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Recent Developments in Manganese, Iron and Cobalt Homogeneous Catalyzed Synthesis of Primary Amines via Reduction of Nitroarenes, Nitriles and Carboxamides

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Abstract. The preparation of primary amines attracts huge attention in the molecular synthetic community. Indeed, amines play a crucial role in chemistry as they are important substructures in a huge amount of drug molecules, agrochemicals, dyes and molecular materials. Compared to stoichiometric reductions using metal hydride based reagents, the catalyzed reduction of nitroarenes, nitriles and carboxamides appears to be an attractive option, mainly when associated to first row transition metals such as manganese, iron, or cobalt. In this short review, we illustrate the progress achieved in homogeneous hydrogenation, hydrogen transfer, hydrogen borrowing and hydrosilylation of nitroarenes, nitriles and carboxamides.

1. Introduction
2. Reduction of nitro derivatives
3. Reduction of nitriles
4. Reduction of primary amides
5. Reductive amination using ammonia as a challenging task
6. Conclusion
7. References

Keywords: iron; manganese; cobalt; homogeneous catalysis; reduction; nitro; carboxamides; nitriles; primary amines

1. Introduction

Amines play a crucial role in the field of synthetic chemistry, particularly primary amines, as they are important substructures in a huge amount of drug molecules, agrochemicals, dyes and molecular materials.^[1] A series of molecules containing a primary amino structure unit are presented in Figure 1 with their corresponding applications.

As pivotal platform in synthesis, the efficient preparation of primary amines is still a topical area of research. The classical access to such primary amines used well known fundamental transformations, such as the Gabriel synthesis, Curtius rearrangement, S_N2 substitution of alkyl halides with ammonia, Staudinger reaction, Béchamp's reduction, etc.^[2] Main of them, even if efficient, either use toxic starting materials or produce by-products. Taking their importance into consideration, research on innovative and efficient methodologies for the preparation of primary amines is still an imperative and ongoing field of study. In addition to the attractive palladium and copper catalyzed amination of organohalides with ammonia,^[3] the most common approaches for their synthesis also include the reduction of nitro or nitrile derivatives, carboxylic derivatives (primary amides, carboxylic acid in the presence of ammonia), reductive amination of aldehydes and ketones, as well as the amination of alcohols via transfer hydrogenation reaction.^[4,5]



Jiajun Wu was born in Liuzhou, Guangxi, P.R. China, in 1993. He received his Bachelor's degree in 2016 from Fujian Normal University under the supervision of Prof. Qiufeng Huang. Then, he moved to

Xiamen University where he worked with Prof. Hui-Jun Zhang and obtained his master degree in 2019. He is currently a PhD candidate working in Prof. Christophe Darcel's research team at the Université de Rennes 1. His research focuses on homogeneous iron catalyzed hydrosilylation and transfer hydrogenation reactions.

Christophe Darcel grew up in the north coast of Brittany and studied chemistry at the Université de Rennes 1, where he obtained his PhD in 1995 under the joint-supervision of C. Bruneau and P. H. Dixneuf on Ru- and Pd-catalyzed transformations of functional alkynes. After a year's post-doctoral stay with W. Oppolzer (Switzerland) working on sultam stereoselective chemistry and application in natural products synthesis, he then joined the group of P. Knochel (Germany) as an Alexander von Humboldt postdoctoral fellow and worked on the development of chiral zinc derivatives. In 1997, he was then appointed at the Université de Cergy-Pontoise as assistant professor, and at the University of Burgundy as associate professor developing in collaboration with S. Jugé P-chirogenic ligands for asymmetric catalysis. In 2007, he became full professor at the Université de Rennes 1. His current research interests concentrate on homogeneous catalysis with particular emphasis on well-defined iron complexes in catalysis.

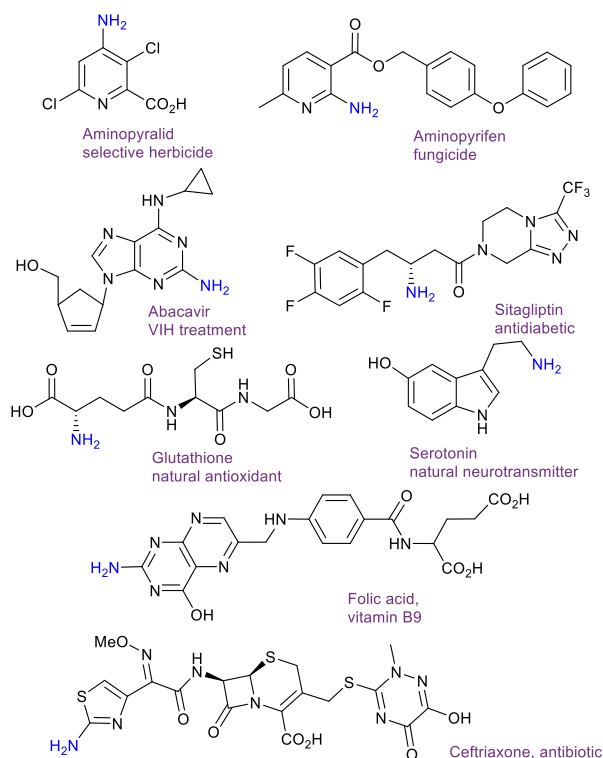


Figure 1. Selected representative examples of molecules containing a primary amino moiety.

Even if such methodologies are well-established, they still suffer from some main limitations such as (i) the lack of selectivity over primary, secondary, and tertiary amines, (ii) the use of tedious multistep process and of harsh reaction conditions, and (iii) sometimes the use of stoichiometric alkali metals.^[6]

Based on the importance of the reduction of carboxylic and nitro derivatives for the production of primary amines, and in the view of the huge increase of the use of non-noble transition metals such as manganese,^[7] iron^[8] and cobalt^[9] in catalyzed reductions, herein we combined the development of the associated both topics within recent decades, including hydrogenation, hydrosilylation, and transfer hydrogenation methodologies. Thus, this review has several main objectives: (a) to provide a concise overview of the literature in the preparation of primary amines from primary carboxamides, nitriles and nitro derivatives, and (b) to show the potential of manganese, iron and cobalt as surrogate transition metals to the noble ones. (Figure 2)

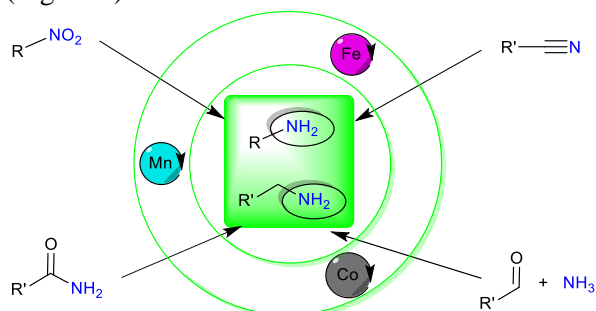


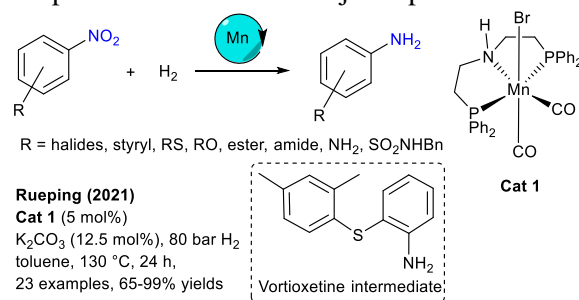
Figure 2. Content of this review

2. Reduction of nitro derivatives

The reduction of the nitro group is one of the most powerful and widely used transformations which permits to incorporate an amino substituent in a molecule.^[10] The classical Béchamp's reduction which used a stoichiometric amount of iron powder in the presence of concentrated hydrochloric acid permitted to produce on industrial scale simple aniline derivatives. The main drawback is clearly the lack of functional group tolerance, and the drastic involved reaction conditions. Thus, in order to synthesize more complex functionalized molecules, catalytic chemoselective nitro reduction protocols have been more recently developed, notably based on hydrogenation, transfer hydrogenation and hydrosilylation.

2.1. Hydrogenation of nitro derivatives

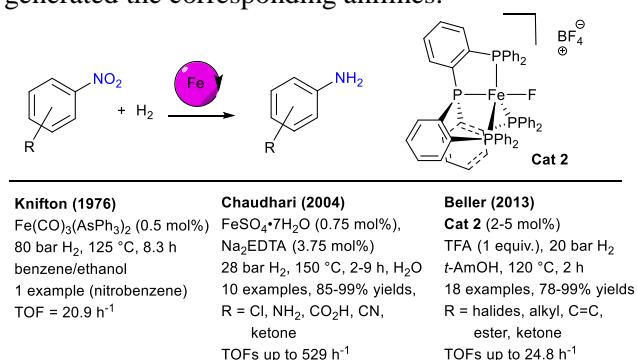
At manganese - Even if manganese catalyzed reduction did a recent breakthrough,^[7] to the best of our knowledge, there is only one recent report by Rueping describing the hydrogenation of nitroarenes to anilines. Thus, using a well-defined PNP pincer complex **Cat 1** (5 mol%) in the presence of 12.5 mol% of potassium carbonate in toluene at 130 °C for 24 h under 80 bar of hydrogen, a huge variety of nitroarenes were efficiently reduced. Noticeably, numerous functional groups such as halides including iodide, esters, amides, sulfonamides, or primary amines were tolerated (Scheme 1).^[11] By contrast, under such conditions, nitriles, alkynes, ketones, and olefins were partially reduced. Interestingly, such reduction was applied for the preparation of Vortioxetine, an antidepressant used to treat major depressive disorder.



Scheme 1. Manganese-catalyzed hydrogenation of nitroarenes to anilines

At iron - Before the beginning of this millennium, only scarce examples of homogeneous iron catalytic systems have been described for the reduction of nitroarenes to anilines. One pioneering contribution of Knifton in 1976 reported the hydrogenation of nitrobenzene catalyzed by two well defined iron complexes, $\text{Fe}(\text{CO})_3(\text{PPh}_3)_2$ and $\text{Fe}(\text{CO})_3(\text{AsPh}_3)_2$ at 125 °C under 80 bar of H_2 .^[12] Noticeably, higher

activity and selectivity were obtained using bis(triphenylarsine)tricarbonyl iron(0). A breakthrough was done three decades later by Chaudhari who identified that the catalytic species *in situ* generated from $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (0.75 mol%) and ethylenediaminetetraacetic acid disodium salt (EDTANa_2 , 3.75 mol%) was particularly efficient in the catalytic hydrogenation of nitroarenes under 28 bar of H_2 at 150 °C, notably working in a water biphasic system.^[13] Nitrile, carboxylic acid, and ketone reducible functional groups were tolerated. Interestingly, using such biphasic system, an easy separation of the catalyst from the mixture can be performed and a significant cumulative TON above 6000 was obtained even if a loss of activity was observed (TOF up to 529 h^{-1} vs 1247 h^{-1} without EDTANa_2). In 2013, Beller reported iron / tetrphosphine based catalysts for the hydrogenation of nitroarenes.^[14] Using 2-5 mol% of the iron-tetraphos complex **Cat 2** associated to 1.0 equiv. of trifluoroacetic acid (TFA) in *tert*-amylalcohol under 20 atm of H_2 at 120 °C for 2 h, the corresponding anilines were produced in 78–99% yields. The *in situ* generated catalytic species from $\text{Fe}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$ and the corresponding tetradentate tris[2-(diphenylphosphino)phenyl]-phosphine led to similar efficiencies. It should be underlined the nice functional groups tolerance of the transformation [ketones, esters, nitriles, styryl, halides (including iodides)]. (Scheme 2) In a mechanism point of view, the catalytic species, $[\text{FeH}(\text{P}_4)]^+$, was generated from the pre-catalyst $[\text{Fe}(\text{P}_4)][\text{BF}_4]$ **Cat 2** by action of H_2 and elimination of HF. Thus, under pressure of H_2 , a diamagnetic species $[\text{FeH}(\text{H}_2)(\text{P}_4)][\text{BF}_4]$ was obtained and reduced ArNO_2 to lead to ArNO and regenerate the $[\text{FeH}(\text{P}_4)]^+$ active species. Two additional cycles then generated the corresponding anilines.

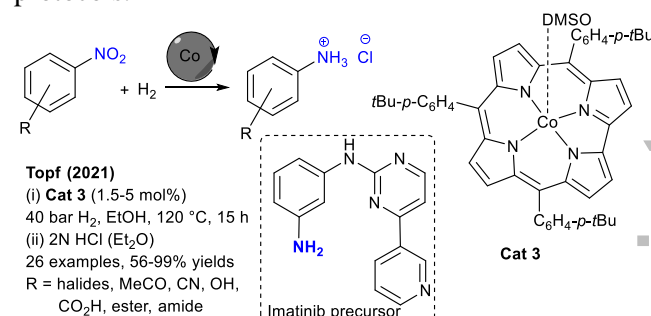


Scheme 2. Iron-catalyzed hydrogenation of nitroarenes to anilines

At cobalt - Similarly to manganese, there are scarce examples of homogeneous cobalt-catalyzed hydrogenation of nitroarenes to anilines. The first report by Topf *et al.* described the use of a cobalt corrole catalyst **Cat 3** (1.5-5 mol%) for the hydrogenation of functionalized nitroarenes in ethanol under 40 bar of H_2 at 120 °C (Scheme 3).

The resulting ammonium salts were obtained in 56-99% isolated yields after an extra step of acidolysis with 2N HCl. Importantly, numerous functional groups were tolerated such as halides (including

iodine), ketones, nitriles, hydroxyls, carboxylic acids & esters, α,β -unsaturated carboxylic acid) and heterocycles.^[15] By contrast, ethenyl group was reduced under such conditions, and even if 3-nitrostyrene can be reduced selectively to 3-aminostyrene, this latter product could not be isolated, due to rapid polymerization. Additionally, a precursor of the anticancer Imatinib drug could be prepared using such conditions, giving an alternative reduction pathway to the traditional Raney nickel or SnCl_2/HCl protocols.



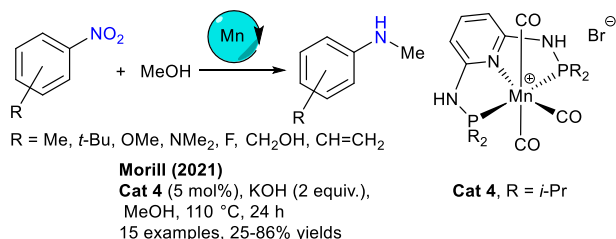
Scheme 3. Cobalt-catalyzed hydrogenation of nitroarenes to anilines.

2.2. Transfer hydrogenation of nitro derivatives

Comparing to the classical hydrogenation reaction performed in autoclaves under high pressure of H_2 , the catalyzed transfer hydrogenation is always an interesting alternative in terms of practical application and convenience, and eco-friendly starting materials can be used as hydrogen donors. Such methodologies were also applied for the reduction of nitroarenes.

At manganese - To the best of our knowledge, there is no report up to today dealing with homogeneous manganese catalysis via transfer hydrogenation producing anilines from nitroarenes. Nevertheless, using methanol as the hydrogen donor, nitroarenes can be reduced to anilines which can be then methylated selectively leading to the corresponding N-methyl arylamines. Indeed, Morrill *et al.* recently described the use of a well-defined PNP pincer Mn(I) cationic complex **Cat 4** (5 mol%) for the conversion of nitroarenes into N-methylanilines in the presence of 2 equiv. of KOH in methanol at 110 °C for 24 h in 25-86% yields (Scheme 4).^[16] It should be underlined that this protocol was highly selective towards mono-methylation, with no dimethylated compound observed. The reaction could be conducted with alkyl, methoxy, dimethylamino, fluoro, CH_2OH and $\text{CH}=\text{CH}_2$ groups. By contrast, starting from hydroxy or amino substituted nitroarenes, no reaction took place and the reaction with CN, CF_3 , COMe substituted nitroarenes and nitroalkanes led to the decomposition of the starting materials.

Additionally, when conducting the reaction with 2-nitro-pyridine, the corresponding 2-aminopyridine, resulting from the transfer hydrogenation, was obtained in 85% yield. Noticeably, when performing the reaction in ethanol instead of methanol, nitrobenzene was selectively reduced to aniline in a moderate 33% NMR yield.

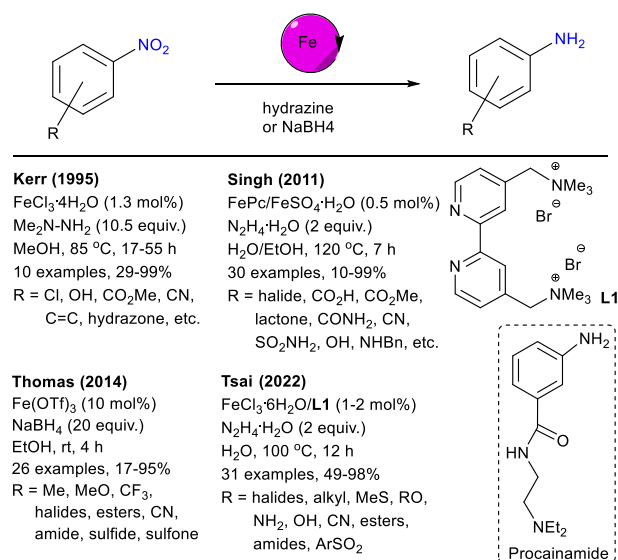


Scheme 4. Manganese-catalyzed transfer hydrogenation of nitroarenes

At Iron - Iron complexes have also been described as efficient catalysts for transfer hydrogenation of nitroarenes. There were pioneering contributions using iron salts or complexes as catalysts and either hydrazine derivatives or NaBH₄ as hydrogen sources to perform this transformation, and representative examples are presented in Scheme 5. Kerr's group disclosed the first report on iron-catalyzed transfer hydrogenation of nitroarenes, using 1.3 mol% of FeCl₃·4H₂O and 10.5 equiv. of N,N-dimethylhydrazine in the presence of charcoal at 85 °C for 17-55 h, thus leading to the corresponding anilines in 29-99% yields.^[17] Later the iron phthalocyanine (FePc) catalytic system in combination with FeSO₄·5H₂O (0.5 mol% for each) in the presence of 2 equiv. of N₂H₄·H₂O was reported for the formation of anilines in a H₂O/EtOH 1:1 mixture by Singh's group in 2011. Conducting the reaction at 120 °C for 7 h, the anilines can be purified with a range of compatible functional groups such as halogen, hydroxy, nitrile, ester, ketone and amide.^[18] Starting from nitroalkanes, no reaction occurred. Recently, Tsai *et al.* have developed a reusable protocol for the reduction of nitroarenes using the commercial FeCl₃·6H₂O salt associated with the cationic 2,2'-bipyridyl ligand **L1** in water at 100 °C.^[19] The catalyst can be reused up to 3 times with a significant decrease of activity (from 99 to 78% yields). Numerous functional groups were tolerated such as halides, sulfide, hydroxyl amino, cyano, ester, amide and sulfonyl. When nitroarenes bearing formyl or acetyl groups were used, the nitro group was reduced to amino, but the carbonyl group also reacted with hydrazine, thus leading to the hydrazone compounds. Using these conditions, Procainamide, which is used for the treatment of cardiac arrhythmias could be obtained in 98% from its corresponding nitro derivative.

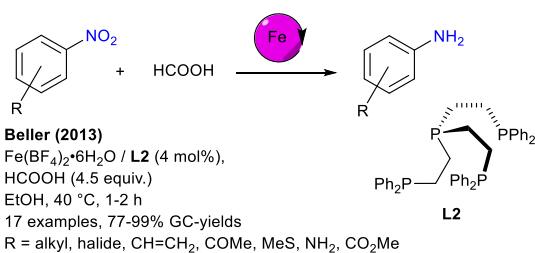
On the other hand, simple iron salts were evaluated using NaBH₄ as the hydrogen source. For example, Thomas and co-workers reported a transfer hydrogenation methodology for the reduction of

nitroarenes using Fe(OTf)₃ as the catalyst in the presence of NaBH₄. Even if 20 equiv. of reductant were required to perform this reduction reaction at room temperature in ethanol, it tolerated trifluoromethyl, ester, amide, nitrile, sulfide and sulfone groups. Aliphatic nitro derivative such as nitrocyclohexane was also reduced to give cyclohexanamine in 20% yield. However, the reaction with 4-nitroacetophenone was not selective as 1-(4-aminophenyl)ethan-1-ol, resulting from the reduction of both functional groups, was obtained.^[20]



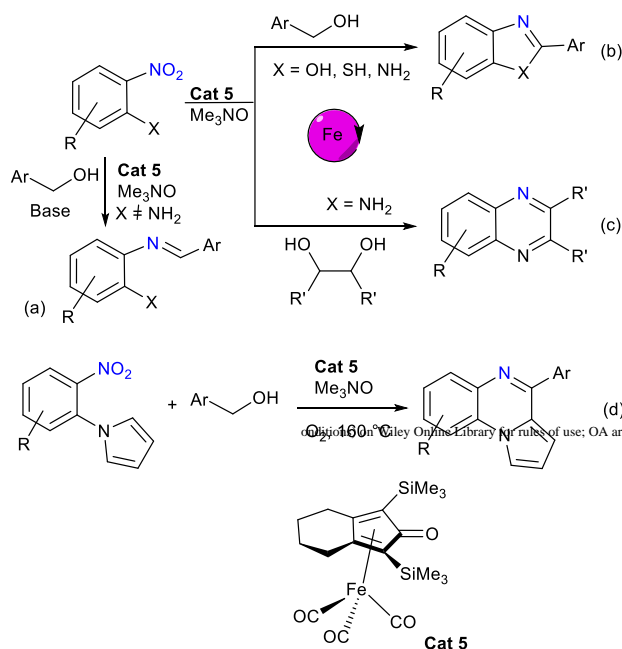
Scheme 5. Iron-catalyzed transfer hydrogenation of nitroarenes with hydrazines or NaBH₄

In addition, formic acid is also an available reagent to act as a hydrogen donor for the reduction of nitroarenes to afford anilines under transfer hydrogenation process. Thus, using tetraphos ligand P(CH₂CH₂PPh₂)₃ **L2** associated to Fe(BF₄)₂·6H₂O catalytic precursor (4 mol%), Beller and co-workers reported an alternative reduction of nitroarenes by transfer hydrogenation with 4.5 equiv. of formic acid in the absence of additional base at 40 °C in ethanol for 1-2 h. The aniline derivatives were obtained in 77-99% yields, with TOF up to 23.3 h⁻¹ (Scheme 6).^[21] The procedure tolerated a large number of functional groups, including ketones, C=C double bonds, esters, thioether, and halide substituents. In a mechanism point of view, the active catalytic species [Fe(**L2**)F]⁺ can react with formate to lead to the corresponding [(HCO₂)Fe(**L2**)F] species which then produced, after β-elimination then non reductive elimination of CO₂, an iron hydride intermediate [(H)Fe(**L2**)F], able to reduce nitro to nitroso. Similar catalytic cycles can then explain the formation of the aniline derivatives.



Scheme 6. Iron-catalyzed transfer hydrogenation of nitroarenes with formic acid.

Up today, no report disclosed the use of tricarbonyl(cyclopentadienone) iron complexes such as **Cat 5** for the reduction of nitroarenes yielding aniline derivatives under transfer hydrogenation conditions. Nevertheless, few reports described their formation as intermediates.

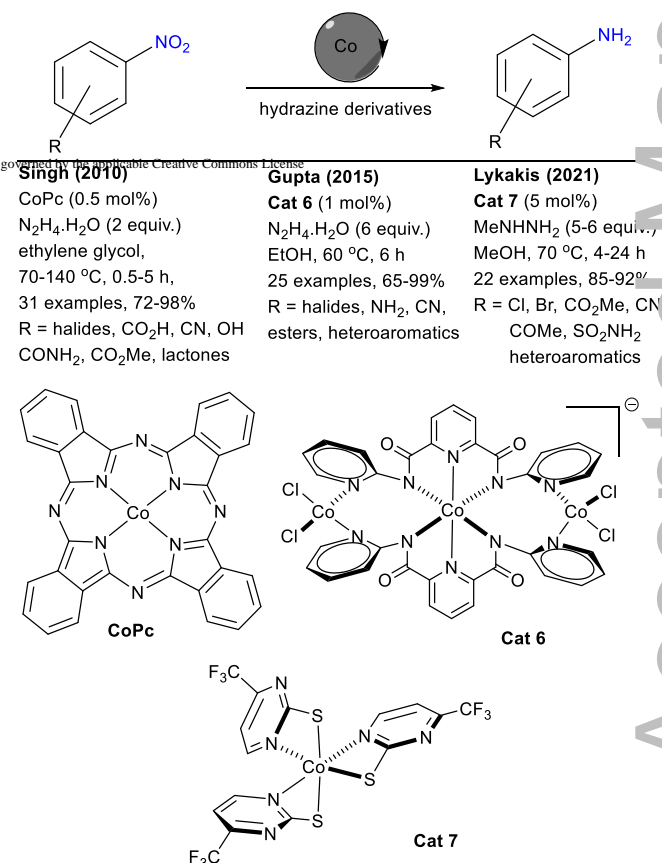


Scheme 7. Iron-catalyzed transfer hydrogenation of nitroarenes to N-heterocycles

Recently, we reported that in the presence of alcohols and 3 equiv. of $\text{K}_3\text{PO}_4 \cdot \text{H}_2\text{O}$, nitroarenes led to the corresponding imines in 30-91% yields when catalyzed by 5 mol% of **Cat 5** associated with 10 mol% of Me_3NO in toluene at 140 °C for 20 h. (Scheme 7a)^[22a] Furthermore, using similar methodology, the preparation of benzimidazoles, benzoxazoles, benzothiazoles and quinoxalines starting from *o*-nitroaniline, *o*-nitrophenol or *o*-nitrothiophenol derivatives, respectively, can be conducted under transfer hydrogenation conditions (Scheme 7b-c).^[22] Additionally, the developed method involving the reduction of nitroarenes to generate the aniline intermediates using **Cat 5** was also applied for the synthesis of pyrrolo[1,2- α]quinoxalines (Scheme 7d).^[23]

At cobalt – Cobalt complexes were also reported as efficient catalysts for the reduction of nitroarenes to give anilines under transfer hydrogenation process, especially using hydrazine as the hydrogen donor, as

shown in the representative examples depicted in Scheme 8. In 2010, Singh and co-workers described such reduction reaction using cobalt phthalocyanine (CoPc, 0.5 mol%) as the catalyst, 2 equiv. of $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ as the reductant in ethylene glycol at 70-140 °C. This methodology was versatile with a series of functional groups, including halides, carboxylic acid, ester, lactone, amide, nitrile, aldehyde, ketone, and olefin.^[24] Similarly to FePc, nitroarenes bearing formyl or acetyl groups led to compounds in which the nitro group was reduced to amino, and the carbonyl group transformed to hydrazone moiety by reaction with hydrazine. Later, a trinuclear cobalt complex $\{\text{Co}^{2+}\text{-Co}^{3+}\text{-Co}^{2+}\}$ (**Cat 6**) was designed by Gupta for the reduction of nitro compounds with 6 equiv. of $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ in ethanol at 60 °C. An interesting functional group tolerance was obtained under these conditions (halides, esters, cyano, amino, heteroaromatics). Importantly, aliphatic nitro substrates such as nitrocyclopentane and 2-methyl-2-nitropropane were reduced in good yields (67 and 80%, respectively).^[25] The reduction of nitroarenes seemed to involve Co(II)-Co(I) cycle and to proceed via the formation of nitrosobenzene then *N*-phenylhydroxylamine and not via azoxybenzene and 1,2-diphenylbenzene.



Scheme 8. Cobalt-catalyzed transfer hydrogenation of nitroarenes with hydrazines

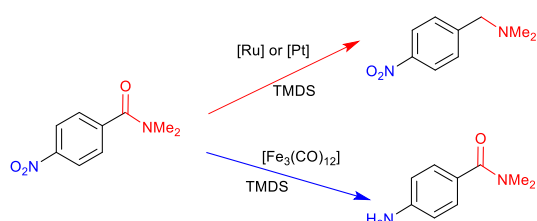
Recently, Lykakis *et al.* have developed a selective and efficient catalytic protocol for such reduction reaction using an easily synthesized tris(*N*-heterocyclic thiamidate) cobalt (III) complex (**Cat 7**)

and 5 or 6 equiv. of methylhydrazine in methanol at 70 °C. Nitroarenes bearing halogens and reducible groups such as ester, lactone, ketone, cyano and sulfonamide were able to undergo this reduction reaction, but no reaction took place with heteroaromatic nitro compounds like 2-nitropyridine, and nitroalkane substrates under such conditions.^[26] To the best of our knowledge, there is no report described homogeneous cobalt catalyzed transfer hydrogenation to generate aniline derivatives starting from nitroarenes using alcohols or formic acid as hydrogen donor.

2.3. Hydrosilylation of nitro derivatives

Besides hydrogenation and transfer hydrogenation, hydrosilanes are milder and higher selective reducing agents in terms of chemoselectivity and functional group tolerance. Thus, hydrosilanes can be considered as interesting alternative reductants, although siloxane waste is an unavoidable by-product.

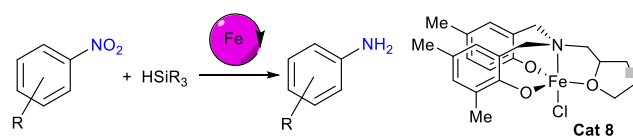
At iron - The reduction of nitroarenes can be also performed via hydrosilylation reaction. In 2009, in a contribution reporting the iron-catalyzed hydrosilylation of carboxamides to the corresponding amines, Nagashima described a single but impressive example in terms of chemoselectivity. Indeed, using $[\text{Fe}_3(\text{CO})_{12}]$ (10 mol%) with an excess of TMDS (10 equiv.) at 100 °C for 24 h, *N,N*-dimethyl-*p*-nitrobenzamide led selectively to the corresponding *N,N*-dimethyl-*p*-aminobenzamide in 77% yield, with the nitro group reduced whereas the tertiary amide group was unchanged.^[27a] Remarkably, when platinum or ruthenium based catalysts, $\text{H}_2[\text{PtCl}_6] \cdot 6\text{H}_2\text{O}$, or $[(\mu_3-\eta^2-\eta^3-\eta^5\text{-acenaphthylene})\text{Ru}_3(\text{CO})_7]$, respectively, were used, a switch of chemoselectivity was observed with the selective reduction of the amide moiety to amine, nitro one staying intact.^[27b,c] Thus, only *p*-NO₂-C₆H₄-CH₂NMe₂ derivative was produced (Scheme 9).



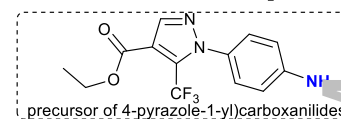
Scheme 9. Switchable chemoselectivity in transition metal-catalyzed hydrosilylation of nitroarenes

One year later, Beller reported a general methodology for the reduction of nitro-substituted (hetero)arenes using an *in situ* formed catalyst from 10 mol% of FeBr_2 and 12 mol% of monophosphine [PPh_3 , $\text{P}(\text{Ph}-4\text{-OMe})_3$ or PPh_2Me] in the presence of 2.5 equiv. of phenylsilane at 110 °C for 16 h with a moderate efficiency (TOF up to 0.6 h⁻¹). The corresponding primary amines were obtained in 25–99% GC-yields with an interesting functional group tolerance including halides (Cl, I), olefins, esters, cyano, benzyl alcohols, etc. (Scheme 10).^[28] Noticeably, ethyl *p*-

nitrocinnamate and *p*-nitrostilbene were selectively reduced without reduction of the conjugated C=C bond, whereas 3-nitrostyrene and 4-nitrophenyl acetate did not lead to the corresponding aniline. Simultaneously, Lemaire *et al.* performed the reduction of nitroarenes using $\text{Fe}(\text{acac})_3$ salt (10 mol%) in the presence of a less expensive silane, TMDS (1.5 equiv.) and the corresponding anilines were isolated in 20–99% yields after a reaction for 24–48 h at 60 °C (Scheme 10). Similarly, a decent efficiency was observed (TOF up to 0.4 h⁻¹) and ester, carboxylic acid or nitrile reducible functional groups were reduced, but not formyl group which was simultaneously transformed to primary alcohol. However, these conditions did not permit to reduce nitroalkanes.^[29]



Beller (2010)	Lemaire (2010)	Thomas (2016)
FeBr_2 (10 mol%), PPh_3 (12 mol%), PhSiH_3 (2.5 equiv.) 110 °C, 16 h, toluene 26 examples, 25–99% yields TOF up to 0.6 h ⁻¹ R = CF ₃ , halides, ester, CN CH ₂ OH, heteroaromatics, conjugated C=C	$\text{Fe}(\text{acac})_3$ (10 mol%), TMDS (1.5 equiv.) 60 °C, 24–48 h, THF 15 examples, 20–99% yields TOF up to 0.4 h ⁻¹ R = Cl, OMe, Br, CN, CO ₂ H, CO ₂ Me, CF ₃	Cat 8 (2 mol%) (EtO) ₃ SiH (4 equiv.) 80 °C, 3–8 h, MeCN 19 examples, 55–98% yields TOF up to 15 h ⁻¹ R = halides, MeS, CN, SO ₂ Me, esters, CF ₃ amide, CH ₂ OH.

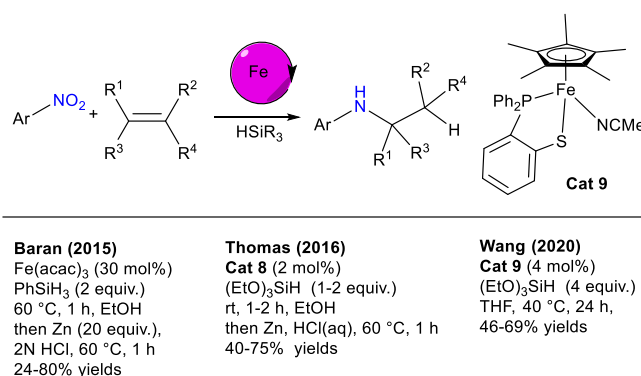


Scheme 10. Iron-catalyzed hydrosilylation of nitroarenes to anilines

In 2016, using a well-defined iron(III) pre-catalyst **Cat 8** (2 mol%), Thomas *et al.* conducted the same reaction in the presence of 4 equiv. of (EtO)₃SiH in acetonitrile at 80 °C for 3–8 h. Noticeably, the efficiency was higher (TOF: 15 h⁻¹) and functional groups such as sulfide, sulfone, ester, amide, nitrile, and halides were tolerated (Scheme 10).^[30] This protocol was used to prepare a precursor of 4-(pyrazole-1-yl)carboxanilides, a series of pharmaceuticals permitting to tune the activity of canonical transient receptor potential channels and thus manage the influx of intracellular calcium cations into mammalian cells (Scheme 10).

On the other hand, iron-catalyzed cascade hydroamination protocols were also developed starting from nitroarenes under hydrosilylation conditions with the generation of aniline intermediates. For example, a general and highly chemoselective one pot reductive hydroamination of olefins was reported by Baran using 30 mol% of $\text{Fe}(\text{acac})_3$ and 2 equiv. of phenylsilane in ethanol at 60 °C for 1 h, and the corresponding secondary arylalkylamines were obtained after a quench step (20 equiv. of Zn powder and 2N HCl) (Scheme 11).^[31] Using the well-defined iron

complex **Cat 8** as the catalyst (2 mol%), Thomas performed similar reactions using 1-2 equiv. of PhSiH_3 in ethanol at rt.^[30,32]



Scheme 11. Iron-catalyzed reductive hydroamination of alkenes with nitroarenes

Recently, Wang *et al.* revealed that a single half-sandwich P-S complex **Cat 9** was also able to perform the similar hydrosilylation transformation of nitroarenes leading to either aniline or N-alkylanilines.^[33]

3. Reduction of nitriles

The catalytic reduction of nitriles provides a valuable alternative for the one-step synthesis of diverse primary amines. Indeed, unsaturated C=C, C=O, C=N bonds, nitriles reduction producing primary amines is challenging and less investigated owing to the high redox potential of C≡N and the decreased selectivity with inevitable side reaction towards the undesired secondary amines.^[34] Herein, the recent developments in nitrile reduction under hydrogenation, transfer hydrogenation and hydrosilylation process are described.

3-1 Hydrogenation of nitriles

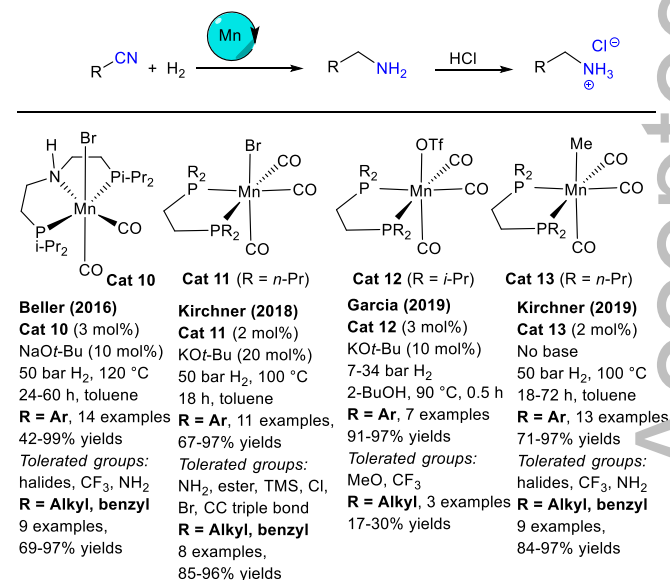
At manganese - When reducing nitriles, the selective issues can make such hydrogenation challenging as in addition to the expected primary amines, a mixture with secondary and tertiary ones can be obtained. The first efficient nitrile hydrogenation with manganese catalysts was reported in 2016 by Beller *et al.* using a MACHO-Mn(I) complex **Cat 10** as the catalyst (3 mol%) in the presence of 10 mol% of *t*-BuONa under 50 bar of hydrogen in toluene at 120 °C for 24 h. This protocol was efficient for the hydrogenation of aliphatic and (hetero)aromatic nitriles, and TOF up to 33 h⁻¹ can be reached (Scheme 12).^[35] A series of groups such as methoxy, halides, CF₃, and amino were tolerated. Additionally, this catalytic system permitted to reduced nitroalkanes with 42-99% yields. Notably the reaction can be scaled up to 5 g scale with 4-trifluoromethylbenzotrile. An outer-sphere mechanism involving a hydride, from the manganese center [(PNP)Mn(CO)₂H], and a proton, from the NH

ligand backbone, transfer to the nitrile moiety was suggested.

One year later, Kirchner described this transformation using a bidentate diphosphine manganese(I)-complex **Cat 11** (2 mol%) in the presence of 20 mol% of potassium *tert*-butoxide in toluene at 100 °C for 18 h under 50 bar of H₂. This hydrogenation exhibited similar scope with the previous one with both (hetero)aromatic nitriles and linear aliphatic (di)nitriles, but with a better TOF (up to 49 h⁻¹).^[36a] Notably, adiponitrile was reduced in hexamethylenediamine in 95% yield. Modifying the structure of the catalyst, substituting the bromide by a methyl (catalyst **Cat 13**, 2 mol%), similar results were obtained (Scheme 12).^[36b]

Garcia also modified the design of the complex **Cat 12**, using a bis(di-isopropylphosphino)ethane ligand, and substituting the bromide by a triflate. **Cat 12** (3 mol%) allowed to perform the reduction at lower pressure (7-34 bar of H₂) and temperature (90 °C) with similar efficiency (TOF up to 120 h⁻¹) (Scheme 12).^[37] The solvent played a crucial role for the selectivity, 2-butanol being better than isopropanol. Noticeably alkanenitrile bearing a cyclopropyl ring can be selectively reduced to the corresponding amine without ring opening. Additionally, dinitriles such as terephthalonitrile and adiponitrile can be also reduced under similar conditions at higher pressure (35 bar) thus leading to diamines in 98 and 53%, respectively.

Using diphosphine based catalysts, an inner sphere mechanism was proposed. A hydride manganese species, (diphos)Mn(CO)₂H, led after coordination of the nitrile then insertion in the Mn-H bond, to a Mn-imine species.

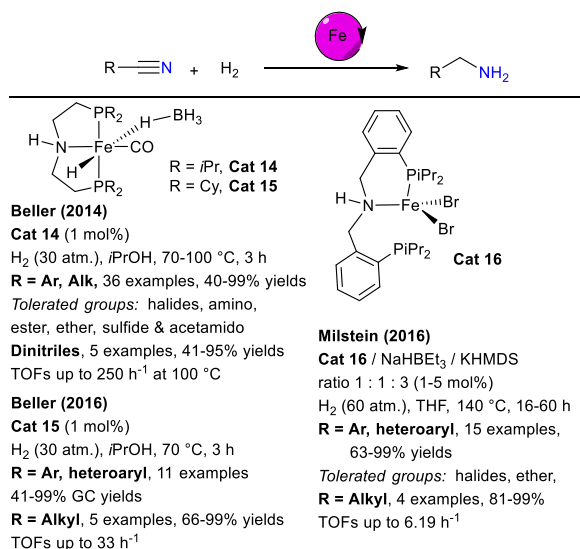


Scheme 12. Manganese-catalyzed hydrogenation of nitriles to primary amines

At iron - Beller first developed the hydrogenation of nitriles to primary amines using 1 mol% of the iron PNP pincer complexes **Cat 14**^[38] and **Cat 15**^[39] under

30 atm. of H₂ in isopropanol at 70-100 °C for 3 h (Scheme 13). Of notable importance, the efficiency of the reduction was high (TOFs up to 250 h⁻¹ at 100 °C) and the scope of the reaction was rather large as aromatic, heteroaromatic, alkyl and dinitriles (including the industrial relevant adiponitrile) were hydrogenated in 40-95% yields when using the catalyst **Cat 15**. Additionally, the functional group tolerance was interesting, as halide, amino, ester, ether, sulfide and acetamido groups were not reduced. When starting from cinnamyl nitrile, the corresponding α,β -unsaturated primary amine can be mainly obtained, while with a small amount of over-reduction amine product.

Few years later, Milstein designed a novel complex **Cat 16** for the selective catalytic homogeneous hydrogenation of (hetero)aromatic, benzylic, and aliphatic nitriles to primary amines (Scheme 13). Indeed, using the catalyst (1-5 mol%) *in situ* generated from **Cat 16**, 1 equiv. of NaBHET₃ and 3 equiv. of KHMDS, the reduction of (hetero)aromatic and alkyl nitriles were conducted under 60 atm. of H₂ in THF at 140 °C for 16-60 h (63-99% yields).^[40] Noticeably, the reduction of crotonitrile led to a mixture of butylamine (66%) and butyronitrile (19%), resulting from the reduction of the α,β -unsaturated double bond.

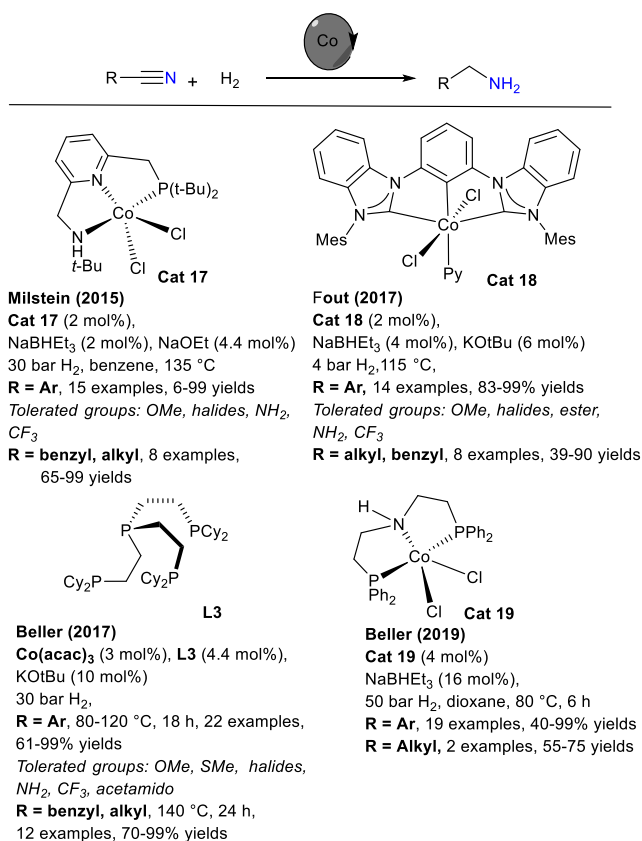


Scheme 13. Iron-catalyzed hydrogenation of nitriles to primary amines

At cobalt - In 2015, Milstein *et al.* described the first contribution dealing with molecular-defined cobalt catalyst for hydrogenation of organonitrile derivatives (Scheme 14).^[41] Using the catalytic system based on 2.2 mol% of the NNP pincer cobalt complex **Cat 17** associated to 2 mol% of NaBHET₃ and 4.4 mol% of NaOEt, both aromatic and aliphatic nitriles could be reduced efficiently under 30 bar of hydrogen at 135 °C leading to primary amines in 6-99% yields, with notably the tolerance of amino, nitro, trifluoromethyl and halide groups.

Two years later, Fout *et al.* described the use of a family of bis-carbene pincer cobalt complexes including **Cat 18** for the hydrogenation of nitriles to primary amines, notably at low pressure (4 bar H₂). Thus, using 2 mol% of **Cat 18** in the presence of 4 mol% of NaBHET₃ and 6 mol% of KO*t*-Bu, various aromatic and aliphatic nitriles were reduced when performing the reaction at 115 °C in toluene. Noticeably, fluoro, chloro, trifluoromethyl, amino and ester were tolerated under such conditions (Scheme 14).^[42] Additionally, the reduction of acetonitrile can be also performed in moderate yield (39%). Interestingly, the mechanism study has shown the crucial role of the NaBHET₃ generating *in situ* a Lewis acid able to coordinate the nitrile substrate thus facilitating a side-on coordination of the nitrile to the cobalt centre, and permitting a pairwise transfer of the hydride through a Co(I/III) redox process.

At the same year, Beller also developed a procedure based on the use of an *in situ* generated catalytic system from Co(acac)₃ (4 mol%) and a tetraphos ligand P(CH₂CH₂PCy₂)₃ **L3** (4.4 mol%) in the presence of 10 mol% of *t*-BuOK under 30 bar of H₂ in *tert*-butanol at 80-140 °C.^[43] Both aryl and alkyl nitriles were reduced with an interesting functional group tolerance including amides, halides, trifluoromethyl, sulfides, amino and heteroaromatic moieties. In 2019, the same group described a series of pincer cobalt complexes, such as **Cat 19**, able to reduce nitriles to primary amines when associated to 16 mol% of NaBHET₃ under 50 bar of hydrogen at 80 °C for 6 h (Scheme 14).^[44] Similar functional group tolerance was observed, but they have highlighted that aldehyde, ketone and ester groups were reduced under such conditions.

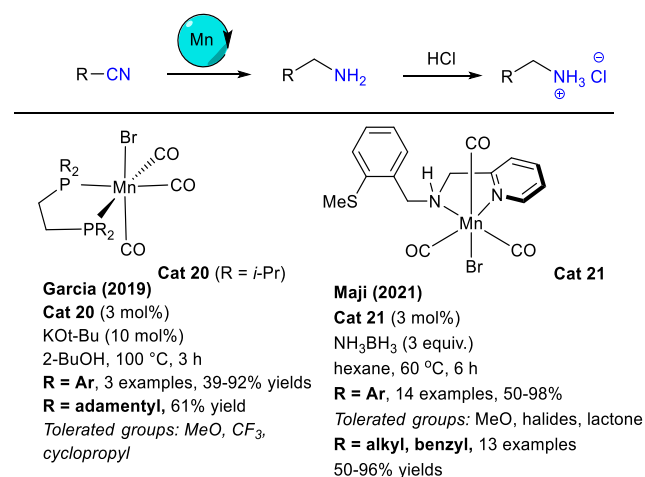


Scheme 14. Cobalt-catalyzed hydrogenation of nitriles to primary amines

3-2 Transfer hydrogenation

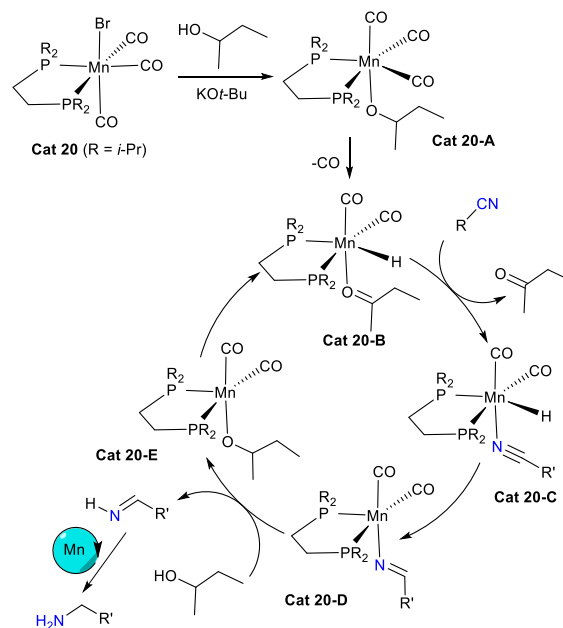
At manganese - The first example of transfer hydrogenation of nitriles using manganese catalyst was described by Garcia and co-workers in 2019, using 3 mol% of catalyst **Cat 20** in the presence of 10 mol% of KOt-Bu in 2-butanol, which is playing the role of solvent and of hydrogen source, at 100 °C for 3 h. After an acidic hydrolysis, primary amines can be isolated, and 4 examples were described (Scheme 15).^[45] Noticeably, when starting from non-hindered alkanenitriles, the corresponding primary amines were not isolated, as the reaction led to imines which resulted from its condensation with 2-butanone, resulting from the dehydrogenation of 2-butanol.

As ammonia borane can also act as the hydrogen source, recently, Maji *et al.* described such reduction reaction using a bench-stable and phosphine-free manganese complex **Cat 21** in hexane at 60 °C for 6 h, which led to the selective formation of primary amines (Scheme 15). This protocol can tolerate halides and lactone decorated aromatic nitriles as well as aliphatic nitriles. However, the reduction of keto groups took place under such conditions.^[46]



Scheme 15. Manganese-catalyzed transfer hydrogenation of nitriles to primary amines

In terms of mechanism, the activation of the pre-catalyst **Cat 20** by 2-butanol and the base led the Mn-alkoxide (diphos)Mn(CO)₃(O-CH(Me)Et) **Cat 20-A** which generated the hydride active species (diphos)Mn(H)(CO)₂(O=C(Me)Et) **Cat 20-B** after non reductive elimination of CO and β-H-elimination.

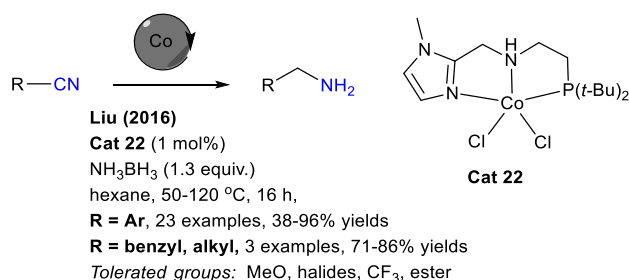


Scheme 16. Proposed mechanism for Mn-catalyzed transfer hydrogenation of nitriles to primary amines

The CO/nitrile L ligand exchange generated (diphos)Mn(H)(CO)₂(N≡C-R) **Cat 20-C** which after insertion of the nitrile moiety in the Mn-H bond led to the (diphos)Mn(CO)₂(N=CH-Ph) **Cat 20-D**. After alcoholysis, the aldimine was produced and the Mn alkoxide **Cat 20-E** was generated. Finally, the active species **Cat 20-B** was regenerated by β-elimination. Using similar cycle, the aldimine was reduced to primary amine. (Scheme 16)

At cobalt - In 2016, the first cobalt-catalyzed transfer hydrogenation reaction of nitriles to produce primary

amines was reported by Liu's group (Scheme 17).^[47] Using the NNP pincer complex **Cat 22** (1 mol%), such reduction reaction was conducted with ammonia borane as the hydrogen source in hexane at 50-120 °C. After 16 h, the corresponding primary (hetero)arylamines can be obtained in 38-96% yields with a series of tolerated functional groups including MeO, halides, ester and CF₃. In addition, aliphatic nitriles were also successfully converted into primary amines. It should be emphasized that the nature of the solvent was essential to control the selectivity, while secondary amines were produced if performing the reaction in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP).

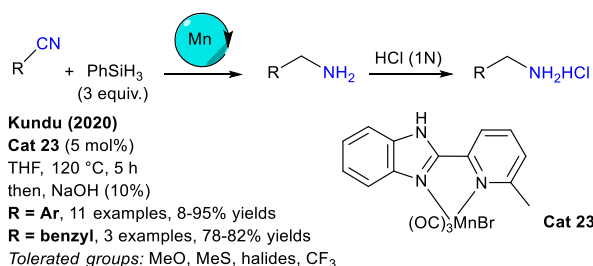


Scheme 17. Cobalt catalyzed transfer hydrogenation of nitriles to primary amines

3-3 Hydrosilylation of nitriles

Nitriles are known to be difficult to reduce selectively to primary amines under hydrosilylation conditions, and there are only scarce examples reported with manganese, iron or cobalt.

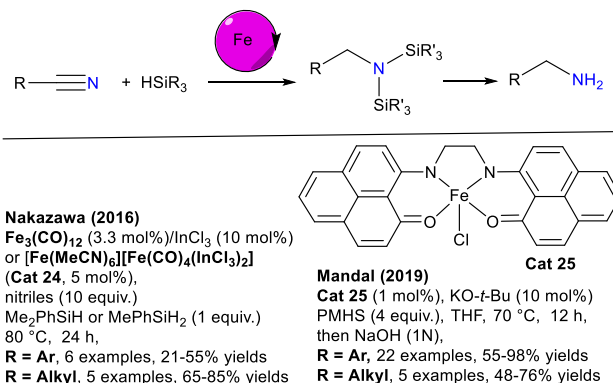
At manganese - The only one report up to date dealing with manganese catalyzed reduction of nitriles to primary amines was reported by Kundu *et al.* Using a bidentate benzimidazole-pyridine manganese complex **Cat 23** (5 mol%) in the presence of 3 equiv. of phenylsilane in THF at 120 °C, various benzonitrile derivatives were reduced to the corresponding primary amines in 8-95% yields. Whereas aromatic, heteroaromatic and benzylnitriles were converted, no reaction took place with aliphatic nitrile such as butanenitrile. Noticeably, the preliminary mechanistic investigations suggested the involvement of radical species during the catalytic reaction (Scheme 18).^[48]



Scheme 18. Manganese-catalyzed hydrosilylation of nitriles to primary amines

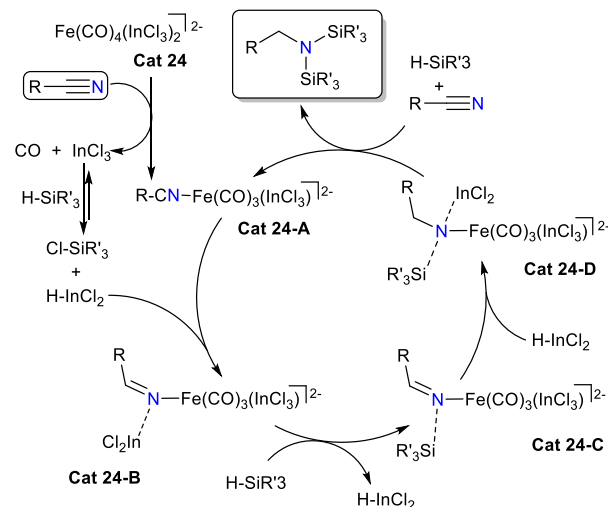
At iron - Nakazawa published the first report describing this selective transformation, using catalytic amounts of a combination of 3.33 mol% of Fe₃(CO)₁₂ and 10 mol% of indium trichloride in the

presence of 1 equiv. of Me₂PhSiH. The double hydrosilylation of acetonitrile (10 equiv.) selectively led to the corresponding disilylamine Me-CH₂-N(SiMe₂Ph)₂ adduct in 78% yield (Scheme 19). It is important to underline that when using 5 mol% of the prepared complex [Fe(MeCN)₆][Fe(CO)₄(InCl₃)₂] **Cat 24**, from Fe₃(CO)₁₂ and InCl₃, similar activity was observed. A variety of alkyl- and aryl-nitriles were reduced to the disilylamines in 21-85% yields (Scheme 19).^[49] Notably, no reaction took place with 2,2-dimethylpropanenitrile, C₆F₅-CN and adiponitrile.



Scheme 19. Iron-catalyzed hydrosilylation of nitriles to primary amines

Based on experimental evidences, the authors proposed the following mechanism. (Scheme 20)



Scheme 20. Proposed mechanism for Fe-In catalyzed hydrosilylation of nitriles

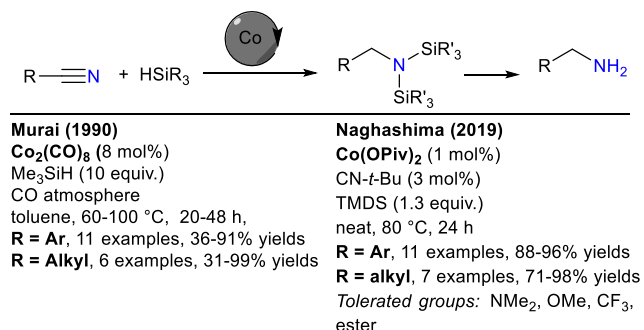
Starting from the iron-indium complex [Fe(CO)₄(InCl₃)₂]²⁻ **Cat 24**, after non reductive eliminations of InCl₃ and CO followed by a non oxidative addition of nitrile, the catalytic species [Fe(CO)₃(InCl₃)(R-CN)]²⁻ **Cat 24-A** was generated. By reaction of the released InCl₃ with hydrosilane, chlorosilane and indium hydride H-InCl₂ were *in situ* produced. Then, **Cat 24-A** reacted with H-InCl₂ leading to the intermediate **Cat 24-B** which thus reacted with hydrosilane to generate silylimine iron species **Cat 24-C**. By a further reaction with H-InCl₂, the latter species led to **Cat 24-D**, which finally in the presence of hydrosilane and nitrile led to the

disilylamine and regenerated the active species **Cat 24-A**.

In 2019, Mandal demonstrated that a well-defined phenalenyl based iron complex **Cat 25** was efficient in the reduction of nitriles to primary amines when conducted in the presence of 10 mol% of *t*-BuOK and 4 equiv. of PMHS in THF at 70 °C. After a basic quench and an acidic hydrolysis, the corresponding alkyl, alkenyl and (hetero)aromatic ammonium salts were isolated 48-98% yields. The transformation tolerated halides and trifluoromethyl groups. (Scheme 19).^[50] By contrast, aldehydes, ketones and esters were simultaneously reduced whereas no conversion were observed with benzonitriles substituted by carboxylic acid, amino, amide and nitro.

At cobalt - In an early report in 1990, Murai described the hydrosilylation of nitriles catalyzed by $\text{Co}_2(\text{CO})_8$ (8 mol%) in the presence of 10 equiv. of HSiMe_3 at 60 °C under CO atmosphere, affording to disilylamines in moderate to good yields. The reaction worked with cyclopropane-carbonitrile and with aromatic nitriles, the ones bearing electron-donating groups being more efficient. To obtain clean reaction with other aliphatic nitriles, higher temperature was required (e.g. 100 °C), but under such harsher conditions, cobalt complex would be decomposed. The addition of a phosphine such as PPh_3 and performing the reaction at 100 °C permitted to conduct more efficiently the reaction with propane-2-nitrile and 2-methylpropane-2-nitrile (Scheme 21).^[51]

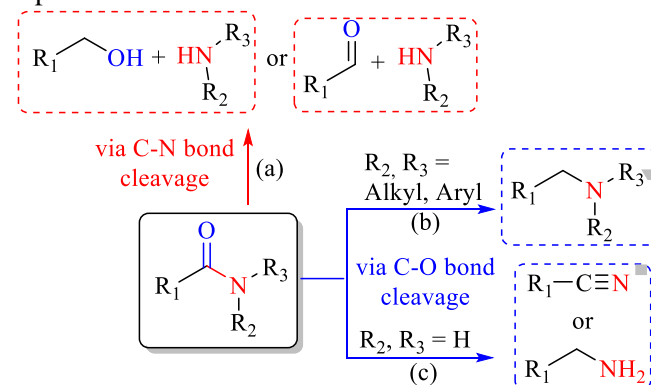
In 2019, Nagashima reported the use of a catalytic system based on $\text{Co}(\text{OPiv})_2$ (1 mol%) and *tert*-butylisocyanide (3 mol%) for the hydrosilylation of nitriles in the presence of 1.3 equiv. of 1,1,3,3-tetramethyldisiloxane (TMDS) at 80 °C under solvent-free conditions. The corresponding primary ammonium salts were produced after acidic hydrolysis in 71-98% yields.^[52] Noticeably, the reaction was efficient with both alkyl and aromatic nitriles and tolerated halides, CF_3 , dimethylamino and ester groups whereas aldehydes and ketones were simultaneously reduced. (Scheme 21)



Scheme 21. Cobalt-catalyzed hydrosilylation of nitriles to primary amines

4. Reduction of primary amides

In the family of carboxylic acid derivatives, there is no doubt that carboxamides are among the most difficult and challenging ones to selectively reduce. Indeed, the reduction of carboxamides can proceed via C–O or C–N bond cleavage and lead to the formation of a number of important compounds (Scheme 22). Herein, the chemoselective reduction of primary amides to primary amines, which has a significant synthetic value for academic and industrial areas, will be reported.

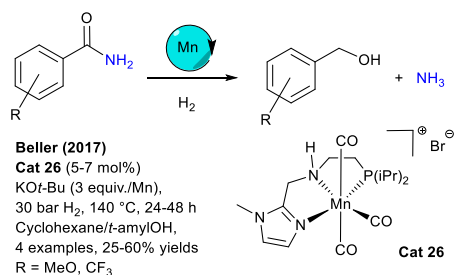


Scheme 22. Reduction of carboxamides through different pathways

4.1 Hydrogenation and transfer hydrogenation of primary amides

The typical C–O bond cleavage of amides results in the formation of amine derivatives via deoxygenation. Alternatively, the hydrogenation of amides can be performed via the C–N bond cleavage thus leading to the corresponding alcohols and amines. This late pathway was mostly achieved with secondary or tertiary carboxamides under hydrogenation conditions. Noticeably, there are only few reports dealing with the hydrogenation of carboxamides using earth abundant first row transition metals such as manganese,^[53] iron^[54] or cobalt.^[55]

On the other hand, the hydrogenation of primary amides is even a more challenging task, and usually leads to primary alcohols and ammonia. To the best of our knowledge, there is only one report dealing with the hydrogenation of primary amides. Thus, using a PNN pincer manganese complex bearing an imidazolyaminolphosphino ligand (**Cat 26**), Beller and co-workers developed an efficient protocol for hydrogenation of a wide range of secondary and tertiary amides to the corresponding alcohols and amines under 30 bar of hydrogen at 100 °C.^[56] This catalytic system can be used for the hydrogenation of four primary (hetero)aromatic amides, and led to the corresponding alcohols and ammonia. (Scheme 23)

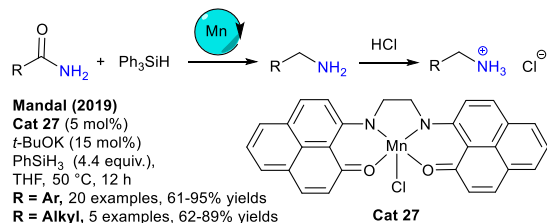


Scheme 23. Manganese-catalyzed hydrogenation of primary amides

4-2 Hydrosilylation of primary amides

Under hydrosilylation conditions, the typical C–O bond cleavage of tertiary and secondary amides usually resulted in the formation of amine derivatives via deoxygenation.^[57] By contrast, the reductions of primary amides performed under hydrosilylation conditions are more difficult tasks to solve. Indeed, dehydration of amides leading to nitrile derivatives is always the observed transformation.^[58]

At manganese – To the best of our knowledge, there is only one report describing the selective hydrosilylation of primary amides producing primary amines using manganese based catalysts. Thus, in 2019, Mandal used 5 mol% of a tetradentate *O,N,N,O*-phenalenyl Mn(III) complex **Cat 27** associated to 15 mol% of *t*-BuOK in the presence of 4.4 equiv. of phenylsilane to perform the reduction of both (hetero)aryl and alkyl primary amides in THF at 50 °C for 12 h. After a basic quench, followed by a HCl treatment, the corresponding ammonium salts were isolated in 61-95% yields; halides and cyclopropyl moieties were tolerated. (Scheme 24) Remarkably, by a slight modification of the reaction conditions (addition of 20 mol% of *N*-methylbenzamide), the selectivity can be switched towards the formation of nitriles.^[59] In a mechanistic point of view, this difference of selectivity, mainly due to the presence of secondary amides, can be explained by a step sequence (i) the dehydration of primary amides to nitriles, then (ii) the reduction of nitriles to primary amines. As secondary amides are a better binding agents than nitriles, this suggests that nitrile is not preferred to bind the Mn(III) center in the presence of a secondary amide, thus avoiding its further reduction.

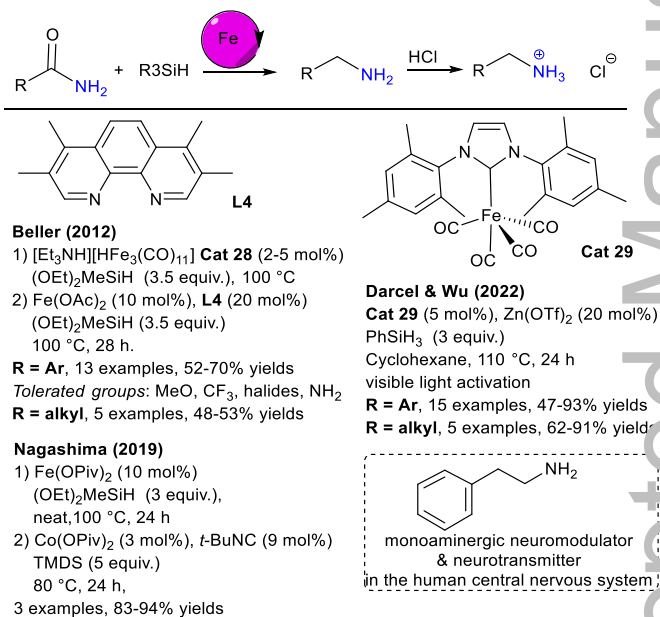


Scheme 24. Manganese-catalyzed hydrosilylation of primary amides to primary amines

At iron – As main of the iron catalysts exclusively led to nitriles from primary amines under hydrosilylation conditions, in order to reverse this selectivity, Beller finely developed a catalytic system based on two

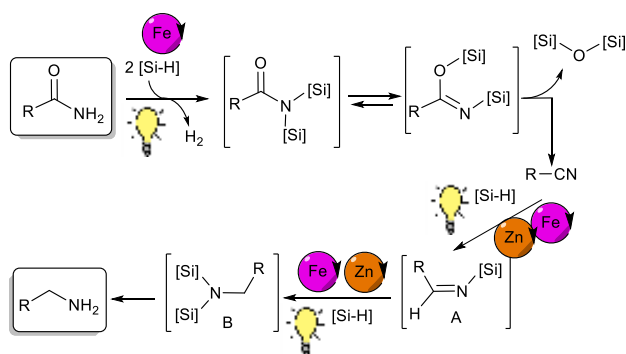
different iron catalytic species, used in a sequential way. Indeed, using the complex [NHEt₃][Fe₃H(CO)₁₁] **Cat 28** (2-5 mol%) with 3.5 equiv. of (EtO)₂MeSiH in toluene at 100 °C, the primary amides were firstly dehydrated to nitriles. Then, they demonstrated that the association of Fe(OAc)₂ (10 mol%) with terpyridine ligand (**L4**, 20 mol%) catalyzed the reduction of nitriles to primary amines at 100 °C for additional 28 h (Scheme 25).^[60] Both aryl and linear alkylamides were reduced in moderate to good yields, and few functional groups were tolerated such as amino, CF₃ and halides.

Similarly, Nagashima used a Fe/Co system to perform similar sequential reduction. Using 10 mol% of Fe(OPiv)₂ in the presence of 3 equiv. of HSiMe(OMe)₂ in neat conditions at 100 °C for 24 h, a nitrile intermediate was *in situ* generated and was sequentially reduced to produce primary amines using a second catalytic system based on 3 mol% of Co(OPiv)₂/9 mol% of *t*-BuNC with 5 equiv. of TMDS at 80 °C for 24 h. After an acidic hydrolysis, 3 examples of primary ammonium salts were isolated in 83-94% yields (Scheme 25).^[52]



Scheme 25. Iron-catalyzed hydrosilylation of primary amides to primary amines

More recently, our group has developed a methodology involving a tandem iron/zinc-catalyzed reductions of primary amides to primary amines under hydrosilylation conditions. By using the combination of 5 mol% of Fe(CO)₄(IMes) **Cat 29** and 20 mol% of Zn(OTf)₂, primary alkyl-, alkenyl- and aryl-amines were selectively and efficiently produced (21 examples, 47-93% isolated yields). Additionally, using such methodology, 2-phenylethylamine, a monoaminergic neuromodulator and a neurotransmitter in the human central nervous system (CNS) can be prepared in 72% yield. Noticeably, when using In(OTf)₃ as co-catalyst, secondary amines were obtained in moderate yields up to 51%. (Scheme 25)^[61]



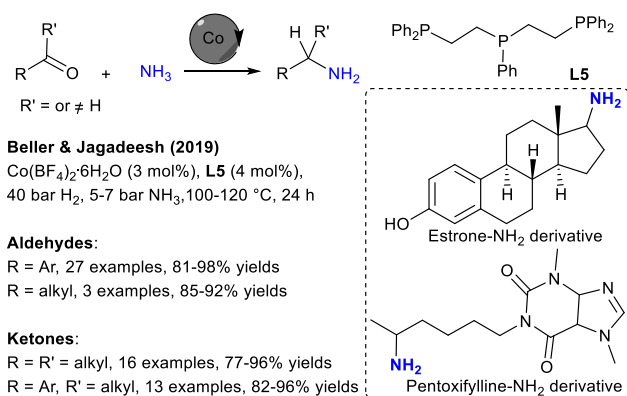
Scheme 26. Proposed mechanism for the Fe/Zn co-catalyzed reduction of primary amides.

Noticeably, the catalytic pathway rationalizing the selective formation of primary amines starting from primary amides involved first a dehydration step leading to the nitrile intermediate.

This step is promoted by both the iron catalyst **Cat 29** and the visible light. The nitrile cannot be reduced under visible light using hydrosilane and iron, but the reduction was performed thanks to the synergic combination of the iron catalyst and the zinc salt under light activation. (Scheme 26)

5. Reductive amination using ammonia as a challenging task

An even more challenging methodology to prepare selectively primary amines is the reductive amination of aldehydes or primary alcohols with ammonia under reductive or hydrogen borrowing conditions, respectively. The main drawback of this transformation is the lack of selectivity to the desired amines.^[62] Additionally, this access to primary amines was scarcely reported using homogeneous catalysts.^[5c,5d] In a pioneering contribution, in 1963, Murakami and Kang described the use of a homogeneous cobalt catalyst *in situ* generated from $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ and KCN for the reductive amination of α -keto acids and esters with ammonium hydroxide by reaction under 49 bar of H_2 at 40–70 °C for 8 h. The corresponding amino-acid derivatives were obtained in 36–95% yields.^[63] After almost a decade, Markó and Bakos have reported that a catalytic species *in situ* generated from $\text{Co}_2(\text{CO})_8$ and tributylphosphine (ratio 1:4) can promote the reaction of acetophenone with ammonia at 150–200 °C, under 100–300 atm of H_2 in ethanol for 6 h. The corresponding 1-phenylethanamine was then obtained in 66% yield with 23% yield of N,N-di(1-phenylethyl)amine.^[64] One of the rare efficient and general examples using cobalt homogeneous catalyst was described in 2019 by Beller and Jagadeesh who used the association of $\text{Co}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$ (3 mol%) and the triphos(bis(2-diphenylphosphinoethyl)phenylphosphine) **L5** (4 mol%) under 5–7 bar of ammonia and 40 bar of hydrogen in trifluoroethanol (TFE) at 100–120 °C for 24 h.



Scheme 27. Cobalt-catalyzed reductive amination of aldehydes with ammonia

Under such conditions, both alkanals and aromatic aldehydes were transformed into the corresponding primary amines in 77–98% yields with interesting functional group tolerance including OMe, OBn, SMe, CF_3 , OCF_3 , esters, C=C bonds, 3,4-methylenedioxy, benzo-1,4-dioxane, methylsulfone, NH_2 , OH and boronic ester (Scheme 27).^[65] This reductive amination has also been applied to ketone containing drugs such as Nabumetone, Pentoxifylline, Azaperone and Estrone.

6. Conclusion

Primary amines being an important class of chemical substances in the industry, huge amount of progress has been made for their formation over the past two decades. Notably, manganese, iron and cobalt catalysis for the reduction of nitro compounds, primary carboxamides and organonitriles leading selectively to primary amines has gathered substantial interest. In this perspective, this review has highlighted the most recent progress and current state of the arts in hydrogenation, transfer hydrogenation and hydrosilylation methodologies for the access to primary amines. Such substitution of noble metals by earth abundant ones in homogeneous reduction catalysis is clearly one of the most significant recent achievements in the field, and should be likely fuel for new research activities. Another important concern deals with the selectivity of the transformation and the associated functional group tolerance, which have been solved by designing molecular catalysts and associating with, for example, hydrosilanes. Additionally, primary amines being a central platform in molecular synthesis, the design of the one-pot reaction involving the reduction of primary carboxamides, organonitriles, and nitro compounds to produce primary amines, should be an interesting perspective.

It thus seems clear that a considerable number of ongoing research contributions is directed towards the discovery of more efficient catalysts based on iron, manganese or cobalt. Noticeably, the direct reduction

of primary amides and the reductive amination involving ammonia still seems a challenging task.

Acknowledgements

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REVIEW

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