

Immobilized Catalysts for Asymmetric Hydrogenation

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Introduction

In a regulatory environment of ever-increasing stringency, extremely high selectivity is required during production of chiral chemical ingredients to maximize purity levels. To achieve the required selectivity, industry has to date relied heavily on homogeneous catalysts.¹ These homogeneous catalysts are by definition soluble in the reaction medium, and thus difficult to remove from liquid reaction products. This creates significant product contamination and catalyst cost issues. The pharmaceutical industry has sought to immobilize homogeneous catalysts by attaching them to solid support materials, so that they can be easily removed from reaction products and reused. At the same time, the immobilized catalyst must maintain the expected catalytic performance. Available supported technologies always show decrease activity or selectivity because of electronic and steric changes to the ligand system due to the chemical modification.^{2,7} In this study we designed new kind of immobilized catalyst, named "Kite-String" immobilized chiral catalyst, which showed high activity and enantio-selectivity comparable to its homogeneous counterpart.

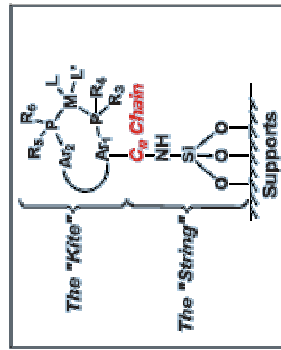


Figure 1. the schematic picture of "Kite-String" immobilized catalyst

Most of the chiral catalysts which include aromatic groups in their ligand structure can be immobilized through this technology.

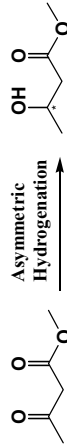
Materials and Methods

Silica surface was modified by special functional groups at first, then (S-) or (R)-Ru(BINAP)Cl₂ was immobilized on silica surface through one step reaction

Results and Discussion

These immobilized catalysts showed 99.00% of ee and 95.98% of conversion in asymmetric hydrogenation of methyl acetoacetate by 3 times recycle. Almost no metal leaching is detectable.

Table 1. Hydrogenation of methyl acetoacetate



Catalyst	Cat. Config.	H ₂ Pressure (psi)	Temp. (°C)	Time (h)	Conv. ^d (%)	ee% ^d
Homo ^a	S	60	100	6	100	98
Homo	S	1,500	25	40	100	99
Homo	R	1,500	25	40	100	99
Homo	R	1,500	100	0.5	100	99
Kite-1, 1 st cycle	S	1,000	100	2	84.23	99
Kite-1, 1 st cycle	S	1,000	100	2	96.45	99
Kite-2, 1 st cycle	S	1,000	100	4	83.39	99
Kite-2, 2 nd cycle	S	1,000	100	6	95.86	99
Kite-2, 3 rd cycle	S	1,000	100	6	95.98	99
Kite-2, 4 th cycle	S	1,000	100	6	95.59	99
Adding K ₂ CO ₃						

^aHomo represent homogeneous(S)- or (R)-Ru(BINAP)Cl₂ catalyst. ^bKite-1 catalyst prepared by first immobilizing BINAP ligand on silica and then adding metal salt RuCl₃·nH₂O. ^cKite-2 catalyst prepared through direct reaction between surface-modified silica and Ru(BINAP)Cl₂. ^dDetermined by HPLC using AGP column.

The advantages of this technology are in three aspects: (1) the active center (the "Kite") is attached to the support by an organic "string". The length, strength and structure of this organic "string" can be adjusted to make the active center high accessible by the reactants without dramatically changing the electronic and steric environment of active center, and thus preserves its original high activity and enantioselectivity. (2) Active chiral center is chemically bonded to the support surface so that almost no metal leaching detectable under various conditions. (3) Preparation cost and time are cut down significantly by only one step reaction between the expensive catalyst and the support with surface modified.

References

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