2,6-Bis(3,5-dimethylpyrazol-1-yl)pyridine: A Useful Pseudo-N_3 Ligand in Efficient Ruthenium(II)-Catalyzed Transfer Hydrogenation of Ketones

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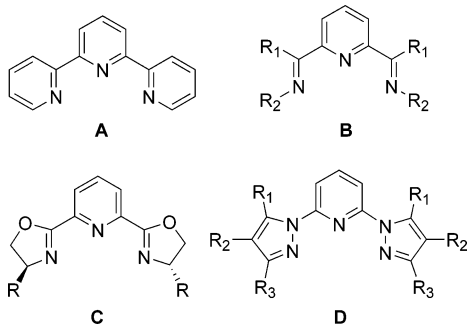
Summary: Transfer hydrogenation of ketones was efficiently carried out with a ruthenium(II) complex bearing the ligand 2,6-bis(3,5-dimethylpyrazol-1-yl)pyridine (Me_4BPPy), i.e., $RuCl_2(PPh_3)(Me_4BPPy)$, in 2-propanol at 82 °C. The single-crystal structure of the complex was first characterized by an X-ray crystallographic study, correcting the mistaken structural assignment of the complex in the literature. The results have demonstrated that the new family of ligands of the type Me_4BPPy can act as pseudo-N_3 ligands to construct transition-metal catalysts.

Nitrogen-containing heterocyclic ligands are receiving more and more attention in the fields of coordination chemistry, homogeneous catalysis, and organic synthesis because organometallic complexes containing nitrogen donor ligands usually exhibit high reactivities.[1] Recently, planar tridentate nitrogen donor (N_3) ligands such as 2,2′:6′,2″-terpyridines (**A**; terpy),[2] 2,6-bis(imino)-pyridines (**B**),[3] and 2,6-bis(oxazolinyl)pyridines (**C**; Pybox)[4] (Chart 1) have been well documented. Other tridentate ligands with a bridging 2,6-pyridyl backbone are also known.[5] Pyrazolato-based transition-metal complexes, in particular, those bearing hydridotris(pyrazolyl)borate (Tp ligand), have been applied as catalysts in some organic reactions.[6] Several 2,6-bis(pyrazol-1-yl)pyridine derivatives of type **D** were synthesized by Jameson et al.[7] However, so far, only five complexes of the same family bearing ligands **D**, i.e., *trans*-$[RuL(X)(PMe_3)_2]^+ClO_4^-$ (**2**: L = ligand **D**; X = Cl,[8] NO_2[9]), have been structurally characterized by X-ray crystallography. Although recently complexes bearing ligands **A**−**C** have been well investigated, ligand **D** has seemingly been forgotten over the past decade. Very recently, Spivak reported the synthesis of the first neutral transition-metal complex of 2,6-bis(3,5-dimethylpyrazol-1-yl)pyridine (Me_4BPPy), i.e., the ruthenium(II) complex $[RuCl_2(PPh_3)(Me_4BPPy)]$ (**1**), and assigned its structure as **E** on the basis of its NMR spectral features (Chart 2),[10a] and Karam documented the synthesis and structural characterization of a cobalt(II) complex of 2,6-bis-(3,4,5-trimethylpyrazol-1-yl)pyridine.[10b]

Chart 1. N_3 and Pseudo-N_3 Ligands



Transition-metal-catalyzed transfer hydrogenation of ketones is currently considered as a promising alternative to the widely used catalytic hydrogenation.[11] Ruthenium(II) complexes are usually used as the most useful potential catalysts for transfer hydrogenation of

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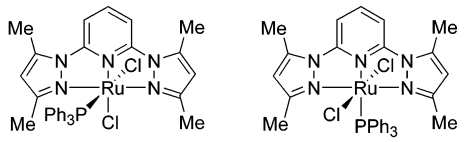
Chart 2. Complex 1



1: $RuCl_2(PPh_3)(Me_4BPPy)$ **E**[10]

ketones. Exploration of new ligands for construction of ruthenium(II) catalysts has been one of the greatest motivations for work in this area. In the course of our ongoing investigation on new pyrazolato-based ligands, we became interested in the structural and catalytic features of ligand **D** based ruthenium(II) complexes. In comparison with ligands **A**−**C**, it is reasonable to consider **D** as a new family of planar tridentate pseudo-N_3 ligands. Herein, we report the first X-ray crystal structure of a neutral ruthenium(II) complex, i.e., $RuCl_2(PPh_3)(Me_4BPPy)$ (**1**), supported by 2,6-bis(3,5-dimethylpyrazol-1-yl)pyridine (Me_4BPPy), correcting the mistaken structural assignment of **1** in the literature,[10a] and transfer hydrogenation of ketones catalyzed by **1** for the first time.

The air-stable complex **1** was prepared from the reaction of $RuCl_3(Me_4BPPy)$ and PPh_3 in the presence of Et_3N in a refluxing ethanolic solution.[10a] A dichloromethane solution of **1** was slowly evaporated at ambient temperature over a period of 2 months to afford single crystals suitable for an X-ray crystallographic study. Spivak et al. assigned the molecular structure of **1** as shown in **E** (Chart 2), in which the two chloride atoms are positioned trans to each other. According to our X-ray crystallographic study on the single-crystal structure of **1**, we conclude that Spivak's structural assignment of complex **1** is incorrect. The perspective view of **1** is shown in Figure 1. In the solid state, complex **1** exhibits a neutral molecular structure in which Me_4BPPy acts as a planar N_3 ligand and the metal center is six-coordinated with the tridentate pseudo-N_3 ligand, two chlorides, and one PPh_3 ligand. A discrete CH_2Cl_2 molecule is present as well.[12] The three Ru−N bond lengths are 1.955(3), 2.078(4), and 2.051(4) Å, respectively, typical of an N_3 ligand. The two chloride atoms are nearly perpendicular to each other (Cl(1)−Ru−Cl(2) = 91.56(4)°). One chloride and the phosphine ligand, and the other chloride and the pyridyl nitrogen atom, are positioned trans (P−Ru−Cl(2) = 176.06(5)°, N(1)−Ru−Cl(1) = 176.97(12)°), respectively. The PPh_3 ligand and its trans partner chloride atom are arranged on the two sides of the pseudo-N_3 ligand plane. In the solid-state structures of **2**, the two PMe_3 ligands are positioned trans to each other, occupying on the two sides of the ligand N_3 planes, and the X moiety is arranged trans to the pyridyl nitrogen atom, respectively.[8,9] It is reasonable to expect that the bulky PPh_3 moiety in complex **1** is positioned above or below the ligand N_3 plane to reduce steric hindrance.

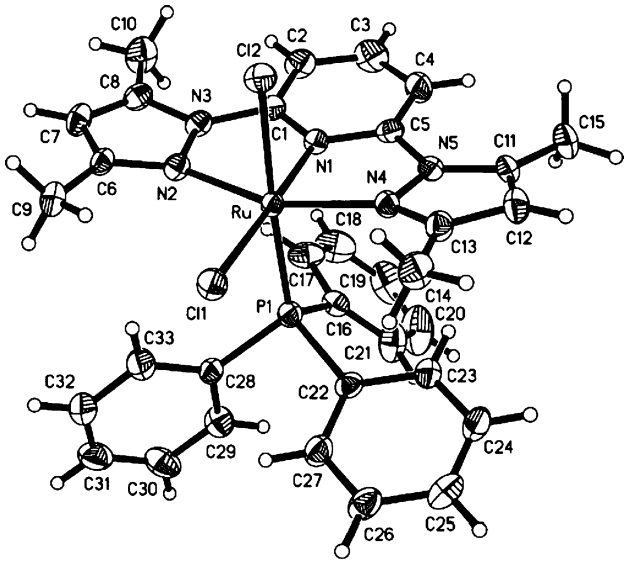


Figure 1. Perspective view of $RuCl_2(PPh_3)(Me_4BPPy)$ (**1**) with the discrete CH_2Cl_2 molecule omitted for clarity. Selected bond lengths (Å) and angles (deg): Ru−N(1), 1.955(3); Ru−N(2), 2.078(4); Ru−N(4), 2.051(4); Ru−Cl(1), 2.4546(12); Ru−Cl(2), 2.4771(13); Ru−P(1), 2.2927(14); N(4)−Ru−N(2), 156.97(15); P(1)−Ru−Cl(1), 88.09(5); P(1)−Ru−Cl(2), 176.06(5); Cl(1)−Ru−Cl(2), 91.56(4); N(1)−Ru−P(1), 94.87(11); N(1)−Ru−Cl(1), 176.97(12).

Transfer hydrogenations of ketones were carried out in 2-propanol at 82 °C with complex **1** as the catalyst and *i*PrOK as the base. Two methods were employed to carry out the catalytic reactions. With method A, the mixture of a ketone and the catalyst was refluxed in 2-propanol at the reaction temperature (82 °C) for 10 min, and then an *i*PrOK solution in 2-propanol was introduced to initiate the reaction. Using method B, the mixture of a ketone, the catalyst, and *i*PrOK in 2-propanol was stirred at room temperature for 10 min and then reacted at 82 °C. In most cases, the catalyst exhibited higher catalytic efficiency with method A than with method B (Table 1). For example, with method A the catalyst showed final TOF values of 5760, 500, and 5880 in the reactions of acetophenone, 3-benzoypyridine, and hexanone, respectively, while final TOF values of 250, 120, and 330 were obtained for the same reactions by means of method B, respectively (entries 1, 14, and 18). Only in several cases, i.e., for the ketones *p*-methoxyacetophenone, α-tetralone, α-indanone, and 2-octanone, did the catalyst exhibit higher efficiency with method B than with method A (entries 11, 16, 17, and 20). Complex **1** as the catalyst exhibited very high catalytic efficiency in the transfer hydrogenation of ketones as compared with other ruthenium(II) catalysts.[11] For acetophenone, 2-methylacetophenone, 2-chloroacetophenone, 3-chloroacetophenone, and hexanone, the reactions were very fast and were finished within 5 min (1/12 h) with 100% selectivity for the corresponding alcohols (entries 1, 3, 4, 7, and 18). In most of the other cases, the ketones reached high conversions within 5 min. The in situ generated hydrides from complex **1** may be the catalytically active species.

In conclusion, complex $RuCl_2(PPh_3)(Me_4BPPy)$ (**1**) has exhibited very high catalytic efficiency in the transfer

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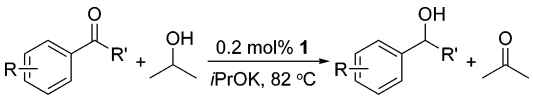
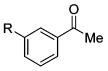
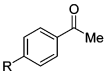
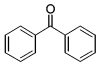
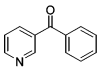
(12) Crystal data for **1**: $C_{33}H_{32}Cl_2N_5PRu{\cdot}CH_2Cl_2$, monoclinic, space group $P2_1/c$, a = 11.7563(9) Å, b = 17.1373(14) Å, c = 17.3475(13) Å, $\alpha = \gamma = 90°$, β = 93.152(2)°, V = 3489.7(5) Å^3, Z = 4, T = 293(2) K, D(calcd) = 1.497 g cm^{-3}, $R(F)$ = 5.09% for 6849 observed reflections ($3.34 \le 2\theta \le 52.00°$).

Table 1. Transfer Hydrogenation of Ketones Catalyzed by 1[f]



Entry	Ketone		Method	Time (h)	Yield (%)[a]	Final TOF (h^{-1})
1		R=Me	A	1/12	96	5760
			B	2	> 99	250
2		R = Et	A	0.75	95	630
			B	3	98	160
3		R = Me	A	1/12	> 99	5940
4		R = Cl	A	1/12	100	6000
5		R= OMe	A	3	97	160
6		R = Me	A	2.5	95	190
7		R = Cl	A	1/12	98	5880
8		R= OMe	B	3	95	140
9		R = Me	A	2	94	240
10		R = Cl	A	0.75	98	650
11		R=OMe	A	4	87	110
			B	3.5	95	140
12			B	3	89[b]	150
13[c]			A	0.5	80[d]	800
			B	4.5	93[b]	100
14			A	1	99	500
			B	4	96	120
15[c]			A	24	81	17
			B	18	74	20
16			A	28	37	7
			B	12	90	38
17[e]			A	13	41	16
			B	9	44	24
18			A	1/12	98	5880
			B	1.5	> 99	330
19			A	1.5	96	320
			B	3	98	160
20			A	3	89	150
			B	1	96	500

[a] GC yield of the corresponding alcohol. [b] Isolated yield by flash column chromatography on silica gel. [c] Catalyst, 0.5 mol %. [d] HPLC yield. [e] KOH as the base. [f] Reaction conditions: **1**/ketone/*i*PrOK = 1/500/25. ketone, 2 mmol; catalyst, 2.8 mg (0.004 mmol); *i*PrOK, 0.1 mmol; 0.1 MPa; 82 °C.

hydrogenation of ketones. The structural confirmation of complex **1** by X-ray crystallography and the present catalytic activity of **1** has revealed promising applications of a new family of planar tridentate pseudo-N_3 ligands, i.e., 2,6-bis(pyrazol-1-yl)pyridines, in transition-metal-promoted catalysis. Investigation of relevant asymmetric transfer hydrogenation and hydrogenation is under way.

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Supporting Information Available: Text, tables, and figures giving experimental procedures and X-ray crystallographic data for **1**; X-ray data are also available as a CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

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