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Efficient and Practical Polymeric Catalysts for Heterogeneous Asymmetric Dihydroxylation of Olefins

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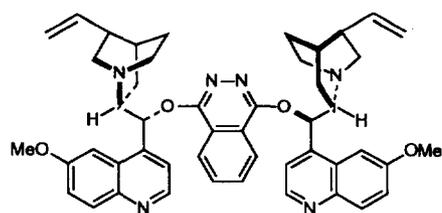
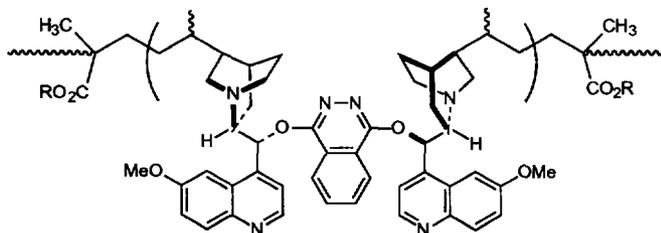
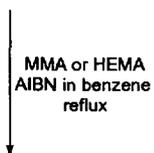
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Abstract: High enantioselectivity (>99% ee) and reactivity in heterogeneous catalytic asymmetric dihydroxylation (AD) of olefins have been achieved using new polymeric cinchona alkaloids containing 1,4-bis(9-*O*-quininyl)phthalazine ((QN)₂-PHAL), which can be synthesized more economically than their homogeneous analogue, 1,4-bis(9-*O*-dihydroquininyl)phthalazine ((DHQ)₂-PHAL). Copyright © 1996 Elsevier Science Ltd

The Sharpless catalytic asymmetric dihydroxylation (AD) of olefins, using catalytic amounts of osmium tetroxide in the presence of cinchona alkaloid derivatives, allows access to a wide variety of enantiomerically pure vicinal diols.¹ However, there are limitations to performing the catalytic AD reaction on a large scale due to the toxicity and high cost of osmium tetroxide and the cinchona alkaloid derivatives. To explore the possibility of the repetitive use of both components, several polymer-bound cinchona alkaloid derivatives have been employed.² However, most of the polymers require complicated synthetic manipulations and, moreover, their catalytic efficiency remains far from satisfactory. Thus, development of synthetically simple and efficient polymers for heterogeneous AD is highly desirable. Very recently, we reported heterogeneous catalytic AD using copolymers of dihydroquinine 4-benzoate with methyl methacrylate (MMA) or 2-hydroxyethyl methacrylate (HEMA), which showed the same selectivity and reactivity with their homogeneous analogues.^{2f} Since it is known that in homogeneous catalytic AD, (DHQ)₂-PHAL gave much better results than the dihydroquinine benzoate derivatives,³ polymeric cinchona alkaloids containing (DHQ)₂-PHAL should also be expected to give better results than the benzoate-type copolymers. Thus, we prepared new polymeric analogues of (DHQ)₂-PHAL and examined their catalytic efficiency resulting the superlative results for the heterogeneous catalytic AD until now. Thus, here we wish to report our preliminary results.

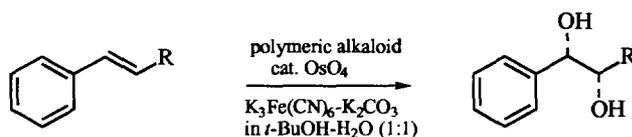
Chiral monomer **1**, 1,4-bis(9-*O*-quininyl)phthalazine ((QN)₂-PHAL) was prepared simply by the reaction of quinine with 1,4-dichlorophthalazine in good yield.⁴ New polymeric analogues of (DHQ)₂-PHAL **2-3**, [poly((QN)₂-PHAL-*co*-MMA) **2**, poly((QN)₂-PHAL-*co*-HEMA) **3**], were prepared by polymerization of (QN)₂-PHAL **1** with methyl methacrylate (MMA) or 2-hydroxyethyl methacrylate (HEMA) in benzene under reflux in the presence of AIBN, respectively.⁵ The nitrogen analysis of copolymers **2** and **3** confirmed 6.32 and 0.4 mol% incorporation of monomeric alkaloid **1**, respectively. The copolymer **2** was obtained in nearly quantitative yield, however, copolymerization of (QN)₂-PHAL with HEMA afforded **3** in very poor yield (7.1%).

1,4-bis(9-*O*-quininyl)phthalazine (1)2, R = CH₃; 3, R = CH₂CH₂OH

To investigate the catalytic efficiency of new polymeric alkaloids **2** and **3**, The heterogeneous ADs with typical substrates such as *trans*-stilbene and methyl *trans*-cinnamate were carried out under standard conditions, in *t*-BuOH/H₂O (1:1) at 10°C using K₃Fe(CN)₆-K₂CO₃ (3 equiv.) as secondary oxidant. The results are summarized in Table 1.

As shown in Table 1, all reactions using copolymers **2** and **3** proceeded very fast and with nearly quantitative enantioselectivities (>99% ee for both substrates) for the diol. Moreover, OsO₄-polymer **2** complex was easily filtered from the reaction mixture and the catalytic efficiency was essentially retained which exhibited a promising reusability. However, copolymer **3** was too highly swelled leading to difficulties in filtration.

In conclusion, we have achieved excellent results for the heterogeneous catalytic AD using copolymers **2**, **3**, which can be synthesized more easily and more economically than their homogeneous analog, (DHQ)₂-PHAL. Thus, we expect this type of polymeric alkaloids can give the possibility to overcome the intrinsic problems of catalytic AD reaction. Further studies are in progress to investigate the catalytic efficiency with other class of alkenes to widen the applicability of this new polymeric system.

Table 1. Heterogeneous AD of olefins using polymeric cinchona alkaloids **2**, **3**^a

Entry	Polymer	Olefin (R=)	Reaction time	% Yield ^b	[α] _D (c, solvent)	% ee ^c	Config. ^c
1	2	Ph	15 h	93	- 92.96 (1.07, EtOH)	>99.9	S,S
2	2	CO ₂ Me	20 h	83	+10.62 (1.02, CHCl ₃)	99.3	2R, 3S
3 ^d	2	Ph	32 h	65	- 93.02 (1.05, EtOH)	>99.9	S,S
4	3	Ph	20 h	87	- 92.99 (1.04, EtOH)	>99.9	S,S
5	3	CO ₂ Me	16 h	82	+10.49 (1.12, CHCl ₃)	98.0	2R, 3S

^a The reaction conditions were not optimized: molar ratio of olefin/OsO₄/polymeric alkaloid = 1/0.01/0.02; reaction temperature (10 °C). ^b Isolated yields by column chromatography. ^c % ee and absolute configurations were determined by comparison of [α]_D²⁰ with literature value.⁶ ^d Reaction was carried out with polymer **2** which had been used in entry 1 without further addition of OsO₄.

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References and Notes

- Review: (a) Johnson, R. A. and Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH publishers: New York, **1993**; pp 227-272. (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483-2547. (c) Lohray, B. B. *Tetrahedron: Asymmetry* **1992**, *3*, 1317-1349.
- (a) Kim, B. M.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3003. (b) Pini, D.; Petri, A.; Nardi, A.; Rosini, C.; Salvadori, P. *Tetrahedron Lett.* **1991**, *32*, 5175. (c) Lohray, B. B.; Thomas, A.; Chittari, P.; Ahuja, J. R.; Dhal, P. K. *Tetrahedron Lett.* **1992**, *33*, 5453. (d) Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron: Asymmetry* **1993**, *4*, 2351. (e) Lohray, B. B.; Nandan, E.; Bhushan, V. *Tetrahedron Lett.* **1994**, *35*, 6559. (f) Song, C. E.; Roh, E. J.; Lee, S. G.; Kim, I. O. *Tetrahedron: Asymmetry* **1994**, *6*, 2687. (g) Achiral polymer-bound OsO₄ has been also used: Cainelli, G.; Contento, M.; Manescalchi, F.; Plessi, L. *Synthesis* **1985**, 45.
- (a) Lohray, B. B.; Kalantar, T. H.; Kim, B. M.; Park, C. Y.; Shibata, T.; Ubi, J. S. M.; Sharpless, K. B. *Tetrahedron Lett.* **1989**, *30*, 2041. (b) Kwong, H. L.; Sorato, C.; Ogino, Y.; Chen, H.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 2999. (c) Shibata, T.; Gilheany, D. G.; Blackburn, B. K.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3817. (d) 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. (e) Amberg, W.; Bennani, Y. L.; Chadha, R. K.; Crispino, G. A.; Davis, W. D.; Hartung, J.; Jeong, K. S.; Ogino, Y.; Shibata, T.; Sharpless, K. B. *J. Org. Chem.* **1993**, *58*, 844.

4. 1,4-Bis(9-*O*-quininyl)phthalazine ((QN)₂-PHAL), **1**: A 500 mL three-neck round-bottom flask equipped with a Dean-Stark-condenser was charged with 25.47 g (78.51 mmol) of quinine, 8.14 g (40.89 mmol) of 1,4-dichlorophthalazine, 16.6 g (120.22 mmol) of K₂CO₃, and 300 mL of anhydrous toluene. After 2 hrs reflux under nitrogen atmosphere, 6.75 g (120.22 mmol) of KOH pellet were added and then the reaction was continued for 14 hrs (The reaction can be followed by TLC using MeOH on silica gel. The R_f of **1** is 0.56.). The light orange solution was cooled to room temperature, mixed with water, and then extracted with EtOAc. The organic layer was washed with water and brine, dried over MgSO₄, and evaporated to dryness. Recrystallization from Et₂O gave 21.7 g of white powder **1**: mp 159-160 °C; [α]_D²³ +348.4 (*c* 1.08, MeOH); ¹³C NMR(CDCl₃) 157.91, 156.65, 147.64, 144.97, 144.91, 142.19, 132.55, 131.79, 127.43, 123.01, 122.67, 122.09, 118.67, 114.53, 102.09, 76.36, 60.30, 56.87, 55.77, 42.75, 39.97, 27.97, 27.79, 23.88; Anal. Calcd for C₄₈H₅₀N₆O₄: C, 74.39; H, 6.50; N, 10.84. Found: C, 74.3; H, 6.69; N, 10.5.

5. (a) Copolymerization of (QN)₂-PHAL with methyl methacrylate (MMA): A solution of (QN)₂-PHAL (3.87 g, 5.0 mmol), MMA (9.51 g, 95.0 mmol) and azobisisobutyronitrile (50 mg) in dry benzene (150 mL) was refluxed under nitrogen atmosphere. After 48 hrs, the solution was poured into *n*-hexane. The precipitate was filtered, washed with *n*-hexane and dried to give 10.5 g of white powder **2**. The component of copolymer **2** was determined by elemental analysis: Anal. Calcd. for a polymer containing 6.32 mol % of (QN)₂-PHAL: C, 64.93; H, 7.52; N, 3.72. Found: C, 64.9; H, 7.67; N, 3.72; IR 1732 cm⁻¹ (CO).

(b) Copolymerization of (QN)₂-PHAL with 2-hydroxyethyl methacrylate (HEMA): A solution of (QN)₂-PHAL (3.20 g, 4.13 mmol), HEMA (10.20 g, 78.38 mmol) and azobisisobutyronitrile (40 mg) in dry benzene (150 mL) was refluxed under nitrogen atmosphere for 48 hrs. The polymer began to precipitate after stirring for 1 hr. The precipitate polymer was filtered, washed twice with 100mL portions of benzene, and dried under vacuo to give 10.45 g of white powder **3**. The component of copolymer was determined by elemental analysis: Anal. Calcd. for a polymer containing 0.40 mol % of (QN)₂-PHAL: C, 55.81; H, 7.71; N, 0.24. Found: C, 55.3; H, 7.67; N, 0.24; IR 1728 cm⁻¹ (CO).

6. (a) Berti, G.; Bottari, F. *J. Org. Chem.* **1960**, *25*, 1286. (b) Denis, J.-N.; Correa, A.; Greene, A. E. *J. Org. Chem.* **1990**, *55*, 1957.

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