

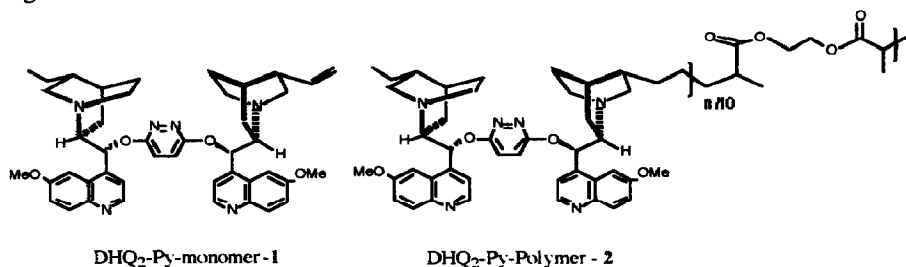
Unprecedented Reactivity and Selectivity in Heterogeneous Asymmetric Catalytic Dihydroxylation of Alkenes**

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Abstract: An unprecedented selectivity and reactivity in heterogeneous asymmetric catalytic dihydroxylation (AD) of olefins has been achieved using 3,6-(9-*O*-bisdihydroquinyl) pyridazine and 3,6-(9-*O*-bisdihydroquinidyl)pyridazine immobilized on ethyleneglycol dimethacrylate polymer backbone.

In the recent years, asymmetric dihydroxylation (AD) of olefins has been of topical interest.¹ Sharpless and co-workers² have developed a number of chiral cinchona alkaloid derivatives furnishing high selectivity in homogeneous AD reactions. However, attempts to achieve identical reactivity and selectivity in heterogeneous catalytic AD reaction remain far from satisfactory. We³ and others⁴ have reported catalytic AD reaction using chiral cinchona alkaloid on different polymer backbones with much inferior reactivity and selectivity which is of vital concern for the practical utilization of this novel methodology in bulk scale synthesis. Here, we wish to report the first example of a new polymer supported bisdihydroquinylpyridazine **2** and the corresponding quinidine derivative which shows nearly the same reactivity and selectivity as that in the case of homogeneous reactions.



The monomer **1** was prepared by the reaction of 3-(9-*O*-dihydroquinyl)-6-chloropyridazine with quinine in *ca.* 80% yield.⁵ The polymer **2** was then prepared using 10% of the monomer and 90% of ethyleneglycol dimethacrylate by radical initiated polymerization in the presence of AIBN to furnish nearly quantitative yield of the polymer **2**.⁶ Polymers containing higher percentage of monomer **1** proved to be less reactive and selective

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in AD reaction. The percentage of alkaloid loaded on the polymer was determined by elemental analysis. These polymers have large pore size and are hydrophilic in nature which facilitate the reactants to penetrate to the catalytic site and thus allow the reaction to proceed with an optimum speed comparable to the homogeneous reaction. The reactions were performed in *t*-BuOH-H₂O (1:1) at ca. 20 °C using K₃Fe(CN)₆-K₂CO₃ (3 equiv.) as cooxidant. As shown in the Table 1 most of the reactions are complete at the same time as in the case of homogeneous reaction ⁷ (Table 1, column 5 vs 6). It is interesting to note that the % ee of the diols obtained by using polymer 2 and DHQ₂-Py ⁷ were largely identical in the case of aromatic class of olefins, however, a significant drop in % ee of the diols was observed in the case of aliphatic di- and monosubstituted class of alkenes.

Table 1: Comparison of % ee of diols obtained in asymmetric dihydroxylation reaction using DHQ₂-Py-Poly-2 versus DHQ₂-Py and DHQ₂-PHAL

S. No.	Olefins	Reaction time	% Yield of diols	DHQ ₂ -Py-Poly-2 ^a	DHQ ₂ -Py ^a	DHQ ₂ -PHAL ^a
1		20 h	87	96 (98) ^b	(99.5) ^c	99.5 (99.5) ^d
2		20 h	89	87 ^e	-	-
3		12 h	90	95 (99) ^e	(93)	97 ^d
4		20 h	82	86 ^e	-	93 ^d
5		48 h	81	(83) ^b	-	(97) ^d
6		24 h	92	45 ^f	93 ^f	-
7		20 h	82	24 ^f	71 ^f	80 ^d
8		48 h	64	48 ^{f,g}	88 ^{f,g}	88 ^d

(a) The configuration of the diols follow the facial selectivity rule. The values in the parenthesis indicate the % ee of the diol obtained by using corresponding DHQD-derivatives and the configuration(s) of the diols are opposite. (b) % ee were determined by ¹H NMR using Eu(hfc)₃ as shift reagent. (c) cited from ref.7 (d) cited from ref. 2 (e) % ee were determined by HPLC on a RP-18 stationary phase using MeOH-H₂O as solvent (flow and the ratio of the solvents varied for different samples). (f) based on comparison of rotation. (g) ¹H NMR of bis MTPA derivative.

The reason for this unexpected behaviour is not well understood at this stage, however, the rate of the reaction in both the cases (homogeneous and heterogeneous) were nearly identical. Salvadori *et. al* 4c have reported AD reaction of olefins using DHQD immobilized on a crosslinked polymer backbone, which resulted in a highly insoluble material. However, these polymers could not be used with K_3FeCN_6 as oxidant. Use of NMO as oxygen source resulted in low enantioselectivity of diols. In contrast, the crosslinked polymers, which we prepared in the form of beads using 10 % of monomer 1, 20 % of ethyleneglycol dimethacrylate as crosslinking agent and 70 % of 2-ethylhexyl acrylate lead to an efficient catalytic turnover in the presence of K_3FeCN_6 . But this polymer did not show any significant advantage over the polymer 2 in terms of reactivity or selectivity. Thus, at least in the case of aromatic alkenes, use of polymer bound DHQ2-Py and DHQD2-Py offers advantages of recovery and recycling of chiral auxiliary without compromising with the reactivity and stereoselectivity of the reaction.

In summary, we have achieved for the first time an unprecedented reactivity and selectivity in heterogeneous AD reaction by immobilising pyridazine based cinchona alkaloid as chiral auxiliary on a polymer backbone which is cheaper than 1,4-(9-*O*-bisdihydroquinidyl)phthalazine (DHQD2-PHAL) and the corresponding quinine derivative (DHQ2-PHAL) without compromising with the reactivity in the AD reaction. Attempts to immobilize DHQD2-PHAL and DHQ2-PHAL are underway.⁸

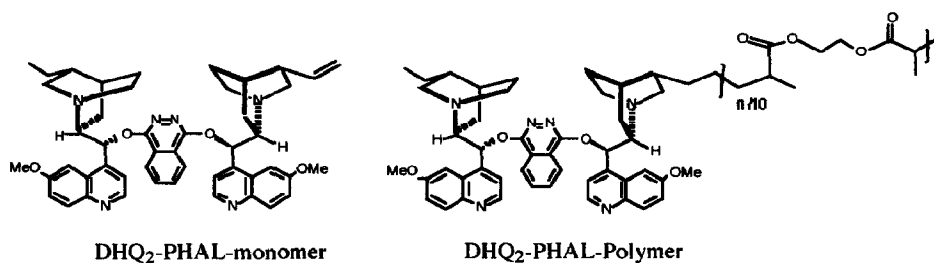
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- 5 Preparation of 1: A suspension of quinine (1.215 g, 3.75 mmol), 3-(9-*O*-dihydroquinyl)-6-chloropyridazine (1.63 g, 3.7 mmol), KOH (0.504 g, 9 mmol) was refluxed in toluene with azeotropic removal of water for 8-9 h. Usual work-up of the reaction mixture furnished monomer 1 (2.1 g, 80 %), mp 120-122 °C. IR (CHCl₃) ν_{max} 2945, 1626, 1518, 1440, 1035 cm⁻¹. ¹H NMR (200 MHz) (CDCl₃) δ : 8.70 (d, *J* = 5 Hz, 2 H), 8.00 (d, *J* = 8.7 Hz, 2 H), 7.5 (d, *J* = 2 Hz, 2 H), 7.42-7.33 (m, 4

H), 7.00 (s, 2 H), 6.74 (d, $J = 5.5$ Hz, 2 H), 5.88 - 5.70(m, 1 H), 5.2 (d, $J = 6.25$ Hz, 1 H), 4.93 (s, 1 H), 3.9 (s, 6 H), 3.47 - 3.3 (m, 2 H), 3.15 - 2.9 (m, 4 H), 2.65-2.45 (m, 3 H), 2.34 - 2.18 (m, 3 H), 1.9 - 1.28 (m, 12 H), 0.85 (t, $J = 6.25$ Hz, 3 H). ^{13}C NMR (50 MHz) (CDCl_3) δ : 161.0, 157.96, 147.59, 144.98, 144.80, 144.62, 142.11, 131.81, 127.52, 121.99, 121.58, 199.10, 119.02, 114.50, 102.28, 60.29, 60.14, 58.67, 56.98, 55.91, 43.01, 42.86, 40.08, 37.76, 28.66, 27.93, 27.91, 25.63, 24.32, 23.94, 12.99. $[\alpha]_D^{25} = +140^\circ$ (c, 1.65, EtOH)

- 6 The polymer **2** was prepared by refluxing a mixture of 3-(9-*O*-dihydroquinyl)-6-(9-*O*-quinyl)pyridazine (0.15 g, 0.207 mmol), ethyleneglycol dimethacrylate (0.37 g, 1.863 mmol, 9 equiv.), AIBN (40 mg) in toluene-methanol (5 mL) for 10 h to furnish nearly quantitative yield of polymer **2**.
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- 8 Preparation of 1-(9-*O*-dihydroquinyl)-4-chlorophthalazine and 1-(9-*O*-dihydroquinyl)-4-(9-*O*-quinyl)phthalazine lead to relatively poor yield under similar conditions employed for the preparation of corresponding pyridazine derivatives. Attempts to optimize the yield are under progress and polymers containing DHQD₂-PHAL and DHQ₂-PHAL will be reported later. These polymers are



expected to give better selectivity as in the case of homogeneous reaction using DHQD₂-PHAL and DHQ₂-PHAL, however, they may not be economically very competitive.

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