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Influence of mass transfer on regio- and enantioselectivity in hydrogenation of 1-phenyl-1,2-propanedione over modified Pt catalysts

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Abstract

The influence of mass transfer limitations on the enantio- and regioselectivity in hydrogenation of 1-phenyl-1,2-propanedione was studied. Gas–liquid mass transfer limitation as well as liquid–solid mass transfer limitation did not influence the enantio- and regioselectivity of the reaction, compared to the performance of the system under kinetic control. Under various regimes, the enantiomeric excess of the (*R*)-1-hydroxy-1-phenylpropanone was about 55% and regioselectivity remained at about 10, which makes process scale-up with respect to enantio- and regioselectivity straightforward.

Keywords: Mass transfer; 1-Phenyl-1,2-propanedione; Pt catalysts

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1. Introduction

In the field of fine chemicals production, replacement of homogeneous catalysts with heterogeneous counterparts is a matter of increasing interest. Heterogeneous catalysts are preferred over homogeneous ones in large-scale production, due to the easy separation and re-use of the former ones. The presence of a solid catalyst complicates the transport processes of gaseous and liquid reactants, namely the liquid-to-solid transport as well as the transport of components into the catalyst pores are involved.

Kinetics of a particular reaction in a laboratory-scale reactor should be measured under kinetic regime, in the absence of internal and external mass transfer limitations. There exist various experimental procedures and theoretical criteria to confirm the kinetic regime [1]. However, in scale-up, the operating conditions are often selected in such a way that the process is at least partly shifted from the kinetic regime to a diffusion-controlled regime. Therefore, it is of utmost importance to know how this shift affects not only the reactant conversion, but also the product selectivities.

In the production of fine chemicals, complex, multi-step organic reactions are involved and the selectivity towards the desired product might be affected by the prevailing regime. Although much effort has been focused on the understanding of the impact of mass transfer on the overall reaction rates, it is however, difficult to predict whether, and how, the selectivity (e.g. chemo-, regio- and enantioselectivity) of the reaction is altered in the diffusion-controlled regime. This calls for thorough investigations of the mass transfer effects.

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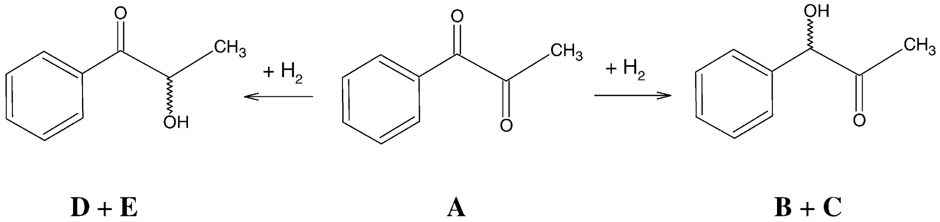

Fig. 1. Simplified reaction scheme. Symbols: **A**, 1-phenyl-1,2-propanedione; **B**, (*R*)-1-hydroxy-1-phenylpropanone; **C**, (*S*)-1-hydroxy-1-phenylpropanone; **D**, (*S*)-2-hydroxy-1-phenylpropanone; **E**, (*R*)-2-hydroxy-1-phenylpropanone.

From the mechanical point of view, one of the most fascinating cases of heterogeneous catalysis is enantioselective hydrogenation, where a chirally modified solid catalyst induces enantiodifferentiation. For this study, 1-phenyl-1,2-propanediones was selected as a model compound and cinchonidine was used as a catalyst modifier. The reaction products, optically active hydroxyketones and diols, are used for synthesis of several pharmaceuticals [2,3]. The effect of mass transfer has been scarcely investigated for this reaction, although the effect of internal mass transfer limitations has been previously reported for 1-phenyl-1,2-propanedione hydrogenation over Pt-MCM-41 catalyst [4]. In enantioselective hydrogenation of α-keto esters over cinchonidine-modified Pt catalysts [5], the enantioselectivity was influenced by mass transfer limitations [6,7].

In this work, the influence of mass transfer limitations on the regio- and enantioselectivity in hydrogenation of 1-phenyl-1,2-propanedione are considered. The performance of the reaction under external mass transfer limitations at the gas–liquid interface and external mass transfer limitations at the liquid–solid catalyst interface are compared to the performance under kinetic regime. The implications of the reactor performance under various regimes and the possible strategies and limitations in the scale-up of the process are discussed. The simplified reaction scheme, relevant for the conversion levels obtained in the present work is illustrated in Fig. 1. Only minor amounts of diols were formed during the residence times used and therefore the considerations can be limited to the hydrogenation of 1-phenyl-1,2-propanedione (**A**) to hydroxyketones (**B**–**E**). The enantiomeric excess (ee) and regioselectivity (rs) are defined as ee $= ([\mathbf{B}] - [\mathbf{C}])/([\mathbf{B}] + [\mathbf{C}])$ and rs $= ([\mathbf{B}] + [\mathbf{C}])/([\mathbf{D}] + [\mathbf{E}])$, respectively.

2. Experimental

Hydrogenation of 1-phenyl-1,2-propanedione (Aldrich 223034, 99%) was carried out over commercial Pt/Al_2O_3 (5 wt.% Pt, Strem Chemicals, mean catalyst particle size 18 μm) catalyst modifier with (−)-cinchonidine (Aldrich C8040-7, 96%) in a semi-batch reactor (Sotelem, $V_L = 50\,\mathrm{cm}^3$) by using ethyl acetate (Lab-Scan, A3511, 99.8%) as a solvent. The reactor was equipped with a vibrating impeller. The hydrogenation experiments were performed at 10 bar H_2 at 20 or 15 °C at 10 bar H_2. Hydrogen was flowed once through the reactor ($100\,\mathrm{cm}^3\,\mathrm{min}^{-1}$). In all of the experiments, the catalyst was reduced at 400 °C for 2 h under flowing hydrogen and modified in situ with cinchonidine. The samples were analysed with a gas chromatograph equipped with an FI-detector and a chiral column (β-dex 225). The details of catalyst characterisation have been reported elsewhere [8].

3. Hydrogenation under mass transfer limitations

3.1. External mass transfer limitations

The hydrogenation reaction with different catalyst masses (56 and 100 mg) and stirring rates (1600, 1700 and 1800 rpm) were investigated at 20 °C and 10 bar. The molar ratio of cinchonidine-to-surface Pt and the reactant concentration were kept constant at 1.1 and $0.05\,\mathrm{mol\,dm}^{-3}$, respectively. A complication arises from the utilisation of different catalyst amounts, which should be kept in mind. As the criteria of kinetic control (rate independent on stirring rate and doubling catalyst amount results in two-fold rate increase) are applied, the specific features of enantioselective hydrogenation should be taken into account. The ee and rs are dependent on the liquid-phase concentration of cinchonidine and also on the cinchonidine-to-surface Pt ratio. Furthermore, the overall reaction rate depends on the amount of the catalyst modifier exhibiting a maximum close to a 1:1 cinchonidine-to-surface Pt molar ratio. Therefore, e.g. when liquid-phase concentration of cinchonidine corresponds to 1:1 cinchonidine-to-surface Pt ratio and the catalyst amount is doubled, cinchonidine-to-surface Pt ratio falls to about 1:2. One would expect a twofold higher reaction rate under kinetic control, however, a less than twofold rate increase is observed due to the decreased rate acceleration effect induced by the modifier at 1:2 cinchonidine-to-surface Pt ratio. Additional complications arise from the reduced enantio- and regioselectivity, which are considerably lowered at 1:2 molar ratio compared to 1:1 molar ratio of cinchonidine-to-surface Pt. If care is not taken, it could well be that one interprets the results as mass transfer effects, however, the origin of observed dependence being just the altered cinchonidine-to-surface Pt ratio.

In the present study, the cinchonidine-to-surface Pt ratio was maintained constant, because relatively low liquid-phase concentrations of cinchonidine were used (close to 1:1 molar ratio of cinchonidine-to-surface Pt). Cinchonidine is known to adsorb relatively strongly on the catalyst surface and therefore, the valid approach at low concentrations is to maintain cinchonidine-to-surface Pt ratio constant. However, at high cinchonidine concentration the comparison at a constant liquid-phase concentration is justified as the modifier coverage does not depend strongly on the liquid-phase concentration.

The hydrogenation rates were independent of the stirring rate. However, the hydrogenation rate was not proportional to the catalyst mass, indicating that external gas–liquid mass transfer affected the overall reaction rate. The reactor productivity was 270 mmol $\mathrm{dm}^{-3}\,\mathrm{min}^{-1}$ when 56 mg of catalyst was used, whereas over 100 mg of catalyst the productivity was 370 mmol $\mathrm{dm}^{-3}\,\mathrm{min}^{-1}$ indicating that the reaction rate was limited by external gas–liquid mass transfer of hydrogen. The ee and rs were 56 and 10%, respectively, and independent of the employed catalyst mass and stirring rate.

3.2. Internal mass transfer limitations

The influence of internal diffusion under employed conditions was estimated by calculating effectiveness factor η_e for pseudo-first order reaction with respect to hydrogen and assuming spherical catalyst particles. The effectiveness factor was solved iteratively utilizing experimentally obtained hydrogenation rates. Details of the procedure are published elsewhere [8]. The obtained effectiveness factor $\eta_e = 0.9999$ showed that influence of internal mass transfer was negligible. In fact this could be expected, because the commercial catalyst used in the experiments was in the form of fine powder (averages particle size below 20 μm). Regardless of the experimentally observed zero order dependence on hydrogen under kinetic control, the assumption of pseudo-first order reaction with respect to hydrogen was justified, as the dependence of effectiveness factor on reaction order is minor at η_e close to one. The reaction conditions employed in the calculations were the most severe ones (the highest reaction temperature and reactant concentration) and therefore, the effect of pore diffusion control was safely discarded in further experiments over the same catalyst, which were carried out at lower temperatures and reactant concentrations.

4. Hydrogenation under kinetic regime

The kinetic regime could be attained by lowering the reaction temperature from 20 to 15 °C and using the initial reactant concentration of 0.025 mol dm^{-3}. Also in these experiments, the cinchonidine-to-surface Pt ratio was maintained constant (1:1). The experiments were carried out at 5 °C lower than the first sequence. The lower temperature and reactant concentration allowed the exclusion of mass transfer limitations. Previously it has been demonstrated for hydrogenation of 1-phenyl-1,2-propanedione (0–25 °C) [9] that both ee and rs were independent on the reaction temperature, thus justifying the comparison of ee and rs at different temperatures. This, however, is only valid as temperature changes slightly. Similarly to the temperature, also the reactant concentration affects the ee and rs to a minor extent.

The kinetic regime was verified experimentally by obtaining initial hydrogenation rate proportional to

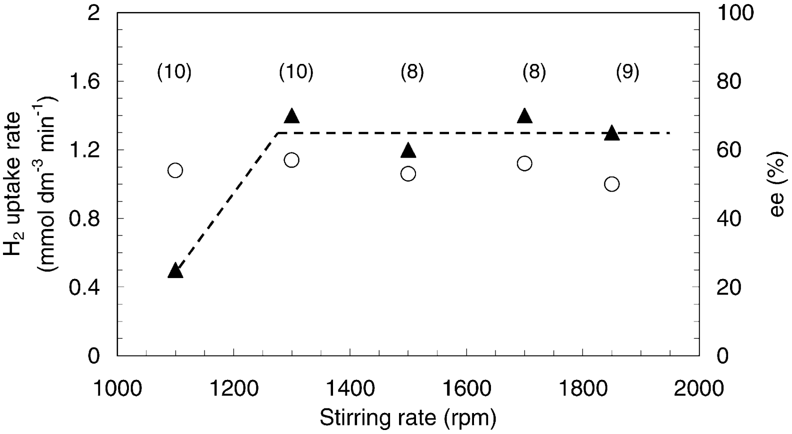

Fig. 2. The initial hydrogen uptake rate (▲) and enantiomeric excess (○) at 80% conversion of dione as a function of stirring speed. Corresponding regioselectivity is given in brackets (rs). Experiments were carried out at 10 bar H_2, 15 °C, c(**A**) = 0.025 M, c(**M**) $= 1.7 \times 10^{-4}$ mol dm^{-3} over 74 mg of catalyst.

catalyst mass (56, 74 and 100 mg catalyst at 1700 rpm) and independent of the stirring rate (1300–1850 rpm). When using the lowest stirring rate (1100 rpm), the reaction rate was significantly suppressed (Fig. 2) by external mass transfer limitations, however, it is noteworthy to observe that the ee and rs remained on the level of kinetic control.

The ee was constant about 55% and it was independent of the stirring rate and the catalyst amount used in the experiments. In these experiments, the catalyst-to-modifier mass ratio was maintained constant. The ee was about 55% also when the stirring rate of 1100 rpm was utilised (Fig. 2). The regioselectivity remained constant, around 10 and was independent on the stirring rate and catalyst mass, even to the lowest stirring rate (1100 rpm). This indicates that the external mass transfer limitations do not affect considerably rs and ee.

5. Discussion

The effects of external mass transfer control (gas–liquid and liquid–solid) on rs and ee were investigated and it can be concluded that ee and rs were practically uninfluenced by external mass transfer limitations. In detailed kinetic experiments, under kinetic control, the reaction order with respect to hydrogen was zero [10], also ee and rs had a zero order dependence on hydrogen pressure. From this zero-order dependence it might be expected that the mass transfer of hydrogen affects only to a minor extent the enantioselectivity and regioselectivity. This differs from what has been previously reported for hydrogenation of α-keto esters over analogous catalytic system, i.e. cinchonidine-modified Pt/Al_2O_3 catalysts. In enantioselective hydrogenation of α-keto esters, the reaction order with respect to hydrogen has been close to one and the enantioselectivity depends considerably on the mass transfer of hydrogen [6].

In all of the experiments the calculated effectiveness factor was about 1 and therefore, the effect of internal diffusion control on selectivity (rs and ee) cannot be evaluated based on present data.

Based on experimental findings is can be concluded that the scale-up of the process becomes easier as mass transfer limitations do not influence the enantio- and regioselectivity to considerable extent. This also implies that ee and rs values obtained outside kinetic regime can be extrapolated to kinetically controlled regime and also compared with ee values obtained under kinetic control.

6. Conclusions

The mass transfer effects in enantioselective hydrogenation of 1-phenyl-1,2-propanedione were studied. The obtained ee and rs were independent on external mass transfer limitations and remained on the same level as under kinetic control. The observed negligible dependence of rs and ee on mass transfer renders the extrapolation of selectivities obtained under kinetic control to mass transfer controlled regime a straightforward task. This implies also an easier scale-up of the process with respect to enantio- and regioselectivity.

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