The final publication is available at

https://doi.org/10.1039/d3gc04175a

Additional Information

Hydrogenation of amides to amines by heterogeneous catalysis: A review

Huiru Yang[1,2], Hermenegildo Garcia*[2], Changwei Hu*[1]

[1]Key Laboratory of Green Chemistry and Technology Ministry of Education, College of Chemistry, Sichuan University Chengdu 610064 (P. R. China), E-mail: changweihu@scu.edu.cn.

[2]Instituto Universitario de Tecnología Química Consejo Superior de Investigaciones Científicas, Universitat Politecnica de Valencia, Av. De los Naranjos s/n, 46022 Valencia (Spain), E-mail: hgarcia@qim.upv.es.

Abstract

Amines are pivotal building blocks for a range of applications, including pharmaceuticals, polymers, agrochemicals and organic synthesis. Hydrogenation of amides using molecular hydrogen via heterogeneous catalysis is considered a promising method for producing amines with considerably high atom efficiency, environmentally friendliness and economic viability. Continued developments have occurred in this area with milestones reached in the hydrogenation of various amides to amines via heterogeneous catalysis. At present, no systematic analysis of the influence of amide structure on their reactivity and the required type of catalyst has been reported. This review describes the most recent advances in catalytic amide hydrogenation, paying a special attention to the influence of structural features (cyclic amides and aliphatic acyclic amides) on catalyst performance. Structural features endow amides with various specific reactivities, reflected in very large differences on the difficulty of hydrogenation and on diverse product selectivity. In addition, insights into the conversion of polyamides, fatty acids and triglycerides to amines are also provided. This review aims to provide new perspectives for designing and applying heterogeneous catalysts adapted to each condition and amide structure.

1. Introduction

Amines are key compounds for the synthesis of dyes, pharmaceuticals, agrochemicals, pigments and polymers (such as Nylon) [1-4]. The applications of polyamides in automotive, aerospace, building construction or health care fields are still expanding. [3, 5, 6] Moreover, amines are also widely present in many of the currently employed drugs. Hence, amines are increasingly important specialty and commodity chemicals. Development of green and sustainable methods for producing amines continues to be sought, especially considering that only very few natural amines are available from biomass. Actually, there are mainly two natural polyamines: poly(ε-L-lysine) produced by *Streptomyces microorganism* [1] and chitosan derived from
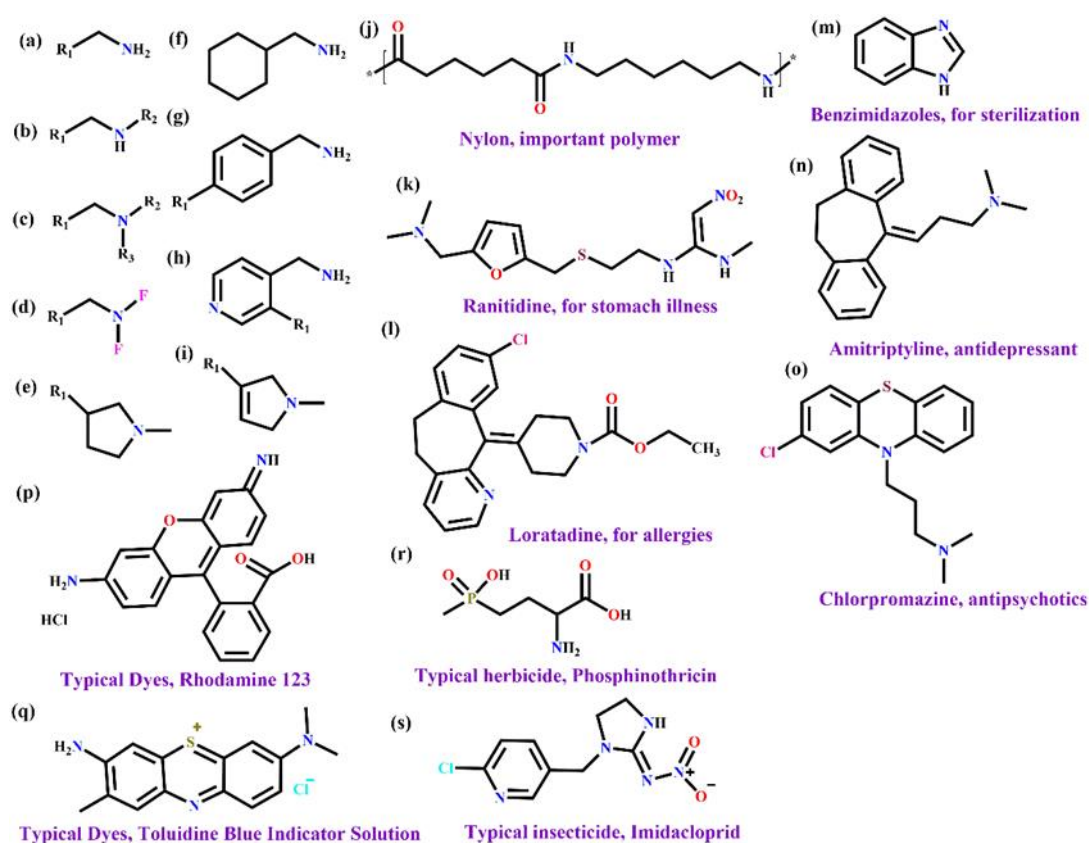

Figure 1. Typical amines (a-i) with different structural features, (j) Nylon 6,6 polymer, (k-o) best-selling nitrogenated pharmaceuticals (p-q) typical dyes and (r-s) typical agrochemicals.

deacetylation of crustacean or insect chitin [7, 8]. Some typical amines with different structural features, such as aliphatic acyclic amines (including primary, secondary and

tertiary amines), cyclic amines, polymers, pharmaceuticals, dyes, and agrochemicals are shown in Fig.1.

The synthesis of amines follows five general routes, as shown in Fig. 2: (a) The direct hydrogenation of nitrile [2, 9], (b) the reduction of nitro compounds [10, 11], (c) the reductive amination of carbonyl compounds (aldehydes and ketones) [12-17], (d) the amination of alcohol with ammonia or amines [18, 19], and (e) the hydrogenation of amides. The route (a) and (b) can only yield primary amines, whereas the remaining methods allow for the production of secondary and tertiary amines depending on the different positions of the functional groups on the substrates. Noticeably, the commonly method for amine industrial production is the amination of alcohol with ammonia or amines, illustrated as route (d). The main drawbacks of this production route are that it needs additional ammonia or amide, and generates a mixture of different amines, which is less selective to one specific amine. Therefore, post-processing treatments are also needed to separate and purify the products obtained. [20-23]
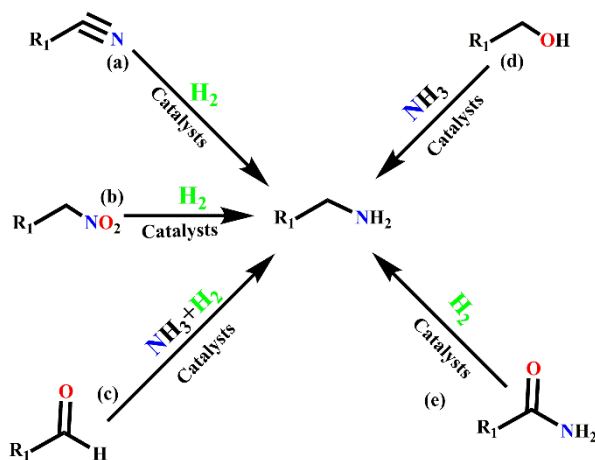

Figure 2. Approaches for amines production.

Amides, being the key functionality present in peptides and proteins from amino acid monomers [3, 24, 25], can be directly extracted from algae [26] and/or can be obtained by amination of bio-based acids [27], making them available from renewable biomass sources. Utilizing the inherent high nitrogen content in natural microalgae (one type of typical biomass) to produce value-added nitrogen-containing compounds such as amides is a promising method, which is of great importance of biomass utilization.

The effects of temperature, metal oxide catalyst (ZrO_2, Al_2O_3, TiO_2, ZnO, MgO, CaO), catalyst amount, and reaction time on the preparation of value-added nitrogen-containing compounds were studied. ZrO_2, as the most effective catalyst, has achieved 6.9 wt% yield of fatty amides under the optimized condition (0.3 g ZrO_2, 300 °C, 6 h). Therefore, the hydrogenation of amides to amines is an attractive process considering amide availability and the atom efficiency of the reaction. The abundance of amides derives from its stable structure, owing to the conjugation effect between N atom lone electron pairs with the carbonyl group. This conjugation between C=O and the N atom renders amides the most stable among all of carbonylic compounds, including aldehydes, ketones, esters, and carboxylic acids, as shown in Fig. 3 (a-b) [28-30], resulting in its low reactivity, particularly toward the nucleophilic attack at the carbonyl group. Besides, the intermolecular hydrogen bonds between amide groups (except the tertiary amides) can further increase the stability of this functionality (Fig. 3 (c)) [29, 31]. It is worth noting that much attention have been paid on the hydrogenation of carboxylic acids, triglycerides, or its derived bio-oils to produce biodiesel. [32-35] The core issue for the hydrogenation of these molecular mentioned above is the designing of catalysts with high hydrogenation efficiency.
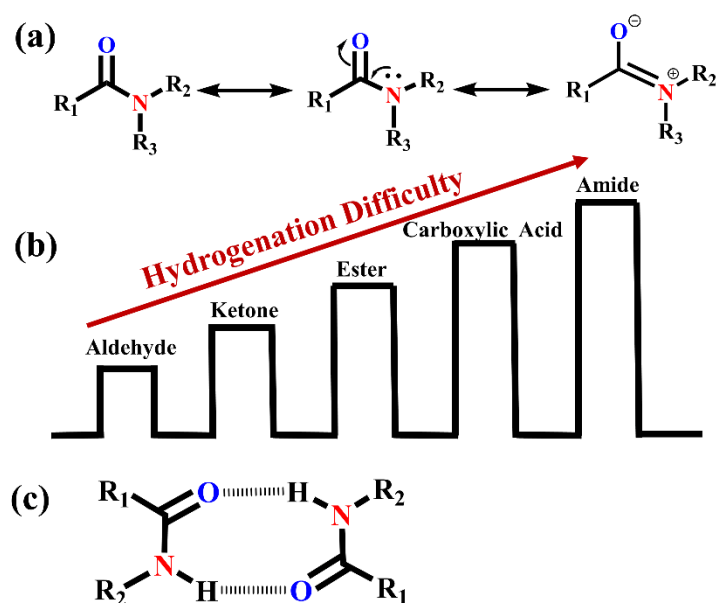

Figure 3. (a) Amide stabilization by resonance, (b) The increase difficulty of the hydrogenation reactions for carboxylic acid derivatives, (c) Intermolecular H bonds that can be established in primary and secondary amides.

Homogeneous catalysis took the lead in the hydrogenation of amides at initial

stage. Two key factors in achieving novel homogeneous catalysts for amide hydrogenation were the control of the metal-ligand interaction to enhance the activity at the metal site and the incorporation of specific ligands in combination with appropriate acidic additives [36]. Metal-complexes with diverse ligands of a wide range of both noble and non-noble metals such as Ir [37], Ru [38, 39], Al [40], Fe [41], Co [42], Mn [31], Zr [43, 44], etc., as shown in Fig.4, have been reported as amide hydrogenation homogeneous catalysts. Even soluble transition metal-free catalysts have also been recently developed for the hydrogenation of amides to amines [45], which is presented as a combined KOtBu/BEt$_3$ catalyst for the deoxygenative reduction of tertiary, secondary, and even notoriously challenging primary amides with pinacolborane (HBpin) at 25-60 °C to form corresponding amines, providing a green protocol for synthesizing high-value pharmaceuticals with amine structure.
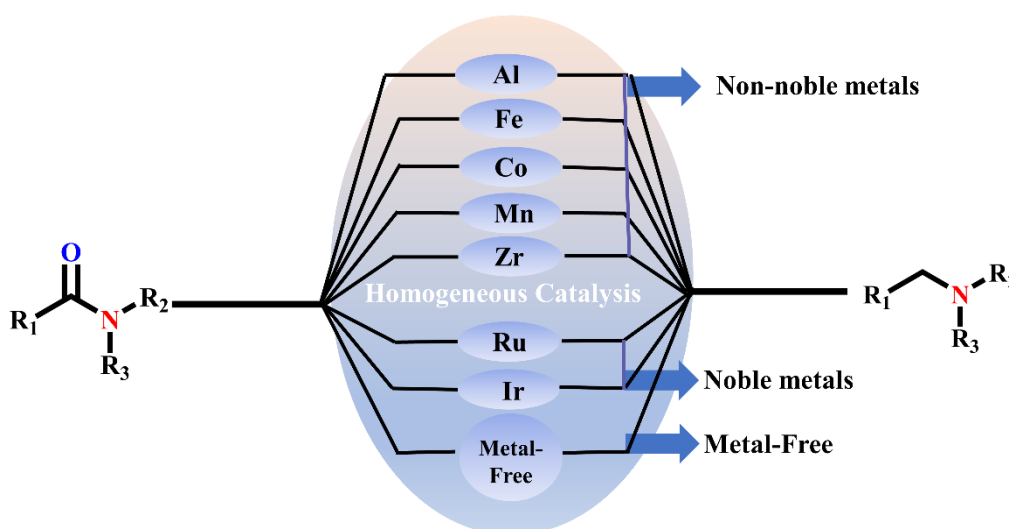

Figure 4. Summary of current homogeneous metal salts and complexes uses as catalysts for amide hydrogenation.

In spite of the higher catalytic activity and the presence of well-defined single sites that generally characterize homogeneous catalysis, they present important drawbacks, such as difficult separation on reaction mixture, cumbersome recycling, the use of costly ligands and difficulty to implement continuous flow processes. For these reasons, heterogeneous catalysis appears to be a considerably more appealing and better suited for industrial production. These general considerations also apply for amide hydrogenation.

The discovery of aggressive metal hydride reagents, specifically lithium aluminum hydride (LAH) in 1947, constituted a breakthrough in the area since it is a general and efficient stoichiometric reagent for amide reduction. The performance of LAH constituted one of the forefronts in organic synthesis, trying to expand the scope of LAH as carbonyl reducing agent [46, 47] to a wide scope of polar X=Y (C=O, N=O, C≡N) functional groups, such as aldehydes, aldimines, ketones, epoxides, esters, carboxylic acids, nitro and nitrile groups, etc. [48]. LAH showed the possibility to reduce amides to amines and this triggered the search for other alternative processes.

In fact, LAH suffers from a significant drawback in terms of its relatively high hazard potential, primarily due to its susceptibility to air and moisture, which renders it unstable. In addition, the stoichiometric LAH reduction suffers from low atom economy, low environmental benignity and poor sustainability.
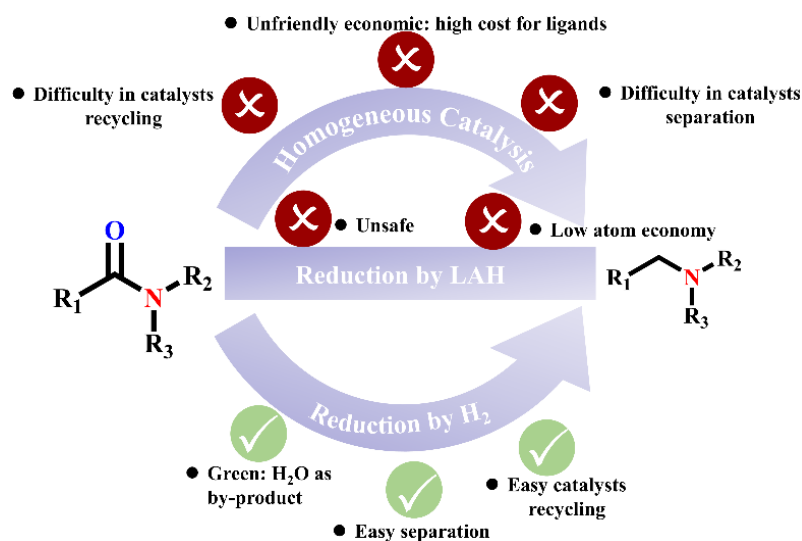

Figure 5. Different approaches for the reduction for amides.

As an alternative, the direct hydrogenation of amides using molecular H_2 promoted by heterogeneous catalysis represents a much greener approach, with considerable economic advantages and better suitability for industrial scale. Undoubtedly, catalytic hydrogenation of amides would serve as a powerful toolkit in organic synthesis and chemical industry. The main differences between homogeneous and heterogeneous catalysis for catalyzing amide to amine are summarized in Fig. 5.
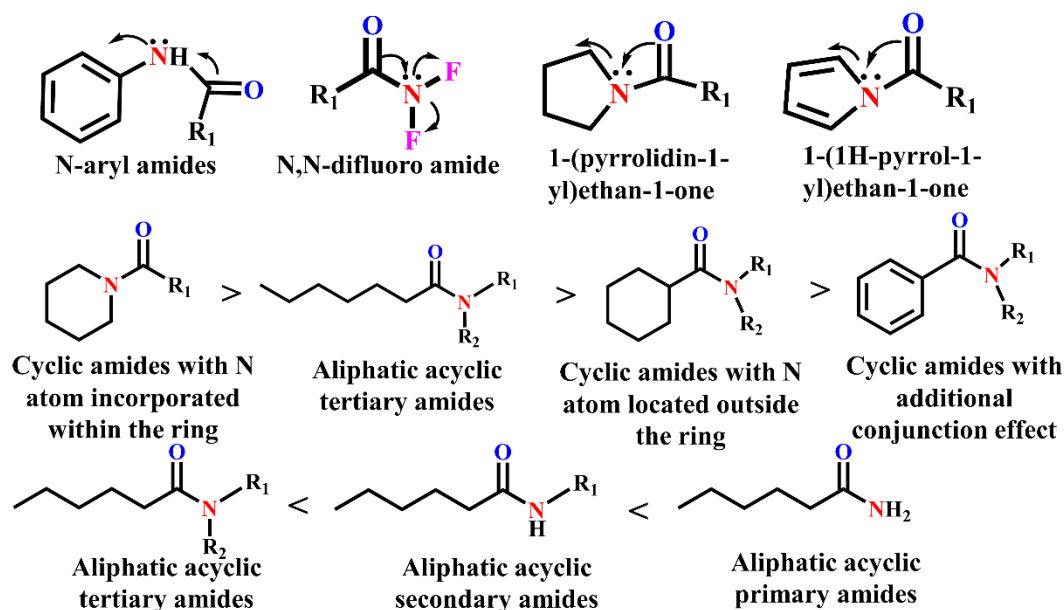
Figure 6. The diagram of conjunction effect between C=O and N atoms in diverse amides, and reactivity order of different amides according to their structure.

As previously mentioned, the carbonyl group in amides is less susceptible to nucleophilic attack among all the carboxylic acid derivatives due to the highest electron density of carbonyl group in amides, primarily caused by the lower electronegativity of N atom compared to the O atom. Hence, it can be anticipated that amides with the N lone electron pair is less available to the carbonyl group such as N-aryl amides, formamides and, as even more pronounced cases such as trifluoromethyl acetamides or amides containing fluorinated or CF_3-substituted aryl groups, would undergo hydrogenation easier and under milder conditions. The relative reactivity order of amides towards catalytic hydrogenation is depicted in Fig. 6. In general, amide structure is the key factor influencing hydrogenation reactivity. Diverse substituents exhibit different electron withdrawing or electron donating effects, thereby affecting the electron density of the carbonyl group. Besides inductive effects, amides with additional conjugation effect, such as those having phenyl substituents have different hydrogenation reactivity. Among cyclic amides, two distinct types can be distinguished: those with nitrogen atoms incorporated within the cyclic structure and those with nitrogen atoms located outside the ring structure. The cyclic amides with nitrogen atoms incorporated within the ring structure are generally more reactive towards

hydrogenation compared to those amides in which the nitrogen atoms are located outside the ring.
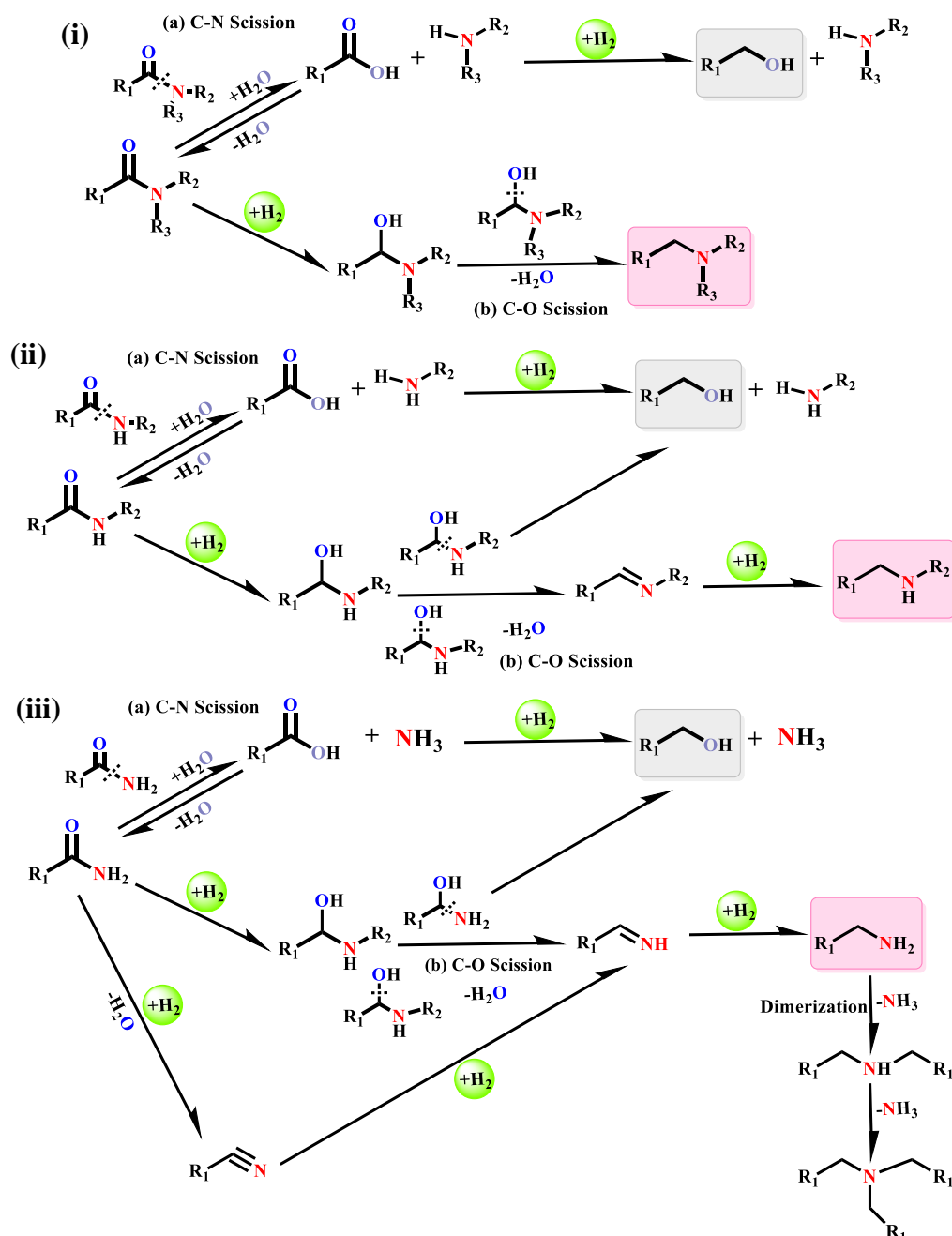
Figure 7. Possible reaction pathways for amide hydrogenation. (i) aliphatic acyclic tertiary amide, (ii) aliphatic acyclic secondary amide, (iii) aliphatic acyclic primary amide. The annotations are (a) C-N hydrogenolysis to alcohol and lower amines, (b) C-O hydrogenolysis forming amines and H_2O.

Regarding aliphatic acyclic amides, the reactivity order (as illustrated in Fig. 6) for hydrogenation is as follows: tertiary amides < secondary amides < primary amides [49]. It is worth noting that the aforementioned reactivity is made under the assumption

that these amides have similar alkyl substituents. However, in reality, the electron density of a specific secondary amide containing an electronegative group may be lower than that of tertiary amides without such groups, making them potentially easier to be hydrogenated.

Additionally, there is still another major challenge for the production of amines via amide hydrogenation besides the difficulty in carbonyl group attack. This is the control of the chemoselectivity (C-N vs C-O hydrogenolysis, in Figure 7) [50-57]. The two alternative bond-breaking possibilities, either C-O bond scission (obtaining higher alkyl chain amines and water) or C-N bond scission (obtaining lower alkyl amines and alcohol) during amide reduction process can result in complex product distribution, as shown in Fig.7. Indeed, theoretical DFT calculations conducted by Cantillo et al. [58] indicate that the cleavage of C-N bonds is energetically more favorable compared to the cleavage of C-O bonds. These calculations suggest a lower energy barrier of approximately 10 kcal mol^{-1} for C-N bonds cleavage with respect to alternative C-O bonds rupture. In general, the choice of hydrogenation catalysts and reaction conditions play a crucial role in determining the products obtained. Consequently, the key challenge in the valorization of amides to obtain amines lies on the design of catalysts with exceptional hydrogenation performance, while displaying high selectivity towards C-O bonds cleavage. This selectivity is important for adequate utilization of amides. It should be noted that alcohols are also actually important sources for the manufacture of cosmetics and consumer chemicals that are widely used, [59-61] and there have been many works that report the cleavage of C-N bonds, leading to the formation of alcohols. Designing catalysts with high selectivity towards C=O or C-N bonds is promising. However, in this review we mainly focus on the hydrogenation of C=O bond, obtaining amines as the final desired product.

It is worth noting that various types of amides, including tertiary, secondary, and primary, can undergo both C-O and C-N bond cleavage. However, the reaction network for primary amides is notably more complex compared to the other two, since these amides can undergo other processes such as direct dehydration to form nitriles,

dimerization, and trimerization, which are not observed for secondary or tertiary amides. These secondary reactions can be particularly prevalent in primary amides with low steric hindrance, such as aliphatic acyclic primary amides. It should be noted that among various types of amides, aliphatic acyclic primary amides are particularly prone to undergo dimerization or trimerization reactions. Therefore, achieving high selectivity in the production of amines from these aliphatic primary amides becomes more challenging due to the required harsher reaction conditions and the potential occurrence of side products. However, it is possible to enhance the selectivity by employing specific strategies to inhibit dimerization reactions. One such approach involves adding NH_3 in the hydrogenation mixture to disfavor di-/oligomerizations and promote the desired amine formation [62].

2. Hydrogenation of amides with different structural features.

Pioneering research by Adkin in 1940s in the field of amide hydrogenation via heterogeneous catalysis reported the use of copper-chromium oxide catalysts under rather drastic reaction conditions of pressure and temperature (175 ºC to 250 °C, 100-300 bar H_2), affording amines through C-O cleavage reaction [63]. Following this groundbreaking work, researchers began to explore the hydrogenation of various types of amides with different structural features. As already mentioned, amides having different structural features exhibit distinct hydrogenation reactivity, regarding both the conversion and selectivity towards amines. Table 1 summarizes activity data reported for the hydrogenation of different types of amides over the last two decades. In the present review, due to the similarity in chemical reactivity we divide these amides into two main categories. One of them is the amides with cyclic structure, and the other one is aliphatic acyclic amides. Cyclic amides can be further classified into cyclic amides with N atoms incorporated within the ring (CANIR) and those with N atoms outside the ring (CANOR). Regarding aliphatic acyclic amides, they are divided into tertiary (AATA), secondary (AASA), and primary amides (AAPA).

Physiochemical features of the solid catalysts reported for amide hydrogenation,

and structure-activity relationships will be commented separately in Section 4.

2.1 Hydrogenation of cyclic amides.

2.1.1   Cyclic amides with N atom incorporated within the ring.

The hydrogenation of cyclic amides with N atoms incorporated within the ring is considered the easiest amide hydrogenation, due to the lowest electronic density of the carbonyl group and the very high selectivity towards the corresponding cyclic amines. In 1996, Fuchikami group reported the hydrogenation of N-acetylpiperidine at 160 ^{o}C, 100 bar H_2 with complete conversion and high yield of N-ethylpiperidine (Table 1, entries 1-3) [64]. N-methylpyrrolidin-2-one (Entry 8) was hydrogenated by Thompson et al. at 120 ^{o}C, 20 bar H_2 with 94% conversion and nearly 93% yield of N-methylpyrrolidine [65]. In this work, a significant solvent effect was observed. The reaction rate depends on the solvent in the following order: hexane > tetrahydrofuran > diethyl ether > methanol > methyl *tert*-butyl ether. This dependency was attributed to differences in the concentration of dissolved hydrogen in each solvent or variations in amide solubility. In 2013, Breit et al. performed successfully the hydrogenation of 108 types of amides to amines at 160 ^{o}C, 30 bar H_2. This comprehensive study demonstrated the general scope of their catalytic system (entries 10-12) [66]. Here, we only comment a few examples among the extensive range of substrates, as summarized in Table S1 of ESI supporting information. Noticeably, most of these amides that were hydrogenated successfully were cyclic amides with N atom incorporated within the ring. The catalysts used in the study based on Pd/Re supported on graphite will be commented in more detail in section 4. In 2016, Kon and co-workers reported the successful complete hydrogenation of N-acetylpiperidine, achieving a 99% yield of the corresponding amine (Table 1, entry 14). The reaction was performed under solventless conditions at 180°C and 50 bar H_2 [67]. In the following year, Kaneda group reported the hydrogenation of 24 types of amides to amines using a bimetallic Pt-V/hydroxyapatite (HAP) catalyst. These hydrogenation reactions were carried out at either 1 bar H_2 and 70 ^{o}C or at 5 bar H_2 and room temperature [68] (Entry 15). The remarkable activity of

this catalyst is evidenced by the substantial decrease in both the required temperature and the hydrogen pressure. These conditions highlight the significant progress on catalyst performance made in this study. Additional data on the catalytic activity pertaining to the hydrogenation of other various amides by Pt-V/HAP can be found in Table S2 of supporting information. In the same year, Shimizu et al. published a study demonstrating that Re/TiO$_2$ catalyst enabled the selective hydrogenation of diverse substrates containing both aromatic and aliphatic moieties at 50 bar H$_2$ and 180-200 ºC [69]. Importantly, when aromatic rings were present in the substrates, amide hydrogenation did not lead to the formation of dearomatized byproducts in spite of the rather drastic conditions (entries 16-17 and Table S3 of supporting information). Tang and co-workers also accomplished the conversion of the same amides studied by Kaneda using indium (In) catalysts supported on a porous carbon material. However, their results showed lower conversion and yields, and the reactions required more rigorous conditions [70] (entry 18 in Table 1), which further proves the superiority of Pt-V/HAP bimetallic catalytic system. The same Pt-V/HAP was also employed to convert N-methylpyrrolidone, resulting in the successful preparation of N-methylpyrrolidine with conversion and yield both exceeding 90 % [71] (entry 25 in Table 1). In the case of N- methylpyrrolidine, the unique experimental advantage was the solventless conditions. When the support was changed to CeO$_2$, the Pt-V/CeO$_2$ developed by Friedrich group was also efficient for 4-acetylmorpholine hydrogenation under rather low temperature with a N-ethylmorpholine yield of 79 % [72] (entry 26 in Table 1).

2.1.2 Cyclic amides with N atoms outside the ring

A significant number of cyclic amides with N atoms located outside the ring have been converted to their corresponding amines through catalytic hydrogenation. Among them, cyclohexanecarboxamide (CyCONH$_2$) comes to be the most common benchmark molecule to compare the activity of various catalysts. Whyman et al. converted CyCONH$_2$ to cyclohexylmethylamine (CyCH$_2$NH$_2$) with 100% conversion

and an approximate yield of 85 % at 160 ºC and 100 bar H_2. Notably, only a small amount of $CyCH_2OH$ was observed, with no $(CyCH_2)_2NH$ (dimers) being detected [73] (Entries 4-5 in Table 1). Subsequently, the same research group carried out the hydrogenation of the same substrate under identical conditions using other different catalysts, but they observed a lower conversion and product yield [74, 75] (Table 1, entries 6-7). Dimerization products were barely detected in all these studies. According to the report by Tomishige et al., a slightly lower yield (55 %) of $CyCH_2NH_2$ was obtained in the hydrogenation of $CyCONH_2$, observing the appearance of a certain amount of $CyCH_2OH$ and dimerization products, implying a low selectivity towards amines [76]. Most recently, Wang group has devoted ~~a~~ significant attention to the hydrogenation of $CyCONH_2$ to $CyCH_2NH_2$, the results being summarized in entries 28-30 of Table 1 [77-79]. Using identical reaction conditions, they provided a comparison among various catalysts concluding that $2Ru1W/SiO_2$ catalyst enables hydrogenation of $CyCONH_2$ more efficiently in terms of both higher conversion and amines yield, for 93.6 % and 84.0 % respectively, than ~~other~~ alternative catalysts. However, the turnover frequency based on interfacial Ru-Mo sites was more than twofold higher than that of Ru-W system. Therefore, it would be of interest to develop advanced Ru-Mo on other supports that would allow a higher active site density than SiO_2.

Besides $CyCONH_2$, cyclic amides with benzene rings such as N-phenyl benzamide have been tested. Luo and co-workers reported the catalytic hydrogenation of N-phenyl benzamide to N-benzyl aniline [80], reaching a remarkably high yield of 93 %. This result was obtained using a specific ratio of amide to $TiCl_4$ to Mg of 1:5:10, with tetrahydrofuran (THF) as the solvent. In 2019, Milstein and co-workers reported the hydrogenation of N-phenyl benzamide to N-benzylaniline using Ag catalyst supported on γ-Al_2O_3, with a complete conversion and 96 % amine yield [81] (entry 19 in Table 1). Notably, the amines obtained here were lighter amines, formed by cleaving C-N bonds, being different from the products reported by Luo described before. The product distribution achieved by Milstein agrees better with the results

reported by Andrés et al. [82] (Entry 23). In the same year, Kadyrov presented a straightforward and versatile method for selectively converting amides to amines. This conversion was achieved by utilizing a protocol involving the addition of CF_3SO_2OMe as alkylating agent, with the reactions being conducted at 150 °C and 40 bar H_2 [83].

2.2 Hydrogenation of aliphatic acyclic amides.

　　As previously mentioned, the hydrogenation activity of these aliphatic acyclic amides follows the reverse order of the electron density of carbonyl group in amides. In the case of having the same substituent, the hydrogenation activity follows the order: tertiary amides < secondary amides < primary amides. Furthermore, it is crucial to note that the selectivity to the desired target amines may differ significantly depending on the substrate due to the varying tendencies to undergo dimerization or even trimerization. As expected in view of the steric encumbrance, aliphatic acyclic primary amines are particularly prone to dimerization, unless additional NH_3 is added to the reaction. For this reason, this class of amides will be discussed separately in this section.

2.2.1 Hydrogenation of aliphatic acyclic tertiary and secondary amides

　　For the aliphatic acyclic tertiary amides, the electron density of the carbonyl group is expected to be the highest among aliphatic acyclic amides. The other two alkyl substituents, being the electron donating groups, contribute to increase the electron density of carbonyl group. As a result, these aliphatic acyclic tertiary amides are expected to be the less reactive in the series of aliphatic acyclic amines towards hydrogenation. However, due to the presence of two substituents attached to the N atom, dimerization reactions are less likely to occur. This steric encumbrance contributes to a high selectivity of amide hydrogenation to the desired amines without the need for additional reagents to inhibit dimerization. Using the same reasoning, in the case of aliphatic acyclic secondary amides, the electron density of the carbonyl group is expected to be intermediate among aliphatic acyclic amides. However, since the nitrogen atom is connected to only one substituent, the likelihood of dimerization

14

increases compared to tertiary amides. This, in turn, results in a slight decrease in the selectivity of the desired amine product. Indeed, the extent of dimerization in aliphatic acyclic secondary amides is influenced by the size of the substituent. Larger substituents or increased steric hindrance around the nitrogen atom hinders dimerization, thereby improving the selectivity of the desired amine product. This factor plays a significant role in determining the extent of dimerization and the resulting selectivity in hydrogenation reactions of aliphatic acyclic secondary amides. In 2021, Kusema reported the hydrogenation of tertiary N,N-dimethyldodecanamide to the corresponding amine with high conversion and yield (94.0 %) at 130 ºC, 30 bar H_2 using Rh-V/Al_2O_3 as catalyst (entry 24 in Table 1) [84]. As expected, the achieved amine selectivity was nearly 100 %. Moreover, the developed catalytic system was also applied to hydrogenate other amides, including those with cyclic structures as well as aliphatic acyclic tertiary, secondary, and primary amides (see Table S4 of supporting information). However, the yields of aliphatic acyclic secondary or primary amides are significantly lower than tertiary amines due to the above-commented dimerization. Therefore, in view of the presence of Rh in the catalysts and the still limited scope there is still much room for improvement regarding the optimal catalyst.

2.2.2 Hydrogenation of aliphatic acyclic primary amides

De Vos and coworkers conducted a pioneering research on the hydrogenation of aliphatic acyclic primary amides in 2019 [62]. They reported that the use of bimetallic Ru-W catalyst in environmentally friendly cyclopentyl methyl ether as solvent to achieve hexanamide hydrogenation reaching complete conversion and up to 83 % hexylamine yield (Entry 21). Additionally, they discovered that the Lewis acid promoter and NH_3 partial pressure played crucial roles in achieving high yields of primary amines. These factors were identified crucial in the hydrogenation process. Meanwhile, the bimetallic Ru-W catalyst was also able to successfully hydrogenate other aliphatic acyclic primary amides with higher number of carbon atoms, as indicated in entry 22 of Table 1. Additionally, a substrate scope investigation was

carried out using the catalytic system, and the comprehensive results can be found in Table S5 of supporting information. Hereafter, Guo et al. reported an efficient Ru/Nb$_2$O$_5$ catalyst for the hydrogenation of propionamide to propylamine, achieving up to 91.4 % yield [85]. Also in this case, the addition of NH$_3$ was found to be essential for achieving high selectivity in the hydrogenation of aliphatic acyclic amides. This is attributed to the low steric hindrance of the desired amines that tend to be dimerize, while the presence of NH$_3$ traps the intermediate resulting in the formation of further primary amines. Later, our group accomplished the hydrogenation of hexanamide as well as other types of aliphatic acyclic primary amides to the corresponding amines by using bimetallic NiMo nitrides catalyst (Ni$_2$Mo$_3$N). Here, high conversion (93.9 %) and hexylamine yield (75.1 %) was obtained under 240 ℃ and 20 bar H$_2$ (Table, Entry 31). [86] The presence of NH$_3$ was essential for the high selectivity of primary amines. Combining intermediate reactivity tests via time-on-stream experiments and literature data, a reasonable reaction pathway for hexanamide conversion over bimetallic Ni$_2$Mo$_3$N catalysts was proposed. According to it, the first step is the addition of hydrogen to the amide, or its tautomer iminol, which affords the corresponding hemiaminal intermediate that can undergo hydrogenolysis producing 1-hexanol via the C-N pathway. Alternatively, the hemiaminal can be dehydrated to give an imine which is further hydrogenated to hexylamine via the C-O break pathway. The obtained hexylamine can undergo further deamination to obtain hexane or dimerization to obtain dihexylamine. Overall, due to the high difficulty in hydrogenation and the low selectivity of products in the case of aliphatic acyclic primary amides, only a few studies have been reported for these substrates and there is much interest in expanding further the scope pf primary alkyl amides that can be successfully converted to the corresponding amines. One specific issue is the compatibility between the Lewis acid site and NH$_3$ that should result in the mutual neutralization, thus, making necessary the use of harsher reaction conditions. It can be anticipated that if the unwanted di-/oligomerization of primary amines is somehow impeded, as for instance using porous catalysts exerting shape selectivity in product formation, the use of NH$_3$ could not be

necessary and, as consequence, the Lewis acid site promotion effect of the catalyst would be more efficient.

3. Derivatization reactions of amides hydrogenation via heterogeneous catalysis

Apart from the direct hydrogenation of amides, various related substrates related to amides, including polyamides, fatty acids, and triglycerides etc., have also been successfully converted into amines in recent years. The conversion of these aforementioned substrates represents also remarkable examples of green processes, as well as valorization of wastes and economy circularity among other benefits.

Developing suitable recycling process for the inevitable plastic waste represents one of the most acute challenges for the 21st Century, Currently, the commonly employed methods for its disposal are landfilling or incineration. However, these methods are ultimately unsustainable considering circular economy principles or the high CO_2 footprint. Landfilling, in particular, falls short as a long-term solution due to the rapid surge in plastic consumption. On the other hand, incineration leads to the emission of significant pollutants. In contrast, the chemical conversion of plastic waste offers a more meaningful and environmentally-friendly approach. Polyamides, as one of the widely used plastic products, are produced in about 6 M metric tons per year only as fibers [87] and have much higher total consumption per year. Consequently, the degradation and valorization of polyamides into amine could be one possible way to recycle part of these polymers at the end of the use. However, one of the main problems for their transformation is the strong internal hydrogen bonds that make these materials insoluble in most common solvents.

De Vos group has made significant contributions to the recycling of polyamides by converting them into amines. In 2022, they reported the ammonolysis hydrogenation of long-chain polyamides using Nb_2O_5+RuWOx/$MgAl_2O_4$ as heterogeneous catalyst, achieving complete depolymerization. The resulting reaction product mixture comprised 62 % of primary amines and 36 % secondary amines [88]. The key step in the depolymerization mechanism is the hydrogenation of in situ-formed primary amides

(or nitriles) to amines, which should occur similarly as previously discussed for aliphatic primary amides. The proposed reaction mechanism is shown in Fig. 8. According to their proposal, the ammonolysis of secondary amides was in essence the reverse reaction of a transamidation. The carbonyl group of the secondary amide coordinates to a Lewis acid site of the catalyst, which activates it for a nucleophilic attack of NH_3. A neighboring acid group can help to stabilize or even activate the leaving group. The secondary amide was cleaved into a primary amine and primary amide. A significant fraction of the in situ-generated primary amide become dehydrated, a process that would be catalyzed by any acid group such as Lewis or Bronsted acid sites.
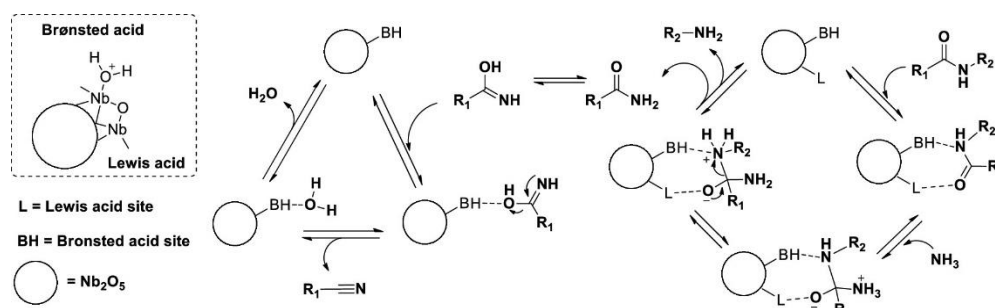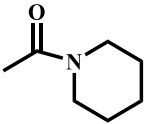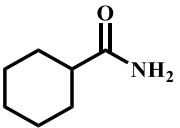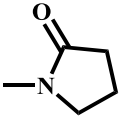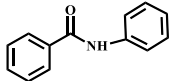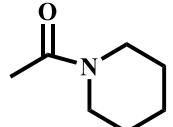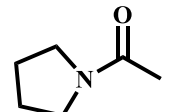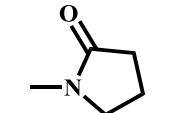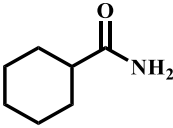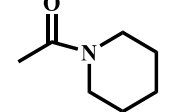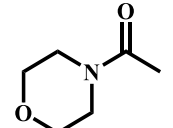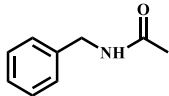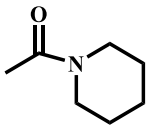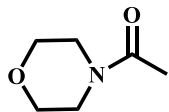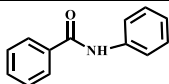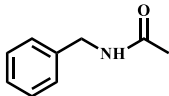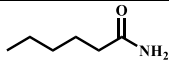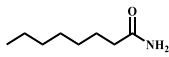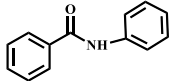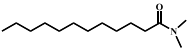

Figure 8. Proposed reaction mechanism for the ammonolysis of a secondary amide and the dehydration of a primary amide with a Nb_2O_5 catalyst. Reproduced from Ref. [88] with permission from American Chemical Society.

Table 1. The activity results for the hydrogenation of amides and ~~used~~ catalysts used over the last two decades.

Entry	Amides	Amide Types	Reaction Conditions	Conversion (%)	Amine yield (%)	Catalysts	Ref.
1				100	96	$Rh_6(CO)_{16}$+ $Re_2(CO)_{10}$	[64]
2		$CANIR^a$	160 °C, 100 bar H_2, 16 h	100	98	$Rh_6(CO)_{16}$+ $Mo(CO)_6$	
3				100	96	$Ru_3(CO)_{12}$+ $Re_2(CO)_{10}$	
4				100	85	$Ru_3(CO)_{12}$+Mo $(CO)_6$	[73]
5		$CANOR^b$	160 °C, 100 bar H_2, 16 h	100	85	$Ru_3(acac)_3$+ $Mo(CO)_6$	
6				77	71	Rh_6CO_{16}+ $Mo(CO)_6$	[74]
7				95	86	$Ru_3(CO)_{12}$+Re $_2(CO)_{10}$	[75]
8		CANIR	120 °C, 20 bar H_2, 24 h	94	> 93	4 wt%Pt-4 wt%Re/TiO_2	[65]

9	<structure: N-phenylbenzamide>	CANOR	Ar atmosphere, room temperature, 4 h	93	> 92	TiCl₄+Mg	[80]
10	<structure: 1-acetylpiperidine>	CANIR		100	> 99		
11	<structure: 1-acetylpyrrolidine>	CANIR	160 °C, 70 bar H₂, 16 h	100	> 99	Pt- Re/graphite	[66]
12	<structure: 1-methylpyrrolidin-2-one>	CANIR		100	> 99		
13	<structure: cyclohexanecarboxamide>	CANOR	140 °C, 80 bar H₂, 24 h	89	55	Rh-MoOx /SiO₂-CeO₂	[76]
14	<structure: 1-acetylpiperidine>	CANIR	180 °C, 50 bar H₂, 24 h, no solvent	100	99	Pt-Nb₂O₅	[67]
15	<structure: 4-acetylmorpholine>	CANIR	1 bar H₂ at 70 °C or 5 bar H₂ at room temperature, 24h	100	99/93	Pt-V/ hydroxyapatite (HAP)	[68]

#	Structure	Type	Conditions			Catalyst	Ref
16		CANOR	180 °C, 50 bar H₂, 24 h	> 95	86	Re-TiO₂	[69]
17		CANIR	180 °C, 50 bar H₂, 24 h	> 99	> 99		
18		CANIR	130 °C, 30 bar H₂, 4 h	85	76	Ir/3.0Mo-KIT6 (Mesoporous Silica)	[70]
19		CANOR	150 °C, 50 bar H₂, 24 h	> 99	96	Ag-γ-Al₂O₃	[81]
20		CANOR	150 °C, 40 bar H₂, 1 h, CF₃SO₂OMe as alkylating agent	> 99	94	5%Pt-C	[83]
21		AAPAᶜ	200 °C, 50 bar H₂, 5 bar NH₃, 16 h	> 99	83	Ru-W/MgAl₂O₄	[62]
22				97	82		
23		CANOR	130 °C, 60 bar H₂, 8 h.	100	> 90	5.3%Pd-In₂O₃	[82]
24		AATAᵈ	130 °C, 30 bar H₂, 1 h	94	94	Rh-V/Al₂O₃	[84]

25		CANIR	220 °C, 20 bar H_2, solvent free	> 90	> 90	Pt-V/HAP	[71]
26		CANIR	90 °C, 30 bar H_2, 3 h	> 79	79	Pt-V/CeO$_2$	[72]
27		AAPA	180 °C, 40 bar H_2, 5 bar NH_3, 12 h.	> 99	73	Ru/Nb$_2$O$_5$-L	[85]
28				93.6	84.0	2Ru1W/SiO$_2$	[77]
29		CANOR	160 °C, 50 bar H_2, 12 h	86.8	61.0	5Ru-Mo/TiO$_2$	[78]
30				90.1	74.8	2Ru-Mo/SiO$_2$	[79]
31		AAPA	200 °C, 20 bar H_2, 3bar NH_3, 4 h	93.9	75.1	Ni$_2$Mo$_3$N	[86]

[a] Cyclic Amides with N atoms In the Ring [b] Cyclic Amides with N atoms Out the Ring.
[c] Aliphatic Acyclic Primary Amides. [d] Aliphatic Acyclic Tertiary Amides.

Hereafter, they developed a sustainable way of recycling polyamides (PA66) to diamines and diamides using a Lewis acid catalyst with NH_3, adding glycerol to dissolve the polymer and favor the ammonolysis [89]. Computational calculations allowed to gain a deeper understanding of the reaction mechanism. These theoretical studies revealed that especially the vicinal diol moieties of these glycol solvents play a key role in activation of the ammonia as nucleophile. This would explain why glycerol is the most effective solvent among many others, as shown in Fig.9.
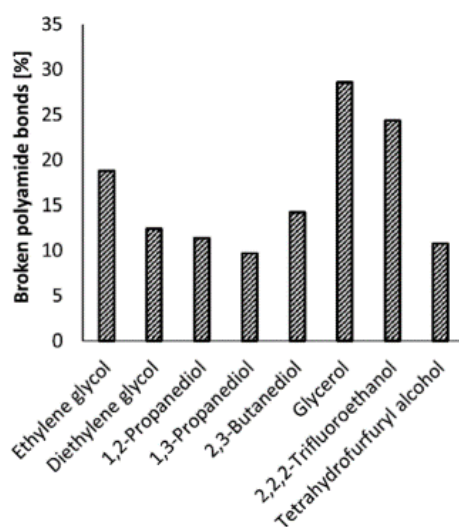
Figure 9. Effect of the reaction solvent on the ammonolysis of PA66. Reproduced from Ref. [89] with permission from The Royal Society of Chemistry.

The conversion of fatty acids to amines is akin to the process of converting amides through reductive amination. Initially, fatty acids undergo conversion into amides by reacting with NH_3, which proves to be a straightforward reaction. Following this, the hydrogenation process of the amides, that is, a slower process takes place. It is of significance to convert carboxylic acids to amines via one-pot tandem process since the value of amines is generally much higher than that of acids or alcohols. De Vos et al. applied Ru-W/MgAl$_2$O$_4$ to accomplish the reductive amination of fatty acids based on their results with amide hydrogenation, which had proved that Ru-W/MgAl$_2$O$_4$ is efficient for the hydrogenation of hexanamide [90]. Using Ru-W/MgAl$_2$O$_4$ as heterogeneous catalyst, up to 99 % selectivity of primary amine with high conversion of the fatty acids was achieved. Additionally, the catalyst was recyclable and tolerant to

common impurities, such as water and cations (e.g. sodium carboxylate). Subsequently, the same group developed new types of catalysts (Ag/TiO$_2$ and Au/TiO$_2$) for the conversion of benzoic acid to benzylamine with H$_2$ and NH$_3$ as reagents [91]. The yield of benzylamine obtained was up to 92 %. Notably, the percentage of noble metal in the catalyst was significantly minimized, with only a mere 0.025 mol % of Au being required for the reaction. Combining experimental results and theoretical calculations, they demonstrated that these catalysts are bifunctional, that is, the catalysts promote the dehydration of both the ammonium carboxylate to the amide and of the amide to the nitrile, while the sites at the metal-support interface promoted the hydrogenation of the in-situ generated nitrile to the amine.
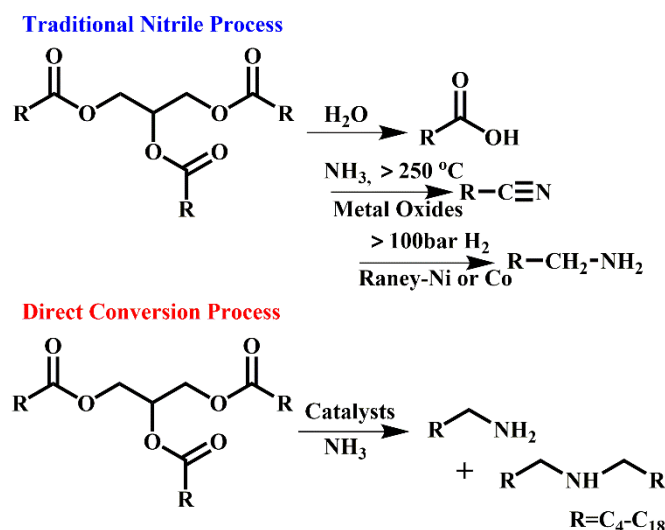
Figure 10. The currently used multi-step industrial pathway to fatty amines (nitrile process) and the direct route based on the tandem process with bifunctional catalysts.

Apart from the reduction of amides derived from polyamides and carboxylic acids, the successful conversion of triglycerides into amines has also been achieved. The reaction sequence in this transformation involves, firstly, the triglycerides extracted from oilseeds undergoing hydrolysis to afford fatty acids, which then react with NH$_3$ in the presence of metal oxide catalysts at high temperature to yield fatty nitriles. Afterwards, a subsequent metal-catalyzed high-temperature hydrogenation of the nitriles under high H$_2$ pressure furnished the targeted fatty amines. Direct conversion using heterogeneous catalysts can achieve high yield and selectivity to amine compared

with the traditional multiple step methods, that in addition require considerable work up, as shown in Fig.10.

A direct conversion of triglycerides into amines by using Zn-Al$_2$O$_3$ or Zn-Cr$_2$O$_3$ catalysts with NH$_3$ or short-chained alkyl amines has been disclosed in a patent by Henkel & Co Ltd [92]. Owing to the still present drawbacks arising from the harsh reaction conditions (200-400 °C; 50-400 bar H$_2$) and the use of over-stoichiometric amounts of catalysts, new types of catalysts or methods with higher efficiency and improved sustainability are highly desired. Recently, Shimizu and co-workers reported the reductive amination of triglycerides directly into fatty amines with up to 91 % amines yield obtained by ZrO$_2$-supported Pt clusters [93]. This transformation represents a substantial advancement in the field, particularly considering the wide availability of oils and fats in Nature. Notably, this catalyst demonstrates a considerable versatility in its capability to convert not only triglycerides, but also amides or nitriles to high-valued amines. By adjusting the metal loading and reaction conditions, the catalyst can be fine-tuned to selectively produce the desired product, expanding its application range. However, it is obvious that further improvements to avoid the use of Pt are is still necessary.

4.   Diverse catalytic systems for amide hydrogenation.

As mentioned previously, a wide range of amides with varying structural features have been studied as starting materials to obtain amines, showcasing the versatility and applicability of this hydrogenation reaction to produce amines from various amides. Many types of catalysts have been designed and implemented for this reaction. The evolution of heterogeneous catalysts for amide hydrogenation has been illustrated in Fig. 11. Advanced characterization techniques have played a pivotal role in uncovering the relevant physicochemical properties and establishing structure-activity relationships in these catalysts. These insights have provided valuable knowledge for developing advanced catalyst generations with enhanced efficiency in amide hydrogenation reactions.

In the early stages of this field, the Cu/CrO_3 catalytic system emerged in 1930s as a highly recommended choice for hydrogenation reactions. Its exceptional hydrogenation ability made it suitable not only for amide hydrogenation, but also for hydrogenation of other functional groups, such as aldehydes, ketones, acids, etc [63]. However, this catalytic system faced limitations due to the requirement of harsh reaction conditions and the use of high valent toxic chromium, which posed environmental and safety concerns. As a result, the widespread application of the Cu/CrO_3 catalytic system was restricted.
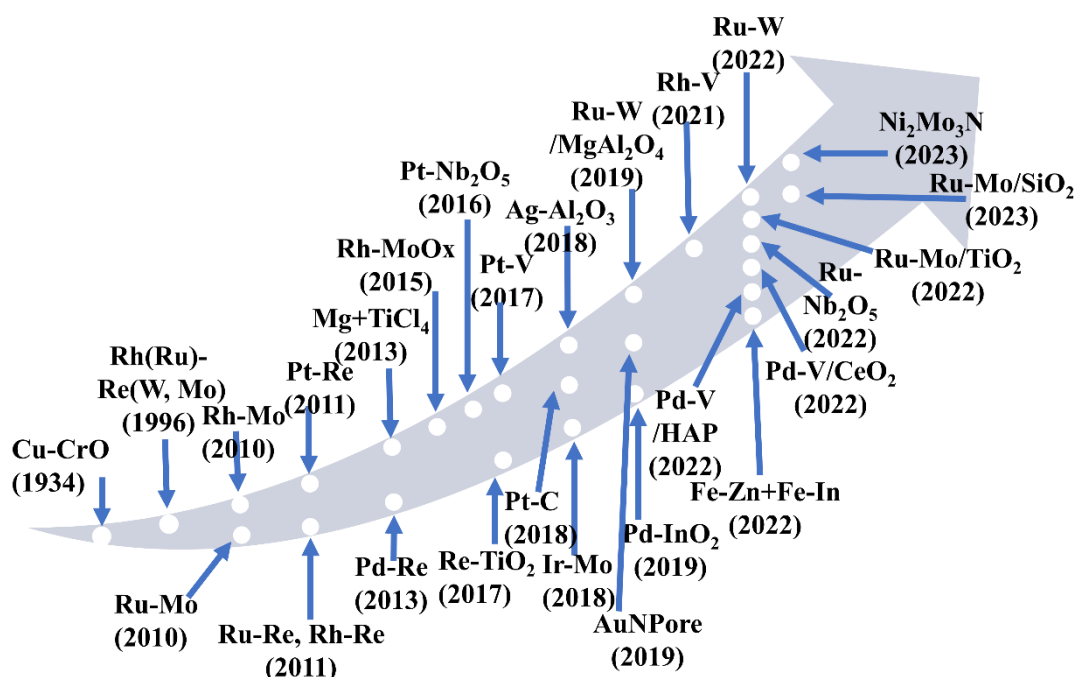
Figure 11. Evolution of heterogeneous catalysts for amides hydrogenation.

With the continuous progress and development of nanoscience and technology, new alternative catalytic systems called bifunctional catalysts were proposed in 1996 by Fuchikami et al. [64], allowing amide hydrogenation to reach a new milestone. The concept of bifunctional catalysts provided a new approach and opened up new possibilities for amide hydrogenation. Bifunctional catalysts provided enhanced efficiency and selectivity in these reactions under milder conditions compared to Cu/CrO_3. In their study, Fuchikami et al. reported that bimetallic catalysts, composed of late transition metals from Group 8 to 10 and early transition metals from Group 6 or 7, exhibit remarkable reducing activity in selectively converting amides into amines.

Particularly effective combinations included rhodium-rhenium, rhodium-molybdenum, and ruthenium-rhenium catalysts, which exhibited excellent performance in the hydrogenation of N-acetylpiperidine. Worth mentioning was the absence of by-products such as hydrocarbons or alcohols, underscoring the high selectivity achieved with these catalysts.

Over the past two decades, Whyman and colleagues have continued to explore and delve deeper into the concept of bifunctional catalysts. Their efforts have focused on understanding the operation mechanism of these catalysts and their applications in various reactions. By building upon the foundation laid by previous studies, they have contributed significantly to the ongoing development and optimization of bifunctional catalysts in the field of catalysis. In this way, in 2010, Whyman and his team developed Rh/Mo catalysts formed in situ using $Rh_6(CO)_{16}$ and $Mo(CO)_6$ as precursors, the resulting catalyst being effective for the liquid phase hydrogenation of $CyCONH_2$ to $CyCH_2NH_2$ in up to 87% selectivity, without the requirement of ammonia to inhibit secondary amine formation [74]. Moreover, variations in Rh/Mo ratio have revealed significant synergistic effects in catalysis, with optimum performance at the value of 0.6. This finding highlighted the importance of carefully tuning the composition of the catalyst for achieving the maximum catalytic activity and selectivity in the hydrogenation process. Moreover, this unsupported Rh-Mo catalyst is found robust. ~~They~~ ,which may be recovered and recycled with only minor loss ~~of~~ in activity, requiring no reactivation procedure other than the application of the standard reaction conditions. Notwithstanding their stability, exposure to CO completely, but reversibly, inhibits the activity, presumably via either/or both (i) stabilization of the metal carbonyl precursors and prevention of active catalyst formation in the case of the 'one-pot' preparations, and (ii) preferential adsorption of CO on active sites on the preformed catalysts. Similar to Rh/Mo, the same authors reported that the Ru/Mo bifunctional catalysts prepared by an analogous method can promote the hydrogenation of $CyCONH_2$ effectively. Similarly, the effect of varying the Ru/Mo ratio on both conversion and yield was also investigated. The results revealed the operation of a

combination of synergistic and poisoning effects, with the optimum Ru/Mo ratio to achieve the highest conversion and selectivity found at 0.5 [73]. By means of extensive characterization using IR spectroscopy, X-ray powder diffraction (XRD), transmission electron microscopy (TEM), energy dispersive X-ray (EDX), and X-ray photoelectron spectroscopy (XPS), it was observed that the active material is comprised of Rh^0 or Ru^0 nanoparticles around 2-4 nm surrounded by Mo in different oxidation states. Stability results showed that complete amide conversions and $CyCOCH_2$ yield remain both essentially constant, although primary amine selectivity decreased slightly during cycles 3-5. This variation in selectivity seems most likely to be a consequence of sequential retention and accumulation of minor amounts of insoluble C-, H-, and N-containing residues on the catalyst surface. Following the successful demonstration of bifunctional catalysts for amide hydrogenation, further studies explored different combinations of metals, leading to additional catalysts, such as Ru-Re, Rh-Re [75], Pt-Re [65] etc. All these catalysts exhibited excellent performance in the hydrogenation of amides, and Ru-Re as well as Rh-Re reported by Whyman et al. exhibited stable catalytic hydrogenation performance, indicating the promising applied prospectives. These findings not only validate the concept of bifunctional catalysts for amide hydrogenation, but also highlight the potential of exploring various metal combinations to further enhance the catalytic efficiency and selectivity in amide hydrogenation.

A Deeper understanding on the mechanism of amide hydrogenation over Pt-Re/TiO_2 catalyst has been achieved clarified by DFT calculating. Specifically, the role of the uncoordinated Re was to activate the C=O and that of the Pt nanoparticles to active hydrogen, removing intermediates from the catalyst surface. The close interaction between the Re and Pt is crucial to the high activity observed [65]. Pt-Re/TiO_2 displays high hydrogenation activity towards N-methylpyrrolidin-2-one conversion. Unfortunately, the loss of activity was observed for the second run, which may be attributed to a decreased interaction between the Pt and Re. Two years later, a breakthrough was achieved by Hamilton group, accomplishing the first continuous flow hydrogenation of amides to amines with the Pt-Re catalyst. To evaluate the stability of

the catalyst over time, the catalytic hydrogenation of N-methylpyrrolidin-2-one in decane was performed under low conversion with a shorter residence time (substrate solution flow rate=0.24 mL/min, H_2 flow=190 mL/min). Fig. 12 presents the conversion and selectivity versus reaction time for hydrogenation of N-methyl propenamide to the corresponding secondary amines [94]. It was found that, Gradual catalyst deactivation was observed with time on stream, and the greatest deactivation (observed as a sharp drop in conversion) occurred within the first four hours on stream. The above results demonstrated the importance of the interaction between two metals.
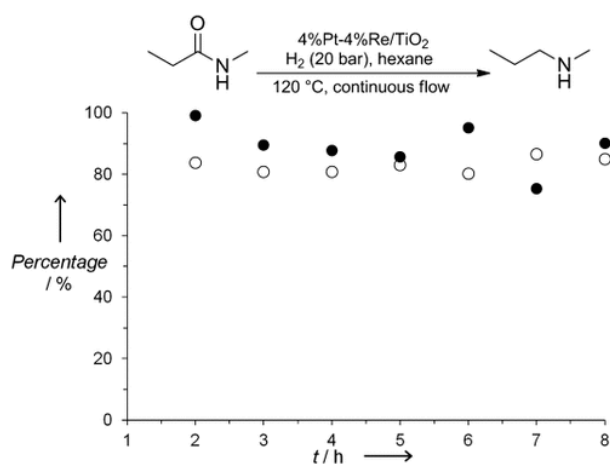
Figure 12. Conversion (●) and selectivity (○) for the catalytic hydrogenation of N-methylpropanamide with 4 %Pt- 4 %Re/TiO_2 as catalyst under continuous flow using a recycled catalyst bed. Reproduced from Ref. [94] with permission from Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

In 2013, Luo's group developed a low-valent titanium catalysts by in situ reduction of $TiCl_4$ with Mg powder in THF. The low-valent titanium catalyst was found to promote the reduction of amides [80]. Unfortunately, this catalytic system has not attracted further attention, primarily because limited scope towards amides containing aromatic rings. Even there were nNo stability data were provided, it can be is anticipated that the stability could be bad since catalysts recycle here is troublesome. It would be, however, important to understand better the origin of the substrate compatibility.

Figure 13. TEM image of Pd/Re-graphite. Reproduced from Ref. [66] with permission from Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

Around the same time, Breit and co-workers reported the hydrogenation of various tertiary and secondary amides at low temperatures and H_2 pressures using a graphite-supported bimetallic Pd/Re catalyst. The advantageou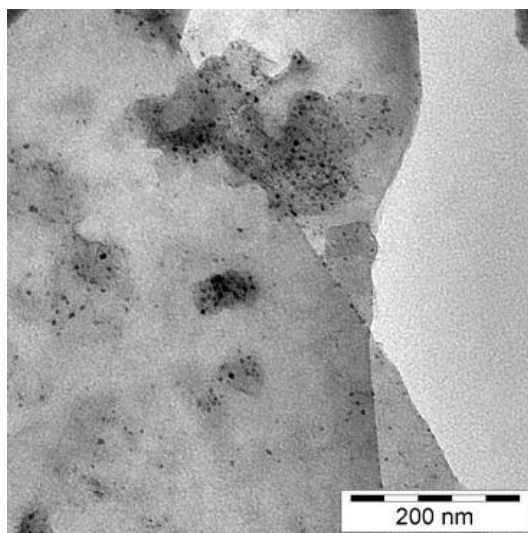s performance of this Pd-Re/graphite catalyst over 43 other different catalysts were established for the catalytic hydrogenation of the N-acetylpiperidine as model substrate. Moreover, graphite-supported bimetallic Pd/Re catalyst was also suitable for converting 108 types of amides to amines. The development of this catalyst was a milestone and it further expanded the toolkit available for amide hydrogenation, offering a promising alternative for achieving high conversion and selectivity under mild reaction conditions. As shown in Fig.13, TEM images revealed the homogeneously dispersed nanoparticles of 2-6 nm deposited on the graphite layers. It was proposed that the high surface/volume ratio achieved for Pd/Re-graphite was the cause of the high reactivity of the catalyst [66]. Besides, the heterogeneous nature of this catalyst makes it easy to separate by simple filtration. After the reduction of N-acetyl piperidine to N-ethyl piperidine, they filtered the catalyst and directly submitted the residue to another hydrogenation under the same reaction conditions. With this procedure, they obtained 80 % conversion from the second run and 70 % from the third run. Other recycling techniques, such as drying and recalcination, preforming the catalyst, or the addition of new substrate after the

reaction, did not improve the results, which implies the unstable nature of this catalyst.

The Rh-MoOx/SiO$_2$+CeO$_2$ catalysts developed by Tomishige et al. showed the best catalytic performance towards CyCONH$_2$ hydrogenation among analogous catalysts with various other metal oxides. The obtained highest yield of CyCH$_2$NH$_2$ was 63 %. Meanwhile, the calcination temperature of added CeO$_2$ was found to cause different catalytic activity [76]. Moreover, the reusability of this catalysts has been reported, and good stability in the structure has been observed by XRD and EXAFS analyses. However, the deposition of organic material on the catalyst in this system clearly limits the long-term use. The development of effective regeneration method without aggregation of active metal particles is a target of further study. The following year, Kon and co-workers synthesized Pt-Nb$_2$O$_5$ catalyst, which convert N-acetylpiperidine completely with 99 % selectivity to the corresponding amine. Based on in-situ IR studies, the authors proposed that the C=O group of amide coordinated to the surface Lewis acid sites, weakening the C=O bond and that the activated amide underwent hydrogen transfer from H species on Pt sites [67]. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis of the filtrate after reaction confirmed that the contents of Pt and Nb in the solution were below the detection limit, indicating the reusability of Pt-Nb$_2$O$_5$.

In 2017, Kaneda and co-workers published a Pt-V/hydroxyapatite (HAP) catalyst, which enabled the mild hydrogenation of amides under 1 bar H$_2$ at 70 $^\circ$C or 5 bar H$_2$ at room temperature [68], providing important design guidelines for the development of advanced catalysts for this process under mild reaction conditions. The mild reaction conditions not only facilitate the highly selective hydrogenation of various amides into their corresponding amines, but also effectively inhibit the unwanted hydrogenation of aromatic rings (arene hydrogenation). Elemental mapping of Pt-V/HAP revealed that V (shown in green in Fig. 14d) and Pt (shown in red in Fig. 14e) were highly dispersed on HAP, and importantly, that V surrounded Pt. Moreover, X-ray absorption near-edge structure studies (Fig.15) further revealed that the V^{5+} species were reduced in situ to V^{3+} by adjacent metallic Pt species with H$_2$.
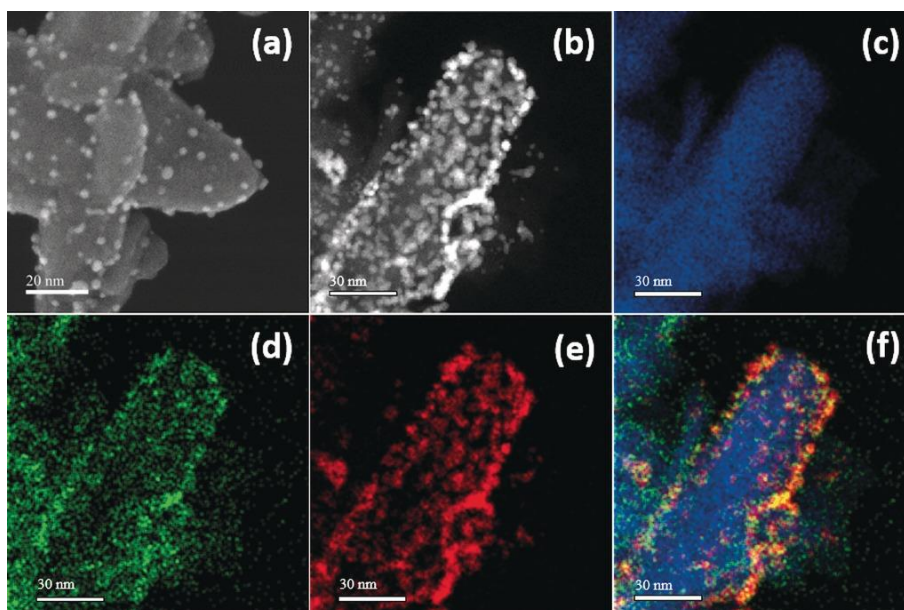
Figure 14. (a) Secondary-electron image of Pt-V/HAP treated with H_2. (b) ADF-STEM image of Pt-V/HAP treated with H_2. Elemental mapping images of (c) Ca, (d) V, and (e) Pt. (f) Composite overlay image formed from (c), (d), and (e). Reproduced from Ref. [68] with permission from Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

The HAP support, can further contribute to the catalytic performance due to both its chemical and thermal stability. Based on these characterization data and DFT calculations, the authors proposed that the origin of the catalytic activity for the bimetallic catalyst was the oxophilic V-decorated Pt nanoparticles, which were 2 nm in diameter. V in Pt-V/HAP was initially present as V^{5+}, but it was reduced by Pt to V^{3+} under H_2, V^{3+} sites are apparently highly suited to activate the amide C=O bonds that undergo hydrogenation due to the hydrogen spillover produced by Pt species. In this way, both V^{3+} and Pt cooperate to the success of the amide hydrogenation. Fig. 15 presents some of the XANES data that were used to characterize the oxidation states of the V and Pt present on HAP. Besides, the Pt-V/HAP catalyst was found to be reusable without any loss of its high activity even after the 10th recycling run. ICP-AES showed the absence of Pt and V species in the filtrate, thus indicating that no metal leaching occurred during the reaction.
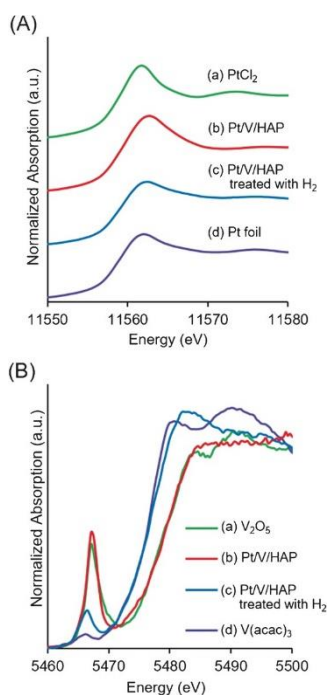
Figure 15. (A) Pt L3-edge XANES spectra of (a) PtCl$_2$, (b) Pt-V/HAP, (c) Pt-V/HAP treated with H$_2$, and (d) Pt foil. (B) V K-edge XANES spectra of (a) V$_2$O$_5$, (b) Pt-V/HAP, (c) Pt-V/HAP treated with H$_2$, and (d) V(acac)$_3$. Reproduced from Ref. [68] with permission from Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

In the same year, Shimizu et al. reported the Re-loaded TiO$_2$ catalysts for the hydrogenation of various secondary or tertiary amides. The Re/TiO$_2$ not only exhibits a wide substrate scope, but also owns stable structure characteristics that high product yield was obtained over the consecutive runs [69]. In 2018, a reusable Ir-Mo/KIT-6 (KIT-6 being one kind of mesoporous silica) catalyst reported by Gao and co-workers was able to hydrogenate N-acetylmorpholine to N-ethylmorpholine with good selectivity [70]. This kind of catalyst with a three-dimensional ordered mesoporous structure was synthesized via a one-pot co-assembly method, as shown in Fig.16. On the catalyst surface, Mo-incorporated KIT-6 (Mo-KIT-6) establishes electronic interactions increasing the proportion of metallic Ir^0 species, disfavoring the easy surface oxidation of ultrafine metal nanoparticles on silica mesoporous-cavities. Subsequently, combined effective H$_2$ activation and hydrogenation ability of metallic Ir^0 sites, determines an outstanding hydrogenation capability of for this catalyst. Recycleing experiments showed that the optimal Ir/3.0Mo-KIT-6 afforded consistent activity and selectivity at a high level in five successive cycles, demonstrating its

satisfactory durability. It should be noted that the slight decrease in conversion can be ascribed to the inevitable loss of catalysts during the recovery by centrifugation.
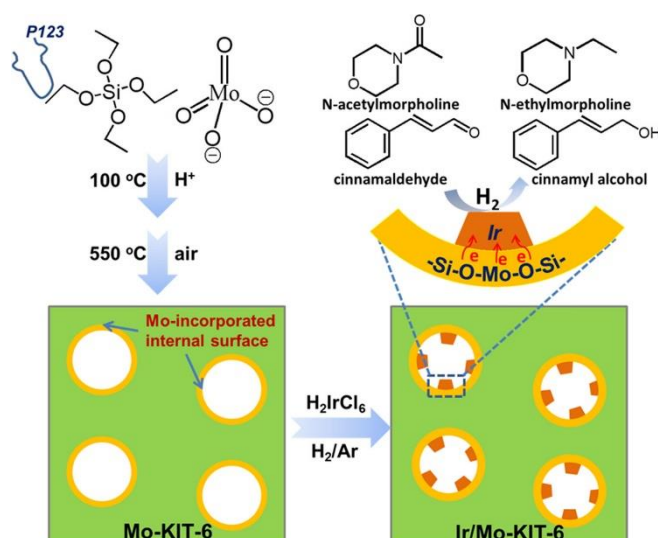

Figure 16. Illustration for the preparation of Mo-KIT-6 and Ir/Mo-KIT-6, indicating the importance of metal-support interactions to boost catalytic hydrogenation. Reproduced from Ref. [70] with permission from American Chemical Society.

The Ag/γ-Al$_2$O$_3$ catalysts reported by Milstein et al. exhibited higher selectivity towards C-N vs. C-O cleavage [81]. One year later, Andrés group reported that Pd-doped In$_2$O$_3$ catalyst prepared by a hydrothermal-assisted microwave heating method followed by calcination exhibited high selectivity towards C-N bond cleavage, reaching high yield of both alcohol and amine partners [82]. It is worth noting that using the Ag/γ-Al$_2$O$_3$ or Pd-doped In$_2$O$_3$ catalysts, amines were not formed through the direct hydrogenation of the carbonyl group. Instead, these catalysts promote the direct cleavage of C-N bonds, leading to the production of shorter chain amines. This product outcome is unique and it highlights the occurrence of specific reaction pathways and mechanisms on these catalysts. The ability to selectively cleave C-N bonds offers alternative possibilities for the synthesis of lower amines (and the corresponding alcohol) from amides and represents a significant advancement in the field of hydrogenation catalysis. In the same year, Terada et al. demonstrated a green and highly efficient heterogeneous catalyst, namely, unsupported nanoporous gold (AuNPore), which was proved to be highly efficient for the reduction of amides to amines. Notably,

this catalytic system utilized hydrosilanes as reductants rather than molecular H_2, which ~~that~~ can be useful in some specific synthesis [95]. Later, Kadyrov and colleagues developed the Pt/C catalysts for the hydrogenation of tertiary amides to produce amines. The conversion is a two-step process, in which amides were initially converted into amide acetals and imido esters through O-alkylation, and then subsequently hydrogenated into amines without isolation of these reaction intermediates [83].

As ~~already~~ mentioned, the $RuWOx/MgAl_2O_4$ catalyst reported by De Vos group became the pioneering example for the hydrogenation of aliphatic acyclic primary amides [62]. In their model reaction using hexanamide as substrate, an impressive yield of hexylamine up to 83 % could be achieved. Beside the NH_3 partial pressure, the effect of the catalyst support, Platinum Group Metal-Lewis acid ratio, H_2 pressure, temperature, solvent tolerance and product stability were also investigated. Both high conversion and amine yield demonstrated the effectiveness of the $RuWOx/MgAl_2O_4$ catalyzing the hydrogenation of aliphatic acyclic primary amides. Additionally, the $RuWOx/MgAl_2O_4$ showed remarkable stability, which could be confirmed by ICP that both Ru and W content in the mixture after reaction were below the detection limits (1 ppb), which represented a leaching below 0.005 % and 0.02 % respectively. Besides, the recorded XRD patterns do not show any Ru peaks and essentially remain the same of the used catalysts, once again illustrating the high stability of the catalyst, making it highly suitable for the hydrogenation of a broad range of amides.

Then, two years later, Pennetier et al. reported the selective transformation of tertiary N,N-dimethyldodecanamide and secondary azepan-2-one to the corresponding amines using V-modified Rh catalyst supported on γ-Al_2O_3 [84]. The structure-activity relationship established that the strong synergistic interaction between Rh and V, and proximity of hydrogenation Rh^0 sites and oxophilic $V^{\delta+}$ sites in the bimetallic Rh-V/Al_2O_3 catalyst, are beneficial for the selective dissociation of C=O bond of the carboxamides into the wanted amines. The close proximity of the active sites in the catalyst facilitated an efficient transfer of reactants, intermediates and active hydrogen, enhancing the overall catalytic performance. The specific interaction between the Rh

and V species in the catalyst structure played a vital role in promoting the desired C=O bond cleavage and minimizing undesirable side reactions. Besides, they also modified industrial hydrogenation catalysts such as Pd/Al_2O_3 by impregnation with Mo species as oxophilic centers to convert amides. Understanding the intricate interplay between catalyst structure and activity provides valuable insights for the design and optimization of bimetallic catalysts for selective amide hydrogenation reactions. The catalyst was reused for at least four cycles without any apparent loss of amide conversion and amine yield. Characterizations, such as XRD, TGA Analysis of used catalysts after recycle tests further proved the stability of this catalyst.

In 2022, a significant number of works have been published that specially focused on the hydrogenation of amides, which indicates that this research field is attracting more attention in the context of biomass valorization and polyamide recycling. Darcel and co-workers developed a kind of tandem Fe/Zn or Fe/In catalyst for the selective synthesis of amines by reducing primary amides under visible light assisted hydrosilylation [96]. Liu et al. achieved the hydrogenation of N-methylpyrrolidone to N-methylpyrrolidine using bimetallic Pt-V/HAP catalysts under advantageous and easily scalable solvent-free continuous flow condition [71].Based on ~~For~~ the investigation of its stability, the catalyst initially showed an excellent catalytic activity and the product yield could reach 89.9 %. With time increasing, the catalyst maintained an excellent catalytic performance during the investigation and the catalyst was only slightly deactivated, with the yield still at 85.2 % at 100 h. The same metals (Pt and V) loaded on CeO_2 has also been reported as efficient catalyst for the hydrogenation amide and could maintain its performance for at least three cycles. [72] In this case, the type of CeO_2 plays a vital role on the catalytic performance, particularly regarding particle morphology. This study also showed that oxygen vacancies on the CeO_2 surface oxidize both Pt and V, poisoning the hydrogenation reaction. In contrast, the absence of oxygen vacancies was found to promote the hydrogenating ability of Pt sites and also improved the ability to participate in the H_2 spillover mechanism and in situ formation of oxophilic V^{3+}.

Also in 2022, Wang group published three papers focused on amide hydrogenation. Firstly, Ru/Nb_2O_5 catalyst was demonstrated to be highly efficient and stable for the selective hydrogenation of propionamide to propylamine, that could be a promising approach for the selective propylamine synthesis [85]. Characterization techniques revealed that Nb_2O_5 can effectively activate the amide C=O group. Moreover, small size Ru particles are very efficient hydrogenation sites. These findings highlight the synergistic effects between Nb_2O_5 and Ru, resulting in an improved overall catalytic performance for the selective amide hydrogenation. Meanwhile, neutralizing the surface acidity of Nb_2O_5 greatly inhibits the side reactions, thereby leading to the enhanced selectivity towards amine. The recycleing experiment results clearly showed that no significant decrease in activity or selectivity was observed during the initial three successive runs, and only a small decline of the catalytic performance was shown in the 4th runs, which should be attributed to the loss of the catalyst during the recovery processes. Similarly, there is are no obvious difference of the fresh and used catalysts according to the XRD patterns. The above results clearly demonstrated the good stability of this Ru/Nb_2O_5 catalytic system for amide hydrogenation. Soon after, Ru-Mo/TiO_2 catalyst was also found to be highly efficient towards the chemoselective reduction of $CyCONH_2$ and it could be reused for eight catalytic cycles without significant loss of reactivity and selectivity of this reaction. [78] In-depth characterization of the catalyst revealed that Ru promotes the reduction of Mo^{6+} to Mo^{5+} and Mo^0, and the resultant low-coordinated Mo^{5+} was responsible for the selective activation of the amide C=O bond, while RuMo alloy promotes the activation of H_2. Additionally, a Ru-W/SiO_2 catalyst was also synthesized, observing a high activity, of 93.6 % in $CyCONH_2$ conversion with 83.7 % selectivity to the corresponding primary $CyCH_2NH_2$ amine [77]. Furthermore, its activity and selectivity remained essentially unchanged after five reaction tests, which was superior to the those reported homogeneous systems. The performance of a series of Ru-W/SiO_2 catalysts with different Ru/Mo atomic ratio critically depended on the synergistic interaction between W and Ru. As depicted in Fig. 17, the domain size of WOx greatly affected the Ru

dispersion. The monometallic Ru/SiO$_2$ catalyst without WOx species showed dispersed Ru NPs with an average size of 1.97 nm. However, the 2Ru1W/SiO$_2$ catalyst gave rise to more uniform and smaller Ru NPs with an average size of 1.68 nm, demonstrating that the presence of WOx species further promotes the dispersion of Ru due to Ru-W bimetallic interactions. Nevertheless, an excessive amount of WOx resulted in the aggregation of Ru NPs, as evidenced by the presence of bigger NPs on the 2Ru3W/SiO$_2$ catalyst. In summary, the sample with the best performance ~~was the one with~~ had a W/Ru atomic ratio of 0.27, with ~~having~~ the smallest Ru-Mo nanoparticles.
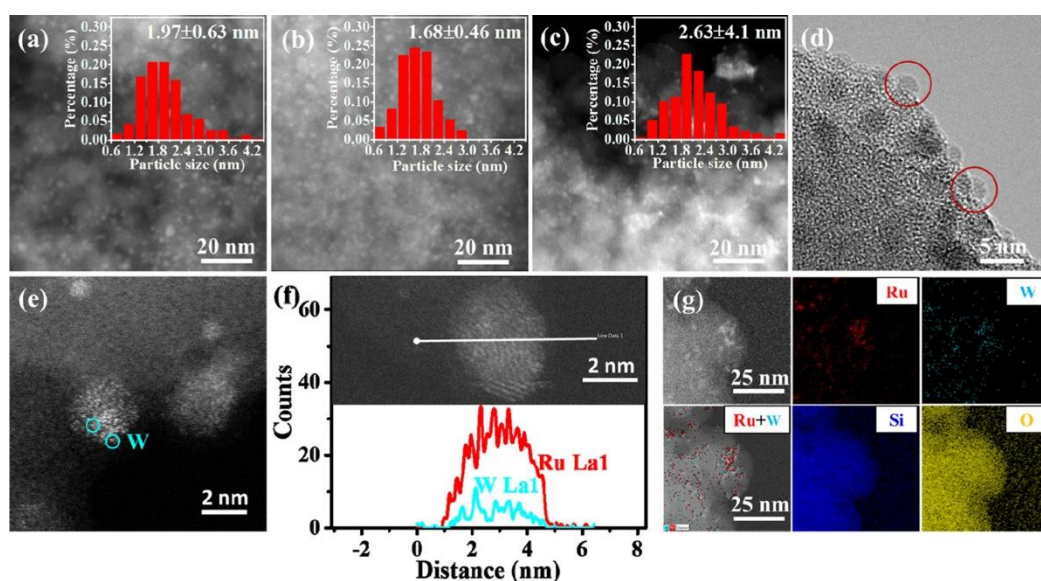

Figure 17. (a-c) HAADF-STEM images and histograms of particle size distributions (insets) of 2Ru/SiO$_2$ (a), 2Ru1W/SiO$_2$ (b), and 2Ru3W/SiO$_2$(c). (d) HRTEM and (e) AC-HAADF-STEM images of 2Ru1W/SiO$_2$ and (f) line-scanning and (g) elemental mapping images of the 2Ru1W/SiO$_2$ catalyst. Reproduced from Ref. [77] with permission from American Chemical Society.

The activity of bifunctional catalysts was found to be significantly influenced by the presence of oxophilic elements. Consequently, the research conducted by the same group also explored catalysts modified by oxophilic elements. In this way, Zhang and co-workers replaced the metal W in Ru-W/SiO$_2$ with Mo to explore the catalytic activity of Ru-Mo/SiO$_2$ for amide hydrogenation [79]. It was found that turnover frequency of Ru-Mo/SiO$_2$ was much higher than that of Ru-W/SiO$_2$, providing further confirmation of the crucial role played by oxophilic elements in the catalytic process. The activity results additionally demonstrated a volcano-shaped relationship between the Mo content and the yield of the target amine. The highest yield was achieved at a

Mo content of 0.2 wt%, corresponding to a Mo/Ru atomic ratio of 0.11. The best-performing catalyst, 2Ru0.2Mo/SiO$_2$ contains Ru NPs of 2 nm decorated with monoatomic Mo^{5+} species, which contrasted with the polymeric MoO$_2$-like species partially covering the Ru surface for the 2Ru3Mo/SiO$_2$ (Figs. 18-19). Recycleing experiment results showed consecutive stable catalytic performance that the catalyst could be reused for at least 6 times without obvious decline in either activity and selectivity. Besides, the HAADF-STEM imaging of the used catalyst revealed that the average size of Ru NPs slightly increased from 1.60 nm to 1.82 nm after 6 recycling tests, and no obvious metal leaching was found. All these results indicated that the Ru-W/SiO$_2$ catalyst structure was stable during the reaction

To summarize, the research on catalysts for amide hydrogenation has predominantly focused on bimetallic catalysts with strong interaction and close spatial proximity. Noticeably, almost all these catalysts contain noble or semiprecious metals. Even though some different catalytic systems (such as Fe-Zn) have been proposed, follow-up reports on these catalytic systems based on abundant elements are rare, possibly due to their limited scopes and/or the instability of their catalyst activity.
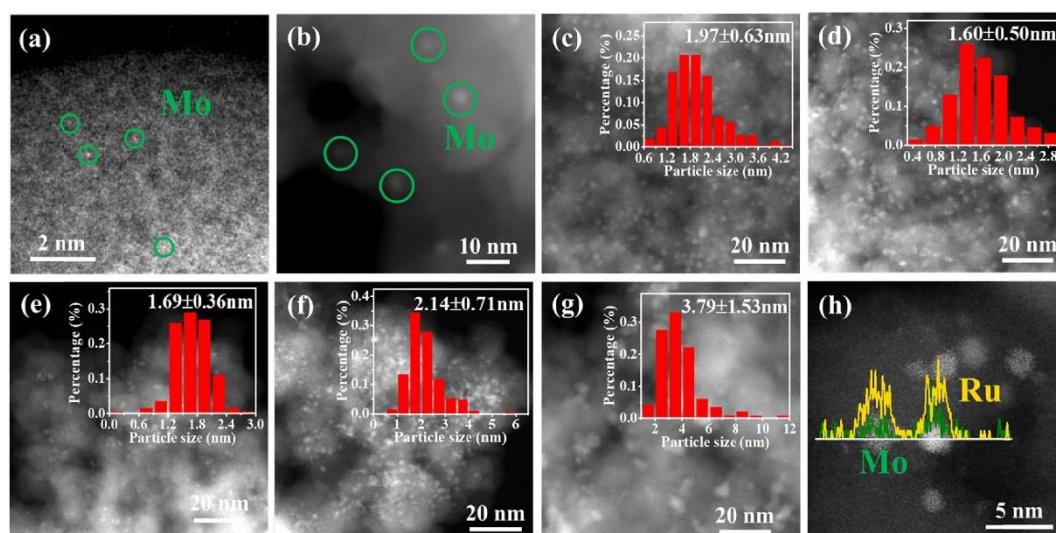
Figure 18. AC-HAADF-STEM images of 0.2Mo/SiO$_2$ (a), 3Mo/SiO$_2$ (b), 2Ru/SiO$_2$ (c), 2Ru0.2Mo/SiO$_2$ (d), 2Ru1Mo/SiO$_2$ (e), 2Ru3Mo/SiO$_2$ (f) and 0.2Mo2Ru/SiO$_2$ (g). The insets are histograms of particle size distributions. (h) Elemental line scanning image of 2Ru0.2Mo/SiO$_2$. Reproduced from Ref. [79] with permission from Elsevier.
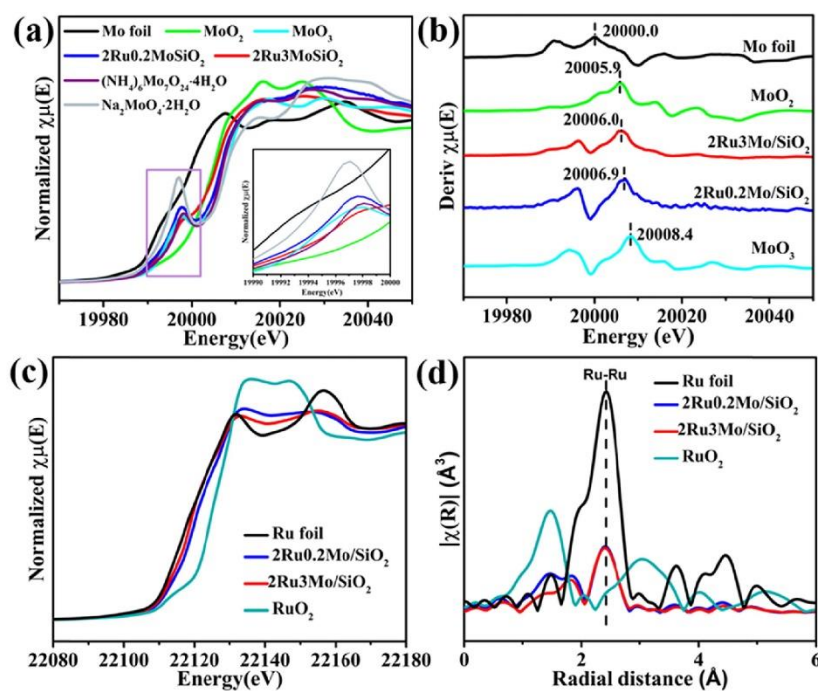
Figure 19. (a) The normalized XANES spectra at Mo K edge of 2RuxMo/SiO$_2$ samples compared to reference Mo compounds; (b) First-order derivative of the XANES spectra at Mo K edge; (c) the normalized XANES spectra at Ru K edge of two 2RuxMo/SiO$_2$ samples compared to two relevant Ru compounds; (d) the k2-weighted Fourier transform EXAFS spectra at Ru K edge in r-space of the 2RuxMo/SiO$_2$ samples and their references. Reproduced from Ref. [79] with permission from Elsevier.

The bifunctional concept proposed in the 1996s has undoubtedly served as the primary guideline for amide hydrogenation in recent years. This concept has spurred extensive research into various types of bifunctional catalysts, with a focus on uncovering their intrinsic properties using advanced characterization techniques and theoretical calculations. Among these catalysts, the one with smaller metal particle sizes and even distribution have demonstrated superior catalytic performance. Moreover, the catalytic performance of bifunctional catalysts is largely governed by the synergistic effects and complementary roles between the two metals and the surface interfaces they create. Designing catalysts with enhanced interaction and larger interfaces between the two metals is crucial to develop more efficient amide hydrogenation catalysts. By maximizing these aspects, the catalytic activity and efficiency should be significantly improved. However, at present, the catalysts are still far from optimal. Developing new types of catalysts for amide hydrogenation that can operate under milder and greener

condition is also particularly desirable. Most of the present catalytic systems still require high H_2 pressure (20-50 bar). Indeed, the use of noble metals in the current state of the art of catalysts for amide hydrogenation absolutely increases the production cost. Therefore, there is still a strong incentive towards developing catalysts that utilize earth abundant metals instead of noble metals. The aim is to find alternative metal catalysts that offer comparable or even superior performance, while diminishing the dependence on critical metals.

Recently, inspired by the superior hydrogenation ability of molybdenum nitrides [97-99], bimetallic NiMo nitride catalysts with Ni atoms embedded into the lattice of molybdenum nitrides were synthesized and employed this catalyst to convert amides. Compared to the traditional programmed temperature nitriding method, the newly hydrothermal synthesis method is easier to operate, environmentally more friendly, and avoids the use of NH_3. The Ni/Mo molar ratio has a significant impact on the structure and performance of the catalysts. Different crystal phases, such as Ni, Ni_2Mo_3N and $Ni_6Mo_6C_{1.06}$ were formed depending on the Ni/Mo molar ratio. [86] The catalyst with Ni/Mo=1:1.5 showed the optimal catalytic performance towards the hexanamide conversion, which is ascribed to the synergistic hydrogenation effect between Ni_2Mo_3N and $Ni_6Mo_6C_{1.06}$. Moreover, the strong interaction between Ni and Mo over this catalyst, and even the cuboid shape with smooth surface also contribute to the outstanding hydrogenation performance. The NiMo bimetallic nitrides catalyst has also been proved to be robust that the catalytic activity is stable without obvious changes in the first 4 runs, whereas the yield of hexylamine decreases slightly in 5th cycle. The characterization results of used catalysts after life-time tests showed that the crystalline Ni_2Mo_3N phase are still presented on the used catalyst without obvious changes in physiochemical properties, demonstrating its stability. Meanwhile, it is found that the used catalysts remain the even cuboid shape with smooth surface, revealed by the SEM and EDX-Mapping. All the results identified the stability of this NiMo nitride catalyst.

From the evolution diagram of the state of the art (Fig. 11), it can be concluded that this field is attracting increasing attention and this interest is expected to continue

over the following years, since amide hydrogenation to amines is considered as a promising synthetic route meeting sustainability principle. New types of catalysts that do not contain noble metals start to step into researcher interests, which provides effective alternatives and could be served as one of the most promising research fields in the future. The increased focus on amide hydrogenation reflects the growing recognition of its importance in the synthesis of amines, which are valuable building blocks and synthetic intermediates in various specialty and biologically active chemicals, including pharmaceuticals, agrochemicals, and materials science. In addition, the importance of amide hydrogenation in polyamide recycling has been widely recognized and is expected to become closer to commercial implementation. Researchers are actively exploring new catalytic systems, and reaction conditions, as well as gaining theoretical and mechanistic insights to enhance the efficiency, selectivity, and sustainability of amide hydrogenation reactions.

5. Conclusions and future prospective

The hydrogenation of a wide range of amides into amines via heterogeneous catalysis using H_2 is one of the most promising routes to realize the upgrading of natural amides, related biomass feedstocks or for the recycling polyamides [29]. Considering the non-negligible importance of this research field, this comprehensive review has compiled essential information, covering most of reported works to date, aiming at providing the readership with an in-depth understanding and insights in the current catalyst design principles to achieve high amide hydrogenation ability towards amines. It has been shown that amide structure, including acyclic or substitution structure, is a key parameter to be considered when selecting catalyst and reaction conditions. Different types of amides with diverse structure features, such as cyclic amides, aliphatic acyclic tertiary, secondary and primary amides, own different electron density of carbonyl group, which results in the diverse difficulty for hydrogenation. The higher the electron density of the carbonyl group, the more difficult to conduct nucleophilic attack and break the C=O bond. Hence, the better of the hydrogenation performance of

the catalyst are required. Moreover, we have also reviewed the process related to amide hydrogenation, including the degradation of polyamides, and the reductive amination of carboxylic acids or triglycerides. The emphasis has been made in providing a comprehensive summary of the different types of catalysts that have been applied in amide hydrogenation, mostly organized in accordance with their chronological order that allows to follow the historic development of the field. It has been shown that significant progress has been achieved in the field of amide hydrogenation through the utilization of bimetallic catalysts with dual functionality. The current knowledge on the parameters that influence the catalytic performance and mechanisms occurring in amide hydrogenation have been highlighted. ~~The d~~Deep insights into catalyst structures have been gained thanks to the recent advance in characterization techniques, as well as by the use of computational calculations to understand the mechanistic pathways. In this way, the progress from the initial studies requiring harsh conditions and characterized by a general lack of selectivity, to the present state using milder conditions and more selective catalysts has been presented.

Despite the considerable progress made in amide hydrogenation, there are still several significant bottlenecks that need to be addressed for the practical application of this reaction. The presence of the noble metals in catalyst composition has discouraged industrial use due to the high cost-effectiveness. Furthermore, high H_2 pressure is also frequently needed, which not only complicates operational workup, but also creates hazard and safety issues that towards industrial applications. In the case of aliphatic acyclic primary amides, NH_3 is also needed to prevent the dimerization, which is not a green approach. Sometimes, these catalysts undergo deactivation or become poisoned during the reaction.

A major limitation of this field is that most supported catalysts are only efficient for the hydrogenation of cyclic amides, and they are not able to hydrogenate aliphatic acyclic amides, especially for the aliphatic acyclic primary amides. In other cases, supported metal nanoparticles catalyze the hydrogenation of aliphatic acyclic secondary and tertiary amides with very low selectivity. These comments clearly

indicate that the currently developed catalytic systems are still far from satisfactory and new advanced catalysts with wide substrate scope are highly wanted.

To address these challenges, it will be necessary to gain a better understanding of the detailed reaction mechanism and reaction intermediates. This knowledge will not only aid in the design of more active catalysts with atomically structured active sites but also should provide insights into the deactivation phenomena that occur during the amide hydrogenation. By unraveling the intricacies of the reaction mechanism and identifying key intermediates, researchers can develop strategies to mitigate catalyst deactivation and enhance catalyst stability, leading to more efficient and sustainable amide hydrogenation processes. Based on this deeper knowledge, it might be possible to overcome some of the above commented limitations for amide hydrogenation especially those derived from C-N cleavage resulting in the appearance of byproducts. Herein, some practical approaches and prospectives are proposed. Firstly, designing catalysts with earth abundant metals is priority. The developed Fe-Zn catalyst has opened a door into this possibility. Meanwhile, the synthesized catalysts should be not only effective for a certain class of amides but also should have a broader substrate scope. Moreover, designing new reactors to separate the amines timely to avoiding their dimerization and to avoid the use of NH_3 will totally make the production process more environmentally friendly and efficient. A catalyst with a wide range of substrate compatibility should allow for greater versatility and applicability in amide hydrogenation reactions. Furthermore, a dedicated focus on the development of more advanced in situ characterization techniques will provide valuable insights into the interactions occurring among the various interfaces and structuration of the active sites on the catalyst and between the catalyst surface and the amide molecules. *Operando* techniques should enable researchers to observe and analyze the catalyst sites under conditions closer to those employed in the reaction, offering a deeper understanding of the catalytic mechanism and the rate determining step. By gaining a more comprehensive understanding at the molecular level, further catalyst optimization for amide hydrogenation can possibly be achieved. Another prospective is extending the

model amides to nitrogen-containing real biomass mixtures to obtain bio-derived amines [100, 101]. Recently, the sustainable production of nitrogen-containing compounds from renewable biomass derivatives such as *chitin*, *microalgae* and *lignin* etc. has attracted much attention with particular interest on the reductive amination of bio-based platform molecules [101-103], which could eventually lead to the amine production from biomass, offering a sustainable and environmentally friendly alternative to conventional amine synthesis.

Overall, the hydrogenation of amides to amines via heterogeneous catalysis offers an alternative to replace traditional organic synthesis methods. The development of highly efficient and selective catalysts for this process is crucial for large-scale implementation of the process. Further research is necessary to develop catalysts which can be universally applied regardless of the amide type and without considering specific tailoring of the catalyst. By focusing on the previously commented points, it should be possible to develop advanced catalytic systems that can contribute to the widespread adoption of amide hydrogenation as a general method for amine production. Proper investments in these improvements can lay the foundation for a more sustainable and environmentally benign future society.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] V. Froidevaux, C. Negrell, S. Caillol, J.P. Pascault, B. Boutevin, Biobased Amines: From Synthesis to Polymers; Present and Future, Chem Rev, 116 (2016) 14181-14224.

[2] Q. Lu, J. Liu, L. Ma, Recent advances in selective catalytic hydrogenation of nitriles to primary amines, Journal of Catalysis, 404 (2021) 475-492.

[3] J.R. Cabrero-Antonino, R. Adam, V. Papa, M. Beller, Homogeneous and heterogeneous catalytic reduction of amides and related compounds using molecular hydrogen, Nat Commun, 11 (2020) 3893.

[4] F. Chen, E. Zhao, T. Kim, J. Wang, G. Hableel, P.J.T. Reardon, S.J. Ananthakrishna, T. Wang, S. Arconada-Alvarez, J.C. Knowles, J.V. Jokerst, Organosilica Nanoparticles with an Intrinsic Secondary Amine: An Efficient and Reusable Adsorbent for Dyes, ACS Appl. Mater. Interfaces, 9 (2017) 15566-15576.

[5] L.-M. Wang, K. Jenkinson, A.E.H. Wheatley, K. Kuwata, S. Saito, H. Naka, Photocatalytic N-Methylation of Amines over Pd/TiO$_2$ for the Functionalization of Heterocycles and Pharmaceutical Intermediates, ACS Sustainable Chemistry & Engineering, 6 (2018) 15419-15424.

[6] L. Jia, X. Tu, K. He, C. Wang, S. Yin, Y. Zhou, W. Chen, Monascorubrin and rubropunctatin: Preparation and reaction characteristics with amines, Dyes Pigm., 170 (2019) 107629-107634.

[7] A. Primo, F. Quignard, Chitosan as efficient porous support for dispersion of highly active gold nanoparticles: design of hybrid catalyst for carbon-carbon bond formation, Chem Commun (Camb), 46 (2010) 5593-5595.

[8] X. Chen, S. Song, H. Li, G. Gozaydin, N. Yan, Expanding the Boundary of Biorefinery: Organonitrogen Chemicals from Biomass, Acc. Chem. Res., 54 (2021) 1711-1722.

[9] P. Scharringer, T. Muller, J. Lercher, Investigations into the mechanism of the liquid-phase hydrogenation of nitriles over Raney-Co catalysts, Journal of Catalysis, 253 (2008) 167-179.

[10] Haydar Göksua, Hakan Sertb, Benan Kilbas, F. Sen, Recent Advances in the Reduction of Nitro Compounds by Heterogenous Catalysts, Curr. Org. Chem., 21 (2017) 794-820.

[11] Z. Shen, L. Hong, B. Zheng, G. Wang, B. Zhang, Z. Wang, F. Zhan, S. Shen, R. Yun, Highly Efficient and Chemoselective Hydrogenation of Nitro Compounds into Amines by Nitrogen-Doped Porous Carbon-Supported Co/Ni Bimetallic Nanoparticles, Inorg. Chem., 60 (2021) 16834-16839.

[12] J. Gallardo-Donaire, M. Hermsen, J. Wysocki, M. Ernst, F. Rominger, O. Trapp, A.S.K. Hashmi, A. Schafer, P. Comba, T. Schaub, Direct Asymmetric Ruthenium-Catalyzed Reductive Amination of Alkyl-Aryl Ketones with Ammonia and Hydrogen, J Am Chem Soc, 140 (2018) 355-361.

[13] X. Tan, S. Gao, W. Zeng, S. Xin, Q. Yin, X. Zhang, Asymmetric Synthesis of Chiral Primary Amines by Ruthenium-Catalyzed Direct Reductive Amination of Alkyl Aryl Ketones with Ammonium Salts and Molecular H(2), J Am Chem Soc, 140 (2018) 2024-2027.

[14] G. Liang, A. Wang, L. Li, G. Xu, N. Yan, T. Zhang, Production of Primary Amines by Reductive Amination of Biomass-Derived Aldehydes/Ketones, Angew Chem Int Ed Engl, 56 (2017) 3050-3054.

[15] H. Qi, F. Liu, L. Zhang, L. Li, Y. Su, J. Yang, R. Hao, A. Wang, T. Zhang, Modulating trans-imination and hydrogenation towards the highly selective production of primary diamines from dialdehydes, Green Chemistry, 22 (2020) 6897-6901.

[16] H. Qi, J. Yang, F. Liu, L. Zhang, J. Yang, X. Liu, L. Li, Y. Su, Y. Liu, R. Hao, A. Wang, T. Zhang, Highly selective and robust single-atom catalyst Ru(1)/NC for reductive amination of aldehydes/ketones, Nat Commun, 12 (2021) 3295.

[17] J. Zhang, J. Yin, X. Duan, C. Zhang, J. Zhang, Continuous reductive amination to synthesize primary amines with high selectivity in flow, Journal of Catalysis, 420 (2023) 89-98.

[18] F. Niu, S. Xie, M. Bahri, O. Ersen, Z. Yan, B.T. Kusema, M. Pera-Titus, A.Y. Khodakov, V.V. Ordomsky, Catalyst Deactivation for Enhancement of Selectivity in Alcohols Amination to Primary Amines, ACS Catalysis, 9 (2019) 5986-5997.

[19] X.-P. Fu, P. Han, Y.-Z. Wang, S. Wang, N. Yan, Insight into the roles of ammonia during direct alcohol amination over supported Ru catalysts, Journal of Catalysis, 399 (2021) 121-131.

[20] H. Huang, Y. Wei, Y. Cheng, S. Xiao, M. Chen, Z. Wei, The Acquisition of Primary Amines from Alcohols through Reductive Amination over Heterogeneous Catalysts, Catalysts, 13 (2023) 1350-1374.

[21] M. Pelckmans, T. Renders, S. Van de Vyver, B.F. Sels, Bio-based amines through sustainable heterogeneous catalysis, Green Chemistry, 19 (2017) 5303-5331.

[22] K. Das, R. Shibuya, Y. Nakahara, N. Germain, T. Ohshima, K. Mashima, Platinum-Catalyzed Direct Amination of Allylic Alcohols with Aqueous Ammonia: Selective Synthesis of Primary Allylamines, Angewandte Chemie International Edition, 51 (2011) 150-154.

[23] P.R. Likhar, R. Arundhathi, M.L. Kantam, P.S. Prathima, Amination of Alcohols Catalyzed by Copper-Aluminium Hydrotalcite: A Green Synthesis of Amines, Eur. J. Org. Chem., (2009) 5383-5389.

[24] R.M. de Figueiredo, J.S. Suppo, J.M. Campagne, Nonclassical Routes for Amide Bond Formation, Chem Rev, 116 (2016) 12029-12122.

[25] L. Hie, N.F. Fine Nathel, T.K. Shah, E.L. Baker, X. Hong, Y.F. Yang, P. Liu, K.N. Houk, N.K. Garg, Conversion of amides to esters by the nickel-catalysed activation of amide C-N bonds, Nature, 524 (2015) 79-83.

[26] L. Liu, Y. Zhou, L. Guo, G. Li, C. Hu, Production of Nitrogen-Containing Compounds via the Conversion of Natural Microalgae from Water Blooms Catalyzed by ZrO_2, ChemSusChem, 14 (2021) 3935-3944.

[27] S. Chakrabortty, S. Zheng, F. Kallmeier, E. Barath, S. Tin, J.G. de Vries, Ru-Catalyzed Direct Asymmetric Reductive Amination of Bio-Based Levulinic Acid and Ester for the Synthesis of Chiral Pyrrolidinone, ChemSusChem, 16 (2023) e202202353.

[28] J. Li, C.Y. Huang, C.J. Li, Deoxygenative Functionalizations of Aldehydes, Ketones and Carboxylic Acids, Angew Chem Int Ed Engl, 61 (2022) e202112770.

[29] A.M. Smith, R. Whyman, Review of methods for the catalytic hydrogenation of carboxamides, Chem Rev, 114 (2014) 5477-5510.

[30] A. J. McAlees, R. McCrindle, Catalytic Hydrogenations of Cyclic Imides and Anhydrides J. Chem. SOC. (C), (1969) 2425-2435.

[31] X. Liu, T. Werner, Indirect reduction of CO_2 and recycling of polymers by manganese-catalyzed transfer hydrogenation of amides, carbamates, urea derivatives, and polyurethanes, Chem Sci, 12 (2021) 10590-10597.

[32] H. Wang, H. Zhou, Q. Yan, X. Wu, H. Zhang, Superparamagnetic nanospheres with efficient bifunctional acidic sites enable sustainable production of biodiesel from budget non-edible oils, Energy Conversion and Management, 297 (2023).

[33] A.H. Abu-Ghazala, H.H. Abdelhady, A.A. Mazhar, M.S. El-Deab, Exceptional room temperature catalytic transesterification of waste cooking oil to biodiesel using environmentally-benign $K_2CO_3/\gamma-Al_2O_3$ nano-catalyst, Chemical Engineering Journal, 474 (2023).

[34] H. Yang, X. Du, X. Lei, K. Zhou, Y. Tian, D. Li, C. Hu, Unraveling enhanced activity and coke resistance of Pt-based catalyst in bio-aviation fuel refining, Appl. Energy, 301 (2021) 117469-117479.

[35] H. Yang, X. Du, L. Zhou, D. Li, C. Hu, Enhanced deoxygenation performance and coke resistance of Ni-based catalysts for jatropha oil conversion by rare earth elements, Fuel, 334 (2023) 126779-126792.

[36] J. Wu, C. Darcel, Recent Developments in Manganese, Iron and Cobalt Homogeneous Catalyzed Synthesis of Primary Amines via Reduction of Nitroarenes, Nitriles and Carboxamides, Advanced Synthesis & Catalysis, 365 (2023) 948-964.

[37] A.K. Ravn, N.M. Rezayee, The Investigation of a Switchable Iridium Catalyst for the Hydrogenation of Amides: A Case Study of C–O Versus C–N Bond Scission, ACS Catalysis, 12 (2022) 11927-11933.

[38] Y. Pan, Z. Luo, X. Xu, H. Zhao, J. Han, L. Xu, Q. Fan, J. Xiao, Ru-Catalyzed Deoxygenative Transfer Hydrogenation of Amides to Amines with Formic Acid/Triethylamine, Advanced Synthesis & Catalysis, 361 (2019) 3800-3806.

[39] L. Gausas, R. Jackstell, T. Skrydstrup, M. Beller, Toward a Practical Catalyst for Convenient Deaminative Hydrogenation of Amides under Mild Conditions, ACS Sustainable Chemistry & Engineering, 10 (2022) 16046-16054.

[40] S. Das, H. Karmakar, J. Bhattacharjee, T.K. Panda, Aluminium complex as an efficient catalyst for the chemo-selective reduction of amides to amines, Dalton Trans., 48 (2019) 11978-11984.

[41] S. Das, B. Wendt, K. Moller, K. Junge, M. Beller, Two iron catalysts are better than one: a general and convenient reduction of aromatic and aliphatic primary amides, Angew Chem Int Ed Engl, 51 (2012) 1662-1666.

[42] V. Papa, J.R. Cabrero-Antonino, A. Spannenberg, K. Junge, M. Beller, Homogeneous cobalt-catalyzed deoxygenative hydrogenation of amides to amines, Catalysis Science & Technology, 10 (2020) 6116-6128.

[43] B. Han, J. Zhang, H. Jiao, L. Wu, Zirconium-hydride-catalyzed site-selective hydroboration of amides for the synthesis of amines: Mechanism, scope, and application, Chinese Journal of Catalysis, 42 (2021) 2059-2067.

[44] L.J. Donnelly, J.C. Berthet, T. Cantat, Selective Reduction of Secondary Amides to Imines Catalysed by Schwartz's Reagent, Angew Chem Int Ed Engl, 61 (2022) e202206170.

[45] W. Yao, J. Wang, A. Zhong, S. Wang, Y. Shao, Transition-metal-free catalytic hydroboration reduction of amides to amines, Organic Chemistry Frontiers, 7 (2020) 3515-3520.

[46] Robert F. Nystrom, W.G. Brown, Reduction of Organic Compounds by Lithium Aluminum Hydride. I. Aldehydes, Ketones, Esters, Acid Chlorides and Acid Anhydrides, Journal of American Chemical Society, 69 (1947) 1197-1199.

[47] A. E. Finholt, A. C. Bond, J.R, I. Schlesinger, Lithium Aluminum Hydride, Aluminum Hydride and Lithium Gallium Hydride, and Some of their Applications in Organic and Inorganic Chemistry,

Journal of American Chemical Society, 69 (1947) 1199-1203.

[48] Lubov Pasumansky, Christian T. Goralski, B. Singaram, Lithium Aminoborohydrides: Powerful, Selective, Air-Stable Reducing Agents, Org. Process Res. Dev., 10 (2006) 959-970.

[49] C.W. Lee, H.M. Ko, Metal-Free Catalytic Reduction of Amides: Recent Progress, Asian Journal of Organic Chemistry, 12 (2023).

[50] J. Coetzee, D.L. Dodds, J. Klankermayer, S. Brosinski, W. Leitner, A.M. Slawin, D.J. Cole-Hamilton, Homogeneous catalytic hydrogenation of amides to amines, Chemistry, 19 (2013) 11039-11050.

[51] J.R. Cabrero-Antonino, E. Alberico, K. Junge, H. Junge, M. Beller, Towards a general ruthenium-catalyzed hydrogenation of secondary and tertiary amides to amines, Chem Sci, 7 (2016) 3432-3442.

[52] Y.Q. Zou, S. Chakraborty, A. Nerush, D. Oren, Y. Diskin-Posner, Y. Ben-David, D. Milstein, Highly Selective, Efficient Deoxygenative Hydrogenation of Amides Catalyzed by a Manganese Pincer Complex via Metal-Ligand Cooperation, ACS Catal, 8 (2018) 8014-8019.

[53] E. Balaraman, B. Gnanaprakasam, L.J.W. Shimon, D. Milstein, Direct Hydrogenation of Amides to Alcohols and Amines under Mild Conditions, The Journal of American Chemical Society, 132 (2010) 16756-16758.

[54] S. Kar, M. Rauch, A. Kumar, G. Leitus, Y. Ben-David, D. Milstein, Selective Room-Temperature Hydrogenation of Amides to Amines and Alcohols Catalyzed by a Ruthenium Pincer Complex and Mechanistic Insight, ACS Catal, 10 (2020) 5511-5515.

[55] J.A. Garg, S. Chakraborty, Y. Ben-David, D. Milstein, Unprecedented iron-catalyzed selective hydrogenation of activated amides to amines and alcohols, Chem Commun (Camb), 52 (2016) 5285-5288.

[56] N.M. Rezayee, D.C. Samblanet, M.S. Sanford, Iron-Catalyzed Hydrogenation of Amides to Alcohols and Amines, ACS Catalysis, 6 (2016) 6377-6383.

[57] J.M. John, S.H. Bergens, A highly active catalyst for the hydrogenation of amides to alcohols and amines, Angew Chem Int Ed Engl, 50 (2011) 10377-10380.

[58] D. Cantillo, Mechanistic Insights on the Ruthenium-Catalyzed Hydrogenation of Amides – C–N vs. C–O Cleavage, Eur. J. Inorg. Chem., 2011 (2011) 3008-3013.

[59] Z. Guo, F. Zhou, H. Wang, X. Liu, G. Xu, Y. Zhang, Y. Fu, Highly selective conversion of natural oil to alcohols or alkanes over a Pd stabilized CuZnAl catalyst under mild conditions, Green Chemistry, 21 (2019) 5046-5052.

[60] J. Wang, R. Nie, L. Xu, X. Lyu, X. Lu, Catalytic transfer hydrogenation of oleic acid to octadecanol over magnetic recoverable cobalt catalysts, Green Chemistry, 21 (2019) 314-320.

[61] Y. Zhou, X. Liu, P. Yu, C. Hu, Temperature-tuned selectivity to alkanes or alcohol from ethyl palmitate deoxygenation over zirconia-supported cobalt catalyst, Fuel, 278 (2020) 118295-118307.

[62] R. Coeck, S. Berden, D.E. De Vos, Sustainable hydrogenation of aliphatic acyclic primary amides to primary amines with recyclable heterogeneous ruthenium–tungsten catalysts, Green Chemistry, 21 (2019) 5326-5335.

[63] Alkins, Hygrogenation of amides to amines, Journal of American Chemical Society, (1934) 247.

[64] Chitaru Hirosawa, Noriko Wakasa, T. Fuchikami, Hydrogenation of Amides by the Use of Bimetallic Catalysts Consisting of Group 8 to 10, and Group 6 or 7 Metals, Tetrahedron Lett., 37 (1996) 6749-6752.

[65] R. Burch, C. Paun, X.M. Cao, P. Crawford, P. Goodrich, C. Hardacre, P. Hu, L. McLaughlin, J. Sá,

J.M. Thompson, Catalytic hydrogenation of tertiary amides at low temperatures and pressures using bimetallic Pt/Re-based catalysts, Journal of Catalysis, 283 (2011) 89-97.

[66] M. Stein, B. Breit, Catalytic hydrogenation of amides to amines under mild conditions, Angew Chem Int Ed Engl, 52 (2013) 2231-2234.

[67] K.-i. Shimizu , W. Onodera, A.S. Touchy, S.M.A.H. Siddiki, T. Toyao , K. Kon, Lewis Acid-Promoted Heterogeneous Platinum Catalysts for Hydrogenation of Amides to Amines, ChemistrySelect, 1 (2016) 736-740.

[68] T. Mitsudome, K. Miyagawa, Z. Maeno, T. Mizugaki, K. Jitsukawa, J. Yamasaki, Y. Kitagawa, K. Kaneda, Mild Hydrogenation of Amides to Amines over a Platinum-Vanadium Bimetallic Catalyst, Angew Chem Int Ed Engl, 56 (2017) 9381-9385.

[69] T. Toyao, S. Siddiki, Y. Morita, T. Kamachi, A.S. Touchy, W. Onodera, K. Kon, S. Furukawa, H. Ariga, K. Asakura, K. Yoshizawa, K.I. Shimizu, Rhenium-Loaded TiO$_2$: A Highly Versatile and Chemoselective Catalyst for the Hydrogenation of Carboxylic Acid Derivatives and the N-Methylation of Amines Using H$_2$ and CO$_2$, Chemistry – A European Journal, 23 (2017) 14848-14859.

[70] T. Chen, Z. Shi, G. Zhang, H.C. Chan, Y. Shu, Q. Gao, Y. Tang, Molybdenum-Incorporated Mesoporous Silica: Surface Engineering toward Enhanced Metal-Support Interactions and Efficient Hydrogenation, ACS Appl. Mater. Interfaces, 10 (2018) 42475-42483.

[71] P. Gao, S. Liu, J. Yang, D. Zhao, Q. Liu, Solvent-free continuous flow hydrogenation of N-methylpyrrolidone to N-methylpyrrolidine catalyzed by bimetallic Pt/V on HAP, Catalysis Science & Technology, 12 (2022) 4605-4612.

[72] M.D. Farahani, C. Moodley, A.S. Mahomed, H.B. Friedrich, Morphology, oxygen vacancies, and other factors affecting the performance of supported bimetallic ceria catalysts, iScience, 25 (2022) 105560.

[73] G. Beamson, A.J. Papworth, C. Philipps, A.M. Smith, R. Whyman, Selective Hydrogenation of Amides using Ruthenium/ Molybdenum Catalysts, Advanced Synthesis & Catalysis, 352 (2010) 869-883.

[74] G. Beamson, A.J. Papworth, C. Philipps, A.M. Smith, R. Whyman, Selective hydrogenation of amides using Rh/Mo catalysts, Journal of Catalysis, 269 (2010) 93-102.

[75] G. Beamson, A.J. Papworth, C. Philipps, A.M. Smith, R. Whyman, Selective hydrogenation of amides using bimetallic Ru/Re and Rh/Re catalysts, Journal of Catalysis, 278 (2011) 228-238.

[76] Y. Nakagawa, R. Tamura, M. Tamura, K. Tomishige, Combination of supported bimetallic rhodium-molybdenum catalyst and cerium oxide for hydrogenation of amide, Sci Technol Adv Mater, 16 (2015) 014901.

[77] Y. Zhang, L. Li, F. Liu, H. Qi, L. Zhang, W. Guan, Y. Liu, A. Wang, T. Zhang, Synergy between Ru and WOx Enables Efficient Hydrodeoxygenation of Primary Amides to Amines, ACS Catalysis, 12 (2022) 6302-6312.

[78] Y. Zhang, F. Zhang, L. Li, F. Liu, A. Wang, Highly Chemoselective Reduction of Amides to Amines over a Ruthenium-Molybdenum Bimetallic Catalyst, ChemistrySelect, 7 (2022).

[79] Y. Zhang, F. Zhang, L. Li, H. Qi, Z. Yu, X. Liu, C. Cao, F. Liu, A. Wang, T. Zhang, Decoration of Ru nanoparticles with mononuclear MoOx boosts the hydrodeoxygenation of amides to amines, Journal of Catalysis, 417 (2023) 301-313.

[80] T. Zhang, Y. Zhang, W. Zhang, M. Luo, A Convenient and General Reduction of Amides to Amines with Low-Valent Titanium, Advanced Synthesis & Catalysis, 355 (2013) 2775-2780.

[81] Y. Xie, P. Hu, T. Bendikov, D. Milstein, Heterogeneously catalyzed selective hydrogenation of

amides to alcohols and amines, Catalysis Science & Technology, 8 (2018) 2784-2788.

[82] I. Sorribes, S.C.S. Lemos, S. Martín, A. Mayoral, R.C. Lima, J. Andrés, Palladium doping of In2O3 towards a general and selective catalytic hydrogenation of amides to amines and alcohols, Catalysis Science & Technology, 9 (2019) 6965-6976.

[83] R. Kadyrov, Reduction of Amides to Amines under Mild Conditions via Catalytic Hydrogenation of Amide Acetals and Imidates, Advanced Synthesis & Catalysis, 361 (2018) 185-191.

[84] A. Pennetier, W.Y. Hernandez, B.T. Kusema, S. Streiff, Efficient hydrogenation of aliphatic amides to amines over vanadium-modified rhodium supported catalyst, Applied Catalysis A: General, 624 (2021).

[85] W. Guo, Q. Xia, H. Jia, Y. Guo, X. Liu, H. Pan, Y. Wang, Y. Wang, Highly selective synthesis of primary amines from amide over Ru-Nb$_2$O$_5$ catalysts, Chem. Asian J., 17 (2022) e202101256.

[86] H. Yang, L. Zhou, H. Chen, Y. Zeng, D. Li, C. Hu, Efficient hydrogenation of aliphatic acyclic amides to amines by bimetallic NiMo nitrides via heterogeneous catalysis, Chem. Eng. J., 473 (2023) 145374-145385.

[87] Production of polyamide fibers worldwide from 1975 to 2021 (in Million Metric Tons). Textile Exchange, 18 Oct 2022.

[88] R. Coeck, A. De Bruyne, T. Borremans, W. Stuyck, D.E. De Vos, Ammonolytic Hydrogenation of Secondary Amides: An Efficient Method for the Recycling of Long-Chain Polyamides, ACS Sustainable Chemistry & Engineering, 10 (2022) 3048-3056.

[89] W. Stuyck, K. Janssens, M. Denayer, F. De Schouwer, R. Coeck, K.V. Bernaerts, J. Vekeman, F. De Proft, D.E. De Vos, A sustainable way of recycling polyamides: dissolution and ammonolysis of polyamides to diamines and diamides using ammonia and biosourced glycerol, Green Chemistry, 24 (2022) 6923-6930.

[90] R. Coeck, D.E. De Vos, One-pot reductive amination of carboxylic acids: a sustainable method for primary amine synthesis, Green Chemistry, 22 (2020) 5105-5114.

[91] R. Coeck, J. Meeprasert, G. Li, T. Altantzis, S. Bals, E.A. Pidko, D.E. De Vos, Gold and Silver-Catalyzed Reductive Amination of Aromatic Carboxylic Acids to Benzylic Amines, ACS Catalysis, 11 (2021) 7672-7684.

[92] M. Biermann, F. Lange, R. Piorr, U. Ploog, H. Rutzen, J. Schindler, R.J.S.i.c.p.t. Schmid, technology, application, Synthesis of surfactants, (1987) 23-132.

[93] M.A.R. Jamil, S. Siddiki, A.S. Touchy, M.N. Rashed, S.S. Poly, Y. Jing, K.W. Ting, T. Toyao, Z. Maeno, K.I. Shimizu, Selective Transformations of Triglycerides into Fatty Amines, Amides, and Nitriles by using Heterogeneous Catalysis, ChemSusChem, 12 (2019) 3115-3125.

[94] J. Coetzee, H.G. Manyar, C. Hardacre, D.J. Cole-Hamilton, The First Continuous Flow Hydrogenation of Amides to Amines, ChemCatChem, 5 (2013) 2843-2847.

[95] Y. Zhao, S. Zhang, Y. Yamamoto, M. Bao, T. Jin, M. Terada, Heterogeneous Catalytic Reduction of Tertiary Amides with Hydrosilanes Using Unsupported Nanoporous Gold Catalyst, Advanced Synthesis & Catalysis, 361 (2019) 4817-4824.

[96] J. Wu, C. Darcel, Tandem Fe/Zn or Fe/In Catalysis for the Selective Synthesis of Primary and Secondary Amines via Selective Reduction of Primary Amides, ChemCatChem, (2022).

[97] Z. Lin, S.R. Denny, J.G. Chen, Transition metal carbides and nitrides as catalysts for thermochemical reactions, J. Catal., 404 (2021) 929-942.

[98] Z. Cheng, W. Qi, C.H. Pang, T. Thomas, T. Wu, S. Liu, M. Yang, Recent Advances in Transition

Metal Nitride‑Based Materials for Photocatalytic Applications, Adv. Funct. Mater., 31 (2021) 2100553‑2100574.

[99] N. Ji, P. Ri, X. Diao, Y. Rong, C. Kim, Supported transition metal (Mo, W) carbide and nitride catalysts for lignin hydrodeoxygenation: interplay of supports, structure, and catalysis, Catal. Sci. Technol., 13 (2023) 2618‑2637.

[100] D. Ruijten, T. Narmon, K. Van Aelst, H. De Weer, R. van der Zweep, T. Hendrickx, C. Poleunis, L. Li, K.M. Van Geem, D.P. Debecker, B.F. Sels, Tertiary Amines from RCF Lignin Mono‑ and Dimers: Catalytic N‑Functionalized Antioxidants from Wood, ACS Sustainable Chemistry & Engineering, 11 (2023) 4776‑4788.

[101] J. He, L. Chen, S. Liu, K. Song, S. Yang, A. Riisager, Sustainable access to renewable N‑containing chemicals from reductive amination of biomass‑derived platform compounds, Green Chemistry, 22 (2020) 6714‑6747.

[102] J. Magano, J.R. Dunetz, Large‑Scale Carbonyl Reductions in the Pharmaceutical Industry, Org. Process Res. Dev., 16 (2012) 1156‑1184.

[103] A. Volkov, F. Tinnis, T. Slagbrand, P. Trillo, H. Adolfsson, Chemoselective reduction of carboxamides, Chem Soc Rev, 45 (2016) 6685‑6697.