend, decreasing the H_2 pressure or reaction temperature would lead to lower catalytic activity. Gratifyingly, complex **8** smoothly catalyzed the hydrogenation of DMO into MG at lower H_2 pressure and/or reaction temperature (entries 6-9). Especially, 95% yield of MG was afforded at room temperature (RT) after an extended reaction time (20 h, entry 7). The TOF is 24 h^{-1}, much higher than that of Ru-Macho catalyst RuH(η^1-BH_4)(CO)[$NH(CH_2CH_2PPh_2)_2$] in hydrogenation of diethyl oxalate under similar reaction conditions.[11a]

After the mono hydrogenation of DMO into MG, we also investigated the catalytic hydrogenation of DMO into EG by **8**. Under the conditions of 100 °C and 50 bar H_2 with 0.2 mol% ruthenium for 4 h, MG and EG were obtained by yield of 83% and 16%, respectively (entry 10). EG was formed via hydrogenation of the mono-hydrogenated product MG.[15] Due to the electron-withdrawing character of ester moiety, DMO is more active than MG to be hydrogenated.[16] The hydrogenation of DMO into EG always requires harsher reaction conditions than that of MG.[16b] As expected, EG was produced as the main product with 97% (entry 11) and 99% yields (entry 13), respectively, after raising the reaction temperature to 120 °C or increasing the amount of **8** to 0.5 mol%.

Finally, the substrate scope of catalytic hydrogenation with **8** was further explored (Table 2). Lactones with different member rings and substituent groups were employed and all smoothly converted into the corresponding diols in yields of 56-96% (entries 1-5). Similarly, MG and methyl lactate both containing hydroxyl group at *α*–position were also hydrogenated into the diols EG and 1,2-propylene glycol in good yields of 99% and 95%, respectively (entries 6 and 7). However, when aromatic substituents were incorporated, the catalytic activity was obviously inhibited. The hydrogenation of the aliphatic ester methyl phenylacetate yielded a phenethyl alcohol of 67% (entry 8). In the case of methyl benzoate, the performance became worse with merely 11% yield of benzyl alcohol (entry 9). The negative effect of phenyl substituents on the reduction of the adjacent ester moiety is probably due to the steric hindrance between the catalyst and the ester substrate.

Table 2 Scope of the hydrogenation of esters into alcohols by **8**.

Entry	Ester	Alcohol	Conv. (Yield) (%)
1			86 (85)
2			82 (80)
3			97 (96)
4			71 (71)
5			93 (56)
6			100 (99)
7			96 (95)
8			69 (67)
9			14 (11)

Reaction conditions: 3.7 mmol ester, 0.5 mol% ruthenium, 5 mol% NaOMe, 10 mL THF, 50 bar H_2, 100 °C, 4 h. The conversion of ester and yield of alcohol were analyzed by GC using *p*-xylene as an internal standard.

Conclusions

In summary, a series of ruthenium complexes **3**-**5** and **7**-**9** bearing mono-N-functionalized secondary amino ligands *o*-$PPh_2C_6H_4NHR$ or $(CH_2NHR)_2$ were synthesized, which exhibit good catalytic activities in hydrogenation of DMO into MG/EG. Remarkable improvement in hydrogenation activity was achieved in comparison with the corresponding primary amino ligand constituted complexes **2** and **6**. Complexes **3** and **8** give the optimal catalytic results by achieving TOF as high as 1520 h^{-1} and 3920 h^{-1}, respectively. Moreover, complex **8** also displays satisfactory activities in the hydrogenation of some other aliphatic esters and lactones. This paves a new route to the design of efficient homogeneous hydrogenation catalysts.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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