Asymmetric Catalytic Dihydroxylation of Alkenes on Polymer Support: Scope and Limitation**

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Abstract: Osmium catalyzed asymmetric dihydroxylation of alkenes has been reported using dihydroquinidine (DHQD) and dihydroquinine (DHQ) on a polystyrene support. Effect of other oxidants and additives has been examined.

Since the discovery of osmium catalyzed asymmetric dihydroxylation of alkenes in the presence of cinchona alkaloid,¹ several modifications in the reaction conditions² and the structure of the chiral auxiliary³ have resulted in considerable higher optical purity of the vicinal diols. To effectively use this reaction for large scale preparative purposes, the cost and toxicity of osmium tetroxide, recycling of osmium tetroxide and the chiral auxiliary, and the ease of isolation of diols must be taken into consideration. Polymer bound cinchona alkaloids have been used earlier in various heterogeneous catalysis.⁴ Recently, Salvadori *et. al* ⁵ have reported 6-46 % ee of the diols at -15 °C emerging from a reaction using DHQD on a polyacrylonitrile support, whereas Kim and Sharpless ⁶ have examined asymmetric dihydroxylation of *E*-stilbene only. Here, we wish to report the use of DHQD and DHQ on polystyrene support, which furnished diols in high yields (79-87%) and good enantioselectivity (22-85 % ee).



We have prepared a series of copolymers of dihydroquinidine (DHQD) 4-vinylbenzoate derivatives with styrene A and 4-phenylstyrene B⁷ and investigated the catalytic asymmetric dihydroxylation of *trans*-stilbene (Table 1). Among all the polymers examined, the one with 10 % of dihydroquinidine or dihydroquinine loaded on polystyrene backbone proved to be the most effective chiral auxiliary with 1 mole % of osmium tetroxide.^{8,9} An increase in the amount of immobilized alkaloid on the polymer support led to an exponential decrease in the rate and enantiomeric purity of the diols (Table 1, entries

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3-5). Similar observations were recorded with the polymers containing dihydroquinine (DHQ). Interestingly, the reaction carried out with the homopolymer of DHQD 4-vinylbenzoate was found to be exceedingly slow (2-3 d) furnishing only 20 % of the nearly racemic hydrobenzoin (Table 1, entry 5). At present, it is difficult to rationalize this observation, however it appears that the binding constant of OsO_4 to the polymer bound alkaloid is higher than the free alkaloid ($K \approx 15 - 30$), presumably due to binding of two quinuclidine moieties to the same osmium tetroxide merely because of proximity. ³

Entry	Polymers A (B) ^a		Reaction	% Yield	% ee ^b	Config.
	n	m	Time		•	
1	9.0	1.0 (B)	24 h	86 (68)	82 (71)	RR
2	9.0	1.0	24 h	79	78	SS °
3	8.0	2.0 (B)	24 h	72 (65)	78 (68)	RR
4	5.0	5.0 (B)	2 d	50 (50)	45 (40)	RR
5	0.0	1.0	2-3 d	20	-	

Table 1: Asymmetric Dihydroxylation of *trans*-Stilbene using Polymer Bound Alkaloid in CH₃CN-H₂O (8:2) at ca. 0 °C in the presence of N-Methyl Morpholine N-oxide (NMO)

a) The numbers in the parenthesis indicate the yields and % ee of the diols obtained when polymer **B** is used in the ratio indicated in the respective entries. b) Enantiomeric excess of the diol was determined by ¹H NMR using Eu(hfc)₃ as shift reagent on the corresponding bisacetate derivatives. c) Polymer containing DHQ was used.

 Table 2: Effect of Reaction Conditions and Oxidants on the Asymmetric Dihydroxylation of trans-Stilbene using 10 % DHQD-Polystyrene (A)

Entry	Reaction ^{•,b} Conditions	Secondary Oxidant	Yield (%)	% ee °
1	36 h (18 h)	NMO	82	85
2	36 h (18 h)	NMO	78	80 ^d
3	24 h, TEAA (18 h)	NMO	32	31
4	24 h	K ₃ [Fe(CN) ₆]	80	85

a) CH₃CN-H₂O (8:2) was used as solvent at ca 0 °C except in entry 4 where *t*-butanol-water (1:1) was used at ca. 20 °C. b) Number in the parenthesis indicates the time of slow addition of olefin. c) In all cases, the absolute configuration of the diol is RR. d) Polymer from entry 1 was recycled.

Subsequently, we have examined the reuse of the polymer, effect of various other secondary oxidants and additives on the rate as well as on the enantiomeric excess of the diol using *trans*-stilbene as the substrate. Recycling of the polymer without any additional amount of OsO_4 resulted in the slightly lower yield and % ee of hydrobenzoin (Table 2, entry 2). It is expected that some amount of OsO_4 might have been washed off during the isolation of the diol, however, the catalytic activity was regained by adding 0.1 mol % of OsO_4 . The addition of tetraethylammonium acetate (TEAA) showed a deleterious effect on the rate, yield and optical purity of the diol (Table 2, entry 3) in contrast to the reaction with the free DHQD-4-chlorobenzoate.^{2a,b} Careful examination of the reaction mixture showed that the addition of TEAA lead to the saponification of the chiral auxiliary from the polymer backbone. The control experiment revealed that dihydroquinidine is a very poor auxiliary for the asymmetric dioxyosmylation reaction.

During the course of our studies, Tsuji et. al ¹⁰ have reported the use of $K_3[Fe(CN)_6]-K_2CO_3$ as a stoichiometric oxidant in the osmium catalyzed vicinal dihydroxylation of alkenes and Sharpless and co-workers ^{2c} have demonstrated its usefulness in the asymmetric version of this reaction. Using Tsuji's condition, high enantiometric excess of the diol was obtained at ca. 20 °C (Table 2, entry 4).

Finally, we have investigated the scope and generality of this reaction using polymer imbibed with 10 % alkaloid. The results are collected in the Table 3. Except for *trans*-methyl cinnamate (and possibly with other α , β -unsaturated esters), the enantiomeric excess of the diols resulting from the asymmetric dihydroxylation of the other alkenes are nearly the same as obtained with the free alkaloid under identical conditions.^{1,2a,b}

Entry	Olefins	Reaction time ^a	% Yield	% ee ^b	Config.°
1	Styrene	12 h	87	48	R
2	E-B-Methyl styrene	12h (5 h)	82	50	RR
3	E-Methyl cinnamate	24 h	78	45	2S,3R
4	E-2-Octene	36 h (21 h)	86	69	RR
5	E-4-Octene	24 h (18 h)	79	60	RR
6	E-5-Decene	24 h (18 h)	81	59	RR
7	1-Decene	19 h	84	22	R

Table 3: Asymmetric Dihydroxylation of Olefins using Polymer A (10 % alkaloid) in CH_3CN-H_2O at ca. 5 °C in the presence of NMO

a) The number in the parenthesis indicates the time of slow addition of olefin. b) Enantiomeric excess were determined by ¹H NMR by (i) shift experiments using $Eu(hfc)_3$ on the corresponding bisacetate derivatives (ii) MTP derivatives and comparison of the optical rotation. c) Absolute configuration were determined by comparison of optical rotation with the known examples.

In summary, using cinchona alkaloid on a polystyrene support, we have been able to prepare chiral diols without sacrificing the yield or the optical purity of the diol. In addition, this process is not only more economical and cost effective but also simple and less toxic. Both osmium tetroxide and chiral auxiliary are recycled several times without isolation and diols are obtained by simple filtration or centrifugation of the reaction mixture.

Acknowledgement: Financial support from DST, New Delhi is gratefully recorded. AT, PC and JRA thank CSIR, New Delhi for graduate fellowship.

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- 7 4-Vinylbenzoate of DHQD and DHQ were prepared by esterification of 4-vinylbenzoyl chloride at ca. 0 °C using DMAP (0.1 equiv.)-triethylamine (2 equiv.) as base in CHCl₃ in 80-89 % yield. (*caution* All operations must be carried out below 20 °C, otherwise it results in the formation of homopolymer). DHQD-4-vinylbenzoate, mp 52 °C $[\alpha]_D = -93.7^\circ$ (c, 1, EtOH). The monomers were polymerized with styrene or 4-phenylstyrene using AIBN as initiator. All the polymers gave satisfactory spectral data and elemental analysis.
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- 9 A typical general procedure is as follows: To a suspension of polymer (0.13 equiv. of alkaloid) in 5 mL acetonitrile: water (8:2) at ca. 0 °C is added OsO_4 (1 mole %, 0. 5 M in toluene), stirred for 45 min. followed by addition of N-methyl morpholine N-oxide (1.5 2 equiv.). The olefin (5 mmol) is then added all at once or slowly. The reaction mixture gradually changed from a heterogeneous to a homogeneous solution in 18-20 h. The reaction is then quenched by addition of water (ca. 5 mL), polymer is removed either by filtration or centrifugation and washed with ether. The combined organic extracts are then evaporated; the residue is dissolved in CH_2Cl_2 (50 mL), washed with brine (20 mL) and dried (Na₂SO₄). The diols are purified either by chromatography or distillation.
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(Received in UK 15 June 1992)