

Communications

Dramatic Rate Acceleration by a Diphenyl-2-pyridylphosphine Ligand in the Hydration of Nitriles Catalyzed by Ru(acac)₂ Complexes

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Summary: New ruthenium(II) complexes having acac (=acetylacetonato) and diphenyl-2-pyridylphosphine as ligands proved to be excellent catalysts for hydration of nitriles to amides under neutral conditions. Among the ruthenium complexes examined, *cis*-Ru(acac)₂(PPh₂py)₂ exhibited the highest activity, with a turnover frequency of up to 20 900 (mol of amide)/(mol of catalyst h).

The catalytic hydration of nitriles is an ideal atom-economical reaction and sustainable method for the preparation of amides. Metalloenzyme^{1a} and heterogeneous transition-metal catalysts^{1b} have been employed in the large-scale industrial production of amides from nitriles. A variety of homogeneous catalysts have also been investigated:^{1c,d} main-group zinc catalysts,^{2a} late-transition-metal catalysts,^{2b,c} and early-transition-metal

catalysts.^{2d,e} Among them, Murahashi's ruthenium system³ and Parkins's platinum complexes⁴ are well-known to exhibit high yields and high turnover numbers. Recently reported heterogeneous catalysts also improved the synthetic efficiency for the preparation of amides.⁵

Here we describe new Ru(acac)₂ complexes having a diphenyl-2-pyridylphosphine (=PPh₂py; **1**) ligand that act as extremely active homogeneous catalysts for the hydration of nitriles. Phosphine **1** is one of the most extensively studied P,N hybrid ligands,⁶ due to its

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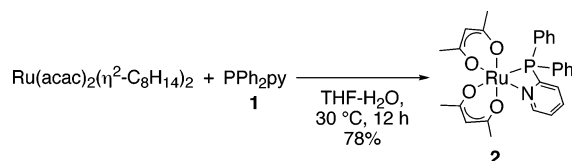
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Scheme 1. Preparation of Ru(acac)₂(κ²-PPh₂Py) (2)


accessibility. Among the hybrid ligands for homogeneous catalytic reactions,⁷ the P,N hybrid ligands have attracted considerable attention, especially in late-transition-metal catalysts.⁸ Grotjahn and co-workers have reported that ruthenium complexes having a bifunctional P,N ligand exhibited an enzyme-like enhancement of rate and selectivity in the anti-Markovnikov hydration of terminal alkynes.⁹ Grotjahn's ruthenium catalysts were inactive for hydration of a nitrile group; however, the P,N ligand system seemed promising as a potential hydration catalyst for other multiple bonds. Therefore, we prepared new ruthenium complexes having the phosphine **1** and acac ligand.¹⁰

A new Ru(acac)₂-PPh₂py complex was prepared by a modifying the procedure for Ru(acac)₂(PR₃)₂ established by Bennett and Ernst.¹¹ Treatment of Ru(acac)₂(η²-C₈H₁₄)₂^{11b} with **1** in a mixed solvent of THF and water at 30 °C gave Ru(acac)₂(κ²-PPh₂py) (**2**) in 78% yield (Scheme 1). Attempts to prepare **2** from the diene complexes Ru(acac)₂(2,3-dimethyl-1,3-butadiene)^{11a} and Ru(acac)₂(isoprene)¹² failed.

An X-ray crystallographic analysis revealed that **2** has a monomeric discrete molecular structure (Figure 1).¹³ The structural parameters for the Ru(acac)₂ unit are

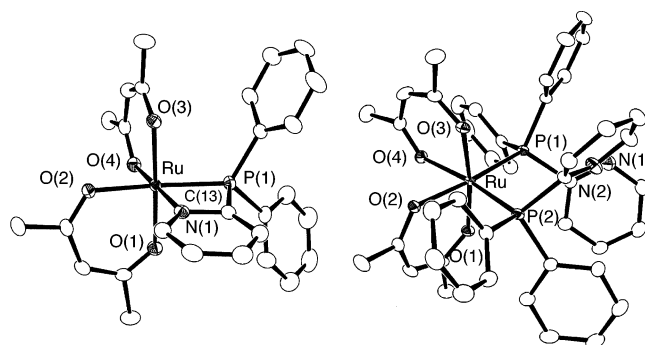
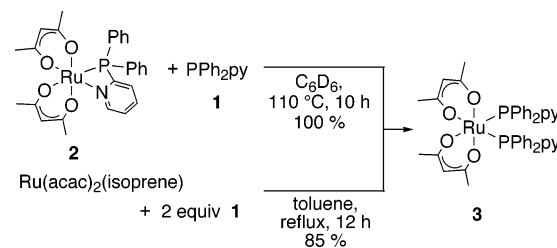


Figure 1. Molecular structures of **2** (left) and **3** (right).

Scheme 2. Preparation of cis-Ru(acac)₂(PPh₂Py)₂ (3)


comparable to those reported for *cis*-Ru(acac)₂(PR₃)₂.¹¹ The O(2)–Ru–P(1) angle (163.10(5)°) deviates from the ideal 180°, whereas the O(1)–Ru–O(3) and O(4)–Ru–N(1) angles are close to 180°. The small bite angle (69.80(6)°) for P(1)–Ru–N(1) is ascribed to the formation of the four-membered chelate ring. The Ru–P(1) and Ru–N(1) distances are shorter than those reported for RuCl₂(κ²-PPh₂Py)(CO)₂ (Ru–P = 2.322(2) Å and Ru–N = 2.119(6) Å).^{10a} The ligand **1** strongly coordinates to the Ru(acac)₂ unit as compared to the RuCl₂(CO)₂ unit.

The solid-state six-coordinate structure is consistent with that observed in solution. Four nonequivalent methyl signals of two acac ligands appeared at δ 1.78, 1.92, 1.95, and 2.20 in the ¹H NMR spectra. A variable-temperature ¹H NMR experiment revealed that **2** maintains a six-coordinate structure from 25 to 75 °C in C₆D₆ solution.

The nitrogen atom of **1** that is coordinated to the ruthenium center proved to be labile. Treatment of **2** with 1 equiv of **1** in C₆D₆ afforded *cis*-Ru(acac)₂(PPh₂py)₂ (**3**) quantitatively (Scheme 2). Complex **3** was also prepared by the reaction of Ru(acac)₂(isoprene)¹² with 2 equiv of **1**. Two phosphorus atoms coordinated to the ruthenium center (δ 57.9 in ³¹P{¹H} NMR). The slightly distorted octahedral structure of **3** was revealed by X-ray crystallographic analysis.¹⁴ The bond elongation of Ru–O lengths trans to the phosphorus atoms (Ru–O(2) = 2.089(1) Å and Ru–O(4) = 2.103(1) Å) is attributed to the trans influence of the PPh₂py ligands (Ru–O(1) = 2.066(2) Å and Ru–O(3) = 2.064(2) Å).

Catalytic hydration of nitriles was examined using benzonitrile as a substrate (Table 1). Treatment of a mixture of benzonitrile with the catalyst **2** and water in 1,2-dimethoxyethane at 180 °C for 3 h afforded

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(13) Crystal data for **2**: C₂₇H₂₈N₂O₄PRu·0.5C₆H₅CH₃; *T* = 150 K, triclinic, *P*1 (No. 2), *a* = 11.0230(8) Å, *b* = 11.207(1) Å, *c* = 12.7551(8) Å, α = 72.3808(7)°, β = 67.497(5)°, γ = 81.631(1)°, *V* = 1386.6(2) Å³, *Z* = 2, *D*_{calcd} = 1.456 g cm⁻³, μ(Mo Kα) = 6.59 cm⁻¹, 11 393 reflections measured, *R*₁ = 0.036, *wR*₂ = 0.089.

(14) Crystal data for **3**: C₄₄H₄₂N₂O₄P₂Ru; *T* = 150 K, triclinic, *P*1̄ (No. 2), *a* = 10.224(1) Å, *b* = 10.799(2) Å, *c* = 17.946(3) Å, α = 75.988(10)°, β = 88.433(10)°, γ = 81.196(6)°, *V* = 1899.7(5) Å³, *Z* = 2, *D*_{calcd} = 1.444 g cm⁻³, μ(Mo Kα) = 5.43 cm⁻¹, 15 740 reflections measured, *R*₁ = 0.034, *wR*₂ = 0.109.

Table 1. Hydration of Benzonitrile Catalyzed by Ruthenium Complexes^a

entry	cat.	additive	time (h)	yield (%)
1	2	none	1	35
2	2	none	3	98
3	3	none	0.17	100
4	<i>cis</i> -Ru(acac) ₂ (PPh ₃) ₂	none	24	66
5	2	1	0.17	99
6 ^b	3	none	3	0
7	RuCl ₂ (κ ² -PPh ₂ py)(CO) ₂	none	3	0
8	[Ru(CO) ₂ (PPh ₂ py)] ₃	none	3	25
9	RuCl ₂ (<i>p</i> -cymene)(PPh ₂ py)	none	3	3
10	RuCl ₂ (κ ² -PPh ₂ py)(CO) ₂	1	3	0
11	[Ru(CO) ₂ (PPh ₂ py)] ₃	1	3	61

^a Reaction conditions: benzonitrile (1 mmol), water (2 mmol), catalyst (0.02 mmol, 2 mol % per benzonitrile), additive (0.02 mmol), DME (0.5 mL), 180 °C. ^b Toluene was used as a solvent.

Table 2. Catalytic Hydration of Benzonitrile^a

entry	cat.	amt of cat. (mol %)	amt of H ₂ O (equiv)	temp (°C)	time (min)	yield (%)	TOF ^d
1	3	0.20	2	180	10	99	2970
2	3	0.024	2	180	10	38	11400
3	3	0.024	4	180	10	85	20900
4 ^b	3	0.20	2	180	10	88	2640
5	3	2.00	2	150	10	74	222
6	3	0.50	4	80	210	trace	0
7 ^c	4	0.50	excess	180	210	10	6

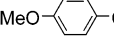
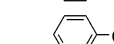
^a Reaction conditions: benzonitrile (1 mmol), DME (0.5 mL).

^b Ligand **1** was added (1:**3** = 4:1). ^c The reaction conditions were the same as in Feringa's report,^{2c} except for the temperature. ^d In units of (mol of amide)/(mol of catalyst) h).

benzamide in 98% yield along with recovered benzonitrile in 2% yield, and no organic byproduct was detected (entry 2). The hydration catalyzed by **3** proceeded to completion within 10 min (0.17 h) (entry 3). This remarkable rate acceleration by ligand **1** was demonstrated by comparison with the hydration catalyzed by a triphenylphosphine analogue of **3** (entry 4). The rapid hydration was also observed when 1 molar equivalent of **1** was added to the reaction mixture of entry 2 (entry 5). Reported Ru–PPh₂py complexes were also examined for the hydration of benzonitrile. A κ²-P,N bidentate complex, RuCl₂(κ²-PPh₂py)(CO)₂,^{10a} was inactive for the hydration and two η¹-P-coordinated complexes, [Ru(PPh₂py)(CO)₃]₃^{10b} and RuCl₂(*p*-cymene)(PPh₂py),^{10f} were slightly effective (entries 7–9). Addition of **1** to the reaction mixture of entry 8 improved the yield of benzamide, although the reactivity was still low (entry 11). These results indicate that the Ru(acac)₂ fragment was also important for the high catalytic activity.

Complex **3** exhibited a remarkably high activity, even at a low concentration of the catalyst (Table 2). The hydration of benzonitrile catalyzed by **3** in DME afforded benzamide in 85% yield, and a TOF of 20900 was achieved (entry 3). The catalytic activity decreased slightly when **1** was added to the reaction mixture of entry 1 (entry 4). The conversion was reduced significantly by decreasing the reaction temperature. Complex **3** gave a trace amount of benzamide at 80 °C (entry 6), whereas almost quantitative formation of benzamide was reported by the platinum catalyst PtH(PPh₂OH)(PPh₂O)₂H (**4**), at a similar reaction temperature.^{2c,4} Complex **4** has been known to be a highly active catalyst; for example, hydration of benzonitrile proceeded with a TOF of up to 518 at about 90 °C.⁴

Table 3. Catalytic Hydration of Various Nitriles Catalyzed by **3^a**

nitrile	time (min)	yield (%)	nitrile	time (min)	yield (%)
	30	93	CH ₃ (CH ₂) ₇ CN	30	93
	30	98	PhOCH ₂ CN	30	95
	30	96	<i>trans</i> -PhCH=CHCN	90	93
	30	99	CH ₂ =CH(CH ₂) ₃ CN	60 ^b	88
	90	95	HC≡C(CH ₂) ₃ CN	60 ^b	0
	60	99	(CH ₃) ₃ CCN	30	75 (96) ^c
Ph(CH ₂) ₂ CN	30	98	Cl ₃ CCN	30	81 (95)

^a Reaction conditions: nitrile (1 mmol), **3** (0.002 mmol, 0.2 mol % per nitrile), H₂O (4 mmol), DME (0.5 mL), 180 °C. ^b 0.04 mmol of **3** was used. ^c Determined by GC.

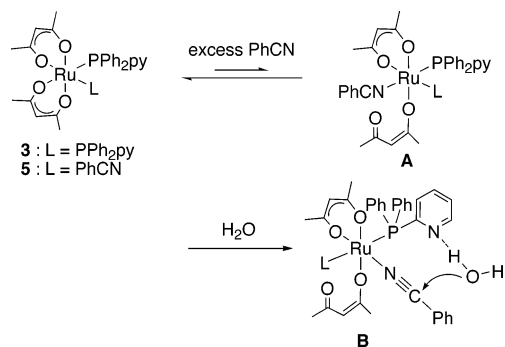
However, at 180 °C, benzamide was obtained in only 10% yield by catalyst **4**. Complex **3** is thermally stable and therefore can act as a catalyst at high temperature with high TOF.

The results of the catalytic hydration of various kinds of nitriles are summarized in Table 3. Hydration of substituted aromatic nitriles gave corresponding amides in almost quantitative isolated yields under similar neutral conditions. Industrially important nicotinamide could be prepared from 3-cyanopyridine in 99% yield. Complex **3** was also effective for hydration of less reactive aliphatic nitriles;^{5c} nonanamide was obtained from nonanonitrile in 93% yield under conditions similar to those for aromatic nitriles. The catalytic hydration proved to be affected by the presence of unsaturated C–C bonds. For example, the hydration of cinnamonnitrile needed 90 min to proceed to completion. 5-Hexenenitrile was hydrolyzed; however, the amount of the catalyst should be increased. Hydration of 5-hexynenitrile with a catalytic amount of **3** did not proceed, and 85% of 5-hexynenitrile was recovered. The catalytic reactivity toward alkynes with **3** shows a sharp contrast to that observed with reported ruthenium catalysts which promote the alkyne hydration without affecting the coexisting nitrile groups.^{9,15} Hydration of trichloroacetonitrile and sterically crowded pivalonitrile with **3** went to completion within 30 min to give the corresponding amides.

In transition-metal-catalyzed hydration of nitriles, it has been considered that a nitrile is activated upon coordination to a vacant site of a transition-metal center, and then, nucleophilic attack of water to the coordinated nitrile occurs.^{1c,d,3,16} To clarify the mechanism catalyzed by Ru(acac)₂–PPh₂Py complexes, stoichiometric hydration of *cis*-Ru(acac)₂(PPh₂py)(PhCN) (**5**) was examined. To our surprise, the coordinated benzonitrile was not hydrolyzed by treatment of **5** with an excess amount of water in DME at 180 °C for even 24 h. In contrast, a

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Scheme 3. Plausible Mechanism for the Catalytic Hydration of Benzonitrile

quantitative formation of benzamide was observed when the reaction was conducted in the presence of 2 mol % of **5** in DME at 180 °C for 3 h. These experiments suggest that the bis(acac) complex **5** is not the active species for this hydration but acts as a precatalyst. The precatalyst **5** could convert to the active species in the presence of an excess amount of benzonitrile.

These preliminary results indicate that the active species would be the complex **A** bearing a monodentate acac ligand (Scheme 3). A bidentate O-bonded acac ligand is known to isomerize to a monodentate O-bonded ligand¹⁷ or C-bonded mode.^{17a,18} Complexes **3** and **5** could be converted to O-bonded **A** in the presence of an excess amount of benzonitrile. At this point, we cannot

exclude the possibility of the formation of the C-bonded acac complex. However, to our knowledge there are no reports on a ruthenium complex having a C-bonded acac ligand. The vacant coordination site for coordination of nitriles would be generated by the dissociation of an oxygen atom caused by the trans influence of the PPh₂py ligand. For **3**, the elongation of the Ru–O bond trans to the PPh₂py ligand was revealed by X-ray analysis. The generated vacant site should be occupied in the presence of **1** (Table 2, entry 4). Nucleophilic addition of water was promoted by coordination to the PPh₂py ligand (Scheme 3, **B**).¹⁹

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Supporting Information Available: Text and figures giving synthetic procedures, characterization data, and ORTEP drawings and CIF files giving X-ray crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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