# Reductive Amination of Cellulosic Biomass Derived Compounds

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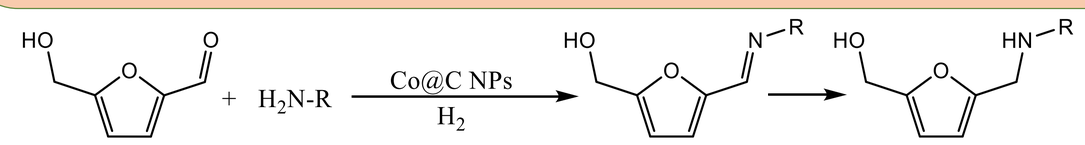
## Introduction

Cellulosic biomass derived 5-hydroxymethyl furfural (HMF) is a renewable platform molecule which can be used as a versatile raw material for the production of many different compounds. N-substituted 5-hydroxymethylfurfurilamines derived from HMF are highly interesting compounds with bioactive properties such as fungicide, bactericide, and pharmacological. They can be achieved via reductive amination of HMF and an amine by the use of a metal catalyst and hydrogen as reducing agent in a one-pot procedure (Scheme 1). Noble metals have been employed in this reaction giving rise to very good results under mild reaction conditions, but, due to their limited availability and high price, more earth-abundant and inexpensive non noble metals have been studied as catalysts.




**Scheme 1.** Direct method for the reductive amination of HMF with primary amines

Recently our group has developed monodispersed metallic Co nanoparticles covered by a thin carbon shell (Co@C NPs) which protects the metal nanoparticles from over-oxidation, leaching and agglomeration (Figure 1). In this work, we have studied the potential of these nanoparticles as hydrogenating catalysts to perform the reductive amination of HMF with different amines under mild reaction conditions.

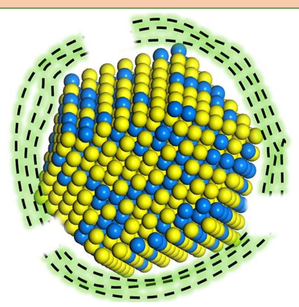
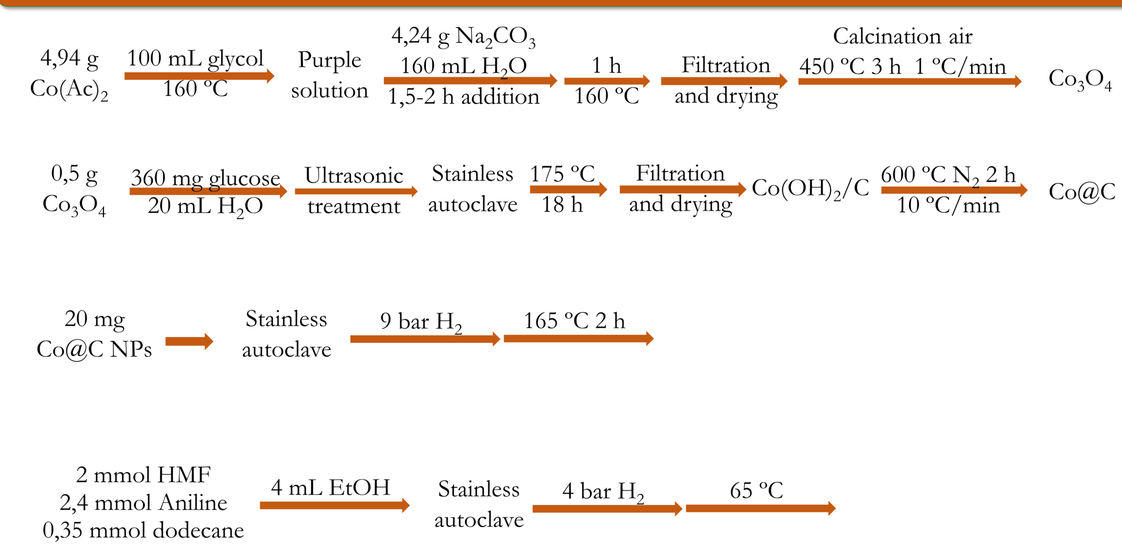


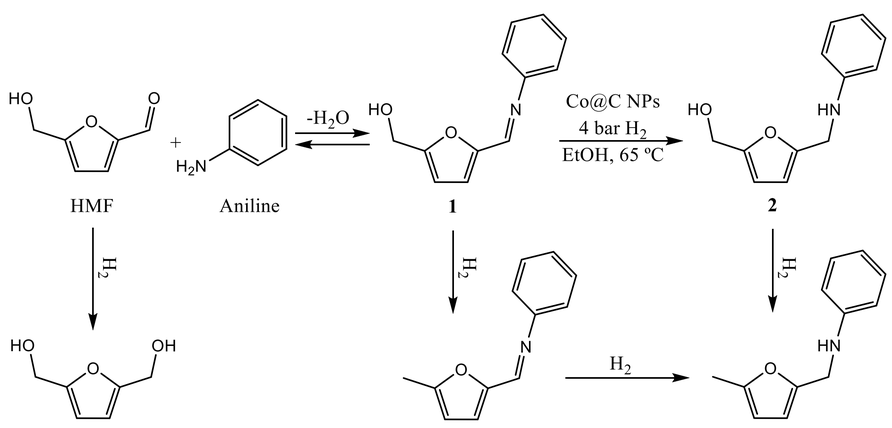
**Figure 1.** Schematic illustration of the structure of Co@C NPs[3a]

## Experimental




## Results

The reaction was performed following the mechanism described in Scheme 2 using HMF and aniline as reagents and Co@C NPs as catalyst. Reaction conditions as well as solvent were optimized resulting in the use of ethanol as solvent, 4 bar of hydrogen pressure and 65 ºC of temperature.




**Scheme 2.** Proposed reaction pathway for the reductive amination of HMF with aniline

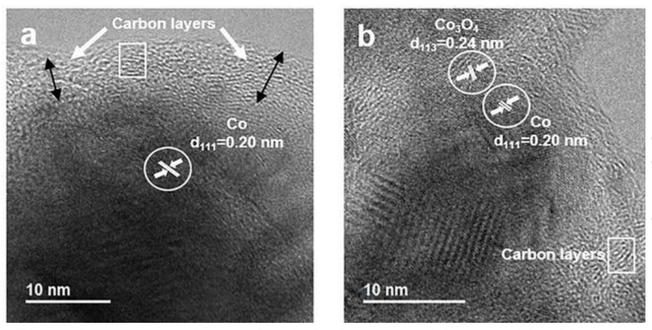



**Figure 2**. a) HRTEM image of a single Co nanoparticle covered by thin carbon layers. b) HRTEM image of surface structures of Co nanoparticle covered by thin carbon layer. The lattice of $Co_3O_4$ can be observed on the outer surface layer of Co@C nanoparticle. [3a]

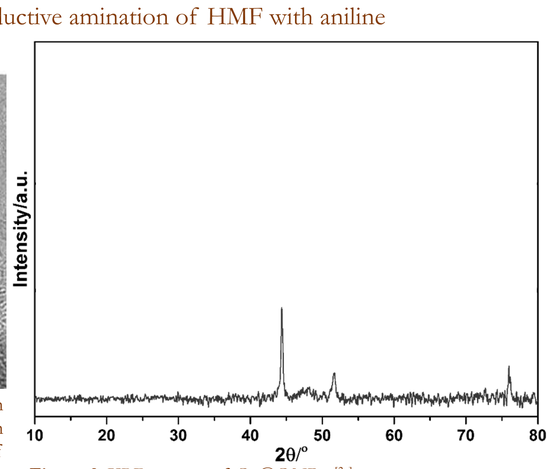



**Figure 3**. XRD pattern of Co@C NPs. [3a]

## Reductive amination of HMF with aniline over different catalysts

Different catalysts were studied in the reaction (Table 1).

***Table 1.*** *Results of the reductive amination of HMF with aniline overdifferent catalysts*

| Entry | Catalyst | r⁰ | Time (h) | Conversion Imine 1 (%) | Yield 2 (%) | Yield 4 (%) | Yield BHMF (%) | TOF ($h^{-1}$)[b] |
|---|---|---|---|---|---|---|---|---|
| 1 | Co@C glucose | 0,34 | 6 | 99 | 98 | 1 | 0 | 1,01 |
| 2 | Co@C EDTA | 0,06 | 21 | 65 | 63 | 1 | 1 | 0,17 |
| 3 | $Co_3O_4$ commercial | 0,01 | 20 | 16 | 15 | 0 | 1 | 0,13 |
| 4 | Ni@C | 0,21 | 20 | 98 | 97 | 0 | 1 | 0,62 |
| 5[d] | Ni:Co@C (1:1) | 0,20 | 18,5 | 92 | 88 | 0 | 1 | 0,58 |

[a] Reaction conditions: imine **1** (2 mmol), 17 mol % of catalyst, EtOH (4 mL), 65 ºC and 4 bar of $H_2$. $r^0$: initial reaction rate of disappearance of imine**1** ($mmol \cdot h^{-1}$). [b] Defined as initial reaction rate divided by mmol of bulk catalyst. [d] Detected some hydrogenation of the furan ring

## Recovery and reuse of Co@C NPs catalyst

The reusability of the Co@C NPs catalyst was studied concluding that it can be reused at least 5 consecutive times without significant loss of activity (Figure 4). The possible leaching of the catalyst was also checked.

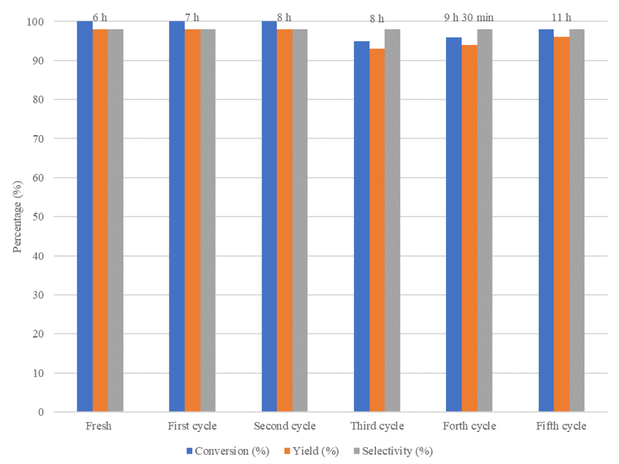



**Figure 4.** Reciclability of Co@C NPs catalyst for the reductive amination of HMF with aniline

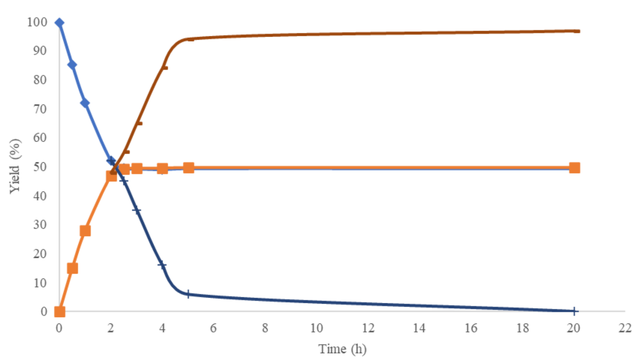



**Figure 5.** Leaching experiment of the reductive amination of HMF with aniline stopped after 2 h of reaction. Reaction conditions: imine **1** (2 mmol), dodecane internal standard (59 mg), Co@C NPs (20 mg), EtOH (4 mL), 65 ºC and 4 bar of $H_2$. Imine **1** (—•—), Amine **2** (—•—), Imine **1** (- - •- -), Amine **2** (- - - -) if the reaction would continue with catalyst.

## Scope of the reaction

The general applicability of the Co@C NPs catalyst for the reductive amination was evaluated performing the reaction using different aldehydes and amines as starting materials.

***Table 2.*** *Results of the reductive amination aniline with different aldehydes*[a]

| Entry | Aldehyde | Time (h) | Conversion Imine (%) | Yield Amine (%) | Selectivity Amine (%) |
|---|---|---|---|---|---|
| 1 | Furfural | 6 | 54 | 54 | 100 |
| | | 21,5 | 93 | 93 | 100 |
| 2 | 5-methylfurfural | 6 | 78 | 78 | 100 |
| | | 21,5 | 99 | 99 | 100 |

[a] Reaction conditions: imine previously formatted with the aldehyde and the aniline (2 mmol), Co@C NPs (20 mg), EtOH (4 mL), 65 ºC and 4 bar of $H_2$.

***Table 3.*** *Results of the reductive amination aniline with different primary amines*[a]

| Entry | Primary amines | Time (h) | Conversion Imine (%) | Yield Amine (%) | Selectivity Amine (%) |
|---|---|---|---|---|---|
| 1 | *p*-Anisidine | 6 | 68 | 67 | 98 |
| | | 19 | 99 | 96 | 97 |
| 2 | *p*-Toluidine | 4 | 99 | 98 | 98 |
| 3 | *o*-Toluidine | 6 | 65 | 63 | 97 |
| | | 20 | 100 | 93 | 93 |
| 4 | 4-Acetyl aniline | 6 | 37 | 34 | 92 |
| | | 20 | 93 | 84 | 90 |
| 5 | Octylamine | 6 | 57 | 52 | 90 |
| | | 20 | 86 | 84 | 97 |

[a] Reaction conditions:imine previously formatted with HMF and the primary amine(2 mmol), Co@C NPs (20 mg), EtOH (4 mL), 65 ºC and 4 bar of $H_2$.

## Conclusion

- The Co@C catalyst prepared from the Co-glucose complex resulted highly active and selective in the reductive amination of HMF with different primary amines under mild reaction conditions to produce a variety of highly valuable N-substituted 5-hydroxymethylfurfurilamines
- Co@C NPs is a stable catalyst that can be reused over several consecutive cycles without loss of activity and selectivity.

## Acknowledgments

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## References

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