**Reductive amination in different solvent systems: reaction network analysis and kinetics**

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**Highlights**

* Formulation of a reaction network for the reductive amination
* Good performance of the RA in homogeneous and thermomorphic solvent systems
* Kinetic description of the RA in two different solvents

**1. Introduction**

The Collaborative Research Center Transregio 63 of the German Research Foundation (DFG) develops methods and strategies to adapt established reactions to substrates from renewable raw materials. Focus of this project is the evaluation of the potential of complex homogeneously catalyzed tandem reactions using the example of the rhodium-catalysed hydroaminomethylation (HAM) of 1-decene. This reaction offers a direct and efficient synthesis of various pharmaceuticals, natural products, agrochemicals and fine chemicals [1]. To acquire detailed knowledge regarding the overall reaction the sub-network of the reductive amination (RA) step is analysed separately.

To recover the expensive Rh-catalysts from the homogeneous reaction solution thermomorphic solvent systems (TMS) are applied. In TMS the separation between products and catalysts is realized by using temperature dependent miscibility gaps in mixture of solvents of different polarity [2]. With regard to process development and optimization detailed knowledge of the reaction rates is necessary. We will report about a kinetic model to describe the reactions in homogeneous solvents and the transferability to TMS systems.

**2. Methods**

RA experiments were conducted in a high-pressure batch reactor system equipped with a gas supplying system and pressure and temperature controllers. The RA was investigated in three different solvent systems (2 homogeneous, 1 TMS) considering the reactants undecanal and diethylamine (DEA) (cundecanal = 0,18 mol/L, nDEA:nundecanal=4:1 and 1:1). The homogeneous solvent systems constituted of isopropyl or methanol (with 1 wt-% dodecane as internal standard respectively), whereas the TMS constituted of methanol and dodecane (wMeOH : wdodecane = 50 : 50). The ligands triphenylphosphine (TPP) and Xantphos (XPH) were investigated, so that the catalyst is formed by Rh(acac)COD and the corresponding ligand (nRh:nP:nundecanal = 1:2:1000). Kinetic experiments were carried out in the temperature and H2 pressure ranges between 85°C…115°C and 10 bar…30 bar, respectively.

**3. Results and discussion**

Based on the experimental results a reaction network for the reductive amination is postulated considering four groups of compounds (Figure 1): the desired product n-amine, the intermediate n-enamine and the side products n-alcohole and aldole.



**Figure 1.** Main and side products of the rhodium-catalysed reductive amination of a linear aldehyde

Concerning the RA performed in methanol with the ligand XPH significant conversion X of the reactant and a high yield Y with respect to the n-amine were observed after 120 min (Xundecanale = 100 %, Yamine = 91 %, Figure 2a). The RA carried out in isopropyl revealed a different behavior. With the ligand TPP the reactant conversion is significantly lower (Xundecanal = 90 %) and the yield is only Yamine = 63 % (Figure 2b). In this case the hydrogenation of the enamine to the amine is clearly inhibited. The reductive amination carried out in the TMS methanol:dodecane = 50:50 showed similar conversions (Xundecanal = 100 %) and yields (Yamine = 85 %) as for the homogeneous solvent methanol.



a)

b)

c)

**Figure 2.** Reductive amination of 1-undecanale at T = 100 °C, pH2 = 20 bar. a) in methanol with XPH, DEA:Sub = 4 b) in isopropyl with TPP, DEA:Sub = 4 c) in TMS (MeOH:dodecane = 50 : 50) with XPH, DEA:Sub = 1

**4. Conclusions**

To describe the experimentally observed trends with a suitable kinetic model, the influence of the solvent composition needs to be considered. Currently the inhibition of the hydrogenation of the enamine to the amine is quantified in more detail in order to provide a quantitative kinetic model for the reaction carried out in the TMS.

**References**

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2. T. Gaide, A. Jörke, K.E. Schlipköter et al., *Appl. Catal. A* **2017**, 532, 50-56