

Hydroaminomethylation in thermomorphic solvent systems

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Abstract

The rhodium catalyzed hydroaminomethylation of 1-octene with morpholine has been studied using temperature-dependent solvent systems (TMS systems). High conversions of the olefin and high selectivities to the amines are obtained in TMS systems consisting of propylene carbonate, an alkane and a semi-polar mediator, although some morpholine reacts with propylene carbonate in a side reaction. With *N*-octylpyrrolidone as mediator the conversion of 1-octene and the selectivity of the corresponding amines reached in each time 92%. After the reaction the catalyst can be easily recovered by a simple phase separation with only a negligible loss of the rhodium catalyst.

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1. Introduction

Various amines can be synthesized in a simple, efficient and atom-economic way by performing a hydroaminomethylation reaction. The hydroaminomethylation is a one pot-reaction consisting of three consecutive steps: In the first step, a hydroformylation of an olefine is performed followed by the reaction of the resulting aldehyde with a primary or secondary amine to give the corresponding enamine or imine. At last this intermediate is hydrogenated to the desired secondary or tertiary amine (see Fig. 1) [1–7].

In most cases, rhodium salts or complexes are used as catalyst. The recovery and reuse of the expensive metal catalyst is one of the most important difficulties in homogeneous catalysis. One concept to overcome this problem is to use multi-phase systems, where the catalyst is dissolved in one phase and the product is located in the other phase. Technical applications for this principle are the Ruhrchemie/Rhône-Poulenc process and the production of α -olefins via the SHOP-process [8]. However, the concept is limited to lower olefins because of the low solubility of higher olefins in the

polar catalyst-phase. This mass transport limitation leads to a deceleration of the reaction and to very low yields.

Therefore, we developed a new recycling concept combining the advantages of a reaction in single-phase systems by overcoming typical mass transport limitations with the advantages of a convenient catalyst recycling in two-phase systems [9,10]. The use of temperature-dependent or thermomorphic multi-component solvent systems (TMS systems) allows to perform a reaction in a single-phase at a high reaction temperature followed by a phase split at a lower temperature. The TMS systems consist of a polar solvent (s1) and non-polar solvent (s2) which show no or at least only very poor solubility for each other. In one of these components the catalyst is dissolved and the other one acts as extraction agent for the reaction products. A semi-polar solvent s3 operates as mediator for the two other solvents. Dependent on the composition and the temperature a mixture of s1, s2, and s3 is either homogeneous or heterogeneous. In the phase diagram, the operating point describes the composition of the solvent system appropriate for the reaction. The miscibility gap between s1 and s2 which describes the extent of the heterogeneous sphere of the solvent system is temperature depending and decreases usually with rising temperature (Fig. 2). The reaction can be carried out in one homogeneous phase and after

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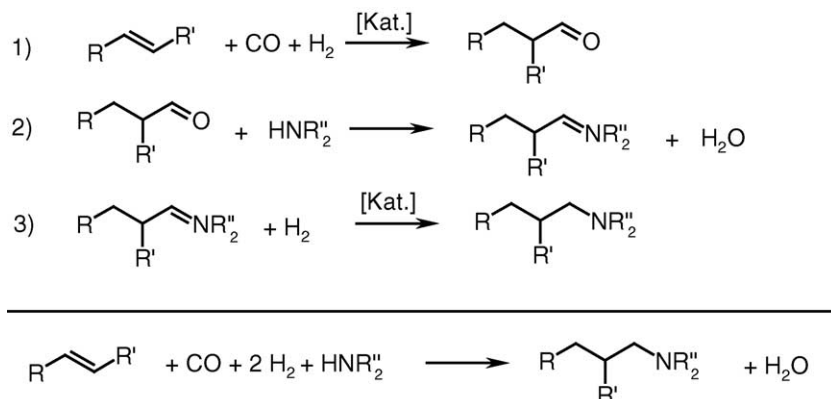


Fig. 1. Reaction steps of the hydroaminomethylation.

cooling down the product mixture the catalyst can be easily recovered by a simple phase separation.

The concept of TMS systems was successfully applied to the isomerizing hydroformylation of *trans*-4-octene [11,12] and to the cooligomerization of fatty acids with ethylene [13,14].

2. Results and discussion

As the hydroformylation is the first step of the reaction, TMS systems, which were used in the isomerizing hydroformylation of *trans*-4-octene, should be applicable to the hydroaminomethylation as well. For this reason propylene carbonate (PC) was chosen as polar solvent for the catalyst and alkanes (an isomeric mixture of dodecane or *n*-hexane) were used as non-polar component *s*2. 1,4-Dioxane, different pyrrolidones (*N*-methylpyrrolidone (NMP), *N*-ethylpyrrolidone (NEP), *N*-cyclohexylpyrrolidone (NCP) *N*-benzylpyrrolidone (NBP) and *N*-octylpyrrolidone (NOP)) or esters of lactic acid (ethyl lactate and butyl lactate) served as mediator *s*3.

As test reaction, we investigated the hydroaminomethylation of 1-octene with morpholine (Fig. 3).

The TMS systems were determined by cloud titrations at different temperatures from 25 to 100 °C. To a mixture of PC and *s*2 the mediator *s*3 was added until a homogeneous solution was obtained. The phase behaviour of the TMS system PC/dodecane/NEP is shown in Fig. 4.

The system is exceptionally temperature-dependent; the miscibility gap is getting smaller with increasing temperature. With the other pyrrolidones the required amount of *s*3 is getting smaller with increasing length of the alkyl chain at the pyrrolidone and the decreasing polarity of the mediator involved:

N-methylpyrrolidone (NMP) > *N*-ethylpyrrolidone (NEP) > *N*-cyclohexylpyrrolidone (NCP) > *N*-octylpyrrolidone (NOP).

N-benzylpyrrolidone (NBP) is one exception, because when this solvent is used, great amounts (>80% of the mixture) of solvent are required. Therefore, no further experiments were performed with NBP. The temperature dependence is decreasing in the same order: NMP > NEP > NCP > NOP (see Fig. 5).

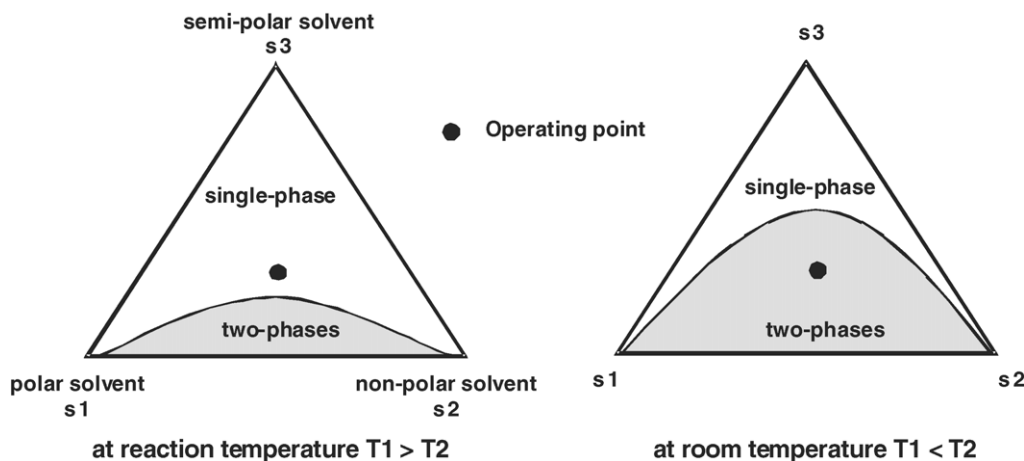


Fig. 2. Principle of temperature depending multi-component solvent systems.

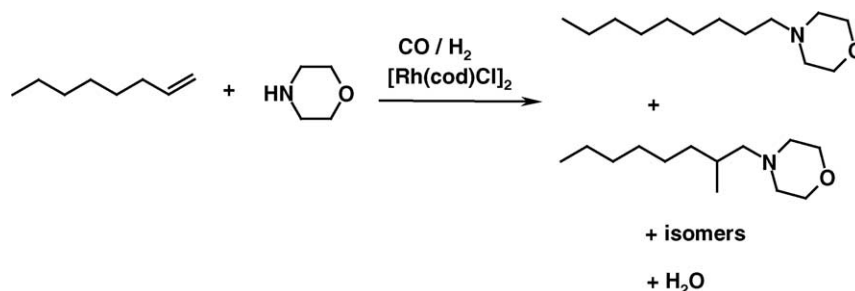


Fig. 3. Hydroaminomethylation of 1-octene with morpholine.

As NMP and NEP are not completely miscible with dodecane at lower temperatures a second miscibility gap between pyrrolidone and the non-polar phase occurs in the TMS systems PC/dodecane/NMP and PC/dodecane/NEP. These solvent systems pass from a system with a closed miscibility gap (with a complete binodal curve) to one with an open miscibility gap at room temperature (compare Fig. 4). This

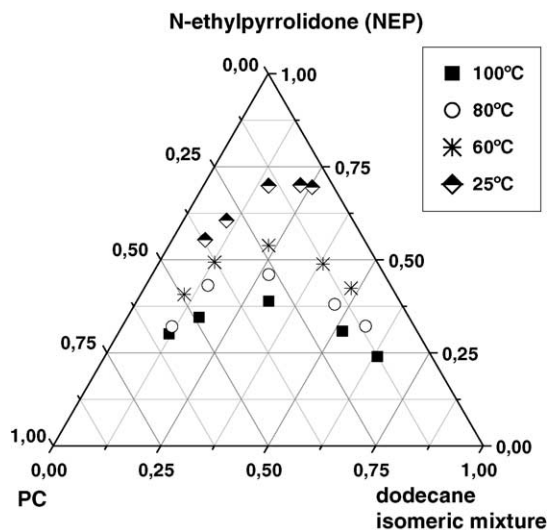


Fig. 4. Thermomorphic solvent system PC/dodecane/NEP.

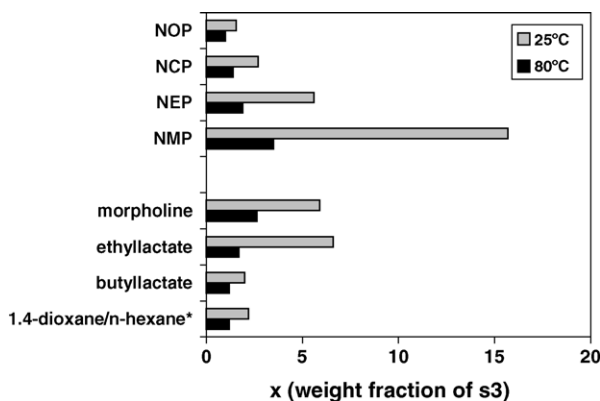


Fig. 5. Required weight ratio PC/dodecane/s3 = 1:1:x for different mediators s3; *PC/n-hexane/1,4-dioxane = 1:0.55:x (x is the required weight to obtain miscibility of the system).

immiscibility of the mediator and the polar phase with the product phase can be used for a convenient recovery of the catalyst.

To determine the appropriate composition of the solvent mixture for the reaction also the influence of the educts 1-octene and morpholine was measured by repeating the cloud titrations with addition of these substances. While the addition of 1-octene has almost no effect on the TMS systems the addition of morpholine leads to a decrease of the mixing gap (see Fig. 6). A smaller amount of s3 is needed to obtain a homogeneous system because morpholine itself is semi-polar and can be used as mediator.

The application of morpholine as s3 was studied in a further test run. In this case, a weight ratio of PC: dodecane: morpholine of 1:1:2.6 is required to get a clear solution at 80 °C (see Fig. 5). The TMS system PC/dodecane/morpholine shows strong temperature dependence. With 1,4-dioxane and the lactates smaller amounts of s3 are necessary, for example a weight ratio of 1:1:1.7 in the TMS system PC/dodecane/butyllactate. The lactates show the same tendency as the pyrrolidones: with increasing chain length and polarity both the amount needed to get a homogeneous phase and the temperature dependency of the solvent systems are decreasing. Similar to the systems with NMP or NEP as s3 the TMS system PC/dodecane/ethylactate changes from a

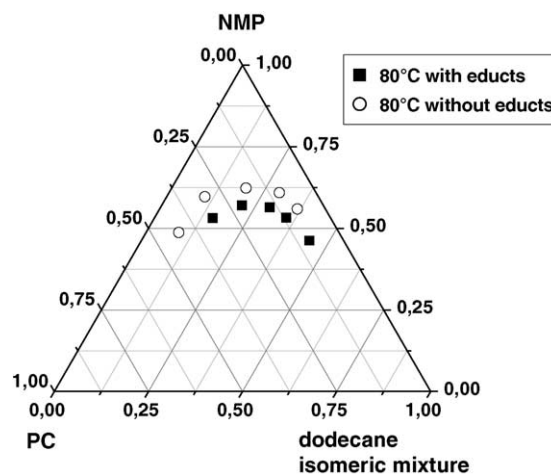


Fig. 6. Influence of the educts 1-octene and morpholine on the TMS system PC/dodecane/NMP.

Table 1
Hydroaminomethylation of 1-octene and morpholine in different thermomorphic solvent systems

Solvent system	Conversion 1-octene [%]	Amine selectivity [%]	<i>n/iso</i>	TON	TOF [h ⁻¹]	Rh loss [%]
PC	97	71	2.0:1	970	485	–
PC/ <i>n</i> -hexane/1,4-dioxane 1:0.55:1.3	97	96	1.4:1	970	485	0.7
PC/dodecane/NMP 1:1:2.65	95	68	3.0:1	950	475	0.4
PC/dodecane/NOP 1:1:0.85	92	92	1.6:1	920	460	1.5
PC/dodecane/NEP 1:1:1.2	97	78	2.1:1	970	485	1.1
PC/dodecane/morpholine 1:1:2.8	98	69	1.8:1	980	490	0.4
PC/dodecane/ethylactate 1:1:1.5	79	50	2.1:1	790	395	0.9
PC/dodecane/butylactate 1:1:1	82	60	1.7:1	820	410	0.8

Reaction conditions: 0.1 mol % [Rh(cod)Cl]₂ based on 1-octene, morpholine/1-octene 1.5:1, 8 bar CO, 39 bar H₂, 125 °C, 2 h, stirrer velocity 1000 rpm.

system with a closed miscibility gap to a system with an open mixing gap at room temperature. In all cases a smaller amount of s3 is required, when the educt morpholine is added, because of its semi-polar nature.

The hydroaminomethylation of 1-octene and morpholine was carried out in PC as a single-phase and in the TMS systems described above. PC and s2 were used in a weight ratio of 1:1 and an appropriate amount of s3 was added to get a homogeneous phase at reaction temperature. As catalyst [Rh(cod)Cl]₂ was used without any further ligand. The results obtained are shown in Table 1.

In all cases a high conversion of 1-octene can be observed, it reaches a level up to 98% after 2 h at 125 °C. The selectivity to the amines is also very high with up to 96% in the TMS system PC/*n*-hexane/dioxane. Without using a ligand only very small *n/iso* ratios can be observed, none of the regioisomers is clearly preferred under the given reaction conditions. The product can be found in both phases with the distribution depending on the mediator. The more polar solvent s3 the more of it and of the product is located in the catalyst phase. Only very small amounts of the possible byproducts nonanal, nonanol or *n*-octane can be detected.

However, an undesired side reaction is observed: morpholine-4-carboxylic acid 2-hydroxy-1-methyl-ethyl ester is formed by the reaction of PC and the educt morpholine via an attack of the nitrogen atom of the morpholine on the carbon atom of the carbonate group. By use of 1,4-dioxane or the pyrrolidones as mediator s3 about 30–45% of the morpholine is consumed by this side reaction. The product of this reaction stays in the PC phase and cannot be extracted to the non-polar product phase. The consumption of the morpholine leads to a lower selectivity to the desired amines. Thus, PC has to be substituted by other polar solvent (e.g. water, methanol or ethylene glycol) in future experiments. The lactates can react with the morpholine, too: first they are cleaved into lactic acid and the corresponding alcohol and then the resulting acid reacts with the amine to the corresponding amide. Overall, the hydroaminomethylation in the TMS systems PC/dodecane/lactate results in a conversion of 1-octene of about 80%, but only in selectivities to the amines of 50–60%. The TMS systems determined for the hydroaminomethylation can also be used for the hydroformylation, where the side reaction with the amine cannot occur.

The rhodium loss to the product phase was investigated by ICP-OES spectrometry. In all cases very low catalyst leaching can be observed, less than 1.5% of the rhodium is extracted (Table 1). The catalyst loss can be correlated to the polarity and the solubility of the mediator s3 in the product phase s2. The less polar s3, the more s3 is dissolved in s2 and the more catalyst is lost.

3. Conclusion

The hydroaminomethylation of 1-octene with morpholine can be performed in various thermomorphic solvent systems consisting of propylene carbonate (PC), an alkane and a semi-polar mediator. High conversions of 1-octene up to 98% after 2 h at 125 °C and good selectivities to the amines up to 96% can be achieved. However, the use of these TMS systems is limited by the occurrence of a side reaction between morpholine and PC, thus requiring in future work a more stable polar solvent. Without use of a ligand almost no regioselectivity is observed. After the reaction and cooling down the reaction mixture, the catalyst can be easily recovered by a simple phase separation. The rhodium leaching to the product phase is very low.

4. Experimental

4.1. Materials

1-Octene (99+%), morpholine (99+%) and the solvents propylene carbonate (99.5%), dodecane (tech.), 1,4-dioxane (99+%), *n*-hexane (95%), *N*-methylpyrrolidone (99%), *N*-ethylpyrrolidone (98%), *N*-cyclohexylpyrrolidone (99%), *N*-benzylpyrrolidone (97%) and ethylactate (97%) were supplied from Acros Organics, *N*-octylpyrrolidone (>98%) and butylactate (97%) were purchased from Fluka. All compounds were used without further purification. The reactions and handling were done under dry argon using standard Schlenk tube techniques. The catalyst [Rh(cod)Cl]₂ was received from Umicore AG & Co. KG, Carbon monoxide (3.7) was obtained from BASF and hydrogen (5.0) from Messer Griesheim.

4.2. Determination of temperature-dependent multi-component solvent (TMS) systems

The TMS systems were determined by performing cloud titrations. 0.6 g of a mixture of propylene carbonate and the alkane (5:1, 3:1, 1:1, 1:3, 1:5 wt. ratio) was transferred into a 5 ml centrifuge glass and warmed in a silicone oil bath under intense stirring. After having reached the desired temperature (100, 80 and 25 °C) the mediator was added drop by drop by a syringe to the biphasic mixture until one homogeneous phase is formed.

4.3. Hydroaminomethylation

In a typical experiment 3 mg (0.006 mmol) of the catalyst $[\text{Rh}(\text{cod})\text{Cl}]_2$, 0.673 g (6 mmol) 1-octene and 0.7839 g (0.9 mmol) morpholine were dissolved in 14 g of the solvent PC or 14 g of the solvent mixture of PC/alkane/s3, respectively. The reaction mixture was saturated with argon and then transferred into an evacuated 70 ml stainless steel autoclave from Parr Instrument company (USA). After reaching a temperature of 125 °C the reaction was started by pressurizing the vessel with 8 bar carbon monoxide and 38 bar hydrogen to a total gas pressure of 46 bar. The autoclave was left for 2 h at 125 °C and a stirrer velocity of 1000 rpm. The reaction was ended by rapidly cooling down the mixture to room temperature. The carbon monoxide and the hydrogen were vented and the biphasic reaction mixtures were separated in a separating funnel. Samples of the catalyst phase and the product phase were taken and analyzed by gas chromatography with 1-octanol as internal standard and toluene as solvent. The catalyst leaching was determined by ICP-spectrometry.

4.4. Analysis and product characterization

Routine gas chromatographic analysis was carried out on a HP 6890 instrument (Hewlett-Packard GmbH, Waldbronn, Germany) equipped with a FI-detector and a HP-5 capillary column (30 m, coating 5% diphenyl-95% dimethylpolysiloxane, diameter 0.25 mm, film thickness 0.25 μm),

connected with an auto-sampler. 1-octanol was used as an internal standard. ICP-OES analysis was carried out on a Iris Interpid DUO ER/S (Thermo Elemental, USA).

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