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Graphical Abstract





TETRAHEDRON LETTERS

Transfer hydrogenation of ketones catalyzed by 2,6- bis(triazinyl)pyridine ruthenium complexes: The influence of alkyl arms

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Abstract—The transfer hydrogenation of ketones catalyzed by transition metal complexes has attracted much attention. A series of ruthenium(II) complexes bearing 2,6-bis(5,6-dialkyl-1,2,4-triazin-3-yl)pyridine ligands (R-BTPs) were synthesized and characterized by NMR analysis and X-ray diffraction. These ruthenium(II) complexes were applied in the transfer hydrogenation of ketones. Their different catalytic activity were attributed to the alkyl arms on the 2,6-bis(5,6-dialkyl-1,2,4-triazin-3-yl)pyridine. As the length of the alkyl arms rising, the catalytic activities of the complex catalysts decreased. By means of 0.4 mol % catalyst RuCl₂(PPh₃)(3-methylbutyl-BTP) in refluxing 2-propanol, a variety of ketones were reduced to their corresponding alcohols with >95% conversion over a period of 3 h. © 2019 Elsevier Science. All rights reserved.

Introduction

Alcohols, especially secondary alcohols, are a class of important organic compounds and have been extensively utilized in organic synthesis and fine chemicals [1]. Among the many methods for the synthesis of alcohols, the transfer hydrogenation (TH) of carbonyl compounds is one of the most effective strategies and has been considered to be a useful alternative method to the widely used catalytic hydrogenation by molecular hydrogen [2]. Transitionmetal-catalyzed TH reactions of ketones have made great success over the past few decades and ruthenium(II) complexes are usually used as the most useful potential catalysts. Much research work has been devoted to the exploration of new ligands for construction of ruthenium(II) catalysts. For example, the versatile ruthenium(II) 2aminomethylpyridine (ampy) complexes reported by Baratta et al. have been used in TH and ATH of ketones as efficient catalysts [3]; Noyori's ruthenium(II) complexes containing N-sulfonylated 1,2-diamines chiral ligands have demonstrated very high catalytic activity in the ATH of ketones [4]; Moreover, the NH functions have possessed beneficial effects on catalytic transformation, ligand assembly, and/or catalyst formation in TH of ketones [5]. Although various ruthenium(II) complex catalysts have been synthesized for TH, chemists are still committed to the development of new and efficient catalytic systems.

2,6-Bis(triazinyl)pyridines (BTPs) are a kind of pyridylbased tridentate *NNN* ligands and have been reported as effective extractants to separate trivalent minor actinides

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(americium and curium) from trivalent lanthanides, which represents a challenging goal for the definition of new methods in the disposal of nuclear wastes [6]. In addition, other metals such as Pd(II), Co(II), Ni(II) and Ca(II) etc. could also be extracted from the highly active liquid wastes with the BTP ligands [7]. We have been interested in developing N-heterocyclic ruthenium(II) complex catalysts for a long time. Various pyridyl-based NNN ruthenium(II) complexes have been synthesized and applied in the TH of ketones [8]. Our group have also reported ruthenium(II) complex based on iBu-BTP ligand, exhibiting moderate to excellent catalytic efficiency in TH of ketones [9]. As different alkyl-substituted BTPs displayed diverse stability towards acidic hydrolysis and radiolytic degradation in the extraction of An(III) from acidic solutions [10], in this paper, we synthesized a series of ruthenium(II) complexes bearing 2,6-bis(triazinyl)pyridine ligands with diverse substituted alkyl groups (R-BTPs), and their catalytic behaviors in the transfer hydrogenation reactions of ketones were investigated.



Conditions: (i) 4Å MS, toluene, N_2 (0.1 MPa), 110 °C, 23 h; (ii) RuCl₂(PPh₃)₃, toluene, N_2 (0.1 MPa), 110 °C, 3 h.

Scheme 1. Synthesis of ligands 3a-d and complexes 4a-d.

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Results and discussions

Ligands **3a-d** were prepared by means of a modified literature procedure (Scheme 1). Dehydrated by heating, pyridine-2,6-dicarbohydrazide imide **1** reacted with 1,2diketones **2a-d** to afford 2,6-bis(5,6-dialkyl-1,2,4-triazin-3yl)pyridines **3a-d**. Then, the reaction of **3a-d** with 1.0 equiv of RuCl₂(PPh₃)₃ [11] in refluxing toluene afforded complexes RuCl₂(PPh₃)(R-BTP) **4a-d**. Complexes **4a-d** were stable when exposed to air at ambient temperature.

The NMR spectra of **4a-d** reveal **3a-d** to be the coordinating ligands. The chemical shifts of the pyridyl CH hydrogen atoms in complexes **4a-d** were shifted upfield by 0.2-0.3 ppm in the proton NMR spectrum compared with the ligand precursors **3a-d**. The ${}^{31}P{}^{1}H{}$ NMR signals of ruthenium(II) complexes **4a-d** reveal a singlet at 41.9, 41.8, 41.7, 41.9 ppm, respectively, suggesting one PPh₃ ligand is presented in the complex.



Figure 1. Molecular structure of complex 4d.

Table 1

Selected bond distances (Å) and angles (°) for complexes 4d and $RuCl_2(PPh_3)(iBu-BTP)$.

Selected bond	4d	RuCl ₂ (PPh ₃)(<i>i</i> Bu-BTP)
Ru–N(1)	1.980(7)	1.982(3)
Ru–N(2)	2.029(6)	2.032(3)
Ru–N(5)	2.047(6)	2.058(3)
Ru–P	2.347(2) 2.3631(11)	
Ru–Cl(1)	2.3798(19) 2.3919(13)	
Ru–Cl(2)	2.4103(19)	2.4110(13)
N(5)–N(6)	1.341(9)	1.341(4)
Cl(1)-Ru-Cl(2)	172.83(7)	174.91(3)
N(1)-Ru-N(2)	78.8(3)	78.85(12)
N(1)-Ru-N(5)	78.7(3)	78.67(12)
N(2)-Ru-N(5)	157.2(3)	156.03(12)
N(1)–Ru–P	176.45(19)	175.80(8)
N(1)-Ru-Cl(1)	89.43(19)	90.05(8)
N(1)-Ru-Cl(2)	85.32(19)	84.96(8)
N(2)-Ru-Cl(2)	95.31(19)	93.88(8)
P-Ru-Cl(1)	93.18(7)	93.83(4)
N(2)-Ru-P	98.81(19)	99.77(9)

We chose complex 4d with cyclopentylethyl as the side arms to further investigate the structure of the ruthenium(II) complex by X-ray crystallographic study. In the solid state, complex 4d exhibits a neutral molecular structure and acts as a planar *pseudo*- N_3 ligand, and the metal center is surrounded by the tridentate pseudo-N₃ ligand, two chlorides, and one PPh₃ ligand. The two chlorides in 4d are closely linear to each other (Cl(1)-Ru-Cl(2), 172.83(7)°) and positioned on the two sides of the pseudo-NNN ligand plane (Figure 1). The three Ru-N, two Ru-Cl and Ru-P bond distances are 1.980(7), 2.029(6), 2.047(6), 2.3798(19), 2.4103(19) and 2.347(2) Å respectively, with 0.0007-0.0161 Å shortened by comparing with RuCl₂(PPh₃)(*i*Bu-BTP) ^[40] (Table 1), revealing that the metal center in 4d was in a much tighter environment than the metal center in $RuCl_2(PPh_3)(iBu-BTP)$. These data suggest that the complex 4d may act as a less catalytically active catalyst than RuCl₂(PPh₃)(*i*Bu-BTP).

Table 2

Optimizing of reaction conditions for transfer hydrogenation .

	+	ч Ч	Ru(II) cat. base, 82 °C	он ↓ +	°,
Entry	Ru(II) cat.	Base	Ketone/base/cat. (molar ratio)	Time (h)	Yield $(\%)^a$
1	4 a	NaOH	500/30/1	2	65
2	4 a	NaOH	250/30/1	2	97
3	4 a	NaOH	250/12.5/1	2	73
4	4 a	NaOH	250/25/1	2	94
5	4 a	NaOH	250/40/1	2	97
6	4 a	iPrOK	250/30/1	2	97
7	4 a	tBuOK	250/30/1	2	98
8	4 a	KOH	250/30/1	2	95
9	4b	NaOH	250/30/1	3	97
10	4c	NaOH	250/30/1	8	96
11	4d	NaOH	250/30/1	9	95
12	Α	NaOH	250/30/1	1.5	97

Conditions: ketone, 2.0 mmol (0.1 M in 20 mL *i*PrOH); 0.1 MPa, 82 °C; ^a GC yield of the corresponding alcohol.

Ruthenium(II) complexes 4a-d have been used as the potential catalysts for TH of ketones. Using 4a as the catalyst, TH of acetophenone was carried out in 2-propanol at 82 °C (Table 2). When NaOH was used as the base, the best molar ratio for ketone/base/catalyst is 250/30/1 (Table 2, entries 1-5). iPrOK, tBuOK and KOH were also tested as the bases. Over a period of 2 h, the corresponding alcohol product from acetophenone reached 97%, 97%, 98%, and 95% yields by GC analysis in the reactions using NaOH, *i*PrOK, *t*BuOK and KOH as the base, respectively (Table 2, entries 2 and 6-8). Thus, NaOH was selected as the reaction promoter. Under optimized conditions, complexes RuCl₂(PPh₃)(R-BTP) with diverse alkyl groups were used as the catalysts in the transfer hydrogenation of acetophenone. To reach >95% yield by GC analysis, the corresponding complexes 4a, 4b, 4c, 4d and

RuCl₂(PPh₃)(*i*Bu-BTP) (A) required 2 h, 3 h, 8 h, 9 h and 1.5 h, respectively (Table 2, entries 2 and 9-12). For a better understanding of the catalytic activity differences between complexes A and 4a-d, the TH reaction kinetics were monitored by means of the reaction of acetophenone (Figure 2). It is clear that as the length of alkyl arms rising, the catalytic activity of complexes A and 4a-c in transfer hydrogenation of ketones reduced. When complex 4d was used as the catalyst under the stated conditions, 9 h was needed to reach 95% conversion. The difference between the catalytic activities of these complexes was presumably attributed to the steric effect of alkyl arms as 4c and 4d have the same number of alkyl carbons. The experimental data further confirms to the result of X-ray crystallographic test. It should be noted that complexes 4a-d could be stored at room temperature over half a year and did not lose their catalytic activity.



Figure 2. Representative reaction kinetics profiles.

Complex 4a was chosed as the catalyst for TH reactions of various ketone compounds. When 0.4 mol % 4a was used in the typical TH reactions (Table 3), most of the ketone substrates were reduced to their corresponding alcohols with >95% conversion over a period of 3 h (Table 3, entries 1, 2, 4, 5, 7, 10-13 and 18-21). When acetophenone is ortho-substituted, the reaction rate will be slowed down because of the steric effect of ortho-position (Table 3, entries 3, 6, 9 and 12). For 2-acetonaphthone and 2-benzoylpyridine, the reaction rates were a little slower under the same conditions, affording the alcohol products at 96% yield in 5 h and 7 h, respectively (Table 3, entries 14 and 15). For 1-tetralone and 9-fluorenone, their corresponding alcohol products were formed in 84% (5 h) and 88% (3 h) yields. The reaction reaches equilibrium and the conversion rate was no significant increase as the time prolonged (Table 3, entries 16 and 17). Benzophenone, cyclic ketones and aliphatic ketones could be efficiently reduced to the corresponding alcohols within 2 h (Table 3, entries 18-21).

Table 3

Transfer hydrogenation reactions catalyzed by Ru(II) complex 4a.

$$\underset{R_1}{\overset{O}{\longrightarrow}} \underset{R_2}{\overset{OH}{\longrightarrow}} + \underset{NaOH, 82 \ ^{\circ}C}{\overset{OH}{\longrightarrow}} + \underset{R_1}{\overset{OH}{\longrightarrow}} + \underset{R_2}{\overset{OH}{\longrightarrow}} + \underset{R_1}{\overset{OH}{\longrightarrow}} + \underset{R_2}{\overset{OH}{\longrightarrow}} + \underset{R_3}{\overset{OH}{\longrightarrow}} + \underset{R_4}{\overset{OH}{\longrightarrow}} + \underset{R_4}{\overset{OH}{\overset{OH}{\longrightarrow}} + \underset{R_4}{\overset{OH}{\longrightarrow}} + \underset{R_4}{\overset{OH}{\overset{OH}{\longrightarrow}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset{OH}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4}{\overset{OH}{\overset{OH}{\overset{OH}{\overset}} + \underset{R_4$$

Entry	Ketone	Time (h)	Yield $(\%)^a$
1	Me	2	97 (95)
2	Et	2	98 (95)
3	CI O Me	10	97 (94)
4	CI	1.5	98 (95)
5	CI Me	3	97 (95)
6	Br O Me	24	96 (92)
7	Br	2	97 (95)
8	Br	6	96 (94)
9	Me O Me	18	91 (90)
10	Me Me	3	97 (96)
11	Me	3	96 (96)
12	OMe O Me	3	95 (93)
13	MeO Me	2	97 (96)
14	Me	5	96 (96)
15	Ph	7	96 (96)
16		5	84 (83)
17		3	88 (88)
18		1.5	98 (97)
19	\bigcirc°	1.5	>99 (90)
20	Ć_ ^{€0}	1	97 (84)
21	Me	2	97 (92)

Conditions: ketone/NaOH/cat. = 250/30/1. ketone, 2.0 mmol (0.1 M in 20 mL *i*PrOH); 0.1 MPa, 82 °C; ^{*a*}GC yield of the corresponding alcohol. Data in parentheses are yields refer to the isolated products.

This ruthenium catalyst has a poor reactivity for the α,β unsaturated ketones. No alcohol product was obtained when chalcone was used as the substrate. The reaction was complicated and 1,3-diphenylpropan-1-one was isolated in 15% yield accompanying by 51% raw material recovery (eq 1). For further application, a scale-up experiment was conducted in the presence of 0.2 mol % **4a**. By means of 90 mmol acetophenone as the substrate, 1-phenylethanol was obtained in 95% yield within 12 h (eq 2), which implicating a potential application of the protocol for the reduction of ketones.

Conclusions

In summary, we have reported a series of ruthenium(II) complexes RuCl₂(PPh₃)(R-BTP) bearing 2,6-bis(5,6-dialkyl-1,2,4-triazin-3-yl)-pyridine ligands. The ruthenium complexes were successfully synthesized, characterized by NMR and X-ray crystallographic analysis, and applied in the transfer hydrogenation of ketones. Their different catalytic activities were attributed to the alkyl groups in the 2,6-bis(triazinyl)pyridine ligands. As the length of the alkyl arms rising, the catalytic activity of the complex catalysts decreased. Various types of ketones were smoothly reduced to the corresponding alcohols as sole products with good catalytic efficiency by 0.4 mol% loading of complex RuCl₂(PPh₃)(3-methylbutyl-BTP) in refluxing *i*PrOH.

Appendix A. Supplementary data

The Supporting Information containing experimental procedures, analytical data, copies of NMR spectra, X-ray crystallographic data of **4d** is available free of charge on the Elsevier Publications website.

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Highlights

- The synthesis of four ruthenium(II) complex catalysts bearing 2,6- bis(triazinyl)pyridine.
- Good catalytic activity of these ruthenium(II) complexes in the transfer hydrogenation of ketones.
- Different catalytic activity of the complex catalysts led by the alkyl arms was discussed.
- The application of 2,6- bis(triazinyl)pyridine in homogeneous catalysis.