Oxidation of Olefins by Palladium(II). 16. A New Palladium(II)-Catalyzed Asymmetric Chlorohydrin Synthesis

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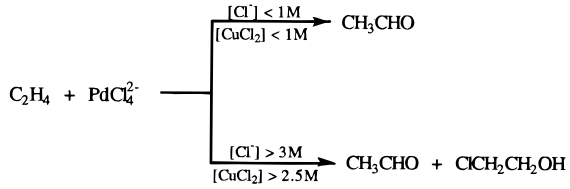
Previous studies showed that palladium(II) catalysts containing a pyridine ligand give mainly ethylene chlorohydrin as a product of the oxidation of ethene in the presence of $CuCl_2$ at $[Cl^-] = 0.2$ M. Under the same conditions $PdCl_4^{2-}$ produced only ethanal. The replacement of pyridine by a chiral monoamine gave a catalyst which oxidized propene and methyl vinyl ketone to optically active chlorohydrins. However, the optical yields were low, with ee's of only 8−12%. The use of chelating diphosphines would be expected to greatly improve optical yields. However, the neutral catalysts containing diphosphine ligands were insoluble in the mixed H_2O−THF (4/1) reaction media. The chiral ligands (*2S*,*4S*)-bis-(diphenylphosphino)pentane ((*S*,*S*)-BDPP), (*2S*,*3S*)-bis(diphenylphosphino)butane ((*S*,*S*)-Chiraphos), and (*R*)−(+)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl ((*R*)-Tol-BINAP) were sulfonated to give water-soluble catalysts. These catalysts gave poor to modest ee's (28−76%) in the oxidation of propene, methyl vinyl ketone, and allyl phenyl ether. In H_2O−THF mixed solvents richer in THF (1/2 H_2O/THF), unsulfonated (*R*)-Tol-BINAP is soluble to some extent. Oxidation of the above olefinic substrates with this system gave the corresponding chlorohydrins with slightly higher enantioselectivities than with the sulfonated catalysts. The absolute configuration of the chlorohydrin from propene with the (*R*)-Tol-BINAP catalyst was *R*. The oxidation of 2,3-dihydrofuran gave chlorohydrins with the *E* conformation. These two stereochemical results are consistent with anti addition to the most stable π-complex followed by a Pd(II)−carbon bond-breaking step which places a chloride from the coordination sphere of Pd(II) on the carbon which is leaving.

Introduction

Presently there are several useful methods for the asymmetric oxygenation of olefins. These include the epoxidation of allylic alcohols (AE),[1a] epoxidation of unfunctionalized olefin,[1b] asymmetric dihydroxylation (AD),[1c] and, more recently, the aminohydroxylation reaction (AA).[2] This paper describes yet another transition-metal-mediated asymmetric oxygenation reaction, the palladium(II)-catalyzed chlorohydrin synthesis.

The Pd(II)-catalyzed oxidation of ethene in aqueous solution (Wacker reaction, Scheme 1) gives exclusively acetaldehyde under the usual Wacker conditions of low $[Cl^-]$ (<1.0 M).[3] Under the same conditions Pd(II) oxidizes α-olefins to methyl ketones and aldehydes. Thus, propene gives a mixture of acetone and propanal. At high $[Cl^-]$ (>2.5 M) and high $[CuCl_2]$ (>3 M) formation of ethylene chlorohydrin becomes a serious side reaction.[3,4] Controversial issues regarding the Wacker oxidation concern the stereochemistry of addition of the elements of Pd(II) and OH to the ethene double bond (hydroxypalladation) under conditions of low and high $[Cl^-]$, as well as the nature of the active intermediate under these two sets of conditions. Recent studies in these laboratories showed that the mode of addition and thus the active Pd(II) species are different at low and high $[Cl^-]$.[5] The intermediate at low $[Cl^-]$ is $PdCl_2(OH)(C_2H_4)$, while the intermediate at high $[Cl^-]$ leading to chlorohydrin is $PdCl_3(C_2H_4)^-$.

Scheme 1



Mechanistic considerations predicted that the addition of a neutral ligand to the coordination sphere of Pd(II) would both retard the Wacker reaction and give chlorohydrin product at much lower $[Cl^-]$ than with $PdCl_4^{2-}$ as the initial Pd(II) species. In fact, $PdCl_3$(pyridine)$^-$ was found to give 2-chloroethanol at $[Cl^-] = 0.2$

(1) (a) Johnson, R. A.; Sharpless, K. B. In "Catalytic Asymmetric Synthesis; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.1. (b) Jacobsen, E. N. In ref 1a, Chapter 4.2. (c) Johnson, R. A.; Sharpless, K. B. In ref 1a, Chapter 4.4.

(2) Li, G..; Chang, H.-T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451−454.

(3) For general discussion and references see: Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; D. Reidel: Dordrecht, Holland, 1980; pp 41−84.

(4) Stangl, H.; Jira, R. *Tetrahedron Lett.* **1970**, 3589−5592.

(5) (a) Francis, J. W.; Henry, P. M. *Organometallics* **1991**, *10*, 3498−3503. (b) Francis, J. W.; Henry, P. M. *Organometallics* **1992**, *11*, 2832−2836. (c) Hamed, O.; Thompson, C.; Henry, P. M. *J. Org. Chem.* **1997**, *62*, 7082−7083.

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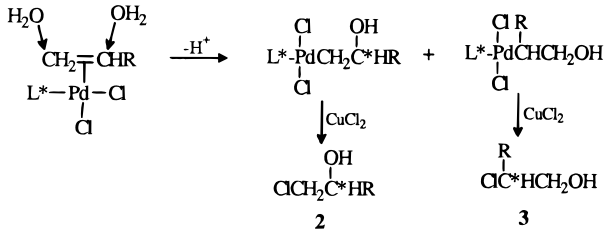
Scheme 2



M and $CuCl_2$ = 4 M.[6] With $PdCl_4^{2-}$, 2-chloroethanol would *not have been formed at any [$CuCl_2$]!* Also, the rate of acetaldehyde formation decreased by a factor of 750. These results open up the possibility of a new asymmetric chlorohydrin synthesis. The incorporation of chiral neutral ligands in the coordination sphere of Pd(II) should lead to catalysts for chiral chorohydrin formation by olefin oxidation.[7]

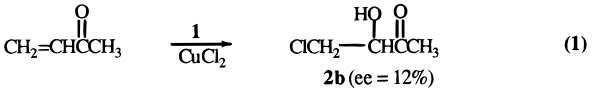
Some of the results of this study have been reported in a preliminary communication.[9]

Results

Oxidation by a Pd(II) Catalyst Containing a Chiral Monodentate Amine. The first catalyst tested was Cl_3PdL^{*-} (**1**; L* = (*S*)−(−)-*N*,*N*-dimethyl-1-phenethylamine). The olefins chosen for these studies were propene and methyl vinyl ketone. Initial studies on the oxidation of propene, carried out at different concentrations of $CuCl_2$ and LiCl, determined optimum conditions for chloropropanol formation. These concentrations were 6.0 M $CuCl_2$ and 0.2 M LiCl.

Oxidation of propene under these conditions gave acetone, 1-chloro-2-propanol (**2a**), and 2-chloro-1-propanol (**3a**) in relative yields of 15%, 67%, and 18%, respectively, as shown by GLC and ^{1}H NMR. Preparative GLC produced a pure sample of **2a**. ^{1}H NMR analysis of the sample in the presence of the lanthanide shift reagent Eu(hfc)$_3$ showed the presence of two enantiomers in relative yields of 45.6% and 54.4% (8.8% ee). Because of the low yield of **3a**, its ee percentage was not determined. As shown in Scheme 2, the two chloropropanols arise from attack of water at each of the two olefinic carbons of the Pd(II) π-complex.

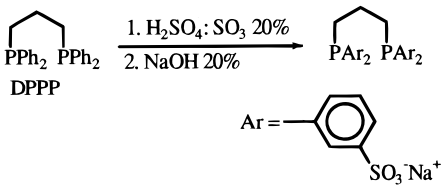
As shown in eq 1, the oxidation of methyl vinyl ketone under the same conditions used above gave only 4-chloro-3-hydroxy-2-butanone (**2b**), which was identified by GLC retention time and ^{1}H and ^{13}C NMR. The ee of **2b** was 12%.



(1)

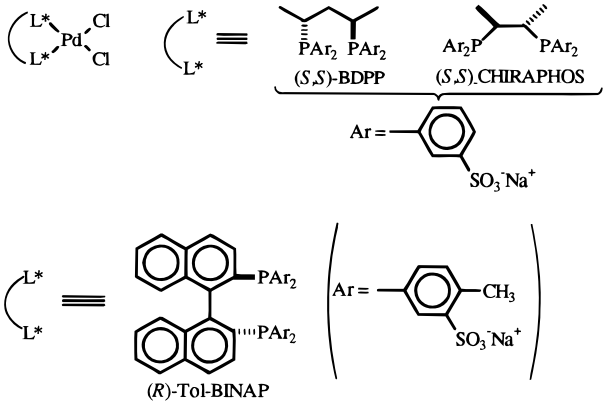
Chiral Sulfonated Phosphines: Synthesis and Use in Asymmetric Synthesis. The initial studies employed the nonchiral diphosphine 1,3-bis(diphenylphosphino)propane (DPPP). The complex [$PdCl_2$-(DPPP)] was prepared by mixing K_2PdCl_4 and the diphosphine in THF and characterized by ^{1}H, ^{31}P, and ^{13}C NMR. Unfortunately this complex was insoluble in aqueous solution. This problem was solved by sulfonating the aryl rings of the DPPP.

Sulfonation of the DPPP was carried out in concentrated sulfuric acid containing 20% SO_3 at room temperature for 24 h followed by neutralization with NaOH.[10] The sulfonated DPPP ligand was characterized by ^{31}P, ^{1}H, and ^{13}C NMR.



The catalyst used in this study was prepared by mixing equimolar amounts of Li_2PdCl_4 and sulfonated DPPP in distilled degassed water. The oxidation was performed in a water−THF mixture (4/1 ratio by volume) in the presence of $CuCl_2$ and LiCl at concentrations of 6.0 and 0.2 M, respectively. As discussed above, these were the optimum conditions for maximizing the yield of the hydroxychlorinated product with the catalyst containing the monodentate chiral amine. Analysis of the product by GLC showed the presence of three products, acetone, 1-chloro-2-propanol (**2a**), and 2-chloro-1-propanol (**3a**), in relative yields of 5%, 88%, and 7%, respectively.

Attention was now turned to the asymmetric oxidation of olefins by a Pd(II) catalyst coordinated to a highly sulfonated chiral diphosphine ligand. The ligands chosen for this purpose were (2*S*,4*S*)-bis(diphenylphosphino)pentane ((*S*,*S*)-BDPP), (2*S*,3*S*)-bis(diphenylphosphino)butane ((*S*,*S*)-Chiraphos), and (*R*)−(+)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl ((*R*)-Tol-BINAP). These



three ligands were sulfonated by a procedure similar to that used in the sulfonation of 1,3-bis(diphenylphosphino)propane. Sulfonation of (*S*,*S*)-BDPP gave a mixture of 18.5% mono-, 6.5% di-, 20% tri-, and 55% tetrasulfonated diphosphine, as determined by ^{31}P NMR. Sulfonation of (*S*,*S*)-Chiraphos gave the tetrasulfonated diphosphine in 76% yield and a 23% mixture of mono-, di-, and trisulfonated phosphines. However,

(6) Francis, J. W.; Henry, P. M. *J. Mol. Catal. A: Chem.* **1995**, *99*, 77−86.

(7) A recent report of the oxychlorination of allylic amines and sulfides is another example of the effect of a neutral ligand on the chlorohydrin formation.[8]

(8) Lai, J.-Y.; Wang, F.-S.; Guo, G.-Z.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 6944−6946.

(9) El-Qisairi, A.; Hamed, O.; Henry, P. M. *J. Org. Chem.* **1998**, *63*, 2790−2791.

(10) Amrani, Y.; Lecomte, L.; Sinou, D.; Bakos, J.; Toth, I.; Heil, B. *Organometallics* **1989**, *8*, 542−547.

Table 1. $^{31}P\{^1H\}$ NMR Data for the Tetrasulfonated Diphosphines andthe Corresponding Pd(II) Complexes

	δ(P) (D_2O)[a]	
ligand	tetrasulfonated ligand	$PdCl_2$ complex
1,3-BPP	−16.31	14.00
(*S*,*S*)-BDPP	0.65	27.00
(*S*,*S*)-CHIRAPHOS	−9.96	57.90
(*R*)-Tol-BINAP	−16.30	16.70

[a] In ppm relative to external H_3PO_4.

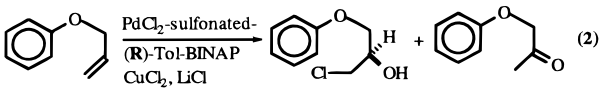
sulfonation of (*R*)-Tol-BINAP gave only one product, which was identified by ^{31}P and ^1H NMR to be tetrasulfonated (*R*)-Tol-BINAP. Table 1 lists the $^{31}P\{^1H\}$ NMR data for the sulfonated phosphines.

The preparation of the sulfonated chiral diphosphine−Pd(II) catalysts involved procedures similar to those described above for the DPPP catalyst. Table 1 summarizes the $^{31}P\{^1H\}$ NMR data for these catalysts. The substrates for the asymmetric oxidation studies were propene, methyl vinyl ketone, and allyl phenyl ether. The conditions were water−THF mixed solvents in the presence of $CuCl_2$ and LiCl at concentrations of 6.0 and 0.2 M, respectively. Table 2 summarizes the results of these studies.

Oxidation of propene by all three catalysts gave a mixture of three products, acetone, **2a**, and **3a**, in relative yields of 5%, 88%, and 7%, respectively. Preparative GLC afforded pure samples of **2a**. Analysis of the samples by ^1H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$ gave the enantioselectivities shown in Table 2.

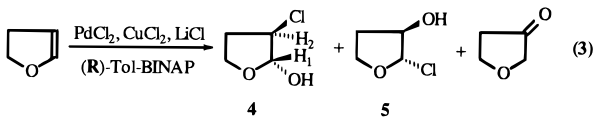
As with the catalyst containing the monodentate chiral amine (eq 1), oxidation of methyl vinyl ketone produced only one product by GLC analysis. Preparative GLC yielded a pure sample of the product. ^1H and ^{13}C NMR analysis identified the compound as 4-chloro-3-hydroxy-2-butanone (**2b**).

Oxidation of allyl phenyl ether in the presence of tetrasulfonated (*R*)-Tol-BINAP afforded two products in relative yields of 84 and 16%. The compounds were identified by ^1H and ^{13}C NMR to be 1-phenoxy-3-chloro-2-propanol (**2c**) and phenoxypropanone (eq 2). The ee of **2c** was 68%.



$PdCl_2$−(*R*)-Tol-BINAP-Catalyzed Oxidation of Olefins. The substrates for the oxidation studies were propylene, methyl vinyl ketone, allyl phenyl ether, and 2,3-dihydrofuran. The catalyst was generated in situ from $PdCl_2(CH_3CN)_2$ and (*R*)-Tol-BINAP in THF. The conditions were a H_2O−THF mixed solvent (1:2) in the presence of $CuCl_2$ (4.0 M) and LiCl (0.2 M). Preparative GLC provided pure samples of the products, which were identified by ^1H and ^{13}C NMR. The ee's were determined by ^1H and ^{13}C NMR using the chiral shift reagent Eu(hfc)$_3$. Table 2 summarizes the results.

Oxidation of propene gave acetone, **2a**, and **3a** in relative yields of 35%, 55%, and 10%, respectively. The ee of **2a** was 56%, and its absolute configuration was *R* as shown by the following procedure. A pure sample of **2a** obtained by preparative GLC was converted into propylene oxide by reacting it with 5% NaOH solution. Comparison of the ^1H NMR spectrum of the oxide in the presence of Eu(hfc)$_3$ with that of an authentic sample from Aldrich confirmed the *R* configuration. Oxidation of methyl vinyl ketone gave 3-chloro-2-hydroxy-2-butanone (**2b**) as the only product in 82% ee and in 78% chemical yield. Allyl phenyl ether gave **2c** in 80% ee and 35% chemical yield. The low yield in this case could be related to low solubility of the allyl phenyl ether in the reaction mixture. Oxidation of 2,3-dihydrofuran gave the three products shown in eq 3 in a

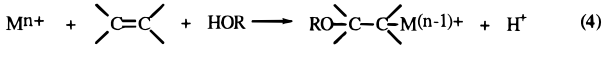


total chemical yield of 75%. The three products were identified as 3-chloro-2-hydroxytetrahydrofuran (**4**), the positional isomer 2-chloro-3-hydroxytetrahydrofuran (**5**), and 3-oxotetrahydrofuran. The three compounds are present in 75%, 5%, and 20% relative yields, respectively. The ee of **4** was determined to be 56%. ^1H NMR analysis showed that H_1 and H_2 have an *E* conformation ($J_{1,2}$ = 2.93 Hz).[11]

Discussion

The development of this new asymmetric synthesis was made possible by a detailed mechanistic knowledge of a very complicated reaction system. The key was the discovery that the hydroxypalladation adduct that was intercepted by $CuCl_2$ at high [Cl^-] was not the same intermediate that decomposed to acetaldehyde at low [Cl^-]. The adduct at low [Cl^-] has a labile aquo ligand, while in the adduct at high [Cl^-] the water is replaced by a nonlabile Cl^-, which inhibits decomposition by hydride transfer. This finding led to the proposal that a catalyst containing a strongly binding neutral ligand such as an amine should stabilize the intermediate so it can be intercepted by $CuCl_2$ at low [Cl^-]. As predicted, the catalyst $PdCl_3$(pyridine)$^-$ gave chlorohydrin at [Cl^-] as low as 0.2 M. In addition the acetaldehyde formation was strongly suppressed.

The reaction to form chlorohydrin, which requires both Pd(II) and Cu(II), is of itself an interesting example of cocatalysis by two metal species. We believe this is a classic example of changing the nature of the metal "leaving group" in a metal ion oxidation of olefins. Many metal ions (Pb^{4+}, Tl^{3+}, Hg^{2+}, Pd^{2+}, and other noble-metal ions) interact with olefins to give oxymetalation adducts such as those shown in eq 4.[12,13] The ability of



this intermediate to oxidatively decompose depends on the nature of the metal species that will be lost in the

(11) Bovey, F. A. *Nuclear Magnetic Resonance Spectroscopy*, Academic Press: San Diego, CA, 1988; p 617.

(12) For a review of olefin oxidation by these metal ions see: Henry, P. M.; Lange, G. L. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1977; Part 2, Chapter 11.

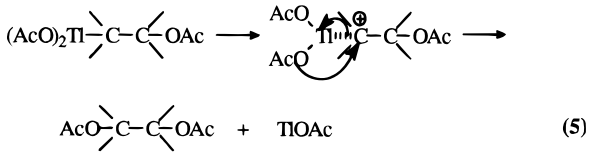
(13) For a comparison of Pd(II) and Tl(III) oxidation mechanisms, see: Henry, P. M. *Adv. Chem. Ser.* **1968**, *70*, 127−154.

Table 2. Results for the Oxidation of Several Olefins by Sulfonated and Unsulfonated Catalysts in the Presence of $CuCl_2$[a]

run	ligand	H_2O/THF	substrate	**2**/**3** ratio[b]	% ee of **2**	turnovers
			Sulfonated Catalysts			
1	(*S*,*S*)-BDPP	4/1	propene	12	28	60[c]
2	(*S*,*S*)-CHIRAPHOS	4/1	propene	12	46	60[c]
3	(*R*)-Tol-BINAP	4/1	propene	12	44	60[c]
4	(*S*,*S*)-CHIRAPHOS	4/1	CH_2=CHC(O)CH_3	>95	64	65[d]
5	(*R*)-Tol-BINAP	4/1	CH_2=CHC(O)CH_3	>95	76	65[d]
6	(*R*)-Tol-BINAP	3/2	CH_2=CHCH_2OPh	>95	68	72[d]
			Unsulfonated Catalyst			
7	(*R*)-Tol-BINAP	1/2	propene	5.5	56[e]	ND[f]
8	(*R*)-Tol-BINAP	1/2	CH_2=CHC(O)CH_3	>95	82	ND[f]
9	(*R*)-Tol-BINAP	1/2	CH_2=CHCH_2OPh	>95	80	ND[f]

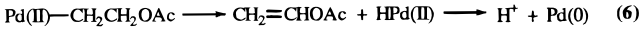
[a] All runs contain 0.1−0.3 mmol of chiral catalyst in 25−50 mL of solvent and are 6 M in $CuCl_2$ and 0.2 M in LiCl. Temperature: 25 °C. The solvent was a H_2O/THF mixture. [b] The reaction mixture also contained varying amounts of the Wacker ketone product (5−30%). [c] Measured by propene uptake using gas burets. [d] Dioxygen is the oxidant; turnovers were measured by O_2 uptake using gas burets. In calculating turnovers dioxygen is assumed to be a four-electron oxidant. [e] Absolute configuration determined to be (*R*) by conversion to the epoxide and comparison with an authentic sample. [f] Not determined.

decomposition. If the original metal ion is Hg(II), the leaving group will be Hg(0), which would be a "poor" leaving group since monatomic zerovalent metal species are unstable in aqueous solution. For that reason the well-known oxymercurials are stable compounds even though Hg(II) is a fairly strong oxidizing agent. However, *their stability would be expected to be decreased by adding excess Hg(II) because the mercury can now leave as Hg(I)−Hg(I) dimers, which* ***are*** *stable species.* In fact, it has been found that the rate of decomposition of allylic mercurials is increased by the addition of extra Hg(II) salts.[14] On the other hand, if the metal ion is lead(IV) or thallium(III) the intermediates are very unstable because these metal ions are vigorous oxidizing agents and Pb(II) and Tl(I), which are stable species in aqueous solution, are "good" leaving groups. The decomposition is of the carbonium ion type, which gives saturated products. An example is the decomposition of the oxythallation intermediate in acetic acid solvent:



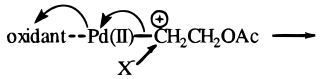
(5)

In oxidations by Pd(II), Pd(0) is the leaving group. Like Hg(0), Pd(0) would be a poor leaving group because it is an unstable species in aqueous solution and oxypalladation adducts would not decompose by carbonium ion mechanisms the way oxythallation adducts do. However, Pd(II), since it is a transition metal, has an alternate means of decomposition, β-hydride elimination. Thus, as shown in eq 6, in acetic acid solution ethene is oxidized to vinyl acetate.



(6)

Apparently oxidants can interact with Pd(II) in the transition state for decomposition, removing two electrons from the Pd(II) so that Pd(0) is not formed but rather Pd(II) is the leaving group.[15] This is similar to the way Hg(II) interacts with mercurials. Equation 7 shows the postulated scheme where the oxidant in the present case is very likely a $CuCl_2$ cluster.[16]



(7)

Although not expected to give high optical yields, the addition of a monodentate chiral ligand to Pd(II) was a logical starting point. As shown in Scheme 2, the enantioselectivities with propene were indeed low, ee = 8.8%. Also, 15% of the product was acetone; therefore, this side reaction was not completely eliminated. A potential complication was the formation of both of the positional isomers, **2a** and **3a**. This result is not surprising, since propene is oxidized to both acetone and propanal under Wacker conditions. These two products also arise from the two possible modes of addition to the double bond. Of course, if the epoxide is the final product and both isomers gave epoxide of the same absolute configuration, there would be no problem. However, because of the small quantities of **3a** produced, its absolute configuration was not determined. Such studies will be described in a future publication.

The oxidation of methyl vinyl ketone gave a somewhat different result. Only one chlorohydrin isomer is formed, and no Wacker oxidation product is observed. This is an encouraging result, since many of the olefins of interest will have groups bulkier than methyl. Unfortunately, the optical purity was again very low (ee = 12%).

The next step was to proceed to bidentate ligands to both improve the optical yields and decrease the carbonyl product side reaction. Thus, if a monodentate ligand decreases the rate of Wacker-type product by a factor of almost 1000, a bidentate ligand would be expected to decrease carbonyl formation even further. At this point a complication arose. With the mixed solvent system initially employed (H_2O/THF = 4/1), these catalysts, being neutral species, were insoluble. Sulfonating the aromatic rings of the diphosphines

(14) Rappoport, Z.; Sleezer, P. D.; Winstein, S.; Young, W. G. *Tetrahedron Lett.* **1965**, 3719−3728.

(15) Henry, P. M. *J. Org. Chem.* **1973**, *38*, 1681−1684.

(16) An alternate mechanism is the transfer of the alkyl to $CuCl_2$ followed by decomposition. However, studies with several noble metals have eliminated this mechanism.[17]

(17) Henry, P. M. *J. Org. Chem.* **1974**, *39*, 3871−3874.

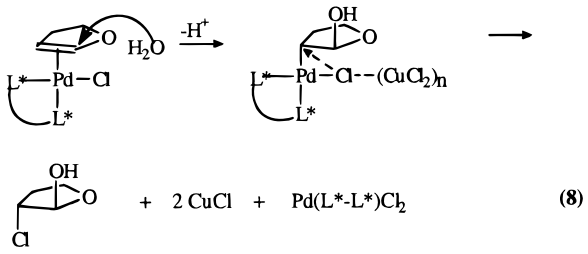
achieved the required solubility. Under the sulfonating conditions employed, the ligands were highly sulfonated, containing mainly the tetrasulfonated species.

As shown in Table 2, these catalysts gave only poor to modest asymmetric inductions. Previous studies suggested that the degree of sulfonation could be an important factor in determining ee values.[10,18] In the hydrogenation of imines by rhodium(I) catalysts containing a sulfonated chiral diphosphine, it was found that the optical purity depended on the degree of sulfonation.[18] When the degree of sulfonation was about 4 (all four aryl rings were sulfonated), the % ee of the product was only 19%. However, when the degree of sulfonation was about 1.5, the optical purity rose to 96% ee. Thus, the use of catalysts with monosulfonated Tol-BINAP probably would increase ee values with the monometallic sulfonated catalysts in the present studies.

The **2**/**3** ratio was high for runs 1−3, indicating that the formation of **3** is not a serious problem. Only propene gave any detectable amount of **3.** Even in this case it was less than 10% of the total. Steric factors must account for this trend in **2**/**3** ratios.

The discovery that mixed aqueous solvents containing greater proportions of THF (1/2 H_2O/THF) dissolved the unsulfonated (*R*)-Tol-BINAP catalyst added a new dimension to the studies. On the basis of the above discussion, the unsulfonated catalysts should give higher enantioselectivities than the sulfonated catalysts. As shown in Table 2, the % ee's were higher than those for the sulfonated (*R*)-Tol-BINAP catalyst listed in Table 2 but the differences were not large.

The stereochemical results with the (*R*)-Tol-BINAP catalyst provides some mechanistic insight on the chlorohydrin synthesis. The configuration of the chlorohydrin **2a** from propene oxidation by this catalyst system was *R*. Molecular models indicate that this result is consistent with anti addition to the most stable π-complex. The mechanistic studies discussed in the Introduction predict anti addition for Pd(II) catalysts containing a neutral ligand. 2,3-Dihydrofuran gave chlorohydrin with the *E* configuration. If the hydroxypalladation is anti, the decomposition must occur from the coordination sphere of the Pd(II) in order to give the overall *E* configuration. This last result is inconsistent with studies on the decomposition of hydroxypalladation adducts formed by exchange of hydroxymercuration adducts with $PdCl_4^{2-}$ in the presence of $CuCl_2$.[19] However, these last experiments were conducted at high [Cl^-], where the mode of decomposition may be different from the conditions of the present experiment. A plausible reaction sequence is shown in eq 8. Although



(8)

Cl^- is shown arising from the coordination sphere of Pd(II), it is also possible that it comes from the coordination sphere of the copper.

The discovery of a new asymmetric chlorohydrin synthesis increases the present stable of transition-metal-catalyzed chiral syntheses. It differs from previous asymmetric oxidation reactions of olefins in that it is a catalytic air oxidation.[1,2] Thus, the $CuCl_2$ regenerates the Pd(II) and the resulting CuCl is readily oxidized by dioxygen to $CuCl_2$ to complete the catalytic cycle. The closest comparison to the present reaction is the Pd(II)-catalyzed synthesis of chiral chlorohydrins using an olefin containing a chiral allylic amine ligand.[8] This very interesting conversion gives a chiral chlorohydrin containing the chiral amine in poor to modest enantioselectivities (ee = 1−77%). As the chiral agent is monodentate, the system is analogous to catalyst **1**. The π-complex formed from catalysts of type **1** is shown in Scheme 2. The fact that the optical yields were generally higher than those obtained with **1** can be rationalized by the fact that, unlike catalyst **1**, the system has a rigid structure. In addition, as opposed to catalyst **1**, the olefin is forced next to the chiral center.

An interesting possibility is the formation of other asymmetric products by variation of reaction conditions. The reaction consists of two distinct steps, addition and decomposition. Nucleophiles other than water could potentially react in the first step. In chloride-free media nucleophiles other than chloride could be involved in the decomposition step and nucleophiles better than water could be the attacking species in the first step. Thus, preparations of chiral bromohydrins and iodohydrins as well as of chiral dibromides are viable possibilities.

Future work will concentrate on defining the scope of the reaction and improving optical yields. The latter effort involves the testing of other chiral auxiliaries and determination of the effect of [Cl^-] and solvent composition on ee percentages. For the sulfonated catalysts the effect of the degree of sulfonation will also be studied.

Experimental Section

General Considerations. GLC analyses were performed on a GOW-MAC 350 gas chromatograph fitted with Carbowax 10 M on 80−100 mesh Chromosorb W-NAW columns. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a 300 MHz Varian VXR 300 spectrometer. Chemical shifts for ^1H and ^{13}C are relative to $(CH_3)_4Si$. ^{31}P chemical shifts are relative to 85% H_3PO_4 at 0.0 ppm. Melting points were recorded on a Laboratory Devices Mel-Temp apparatus using a calibrated thermometer.

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

Materials. $PdCl_2$ was purchased from Alfa AEsar and used without further purification. DPPP, (*S*,*S*)-BDPP, (*S*,*S*)-Chiraphos, and (*R*)-Tol-BINAP were obtained from Strem Chemical Inc. and used without further purification. (*S*)-(−)-*N*,*N*-dimethyl-1-phenethylamine was purchased from Aldrich and used as received. THF was dried over sodium benzophenone ketyl and distilled and stored over CaH_2 under Ar. All other chemicals were of reagent grade. Europium(III) tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] (Eu(hfc)$_3$), propene, and (*S*)-propylene oxide were obtained from Aldrich Chemical Co. Allyl phenyl ether was obtained from Fluka Chemical Corp. All chemicals were used as received.

(18) Bakos, J.; Orosz, A.; Heil, B.; Laghmari, M.; Lhoste, P.; Sinou, D. *J. Chem. Soc., Chem. Commun.* **1991**, 1684−1685.
(19) Bäckvall, J. E.; Åkermark, B.; Ljunggren, S. O. *J. Am. Chem. Soc.* **1979**, *101*, 2411−2416.

General Procedure for the Catalytic Oxidation of Olefins. In a typical experiment a 250-mL two-necked cone-shaped flask, with indented sides to increase the efficiency of stirring, was equipped with a magnetic stirring bar, subseal septum and vacuum adapter. The flask was charged with 20 mL of H_2O, 5 mL of THF, 10.09 g (75 mmol) of $CuCl_2$, 0.212 g (5 mmol) of LiCl, and 0.1 mmol of catalyst. The flask was then placed in a constant-temperature bath at 25 °C and connected to the gas uptake system.[20] The system was evacuated for 10 min on the vacuum line with the stirrer running. The stirring was stopped and the system pressurized to 1 atm with dioxygen. The olefin was added to the reaction mixture by syringe. In the case of propene oxidation, propene was the gas rather than oxygen; therefore, the reaction was followed by propene uptake. The mercury in the gas buret and the leveling bulb were equalized, and a reading was taken. The stirrer was turned on to start the reaction. The pressure was kept constant at 1 atm by continuously leveling the mercury in the gas buret and bulb. Gas uptake readings were taken at regular intervals. The reaction was allowed to run until the reaction mixture was at least 0.25 M in total oxidation product. The oxidation product was separated from the reaction mixture by continuous extraction with ether overnight. The ether was dried over anhydrous $MgSO_4$ and removed by distillation. Analysis of the product was carried out by GLC and ^{1}H and ^{13}C NMR.

Preparation of a Pd(II) Complex with a Chiral Monodentate Amine, 1. A 0.72 g (2.2 mmol) sample of K_2PdCl_4 and 0.36 mL of (*S*)-(−)-*N*,*N*-dimethyl-1-phenethylamine (2.2 mmol) were suspended in 15 mL of dry THF under Ar and stirred at room temperature for 24 h. The resulting brownish yellow solid was collected by filtration, washed with ether, and dried under vacuum to give 0.51 g (72% yield) of **1**: mp 142−145 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.50 (m, 5H), 4.28 (q, 1H), 2.57 (s, 3H), 2.47 (s, 3H), 1.29 (d, 3H).

Oxidation of Propene Catalyzed by 1. The flask was charged with H_2O (25.0 mL), $CuCl_2$ (6.0 M), LiCl (0.2 M), and Pd(II) complex **1** (0.15 g; 0.5 mmol). GLC analysis and preparation of the 2,4-DNP derivative showed the presence of acetone, 2-chloro-1-propanol (**3a**), and 1-chloro-2-propanol (**2a**) in relative yields of 15%, 18%, and 67%, respectively. A pure sample of **2a** was collected by preparative GLC and analyzed by ^{1}H NMR. The ^{1}H NMR in the presence of Eu(hfc)$_3$ showed the ee to be 8.8%.

Oxidation of Methyl Vinyl Ketone Catalyzed by 1. Oxidation of methyl vinyl ketone by the procedure described above afforded only one product. GLC and ^{1}H and ^{13}C NMR identified the product as 4-chloro-3-hydroxy-2-butanone (**2b**). ^{1}H NMR ($CDCl_3$): δ 4.30 (t, 1H), 3.90 (dd, 2H), 2.56 (s, 1H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 203.0, 62.5, 63.7, 27.6.

Preparation of Sulfonated Phosphine: General Procedure. To 1 mmol of diphosphine in 0.5 mL of sulfuric acid in a two-necked flask under Ar at 0 °C was added 6.0 mL of sulfuric acid containing 20% SO_3 slowly over a period of 6 h. After 24 h of stirring at room temperature, the mixture was poured slowly onto 50 g of ice and neutralized with 20% NaOH at 0 °C. After filtration the solution was poured into 50 mL of methanol and the solid precipitate was extracted with methanol (2 × 50 mL). The layers were combined and the solvent evaporated under vacuum. The residue was then dissolved in a minimum amount of water and poured into methanol. The solid which was produced was removed by filtration and the filtrate evaporated to give the crude tetrasulfonated diphosphine. The crude product was recrystallized from aqueous methanol several times.

Preparation of Sulfonated DPPP. ^{31}P NMR (D_2O): δ −16.32. ^{1}H NMR (D_2O): δ 7.65 (m, 8H), 7.25 (m, 8H), 2.05 (t,4H), 1.31 (m, 2H). ^{13}C NMR (D_2O, DMSO): δ 21.5 (s, C-2), 29.5 (t, C-1, C-1′), 127.8 (s, C-4 ar), 130.6 (s, C-5 ar), 130.88 (d, C-2 ar), 136.1 (d, C-6 ar), 139.5 (d, C-1 ar), 145 (d, C-3 ar).

Preparation of Sulfonated (*S*,*S*)-BDPP. ^{31}P NMR (D_2O): δ 0.65. ^{1}H NMR (D_2O): δ 8.4−7.8 (m, 8H), 7.5−7.2 (m, 8H), 1.1 (m, 2H), 2.5 (m, 2H), 0.85 (b, 6H).

Preparation of Sulfonated (*S*,*S*)-Chiraphos. ^{31}P NMR (D_2O): δ −9.96. ^{1}H NMR (D_2O): δ 7.70−6.90 (m, 16H), 2.20 (b, 2H), 0.84 (b, 6H).

Preparation of Sulfonated (*R*)-Tol-BINAP. ^{31}P NMR (D_2O): δ −16.3. ^{1}H NMR (D_2O): δ 8.60 (d, 4H), 7.80 (d, 4H), 7.40 (b, 4H), 6.90−6.40 (m, 12H), 3.20 (s, 12H).

Preparation of Sulfonated Diphosphine-$PdCl_2$: General Procedure. A. To an aqueous solution of 0.1 M of K_2PdCl_4 (0.1 mmol in 1 mL of H_2O) under Ar was added a solution of sulfonated diphosphine (0.12 mmol in 4 mL of H_2O). The resulting solution was stirred for 1 h. Then it was transferred to the oxidation apparatus to be used *in situ*.

B. To a solution of $PdCl_2(PhCN)_2$ (0.01 mmol) in benzene (1 mL) under Ar was added a solution of tetrasulfonated diphosphine (0.012 mmol in 5 mL of degassed H_2O). The mixture was stirred for 1 h. Then the aqueous layer was transferred via a syringe to the oxidation apparatus to be used in situ. The complexes were characterized by ^{31}P NMR.

$PdCl_2$-Sulfonated (*R*)-Tol-BINAP-Catalyzed Oxidation of Allyl Phenyl Ether. Oxidation of allyl phenyl ether gave two products in relative yields of 84 and 16%. Preparative GLC yielded pure samples of these two compounds. ^{1}H and ^{13}C NMR identified the compounds as 1-phenoxy-3-chloro-2-propanol (**2c**) and phenoxypropanone, respectively. ^{1}H NMR of **2c** ($CDCl_3$): δ 7.33 (t, 2H), 7.00 (t, 1H), 6.90 (d, 2H), 4.25 (m, 1H), 4.10 (dd, 2H), 3.75 (dd, 2H), 2.65 (db, 1H, OH). ^{13}C NMR of **2c** ($CDCl_3$): δ 158.1,129.5, 121.4, 114.6, 70.0, 68.5, 46.0.

$PdCl_2$−(*R*)-Tol-BINAP-Catalyzed Oxidation of Olefins. The procedure was similar to that described for the sulfonated catalysts. The catalyst was prepared by adding (*R*)-Tol-BINAP (117.0 mg, 0.172 mmol) to a solution of $PdCl_2(CH_3CN)_2$ (39.0 mg, 0.15 mmol) in THF (5 mL). The solution was stirred under Ar at room temperature for about 30 min. The yellow clear solution which was produced was transferred to the oxidation apparatus for use *in situ*.

Oxidation of 2,3-Dihydrofuran. This oxidation afforded three products in relative yields of 20%, 75%, and 5%. ^{1}H and ^{13}C NMR identified the products as 3-oxotetrahydrofuran, 3-chloro-2-hydroxytetrahydrofuran (**4**), and 2-chloro-3-hydroxytetrahydrofuran (**5**), respectively. Spectral data of the products were as follows. 3-chloro-2-hydroxy-tetrahydrofuran: ^{1}H NMR ($CHCl_3$) δ 5.48 (d, $J_{1,2}$ = 2.93 Hz, 1H), 4.26 (d, 1H), 4.19 (m, 2H), 2.78 (b, 1H, OH), 2.65 (m, 1H), 2.15 (dd, 1H); ^{13}C NMR ($CDCl_3$) δ 103.2, 67.1, 61.1, 33.0. 3-oxotetrahydrofuran: ^{1}H NMR ($CHCl_3$) δ 5.10 (dd, 2H), 3.70 (m, 2H), 2.02 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 207.3, 103.6, 62.6, 32.4. The ^{13}C NMR of spectra **4** in the presence of Eu(hfc)$_3$ showed the ee to be 56%.

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(20) For a similar apparatus see ref 1, p 57.