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## COMMUNICATION

## Selective hydration of nitriles to amides catalysed by PCP pincer supported nickel(II) complexes

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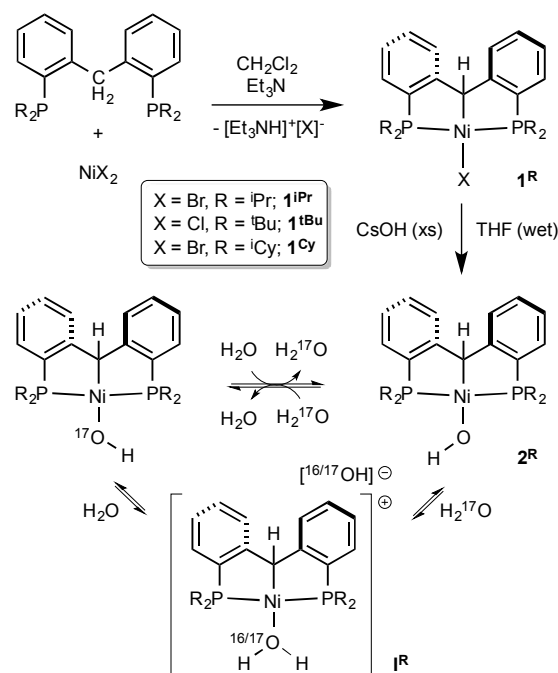
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**The (PCP)Ni-OH complexes  $2^R$  ( $R = ^iPr, ^tBu, Cy$ ) are effective catalyst precursors for the selective hydration of nitriles to the corresponding amides under relatively mild conditions (80 °C) and low catalyst loadings (0.05-0.5%). Substrate scope includes aliphatic, vinylic and aromatic nitriles, but substrates with protic groups poison the catalyst abruptly. The catalysts are effective because the electron rich nature of the PCP ligands and their steric bulk renders the hydroxo group labile.**

While the hydration of nitriles to form organic amides may seem a rather mundane transformation, the enormous scale upon which this is done gives this reaction economic and environmental significance that few other chemical conversions have.<sup>1</sup> For example, hydration of acrylonitrile to give acrylamide, the monomer for polyacrylamide, produces  $10^5$ - $10^6$  metric tonnes per annum.<sup>2</sup> The processes utilized suffer from poor selectivity, and over hydration to acrylic acid adds separation and waste disposal costs to the industry. While the use of biocatalytic routes improves selectivity,<sup>3</sup> these processes can be more expensive to operate. Therefore, there has been interest in the development of homogeneous catalysts that selectively mediate the conversion of nitriles to amides.<sup>4-6</sup> While there have been some notable successes, many of the catalysts investigated so far are based on precious metals, particularly ruthenium<sup>4,7</sup> and platinum<sup>8</sup> and lack suitable activity levels for enablement on the scales necessary. We describe here a family of comparatively active catalysts based on the earth abundant metal nickel, supported by electron rich PCP pincer ligands developed recently in our laboratories.<sup>9</sup> To our knowledge, only one homogeneous nickel-based catalyst has been reported<sup>10</sup> to date. Here, a Ni(0) catalyst precursor mediated the hydration of benzonitrile and acetonitrile under rather forcing conditions (140-180 °C). Low conversions were observed (6-68% for benzonitrile, 1-10%

for acetonitrile) and low turn over numbers (TON = 40-984 for benzonitrile, 17-257 for acetonitrile) were achieved.

The catalysts employed here are the Ni(II) (PCP)NiOH complexes  $2^R$  ( $R = ^iPr, ^tBu, Cy$ ) prepared as depicted in Scheme 1. The pincer ligand attachment protocol used is improved over that which we initially reported<sup>11</sup> by the inclusion of Et<sub>3</sub>N to remove the HX produced in the C-H activation reaction between the proligands and

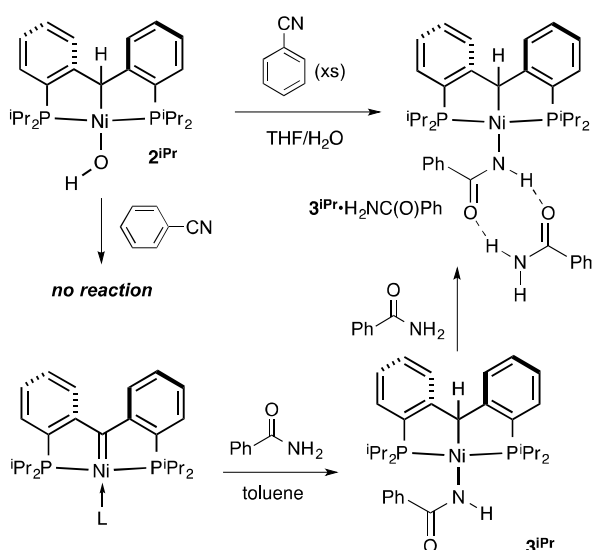


Scheme 1. Synthesis of catalysts  $2^R$  and exchange processes associated with the hydroxo group.

NiX<sub>2</sub>. In this way, the (PCP)NiX compounds **1**<sup>R</sup> can be obtained in yields of over 90%.

These compounds were fully characterized, and the X-ray structure determinations for the chloro derivative **1**<sup>tBu</sup> and the bromo complex **1**<sup>cy</sup> are included in the ESI (Figures S1 and S2). Conversion to the hydroxo derivatives was accomplished by treatment with an excess of CsOH in degassed, wet THF. In addition to ligand resonances, isolated hydroxo compounds **2**<sup>R</sup> exhibit characteristic signals at 4.73–4.84 ppm for the benzylic proton on the PCP ligand and triplets at -2.94 to -3.22 ppm (<sup>2</sup>J<sub>HP</sub> ≈ 5–6 Hz) for the O–H protons in the <sup>1</sup>H NMR spectra. The latter resonances broaden in the presence of small amounts of water, and disappear when D<sub>2</sub>O is added; the benzylic protons do not exchange with the deuterium in D<sub>2</sub>O, indicating that PC<sub>carbene</sub>P species<sup>31</sup> are not formed via elimination of water from compounds **2**<sup>R</sup>. However, when <sup>17</sup>O enriched **2**<sup>iPr</sup> was treated with H<sub>2</sub>O water, rapid depletion of label from the Ni-<sup>17</sup>OH moiety was observed (Figure S3). This demonstrates that the hydroxo group in these compounds is labile under these conditions, presumably mediated by the cationic species **I**<sup>R</sup> (Scheme 1) perhaps formed upon protonation of the hydroxo group. It is also conceivable that direct dissociation of the OH ligand occurs; the Ni–O bond distance of 1.978(2) Å found for **2**<sup>iPr13</sup> is longer than any reported in related Ni–OH compounds<sup>32–37</sup> and the C<sub>sp3</sub> anchoring group of the PCP pincer ligand should have a strong *trans* influence.<sup>18</sup>

In either case, the lability of the hydroxo group in compounds **2** in polar solvent environments suggested to us that nitriles might undergo facile hydration in the presence of a cationic species such as **I**<sup>R</sup>. When **2**<sup>iPr</sup> was treated with an excess of benzonitrile in THF, no reaction was observed either visually or spectroscopically; however, addition of water to this solution resulted in rapid conversion of hydroxo **2**<sup>iPr</sup> to a new compound characterized by a broadened peak in the <sup>31</sup>P NMR spectrum at ≈ 45 ppm, shifted downfield from that observed for **2**<sup>iPr</sup> at 39.3 ppm. Furthermore, slow conversion of benzonitrile to benzamide was observed over the course of several hours. The spectroscopic features of this mixture were difficult to



Scheme 2. Hydration of benzonitrile using **2**<sup>iPr</sup>; catalyst resting state.

interpret because of broadening and the presence of the various components in excess, but crystals deposited from solutions left standing for > 24 hours and were subjected to diffraction analysis. In this way, the new compound was identified as the κ<sup>1</sup> amidate **3**<sup>iPr</sup>•H<sub>2</sub>NC(O)Ph (Scheme 2). The molecular structure of this compound is shown in Figure 1, along with selected metrical parameters. The broadness in the NMR spectra of this compound is no doubt attributable to dynamic processes involving the hydrogen bonded benzamide molecules in the product, further complicated by the presence of excess H<sub>2</sub>O in the solutions. Amidate **3**<sup>iPr</sup> can be prepared free of hydrogen bonding partners by treating the known (PC<sub>carbene</sub>P)Ni(NC<sup>t</sup>Bu) complex<sup>31</sup> with one equivalent of dry benzamide. The N–H bond adds across the Ni=C linkage to cleanly deliver **3**<sup>iPr</sup>; the X-ray structure of this species has also been determined (Figure S4) and the numbers in parentheses in the caption for Figure 1 indicate the distances and angles found for this species as a comparison. The lack of hydrogen bonding partners for **3**<sup>iPr</sup> sharpens the NMR resonances, and in the <sup>1</sup>H NMR spectrum a signal at 3.50 ppm may be assigned to the N–H moiety, and a sharp resonance at 45.8 ppm is observed in the <sup>31</sup>P NMR spectrum. Addition of an excess of benzamide in wet THF to this sample reproduces the NMR features of **3**<sup>iPr</sup>•H<sub>2</sub>NC(O)Ph.

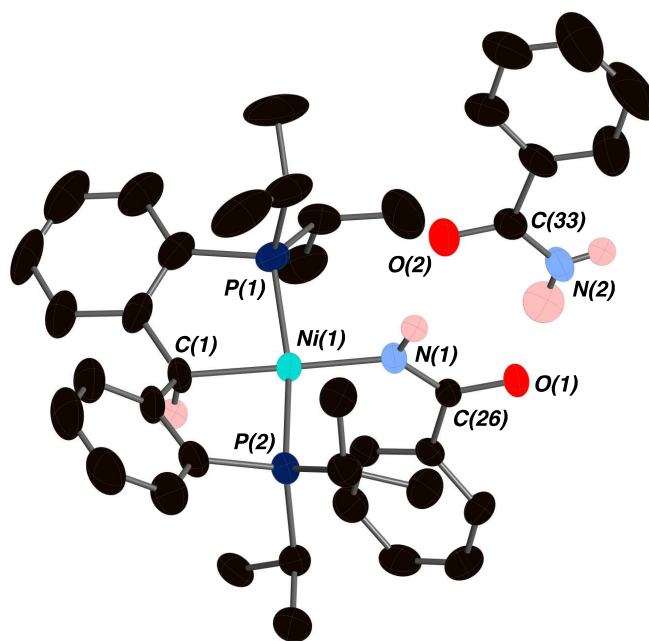
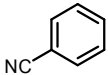
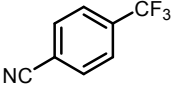
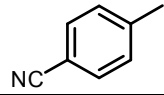
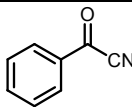
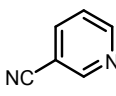
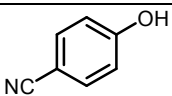







Figure 1. Molecular structure of **3**<sup>iPr</sup>•H<sub>2</sub>NC(O)Ph. Most hydrogen atoms are omitted for clarity; a second molecule of benzamide H-bonded through N(2) is also not shown. Selected bond distances, non-bonded distances (Å), angles and dihedral angles (°); numbers in square brackets are the metrical parameters for **3**<sup>iPr</sup>, included for comparison: Ni(1)–C(1), 1.990(4) [**1.973(4)**]; Ni(1)–P(1), 2.1550(12) [**2.1544(10)**]; Ni(1)–P(2), 2.1992(12) [**2.2165(11)**]; Ni(1)–N(1), 1.914(3) [**1.902(3)**]; N(1)–C(26), 1.308(5) [**1.313(6)**]; C(26)–O(1), 1.272(4) [**1.232(5)**]; N(1)–O(2), 3.128; O(1)–N(2), 2.870; P(1)–Ni(1)–N(1), 93.69(10) [**95.01(11)**]; N(1)–Ni(1)–P(2), 95.26(10) [**96.94(11)**]; C(1)–Ni(1)–P(1), 85.66(13) [**85.77(12)**]; C(1)–Ni(1)–P(2), 85.27(13) [**83.62(12)**]; P(1)–Ni(1)–N(1)–C(26), 120.26 [**123.35**]; P(2)–Ni(1)–N(1)–C(26), 73.59 [**72.80**].

Species **3**<sup>iPr</sup>•H<sub>2</sub>NC(O)Ph likely forms from a cation **I**<sup>iPr</sup> via displacement of the aquo ligand by benzonitrile and nucleophilic attack by

**Table 1.** Catalyst and substrate scope for the hydration of nitriles using nickel hydroxo compounds  $2^R$ .

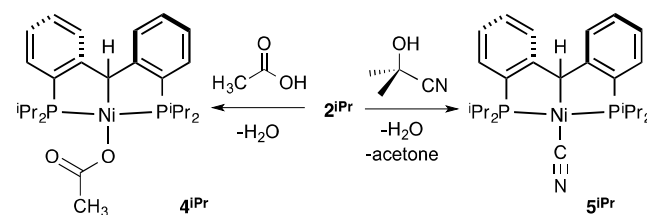
Substrate	Entry	Cat (%)	Time (h)	Yield (%)	TON
	1a	$2^{iPr}$ , 0.1	9	95 <sup>a</sup>	950
	1b	$2^{Cy}$ , 0.1	6.5	99 <sup>a</sup>	990
	1c	$2^{tBu}$ , 0.1	3	99 <sup>a</sup>	990
	1d	$2^{tBu}$ , 0.05	10	88	1750
	2	$2^{tBu}$ , 0.5	1	100	200
	3	$2^{tBu}$ , 0.5	6	98 <sup>a</sup>	196
	4	$2^{tBu}$ , 0.5	0.5	100	200
	5a	$2^{iPr}$ , 0.5	1	95 <sup>a</sup>	950
	5b	$2^{tBu}$ , 0.5	0.5	99 <sup>a</sup>	990
	5c	$2^{tBu}$ , 0.05	6	88	2000 <sup>c</sup>
	6	$2^{tBu}$ , 0.5	24	0	-
CH <sub>3</sub> CN	7a	$2^{iPr}$ , 0.1	2	47	470
	7b	$2^{iPr}$ , 0.5	2	92 <sup>a</sup>	200
	7c	$2^{tBu}$ , 0.5	1	32	64
	8a	$2^{iPr}$ , 0.5	3	99 <sup>a</sup>	200
	8b	$2^{tBu}$ , 1	4	95 <sup>a</sup>	190
	9a	$2^{iPr}$ , 0.5	6	95 <sup>a</sup>	190
	9b	$2^{tBu}$ , 1	8	95 <sup>a</sup>	95
	10a	$2^{iPr}$ , 0.5	0.5	50 <sup>b</sup>	100
	10b	$2^{tBu}$ , 0.5	1	45 <sup>b</sup>	90
	11a	$2^{iPr}$ , 0.2	3	99 <sup>a</sup>	500
	11b	$2^{tBu}$ , 0.1	6	100	1000
	12	$2^{iPr}$ , 0.5	-	0	-

<sup>a</sup> Isolated Yield, <sup>b</sup> Full conversion observed but low selectivity, <sup>c</sup> Maximum achieved TON.

hydroxide on the coordinated nitrile;<sup>5</sup> tautomerization of the kinetic product of this sequence would yield  $3^{iPr}$ . This appears to be the resting state of the nickel as the reaction turns over; only  $3^{iPr} \cdot H_2NC(O)Ph$  is observed as the ongoing conversion of benzonitrile

to benzamide is monitored by NMR spectroscopy. The reaction is slow at room temperature, and use of THF as a solvent for larger scale catalytic runs lead to solubility problems. Through optimization, we found that iso-propanol/water mixtures, spiked with a small amount of *d*<sup>8</sup>-THF for NMR spectroscopic purposes, was the best medium for the reaction; running the reactions at a temperature of 80 °C gave convenient rates.

A study of the catalyst precursor and substrate scope for nitrile hydration was conducted using these standard conditions (Table 1). A comparison of the three catalyst precursors  $2^R$  for the hydration of benzonitrile showed that the catalyst with the di-tert-butyl phosphine was more active than the iso-propyl or cyclohexyl substituted catalyst precursors (Table 1, entries 1a-d, Figure S5) for this substrate. Indeed,  $2^{tBu}$  was the most active catalyst for all aryl nitriles examined (entries 2-5). When  $2^{Cy}$  was employed, it exhibited average performance and so was not examined in any further detail. For aliphatic nitriles, however,  $2^{iPr}$  was competitive, perhaps somewhat superior, in terms of performance (entries 7-9). In the case of acetonitrile (entry 7), at lower catalyst loadings of  $2^{iPr}$ , the reaction stopped at ~50% conversion; this was due to the conversion of the catalyst to the  $\kappa^1$  acetate complex  $4^{iPr}$  (Scheme 3). Formation of  $4^{iPr}$  was ascribed to the presence of traces of acetic acid in the substrate feed, rather than over hydration of the acetamide product, since higher catalyst loadings resulted in full conversion, and prolonged exposure of pure acetamide to catalytic conditions did not produce acetic acid or  $4^{iPr}$ . Compound  $4^{iPr}$  was separately synthesized from  $2^{iPr}$  and acetic acid and fully characterized, including via X-ray crystallography (Figure S6).



Scheme 3. Catalyst poisoning processes with protic impurities.

Unfortunately, acrylonitrile underwent competitive reactions involving the C=C double bond (entry 10), and only 45-50 % conversion to acrylamide was observed. The main side reaction involved addition of iso-propanol to the double bond, followed by hydration of the amide. However, when methylacrylonitrile was subjected to catalytic conditions, selective conversion to the amide was observed (entry 11). Substrates with protic groups (entries 6 and 12) were not tolerated, since these species led to immediate catalyst poisoning. In the case of the acetone cyanohydrin substrate, treatment of the catalyst precursor  $2^{iPr}$  with even one equivalent results in rapid conversion to the cyano complex  $5^{iPr}$  (Scheme 3) which was isolated and characterized by X-ray crystallography (Figure S7) and spectroscopic methods. Details on the path by which  $5^{iPr}$  forms are not available, but could involve either formation of the alkoxide followed by  $\beta$ -cyano elimination, or (more likely) via direct reaction of  $2^{iPr}$  with hydrogen cyanide, which is present in equilibrium with the cyanohydrin in water.<sup>5</sup>

## Conclusions

Despite these limitations, the catalysts  $2^R$  can be regarded as being comparatively quite active and robust when evaluated against other homogeneous systems.<sup>5</sup> Furthermore, the use of an earth abundant metal is an attractive feature of this chemistry, and the catalysts disclosed here are more active than any nickel-based catalysts systems reported to date. The detailed mechanism by which these catalysts turnover is currently under investigation, focusing on how the resting state of the catalyst, of  $3^{iPr} \bullet H_2NC(O)Ph$ , releases product. For example, it is not clear if the catalytic cycle is completed by regeneration of the hydroxo complex  $2^{iPr}$ , or if a cationic nitrile adduct akin to  $1^{iPr}$  (Scheme 1) arises directly from  $3^{iPr} \bullet H_2NC(O)Ph$  without formation of  $2^{iPr}$ .

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This work was supported by the Natural Sciences and Engineering Research Council of Canada. W.E.P. also thanks the Canada Research Chair secretariat for a Tier I CRC (2013-2020).

## Notes and references

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Electronic Supplementary Information (ESI) available: General and detailed experimental data, thermal ellipsoid depictions of  $1^{tBu}$ ,  $1^{Cy}$ ,  $3^{iPr}$ ,  $4^{iPr}$  and  $5^{iPr}$ , <sup>17</sup>O NMR spectra and catalytic speciation plots, and crystallographic data in CIF format (CCDC 1039461-1039466). See DOI: 10.1039/c000000x/

1. E. L. Downs and D. R. Tyler, *Coord. Chem. Rev.*, 2014, 280, 28-37.
2. A. Goto, K. Endo and S. Saito, *Angew. Chem. Int. Ed.*, 2008, 47, 3607-3609.
3. S. Prasad and T. C. Bhalla, *Biotechnol. Adv.*, 2010, 28, 725-741.
4. R. García-Álvarez, J. Francos, E. Tomás-Mendivil, P. Crochet and V. Cadierno, *J. Organomet. Chem.*, 2014, 771, 93-104.
5. T. J. Ahmed, S. M. M. Knapp and D. R. Tyler, *Coord. Chem. Rev.*, 2011, 255, 949-974.
6. V. Y. Kukushkin and A. J. L. Pombeiro, *Inorg. Chim. Acta*, 2005, 358, 1-21.
7. E. Tomas-Mendivil, F. J. Suarez, J. Diez and V. Cadierno, *Chem. Commun.*, 2014, 50, 9661-9664.
8. T. Ghaffar and A. W. Parkins, *J. Mol. Cat. A: Chem.*, 2000, 160, 249-261.
9. R. J. Burford, W. E. Piers and M. Parvez, *Organometallics*, 2012, 31, 2949-2952.
10. M. G. Crestani, A. Arévalo and J. J. García, *Adv. Synth. Catal.*, 2006, 348, 732-742.
11. D. V. Gutsulyak, W. E. Piers, J. Borau-Garcia and M. Parvez, *J. Am. Chem. Soc.*, 2013, 135, 11776-11779.
12. A. Castonguay, A. L. Beauchamp and D. Zargarian, *Inorg. Chem.*, 2009, 48, 3177-3184.
13. J. Cámpora, P. Palma, D. del Río and E. Álvarez, *Organometallics*, 2004, 23, 1652-1655.
14. T. J. Schmeier, A. Nova, N. Hazari and F. Maseras, *Chem. Eur. J.*, 2012, 18, 6915-6927.
15. D. Adhikari, S. Mossin, F. Basuli, B. R. Dible, M. Chipara, H. Fan, J. C. Huffman, K. Meyer and D. J. Mindiola, *Inorg. Chem.*, 2008, 47, 10479-10490.
16. D. Huang, O. V. Makhlynets, L. L. Tan, S. C. Lee, E. V. Rybak-Akimova and R. H. Holm, *Inorg. Chem.*, 2011, 50, 10070-10081.
17. D. Powell-Jia, J. W. Ziller, A. G. DiPasquale, A. L. Rheingold and A. S. Borovik, *Dalton Trans.*, 2009, 2986-2992.
18. D. Gelman and S. Musa, *ACS Catal.*, 2012, 2, 2456-2466.

## Graphical Abstract

Nickel (II) hydroxo compounds supported by an electron rich PCP pincer ligand are active catalysts for the selective hydration of a variety of nitriles at low catalyst loadings and mild conditions.

