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Homogeneous Hydrogenation of Nitriles Catalyzed by Molybdenum and Tungsten Amides

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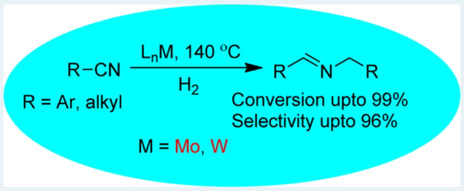
S Supporting Information

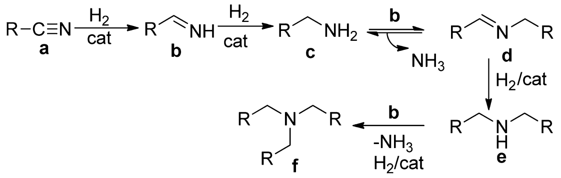
ABSTRACT: Low-valent molybdenum and tungsten amides M(NO)(CO)(PNP) {M = Mo, **1a**; W, **1b**; PNP = N(CH$_2$CH$_2$P^{i}Pr$_2$)$_2$} were found to be active catalysts for the hydrogenation of various nitriles to the corresponding imines, primary amines, and N-substituted imines with high selectivity for the latter type of product. A wide range of p- and m-substituted aromatic nitriles—*p*-methyl, *p*-methoxy, *p*-bromobenzonitriles; 3-trifluoromethylbenzonitrile, m- and p-disubstituted benzonitrile; the heterocyclic 2-thiophencarbonitrile; and the aliphatic nitriles cyclohexylcarbonitrile and benzylcyanide—could be hydrogenated at 140 °C and 60 bar H$_2$ in THF with high yields. TOFs were found to be between 0.4 and 36 h^{-1}.



KEYWORDS: *nitrile hydrogenation, secondary imines, molybdenum, tungsten, amides*

Particularly challenging in homogeneous catalysis research is the hydrogenation of nitriles[1] resulting in the production of amines and imines, which are useful synthetic precursors for pharmaceuticals and agrochemicals.[2,3a,b] Often, the catalytic hydrogenation of nitriles displays low selectivities forming imines and amines, and the amines could consist of a mixture of primary, secondary, and tertiary amines.[3] The imines are intermediates on the way to amines, which can subsequently react with the formed primary or secondary amines by expulsion of NH$_3$ to give new N-substituted imines and enamines, respectively. Concomitant hydrogenation of these leads to formation of the secondary and tertiary amines (Scheme 1). Alternatively, the secondary and tertiary amines could be formed via direct hydrogenolysis of gem diamines.[3a]

Scheme 1. General Scheme for the Hydrogenation of Nitriles to Form Primary, Secondary and Tertiary Amines via Imine Intermediates



However, reports on homogeneous nitrile hydrogenations are rare. They normally require precious metal catalysts, such as ruthenium,[4] rhodium,[1b] and iridium,[5] which may also invoke a toxicity issue. In 2008, Beller and co-workers reported ruthenium phosphine catalysts based on dppf[6] or PPh$_3$[7] ligands for the hydrogenation of a variety of aromatic and aliphatic nitriles showing high catalytic activity with selectivities for primary amines, albeit these reactions required the addition of KO*t*Bu as a base. Our group has recently developed a rhenium-based catalyst, which was found to be active in the hydrogenation of various aliphatic and aromatic nitriles forming a mixture of N-substituted imines (**d**) and secondary amines (**e**) along with tertiary amines (**f**).[8] In most cases of these hydrogenations the secondary amine (**e**) was the predominant type of product. Related to this possibility of secondary amine formation, a challenging goal would be to find ways to direct the hydrogenation of nitriles to the production of secondary imines.[9] Indeed, in a recent report, Milstein and co-workers have demonstrated that the hydrogenation of nitriles in the absence and presence of added amines could selectively yield secondary imines under mild and neutral pH conditions employing PNN-based Ru pincer complexes as catalysts.[10] Moreover, Sabo-Etienne et al. have observed formation of *N*-benzylidene-1-phenylmethaneamine during the hydrogenation of benzonitrile and were able to obtain this compound selectively when the reaction was carried out in the absence of a solvent.[11]

Today's chemistry focuses on cheaper, greener, and atom-economic ways to carry out organic transformations.[12,13] In this respect, iron, molybdenum, and tungsten catalysts would be appropriate alternatives to those with precious metal centers reaching a new stage of homogeneous catalysis with the issue of "Cheap Metals for Noble Tasks".[14] These metals are earth-abundant, have low toxicity, and are environmentally benign. In fact, recently we were able to demonstrate the catalytic efficiency of suitably substituted molybdenum- and tungsten-based catalysts in imine hydrogenations[15,16] and in related hydrosilylations of various aldehydes and ketones.[17]

In a previous publication,[15] we demonstrated that molybdenum and tungsten amide complexes M(NO)(CO)-

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(PNP) $\{M = Mo, \mathbf{1a}; W, \mathbf{1b}; PNP = N(CH_2CH_2P^iPr_2)_2\}$ (Figure 1) enable heterolytic splitting of H_2-producing bound hydrides and protons. Compounds **1a**,**b** were found active catalysts in such bifunctional hydrogenations of *N*-aryl-substituted imines with hydride transfer to the C_{imine} atom and proton transfer to the N_{imine} atom; however, *N*-alkyl-substituted secondary imines could not be hydrogenated. This was explained in terms of the indicated metal-based "ionic" catalytic reaction course. The alkyl-substituted imine/amine pairs generally possess high basicities, and the amines of type **c** are more basic than the corresponding imines of type **b** (Scheme 1). Therefore, the more basic product amines are anticipated to consume a significant proportion of the protons and in this way hinder imine activation by protonation. Furthermore, the alkyl amines would also be stronger ligands and could block the metal centers by coordination. Aryl-substituted imine/amine pairs are expected to show generally lower basicities, but the aryl imines of type **b** of Scheme 1 would be the stronger bases and could be activated by protonation to form iminium cations ready for hydride transfer generating amines of type **c**.[16] Therefore, catalytic aryl nitrile reductions are expected to initially lead to primary amines, which provide the perspective to form in a subsequent reaction secondary *N*-aryl,alky-substituted imines of type **d** (Scheme 1), which as derived in the beginning of this paragraph are expected to be reluctant to undergo hydrogenations with the given set of catalysts. With this in mind, we commenced to investigate challenging highly selective catalytic nitrile hydrogenations.

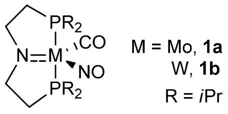


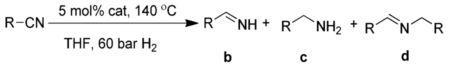
Figure 1. Catalysts for nitrile hydrogenation.

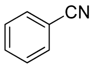
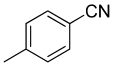
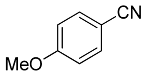
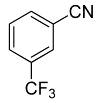
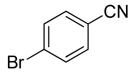
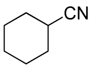
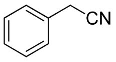
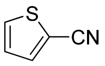
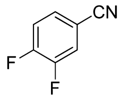
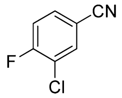
Herein, we communicate the first examples of molybdenum (**1a**)- or tungsten amide (**1b**)-catalyzed homogeneous hydrogenation of nitriles leading prevalently to formation of secondary imines (**d**). The synthetic versatility of imines promises a broad application range for them in laboratory and industrial processes.[18] Therefore, we believe that the formation of secondary imines as predominant products from readily available nitriles has a considerable synthetic potential.

Both complexes **1a** and **1b** were applied in these homogeneous nitrile hydrogenations requiring no additive or cocatalyst. Formation of a mixture of products was observed, but dibenzylimines (**d**) (Scheme 1) were strongly prevailing in the range of products. Product admixtures of minor amounts were benzylimines (**b**) and benzylamines (**c**), but dibenzylamines (**e**) or tertiary amines (**f**) were not detected either as products or as reaction intermediates, as revealed by GC/MS probing. Apparently, the higher N-substituted imines (**d**) are formed via attack of the intermediate imines (**b**) by the primary amines (**c**) producing gem-diamines followed by expulsion of ammonia.

Initially, hydrogenation of benzonitrile was carried out at room temperature with a loading of 5 mol % of the catalyst **1a** under 60 bar H_2 in THF. However, the GC/MS analyses revealed after 14 h the formation of only 3% *N*-benzylidenebenzylamine (Table 1, entry 1, first row). When the temperature was raised to 140 °C with otherwise the same conditions, an initial TOF of 36 h^{-1} could be achieved, corresponding to a conversion of 90% after an initial 30 min. The reaction was completed in <4 h, yielding 10% benzylimine and 90% *N*-benzylidenebenzylamine (Table 1, entry 1, middle row). No benzylamine could be detected as revealed by GC/MS analysis. Exploring the scope of this catalytic reaction by

Table 1. Hydrogenation of Aromatic and Aliphatic Nitriles Catalyzed by 1a and 1b



Entry[a]	Substrates	Cat	Time (h)	Initial TOF (h^{-1})[b]	Conv[c] (%)	Sel (%) (b:c:d)[c]
1		1a	14	ND	3[d]	0:0:100
		1a	<4	36	>99	10:0:90
		1b	14	0.4[e]	91	26:0:74
2		1a	<6	36	>99	0:10:90
		1b	16	ND	3	0:0:100
		1b	16	ND	19	0:0:100[f]
3		1a	< 6	ND	>99	0:7:93
4		1a	< 6	6	>99	0:22:78
		1b	14	-	0	0
5		1a	8	16	98	4:0:96
6		1a	< 4	34	>99	0:22:78
		1b	16	ND	14	0:0:100
7		1a	14	3	40	0:0:100
8		1a	< 8	4	>99	43:8:49
		1b	14	-	0	0
9		1a	6	8	>99	4:0:96
10		1a	14	ND	22	54:0:46

[a]Unless otherwise stated, 5 mg of the catalyst **1a** or **1b**, 20 equiv substrate relative to catalyst, 140 °C temperature, 60 bar H_2, and 2 mL of THF as solvent were used as reaction conditions. [b]Initial TOFs were determined after 30 min by GC/MS. [c]Conversions and selectivity were determined by GC/MS on the basis of substrate consumption. [d]At room temperature [e]TOF was determined after initial 1 h. [f]150 °C temperature was used. ND = initial TOFs were not determined. Sel = selectivity.

application of a variety of nitriles, the reaction of 4-methylbenzonitrile and 4-methoxybenzonitrile resulted under the same conditions (60 bar H_2 and 140 °C) and with a loading of 5 mol % of **1a** in THF in the formation of *N*-(4-methylbenzylidene)-1-(*p*-tolyl)methanamine and *N*-(4-methoxybenzylidiene)-1-(4-methoxyphenyl)methanamine, respectively, showing complete conversion in <6 h (90% and 93% selectivity of the secondary imine; entries 2 and 3). Compound **1a** was also found to be active in the hydrogenation of the sterically more hindered 3-trifluoromethylbenzonitrile, which was completely converted to the corresponding primary amine of type **c** and to the secondary imine of type **d** with 22% and 78% selectivity, respectively (Table 1, entry 4). In the hydrogenation of *p*-bromobenzonitrile, applying **1a** (5 mol %) as a catalyst at 140 °C under 60 bar H_2 in THF (Table 1, entry 5), a selectivity of 96% was observed for the generation of the corresponding *N*-(4-bromobenzylidene)-1-(4-bromophenyl)methaneamine.

The potential of the catalyst was further probed by employing more challenging alkyl and functionally substituted heterocyclic nitriles. Cyclohexylcarbonitrile could be fully hydrogenated to the corresponding primary amine and the secondary imine with 22% and 78% selectivity, respectively, with 5 mol % of the catalyst **1a** under 60 bar H_2 at 140 °C, giving an initial TOF of 34 h^{-1} (Table 1, entry 6). Benzylcyanide could also be hydrogenated, revealing the formation of exclusively secondary imine in moderate 40% yield after 14 h of reaction time (Table 1, entry 7). However, the reaction was slow, with an initial TOF of only 3 h^{-1}. 2-Thiophencarbonitrile was hydrogenated completely to the corresponding primary amine, and primary and secondary imines, within 8 h (Table 1, entry 8), employing **1a** as the catalyst with an initial TOF of 4 h^{-1}. The selectivity of the corresponding secondary imine was 49%. Surprisingly, m- and p-dihalosubstituted benzonitriles were also efficiently hydrogenated using catalyst **1a**. For example, 3,4-difluorobenzonitrile exhibited complete conversions, with transformation to the corresponding secondary imine (96%) and 4% of the primary amine after 6 h using 5 mol % of the catalyst **1a** at 140 °C under 60 bar H_2 (initial TOF of 8 h^{-1}) (Table 1, entry 9). As an example of lower catalytic conversion, 3-chloro-4-fluorobenzonitrile was found to be very sluggishly hydrogenated, with a conversion of only 22% after 12 h under otherwise the same conditions as in the experiments before with 46% selectivity of the corresponding secondary imine (Table 1, entry 10).

The scope of the nitrile hydrogenations could be extended further by applying the tungsten analogue **1b** as the catalyst. As for **1a**, 5 mol % of **1b** was used in the prototypic benzonitrile hydrogenation in THF at 140 °C under 60 bar H_2, which furnished 91% conversion to the corresponding imine (**b**, 26%) and dibenzylimine (**d**, 74%) after 14 h of reaction time, as revealed by the GC/MS, albeit a very low TOF of 0.4 h^{-1} in the first hour (Table 1, entry 1, last row). Nonetheless, only 3% catalytic conversion of *p*-methylbenzonitrile to the corresponding dibenzylimine *N*-(4-methylbenzylidene)-1-(*p*-tolyl)methaneamine could be observed after 16 h when 5 mol % of catalyst **1b** was used (140 °C, 60 bar H_2) (Table 1, entry 2, middle row). Raising the temperature to 150 °C (otherwise keeping the same conditions) showed only little improvement in the catalytic performance (19%, Table 1, entry 2, last row). It was a somewhat unexpected result to find that attempts of hydrogenations of 3-trifluoromethylbenzonitrile and 2-thiophencarbonitriles using **1b** as a catalyst (5 mol %) did not occur at all at 140 °C under 60 bar H_2 in THF (Table 1, entries 4, and 8). Exclusive formation of secondary *N*-(cyclohexylmethelene)-cyclohexanemethanamine was observed when the aliphatic cyclohexylcarbonitrile was hydrogenated at 140 °C under 60 bar H_2 using catalyst **1b**, furnishing a quite low yield (14%) after 16 h as revealed by GC/MS (Table 1, entry 6, last row).

To summarize, we could demonstrate for the first time the catalytic application of non-noble molybdenum and tungsten complexes {M(NO)(CO)(PNP) M = Mo, **1a**; W, **1b**} in homogeneous hydrogenations of a variety of nitriles: p-substituted benzonitriles; *p*-methyl, *p*-methoxy, *p*-bromo benzonitriles; 3-trifluoromethylbenzonitrile, disubstituted benzonitriles (meta and para), heterocyclic 2-thiophencarbonitrile, aliphatic cyclohexylcarbonitrile, and benzylcyanide could be converted to their corresponding secondary imines (**d**) with moderate to good selectivity along with the formation of primary imines (**b**) and the primary amines (**c**) in most of the cases. Excellent conversions were achieved applying particularly the molybdenum system **1a** as the catalyst. This exploration showed that middle transition element complexes when equipped with an appropriate ligand environment are capable of taking the role of precious platinum group metal catalysts, and it seems therefore worthwhile to make efforts extending this fundamental finding to optimize via ligand "tuning" of the catalysts the activities of these catalyses.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and the GC/MS data of the substrates and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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