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Oxidation of olefins by palladium(II). 18. Effect of reaction conditions, substrate structure and chiral ligand on the bimetallic palladium(II) catalyzed asymmetric chlorohydrin synthesis

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Abstract

The effect of electronic factors, solvent composition, identity of the chiral bidentate, and olefin structure on the yields and enantioselectivities of the asymmetric chlorohydrin synthesis were investigated. Electronic effects on the chlorohydrin reaction were tested by oxidation of phenyl allyl ether *p*-substituted by H, Cl, CH_3O and CN. All species gave same similar yields and enantioselectivities indicating that electronic effects are not important. Varying the solvent composition of the THF–H_2O mixtures indicated that the optimal solvent mixture contains more than 85% THF. Variation of added [Cl^-] indicated that the added chloride had to be greater than 0.2 M for high yields and %ee's. Under ideal conditions the enantioselectivities of the chlorohydrins from the phenyl allyl ethers were more than 90%ee. Vinylacetic acid, methyl acrylate and *trans*-cinnamaldehyde were unreactive under the usual reaction conditions while 2-hydroxy-3-butene and allyl acetate give lower %ee's than did the phenyl allyl ethers. Styrene and α-methylstyrene gives comparable rates of reactions but the %ee's were lower with the latter. (2,6-Diisopropyl)phenyl allyl ether and 2-hydroxy-3-butene give high %ee's indicating that steric hindrance was not a major factor. All of the chiral bridging ligands tested gave satisfactory results except for DACH. A strange case was BZOX which did not give any induction at all. Structural studies showed the ligands are not large enough to bridge both Pd(II) in the bimetallic catalyst so one Pd(II) contained both ligand groups of the bidentate ligand and was thus unreactive. The other Pd(II) of the dimer was reactive but did not contain any chiral ligands to induce optical activity.

Keywords: Palladium(II); Catalysis; Asymmetric; Olefins; Chlorohydrins

1. Introduction

Presently there are five general methods for the asymmetric oxygenation of olefins. The first developed was the Sharpless epoxidation of allylic alcohols with hydroperoxides catalyzed by titanium(IV)-chiral diethyltartrate complexes which were discovered in 1980 [1]. Of many asymmetric transformations, one of the simplest and most useful is the conversion of allyl alcohol to chiral glycidol. Despite its usefulness, the Sharpless epoxidation is restricted to oxidation of allylic alcohols. The Jacobson epoxidation procedure does not suffer from this limitation [2]. Macrocyclic complexes of Mn(III) prepared from chiral diamines catalyze the epoxidation of unfunctionalized olefins by hydroperoxides. Recent synthetically useful variations of this chemistry include the kinetic resolution of epoxides by reaction with azide (metal = Cr) to give hydroxy azides [3], hydrolysis with water (metal = Co) to give glycols [4], and carbonylation with CO to give β-hydroxyesters [5]. The third asymmetric oxidation procedure consists of the vicinal hydroxylation of olefins by Os(VIII) catalysts [6]. A well-known reaction is the osmium tetroxide catalyzed oxidation of olefins by H_2O_2. The asymmetric version, as with the previous two systems discussed, involves the addition of an appropriate chiral ligand to the coordination sphere of the Os(VIII). This system does not require another functional group, such

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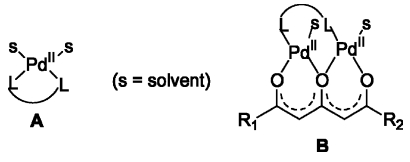
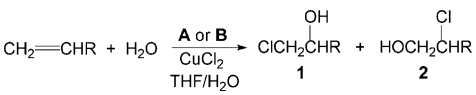
as OH in the Ti catalyzed epoxidation, to obtain enantioselectivity. Thus the asymmetric dihydroxylation is a general reaction, a trait that has made it useful for the preparation of many chiral biologically active compounds. The fourth synthesis is the osmium catalyzed aminohydroxylation reaction [7]. Another of the reactions uncovered by Dr. Sharpless, this synthesis could be particularly useful in drug manufacture. The fifth is the chiral Pd(II)-catalyzed allylic acetoxylation [8]. However the enantioselectivities realized to date have been very low ($< 5\%$).

Papers 16 [9] and 17 [10] of this series described the newest procedure, the asymmetric synthesis of chlorohydrins by the oxidation of olefins using mono- and bimetallic Pd(II) complexes containing chiral auxiliaries (**A** and **B**), in the presence of $CuCl_2$ (Scheme 1). The $CuCl_2$ is necessary for the formation of the chlorohydrin products. In its absence only ketones and aldehydes are produced. These studies used α-olefins as the main substrates.

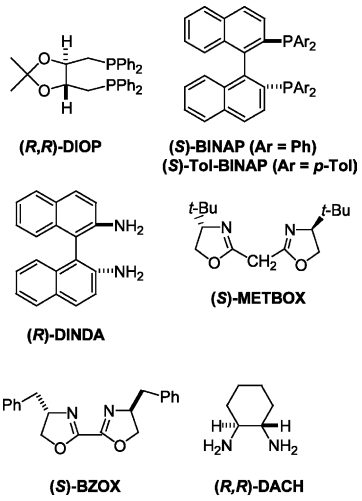


Catalyst **A** gave modest to good enantioselectivities (ee = 28–82%) while catalyst **B** generally gave higher enantioselectivities (50–94%). One reason for the lower enantioselectivities for the monometallic catalysts is the fact that the ligands were sulfonated to increase solubility in the reaction media and sulfonation is known to decrease optical yields [11]. However, monometallic catalysts with ligands that were not sulfonated still gave lower enantioselectivities than the corresponding bimetallic catalysts.

The present paper will explore further the effect of chiral ligand, substrate structure and reaction conditions on the oxidation of α-olefins by the bimetallic catalysts, **B**. The studies described in paper 17 used (1*R*,2*R*)-(−)-1,2-diaminocyclohexane (1*R*,2*R*-DACH), (+)- and (−)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((+) and (−)-DIOP), and (*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl {(*S*)-BINAP}. The present study will include these ligands and, in addition, (*S*)-(−)-2,2′-bis(ditolylphosphino)-1,1′-binaphthyl {(*S*)-Tol-BINAP}, (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine ((*R*)-DINDA), 2,2′-methylenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] ((*S*)-METBOX), and 2,2′-methylenebis[(4*S*)-4-benzyl-2-oxazoline] ((*S*)-BZOX).



Scheme 1. Chlorohydrin reaction.



2. Results and discussion

2.1. Electronic effects, solvent composition and chloride concentration

Table 1 lists a series of runs which test electronic effects, chloride concentration and solvent composition on the yields and enantioselectivity of the chlorohydrin product.

First, in regard to electronic effect, runs 3, 6, 8 and 10 have about the same [Cl^-] (0.2–0.3 M) and % THF (85–92%) but have different para substitutions on the benzene rings. These include the hydrogen, the electron withdrawing CN and Cl, and the electron releasing group CH_3O. The yields of **1** were greater than 85% and the ee varied between 85 and 93% and there is no systematic dependence on the electron withdrawing or releasing properties of the substitution. This result is not surprising since electron effects are apparently not important in Pd(II) catalytic chemistry. Thus, in the Wacker oxidation of α-olefins in aqueous solution, both acetaldehydes and ketones are formed with ketones predominating [12]. The order of rates for the reaction is ethene > propene > isobutene [13]. On the other hand, the reaction of α-olefins with Tl(III) give only ketones and the order of rates is isobutene > propene > ethene [14].

The results are summarized in Scheme 2. Since Pd(II) hydroxypalladation does have any appreciable carbonium ion character, it gives both **3** and **4** which decompose to ketones and acetaldehydes respectively. Since the reaction is mainly controlled by stereo chemistry factors, increasing substitution on the double bond retarded the reaction. On the other hand, the addition of Tl(III) and hydroxyl to olefins has considerable ionic character. This results in exclusively Markovnikov addition to give

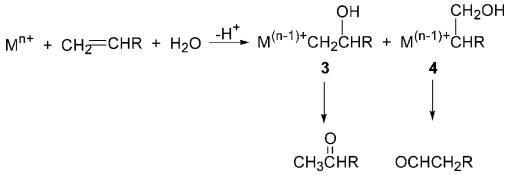
Table 1
Results for the oxidation of several para-substituted phenyl allyl ethers

Run	L*–L*	[LiCl], (M)	Substrate, *p*-X–PhOCH$_2$CH=CH$_2$	% THF	Yield of **1**	%ee of **1**
1	(*S*)-BINAP	0.3	X = H	30	82 [b]	84
2	(*S*)-BINAP	0.3	X = H	60	90 [b]	80
3	(*S*)-BINAP [a]	0.3	X = H	92	92	93
4	(*S*)-Tol-BINAP	0.00	X = Cl	92	70	52
5	(*S*)-Tol-BINAP	0.05	X = Cl	92	75 [b]	75
6	(*S*)-BINAP	0.24	X = Cl	85	> 90	92
7	(*S*)-Tol-BINAP	2.0	X = Cl	92	92 [b]	92
8	(*S*)-Tol-BINAP	0.3	X = OCH$_3$	85	> 90	88
9	(*S*)-Tol-BINAP	2.3	X = OCH$_3$	85	90	89
10	(*S*)-Tol-BINAP	0.2	X = CN	85	> 85	85
11	(*S*)-Tol-BINAP	1.7	X = CN	93	> 95	94

All runs contain 0.05–0.12 mmoles of chiral catalyst in 20–30 ml of solvent and are 2.1–3.5 M in $CuCl_2$. Temperature = 25 °C. The solvent was a H_2O–THF mixture containing 54–93% THF by volume. Catalyst turnovers were between 150 and 200.

[a] Data from reference [10].

[b] Dioxygen is oxidant; turnovers measured by O_2 uptake using gas burets. In calculating turnovers dioxygen is assumed to be a four electron oxidant.



Scheme 2. Oxidation of olefins by Pd(II), Tl(III) and Hg(II).

3 which give ketone as the only carbonyl product. Thus, since electronic factors predominated, increased substitution increases the rate of the reaction. A similar case is Hg(II) which produces the stable oxymercuration adducts **3**. As with Tl(III), since only Markovnikov addition is observed, the rate increased with increasing substitution on the double bond [15]. The δ for the reaction was found to be -2.77 which is close to that expected for a free carbonium ion in the transition state.

Electronic effects do play some role in altering the **3**–**4** ratio. In the study of the oxidation of some *p*-substituted styrenes in THF–H_2O mixtures, it was observed that electron-releasing groups on the aromatic ring favored phenylacetophenone formation and electron-withdrawing groups favored phenylacetaldehyde formation [16]. In the chlorohydrin reaction this directing influence cannot be a factor since only the **1** isomer is observed in all cases. However the electronic releasing *p*-CH_3O group does give some acetaldehyde so the electronic factor is of some importance in carbonyl formation.

The composition of the solvent makes a fairly small but appreciably affect on %ee. Thus, in runs 1–3 the only variation in reaction conditions is the solvent composition. When the %THF drops from 92 to 60% the %ee falls to 80%. Reducing the %THF further to 30% does not decrease the %ee further. The reason this solvent dependance of %ee is not clear but the remainder of the runs contained more than 85% THF to ensure maximum values of enantiospecificity.

The added [Cl^-] content to the reaction mixture had a larger effect than the solvent composition. In runs 4–7 the major variation of the reaction is the added [Cl^-] content. Apparently at least $\sim$0.2 M excess [Cl^-] must be added to achieve the maximum %ee. The optical purity decreased sharply in going to 0.06–0.00 M added [Cl^-]. In such a complicated system it is difficult to define the exact role of the added [Cl^-]. In these heterogeneous reaction mixtures the chloride may be bringing more cupric chloride into solution as the $CuCl_3^-$ ion. Increasing the added [Cl^-] above 0.2 M does not to have any further effect on %ee's (compare runs 6 and 7). However, with the *p*-CN substituted phenylallyl ether (PAE), [Cl^-] does seem to make an appreciable difference.

2.2. Effect of olefin structure

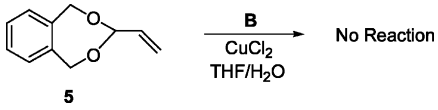
Table 2 lists the results for the oxidation of several olefins containing different functional groups and of different stereo chemistry requirements. The first five runs test the reactivity of acids, esters, aldehydes and alcohols. The fact that vinylacetic acid, methyl acrylate and *trans*-cinnamaldehyde were inactive was a surprise although these functional groups had not been tested previously. The acid and esters groups must deactivate the double bond to attack of Pd(II) and water.

On the other hand, the failure of *trans*-cinnamaldehyde was not surprising since aldehydes tend to be poor candidates for asymmetric synthesis because of side reactions. To overcome this problem, this reaction was tested on acrolein benzene-1,2-dimethanol acetal (**5**), a masked glyceraldehyde used successfully in the asymmetric dihydroxylation reaction (Scheme 3). Unfortu-

Table 2
Effect of olefin structure on rate of dioxygen uptake with (*S*)-Tol-BINAP as chiral ligand

Run	Substrate	Rate, M h^{-1}, $\times 10^3$	Yield of **1**	%ee
1	CH_2=$CHCH_2CO_2H$	0	0	0
2	CH_2=$CHCO_2CH_3$	0	0	0
3	*t*-PhCH=CHCHO	0	0	0
4	CH_2=$CHCH(OH)CH_3$	2.8	75	70
5	$AcOCH_2CH$=CH_2	1.9	75	66
6	Styrene	0.74	85 [a]	80
7	(2,6-diisopropyl)PAE	0.27	> 95	84
8	α-Methyl styrene	0.45	> 90	70
9	2-Methyl-1-butene	1.4	57	86

All runs contain 0.05–0.12 mmol of chiral catalyst in 20–30 ml of solvent and are 2.1–3.5 M in $CuCl_2$. Temperature = 25 °C. [LiCl] = 0.3–0.4 M. The solvent was a H_2O–THF mixture containing 90% THF by volume. Catalyst turnovers were between 150 and 200.
[a] Absolute configuration is *R*.



Scheme 3. Reaction of acrolein benzene-1,2-dimethanol acetal.

nately, none of the chlorohydrin was formed. It is possible that polymerization had occurred.

The enantioselectivities of 3-hydroxy-2-butene and allyl acetate were low compared with the ethers in Table 1. This could result from the presence of the hydroxy and acetate groups. These groups could interact with the Pd(II) and thus interfere from the olefin forming a good fit into the pocket formed by the chiral ligand bonded to the Pd(II). By comparison the oxidation of allyl alcohol gave low %ee's and a fair amount of the **2** isomer [10]. In addition both 1-hydroxyacetone and 3-hydroxypropanal were found in about equal amounts. This suggests that the hydroxy group have a strong directing effect on the mode of hydroxypalladation. This directing effect of the hydroxy group has been observed previously [17]. Possibly the acetate group in allyl acetate also exerts a directing influence.

Runs 6–9 test the effect of increasing substitution on rates and products. Styrene is the least substituted and thus is a model for comparison with other olefins. (2,6-diisopropyl)PAE tests the effect of *o*-substitutions on the phenyl ring. This type of steric hindrance is apparently not an important factor since the yields and %ee's compare well those in Table 1. Runs 8 and 9 are examples of α-olefins with two substitutions on one carbon of the double bond. In both runs the yields were low and with α-methylstyrene the %ee were also lower than the other three runs of the series. Some dimeric product was detected in the run. This dimerization is the predominate reaction in acetic acid [18].

The rates of the reactions in Table 2 are noteworthy mainly because they vary over a short range, a factor of only ten. As expected, they are, in general, faster for the monosubstituted olefins. However 2-methyl-1-butene is about twice as fast as styrene indicating that the phenyl group exerts more steric influence than two methyl groups. As expected, (2,6-diisopropyl)PAE and α-methylstyrene were the slowest reacting olefins.

2.3. Comparison of various chiral ligands

Table 3 lists the results of oxidations of phenyl allyl ethers by several chiral ligands. As reported previously, DIOP was not as effective as BINAP and DACH was somewhat inferior to both. The newer ligands, DINDA and METBOX were about as effective at BINAP in producing high %ee's. The lower enantioselectivity displayed with METBOX in the 1-naphthy allyl ether oxidation is to be expected since that substrate gives lower %ee's when oxidized by a catalyst in which BINAP is the ligand.

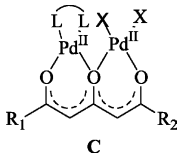
What stands out in Table 3 is the result when BZOX is the ligand. The yield of chlorohydrin product is high

Table 3
Results for the oxidation of phenyl allyl ether (PAE) and substituted phenyl allyl ethers by several chiral ligands

Run	L*–L*	Substrate	Yield of **1**	%ee
1	(*R*)-DINDA	PAE	90 [b]	86
2	(*S*)-METBOX	PAE	90 [b]	90
3	(*S*)-BZOX	PAE	90 [b]	0
4 [a]	(*S*)-BINAP	PAE	92	93
5 [a]	(−)-DIOP	PAE	88	85
6 [a]	(−)-DACH	PAE	40	60
7	(*R*)-DINDA	(4-CN) PAE	87	92
8	(*S*)-METBOX	1-naphthyl allyl ether	70 [a,b]	82
9	(−)-DIOP	(4-OMe) PAE	90	86

All runs contain 0.05–0.12 mmoles of chiral catalyst in 20–30 ml of solvent and are 2.1–3.5 M in $CuCl_2$. Temperature = 25 °C. The solvent was a H_2O–THF mixture containing 54–93% THF by volume. Catalyst turnovers were between 150 and 200.
[a] Data from reference [10].
[b] Dioxygen is oxidant; turnovers measured by O_2 uptake using gas burets. In calculating turnovers dioxygen is assumed to be a four electron oxidant.

but there was absolutely no chiral induction. METBOX and BZOX are similar in structure with the latter having one less CH_2 groups separating the two nitrogen donors. This suggests that the METBOX catalyst have the structure **B** while the BZOX catalyst **C**. The Pd(II) which contains the bidentate ligand has no labile coordinate sites and is thus inactive. The other Pd(II) has two labile coordinate sites and is thus reactive but it gives no chiral induction since it has no chiral ligand. To test this possibility both catalysts were prepared using the symmetric triketone, 2,4,6-heptanetrione. The two terminal CH_3 had an identical signal at 1.76 ppm in the ^{1}H-NMR for the METBOX containing catalyst indicating a symmetrical structure. However the signals for the terminal methyl groups in the BZOX catalyst had different values (2.00 and 2.19 ppm) indicating the non-symmetrical structure **C**. Note that BZOX might a very effective ligand for a monometallic catalyst.



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3. Conclusions

The conditions which favor the high yields and enantioselectivity in the chlorohydrin reaction by bimetallic catalysts in THF–H_2O mixtures are further defined. They include high THF content ($>85\%$) and [Cl^-] of at least 0.2 M. A series of runs with *p*-substituted phenyl allyl ethers confirm that electronic effects are not importance in yield and purity of the product. Several bidentate chiral ligands were found to be effective in producing chlorohydrins of high optical purity. However the chain between the two ligands must be long enough to bridge both of the two Pd(II)'s or an inactive catalyst will result. Aldehydes and acids and their esters are unreactive but alcohol and the esters are reactive. With simple α-olefins steric hindrance does not play a major role.

4. Experimental

4.1. General

All ^{1}H-, ^{13}C-, ^{31}P-NMR spectra were recorded on a Varian VXR 400S NMR spectrometer. Chemical shifts for ^{1}H and ^{13}C are relative to $(CH_3)_4Si$. ^{31}P chemical shifts are relative to 85% H_3PO_4 at 0.0 ppm. IR spectra were recorded on a Perkin–Elmer Model 1310 Infrared spectrometer or an ATI Mattson Genesis series FT-IR spectrometer. Melting points were recorded on a Laboratory Devices Mel-Temp apparatus using a calibrated thermometer. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. GLC analyses were carried out on a GOW-MAC gas chromatograph (Model 350) or a Perkin–Elmer Autosystem XL GC. Optical rotations were measured using a Perkin–Elmer Model 341 polarimeter.

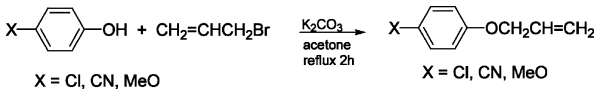
(+)- And (−)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (DIOP), (1*R*,2*R*)-(−)-1,2-diaminocyclohexane (1*R*,2*R*-DACH), (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine (*R*)-DINDA), 2,2′-methylenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] ((*S*)-METBOX), and 2,2′-methylenebis[(4*S*)-4-benzyl-2-oxazoline] ((*S*)-BZOX). tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphoratol], europium(III) derivative (Eu(hfc)$_3$), sodium hydride (60% dispersion in mineral oil), styrene, methyl acrylic, acrolein, vinylacetic acid, trans-cinnamaldehyde, 3-buten-2-ol, α-methylstyrene, 2-methyl-1-butene, 2,4-pentanedione α-styrene oxide and dehydroacetic acid were obtained from Aldrich Chemical Co. (*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl {(*S*)-BINAP} was obtained either from Fisher Scientific or Strem Chemicals. (*S*)-Tol-BINAP and tetrakis(acetonitrile)palladium(II) tetrafluoroborate, 98%, were obtained either from Strem Chemicals or Aldrich. Allyl phenyl ether was obtained from Fluka Chemical Corp. All chemicals were used as received. The preparation of 1-phenyl-1,3,5-hexanetrione (PHT), 2,4,6-heptanetrione (HpT) and allyl-α-naphthyl ether was described previously [10]. Solvents were reagent grade. Dichloromethane, diethyl ether, tetrahydrofuran, and acetonitrile were dried over calcium hydride (CaH_2) and distilled and stored under argon. The preparation of the polyketones required moisture exclusion techniques. All reaction glassware was dried overnight at 110 °C before use. The apparatus was assembled and lightly flamed while passing argon through the system. Moisture sensitive solvents and solutions were transferred via cannulas and/or syringes. Reflux reactions under nitrogen or argon were normally performed in a three-neck round bottom flask fitted with a condenser, an inert gas adapter and a suba seal septum. Reagents were introduced through the neck with the septum. The reactions were accomplished under a slight positive pressure of the inert gas.

The %ee was determined by using ^{1}H- or ^{13}C-NMR in the presence of chiral Eu(hfc)$_3$. A range of 0.1–0.3 mol ratio of Eu(hfc)$_3$ with respect to the chiral material was used.

4.2. Preparation of reactants and ligands

4.2.1. Preparation of 4-substituted phenyl allyl ether

These substrates were prepared by a literature procedure [19] according to Scheme 4.



Scheme 4. Preparation of 4-substituted phenyl allyl ethers.

4.2.1.1. X = Cl. 4-Chlorophenol (10.0 g, 0.078 mol), 14.1 g (0.117 mol) of allyl bromide, and 16.2 g (0.117 mol) of potassium carbonate were mixed together in 60 ml acetone and refluxed for 2 h. Acetone was removed by rotary evaporator and the residue extracted with Et_2O (3×50 ml). The ether layer was dried over anhydrous $MgSO_4$ and then evaporated. The residue was charged on a silica gel column chromatography. The column was eluted with 10% EtOAc–Hexane to afford a yellow oil product. The yield was 83%; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 4.50$ (dd, 2H, $J = 3.00$, 5.26 Hz), 5.28 (dd, 1H, $J = 1.38$, 10.49 Hz), 5.38 (dd, 1H, $J = 1.59$, 17.27 Hz), 6.05 (m, 1H), 6.84 (dd, 2H, $J = 2.14$, 6.73 Hz) and 7.22 (dd, 2H, $J = 2.21$, 6.80 Hz) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 68.90$, 104.82, 115.90, 119.76, 129.43, 135.40, and 156.82 ppm.

4.2.1.2. X = CN. Same procedure was used as in Section 4.2.1.1, except 4-cyanophenol allyl ether used. The yield was 85%; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 4.57$ (d, 2H, $J = 5.18$ Hz), 5.29–5.44 (ddd, 2H, $J = 1.37$, 10.35, 17.27 Hz), 6.00 (m, 1H), 6.96 (d, 2H, $J = 8.80$ Hz) and 7.57 (d, 2H, $J = 8.80$ Hz) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 68.94$, 103.97, 115.33, 118.29, 119.00, 131.93, 133.77 and 161.63 ppm.

4.2.1.3. X = MeO. Same procedure was used as in Section 4.2.1.1, except 4-methoxyphenol allyl ether used. The yield was 87%. 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 3.75$ (s, 3H), 4.46 (dt, 2H, $J = 1.50$, 5.30 Hz), 5.24 (dd, 1H, $J = 1.50$, 10.50 Hz), 5.36 (dd, 1H, $J =$ 1.50, 17.30 Hz), 6.03 (m, 1H) and 6.83 (m, 4H) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 69.40$, 70.21, 115.88, 119.76, 129.43, 135.50, 152.52 and 154.30 ppm.

4.2.2. Preparation of 2,6-diisopropylphenyl allyl ether

An 13.9 g (0.078 moles) sample of 2,6-diisopropylphenol, 14.1 g (0.117 moles) of allyl bromide, and 16.2 g (0.117 moles) of potassium carbonate were mixed together in 60 ml acetone and refluxed for 24 h. Acetone was removed by rotary evaporator and the residue extracted with Et_2O (3×50 ml). The ether layer was dried over anhydrous $MgSO_4$ and then evaporated. The residue was charged on a silica gel column chromatography. The column was eluted with 5% EtOAc–hexane to afford a yellow oil product. The yield was 95%; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 1.25$ (d, 12H, $J = 6.8$ Hz), 3.36 (septet, 1H, $J = 6.98$, 13.89 Hz), 4.30 (dt, 2H, $J =$ 1.59, 3.50 Hz), 5.30 (dt, 1H, $J = 1.27$, 10.48 Hz), 5.47 (dt, 1H, $J = 1.59$, 17.15 Hz), 6.13 (m, 1H) and 7.11 (s, 3H) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 24.06$, 26.49, 75.41, 116.84, 123.96, 124.56, 134.12, 141.87, 153.37 ppm.

4.2.3. Preparation of 3-vinyl-1,5-dihydro-3H-2,4-benzodioxepine [20]

A solution of 1,2-benzenedimethanol (**6**, 4.14 g, 30.0 mmol), trimethylorthoformate (3.18 g, 30.0 mmol), and a trace amount of *p*-toluene sulfonic acid in 1,2-dimethoxy ethane (DME) (15 ml) was stirred at room temperature (r.t.) for 1 h (Scheme 5). The reaction mixture was diluted with Et_2O and washed with sodium bicarbonate. The ether layer was dried over anhydrous $MgSO_4$. Solvent was removed by rotary evaporator, and ^{1}H-NMR for the residue indicated compound **7** obtained. The residue was redissolved in 15 ml DME. To this solution was added, acrolein (2.0 ml, 30 mmol) and a trace amount of *p*-toluene sulfonic acid. The reaction mixture was stirred for 1 h at r.t. Same work up was used as in preparation of compound **7**. Compound **5** was obtained in 70% yield; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 4.85$–4.97 (q, 4H), 5.33–5.37 (dd, 2H, $J = 1.46$, 10.53 Hz), 5.50–5.56 (d, 1H, $J = 17.36$ Hz), 5.89–5.99 (m, 1H), 7.13–7.25 (m, 4H) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 69.96$, 104.20, 118.40, 126.10, 127.20, 134.60, 138.71 ppm.

4.3. Catalyst preparation

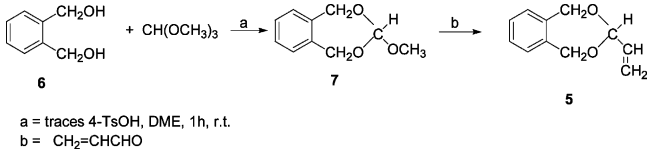
The procedure for catalyst preparation have been described [10].

4.3.1. $[Pd_2(MeCN)_2(PHT)(Tol\text{-}BINAP)](BF_4)_2$

The yield was 83%. Anal. Calc. for $Pd_2C_{64}H_{58}N_2O_3P_2B_2F_8$: C, 56.87; H, 4.33; N, 2.07; P, 4.58. Found: C, 56.27; H, 4.23; N, 2.10; P, 4.52%. ^{1}H-NMR (DMSO): $\delta = 1.77$ (s), 2.02 (s), 2.37 (s), 2.47 (s), 6.21 (s), 6.55 (dd, $J = 4.0$, 9.6 Hz), 6.65 (br), 6.86 (d, $J = 2.0$ Hz), 7.22 (t, $J = 6.8$ Hz), 7.40 (t, $J = 7.6$ Hz), 7.56 (br.t), 7.77–7.89 (m), 7.92 (m), 8.18 (br.s) ppm. ^{13}C-NMR (DMSO): $\delta =$ 1.2, 20.9, 21.1, 110.2, 113.6, 113.7, 120.7, 121.3, 124.0, 125.8, 126.8, 127.5, 128.2, 128.6, 129.1, 129.3, 129.8, 131.3, 132.2, 134.4, 135.2, 139.0, 142.3, 143.5, 162.5, 165.8, 178.8, 180.4, 185.9 ppm. ^{31}P-NMR (DMSO): $\delta =$ 31.3 ppm

4.3.2. $[Pd_2(MeCN)_2(PHT)(DINDA)](BF_4)_2$

The yield was 85%. Anal. Calc. for $Pd_2C_{36}H_{34}N_4O_3B_2F_8$: C, 45.18; H, 3.58; N, 5.85. Found: C,



Scheme 5. Preparation of 3-vinyl-1,5-dihydro-3H-2,4-benzodioxepine.

45.12; H, 3.64; N, 5.75%. ^{1}H-NMR (DMSO): $\delta = 1.77$ (s), 2.06 (s), 2.37 (s), 3.56–3.63 (br.s), 6.21 (s), 6.80 (s), 6.84 (d, $J = 2.0$ Hz), 6.92 (d, $J = 8.4$ Hz), 7.38 (t, $J = 7.6$ Hz), 7.43 (d, $J = 8.4$ Hz), 7.57 (q, $J = 6.8$ Hz), 7.76 (d, $J = 8.8$ Hz), 7.91 (dd, $J = 2.0$, 8.0 Hz), 8.10 (d, $J = 8.4$ Hz), 8.20 (d, $J = 8.8$ Hz), 8.23 (d, $J = 8.4$ Hz) ppm. ^{13}C-NMR (DMSO): $\delta = 1.1$, 18.0, 110.1, 113.6, 118.1, 120.7, 121.4, 121.8, 124.8, 125.8, 127.5, 128.7, 129.1, 131.1, 131.4, 132.0, 133.0, 136.7, 163.9, 176.8, 179.5, 183.6 ppm.

4.3.3. $[Pd_2(MeCN)_2(HpT)(BZOX)](BF_4)_2$

The yield was 87%. Anal. Calc. for $Pd_2C_{31}H_{36}N_4O_5B_2F_8$: C, 40.00; H, 3.90; N, 6.02. Found: C, 40.02; H, 3.87; N, 6.08%. ^{1}H-NMR ($CDCl_3$): $\delta = 1.39$ (d, $J = 6.4$), 1.45 (d, $J = 6.4$), 2.00 (s), 2.19 (s), 2.71 (s), 3.03 (m), 3.12 (m), 3.36 (m), 3.68 (m), 4.49–4.76 (m), 5.90 (s), 6.00 (s), 7.26–7.42 (m) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 1.9$, 18.0, 20.1, 30.4, 38.4, 38.8, 43.4, 55.4, 63.3, 63.4, 78.2, 103.9, 113.6, 118.1, 120.7, 127.6, 128.5, 128.8, 129.2, 129.4, 129.6, 129.9, 134.6, 161.6, 174.5, 178.4, 196.5 ppm.

4.3.4. $[Pd_2(MeCN)_2(HpT)(METBOX)](BF_4)_2$

The yield was 87%. Anal. Calc. for $Pd_2C_{26}H_{42}N_4O_5B_2F_8$: C, 35.60; H, 4.83; N, 6.39. Found: C, 36.01; H, 4.87; N, 6.48%.^{1}H-NMR (DMSO): $\delta = 0.93$ (s), 0.99 (s), 1.09 (s), 1.25(s), 1.26 (s), 1.28 (s), 1.76 (s), 2.20 (t, $J = 7.6$ Hz), 2.65 (t, $J = 7.6$ Hz), 3.14 (m), 3.62 (m), 6.69 (br s), 7.29 (br s), 8.16 (br s) ppm. ^{13}C-NMR (DMSO): $\delta = 1.3$, 18.0, 20.1, 25.6, 26.0, 26.3, 26.8, 41.8, 53.6, 67.8, 70.7, 71.5, 103.4, 104.0, 105.6, 118.9, 161.9, 166.3, 166.7, 171.6, 177.9 ppm.

4.4. Oxidation reactions

4.4.1. Oxidation procedure

To provide good gas liquid mixing, the reactions were run in creased flasks at 25 °C at a constant pressure of one atmosphere of dioxygen. The progress of some of the oxidations was followed by dioxygen uptake measured by gas burets thermostated at 25 °C. The reaction vessel was a 250 ml two-necked coned shaped flask with the sided indented at four places to increase stirring efficiency. The apparatus is similar to that previously described [21]. In a typical run the flask containing 30–50 ml of reaction mixture was placed in a constant temperature bath and connected to the gas buret. The system was then evacuated for 10 min on the vacuum line with stirrer running. The stirring was stopped and the system pressurized to 1.0 atm with dioxygen. The mercury in the gas buret and the leveling bulb were equalized and a reading taken. The stirrer was then activated. Atmospheric pressure was maintained by continuously leveling the mercury in the gas buret. The volume of dioxygen consumed was measured at regular time intervals (t) to give a series of readings (V_t). In all runs the gas uptake was a linear function of time. For the runs in which the dioxygen uptake was measured, the yields were based on dioxygen consumed. For the others it was based on recovered starting material.

The products were extracted with Et_2O (3×50 ml) and then dried over anhydrous $MgSO_4$. Ether was evaporated and the volume reduced to ~ 1.0 ml. This volume was charged on a silica gel (60–200 mesh) column chromatography. The column was eluted with 80% petroleum ether in CH_2Cl_2 to elute starting material and carbonyl product. Then, the column was eluted with 20% petroleum ether in CH_2Cl_2 to give the chlorohydrin. The %ee was determined by ^{1}H-NMR in the presence of chiral Eu(hfc)$_3$.

4.4.1.1. Oxidation of allyl phenyl ether. The oxidation has been described [10]. The spectra data (^{1}H-NMR, ^{13}C-NMR) of the 1-chloro-3-phenoxy-2-propanol product were identical with those reported [22].

4.4.1.2. Oxidation of (4-chloro)phenyl allyl ether. The ketone product was confirmed to be (4-chloro)-1-phenoxyacetone; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.28$ (s, 3H), 4.02 (s, 2H), 6.82 (d, 2H, $J = 9.0$ Hz), 7.22 (d, 2H, $J = 7.35$ Hz) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 26.59$, 73.28, 115.81, 129.50, 143.03, 156.25, 204.90 ppm.

The major product was confirmed to be (4-chloro)-1-phenoxy-3-chloro-2-propanol; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.55$ (s.br, OH), 3.73–3.81 (ddd, 2H, $J =$ 5.38, 11.27, 18.20 Hz), 4.05–4.07 (dd, 2H, $J = 1.17$, 5.21 Hz), 4.22 (m, 1H), 6.86 (d, $J = 9.0$ Hz), 7.23-7.26 (dd, 2H, $J = 1.95$, 7.35 Hz) ppm. ^{13}C-NMR ($CDCl_3$) $\delta =$ 45.94, 68.96, 69.83, 115.86, 129.39, 135.41, 156.75 ppm. Anal. Calc. For $C_9H_{10}Cl_2O_2$: C: 48.90; H: 4.56; Cl: 32.07. Found: C: 49.24; H: 4.60; Cl: 31.95%. $[\alpha]_D^{20} = +0.51°$ ($c = 3.33$, CH_2Cl_2) (ee = 92%).

4.4.1.3. Oxidation of (4-methoxy)phenyl allyl ether. The first fraction was obtained in a 8% yield and found to be a mixture of (4-methoxy)-1-phenoxyacetone and (4-methoxy)-3-phenoxypropanal. Their ratio was obtained by ^{1}H-NMR and found to be 69%: 31% respectively; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.25$ (s, 3H), 2.85 (m, 2H), 3.73 (s, 3H), 3.75 (s, 3H), 4.25 (d, 2H), 4.47 (s, 2H), 6.80 (s, 8H), 9.84 (t, 1H) ppm. The second fraction was obtained in $>90\%$ yield and found to be (4-methoxy)-1-phenoxy-3-chloro-2-propanol; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.54$ (d, OH, $J = 5.7$ Hz), 3.71–3.80 (m, 2H), 3.75 (s, 3H), 4.01–4.03 (dd, 2H, $J = 1.53$, 5.00 Hz), 4.16 (m, 1H), 6.83 (s, 4H) ppm. ^{13}C-NMR ($CDCl_3$): $\delta =$ 46.02, 55.78, 69.40, 70.00, 114.72, 115.63, 152.63, 154.29 ppm. Anal. Calc. For $C_{10}H_{13}ClO_3$: C: 55.44; H: 6.05; Cl: 16.36. Found: C: 56.83; H: 5.95; Cl: 15.83%. $[\alpha]_D^{20} = +0.70°$ ($c = 1.6$, CH_2Cl_2) (ee = 86%).

4.4.1.4. Oxidation of (4-cyano)phenyl allyl ether. The first fraction contained 25% of the original starting material. The second fraction contained a 75% conversion to (4-cyano)-1-phenoxy-3-chloro-2-propanol; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.50$ (d, OH, $J = 5.7$ Hz), 3.71–3.81 (ddd, 2H, $J = 5.38$, 11.27, 18.20 Hz), 4.14–4.24 (dd, 2H, $J = 1.17$, 5.21 Hz), 4.26 (m, 1H), 6.98 (d, 2H, $J = 9.0$ Hz), 7.61 (d, 2H, $J = 7.35$ Hz) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 45.84$, 68.86, 69.60, 104.89, 115.27, 118.77, 134.02, 161.34 ppm. Anal. Calc. For $C_{10}H_{10}ClNO_2$: C: 56.75; H: 4.76; Cl: 16.75, N: 6.62. Found: C: 57.88; H: 4.63; Cl: 16.50; N: 6.31%. $[\alpha]_D^{20} = +90.3^\circ$ ($c = 0.35$, CH_2Cl_2) (ee = 94%).

4.4.1.5. Oxidation of (2,6-diisopropyl)phenyl allyl ether. The first fraction contained 40% of the starting material. The second fraction contained a 60% conversion to (2,6-diisopropyl)-1-phenoxy-3-chloro-2-propanol; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 1.24$ (d, 12H, $J = 7.2$ Hz), 2.60 (d, OH, $J = 5.7$ Hz), 3.30 (septet, 2H, $J = 6.99$ Hz), 3.81 (dd, 2H, $J = 5.55$, 9.68 Hz), 3.88 (t, 1H, $J = 5.24$ Hz), 4.06 (m, 1H), 4.23 (m, 1H), 7.14 (s, 3H) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 23.99$, 24.05, 26.40, 26.44, 45.69, 70.49, 74.17, 124.15, 125.04, 141.59, 152.06 ppm.

4.4.1.6. Oxidation of 3-vinyl-1,5-dihydro-3H-2,4-benzodioxepine. ^{1}H and ^{13}C-NMR analysis of the product indicated that no chlorohydrin was present. It might be a polymerized product obtained and no further investigation was taken.

4.4.1.7. Oxidation of styrene. The first fraction was obtained in a $\sim 5\%$ yield and found to be a mixture of acetophenone and 2-phenyl acetaldehyde in a ratio of 2:1 respectively; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.15$ (s, 3H), 3.67 (d, 2H, $J = 6.80$ Hz), 7.20–7.60 (m, 10H), 9.75 (t, 1H, $J = 5.24$ Hz). The second fraction was obtained in a 85% yield and found to be 1-phenyl-2-chloro ethanol. The spectra data (^{1}H-NMR, ^{13}C-NMR) of the 1-chloro-3-phenoxy-2-propanol product were identical with those reported [23].

A sample from 2-chloro-1-phenylethanol (styrene chlorohydrin) was reacted with 2 ml 30–40% NaOH solution at r.t. The reaction mixture was stirred for 30 min. Styrene oxide was extracted with $CDCl_3$. The spectra date (^{1}H-NMR, ^{13}C-NMR) were identical with those reported [24]. The %ee was determined by ^{1}H-NMR in the presence of chiral Eu(hfc)$_3$ and found to be 78%. The absolute configuration of styrene oxide was determined by comparison with ^{1}H-NMR of the authentic sample of (*R*)-styrene oxide in the presence of 0.2 mol ratio of Eu(hfc)$_3$. The configuration was found to be (*S*)-styrene oxide. Since the configuration was reversed in forming the oxide the starting chlorohydrin was (*R*).

4.4.1.8. Oxidation of 2-methyl-1-butene. The chlorohydrin product was obtained in a 60% yield based on oxygen uptake and found to be a mixture of 2-methyl-1-chloro-2-butanol and 2-methyl-2-chloro-1-butanol. The ratio of these two was obtained by GC and found to be 95:5% respectively; 400 MHz; ^{1}H-NMR ($CDCl_3$) for 2-methyl-1-chloro-2-butanol (major product): $\delta = 0.90$ (t, 3H, $J = 7.40$ Hz), 1.18 (s, 3H), 1.52 (q, 2H, $J = 7.6$ Hz), 2.36 (br., OH), 3.65(s, 2H) ppm. ^{13}C-NMR ($CDCl_3$) $\delta = 8.52$, 15.19, 28.58, 36.28, 67.68 ppm.

4.4.1.9. Oxidation of α-methyl styrene. Two fractions were collected by column chromatography. The first fraction was found to be the starting material and some Diels Alder products. The second fraction was obtained in a 40% conversion relative to starting material and found to be 1-chloro-2-phenyl-2-propanol; 400 MHz; ^{1}H-NMR ($CDCl_3$): $\delta = 2.11$ (s, 3H), 4.04 (q, 2H, $J = 11.4$ Hz), 4.48 (s, OH), 7.33–7.41 (m, 3H), 7.56–7.58 (d, 2H, $J = 7.2$ Hz) ppm. ^{13}C-NMR ($CDCl_3$): $\delta = 28.20$, 54.59, 70.54, 126.40, 128.40, 128.52, 141.47 ppm.

4.4.1.10. Oxidation of allyl acetate. The first fraction contained recovered starting material. The second was pure 3-chloro-2-hydroxypropyl acetate. 400 MHz ^{1}H-NMR ($CDCl_3$): $\delta = 2.09$ (s, 3H), 2.36 (s, OH), 3.58–3.63 (dd, 2H, $J = 5.4$, 9.4 Hz), 4.06 (m, 1H), 4.19 (d, 2H, $J = 5.2$ Hz) ppm. ^{13}C-NMR ($CDCl_3$) $\delta = 20.80$, 45.97, 65.29, 69.62, 71.09 ppm.

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