Short Note

Dichloro(η^6-*p*-cymene)(*P,P*-diphenyl-*N*-propyl- phosphinous amide-κP)ruthenium(II)

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Abstract: The title compound, i.e., [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**), was obtained in a 71% yield by reacting a toluene solution of the chlorophosphine complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**) with two equivalents of *n*-propylamine at room temperature. The aminophosphine complex **2** was characterized by elemental analysis, multinuclear NMR (^{31}P{^{1}H}, ^{1}H and ^{13}C{^{1}H}) and IR spectroscopy. In addition, its catalytic behavior in the hydration of benzonitrile was briefly explored.

Keywords: aminophosphines; ruthenium; half-sandwich complexes; chlorophosphines; nitrile hydration

1. Introduction

Aminophosphines R$_n$P(NR'$_2$)$_{3-n}$ (n = 0–2; see Figure 1), also referred to as aminophosphanes or phosphinous amides, are a well-known class of phosphorus compounds with a multitude of applications in heterocyclic, coordination and organometallic chemistry and homogeneous catalysis [1,2].
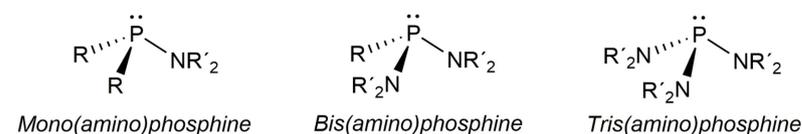

Figure 1. Generic structures of mono-, bis- and tris(amino)phosphines.

In particular, studies carried out by our group and others have shown the usefulness of aminophosphines as auxiliary ligands in metal-catalyzed nitrile hydration reactions [3–9]. It should be emphasized at this point that the catalytic hydration of nitriles is an important transformation in current and future sustainable chemical technologies since it represents a simple, efficient and atom-economical route to obtain primary amides, which are structural units present in a large variety of biologically active compounds, natural products, polymers and synthetic intermediates [10–12]. A metal–ligand cooperative effect involving the simultaneous activation of the nitrile substrate, by coordination with the metal, and the water molecule, by hydrogen bonding with one of the amino groups of the ligand (Figure 2A), has been commonly proposed to explain the superior activities of aminophosphine-based metal catalysts when compared with analogous systems containing classical phosphines PR$_3$ (R = alkyl or aryl group) [3–8]. However, recent observations have questioned this assumption and pointed to a different role of aminophosphines, which could act as precursors of phosphinous acids R$_n$P(OH)$_{3-n}$ by hydrolysis of the P-N bonds during the catalytic reactions [9]. Phosphinous acids are particularly effective ligands in the hydration of nitriles, facilitating the reaction through the generation of a highly reactive five-membered metallacyclic intermediate (Figure 2B) by intramolecular addition of the P-OH group to the metal-coordinated nitrile [13,14].
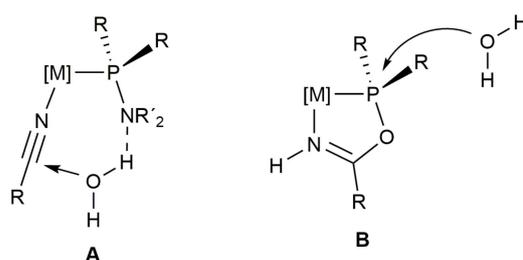
Figure 2. Structure of the intermediate species (**A**,**B**) commonly proposed in the catalytic hydration of nitriles with aminophosphine and phosphinous acid ligands, respectively.

Different ruthenium, osmium and rhodium complexes containing *N,N*-disubstituted mono-, bis- and tris(amino)phosphines have been explored to date in nitrile hydration reactions [3–9]. Conversely, *N*-monosubstituted aminophosphines have not yet been tested. This fact prompted us to synthesize a representative complex containing one of these ligands, namely [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**), and study its behavior in the hydration of the model benzonitrile substrate. A half-sandwich (η^6-*p*-cymene)–ruthenium(II) complex was chosen as the [RuCl$_2$(η^6-*p*-cymene)] fragment represents an excellent platform for the screening of ligands [15]. Details on the preparation, characterization and catalytic activity of the novel ruthenium(II) complex **2** are herein presented.

2. Results and Discussion

The condensation of chlorophosphines with amines is the most widely used method for the preparation of aminophosphines [1,2]. This aminolysis process also occurs when the chlorophosphine is coordinated to a metal [16–18]. Following this route, complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**) was obtained in a 71% yield by reacting a toluene solution of [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**), a compound previously described by us [19], with a two-fold excess of *n*-propylamine (Scheme 1). The reaction proceeded rapidly at room temperature, generating the insoluble ammonium salt [^{n}PrNH$_3$]Cl (**3**) as a by-product, which could be easily separated from the desired aminophosphine–ruthenium(II) complex **2** by filtration (see details in Section 3).
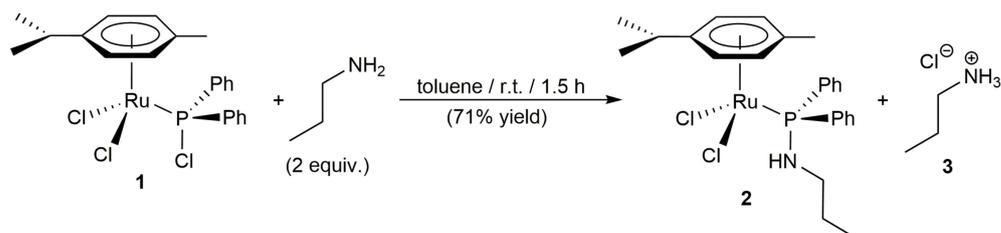
Scheme 1. Synthesis of the aminophosphine–ruthenium(II) complex **2**.

Characterization of the novel Ru(II) complex **2**, isolated as an air-stable orange solid, was straightforward following the analytical and spectroscopic data obtained (details are given in the Section 3). In particular, the ^{31}P{^{1}H} NMR spectrum was very informative, showing the presence of a singlet signal at δ_P 59.5 ppm, shielded with respect to that of the starting material **1** (δ_P 96.6 ppm) [19], and featuring the expected deshielding when compared to that of the corresponding free ligand Ph$_2$PNH^{n}Pr (δ_P 40.9 ppm) [20]. The ^{1}H and ^{13}C{^{1}H} NMR spectra of complex **2** fully confirmed the formation of the aminophosphine Ph$_2$PNH^{n}Pr, showing, in addition to the expected resonances for the Ph units, the following characteristic signals: (*i*) (^{1}H NMR) a broad signal at δ_H 3.04 ppm for the NH proton, two separated multiplets in the δ_H range of 1.28–2.43 ppm and a triplet at δ_H 0.69 ppm ($^3J_{HH}$ = 7.4 Hz) corresponding to the CH$_2$ and CH$_3$ protons, respectively, of the *n*-propyl group, and (*ii*) (^{13}C{^{1}H} NMR) two doublets at δ_C 24.3 ($^3J_{PC}$ = 5.4 Hz; PNHCH$_2$CH$_2$) and 44.6 ($^2J_{PC}$ = 11.0 Hz; PNHCH$_2$) ppm and a singlet at δ_C 11.2 ppm

(CH$_3$). On the other hand, in accordance with the presence of a symmetry plane in the molecule, only two signals for the aromatic CH protons (doublets at δ_H 5.09 and 5.27 ppm with a mutual $^3J_{HH}$ coupling constant of 5.6 Hz) and carbons (doublets at δ_C 86.1 and 91.0 ppm with $^2J_{PC}$ coupling constants of 6.0 and 4.1 Hz, respectively) of the η^6-coordinated *p*-cymene ring were observed in the ^{1}H and ^{13}C{^{1}H} NMR spectra. Resonances for the aromatic quaternary carbons (singlets at δ_C 93.7 and 107.9 ppm), and the methyl (singlet at δ_C 17.4 ppm) and isopropyl substituents (singlets at δ_C 21.3 (Me) and 30.0 (CH) ppm) of the arene ligand, were additionally observed in the ^{13}C{^{1}H} NMR spectrum. The Me and ^{i}Pr groups also left their typical mark on the ^{1}H NMR spectrum in the form of a singlet signal at δ_H 1.96 ppm for the former, and as a septuplet (δ_H 2.61 ppm; $^3J_{HH}$ = 6.9 Hz, C*H*Me$_2$) and a doublet (δ_H 0.84 ppm; $^3J_{HH}$ = 6.9 Hz, CH*Me$_2$*) for the latter. Complex **2** was further characterized by IR spectroscopy, the most characteristic band in the spectrum being associated with the ν(N-H) absorption at 3367 cm^{-1}. Unfortunately, all attempts to obtain suitable crystals for the structural determination of complex **2** by single-crystal X-ray diffraction were unsuccessful.

The catalytic potential of [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**) was subsequently evaluated, employing benzonitrile as the model substrate. As shown in Table 1, when performing the hydration reaction in pure water at 80 °C with 2 mol% of complex **2**, the desired benzamide was generated in a 89% yield after 5 h (entry 1; TOF = 8.9 h^{-1}), a result clearly inferior to that obtained when the parent complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**) was employed as a catalyst (95% yield after only 1 h of heating; TOF = 47.5 h^{-1}; entry 2). As discussed in a previous work [19], the high catalytic activity of **1** is related to its ability to rapidly transform in the reaction medium into the diphenylphosphinous acid complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$OH)] (**4**), which acts as the catalytically active species, by hydrolysis of the P-Cl bond of the coordinated chlorophosphine. Indeed, when the isolated complex **4** was employed, under identical reaction conditions, quantitative formation of benzamide was observed after only 30 min (TOF = 100 h^{-1}; entry 3). In order to determine whether **4** participates in the hydration process when [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**) is employed as the ruthenium source, the behavior of **2** towards water was explored. To this end, an NMR tube containing **2** dissolved in a THF/D$_2$O (1:1 *v*/*v*) mixture was heated in an oil bath at 80 °C for 3 h. The ^{31}P{^{1}H} NMR spectrum subsequently recorded did not show the presence of **4** and only the singlet signal of **2** was present (a copy of the spectrum is given in the Supplementary Materials file). Based on this observation, an intermediate of type A (see Figure 2) would be most likely involved in the hydration process.

Table 1. Hydration of benzonitrile into benzamide catalyzed by complexes **1**, **2** and **4** in water [1].
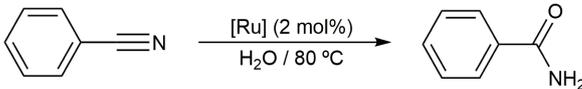
Entry	Catalyst	Time (h)	Yield (%) [2]
1	[RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**)	1 (5)	14 (89)
2	[RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**)	1	95
3	[RuCl$_2$(η^6-*p*-cymene)(PPh$_2$OH)] (**4**)	0.5	> 99

[1] Reactions performed under Ar atmosphere using 1 mmol of benzonitrile (0.33 M in water). [2] Yield of benzamide determined by gas chromatography (uncorrected GC areas).

3. Materials and Methods

The manipulations were carried out under an inert atmosphere (Ar) using vacuum-line and standard Schlenk or sealed-tube techniques. All reagents employed in this work were obtained from commercial suppliers and used as received, with the exception of complexes [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**) [19] and [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$OH)] (**4**) [21], which were synthesized following the methods reported in the literature. Organic solvents were purified by standard methods prior to use [22]. NMR spectra were recorded

at room temperature on Bruker DPX-300 (^{31}P{^{1}H} and ^{1}H) or AV-400 (^{13}C{^{1}H} and DEPT-135) instruments (Billerica, MA, USA). For the ^{13}C and ^{1}H NMR chemical shifts, the residual signal of the deuterated solvent (CDCl$_3$) was employed as a reference, while, for the ^{31}P NMR ones, 85% H$_3$PO$_4$ was used as an external standard. A PerkinElmer 1720-XFT spectrometer (Waltham, MA, USA) was employed for the IR measurements. GC measurements were performed on a Hewlett Packard HP6890 apparatus (Palo Alto, CA, USA) equipped with a Supelco Beta-Dex™ 120 column (30 m length, 250 mm diameter).

3.1. Dichloro(η^6-p-cymene)(P,P-diphenyl-N-propyl-phosphinous amide-κP)ruthenium(II) (**2**)

To a solution of the chlorophosphine complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**) (0.100 g, 0.190 mmol) in 20 mL of toluene, ^{n}PrNH$_2$ was added (31.3 μL, 0.380 mmol), and the mixture was stirred at room temperature for 1.5 h. A white precipitate of the ammonium salt [^{n}PrNH$_3$]Cl (**3**) appeared and was removed by filtration. The filtrate was then evaporated to dryness, and the resulting oily residue was dissolved in the minimum amount of CH$_2$Cl$_2$ (ca. 3 mL). Addition of hexane (15 mL) precipitated an orange solid, which was washed twice with 10 mL of hexane and vacuum-dried. Yield: 0.074 g (71%). The characterization data for complex **2** are as follows: ^{31}P{^{1}H} NMR (121 MHz, CDCl$_3$): δ = 59.5 (s) ppm. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.95–7.90 (m, 4H, CH of Ph), 7.50 (br s, 6H, CH of Ph), 5.27 (d, 2H, $^3J_{HH}$ = 5.6 Hz, CH of cymene), 5.09 (d, 2H, $^3J_{HH}$ = 5.6 Hz, CH of cymene), 3.04 (br s, 1H, NH), 2.61 (sept, 1H, $^3J_{HH}$ = 6.9 Hz, C*H*Me$_2$), 2.43–2.37 (m, 2H, NHC*H$_2$*CH$_2$Me), 1.96 (s, 3H, Me of cymene), 1.28–1.16 (m, 2H, NHCH$_2$C*H$_2$*Me), 0.84 (d, 6H, $^3J_{HH}$ = 6.9 Hz, CH*Me$_2$*), 0.69 (t, 3H, $^3J_{HH}$ = 7.4 Hz, NHCH$_2$CH$_2$*Me*) ppm. ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ = 134.5 (d, $^1J_{PC}$ = 52.1 Hz, C$_{ipso}$ of Ph), 132.9 (d, J_{PC} = 10.1 Hz, CH$_{ortho}$ or CH$_{meta}$ of Ph), 130.6 (s, CH$_{para}$ of Ph), 128.0 (d, J_{PC} = 10.0 Hz, CH$_{ortho}$ or CH$_{meta}$ of Ph), 107.9 (s, C of cymene), 93.7 (s, C of cymene), 91.0 (d, $^2J_{PC}$ = 4.1 Hz, CH of cymene), 86.1 (d, $^2J_{PC}$ = 6.0 Hz, CH of cymene), 44.6 (d, $^2J_{PC}$ = 11.0 Hz, NHCH$_2$CH$_2$Me), 30.0 (s, CHMe$_2$), 24.3 (d, $^3J_{PC}$ = 5.4 Hz, NHCH$_2$CH$_2$Me), 21.3 (s, CH*Me$_2$*), 17.4 (s, Me of cymene), 11.2 (s, NHCH$_2$CH$_2$*Me*) ppm. IR (KBr): ν = 3367 (s), 3055 (m), 2963 (m), 2914 (m), 2866 (m), 1463 (m), 1439 (s), 1408 (m), 1386 (m), 1353 (w), 1259 (w), 1235 (w), 1189 (w), 1129 (m), 1119 (s), 1100 (s), 1057 (m), 1033 (m), 1011 (m), 900 (w), 865 (w), 797 (w), 746 (s), 698 (s), 501 (s), 553 (m), 479 (m) cm^{-1}. Elemental analysis calcd. (%) for C$_{25}$H$_{32}$Cl$_2$NPRu: C 54.65, H 5.87, N 2.55; found: C 54.71, H 5.80, N 2.60.

3.2. General Procedure for the Catalytic Hydration of Benzonitrile

Under an argon atmosphere, benzonitrile (0.103 mL, 1 mmol), water (3 mL) and the corresponding ruthenium(II) complex (0.02 mmol) were introduced into a Teflon-capped sealed tube, and the reaction mixture was stirred at 80 °C for the indicated time (see Table 1). Conversion of benzonitrile into benzamide was determined by taking a sample of ca. 10 μL, which, after extraction with CH$_2$Cl$_2$ (3 mL), was analyzed by gas chromatography.

4. Conclusions

In summary, the novel aminophosphine–ruthenium(II) complex [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$NH^{n}Pr)] (**2**) has been synthesized in high yield by aminolysis of [RuCl$_2$(η^6-*p*-cymene)(PPh$_2$Cl)] (**1**) with propylamine, and analytically and spectroscopically characterized. Although **2** proved to be catalytically active in the hydration of benzonitrile in bulk water, its effectiveness was much lower than that shown by **1** due to the reluctance of the coordinated PPh$_2$NH^{n}Pr ligand to hydrolyze into the phosphinous acid PPh$_2$OH.

Author Contributions: Conceptualization, V.C.; synthesis and characterization of compound **2**, and catalysis test, R.G.-F.; original draft preparation, P.C.; review and editing, V.C. All authors have read and agreed to the published version of the manuscript.

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