Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 897–900

TETRAHEDRON:
ASYMMETRY

Use of heterogenized dialdimine ligands in asymmetric transfer hydrogenation

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Received 17 December 1997; accepted 12 February 1998

Abstract

Heterogenized dialdimine ligands complexed to iridium were tested in the asymmetric transfer hydrogenation of acetophenone. E.e.s of up to 70% were achieved but the recycling was unsatisfactory. When such ligands were used in asymmetric epoxidation of styrene, a modest e.e. of 15% was achieved. © 1998 Elsevier Science Ltd. All rights reserved.

Nowadays, due to their availability, lower cost and toxicity, the use of chiral dinitrogen ligands is of increasing interest in asymmetric synthesis. As examples, chiral bisoxazolines chelated to rhodium or iridium were efficient for hydrosilylation or reduction of ketones; chelated to copper, they have been used for asymmetric cyclopropanation of styrene with alkyl diazoacetates. Bisoxazoline palladium complexes have been used as enantioselective catalysts for allylic nucleophilic substitution.[1] We have developed the use of chiral diamines complexed to rhodium, iridium and even cobalt for asymmetric reduction of C=C or C=O bonds.[2] Jacobsen developed the use of chiral bis(salicylidene)ethylenediamine manganese complexes in the asymmetric epoxidation of cis double bonds.[3] Similar aldiminato–cobalt complexes allowed borohydride reduction of ketones with high enantiomeric excess.[4] Our interest in preparing configurationally heterogenized ligands prompted us to synthesize polymerizable dialdimine ligands from hydroxy or dihydroxy benzaldehyde. Copolymerization with styrene and divinylbenzene (DVB) and their use in asymmetric iridium-catalyzed transfer hydrogenation or manganese-catalyzed epoxidation will be discussed.

Polymerizable ligands were synthesized by reacting 4-chloromethylstyrene with 4-hydroxybenzaldehyde or 2,4-dihydroxybenzaldehyde, and then the diimine was obtained after condensation with the enantiomerically pure (1R,2R)-cyclohexanediamine (Scheme 1).[5] Modest non-optimized global yields of 30–40% were achieved.

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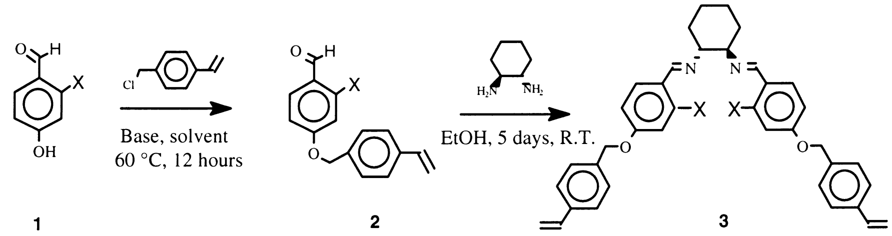
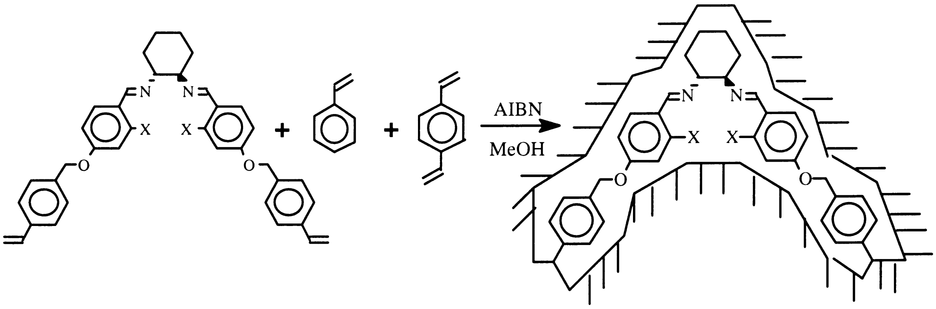
PII: S0957-4166(98)00067-6



a : X= H
b : X= OH

Scheme 1. Synthesis of dialdimine ligands

Table 1
Preparation of polymerized diimine[6]



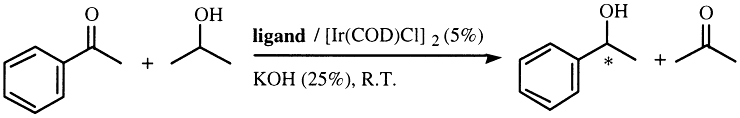
Polymer	Diimine	Styrene/3	DVB/3	Degree of crosslinking (%)(a)	Yield (%)
4	**3a**	11	0	15	75
5	**3a**	0	9	100	88
6	**3a**	4.5	4.5	71	56
7	**3b**	4.5	4.5	71	70

(a) degree of crosslinking = (2nDVB + 2n'diimine)/(2nDVB + 2n'diimine + n"Styrene)

The monomers **3a** and **b** were then copolymerized with various quantities of styrene and/or divinylbenzene in order to prepare polymers with different degrees of crosslinking. These polymers were obtained in reasonable yields (Table 1).

These ligands were first tested for the asymmetric reduction of acetophenone with iso-propanol as the hydride source. As the iridium gave the better results in terms of conversion and enantioselectivity we focussed only on this metal (attempts to realize the reduction with cobalt or ruthenium-based catalysts were unsuccessful). The influence of the polymeric nature and the recycling of the catalyst were evaluated. Amazing increases of enantioselectivity were achieved using the polymerized diimine compared to the homogeneous ligand (entries 1 and 4, Table 2). In addition, this higher selectivity was not observed when the complex was prepared previously before the addition of the substrate (entries 2 and 3): lower enantioselectivity, similar to that obtained in homogeneous conditions, was achieved. Probably different active species are involved.

Table 2
Catalytic hydrogen transfer reduction of acetophenone[a]



Entry	Ligand	Time (h)	Conversion (%)	e.e. (%) (conf)
1	monomer **3a**	18	95	22 (S)
2	polymer **4** (b)	18	95	57 (S)
3	polymer **4** (b,c)	18	90	23 (S)
4	polymer **4**	7	97	55 (S)
5	polymer **6**	7	90	70 (S)
6	polymer **5**	7	95	64 (S)
7	polymer **6** (d)	7	95	63 (S)
8	polymer **6** (d,e)	7	18	44 (S)
9	polymer **7**	7	46	21 (S)

a) In a typical experiment, iridium precursor, ligand (ligand/metal = 2), KOH, iPrOH and the substrate were mixed together under argon atmospher. Conversion and e.e. were determined by G.C. analysis (SGE Cydex B column) ; b) ligand/metal = 1 ; c) the polymer and the metallic precursor were mixed together overnight in solution of KOH in iPrOH before the addition of acetophenone d) ligand/metal = 10; e) recycled catalyst.

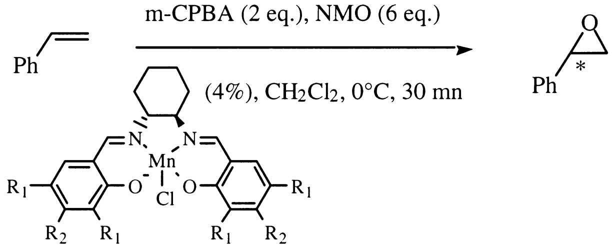
From the influence of the nature of the polymer it is clear that there is an effect due to the degree of crosslinking: when it increased from 15% to 71% (entries 4 and 5) a higher enantiomeric excess was observed. However the rise in the degree of crosslinking from 71 to 100% gave no significant difference (entries 5 and 6).

The test of the catalyst recycling was performed with a ligand to metal ratio of 10 to 1, as this ratio affects neither the conversion nor the enantioselectivity (entries 5 and 7). The catalyst was carefully separated from the reaction mixture and reused in a new reaction (entries 7 and 8). Unfortunately we noticed an important loss in activity and a lower enantiomeric excess. It seems that there is partial leaching of the metal in solution. We are not able at the moment to improve the stability of the heterogenized complex.

As the best result in terms of conversion and enantioselectivity was obtained with the **3a**-based polymer prepared with a 71% degree of crosslinking (polymer **6**, entry 5), we prepared a similar polymer starting from ligand **3b** (polymer **7**). Unfortunately, lower conversion and enantioselectivity were achieved (entry 9). Therefore we decided to test this ligand **3b** and its polymerized analogue **7** in manganese-catalyzed asymmetric epoxidation of styrene as done recently with a similar compound.[7] A combination of m-chloroperbenzoic acid and N-methyl-morpholine-N-oxide was chosen as the oxidation system (Table 3).[8]

These preliminary results showed that lower conversion and enantioselectivity were obtained using the ligand **3b** compared to the Jacobsen's ligand. Low improvement of the enantioselectivity was achieved using the heterogenized ligand **7**. The same value was described in a recent work using an analogous polymeric catalyst.[7] The design of the ligand has to be improved in order to obtain better results in heterogeneous conditions and to recycle the catalyst.

Table 3
Asymmetric epoxidation of styrene



Entry	R_1	R_2	conversion (%)	e.e. (%) (conf.)	Remark
1	t-Bu	H	95	40 (R)	Jacobsen's catalyst
2	H	OR	32	10 (R)	homogenous
3	H	OR	32	15 (R)	heterogeneous

Nevertheless, this work showed that it is possible to prepare easily polymerizable imines and to use such polymers in asymmetric reduction or oxidation reactions even if the structures of the monomers have to be optimized in order to increase the enantioselectivity of the reactions.

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6. Typical experiment (polymer **6**): In a flask containing 15 mg of AIBN, a solution of 100 mg of **3a**, 93 µL of styrene and 145 µL of divinylbenzene were added. The flask was flushed with argon, then it was closed and the polymerization was carried out at 50°C for 48 h. The solvent was removed in vacuo and the polymer was crushed, washed twice with isopropanol (30 mL) and dried in vacuo (m=160 mg, 56% yield).
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