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Heterogeneous Enantioselective Dihydroxylation of Aliphatic Olefins: A Comparison Between Different Polymeric Cinchona Alkaloid Derivatives

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Abstract:Two new polymeric cinchona alkaloid derived ligands were synthetized and used in the asymmetric dihydroxylation of aliphatic olefins, obtaining for the first time in the reaction performed in the heterogeneous phase enantioselectivity up to 88%.

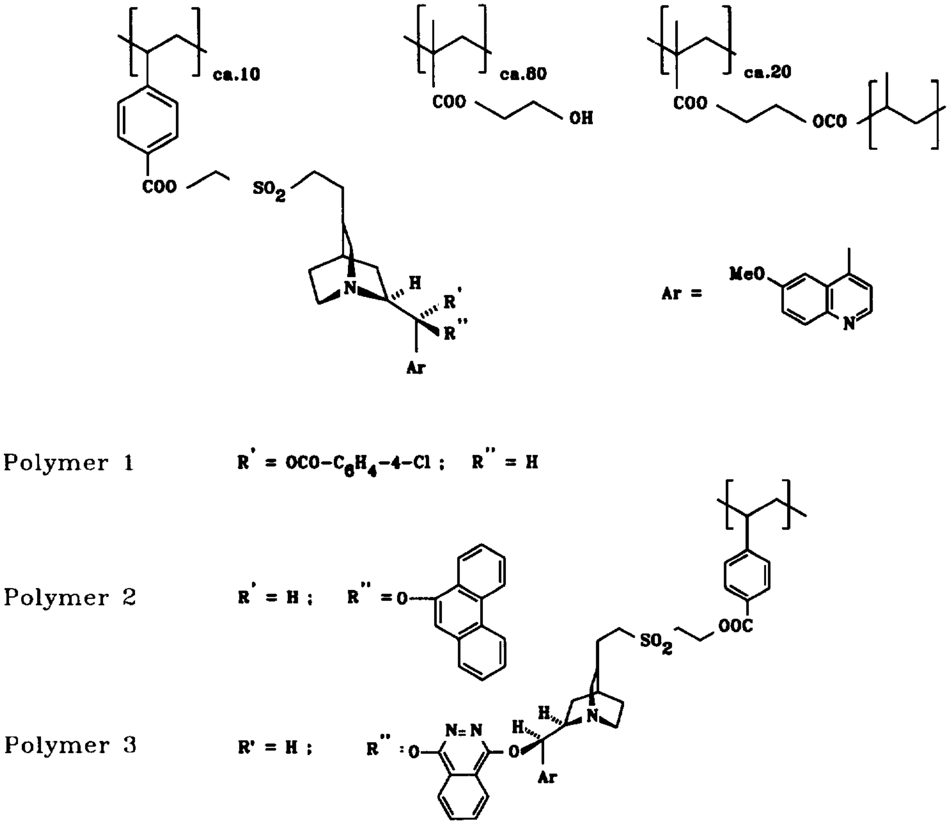
The asymmetric cis dihydroxylation of olefins in the homogeneous phase has been improved steadily in the recent years thanks to the development of more effective cinchona alkaloid derived ligands, reported by the Sharpless group[1].

Attempts to employ polymer bound alkaloid derivatives in the heterogeneous dihydroxylation reaction conditions have been made in order to improve the convenience and economy of the process[2]. Up to date, very promising results were obtained by using as substrates aromatic olefins with different polymeric supports; on the contrary with the mono and di-substituted aliphatic olefins poor enantiomeric excesses were observed.

We have recently reported[3] the synthesis and use of crosslinked polymer **1**, containing 4-chlorobenzoate of quinine, spaced from the main polymeric chain, which provided in a heterogeneous process diols with e.e. comparable to those obtained by the homogeneous reaction conditions, expecially with aromatic olefins.

In the continous effort to further improve the enantioselectivity in the asymmetric dihydroxylation of aliphatic olefins, we have synthetized the polymeric ligands **2** and **3**, containing respectively the phenantryl ether of dihydroquinidine and 1,4-bis-(dihydroquinidinyl)phtalazine, spaced from the main polymeric chain by the same spacer group used for the polymer **1**[4].

We have tested the discriminating power at the corresponding polymer supported catalysts in the reaction with two aliphatic olefins, 1-decene and 5-decene, used as reference substrates and which previously gave[2f] very low enantiomeric excess.



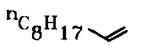
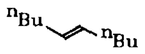
Polymer 1 $R' = OCO-C_6H_4-4-Cl$; $R'' = H$

The polymer **2** and **3** were obtained by radical copolymerization of the cinchona alkaloid derived monomers[5] with hydroxyethyl methacrylate, using ethylene glycol dimethacrylate as crosslinking agent. These polymers were continously extracted with acetone and methanol to avoid the presence of non reacted chiral monomers or soluble chiral oligomers and then characterized by elemental analysis.

As we have already noted[3], these polymers contain free alcoholic pendent groups that enable them to swell very well in polar protic solvents used for the asymmetric dihydroxylation.

The enantiomeric excesses obtained with the new polymeric ligands **2** and **3** are reported in Table and compared with those obtained by using polymer **1**[3].

Table : Enantiomeric Excesses[a] (%e.e.) Obtained Using Polymers 1-3

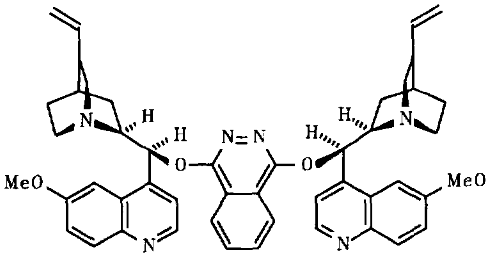
olefin	Polymer 1	Polymer 2	Polymer 3
	50	60	70
	75	88	86

[a] The asymmetric dihydroxylation runs were carried out as described in ref.3., using $K_3Fe(CN)_6$ as secondary oxidant in $^tBuOH:H_2O$ 1:1 as solvent. The chemical yields of the diols were 68-80%. The e.e.'s were measured using NMR analysis (200 MHz) of the bis MTPA esters of the diols. The configuration of the resulting diols are S (S,S for decane-5,6-diol), when using polymer 1 containing a quinine derivative, and R (R,R for decane-5,6-diol) when using polymers 2 and 3 containing quinidine derivatives.

Both with mono and disubsituted aliphatic olefins a significant improvement in the extent of enantioselectivity was observed. By using polymer 2 and 3, we have reached 70 % of e.e. with the terminal olefin and of 88% with the internal one.

Polymers 1-3 were recycled three times and used in the same reaction conditions, obtaining reactivities and enantioselectivities comparable to those observed in the first run.

Should be noted that we have also tried to polymerize the chiral ligand 4 directly with ethylene glycol dimethacrylate in toluene at 80°C for 50 hours, using AIBN as radical initiator.



4

After repeated extraction of the crude material with acetone, a white solid was obtained with only 15% yield which was used in the asymmetric dihydroxylation of *trans*-stilbene, obtaining a product with high e.e. (≥98%). Nevertheless, the U.V. spectrophotometric analysis of the polymer washings, examined time to time after prolonged extraction time (until 7 days), showed a significant absorption maximum corresponding to the chiral monomer. So we concluded that, due to the high percentage of the crosslinking agent, the monomer was not completely bounded to the polymeric matrix but in some extent absorbed in the swelled polymer. Indeed we were afraid that the reaction can occur, at least in part, in the homogeneous phase, making this polymeric material not proper to be used as heterogeneous catalytic precursor.

In conclusion we have demonstrated that in the heterogeneous asymmetric dihydroxylation of olefins it is important to use either a suitable polymeric support or the "best substituent" on the alkaloid moiety, in order to obtain high enantiomeric excesses.

Further studies are in progress to optimize the experimental reaction conditions in order to use the heterogeneous process for large scale synthesis.

REFERENCES AND NOTES

1. (a) Sharpless, K. B.; Amberg, W.; Beller, M.; Chen, H.; Hartung, J.; Kawanami, Y.; Lübben, D.; Manoury, E.; Ogino, Y.; Shibata, T.; Ukita, T. *J. Org. Chem.* **1991**, *56*, 4585. (b) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.S.; Kwong, H.L.; Morikawa, K.; Wang, Z.M.; Xu, D.; Zhang, X. L. *J. Org. Chem.* **1992**, *57*, 2768. (c) Crispino, G. A.; Jeong,K.S.; Kolb, H. C.; Wang, Z.M.; Xu, D.; Sharpless, K. B. *J. Org.Chem.* **1993**, *58*, 3785.
2. (a) Pini, D.; Rosini, C.; Nardi, A.; Salvadori, P. *Fifth IUPAC Symposium On OrganometallicChemistry Directed Towards Organic Synthesis*, Abstracts PS1-67, Florence (ITALY), October 1-6, **1989**.(d) Kim, B. M.; Sharpless, K. B. *Tetrahedron Lett.***1990**, *31*, 3003. (c) Pini, D.; Petri, A.; Nardi, A.; Rosini, C.; Salvadori, P. *Tetrahedron Lett.* **1991**, *32*, 5175. (d) Lohray, B.B.; Thomas, A.; Chittari, P.; Ahuja, J. R.; Dhal, P. K. *Tetrahedron Lett.* **1992**, *33*, 5453. (e) Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron: Asymmetry* **1993**, *4*, 2351. (f) Lohray, B.B.; Nandanan, E.; Bhushan, V. *Tetrahedron Lett.* **1994**, *35*, 6559.
3. Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron* **1994**, *50*, 11321.
4. It was noted[6] that quinine derivatives employed as chiral catalysts in the asymmetric dihydroxylation of olefins gave a lower e.e. (~10%) than the corrisponding quinidine derivatives.
5. The chiral spaced monomers were synthetized following the same reaction scheme as that reported[3] for the synthesis of the monomer containing the 4-chlorobenzoate group. The quinidine derivatives were prepared following the experimental procedure reported by Sharpless[7].
6. Jacobsen, E.N.; Marko', I.; Mungall, W.S.; Scroeder, G.; Sharpless, K.B. *J.Am.Chem.Soc.* **1988**, *110*, 1968.
7. Amberg, A.; Bennani, Y.L.; Chadha, R.K.; Crispino, G.A.; Davis, W. D.; Hartung, J.; Jeong, K.; Ogino, Y.; Shibata, T.; Sharpless, K.B. *J. Org. Chem.* **1993**, *58*, 844.

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