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Effect of ultrasound in enantioselective hydrogenation of 1-phenyl-1,2-propanedione: comparison of catalyst activation, solvents and supports

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Abstract

The enantioselective hydrogenation of 1-phenyl-1,2-propanedione was carried out over Pt/Al_2O_3, Pt/SiO_2, Pt/SF (silica fiber), Pt/C catalysts modified with cinchonidine under ultrasonic irradiation. The initial rate, regioselectivity and enantioselectivity were investigated for different catalyst pretreatments, solvents and ultrasonic powers. The ultrasound effects were very catalyst dependent. The sonication significantly enhanced enantioselectivity and activity of the Pt/SF (silica fiber) catalyst. For the other Pt supported catalysts the reaction rate, enantioselectivity and regioselectivity increased moderately. The choice of solvent influenced the impact of ultrasound effect, namely in mesitylene, which has the lowest vapor pressure, the highest ultrasound enhancement was observed. The effect of sonication on catalysts surface was studied by transmission electron microscopy and scanning electron microscopy (SEM). No significant change in the metal particle size distribution due to sonication was observed. However, in the case of the Pt/SF catalyst, acoustic irradiation induced morphological changes on the catalyst particle surface (SEM), which might be the cause for enhancement of the initial reaction rate and enantioselectivity.

Keywords: Ultrasound; Enantioselective hydrogenation; Regioselectivity; Diketone; Pt catalysts

1. Introduction

In the production of optically pure chemicals (e.g. pharmaceuticals, agrochemicals, fragrances, sweeteners, etc.), utilization of heterogeneous catalysis, which combine easy catalyst separation and handling and lower catalyst cost (compared to chiral homogeneous catalysts) is particularly attractive. Cinchona alkaloid modified Pt catalysts for the hydrogenation of α-keto esters are extensively studied highly enantioselective chirally modified heterogeneous catalytic systems originally discovered by Orito et al. in the late 1970s [1]. Enantiomeric excesses approaching 98% have been reported [2]. Recent progress and developments have been summarized in excellent reviews [3–5]. The Orito reaction is very substrate specific and enantiomeric excesses approaching 95% has been achieved only with a few substrates. However, many substrates [3–5] can be hydrogenated with a moderate enantiomeric excess (40–60%). Therefore, all possible ways which enhance enantioselectivity and also catalyst activity and durability are of

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particular interest to those trying to expand the application areas of the Orito reaction.

A promising way the enhance catalyst activity, durability, and (enantio)selectivity is to apply on-line acoustic irradiation either during the course of reaction [6–16] or to pre-treat catalysts with ultrasound [17–28]. A cause for the often observed rate enhancement in the presence of ultrasound can be the cavitation effect, near a catalyst surface, when cavity collapse is non-spherical and drives high-speed jests of liquid onto the catalyst surface. These jets and associated shock waves can cause substantial surface damage and expose fresh, highly active surfaces [29]. The sonic treatment can change the catalyst morphology and particle size [30] and when applied on-line it can improve mass transfer as well as help to reactivate the catalyst. Sonication has been reported [22] to enhance enantioselectivity e.g. in ethyl pyruvate hydrogenation the highest *ee* of 97.1% ever reported for this reaction was obtained over an ultrasound treated catalyst. This positive ultrasound effect in Pt cinchona alkaloid system is explained by ultrasound induced catalyst morphological and surface cleaning effects as well as by enhanced adsorption of the cinchona alkaloid, thus providing higher coverage of chirally modified sites [31].

In this work, enantioselective hydrogenation of 1-phenyl-1,2-propanedione was used as a model reaction. The reaction has been studied extensively [32–36] and up to now the highest *ee* under maximum product yield has been 70% [37]. The main product of 1-phenyl-1,2-propanedione (**A**) hydrogenation was (*R*)-1-hydroxy-1-phenylpropanone (**B**, Fig. 1), which is a key intermediate in the synthesis of e.g. L-ephedrine [38]. In the first hydrogenation step the reaction produces four hydroxyketones (**B**, **C**, **D** and **E**, Fig. 1) and in the consecutive second hydrogenation step completely hydrogenated diols (**F**, **G**, **H**, and **I**, Fig. 1). Typical product distribution during hydrogenation of A is shown in Table 1. In the present work only the first hydrogenation step is considered. However, as the reaction proceed further to diols at long reaction times kinetic resolution of intermediate (*R*)- and (*S*)-hydroxyketones increases the product *ee* [39] at reactant conversions above 90%. Over 90% *ee*s of the main product **B** have been reported albeit with reduced product yield [39,40]. In the present study the role of kinetics resolution was small due to relatively short reaction times e.g. the 47% *ee* (at 50% conversion) could be increased up to 60% *ee* (at 98% conversion). More detailed treatment of kinetic resolution can be found elsewhere [39,40]. The complexity of hydrogenation of **A** makes it an interesting model molecule for investigating possibilities to enhance regio-, enantio- and diastereoselectivity as well as catalyst durability by means of on-line acoustic irradiation.

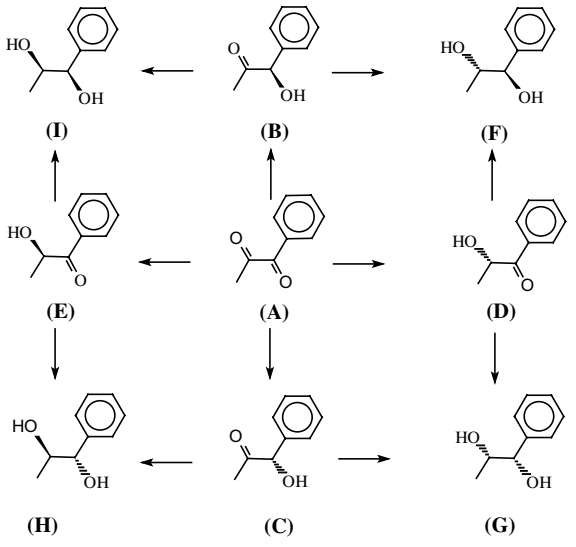

Fig. 1. Reaction scheme of 1-phenyl-1,2-propanedione hydrogenation. (**A**) 1-Phenyl-1,2-propanedione, (**B**) (*R*)-1-hydroxy-1-phenylpropanone, (**C**) (*S*)-1-hydroxy-1-phenylpropanone, (**D**) (*S*)-2-hydroxy-1-phenylpropanone, (**E**) (*R*)-2-hydroxy-1-phenylpropanone, (**F**) (1*R*, 2*S*)-1-phenyl-1,2-propanediol, (**G**) (1*S*, 2*S*)-1-phenyl-1, 2-propanediol, (**H**) (1*S*, 2*R*)-1-phenyl-1,2-propanediol, (**I**) (1*R*, 2*R*)-1-phenyl-1, 2-propanediol.

Table 1
Product distribution and conversion (X) of **A** over cinchonidine modifier Pt/Al_2O_3 catalyst in toluene under ultrasound (30 W)

Time/min	X (%)	**A**[a]	**B**[a]	**C**[a]	**D** + **E**[a,b]	**F**[a]	**H**[a]	**G** + **I**[a,b]
3	13.8	86.2	7.1	3.2	1.9	0.0	0.0	0.0
15	51.6	48.4	30.2	10.7	7.8	0.9	0.4	0.3
45	84.5	15.5	47.8	15.4	11.9	4.2	2.2	2.0
80	96.5	3.5	50.1	14.5	12.8	9.2	4.8	4.5
120	98.1	1.9	46.0	11.4	10.8	14.5	8.0	7.2

[a] Dimensionless concentration (%), $c/c^0_{\mathbf{A}} \times 100\%, c^0_{\mathbf{A}} = 19$ mmol/l.
[b] Enantiomers could not be separated in GC.

2. Experimental

2.1. Experimental and reactor set-up

1-Phenyl-1,2-propanedione (Aldrich, 99%) was hydrogenated in a pressurized reactor (300 ml) in presence and absence of ultrasound. Four different Pt catalysts were tested in enantioselective hydrogenation of 1-phenyl-1,2-propanedione: 5 wt.% Pt/Al_2O_3 (S = 95 m^2/g, Strem Chemicals Inc.), 5 wt.% Pt/SF crushed silica fiber (S = 59 m^2/g), 5 wt.% Pt/SiO_2 (prepared by incipient wetness method using hexachloroplatinic acid (Degussa) and commercial silica (S = 379 m^2/g, Merck 7734)), 5 wt.% Pt/C (S = 797 m^2/g, Johnson Matthey) catalyst. The preparation of the 5 wt.% Pt/SF crushed silica fiber catalyst is described elsewhere [34]. The