Asymmetric Dihydroxylation of Olefins in $(DHQD)_2$PHAL-Immobilized Silica Gel-Water Disperse System. An Approach to Fe/Os-Mediated Electrooxidation (Ex-cell Method)

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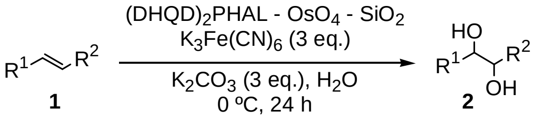
Os-catalyzed asymmetric dihydroxylation (ADH) of olefins by using cinchona alkaloid type ligand, such as $(DHQD)_2$PHAL, is an important reaction and widely used in synthesis of optically active natural compounds. To perform the ADH reaction in a large scale, however, there is limitation because of high cost of the ligands. To overcome this problem, immobilization of the ligand on to solid support, such as polymers and silica gels, have been reported. So far reported methods, however, the ligands were immobilized by anchoring the cinchona alkaloid moieties[1] and there is no report that the ligand is immobilized by anchoring the core unit, which is far from chiral center.

In this paper are described 1) immobilization of the ligand on silica gel at central diazanaphthalene unit and 2) ADH reaction by using chiral ligands-immobilized silica gel in an *aqueous* $K_3Fe(CN)_6$. The aqueous oxidant can be re-generated by electrooxidation and used repeatedly,[2] thereby offering a new "ex-cell" electrooxidation method.



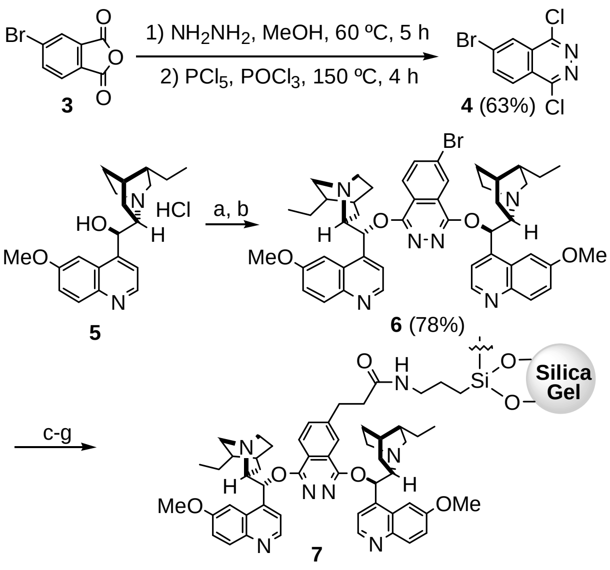
$(DHQD)_2$PHAL-immobilized silica gel was prepared as illustrated in Scheme 1, and *ca*. 0.06 mmol/g-SiO_2 of $(DHQD)_2$PHAL was immobilized.

A representative procedure of ADH is as follows. (DHQD)PHAL-SiO_2 (471 mg) was treated with aq. $K_2OsO_2(OH)_4$ (6 mg/3 mL) at room temperature for 3 h. The silica gel was filtered and dried to give chiral Os-immobilized silica gel reagents. To the silica gel was added acetone solution (2 mL) of 1-vinylnaphthalene (**1a**, 163 mg, 1.1 mmol), and the mixture was stirred for few minutes. After evaporation of most of acetone, an aqueous solution (10 mL) of $K_3Fe(CN)_6$ (1.05 g, 3.2 mmol) and K_2CO_3 (443 mg, 3.2 mmol) was added to the residue. The resultant suspension was stirred at 0 °C for 24 h. The silica gel was filtered and washed with acetone. The acetone washings was concentrated under reduced pressure, and the residue was recrystallized (MeOH) to give 1-(1-naphthyl)-1,2-ethanediol (**2a**, 187 mg, 0.99 mmol, 93%). Enantiomeric excess (ee%) was, however, estimated to be only 8% by HPLC.

The results of ADH reaction with several olefins are summarized in Table 1. In the case of *p*-chlorostyrene (**1b**) and *trans*-1-phenyl-1-propene (**1c**), the desired diols, **2b** and **2c**, were obtained in moderate yields with moderate to high ee% value. Notably, 1-phenyl-1,2-propanediol (**2c**) was obtained in 75% yield and 97%ee when *t*-BuOH was used as a co-solvent, which is comparable with the ADH using $(DHQD)_2$PHAL-immobilized silica gel by anchoring the cinchona alkaloid moieties.[1]

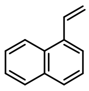
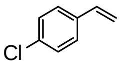
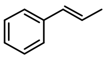
Recycle use of the silica gel and electrochemical re-generation of $[Fe^{III}(CN)_6]^{3-}$ have been investigated and will be discussed.

Scheme 1. Preparation of $(DHQD)_2$PHAL-Immobilized Silica Gel



a) NaH, THF, 70 ºC, 1 h. b) **2**, THF, 70 ºC, 24 h. c) CH_2=CHC(O)OMe, $Pd(OAc)_2$, P(*o*-tolyl)$_3$, NEt_3, DMF, 90 ºC, 48 h, 90%. d) 5% Pd-C, H_2, MeOH, 15 h, 53%. e) 5% NaOH (0.5 mL), MeOH (2.0 mL), room temp., 98%. f) $H_2N(CH_2)_3Si(OEt)_3$, WSCI, THF, 75 ºC, 20 h. g) Silica gel, room temp., 48 h.

Table 1 ADH by Using $(DHQD)_2$PHAL-Immobilized Silica Gel-Water Disperse System

Entry	1		2	
			Yield (%)[a]	Ee (%ee)
1		**1a**	97 (93 : 4)	8[c]
2		**1b**	78(13 : 65)[b]	74[c]
3		**1c**	45 (8 : 37)[b]	91[d]
4[e]			75[b]	97[d]

[a] Isolated yields. [b] When the diol was easily soluble in aq. phase, the silica gel was filtered and washed with ethyl acetate. The combined filtrate and washings were extracted with ethyl acetate to obtain crude products. [c] HPLC (Chiralcel OD). [d] HPLC (Chiralcel BG). [e] A mixture of H_2O (7 mL) and *t*-BuOH (5 mL) was used as a solvent.

References: 1. Song, C. E. *et al*., *Tetrahedron: Asymmetry*, **8**, 841 (1997). 2. Torii, S. *et al., J. Org. Chem*., **61**, 3055 (1996).