ISGC 2022

N°23 / OC
TOPIC(s) : Clean reactions / Waste and side streams valorization

Reductive amination of aliphatic and benzylic carboxylic acids

AUTHORS

Robin COECK / KU LEUVEN, CELESTIJNENLAAN 200F (BOX 2454), LEUVEN (HEVERLEE)
Dirk DE VOS / KU LEUVEN, CELESTIJNENLAAN 200F (BOX 2454), LEUVEN (HEVERLEE)

PURPOSE OF THE ABSTRACT

Introduction

Amines are important compounds in the chemical and pharmaceutical industry. Historically, amination of oil-based alcohols, aldehydes and ketones is one of the most popular methods for amine synthesis. Although progress has been made in producing amines from bio-based compounds, the reductive amination of carboxylic acids could be a desirable complementary method for sustainable amine synthesis. Carboxylic acids are generally cheap, often bio-based and readily available, making them suitable platform chemicals. Currently, carboxylic acids can be converted to the corresponding primary amines via multi-step pathways. Nevertheless, a one-pot synthesis of primary amines from carboxylic acids (utilizing solely NH_3 and H_2) would be a significant improvement regarding energy cost, reactor cost and product isolation. Here, we report the use of heterogeneous metal catalysts for the direct synthesis of aliphatic and benzylic primary amines from carboxylic acids. Reactions were performed in the green and benign cyclopentyl methyl ether.

Results and discussion

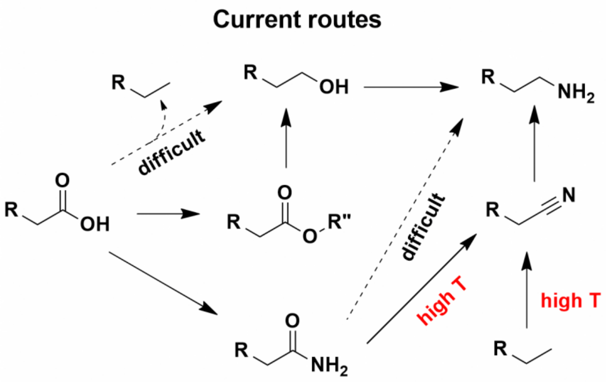
For the synthesis of aliphatic primary amines, a ruthenium-tungsten bimetallic catalyst was utilized. A time profile revealed that at the onset of the reductive amination, the acid is quite rapidly converted to the amide, even in the absence of H_2. Further investigation revealed that the dehydration of the ammonium carboxylate is catalyzed by the acid or basic support, e.g. amidation of octanoic acid with the rather basic $MgAl_2O_4$ and ZrO_2 yielded 82% and 85% octanamide respectively, while Nb_2O_5, featuring both Brønsted and Lewis acid sites, yielded 75% octanamide and was even able to promote the dehydration to the nitrile, resulting in 10% octanenitrile. The hydrogenation of the in-situ generated amide took place on the Ru-W interphase, yielding mainly primary amines with secondary amines as the lesser side-product. A catalyst evaluation revealed that RuWOx catalysts are superior in comparison with commercial PGM/C catalysts. Also the highly active amide hydrogenation catalyst PtV/HAP, described by Mitsudome et al., was outperformed. Additional experiments revealed that RuWOx-catalysts, with insoluble TiO_2 or ZrO_2 supports, showed good recyclability and were tolerant for common impurities in industrial streams of (bio-based) carboxylic acids such as cations, e.g. Na-salts, or water. Finally, an extensive substrate scope investigation was performed. High yields for a wide variety of carboxylic acids could be achieved (70-96%). For alfa-branched carboxylic acids, e.g. 2-methylbutanoic acid, condensation reactions towards secondary amines are nearly completely halted, leading to extremely high selectivities for primary amines (up to 99%).
Ru-based catalysts are less suitable for reactions with aromatics, since Ru readily hydrogenates aromatic rings. Therefore Ag/TiO_2 and Au/TiO_2 catalysts were developed for the reductive amination of benzoic acids (or benzamides) to benzylamines. While in previous experiments the in-situ generated amide was directly hydrogenated, now the amide is first dehydrated toward a nitrile (catalyzed by the support) after which the reduction toward an amine takes place (catalyzed by the metal). This led to some interesting kinetics. After optimization of the reaction conditions and minimization of the metal loading to only 0.025 mol% Au, yields of up to 92% benzylamine were obtained with H_2 and NH_3 as the only reagents. The catalysts also showed good

recyclability and could be reused at least 4 times.

Conclusions

The reductive amination of carboxylic acids using solely H2 and NH3 is a green and interesting method for the synthesis of primary amine. Two catalytic systems were developed that are both recyclable and relatively cheap. An extensive substrate scope investigation was performed. Good yields and selectivities for the corresponding primary amine were achieved for a wide variety of amines, with values up to 96% and 99% respectively.

FIGURES



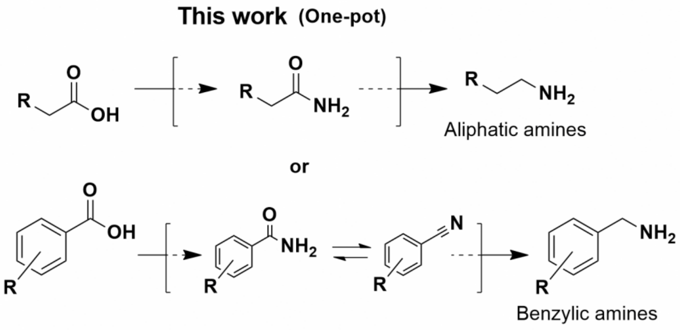


FIGURE 1

Figure 1

Classical pathways to amines from carboxylic acids.

FIGURE 2

Figure 2

Direct synthesis of primary amines from carboxylic acids

KEYWORDS

Reductive amination | Amines | Heterogeneous catalysis | Carboxylic acids

---

BIBLIOGRAPHY

[1] R. Coeck, S. Berden, D. E. De Vos, Green Chem. 2019, 21, 5326.

[2] E. Hernández-Ramírez, J. A. Wang, L. F. Chen, M. A.Valenzuela, A. K. Dalai, Appl. Surf. Sci. 2017, 399, 77.

[3] T. Mitsudome, K. Miyagawa, Z. Maeno, T. Mizugaki, K. Jitsukawa, J. Yamasaki, Y. Kitagawa and K. Kaneda, Angew. Chemie, 2017, 129, 9509.