IMMOBILIZATION OF OPTICALLY ACTIVE RHODIUM COMPLEX ON MCM-41 FOR HYDROGENATION OF \(\alpha\)-(ACETYLAMINO)CINNAMIC ACID.

PART II. ENANTIOSELECTIVE CATALYTIC HYDROGENATION

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Abstract: A new supported heterogeneous catalyst has been synthesized through the anchoring of 3,4-(R,R)-bis(diphenylphosphino)pyrrolidine rhodium complex to the surface of MCM-41 mesoporous material. The catalyst showed to be highly active in the enantioselective hydrogenation of \(\alpha\)-(acetylamino)cinnamic acid.

Key words: mesoporous materials, MCM-41, Rhodium complex, enantioselective catalyst, hydrogenation, cinnamic acid

INTRODUCTION

The optically active rhodium complexes have been widely reported as efficient catalysts for a broad range of organic reactions [1, 2]. Rhodium complexes of 1,2-diphosphino ligands which have been used for asymmetric hydrogenation of N-acyldehydroamino acids have been known for 30 years. Brown [3] and Landis [4] have used either Dipamp:
(R,R)-1,2-ethanediylbis[(o-methoxyphenyl)phenylphosphine] [5] or Chiraphos: (S,S)-2,3-bis(diphenylphosphino)butane [6] complexes as catalysts for clarifying the mechanism of this reaction. Nagel [7] has synthesized new optically pure 3,4-bis(phosphanyl)pyrrolidine ligands. The rhodium complexes have been used as catalysts for the hydrogenation of cinamic acid and its methyl ester and unfunctionalized ketones. Their catalytic activity strongly depends on the ligands structure: those bearing phenyl groups axial and methyl groups equatorial, give higher optical yields than their counterparts with methyl groups axial and phenyl groups equatorial.

With the success and diversity of chiral 3,4-bis(phosphanyl)pyrrolidine catalysts in enantioselective homogeneous phase, attention has also been turned to the development of heterogenized systems which may be of significant industrial interest. The problems associated with the recovery of homogeneous catalysts, their separation from the reaction products [8] and the difficulties associated with the recycling of the catalytic species have in part been addressed by immobilization on a heterogeneous solid support such as polymers or silicas [9]. Mesoporous material MCM-41 is suitable for use as catalyst support because it possesses large pores, controllable narrow pore-size distribution and high surface area. The pore size allows passage of large molecules such as organic reactants and metal complexes through the pore to react to the surface of the channel [10]. Crosman et al. realized a very straightforward for immobilizing rhodium diphosphine complexes on aluminated SBA-15. New heterogeneous chiral catalysts showed high activities and excellent chemo- and enantioselectivities during the hydrogenation of different prochiral olefins [11]. The immobilization of the rhodium complexes within sol-gel materials allows a better and easier separation of these catalysts from solution and facilitates their reuse, which greatly improves the productivity of the catalyst. Different mesoporous silica materials were used as support materials in order to adapt the catalyst to the substrate of the reaction [12, 13]. The hydrogenation of itacinic acid and its derivates was carried out with sol-gel building agent entrapped Rh/BPPM catalysts in methanol solutions. About 90–99% enaniomeric excess (e.e.) were achieved for the hydrogenation of itacinic acid to (S)-(−)-2-methyl succinic acid [14].

The research in this paper was focused on the use of immobilized 3,4-(R,R)-bis(diphenylphosphino)pyrrolidine rhodium complex for enantioselective hydrogenation of α-(acetylamino)cinnamic acid.

**EXPERIMENTAL PART**

In order to characterize the activity and stability of supported rhodium complex the experiments were performed in different conditions – a batch reactor and a stream reactor.

In the case when hydrogenation was carried out in a stream reactor, the catalyst was placed in a reactor in Ar atmosphere. H₂ pressure was 85 bar at room temperature, flow speed – 0.5 ml/min, substrate – 0.1 M α-(acetylamino)cinnamic acid in MeOH, catalyst – 1 g MCM-41 and 0.01 g rhodium complex. The experiment was carried out for 150 h.
A part of experiments were performed in a stainless-steel autoclave with a volume 80 ml as a batch reactor. The substrate (0.564g) dissolved in 40ml MeOH and the catalyst (1g MCM-41 and 2.43 μmol rhodium complex) were placed in the autoclave. The autoclave was closed, thoroughly evacuated and flushed at least three times with 1 atm of Ar to ensure a completely oxygen-free environment. The evacuated autoclave was filled with hydrogen (P(H₂) – 25 atm, temperature 25°C) and the reaction started with rapid stirring.

In all cases the quantitative hydrogenation was confirmed using a ^1H NMR spectrum. The products of reaction were analyzed by GC. The optical yield was determined by comparison with the specific rotations of the pure enantiomers [(S)-N-acetylphenylalanine, [α]_D²² = 47.4.

RESULTS AND DISCUSSION

The supported catalyst was tested for enantioselective hydrogenation of α-(acetylamino)cinnamic acid in methanolic solution to (S)-N-acetylphenylalanine (Scheme 1).

Scheme 1. Enantioselective hydrogenation of α-(acetylamino)cinnamic acid to (S)-N-acetylphenylalanine over [3,4]-bis(diphenylphosphino)pyrrolidine-P,P’](1,5-cyclooctadien)rhodium complex – MCM-41.

In the stream reactor, at the beginning of the reaction the conversion was about 95–96% and the optical yield was 93.04% enantiomeric excess (e.e.) (Figs. 1 and 2). During the hydrogenation conversion remained comparatively constant ~ 97% and the optical yield remained up to 94.0%.

Figure 1. Enaniomeric excess (%) of (S)-N-acetylphenylalanine
In the batch reactor up to 98.28 % e.e. was achieved. The catalyst was reused three times and after every run it was washed with MeOH and COD. The activity of the catalyst was preserved high during the runs (Table 1). A substrate/catalyst ratio of 1000:1 was used. In all cases MeOH was used as a solvent. Previous investigations have shown that MeOH is a better environment than CH₂Cl₂ for this reaction [15].

**Table 1. Hydrogenation of α-(acetylamino)cinnamic acid.**

<table>
<thead>
<tr>
<th>Catalyst Run</th>
<th>Turnover (%)</th>
<th>ee(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>98.28</td>
<td>96.56</td>
</tr>
<tr>
<td>2-1</td>
<td>96.72</td>
<td>93.44</td>
</tr>
<tr>
<td>2-2</td>
<td>90.25</td>
<td>80.50</td>
</tr>
<tr>
<td>2-3</td>
<td>89.51</td>
<td>79.02</td>
</tr>
<tr>
<td>3-1</td>
<td>96.31</td>
<td>92.62</td>
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<tr>
<td>3-2</td>
<td>91.17</td>
<td>82.34</td>
</tr>
<tr>
<td>3-3</td>
<td>91.13</td>
<td>82.26</td>
</tr>
</tbody>
</table>

Solvent – MeOH 40 ml; p(H₂) = 25 atm.; T = 25°C; substrate α-(acetylamino)cinnamic acid; molar ratio substrate : catalyst = 1000 : 1.

In the rhodium complex of optically active diphosphines, the conformation of the chelating ligand determines the prevailing product configuration. Normally λ-chelate gives the (S)-enantiomer and a δ-chelate the (R)-enantiomer. Each phosphorous atom in the rhodium complex was attached with two phenyl groups. In the square-planar rhodium complex the equatorial phenyl groups control the stability of the diastereomeric substrate complexes. The axial groups have a little influence. In the octahedral dihydrido complex the axial phenyl groups dominate with their influence on the stereochemistry. The axial phenyl groups direct the reaction, during hydrogen activation, in the opposite sense com-
pared with that of the equatorial phenyl groups – substance equilibrium. This is expected because the handedness of the chiral array of the two axial groups is opposite to the array of the two equatorial groups.

CONCLUSIONS

The results obtained using the catalyst supported on MCM-41 indicate that the structure of the solid support does not influence the activity of the catalyst. The new supported catalyst possesses high catalytic activity for enantioselective hydrogenation of α-(acetylamino)cinnamic acid and we have demonstrated that it has a long life span, and it could be used more than once with good optical yields.

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REFERENCES


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