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New Polymer Supported Cinchona Alkaloids for Heterogeneous Catalytic Asymmetric Dihydroxylation of Olefins

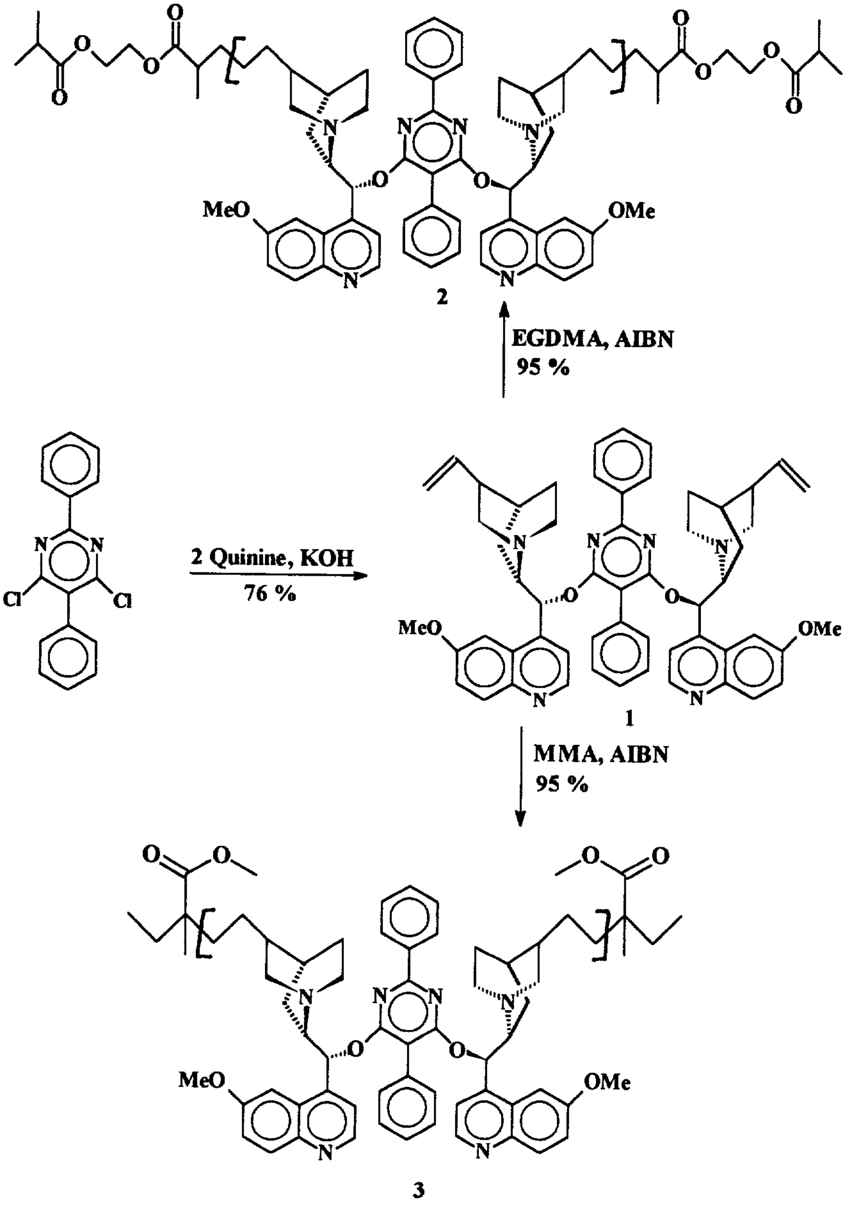
E. Nandanan, A. Sudalai* and T. Ravindranathan*

Division of Organic Chemistry: Technology
National Chemical Laboratory, Pune-411 008, INDIA.

Abstract: *Two new polymeric cinchona alkaloid derived ligands were synthesized and utilized in the asymmetric dihydroxylation of olefins, exhibiting high enantioselectivities in the case of aliphatic terminal olefins under heterogeneous phase.* © 1997 Elsevier Science Ltd.

Sharpless catalytic asymmetric dihydroxylation (ADH) of olefins using catalytic amounts of osmium tetroxide in the presence of cinchona alkaloid derivatives, leading to a wide variety of enantiomerically pure vicinal diols, has become one of the most useful and reliable organic reactions.[1] Further, to explore the possibility of recycling both the expensive OsO_4 and the chiral ligand, a variety of polymer bound cinchona alkaloid derivatives have been employed.[2] However, most of the polymers required complicated synthetic manipulations and their catalytic efficiency was, usually, not sufficient for practical purposes, especially in the case of aliphatic terminal olefins. Thus, the development of synthetically simple and efficient polymers for heterogeneous ADH of aliphatic terminal olefins is strongly needed. It has been well established that bis-cinchona alkaloid substituted pyrimidine ligands were known to give improved enantioselectivity in the ADH of monosubstituted terminal olefins under homogeneous conditions.[3] In this paper, we describe the synthesis of two new polymers **2** & **3** and their improved catalytic activity in the heterogeneous catalytic ADH of terminal olefins.

The chiral monomer, **1**, was prepared by the condensation reaction of 2,5-diphenyl-4,6-dichloropyrimidine with quinine in 78 % yield.[4] The polymers **2** and **3** were obtained by radical copolymerization of the cinchona alkaloid derived monomer **1** with ethylene glycol dimethacrylate (EGDMA) and methyl methacrylate (MMA) respectively,[5] [Scheme-1]. These polymers were continuously extracted with acetone and methanol to avoid the presence of any unreacted chiral monomer,**1**, or soluble chiral oligomers and characterized by elemental analysis. The nitrogen analysis of copolymers **2** and **3** confirmed approximately 11 and 10 mole % incorporation of monomeric alkaloid **1** respectively.



Scheme 1

The heterogeneous catalytic ADHs were carried out using copolymers **2** and **3** with variety of olefins and the results were summarized in Table **1**. As can be seen from Table **1**, high chemical yields were observed with nearly all olefins studied. Both aliphatic and aromatic olefins, terminal and internal, were screened and the reaction proceeded with good extent of enantioselectivity (84 % in the case of *trans*-stilbene). It is particularly noteworthy that the enantioselectivities and rates of reaction for terminal olefins, the most common and most useful class of olefins, show significant improvement. By using polymer **2**, we have reached 76 % ee with the aliphatic olefins. It is reasoned that these polymers **2** and **3** have large pore size and are hydrophilic in nature, It thus facilitates the reactants to penetrate to the catalytic site and allow the reaction to proceed with optimum speed comparable to the homogeneous reaction.

Table **1** : Heterogeneous catalytic asymmetric dihydroxylation of olefins using polymeric cinchona alkaloids **2** and **3**[a]

Entry	Olefin	Polymer	t/h	% Yield[b]	% ee[c]
1	Allyl bromide	2	20	62	61
2	1-Decene	2	20	80	64
3	3,3-Dimethyl-1-butene	2	20	80	76
4	Vinylcyclohexane	2	20	78	67
5	Styrene	2	12	92	67
		3	12	85	60
6	α-Methylstyrene	2	20	84	52
7	E-Ethylcinnamate	2	34	72	70
8	E-Stilbene	2	24	92	84
		2[d]	72	10	83

(a) molar ratio of olefin : OsO_4 : Polymeric alkaloid = 1 : 0.0025 : 0.005, temp 20 °C, (b) isolated yield after chromatographic purification, (c) % ee was determined by comparison of $[\alpha]_D^{20}$ with literature values.[6, 1a] (d) the polymeric alkaloid **2** was recovered and reused without adding further OsO_4.

The OsO_4-polymer **2** complex was filtered and recycled once in the case of *trans*-stilbene and it was observed that the enantioselectivity of the polymer-OsO_4 complex was almost retained but the catalytic activities were decreased which may be due to the loss of OsO_4 during the filtration (entry-8). In conclusion, we have achieved improved enantioselectivities for the heterogeneous catalytic ADH of aliphatic terminal olefins using copolymers **2** and **3** which can be synthesized more easily and economically. In addition, the polymer**2**-OsO_4 complex exhibited a promising reusability, even though the catalytic efficiency of the recovered polymeric catalyst was decreased. Further, the compatability of the polymer support with the protic polar solvent mixture (*t*-BuOH : H_2O) was increased by increasing the polarity of the polymer backbone.

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4. Preparation of chiral monomer, **1**: A mixture of 4,6-dichloro-2,5-diphenylpyrimidine (290 mg; 1 mmol), quinine (648 mg, 2 mmol) and KOH (560 mg, 10 mmol) in dry toluene (30 ml) was stirred at RT for 10 min. and refluxed for 12 h with the azeotropic removal of water under argon atmosphere. Cooled to RT and water was added to it and extracted with EtOAc. The crude product was purified by flash column chromatography using MeOH : EtOAc (3 :7) as eluant to furnish a pale yellow solid (692 mg; 80 %) m.p. 93-95 °C; IR (Nujol): ν_{max} 2855, 1555, 1516, 1461, 1403 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$):δ 1.2-1.4 (m, 4H), 1.6-1.8 (m, 4H), 2.3 (m, 6H), 2.65 (m, 2H), 3.05-3.3 (m, 6H), 3.98 (s, 6H), 4.9 (m, 4H), 5.65 (m, 2H), 7.0-7.15 (m, 4H), 7.25-7.65 (m, 14H), 8.05 (d, J = 9.2 Hz, 2H), 8.67 (d, J = 5.4 Hz, 2H)); ^{13}CNMR (50 MHz, $CDCl_3$):δ 21.9, 26.4, 27.3, 38.9, 43.1, 56.1, 56.4, 59.1, 76.7, 101.1, 114.8, 117.9, 118.7, 122.3, 126.4, 128.2, 128.6, 129.4, 129.8, 131.2, 131.9, 135.4, 140.7, 143.4, 144.6, 147.2, 158.5, 159.8, 162.5, 166.1; Analysis: Calculated for $C_{56}H_{56}N_6O_4$; C = 76.72 %, H = 6.39 %, N = 9.58 %, Found: C = 76.86 %, H = 6.05 %, N = 9.52 %.
5. Polymerization of chiral monomer to polymer **2**: Radical copolymerization of monomer **1** (220mg, 0.25 mmol) with ethylene glycol dimethacrylate (465mg, 2.25 mmol) using AIBN as initiator was carried out in benzene : MeOH (1 : 1) at reflux temperature for 5 h. The precipitated polymer 2 was filtered and continuously extracted with MeOH and acetone to remove any soluble chiral monomer. Yield: 95 % ; IR (Nujol) :ν_{max} 1731, 1461, 1377, 1120 cm^{-1}; Analysis : Found C = 58.17 %, H = 6.50 %, N = 4.05 %. Similarly polymer **3** was prepared by taking methyl methacrylate (234mg, 2.34 mmol). Yield : 95 %; Analysis: Found: C = 62.25 %, H = 7.04 %, N = 3.95 %.
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