Pergamon

Tetrahedron Letters, Vol. 36, No. 48, pp. 8779-8782, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01874-3

"Molecular Imprinting Effect" in the Synthesis of Immobilized Rhodium Complex *Catalyst* (IRC *cat*)

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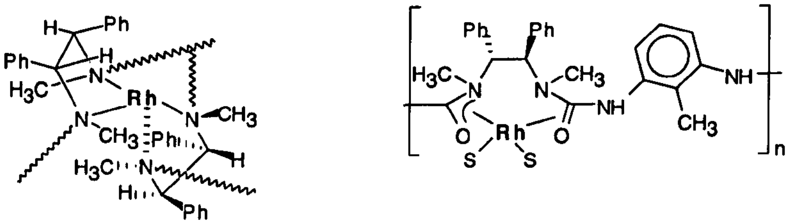
Abstract: a new concept has been tackled with the utilization of a polymerized rhodium complex with an asymmetric catalysic application. Furthermore, this new method of preparing heterogeneous catalyst has allowed to bring to the fore a molecular imprinting effect during the polymerization : an increase of enantioselectivity has been obtained by molecular imprinting.

Since the early 70s[1] the advances made in the field of molecular imprinting have been considerable, especially in the synthesis of material for racemic resolutions[2]. Nevertheless, few works are dealing with the use of such materials for their catalytic activity especially in the field of enantioselective synthesis. Main results are obtained by miming enzymes or abzymes, for example by printing a transition state analogue of hydrolysis. So, Shea and Mosbach[3] have reported imprinted polymers with enantioselective activity in the hydrolysis of *D,L*-aminoesters. Akermark[4] have reduced regioselectively steroid 3- and 17-ketones using $LiAlH_4$ activated templated polymers.

From the seminal work of Kagan and Stille,[5] interest in new methods for the preparation of supported catalysts is still growing. We wish to use " Molecular Imprinting effect" to reach highly enantioselective catalytic reaction. Recently, we reported[6] the utilization of a rhodium(I) complex deposited on chiral polymers in hydride transfer reduction of acetophenone. We develop here a new method for the preparation of heterogeneous asymmetric catalysts (Scheme 1 with a chlorine atom instead of a phenylethoxy group).[7a] It consists of immobilizing a preformed [rhodium(I)-(*N,N'*-dimethyl-1,2-diphenylethane diamine **1**)$_2$] complex by polyaddition with a mixture of di and triisocyanate. Then this new material could be used as catalyst in hydride transfer reduction. It has to be noted that with deposited rhodium on chiral polymer, opposite enantiodifferentiation was obtained which can be explained by a distinct complexation of rhodium (Figure 1). When the catalysts were obtained by deposition of rhodium(I) on a poly(urea) synthesized beforehand, the low mobility of the polymer chains allows the coordination of only two nitrogen atoms to the metal.



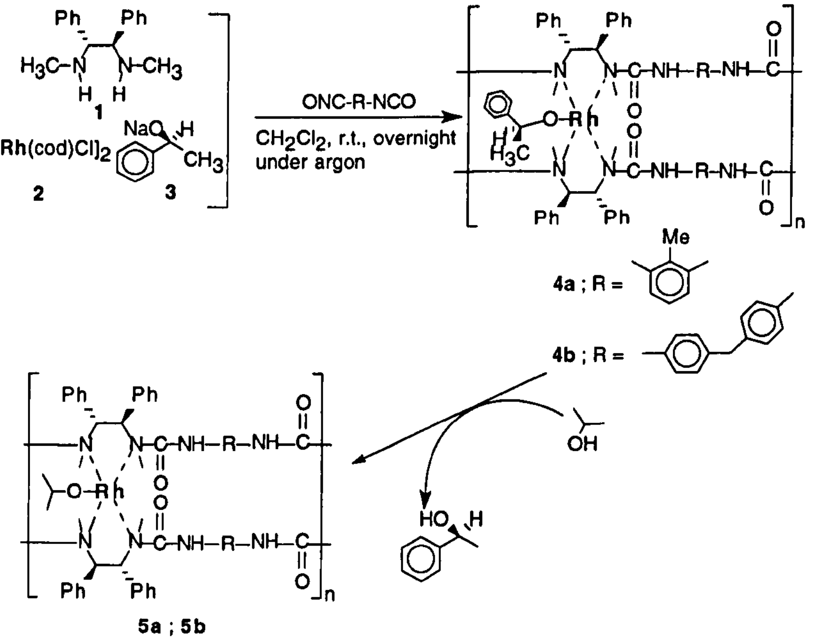
Polymerized rhodium complex

Deposited rhodium on poly(urea)

Figure 1 : Proposed structures for heterogeneous catalysts

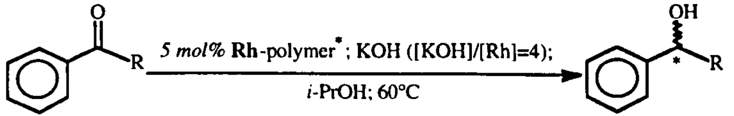
This new catalyst preparation allows us to polymerize the chiral rhodium complex in the presence of optically pure 1-(*S*)-phenylethanol as template[7b] in order to increase enantioselectivity. Scheme 1 describes the principle : [bis(diamine **1**)-rhodium] catalyst is prepared in a dichloromethane solution of sodium 1-(*S*)-phenylethanolate **3**. This complex is polymerized by addition of diisocyanate. The imprinted polymer **4** is washed with an excess of 2-propanol in order to eliminate the template (the elimination is monitored by GC on a chiral Cydex B *SGE* column, 25m x 0.25 mm Ø with the other enantiomer as internal reference). The polymer **5** is dried and used in hydride transfer reduction.

Scheme 1



Comparison between the homogeneous catalysis and the immobilized rhodium complex is summarized in Table 1. In homogeneous phase diamine **1** with (*R*,*R*) configuration leads to 55% enantiomeric excess (e.e.) of 1-(*S*)-phenylethanol (entry 1). Polymerized (*R*,*R*) rhodium complex (entry 2) allows a lower selectivity of the same enantiomer to that observed in homogeneous phase. We have proposed[8] a [bis(diamine **1**)-Rh] complex in the catalytic cycle for the homogeneous phase. In the case of polymerized complex, we assume that we polymerized a rhodium complex close to this working in homogeneous phase (Figure 1). Without template (entry 2), acetophenone reduction leads to 33% e.e. of 1-(*S*)-phenylethanol. The polymerized [bis-((*R*,*R*)-diamine **1**)-1-(*S*)-phenylethoxy-rhodium] complex allows an increase of 10% e.e. in imprinted alcohol whereas the utilization of [bis-((*R*,*R*)-diamine **1**)-1-(*R*)-phenylethoxy-rhodium] complex shows a light decrease of it (entries 3 and 4). This result may be close to a molecular imprinting effect.

Table 1 : Utilization of an imprinted polymerized rhodium complex[9]



Entry	Polymer*	R	Catalyst	Inductor Config.	Conversion (%)	Time (day)	e.e. (%)[a] (Config.)
1	diamine **1**	CH_3	Homogeneous	(*R*,*R*)	100	3.5	55 (*S*)[b]
2	**5a**	"	Heterogeneous : Polymerized Complex	(*R*,*R*)	44	1	33 (*S*)
3	**5a**	"	(*S*) Templated polymerized complex	(*R*,*R*)	42	1	43 (*S*)
4	**5a**	"	(*R*) Templated polymerized complex	(*R*,*R*)	40	1	30 (*S*)
5	**5b**	"	Polymerized complex	(*S*,*S*)	98	1	25 (*R*)
6	**5b**	"	(*R*) Templated polymerized complex	(*S*,*S*)	89	1	43 (*R*)
7[c]	**5b**	C_2H_5	Polymerized complex	(*S*,*S*)	96	6	47 (*R*)
8[c]	**5b**	"	(*R*) Templated polymerized complex	(*S*,*S*)	91	9	66 (*R*)

[a] The enantiomeric excesses are determined by GC with a maximum error of 0.6%. [b] 55% e.e.of (*R*)-phenylethanol is obtained with (*S*,*S*)-diamine. [c] reduction realised at 25°C.

The best effects were obtained when a commercial mixture of di and triisocyanate is used for polyaddition. The cross-linked rigid polymer synthesized in that way permits an increase of 18% e.e. in the case of acetophenone reduction (entries 5 and 6). In order to determine the versatibility of our material, we have reduced with the same polymer **5b**, propiophenone which is sterically close to acetophenone. A similar increase of 19% e.e. between unimprinted and imprinted polymer is observed (entries 7 and 8). On the other hand, no gain of enantiomeric excess is observed in the reduction of 4'-trifluoromethylacetophenone (23% e.e.) with only 28% conversion in 14 days which indicates that the imprint effect is only observable with substrates having a structure closely related to the imprinted molecule.

In conclusion, we have shown that it is possible to imprint an optically pure rhodium complex in an organic matrix and to use the heterogeneous catalyst in asymmetric catalysis with an obvious template effect. This new methodology may lead to an improvement of the usefulness of enantioselective heterogeneous catalysis. Further experiments on using these new materials are under investigation.

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7. (a) The polymerized complex was prepared as below but without template.

   (b)*Typical procedure for imprinted polymerized rhodium complex synthesis* : in a round bottom flask under an inert dry atmosphere of argon, 750 mg (3.12 mmol) of (1*S*,2*S*)-*N*,*N'*-dimethyl-1,2-diphenylethane diamine **1** are dissolved in 4 mL of dichloromethane freshly distilled from P_2O_5. 78 mg (0.32 mmol) of catalytic precursor ($[Rh(C_8H_{12})Cl]_2$) are added and the solution is stirred.

   Preparation of sodium 1-phenylethanolate **3** : 9 mg (0.33 mmol) of NaH 98% are introduced in a second round bottom flask. Then, 1.5 mL of dichloromethane freshly distilled from P_2O_5 and 36 µL (0.3 mmol) of optically pure (*R*)-1-phenylethanol are added. This solution is stirred one hour before being introduced in the flask containing the rhodium complex. After 2 hours stirring, a solution of 1.08 g (4.32 mmol) of a commercial mixture of di and triisocyanate (diphenylmethane diisocyanate, *MERCK*, Art. 820797; diisocyanates : 65%, triisocyanates : 30%) in 1.5 mL of dichloromethane is added. The polyaddition is exothermic. The solution was stirred overnight at room temperature. The solvent is evaporated and the polymer is crushed and washed with 500 mL of 2-propanol during 24 hours. Finally, it is filtered through a *Millipore* filter (vv type, pore size 0.10 µm) and dried.
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9. *Typical procedure for heterogeneous hydride transfer reduction* : polymerized complex (35 mg; 6 10^{-3} mmol of rhodium that is *5 mol%*) is dried under vacuum during 3 hours. Then 2 mL of a 1.3 10^{-2} mol.L^{-1} potassium tert-butoxide solution in 2-propanol is added under an inert atmosphere of argon. 15µL (0.11 mmol) of substrate is introduced with a syringe. Conversion and enantiomeric excess are monitored by GC. The different experiments are performed 5 times.

(*Received in France* 30 *June* 1995; *accepted* 29 *September* 1995)