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Ruthenium-Catalyzed Hydrogenation of Nitriles: Insights into the Mechanism

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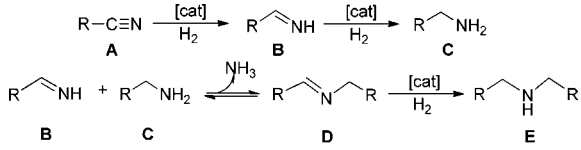
When considering the tremendous importance of adiponitrile as a precursor to hexamethylenediamine, a key component for the synthesis of the Nylon-6,6, it is rather surprising that the hydrogenation of nitriles into primary amines has received little interest among the organometallic community.[1] One of the main problems remains selectivity, as imines (**B** and **D**) or secondary amines (**E**) are very often observed as side products (Scheme 1).

Scheme 1. Hydrogenation of Nitriles (**A**) to Primary Amines (**C**) and Secondary Reaction with the Intermediate Imines (**B**)



The group of Beller has very recently addressed this problem by using Ru(cod)(methylallyl)$_2$ as a catalyst precursor and benzonitrile as the model substrate.[2] Indeed, ruthenium is a key metal in hydrogenation,[3] and in this area, the bis(dihydrogen) ruthenium complex $RuH_2(H_2)_2(PCy_3)_2$ (**1**) deserves specific attention.[4] In 1996, its use as a catalyst precursor for nitrile hydrogenation was disclosed by Beatty and Paciello in a series of patents.[5] The optimal conditions involved 0.1 mol % of catalyst, a dihydrogen pressure in the range of 50−70 bar, and a temperature in the range of 80−100 °C. Recently, Morris *et al.* compared the performance of **1** with that of hydride ruthenium complexes incorporating a tetradentate ethP$_2$(NH)$_2$ ligand {ethP$_2$(NH)$_2$ = [PPh$_2$(*o*-C$_6$H$_4$)(CH$_2$NHCH$_2$)]$_2$}.[6]

We have recently shown that a small variation in the cycloalkylphosphine can induce dramatic changes in the properties of the corresponding bis(dihydrogen) complex. In 2005, we prepared the new complex $RuH_2(H_2)_2(PCyp_3)_2$ (**2**), incorporating two tricyclopentylphosphines ($PCyp_3$).[7] **2** displays as the analogous PCy_3 complex two labile dihydrogen ligands. However, it has shown very different behavior, in particular regarding dehydrogenation processes.[8] Moreover, the superior activity of **2** as a catalyst precursor for the Murai reaction and for H/D exchange pushed us to investigate its activity for nitrile reduction. Herein, we describe the results of a catalytic investigation of benzonitrile reduction by **2** at ambient temperature and mild pressure and the first example of a catalyst resting state resulting from C−H activation and trapping of the intermediate imine **B**.

The catalytic experiments were performed at ambient temperature with 3 bar H_2 in pentane or THF or in absence of any solvent, with a catalyst:benzonitrile ratio of 1:200 or 1:500. The main results are summarized in Table 1. Conversion of benzonitrile is given after 2 or 24 h of reaction, with the corresponding selectivity in benzylamine **C** and dibenzylimine **D** (Scheme 1, R = Ph). The formation of dibenzylamine **E** was never detected. The concentrations of benzonitrile and the resulting hydrogenated products were monitored over the course of the reaction by gas chromatography.

Table 1. Catalytic Hydrogenation of Benzonitrile (**A**) into Benzylamine (**C**) and Dibenzylimine (**D**) with Complex **2**, **3**, or **5** (Scheme 2) at 22 °C and 3 bar H_2

			conversion of **A** (%)[c]		product ratio **C**:**D** (%)[c]	
entry	cat.[a]	solvent	2 h	24 h	2 h	24 h
1	**2**	pentane	94	94	94:6	94:6
2	**2**	THF	56	96	96:4	99:1
3	**2**[b]	THF	62	98	22:77	96:4
4	**2**	none	84	97	0.1:99.9	89:11
5	**3**	THF	68	97	96:4	99:1
6	**5**	THF	68	96	98:2	99:1

[a] Catalyst and benzonitrile in a 1:200 ratio unless otherwise stated. [b] Catalyst and benzonitrile in a 1:500 ratio. [c] Determined by GC.

A typical plot of the change in concentrations over time is shown in Figure 1. This plot reveals that dibenzylimine **D** is formed as an intermediate product and then converted to benzylamine **C**.

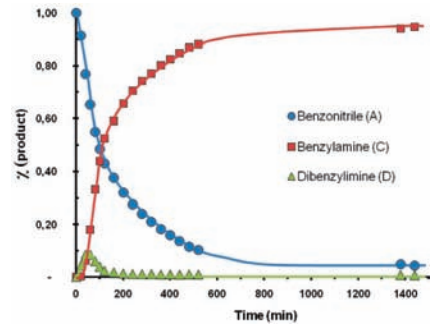


Figure 1. Hydrogenation of benzonitrile with 0.5% **2** in THF at 22 °C and 3 bar H_2.

We conducted a series of experiments at both the stoichiometric and catalytic levels to gain information on the mechanism of the reaction. Monitoring of the catalytic reaction by ^{1}H and ^{31}P{^{1}H} NMR was carried out using a THF-d_8 solution in a Quick Pressure Valve NMR tube (Supporting Information, Figures 1S and 2S). Initially, the addition of 500 equiv of benzonitrile to **2** was performed, and NMR spectra were recorded. At 223 K, the disappearance of **2** was immediately observed, with concomitant formation of two new species, characterized by two ^{31}P signals at 43.6 ppm (**3**) and 65.3 ppm (**4**) and two ^{1}H triplets in the hydride region at −11.36 ppm (**3**) and −14.68 ppm (**4**) (Scheme 2). We then pressurized the tube with 3 bar H_2 at ambient temperature. New NMR spectra were recorded showing an increase of the signals corresponding to **3** and detection of a new species **5** characterized by a ^{31}P NMR signal at 56.7 ppm and a broad hydride signal at −8.70 ppm. Further monitoring after 60 and 105 min showed the disappearance of **4**. After 105 min, **3** was the only organometallic species detected, together with a weak ^{31}P NMR signal at 5 ppm characteristic of free $PCyp_3$.[9] In view of these NMR data, we carried

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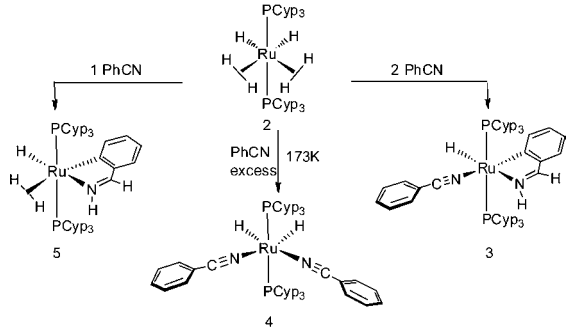
out stoichiometric reactions. The addition of 1 equiv of PhCN to **2** in THF-d_8 at ambient temperature led to signals corresponding to species **5** seen during the catalytic experiments. No other species could be detected apart from **2** and **5**. Complex **5** could be isolated in good yield and fully characterized as a hydrido(dihydrogen) cyclometalated species by multinuclear NMR, IR, and X-ray diffraction (Supporting Information). It is remarkable that the reaction leads to benzylimine formation (**B**), the first hydrogenation intermediate in benzonitrile hydrogenation, and through C−H activation gives rise to the formation of the orthometalated complex **5**. The X-ray and spectroscopic data follow those reported for other orthometalated complexes.[10]

Scheme 2. Benzonitrile Hydrogenation versus Coordination



When 2 equiv of PhCN was added to **2**, the signals corresponding to **5** and **3** also seen in the catalytic experiments were observed, prior to full conversion to **3**. Complex **3** could also be isolated and fully characterized by multinuclear NMR, IR and X-ray diffraction (Figure 2 and Supporting Information). **3** displays a structure very similar to that of **5**, except with the dihydrogen ligand replaced by a benzonitrile end-on coordinated to the metal through nitrogen. It is remarkable that in **3**, two different activation stages of benzonitrile are present: a very early stage with one PhCN acting as a two-electron donor ligand, and the first hydrogenation step with the imine coordinated to the metal thanks to C−H activation.

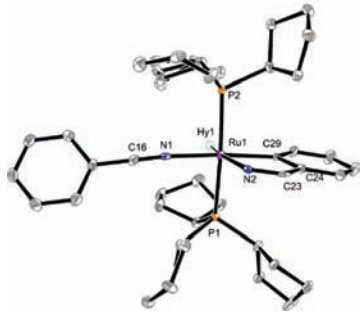


Figure 2. X-ray structure of **3**.

It turned out to be impossible to isolate **4**, the first species observed when mixing **2** with benzonitrile in the absence of H_2 at 223 K. Monitoring the mixture up to ambient temperature showed the conversion of **4** into **3**. We tentatively propose that **4** is the dihydride complex $RuH_2(PhCN)_2(PCyp_3)_2$, resulting from the substitution of the two dihydrogen ligands in **2** by two PhCN, end-on coordinated through nitrogen to the ruthenium center.[11] Having established the identities of **3** and **5**, we tested their catalytic activity and found, as shown in Table 1, entries 5 and 6, data very similar to those reported in entry 2 when using **2** as a catalyst precursor (see also Supporting Information, Figure 3S and Table 1S).

In summary, benzonitrile hydrogenation into benzylamine is readily achieved under mild conditions by the bis(dihydrogen) complex **2** incorporating tricyclopentylphosphines. A key event in this system is *ortho*-directed C−H activation within the aryl group, which induces fast cyclometalation and trapping of the intermediate imine to generate **3**, the catalyst resting state. With the coordination and cyclometalation of arylimines previously observed for different metals,[10] the isolation of the cyclometalated imine adducts **3** and **5** from benzonitrile provides useful insight into the hydrogenation mechanism. Theoretical studies and reactivity toward other nitriles are the subject of ongoing research, and the role of ammonia in promoting the formation of benzylamine will be especially analyzed.

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Supporting Information Available: Full details of the synthesis and characterization of new compounds, standard catalytic procedures, as well as X-ray data in CIF format for **3**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) We could isolate and fully characterize (X-ray structure) the analogous bis(acetonitrile) complex $RuH_2(CH_3CN)_2(PCyp_3)_2$ (**6**) (see Supporting Information).

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