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Novel Horseradish Peroxidase Catalysed Enantioselective Oxidation of 2-Naphthols to 1,1'-Binaphthyl-2,2'-diols

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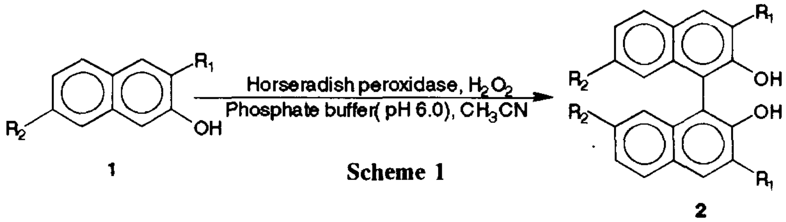
Abstract: Enantioselective oxidation of 2-naphthols to 1,1'-binaphthyl-2,2'-diols catalysed by horseradish peroxidase is described. © 1997 Elsevier Science Ltd.

Horseradish peroxidase (EC 1.11.1.7) is a metalloporphyrin enzyme which has been thoroughly studied for its organic and inorganic oxidation reactions.[1] However, recently this enzyme has once again come into focus with the discovery of its remarkable enantioselective reactions, viz., i) enantioselective oxidation of unsymmetrical sulfides to sulfoxides[2] and ii) enantioselective reduction of racemic hydroperoxides to alcohols.[3] Now we report here another new reaction: enantioselective oxidation of 2-naphthols, **1a-1d** to 1,1-binaphthyl-2,2'-diols, **2a-2d** catalysed by horseradish peroxidase (**Scheme 1**). The representative results were given in Table 1.

The oxidation[4] of naphthols, **1a-1d** were carried out with horseradish peroxidase in phosphate buffer at pH 6.0, using acetonitrile as cosolvent and 5% H_2O_2 as oxidant and maintaining the reaction temperature at 20°C.



Scheme 1

Because of growing importance to binaphthyl derivatives as chiral auxillaries in organic synthesis,[5] there is considerable quest in recent years for developing new enantioselective methods for preparation of binaphthols. There are four enantioselective routes known earlier for direct conversion of 2-naphthols to binaphthols : i) an intermolecular Ullman coupling,[6] ii) a nucleophilic aromatic substitution,[7] iii) an oxidative dimerisation of 2-naphthols with Copper(II) amine complexes as oxidant[8] and iv) electrocatalytic oxidative coupling.[9] The results observed in the present enzyme catalysed oxidation reaction are comparable with those of existing methods.

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Table 1: Horseradish Peroxidase Catalysed Enantioselective Oxidation of 2-naphthols

Entry	Naphthol, 1	Yield(%)[a], 2	% e.e[b]	Config[b]
1a	$R_1=R_2=H$	75	52	R
1b	$R_1=$ Br; $R_2=H$	80	64	R
1c	$R_1=H$; $R_2=$COOMe	65	45	R
1d	$R_1=H$; $R_2=CH_3$	60	38	R
1e	$R_1=H$; $R_2=$COOH	10	-	-

[a] All are isolated yields. [b] Absolute configuration and enantiomeric excess were found out by comparing the optical rotations from literature[10].

In summary, this work identifies a novel enantioselective reaction catalysed by horseradish peroxidase and is the first application of enzyme catalysis using horseradish peroxidase for synthesis of binaphthols directly from 2-naphthols.

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4. In a general procedure, 2-naphthol, **1a** (500mg, 3.5mmol) and horseradish peroxidase (10mg, 1000 units, type 1 from Sigma, USA) and phosphate buffer (0.05M, pH6.0, 20 mL) and acetonitrile (30 mL) were taken in a conical flask and stirred at 20°C. To this 5% H_2O_2 was added slowly (ca. 2.4ml) for 1 hour. The reaction was monitored by TLC. When the starting material was consumed, the crude product was extracted with ethylacetate, washed with water and dried over sodium sulfate.The solvent was evaporated under vacuum and purification of crude product by column chromatography gave **2a** (370 mg, 75%); ^{1}HNMR(CDCl$_3$,200MHz): δ 7.06(2H, s), 7.22(2H, m), 7.28(2H, m), 7.35(2H,d), 7.88(2H, d), 7.89(2H,d), 7.91(2H, d) ppm. Mass spectrum : 286(M$^+$).
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10. 1a:$[\alpha]_D=17.7$ (C, 1.0, MeOH){lit$[\alpha]_D=34.10$}1b: $[\alpha]_D=-62.73$ (C,1.0, MeOH){lit $[\alpha]_D=-97.8$} 1c:$[\alpha]_D=34.7$ (C, 1.0, MeOH){lit $[\alpha]_D=77.10$}1d $[\alpha]_D=$ 16.71 (C,1.0, MeOH){lit $[\alpha]_D=44.2$} Ref: J. Cuntze, J.; Owens, L.; Alcazar. V.; Seiler, P.; Diedrich., F.; *Helv.Chim.Acta*, **1995**, *78*, 367; Cram, D.J.; Helgeson, R.C.; Peacock, S.C.; Kapalan, L.J.; Domeier, L.A.;Moreau, P.; Konga, K.; Mayer, J.M.; Chao, Y.; Siegel, M.G.; Hoffman, D.H.; Sogah, G.D..Y.; J. Org. Chem., 1978, 43, 1930.

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