Ruthenium(II) complex catalysts bearing a 2,6-bis(tetrazolyl)pyridine ligand for the transfer hydrogenation of ketones

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ABSTRACT

Three ruthenium(II) complex catalysts bearing 2,6-bis(tetrazolyl)pyridine were synthesized, structurally characterized, and applied in the transfer hydrogenation of ketones. Their different catalytic activities were attributed to the different phosphine ligands on the 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine ruthenium(II) complexes, with that based on 1,4-bis(diphenylphosphino)butane exhibiting better catalytic activity. A variety of ketones were reduced to their corresponding alcohols with >95% conversion.

1. Introduction

Nitrogen-containing ligands have been widely used in coordination chemistry and homogeneous catalysis owing to ease of manipulation and the high catalytic activity of their transition metal complexes [1–5]. Many pyridyl-based symmetric ligands, such as 2,2’:6,2’’-terpyridines [6–10], 2,6-bis(oxazolinyl)pyridines [11–15], 2,6-bis(imino)pyridines [16–20], and 2,6-bis(pyrazoyl)pyridines [21–25] have been reported and applied in organic synthesis and homogeneous catalysis.

2,6-Bis(tetrazolyl)pyridines are pyridyl-based multidentate chelating agents containing nine N atoms, and their metal complexes have been applied in functional materials fabrication, coordination chemistry, and catalysis. These ligands can be used in the synthesis of luminescent materials using a self-assembly strategy. Both visible and near-infrared (IR) luminescence emissions of lanthanide cations (Pr, Nd, Sm, Eu, Tb, Dy, Ho, Er, Tm, and Yb) can be efficiently sensitized using 2,6-bis(tetrazole)pyridine [26,27]. Furthermore, platinum(II) complexes bearing 2,6-bis(tetrazolyl)pyridine can be used as luminescent films, dopants for OLEDs, and to form supramolecular polymeric nanofibers [28–31]. Ruthenium complexes based on mixed ligands 2,2’:6,2’’-terpyridine and 2,6-bis(tetrazole)pyridine have been reported and used in dye-sensitized solar cells to afford novel ruthenium dyes [32–34]. These ligands can also be coordinated with other metals, such as a reported series of homoleptic complexes of 2,6-bis(tetrazole)pyridine with CoII, NiII, CuII, and ZnII [35]. Furthermore, 2,6-bis(tetrazolyl)pyridine ligands can recover trivalent minor actinides effectively and selectively from HNO3 media, while exhibiting weak or almost no extraction of trivalent lanthanides with similar chemical properties [36,37]. However, 2,6-bis(tetrazolyl)pyridine ligands have rarely been applied in catalytic reactions. In 2016, zinc polymers based on...
2.1. Versatile ruthenium(II) 2-aminomethylpyridine (ampy) complexes have been reported by Baratta et al. [44–49] and demonstrated very high catalytic activity in the TH and asymmetric TH (ATH) of ketones. Moreover, Noyori ruthenium(II) complexes, containing N-sulfonated 1,2-diamines as chiral ligands, have been used as efficient catalysts for the ATH of ketones and imines [50–55]. Furthermore, transition-metal complexes bearing a ligand with NH functionality also exhibit high catalytic activity in transfer hydrogenation reactions [56–59]. Although various ligands and their transition-metal complexes have been synthesized for TH, the development of efficient catalytic systems is still needed. We have been interested in developing N-heterocyclic ligands and the corresponding highly effective catalyst system for application in homogeneous catalysis. Various pyridyl-based N-containing ligands and their ruthenium(II) complexes have been reported and applied to the TH of ketones [60–65]. Herein, we describe the synthesis and structural characterization of ruthenium(II) complexes of 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine with different phosphorus ligands and their catalytic behavior in TH reactions of ketones.

2. Experimental

2.1. General considerations

All manipulation of air- and moisture-sensitive compounds was carried out under a nitrogen atmosphere using standard Schlenk techniques. Solvents were dried and distilled prior to use according to literature methods. 1H and 31P{1H} NMR spectra were recorded on a Bruker DRX-400 spectrometer (Bruker, Germany) and all chemical shift values are referenced to δMe = 0.00 ppm or CDC6D6 (δ(H), 7.26 ppm and δ(C), 77.16 ppm). HRMS analysis was performed by the Analysis Center, Dalian University of Technology. All melting points are uncorrected. Thin-layer chromatography (TLC) analysis was performed using glass-backed plates coated with silica gel (0.2 mm). Flash column chromatography was performed on silica gel (200–300 mesh). All chemical reagents were purchased from commercial suppliers and used as received unless otherwise indicated.

2.2. Preparation of ligand and ruthenium complexes

4-Chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine (2). A mixture of N,N,N′,N′-di-p-tolylpyridine-2,6-dicarboxamide (1) (20.0 g, 58 mmol), PCl3 (24.2 g, 116 mmol), and SOCl2 (120 mL) were heated at 80 °C for 3 h. Excess SOCl2 was removed under reduced pressure and the resulting imidoyl chloride was dissolved in CH2Cl2 (100 mL). This solution was then added drop-wise to a stirred suspension of NaN3 (13.6 g, 209 mmol) in DMF (100 mL). After addition was completed, stirring was continued for 16 h at room temperature. The reaction mixture was then treated with water, the organic layer was separated and washed with water (3×200 mL), and all volatiles were removed under reduced pressure. The resultant residue was purified by column chromatography on silica gel (eluent: petroleum ether (60–90 °C)/CH2Cl2 = 2:1, v/v) to afford 2 as a white solid (87.7 g, 35%). m.p. 247–248 °C. 1H NMR (CDCl3, 400 MHz, 25 °C) δ 8.28, 8.28 (s, 2 H, pyridyl CH), 7.11 (d, 4H, J = 8.2 Hz) and 6.92 (d, 4H, J = 8.3 Hz) (both p-tolyl CH), 2.38 (s, 6 H, p-tolyl CH3). 31P{1H} NMR (CDCl3, 100 MHz, 25 °C) δ 150.7, 147.1, 145.8, 140.6, 131.8, 129.8, 127.2, 124.8, 21.4. HRMS Calcld. for C23H19ClN5O 429.1217; Found: 429.1212.

Ruthenium complex 3a. Under a nitrogen atmosphere, a mixture of 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine (2) (215 mg, 0.5 mmol), RuCl2(PPh3)3 (480 mg, 0.5 mmol), and CH2Cl2 (40 mL) was stirred at 40 °C for 4 h. After cooling to ambient temperature, all volatiles were evaporated under reduced pressure. The resultant residue was purified by flash chromatography on silica gel (eluent: CH2Cl2/CH3OH = 2:1, v/v) at room temperature. Purification of ruthenium(II) complex 3a as a reddish brown solid (479 mg, 85%). m.p. >155 °C dec. 1H NMR (CDCl3, 400 MHz, 25 °C) δ 7.56, 7.40, 7.33, 7.27, 7.13, and 6.72 (each m, 10:9:3:6:6:6 H, aromatic CH), 2.56 (s, 6 H, p-tolyl CH3). 13C{1H} NMR (CDCl3, 100 MHz, 25 °C) δ 153.25, 152.32, 146.58, 145.11, 144.2, 134.8, 134.7, 134.2, 133.7, 133.3, 133.2, 131.6, 130.8, 129.9, 129.8, 129.3, 128.7, 128.6, 128.5, 127.8, 127.7, 125.5, 125.3, 21.5. 31P{1H} NMR (CDCl3, 162 MHz, 25 °C) δ 40.4, 35.0.

Ruthenium complex 3b. Under a nitrogen atmosphere, a mixture of 1,4-bis(diphenylphosphino)butane (512 mg, 1.2 mmol), RuCl2(PPh3)3 (959 mg, 1.0 mmol), and CH2Cl2 (50 mL) was stirred at room temperature for 2 h. Then, 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine (2) (429 mg, 1.0 mmol) was added and the mixture was stirred at 40 °C for 4 h. After cooling to ambient temperature, all volatiles were evaporated under reduced pressure. The resultant residue was purified by flash chromatography on silica gel (eluent: AcOEt/CH3OH = 5:1, v/v). Recrystallization in hexane–CH2Cl2 (3:1, v/v) at room temperature gave ruthenium(II) complex 3b as a reddish brown solid (754 mg, 71%). m.p. >180 °C dec. 1H NMR (CDCl3, 400 MHz, 25 °C) δ 7.95, 7.62, 7.45, 7.36, 7.28, 7.07 and 6.86 (each m, 48:6:24:2:4:2:4 H, aromatic CH), 2.33, 2.37, 2.11 and 1.79 (each m, 4×CH3), 2.57 (s, 6 H, p-tolyl CH3). 13C{1H} NMR (CDCl3, 100 MHz, 25 °C) δ 153.2, 145.7, 144.8, 144.4, 136.4, 136.0, 134.0, 133.9, 132.7, 132.2, 131.8, 131.6, 131.5, 131.0, 130.2, 129.3, 129.2, 128.1, 128.0, 125.6, 124.3, 33.0, 32.7, 29.3, 29.1, 26.1, 21.7, 20.1. 31P{1H} NMR (CDCl3, 162 MHz, 25 °C) δ 40.4, 33.9.

Ruthenium complex 3c. Under a nitrogen atmosphere, a mixture of 1,5-bis(diphenylphosphino)pentane (106 mg, 0.24 mmol), RuCl2(PPh3)3 (193 mg, 0.2 mmol), and CH2Cl2 (10 mL) was stirred at room temperature for 2 h. Then 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine (2) (86 mg, 0.2 mmol) was added and the mixture was stirred at 40 °C for 4 h. After
cooling to ambient temperature, all volatiles were evaporated under reduced pressure. The resultant residue was purified by flash chromatography on silica gel (eluent: CH2Cl2/MeOH = 5:3, v/v). Recrystallization in hexane–CH2Cl2 (3:1, v/v) at room temperature gave ruthenium(II) complex 3c as a reddish brown solid (154 mg, 74%). m.p. >193 °C dec. 1H NMR (CDCl3, 400 MHz, 25 °C) δ 7.87, 7.58, 7.44, 7.38, 7.30, 7.23, 6.96, and 6.74 (each m, 4:8:2:4:2:4 H, aromatic CH), 2.52 (s, 6 H, p-tolyl (CH3)), 2.44, 2.17, 1.92, 1.66, and 1.46 (each m, 5 CH2). 13C{1H} NMR (CDCl3, 100 MHz, 25 °C) δ 153.1, 145.3, 145.0, 144.3, 143.0, 136.5, 133.9, 133.8, 131.7, 130.8, 130.0, 129.0, 128.9, 128.8, 127.9, 127.8, 125.4, 123.9, 27.6, 27.3, 26.5, 26.33, 26.26, 26.2, 21.5, 19.85, 19.79, 19.7. 31P{1H} NMR (CDCl3, 162 MHz, 25 °C) δ 41.8, 32.2.

2.3. General procedure for TH of ketones catalyzed by 3

Under a nitrogen atmosphere, a mixture of ketone (2 mmol), catalyst 3 (0.01 mmol), and 2-propanol (18 mL) was stirred at 82 °C for 10 min. Then, iPrOK solution in 2-propanol (2.0 mL, 0.1 mol/L, 0.2 mmol) was introduced to initiate the reaction. The reaction mixture was stirred at reflux. After the stated time, 0.1 mL of the reaction mixture was sampled and immediately diluted with 0.5 mL of 2-propanol precooled to 0 °C, and filtered through a short pad of celite to quench the reaction by time. 0.1 mL of the reaction mixture was sampled and immediately diluted with 0.5 mL of 2-propanol precooled to 0 °C, and filtered through a short pad of celite to quench the reaction by removing the complex catalyst. The resultant filtrate was used for GC analysis. After the reaction was finished, the mixture was condensed under reduced pressure and subjected to flash silica gel chromatography to afford the alcohol product. The alcohol products were identified by comparison with authentic samples using NMR and GC analyses.

3. Results and discussion

A mixture of N2,N3-di-p-tolylpyridine-2,6-dicarboxamide 1, PCl5 and SOCl2 were heated to afford an imidoyl chloride. The ligand, 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetraz-ol-5-yl)pyridine 2, was then obtained by cycladdition of the imidoyl chloride to NaN3 in DMF. Treatment of ligand 2 with ruthenium compounds in CH2Cl2 gave complexes 3a-c under reaction conditions (iii) or (iv) (Scheme 1). Due to cyclic tension, complexes 3 with 2, 3, or 6-carbon alkyl chains between the two phosphorus ligands were not obtained under the same conditions. Complexes 3a-c were stable when exposed to air at ambient temperature.

The structures of complexes 3 were supported by NMR analysis in solution. The chemical shifts of the pyridyl CH hydrogen atoms in complexes 3 were shifted upfield by 0.3–0.7 ppm in the proton NMR spectrum compared with those of ligand precursor 2. Complexes 3a-c showed two signals in the 31P{1H} NMR spectra, suggesting that the two phosphorous groups were positioned in different environments. Single crystals of 3b suitable for X-ray crystallographic study were obtained to further validate the complex structure [66]. In the solid state, the cationic metal center of complex 3b was surrounded by tridentate NNN ligand 2, two PPh2 ligands, and a chloride anion, with another dissociated chloride anion in the vicinity (Fig. 1). The P(1)–Ru–P(2) angle in 3b was 92.54°, suggesting that the two PPh2 ligands were almost orthogonal to each other. P(1) and Cl(1) were almost linear to each other (P(1)–Ru–Cl(1), 171.32°) and positioned on two sides of the ligand plane. The presence of three Ru–N bonds (2.058(2), 2.079(2), and 2.096(2) Å), two Ru–P bonds (2.3186(8) and 2.3467(9) Å), an Ru–Cl bond (2.4538(8) Å), a N(5)–Ru–P(2) angle of 171.79(6)°, and a P(1)–Ru–Cl(1) angle of 171.32(3)°

![Fig. 1. Molecular structure of 3b with a H2O molecule and chloride anion omitted for clarity.](image-url)
identified a six-coordinate metal center in complex 3b with a distorted bipyramidal environment.

Ruthenium(II) complexes 3a–c were tested as catalysts in the TH of ketones (Table 1). Using 0.5 mol% of 3 as catalyst, with a molar ratio of 200/20/1 for ketone/base/catalyst and iPrOK as the base promoter, transfer hydrogenation of acetophenone was conducted in 2-propanol at 82 °C. To achieve >96% yield, corresponding complexes 3a, 3b and 3c were reacted for 1 h, 1.5 h, and 2 h, respectively (Table 1, entries 1–3). Further research into the catalyst activities was performed using 3a and 3b. For o-methylacetophenone, both catalysts required 3 h to reach 97% conversion (Table 1, entries 4 and 5). When o-chloroacetophenone was tested, 3b showed better catalytic activity, with only 20 min needed to reach 97% conversion (Table 1, entries 6 and 7). Furthermore, for cyclohexanone, 3b showed better catalytic activity than 3a (Table 1, entries 8 and 9). Next, 0.5 mol% 3b as catalyst was used in typical reactions, exhibiting very good catalytic activity for the transfer hydrogenation of o-, m-, and p-chloroacetophenone and achieving >97% conversions for these ketones in 20–40 min (Table 1, entries 7, 12, and 13). Electron-donating substituent-bearing aromatic ketones o-, m-, and p-methylacetophenone required a longer time to be transformed into the target reduction products (Table 1, entries 5, 10, and 11). Propiophenone, 2-acetonaphthone, 2-benzoylpyridine, and benzophenone were also smoothly reduced to their corresponding alcohols in 93%–96% conversions within 1–2 h (Table 1, entries 14–17). Due to the rigidity of the carbonyl rings, 1-tetralone and 9-fluorenone proceeded with the poorest reaction activity affording 70% and 83% conversion after 2 and 0.5 h, respectively, with extended reaction times producing no improvement (Table 1, entries 18 and 19). For the reduction of aliphatic ketones, cyclohexanone and linear 2-heptanone achieved >95% conversions in 40 min and 3 h, respectively (Table 1, entries 9 and 21), while cyclopentanone was reduced to its desired alcohol in 90% conversion in 2 h, with no further transformation taking place when the reaction time was extended (Table 1, entry 20). The difference between the catalytic activity of complexes 3a–c in the TH

Table 1
Transfer hydrogenation of ketones catalyzed by complexes 3a–c.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ru(II) cat.</th>
<th>Ketone</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Entry</th>
<th>Ru(II) cat.</th>
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Conditions: Ketone, 2.0 mmol (0.1 mol/L in 20 mL of iPrOH); catalyst, 0.5 mol% 3; ketone/iPrOK/catalyst = 200:20:1; 0.1 MPa N₂, 82 °C.

* Determined by GC analysis.
Ru(II) catalyst for the transfer hydrogenation of ketones.

References

Graphical Abstract

Ruthenium(II) complex catalysts bearing a 2,6-bis(tetrazolyl)pyridine ligand for the transfer hydrogenation of ketones

Liandi Wang *, Tingting Liu
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Three ruthenium(II) complex catalysts bearing 2,6-bis(tetrazolyl)pyridine were synthesized and applied in the transfer hydrogenation of ketones. Their different catalytic activities were attributed to the phosphine ligands in the 4-chloro-2,6-bis(1-(p-tolyl)-1H-tetrazol-5-yl)pyridine ruthenium(II) complexes. The ruthenium(II) complex based on 1,4-bis(diphenylphosphino)butane exhibited better catalytic activity, reducing a variety of ketones to their corresponding alcohols with >95% conversion.

[66] CCDC 1007204 contained the supplementary crystallographic data for 3b. Copies of this information could be obtained free of charge from the Cambridge Crystallographic Data Centre.
吡啶基桥联双四唑钌(II)配合物催化酮的转移氢化反应

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摘要：含氮配体具有稳定性好、易于合成等优点，而且其过渡金属配合物表现出较高的催化活性，因此在配位化学和均相催化等研究领域受到了广泛关注。基于吡啶骨架的三齿NNN配体具有良好的配位能力和丰富的配位模式，如吡啶桥联的对称配体2,2':6',2''-三吡啶、2,6-双噁唑啉基吡啶、2,6-双亚胺基吡啶和2,6-双吡唑基吡啶等在有机合成及配合物催化剂制备等方面得到广泛应用。2,6-双四唑基吡啶也是基于吡啶的多齿配体，已被用于合成发光材料或高效回收次锕系元素等，但是其在催化领域的应用较少。

过渡金属催化的不饱和化合物的转移氢化反应具有反应条件温和、不直接使用氢气等优点，因而受到越来越多的关注。一系列优异的配体及配合物在转移氢化反应中脱颖而出，如对甲苯磺酰手性二胺配体、2-甲胺基吡啶钌配合物、配体中含有NH官能团的过渡金属配合物等。我们也报道了几种吡啶基桥联的含氮配体及其钌配合物，并应用于催化酮的转移氢化反应。在此基础上，本文合成了三种连有不同膦配体的2,6-双四唑基吡啶钌配合物，并用于催化酮的转移氢化反应。

从A²,N²-N,N-N基甲苯磺酰二胺(1)出发，经氯代环化两步反应合成4-氯吡啶基桥联双四唑化合物(2)，配合物2与RuCl2(PPh3)3在对应的反应条件下制得三种连有不同膦配体的2,6-双四唑基吡啶钌配合物(3)，其分子结构通过核磁共振波谱和X射线单晶结构测定得到确认。将这三种钌配合物应用于催化酮的转移氢化反应，当催化剂用量为0.5 mol%时，在异丙醇回流条件下，比较连有不同膦配体的2,6-双四唑基吡啶钌配合物的催化活性。膦配体为1,4-双(二苯基膦)丁烷的钌配合物3b表现出更高的催化活性，含有双三苯基膦的钌配合物3a则表现出与3b相当或略低的催化活性，含有1,5-双(二苯基膦)戊烷的钌配合物3c活性最差。以3b为催化剂拓展了一系列酮底物，取代的芳香酮、链状和环状的脂肪酮都可以高效地被还原，大部分酮底物以>95%的转化率还原成相应的醇。含有氯取代基的苯乙酮对反应有较大的加速作用，反应时间更短，转化率更高，由于羰基环的张力，1-四氢萘酮与9-芴酮转化率略低。

结合实验结果与相关文献，提出了一条基于Ru-H活性中间体的内层反应机理：钌配合物在iPrOK作用下生成Ru(II)-烷氧基中间体I，随后发生β-H消除反应脱去一分子丙酮得到Ru-H配合物，Ru-H配合物与酮底物作用经过渡态II生成另一分子Ru(II)-烷氧基中间体II，随后异丙醇与烷氧基发生交换生成目标产物，同时生成中间体I完成催化循环。

关键词：2,6-双四唑基吡啶；钌；转移氢化；酮；均相催化

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