INFLUENCE OF SOLUTION IONIC STRENGTH ON AGGREGATION OF NOVEL WATER SOLUBLE PHOSPHINES AND TWO PHASE CATALYSIS

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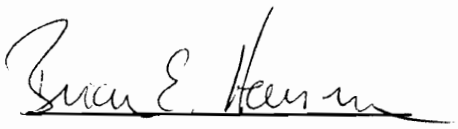

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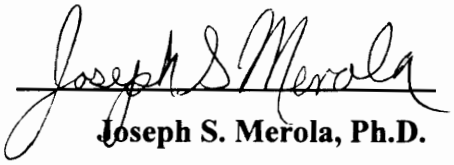

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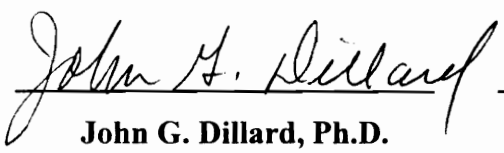

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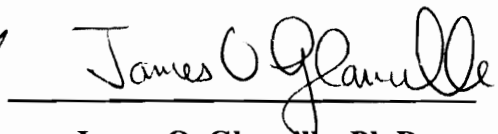

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by

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ABSTRACT

The preparation of new water soluble phosphines for organometallic chemistry and catalysis in water is important to the development of environmentally benign homogeneous catalysts. A series of steric demanding surface active phosphines have been synthesized and fully characterized. Two phase hydroformylation of 1-hexene and 1-octene with rhodium complexes of these water soluble phosphines has been investigated. The results indicate that both reaction activity and selectivity for these water insoluble olefins are significantly better than the rhodium/TPPTS system which is used commercially for hydroformylation of propene. Quantitative measurement of the aggregation of these surface active phosphines has been done. It is proposed that rate and selectivity enhancements are due, in part, to the aggregation of the ligand.

Ionic water soluble phosphines and their metal complexes are strong electrolytes. Salt addition for various purposes is a common technique in the aqueous phase chemistry. In the case of water soluble catalysis, the solution ionic strength may be expected to influence the stability of catalytic intermediates which in turn could have a decisive influence on the catalytic activity and selectivity. Reported here is the first study that systematically investigates the effect of ionic strength on aqueous phase catalysis. The study provides the basic understanding of the relationship between solution ionic strength and hydroformylation rate and selectivity in the aqueous phase.

The organometallic chemistry and catalysis with water soluble bis-diphenyl phosphine-chelates have been fully investigated. But the preparation of this class of ligands suffers from low yield and uncertainty of the site of sulfonation. Introduction of α-ω diphenylalkyl group into a chelating phosphine via $LiP[C_6H_4(CH_2)_XC_6H_5]_2$ results in a new class of chiral chelating phosphines which can be easily sulfonated. This highly efficient, well defined sulfonation method leads to surface active phosphines which are sterically and electronically similar to those bis-diphenyl phosphine-chelates. (*S, S*) tetra-sulfonated 2,4-bis-diarylphosphinopentane has been successfully synthesized and its applications in aqueous phase hydrogenation shows improved reaction rate and enantioselectivity compared to its non-surface active analogs.

ACKNOWLEDGMENTS

The completion of this thesis is by no means a solo effort. I am indebted to a number of individuals for their input and guidance throughout the arduous process of completing doctoral work. First and foremost I thank Dr. Brian Hanson, my advisor, boss, mentor and friend. He provided the opportunity, the environment, and the encouragement for me to grow. His guidance and support created an excitement for me within this field, and I thank him for pointing the way towards a new and bright direction for my life. It has been an honor and a privilege to work under his direction. I wish I could put words in the best way to express my gratitude to him.

I would also like to express my deep gratitude to my committee members, Drs. Joseph Merola, Karen Brewer, John Dillard and James Glanville for their guidance to the development and completion of this study and to my professional development.

I thank people in the inorganic division of the Chemistry Department at Virginia Tech for their friendship and help. These wonderful people made my tenure at Blacksburg a truly memorable one. I owe a debt of appreciation to Dr. Tamás Bartik and Dr. Berit Bartik, two remarkable chemists, for their contribution to this dissertation. I also like to thank Dr. Barbara B. Bunn. Her help and friendship are invaluable.

For my becoming Dr. Ding, the most credit must go to my parents. For they, more than anyone else, know what I have gone through to get here; geographically

thousands miles away from my homeland and academically a higher level from where I started.

Finally, I wish to dedicate this dissertation to my wonderful wife, Ruli. You not only provided the inspiration that kept me going but you were always there when I needed you. Your devotion and love have made the past four years the most fulfilling and rewarding time of my life. Most of all I thank you for pinning your faith on me. May we achieve our dreams together.

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Literature Survey and Objectives of the Research

1.1 Introduction to Two Phase Catalysis With Water Soluble Phosphines

Homogeneous catalysis, as a result of the rapid development of modern organometallic chemistry, has many characteristics that are favorable for commercial application. Most importantly homogeneous catalysts give high activity and selectivity even under mild reaction conditions [1]. Because the catalyst is a molecular species, reaction selectivity can, in principle, be achieved by tuning the coordination sphere of the metal. However, homogeneous catalysts are usually sensitive to air and moisture, this as well as the difficulty in separation of the catalyst from organic products, limits the application of homogeneous catalysts in the chemical industry.

The homogeneous catalysts which are applied in commercial syntheses are often not recovered in the production. But in the case where the catalyst is too expensive to lose or undesirable to be left in the product or discharged to the environment, its separation from the reaction mixture must be achieved. One common method for separation is distillation. However, if the products have relatively high boiling points or the catalyst is somewhat thermally unstable, different approaches need to be applied. Of many potential solutions to the problem, immobilization of the catalyst on a solid has received a great deal of attention [2]; for example immobilization has been achieved by

coordinating the metal or metal complexes to a functionalized organic polymer [3] or inorganic support [4] and dissolving the catalyst in a supported liquid phase [5]. These methods all address the issue of product/catalyst separation, and generally offer the advantages of a heterogeneous system. However, in spite of considerable effort commercial applications have not been found for immobilized catalysts perhaps due to the leakage of expensive metal as well as low reactivity and selectivity in some cases.

Another approach to the problem of product/catalyst separation is to introduce a secondary liquid phase that contains the catalyst and is immiscible with products of the reaction. The separation of products and complete recovery of the catalyst, in the immiscible phase, can then be acccomplished by a simple phase separation. The technical and commercial feasibility of this scheme for catalyst recovery is demonstrated by the "Shell Higher Olefin Process"(SHOP) [6]. In this process ethylene is catalytically oligomerized by an organonickel catalyst in a polar phase of 1, 4-butanediol, and the oligomers generated by the reaction form a secondary phase which is immiscible with 1, 4-butanediol. Therefore the products can be removed without distillation.

Among polar solvents which may be a candidate for the secondary phase water is excellent choice. A rhodium based hydroformylation system with the modification of water soluble phosphines has been realized industrially in the "Ruhrchemie/Rhone Poulenc Process" for the production of butyraldehyde [7].

Water is a highly polar solvent, hydrogen bonding and the presence of ionic species may change the nature and the outcome of a reaction that operates in water.

Catalytic reactions in aqueous phase may show surprising changes of reaction reactivity and selectivity. The reactivity of a two phase catalysis is strongly dependent on the solubility of the organic reactants. For example, the two phase hydroformylation of propene, the Ruhrchemie/Rhone Poulenc process, has a comparable reaction rate to a homogeneous system due to relatively high water solubility of propene, while mass transfer limitation causes a considerably lower activity for similar reactions with higher olefins, such as 1-hexene and 1-octene [8]. The selectivity of a two phase catalyst is also profoundly influenced by water. Since most of the water soluble catalysts are ionic species, tuning the coordination sphere of the metal center by altering the ionic strength of the aqueous medium may result in a change of reaction selectivity.

In addition to these advantages, water is an environmentally benign solvent. Operation of a chemical process in which organic solvents are minimized is attractive to industry. This is one of the reasons behind the bloom of activities in the research on water soluble catalysis. All the efforts will likely contribute to future water based large scale processes.

Homogeneous catalysts are transition metal complexes with various kinds of ligands, such as phosphines. The ligands electronically and sterically modify the coordination sphere of the metal for better reactivity and selectivity. The water solubility of these complexes can be achieved by introducing polar functional groups to the ligand. Surveys of water soluble ligands and their applications to catalysis can be found in several review articles [9 - 12].

Herrmann and Kohlpaintner have written a comprehensive review on the water soluble ligands, their metal complexes and related catalysis [12]. Although virtually all the available methods for introducing water soluble functionalities are discussed, most attention is given to the direct sulfonation of arylphosphines, which is the most widely used method to convert phosphines into their water soluble derivatives. The preparation and purification of sulfonated phosphines are described in detail. The use of water soluble phosphines in hydroformylation, asymmetric hydrogenation and other catalytic reactions, as well as supported aqueous phase catalysis is covered. Many new concepts and latest trends in the research of water soluble catalysis are included.

Another comprehensive review on the similar subjects was written by Kalck and Monteil [11]. The preparation of water soluble ligands, especially sulfonated phosphines is fully discussed. Metal complex chemistry with water soluble ligands and related biphasic catalysis are also covered.

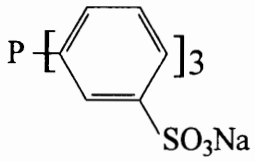
The most successful industrial application of the rhodium/*m, m, m*-trisulfonated triphenylphosphine (TPPTS) system is the hydroformylation of propylene, Ruhrchemie/Rhône-Poulene process. Technical aspects of this process are described in detail by Cornil et al [13]. Commercial applications of water soluble catalysts to various system are also briefly reviewed.

1.2 The Preparation of Water Soluble Phosphines

Water solubility of a phosphine is commonly created by the incorporation into the phosphine of polar functional groups, such as sulfonate [14 - 17], carboxylate[18 - 20], hydroxyl [21, 22], phosphonium [23] or ammonium [24 - 27]. The majority of water soluble phosphines, however, are prepared by direct sulfonation to generate sulfonated arylphosphines. The method is straightforward but somewhat laborious. Sulfonated phosphines are highly water soluble and similar to their non-functionalized analogs in their coordination chemistry. Introduction of sulfonate groups to arylphosphines make the phosphines slightly more electron withdrawing [28]; and the *meta*-sulfonated triarylphosphines are sterically bulkier. Trisulfonated triphenylphosphine (TPPTS), for example, is about 20% bigger than triphenylphosphine. The Tolman cone angle for TPPTS is estimated to be 170° while the value for triphenylphosphine is 145° [28, 29]

The report of direct sulfonation of a phosphine was first made by Ahrland, Chatt, Davies and Williams in 1958 [30]. By dissolving triphenylphosphine into fuming sulfuric acid (SO_3/H_2SO_4), the monosulfonated triphenylphine (TPPMS), $Ph_2P[m\text{-}C_6H_4SO_3Na]$, was isolated upon neutralizaton with NaOH. The *para* and *ortho* monosulfonated triphenylphosphines are prepared by nucleophilic substitution rather than direct sulfonation [31, 32]. The method suffers from the low solubility of sulfonated compounds in common organic solvents. Therefore, with few exceptions, it is limited to the synthesis of monosulfonated phosphines.

Kuntz [33] modified the sulfonation conditions of Chatt et al [30] to achieve a higher degree of sulfonation. The tris(*m*-sodium sulfonatophenyl)phosphine (TPPTS) (**1**) was therefore obtained. Introduction of sulfonate groups to the position other than *meta* in triphenylphosphine requires an alternative approach. $P[p\text{-}C_6H_4\text{-}SO_3K]_3$, $PhP[p\text{-}C_6H_4\text{-}SO_3K]_2$, and $Ph_2P[p\text{-}C_6H_4\text{-}SO_3K]$ were prepared by nucleophillic substitution of aromatic fluorine in $p\text{-}F\text{-}C_6H_4\text{-}SO_3K$ with PH_3 or primary and secondary phosphines in the superbasic medium [34]. The crystal structure of $P[p\text{-}C_6H_4\text{-}SO_3K]_3$ suggested that the *para, para, para*, trisulfonated triphenylphosphine is sterically similar to triphenylphosphine [34].



Tris(*m*-sodium sulfonatophenyl)phosphine (TPPTS) (**1**)

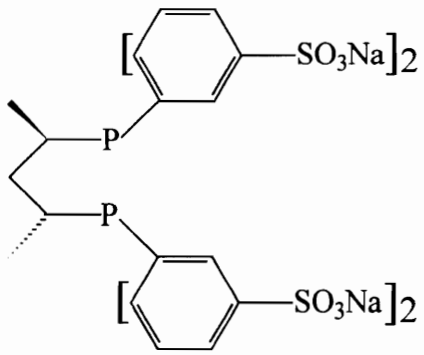
Since the success in the synthesis of TPPTS, many research groups have focused on the detailed preparation and purification of this important water soluble ligand on the laboratory scale mainly for the purpose of catalytic studies and complex chemistry. The basic laboratory procedure consists of the reaction of triphenylphosphine with H_2SO_4/SO_3 followed by the neutralization of the mixture with aqueous NaOH. The final product, TPPTS, is obtained by selective precipitation. A comprehensive spectroscopic

documentation of mono, di, trisulfonated triphenylphine and their oxides along with a complete procedure of direct sulfonation of triphenylphosphine to yield TPPTS was given by Hanson and co-workers [35]. It was demonstrated that ^{1}H NMR, as the most sensitive spectroscopic technique to the extent of the sulfonation, can be applied to monitor the progress of sulfonation. The attached ^{1}H NMR data of TPPTS and its oxide provide an alternative method to estimate the extent of oxidation. Gel-permeation chromatography has also been proven to be useful for the purification of TPPTS and its transition metal complexes [36-38].

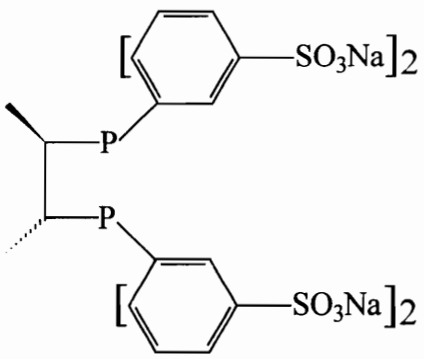
The synthesis of TPPTS on a large scale for commercial application, however, is done with a different work-up method. Sulfonated triphenylphosphine in its acid form is extracted into a hydrocarbon solvent with trioctylamine as in situ phase transfer agent. Sodium salt of trisulfonated triphenylphosphine is obtained by subsequent reaction with NaOH. This method avoids the generation of Na_2SO_4 which may be difficult for disposal in large quantity [39].

Because of the potential pharmaceutical application, much of the effort in this area has been directed toward the preparation of water soluble chiral diphosphines for two phase asymmetric hydrogenation [40 - 42]. However, the reactivity of the water soluble catalysts is somewhat limited by the solubility of the organic substrate in aqueous phase. The synthesis of water soluble phosphines has reached a stage that it is possible now to tailor the structure of a phosphine for improved reactivity while retaining excellent water solubility for good catalyst separation. Direct sulfonation has also proven to be a useful

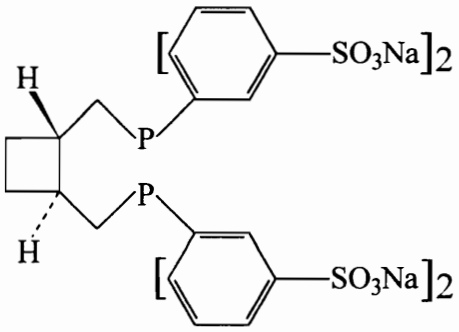
method for synthesizing water soluble chelating phosphines with *diphenylphosphino* functionality, such as BDPP, prohos, chiraphos, cyclobutaneDIOP [43], BISBI [44] and BINAP [40]. (Figure 1.1)



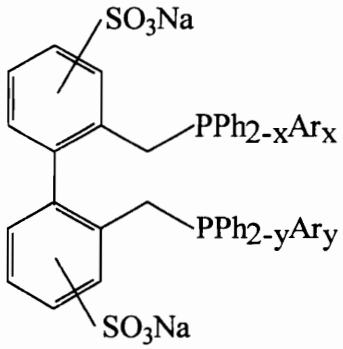
Tetrasulfonated BDPP



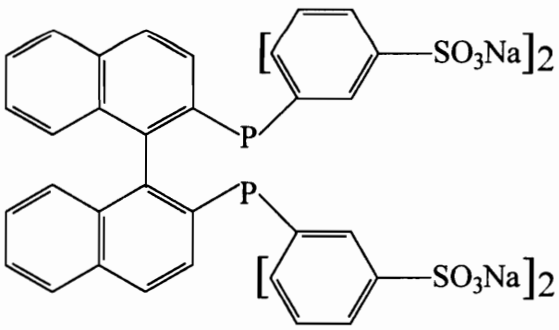
Tetrasulfonated Chiraphos



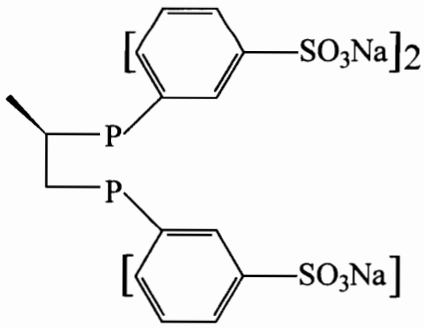
Tetrasulfonated CyclobutaneDIOP



Multisulfonated BISBI



Tetrasulfonated BINAP



Tetrasulfonated Prophos

Figure 1.1 Sulfonated Chelating Phosphines

Although the direct sulfonation of biphosphines often results in a mixture with different degrees of sulfonation, these water soluble chelates give promising results in two phase catalysis. Water soluble rhodium catalysts with multisulfonated BISBI made from the reaction with oleum (65% SO_3) provide outstanding selectivity to linear aldehyde in the two phase hydroformylation of propene even at relatively low phosphine to rhodium ratio [8]. Even better catalytic results were obtained with rhodium catalysts of multisulfonated 2, 2'-Bis(diphenylphosphinomethyl)-1, 1'-binaphthalene (BINAS) [45].

BINAP was also sulfonated with only a little oxidation in concentrated H_2SO_4 with up to 40% SO_3 [40]. Ethylene glycol, rather than water, was used as the catalytic phase of a supported liquid phase system to prevent cleavage of the Ru-Cl bond which is thought to be critical to high enantioselectivity of the hydrogenation to produce (*S*)-naproxen. 96% e.e of (*S*)-naproxen was achieved [46].

Most of the sulfonated chiral biphosphines, however, give relatively poor enantioselectivity in the hydrogenation of prochiral substrates compared to their non-water soluble analogs. The reason for lower enantioselectivity, although not clear at this moment, is perhaps caused by additional chirality arising from the low degree of sulfonation [46]. On the other hand, Sinou et al demonstrated that a mixture of *mono, bi, tri*-sulfonated BDPP gives better enantioselectivity in the hydrogenation of cinnamic acid derivatives compared to tetra-sulfonated analog [43]. Mono-sulfonated BDPP gives the

best enantiomeric excess of all sulfonated phosphine analogs for imine hydrogenation [47].

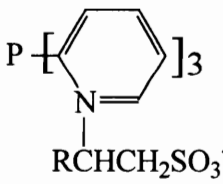
Direct sulfonation of chelating phosphines often requires harsh conditions and long reaction times. A mixture of SO_3 and concentrated H_2SO_4 is usually applied to the reaction as a means to introduce sulfonate group to aryl phosphines. A high degree of sulfonation can only be possible with the addition of SO_3. Even with SO_3 however sulfonation requires several days to achieve. After the reaction large amounts of Na_2SO_4 are generated from the neutralization with NaOH.

Since SO_3 is a strong oxidizing agent and the reaction time for direct sulfonation is long, the reaction produces a significant amount of phosphine oxide along with phosphines with different degrees of sulfonation. Although it has been recently reported by Herrmann et al that oxidation of the phosphine can be virtually eliminated during the sulfonation of phenylphosphines when the reaction is done in the presence of a large excess of orthoboric acid, the new sulfonation conditions still require oleum and long reaction time [48].

All these difficulties complicate the purification of sulfonated products and contribute to a poor yield of sulfonation products (10-30% for diphosphines). Therefore, the conventional direct sulfonation is not very suitable for chiral water soluble phosphine synthesis, since a large portion of expensive chiral phosphine is going to be sacrificed in direct sulfonation. Yields for the direct sulfonation of chiral phosphines such as BDPP and BINAP are not reported [40, 41].

Other than functionalization of an aryl group directly bound to phosphorus, sulfonate groups can also be introduced to an aliphatic chain of a diphenyl or diaryl alkylphosphine by the attack of a nucleophilic alkali metal phosphide to sulfones [49]. The method opens a route to different alkali metal salts of sulfonated phosphines, which may be important to catalysis in water. These sulfonates can be further converted into the free sulfonic acids by ion exchange.

A similar methodology was applied by Fell and co-workers to sulfoalkylate tris(2-pyridyl)phosphine with alkyl-1, 2-sultone(C_3 - C_{14}). Phosphines with long alkyl chains in this series are surface active (**2**). Therefore higher olefins, such as 1-tetradecene, can be satisfactorily hydroformylated with rhodium complexes of these phosphines under two phase conditions [50].



Sulfoalkylated tris(2-pyridyl)phosphines (**2**)

A series of water soluble phosphines, $P[(CH_2)_n(C_6H_4\text{-}p\text{-}SO_3Na)]_3$ (n = 1, 2, 3, 6.) were prepared by direct sulfonation of the corresponding tri-ω-phenylalkylphosphines. The presence of the linear methylene chain makes sulfonation easier. Only concentrated

sulfuric acid (no SO_3) is required to complete trisulfonation for n≥3. The electronic and steric parameters of these water soluble phosphines were determined spectroscopically. It was found that the phosphines have similar electron-donor character as the trialkylphosphine $P(n\text{-}Bu)_3$ when the methylene chain is sufficiently long [28].

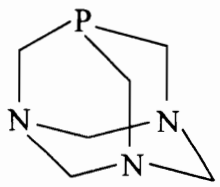
Besides sulfonate, many other highly polar functionalities can also give phosphines water solubility. Hanson and co-workers successfully synthesized a series of analogs of diphosphines, such as BDPP, Chiraphos, and DIOP, bearing $-P[C_6H_4NMe_3^+]_2$ functionalities [51]. These quaternized amine groups provide water solubility to phosphines and their metal complexes. Two phase asymmetric hydrogenation of cinnamic acid derivatives with rhodium complexes of these ligands was carried out. It was found that the quaternized amine groups do not affect the enantioselectivity compared to non-functionalized analogs [27].

The synthesis of a water soluble phosphine $P(CH_2OH)_3$ and its metal complexes with nickel, palladium and platinum were described by Pringle et al [52]. It was concluded that although the coordination properties of $P(CH_2OH)_3$ are expected to be similar to small trialkylphosphines, such as PMe_3 and PEt_3, the hydrogen bonding among coordinated $P(CH_2OH)_3$ may play a role in the stability of the complex. The complexes with $P(CH_2OH)_3$ are air stable.

Linear triphosphine ligands can also be modified with polar water soluble functionalities. DuBois et al synthesized water soluble triphosphines, $RP(CH_2CH_2PR'_2)_2$

(R = hydroxylalkyl, R' = alkylphosphonate). The hydroxyl group is introduced to the central phosphorus atom by free-radical addition of a secondary phosphine to allyl alcohol. The terminal phosphorus atoms are modified for the water solubility with diethyl phosphonate groups [53].

Another air-stable and water soluble phosphine, 1, 3, 5-Triaza-7-phosphaadamantane (PTA) (**3**) was first prepared by Daigle et al [54]. Water soluble complexes $RuCl_2(PTA)_4$ and $RhCl(PTA)_3$, were prepared and characterized by X-ray crystallography. It was found that $RuCl_2(PTA)_4$ is also an active hydrogenation catalyst for unsaturated aldehydes to unsaturated alcohols under two phase conditions. $RhCl(PTA)_3$, however, catalyzes olefin hydrogenations [55].



1, 3, 5-Triaza-7-phosphaadamantane (PTA) (**3**)

Water solublility can also be imparted by phosphonium salts. A series of phosphonium phosphines$(Ph_2P(CH_2)_nPMe_3)X$ (n = 2, 3, 4, 6, 10.) was synthesized by Baird and co-workers. $[(NBD)RhCl]_2$ reacts with two equivalents of the phosphine to give a water soluble hydrogenation catalyst. The catalytic results suggested that the

length of the aliphatic chain in the phosphine influences the activity. The highest activity is reached when n = 4, and the a stable emulsion is formed with phosphine of longest methylene chain [56].

Besides base-catalyzed coupling reaction, the free radical addition of diphenylphosphine, phenylphosphine and ethylenebis(phenylphosphine) to unsaturated carboxylic acids offers an alternative for the introduction of carboxylic acid functionality to phosphines [57].

1.3 History of Hydroformylation and Its Mechanisms With Rhodium Catalysts

In 1938, the production of large quantities of higher hydrocarbons including oxygen containing compounds was observed when ethylene was added to CO and H_2 over a Co-Cu-Mn oxide Fischer Tropsch catalyst [58]. Subsequently Otto Roelen investigated the effect of added olefins to Fischer Tropsch catalysts and identified aldehydes as one of the oxygen containing components [59]. (Equation 1.1).

Equation 1.1 Oxo Reaction of Olefin (hydroformylation)

$$\text{Olefin} + CO + H_2 \rightarrow \text{aldehyde} + \text{alcohol}$$

Under high pressure of hydrogen and carbon monoxide, olefins catalyzed by various metal oxides produce aldehydes which are one carbon heavier than the original

olefins. Alcohols in oxo reaction are formed from the reduction of aldehyde. With respect to mechanism, it was determined in the late 40's that $HCo(CO)_4$ is the active species, or at least a precursor to an active species [60]. Homogeneous hydroformylation with cobalt is practiced industrially.

Hydroformylation with rhodium catalysts was developed much later, and gained attention upon the publication of Evans, Osborn, and Wilkinson's landmark work on the hydroformylation of alkenes by homogeneous rhodium catalysts with triphenylphosphine in 1968 [61, 62]. The industrial significance attacted a great deal of the interest in rhodium hydroformylation and resulted in a phenomenal growth of research, both academic and industral, in this area. Driven by the increasing demand for oxo products such as plasticizer and detergent alcohols, the low pressure process for the hydroformylation of propylene utilizing rhodium/triphenylphosphine was finally developed by the joint effert of the Union Carbide, Davy International Ltd., and Johnson Matthey. The process involves $HRh(CO)(PPh_3)_3$, which is generated in situ, as the catalyst precursor.

Because of its commercial significance, the mechanism of rhodium catalyzed olefin hydroformylation with $HRh(CO)(PPh_3)_3$ and related compounds has been widely investigated [61, 63 - 82]. Many factors which may play a role in determining the outcome of hydroformylation are now understood from the mechanistic point of view. Side reactions, such as isomerization of an olefin, hydrogenation of the substrate and product, have also been considered as mechanistically related phenomena.

The generally accepted mechanism for hydroformylation of α-olefin with $HRh(CO)(PPh_3)_3$ is shown in Figure 1.2. Related side reactions, hydrogenation and isomerization, are also included schematically [63].

The mechanism for hydroformylation reveals that the selectivity to linear aldehyde is controlled by the way of metal hydride migration to π bonded olefin substrate. Anti-Markownikov addition of hydride results in a linear aldehyde while Markownikov addition leads to branched aldehyde. Two factors, the acidity of the hydride and the steric constraints of the ligands, control the selectivity of the addition. Sterically demanding ligands such as triarylphosphines are expected to favor linear aldehyde formation by anti-Markownikov addition.

The isomerization and hydrogenation mechanisms share many intermediates with the hydroformylation reaction. Therefore careful control of reaction conditions is necessary to direct the catalytic reaction to the desired products. It has been shown that excess ligand such as triphenylphosphine can minimize the occurrence of isomerization and high partial pressure of CO prevents both isomerization and hydrogenation [83, 84].

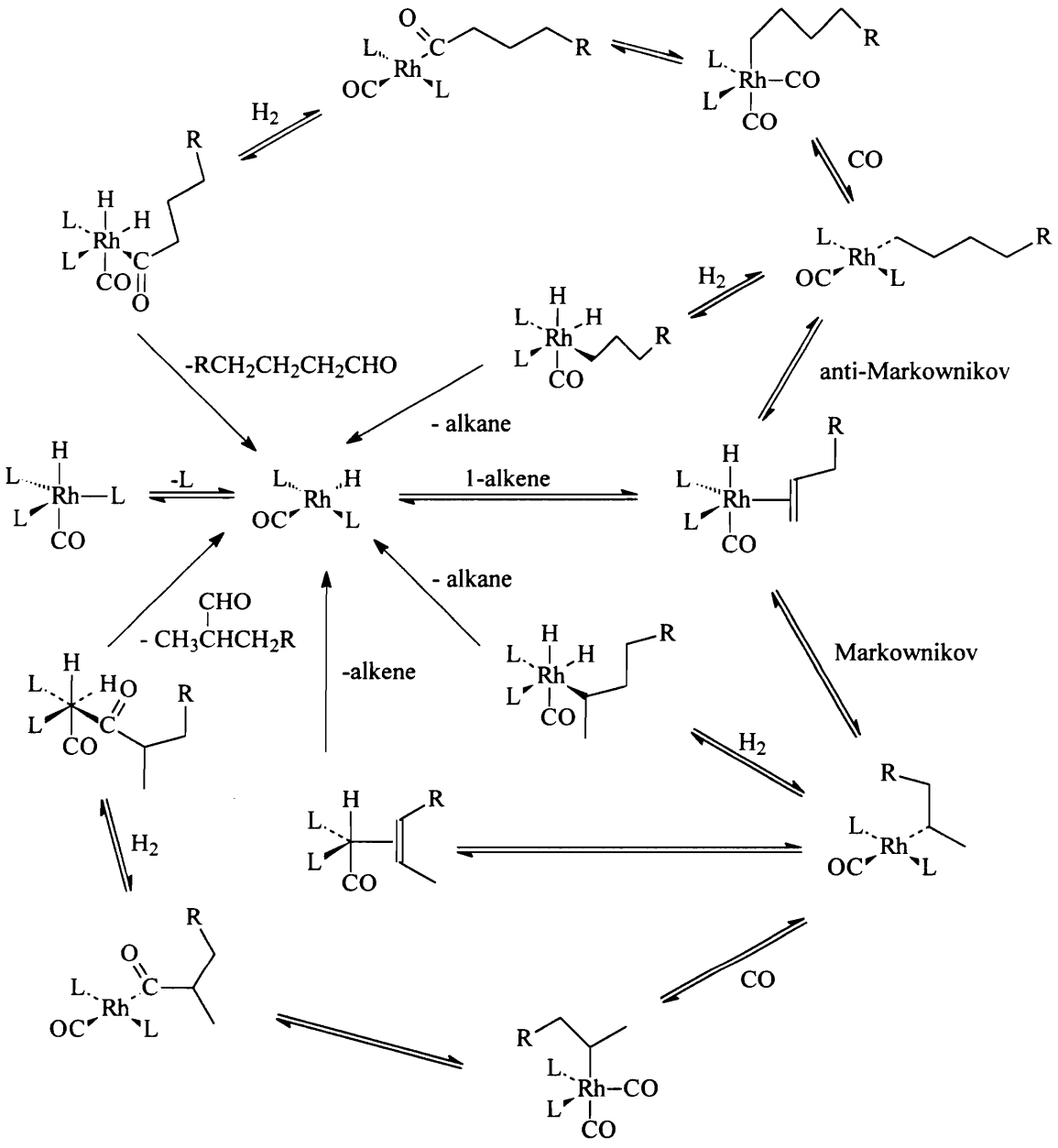


Figure 1.2 Schematic Representation of Possible Reaction Mechanisms for Hydroformylation, Isomerization and Hydrogenation of 1-alkene by $HRh(CO)(PPh_3)_3$ Catalyst (L = PPh_3) (modified from [63])

Results from many studies [61, 64-75] suggest that the equilibria represented by Figure 1.3 take place under hydroformylation conditions and each of these species may act as the precursor to a catalytically active species that can operate in the catalytic cycles. Because of the catalytic cycle starts at $HRh(CO)(PPh_3)_3$ (I) and the system is usually operated under large excess of PPh_3, the concentrations of III and IV are minimized and the most predominant species are I and II. Both I and II can lose a PPh_3 to generate 16 electron species, V and VI respectively, which are catalytically active towards hydroformylation.

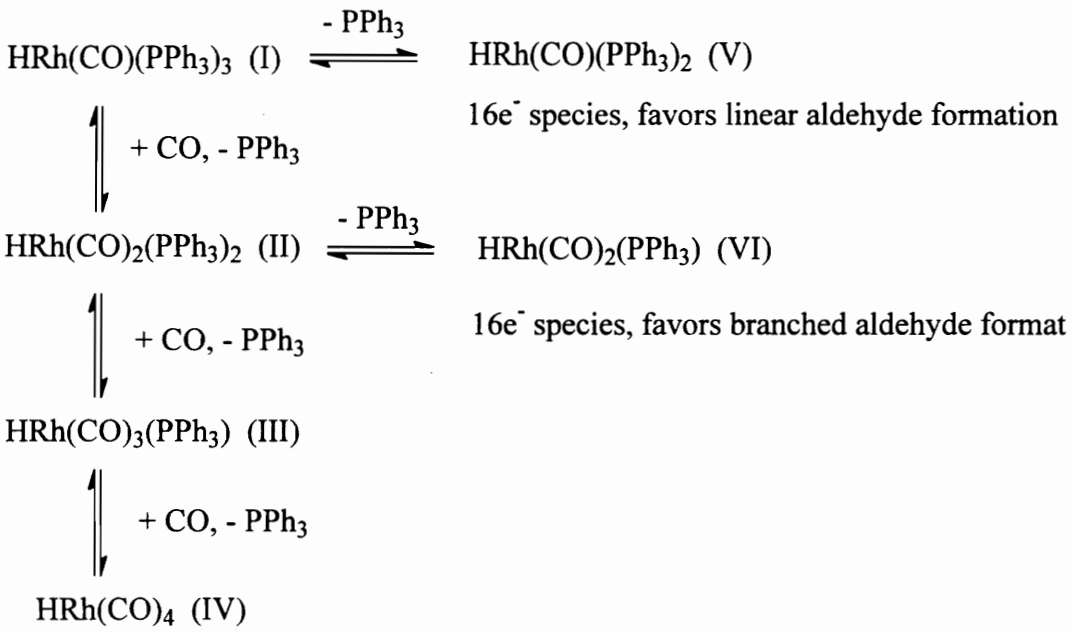


Figure 1.3 Possible Equilibria in Rh/PPh_3 System in the Presence of CO/H_2

The dissociative mechanism originally proposed by Wilkinson [61] is generally considered to be operative with oxidative addition of hydrogen as the rate determining step. A large excess of sterically demanding ligands, such as PPh_3, is required for good selectivity to linear aldehydes, however excess phosphine also reduces the reaction rate.

High concentrations of PPh_3 favor V over VI. If catalysis proceeds via the 16 e^- complexes V and VI then excess phosphine forces the catalysis to go through the more sterically demanding intermediate V. This can explain the higher proportion of linear product obtained in the presence of excess phosphine. Therefore V is more selective compared to VI.

Since the successful synthesis of trisulfonated triphenylphosphine in 1975, the research activity in the area of two phase hydroformylation has been high. However fundamental understanding of the hydroformylation mechanism in aqueous solution is still lacking. It is in part due to the difficulties in gathering spectroscopic evidence, such as NMR and IR information, for ionic species in water. It has been generally accepted that hydroformylation mechanism with Rh/TPPTS operates in water with dissolved organic substrates in a fashion similar to that with Rh/triphenylphosphine [7].

Seven ruthenium complexes with TPPTS were prepared by Basset et al.[85]. Those complexes seem to have same structure as their PPh_3 analogs. It was concluded from spectroscopic evidence that the difference between PPh_3 and TPPTS in their binding ability is mainly steric, not electronic. Only a minor electronic influence of the sulfonate

substituent on the nature of M-P bond was found by infrared spectroscopy and ^{13}C and ^{31}P NMR spectroscopy. This conclusion is further supported by the M-P bond distance from the crystallographic data collected by Darensbourg and his co-workers [29]. A crystal structure of $W(CO)_5$(TPPTS) with 4,7,13,16,21,24-Hexaoxa-1,10-diazabicyclo[8,8,8]hexacosane (Kryptofix-221) was successfully obtained. Although PPh_3 and TPPTS are similar electronically, TPPTS is approximately 20% larger; the W-P bond distance is 2.554Å in $W(CO)_5$(TPPTS), a normal distance for W-P bonds.

The only reported crystal structure of a TPPTS complex in the absence of crown ethers was obtained by Hanson et al [86]. The structure of $Co_2(CO)_6TPPTS_2$ therefore provided valuable information about the interaction between sulfonate and counter ions. In the solid state, hydrophobic layers of $Co_2(CO)_6TPPTS_2$ are separated by hydrophilic planes of sodium cations and solvent.

Kinetic investigation of TPPTS dissociation from $M(CO)_5$(TPPTS) (M = Cr, Mo, W) in the presence of a high pressure of CO indicated that the rate and activation parameters for TPPTS are similar to those determined for the corresponding PPh_3 complexes. A stabilizing effect was observed for the *cis*-$Mo(CO)_4(TPPTS)_2$ in which it was proposed that the Na^+ cation bridges sulfonate groups via intramolecular interligand interactions. An intramolecular rearrangement from *cis*-$W(CO)_4(TPPTS)_2$ to *trans*-$W(CO)_4(TPPTS)_2$ under CO was also observed [15].

Although the water soluble phosphines and their transition metal complexes often display spectroscopic properties similar to their water-insoluble analogs and consequently

they are often assumed to have the same catalytic properties and follow a similar mechanism, water can play a role in aqueous catalysis in unanticipated ways, and many factors need to be taken into account that are irrelevant in organic solvents. For example (1-hydroxyalkyl)phosphonium salts were prepared by mixing TPPMS and corresponding alkylaldehydes in acidic medium. It is suggested that the formation of phosphonium salts often occurs, particularly in protic solvents, in the catalytic hydroformylation. This results in the loss of phosphines and may account in part for the large excess phosphine requirement in these processes. The solvent, water, can influence the formation of phosphonium salts by protonation of the anionic intermediate and hence may influence the selectivity and reactivity [87].

Sinou et al investigated the role of water in asymmetric hydrogenation with rhodium complexes of several sulfonated biphosphines [41, 88]. Deuterium incorporation was found in the product from the hydrogenation of cinnamic acid derivatives when deuterium oxide was used in place of water. Therefore, in an aqueous catalytic system water can serve not only as a solvent but also as a reactant.

1.4 The Limitation of Two Phase Reactions With Water Soluble Catalysts

The two phase hydroformylation of propene, the Ruhrchemie/Rhone Poulenc process, is the first successful commercial application of a water soluble phosphine [7]. In addition to the easy separation of the Rh catalyst from the substrate and products as the most obvious advantage, the Rh/TPPTS catalyst also offers high selectivity. The

normal to branched (n/b) butylaldehyde ratio is >95:5 compared to a typical n/b of 90:10 given by homogeneous Rh/triphenylphosphine system [13].

The major limitation of two phase hydroformylation perhaps is the solubility of olefin, especially higher olefins, in water. Studies have shown that the hydroformylation of olefins under two phase conditions actually occurs in the aqueous phase [7, 12]. Therefore the activity of the catalytic system is limited by the concentration of olefins in water. The Ruhrchemie/Rhone Poulenc process has good activity for propene hydroformylation since propene has significant solubility in water. However the same system is not commercially viable for higher olefins due to limited solubility.

A potential solution to enhance the solubility of an organic substrate in water may be the introduction of a surfactant. As a matter of fact, surfactants are commonly used as additives in two phase catalysis to increase the mixing of two phases. It has been shown that the addition of a surfactant to a Rh/TPPTS hydroformylation catalyst increases the reaction activity of two phase hydroformylation of 1-hexene [89]. Overuse of surfactants should be avoided since the formation of highly stable emulsions is in conflict with the goal of two phase systems, namely easy product-catalyst separation. A new class of phosphine ligands, sulfoalkylated tris(2-pyridyl)phosphines(**2**), is strictly designed to be surface active [50]. Although the rate of hydroformylation of liquid olefins with these surface active phosphines has been significantly improved, a stable emulsion is formed. Also selectivity toward linear aldehydes is limited.

Another approach is to design a phosphine which has some characteristic features of a surfactant, but is not expected to stabilize emulsions. The surface active phosphine is defined as a phosphine which bears a hydrophobic end and several hydrophilic ends can serve not only as a phosphine ligand to satisfy the coordination chemistry of the central metal atom, but function as a surfactant as well. The suface activity of such phosphine is shown as its ability of aggregation in aqueous solution and aggregation of phosphines may improve the solubility of organic substrates in water. Since the surface activity of such phosphine does not arise from external additives, the activity and the selectivity of such catalysts can be studied and understood mechanistically by simplifying two separate issues, namely the electronic and steric aspect of a phosphine and the surface active feature of an external additive, into a single issue of surface active phosphine. In other words, by introducing a surface active phosphine, the position of the hydrophilic functionality to the metal center is well defined.

Many of the sulfonated phosphines reported in the literature are expected to be surface active. Wilkinson et al. noted the surface active character of TPPMS as a water soluble ligand for the two phase hydroformylation of 1-hexene [14]. More recently, Hanson et al. synthsized a series of trisulfonated tris(ω-phenylalkyl)phosphines $P[(CH_2)_x(p\text{-}C_6H_4SO_3Na)]_3$, x = 1, 2, 3, 6 [28]. These sulfonated phosphines have a well separated hydrophobic part and three hydrophilic ends. The two phase hydroformylation of 1-octene with these phosphines, especially with trisulfonated tris(6-

phenylhexyl)phosphine, showed better reactivity and moderately enhanced selectivity at low ligand to rhodium ratios. Unfortunately the activity of the catalyst dropped to almost zero at the high ligand to rhodium ratios necessary for the long term stability of the Wilkinson type catalysts [28]. This outcome is not surprising since these phosphines are electron donating and tend to block all the coordination sites of rhodium at high ligand to rhodium ratio. Because of relatively small cone angle of these phosphines, the reaction selectivity showed no improvement compared to Rh/TPPTS system.

Based on the experimental observations with tris(ω-phenylalkyl)phosphines, it is obvious that a class of surface active phosphines which are electron-withdrawing and steric demanding would be more suitable as ligands for Wilkinson type catalysts.

1.5 Influence of Salt on the Reactivity and Selectivity of Aqueous Hydroformylation

Since the successful synthesis of TPPTS, the development of aqueous phase hydroformylation has attracted wide attention. Several factors not encountered in nonaqueous homogeneous system are now important in the two phase catalysis with water soluble catalysts derived from TPPTS. First, the solubility of the substrate in water is significant in determining the reaction rates of a two phase hydroformylation reaction. Second, the catalyst and all proposed intermediates in the homogeneous system are neutral whereas all the rhodium-TPPTS complexes are inherently ionic due to the charge on the sulfonate groups. Third, although aqueous phase rhodium catalysts derived from

TPPTS are generally considered to be similar to Rh/PPh_3 system mechanistically, dynamic NMR study on the exchange of water soluble rhodium hydroformylation catalyst $HRh(CO)(TPPTS)_3$ with free TPPTS performed by Horvath and co-workers has indicated a special stability for water soluble rhodium complexes of TPPTS [90]. Specifically it was shown that the dissociation of TPPTS from $HRh(CO)(TPPTS)_3$ has an activation barrier of 30.2 kcal/mol. For comparison similar NMR studies on the corresponding dissociation of PPh_3 from $HRh(CO)(PPh_3)_3$ led to an estimated 19 kcal/mol activation barrier for the exchange of triphenylphosphine [72].. It was found that $HRh(CO)(TPPTS)_3$ does not form new species, such as $HRh(CO)_2(TPPTS)_2$, even under 200 atm of CO/H_2 (1/1). While the Rh/triphenylphosphine system under 30 atm shows that $HRh(CO)_2(PPh_3)_2$ is the only species detectable. It was concluded that the high stability of $HRh(CO)(TPPTS)_3$ contributes to the observed high selectivity to linear aldehyde in aqueous hydroformylation system with rhodium-TPPTS catalyst. Specifically the reaction equilibria depicted in Figure 1.4 lie in favor of $HRh(CO)(TPPTS)_3$, especially when a system as Ruhrchemie/Rhone Poulenc Process which contains large excess of TPPTS. This leads to catalysis via $HRh(CO)(TPPTS)_2$ as active intermediate. This behavior was attributed by Horvath et al. to the hydrogen bonding between sulfonate groups and water.

$$HRh(CO)(TPPTS)_3 \underset{+\,CO}{\overset{-TPPTS}{\rightleftharpoons}} HRh(CO)_2(TPPTS)_2$$

$$\overset{-TPPTS}{\underset{+\,CO}{\rightleftharpoons}} HRh(CO)_3(TPPTS) \overset{-TPPTS}{\underset{+\,CO}{\rightleftharpoons}} HRh(CO)_4$$

Figure 1.4 Possible Equilibria in Aqueous Rh/TPPTS Hydroformylation System

An examination of the patent literature on hydroformylation catalysts derived from rhodium and TPPTS reveals that in nearly all reported patent examples an additional salt is added to the aqueous phase [33, 91, 92]. Typically these are either ionic surfactants or sodium phosphates, e.g. Na_2HPO_4; the role of the added ionic component is apparently to either improve the mixing of the two phases, in the case of a surfactant, or to control the reaction pH. In these specific patent examples with either propylene and hexene high selectivity for the linear aldehydes in the hydroformylation reactions is commonly observed. In contrast to these reported high selectivity of Rh/TPPTS hydroformylation, the catalysts without added salt, buffer or surfactant and have a low rhodium concentration give low selectivity, usually in the range 2.5-5.0. The influence of solution ionic strength on selectivity may be due to control of the geometry of catalytic intermediates.

Ionic water soluble phosphines, such as sulfonated phosphines, and their metal complexes are strong electrolytes. Since addition of salt greatly changes the solution

ionic strength, the presence of added salt is expected to influence the relative stability of catalytic intermediates. Thus the salt addition may be expected to have an effect on the activity and selectivity of water soluble catalysis.

Although the influence of additional salt on the catalytic activity and selectivity is observable, a systematic study on this subject has never been done.

1.6 Objectives of the Research

This thesis consists of two integral parts. Part 1 contains the synthesis and the two phase catalytic application of a series of novel surface active phosphines. Surface active phosphines are those phosphines which are designed to form small aggregates and to increase the solubility of organic substrate in water. Since the salt addition promotes the aggregation of these phosphines, the effect of solution ionic strength on the reaction activity and selectivity of aqueous catalysis is also investigated. The synthesis of surface active chiral chelating phosphines and their application in two phase asymmetric hydrogenation are described in Part 2.

One objective of Part 1 is to synthesize in high yield a series of steric demanding phosphines which can be sulfonated easily to generate both water solubility and surface activity. The surface activity of these phosphines, which is expected to play an important role on the outcome of aqueous catalysis, is characterized quantitatively by dynamic light scattering experiments. The two phase hydroformylation of a water insoluble olefin, 1-octene, is carried out for the purpose of demonstrating enhanced reaction rate and

selectivity with these surface active phosphines compared to the two phase hydroformylation with rhodium-TPPTS under similar catalytic conditions.

Because the solution ionic strength of the aqueous phase has a strong influence on the reaction activity and selectivity of two phase hydroformylation, the other objective of part 1 is to systematically investigate the influence of salt addition on the two phase hydroformylation of higher olefins. Studies of added salt on catalytic behavior provide additional information which supports the influence of surface active phosphines on the activity and selectivity of two phase hydroformylation of 1-octene as described previously.

Dissociation of TPPTS from $HRh(CO)(TPPTS)_3$ is considered a key step to generate active hydroformylation species. In order to further understand the fundamental reasons for the effect of ionic strength on the selectivity of aqueous hydroformylation, the influence of salt on the TPPTS/$HRh(CO)(TPPTS)_3$ exchange is studied. This study provides valuable insight on the relationship between solution ionic strength and the relative stability of catalytically active species which have decisive influence on the hydroformylation selectivity. On the other hand, the different results from TPPTS and surface active phosphines obtained by dynamic light scattering experiments are used to explain the observed difference in hydrofromylation activity.

A related objective is to study the role of the charge and size of the cation in determining the conformation of coordinated phosphine in transition metal complexes of sulfonated phosphines, as indicated by several crystal structures of metal complexes with

TPPTS [86, 87]. Investigation of the role of different cations in determining the reaction selectivity of aqueous hydroformylation is carried out.

The objective of part 2 is to establish a novel synthetic route to chelating phosphines, especially chiral biphosphines. Instead of a diphenylphosphino group, pendant diarylphosphino groups are introduced to biphosphines to generate a class of ligands which are easily sulfonated and have surface activity. Dynamic light scattering gives a quantitative measurement of aggregation. Two phase asymmetric hydrogenation of cinnamic acid derivatives is carried out to demonstrate that the rhodium catalysts with these surface active chiral phosphines are better in activity and enantioselectivity than their non-surface active analogs.

The two parts of the thesis are integrated by two main themes important for industrial applications of aqueous catalyses. First, the limited water solubility of a organic substrate impairs the catalytic activity of a water based system. This thesis demonstrates the potential of surface active phosphines to overcome the solubility problem. Second, selectivity of a catalyst is always critical for industrial applications. It is shown here for the first time that common additives in an aqueous catalytic system, salts and any other ionic species, have strong influence on reaction activity and selectivity and allow manipulation of reaction products, yields and rate.

Chapter 2

Effect of Aggregation of Water Soluble Phosphines and Solution Ionic Strength on Two Phase Hydroformylation of Olefins

2.1 Novel Sterically Demanding and Electron Withdrawing Phosphines

A class of novel phosphine, which have a combination of structural features of triphenylphosphine and tris(ω-phenylalkyl)phosphines [28], is synthesized and the rhodium catalysts with trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines are tested for hydroformylation activity under two phase conditions.(Figure 2.1)

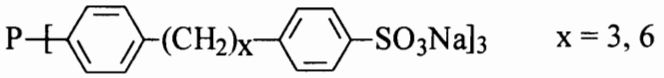


Figure 2.1 Trisulfonated Tris[*p*-(ω-phenylalkyl)phenyl]phosphines

A surface active phosphine which is electronically and sterically similar to triphenylphosphine may be a good candidate for hydroformylation of higher olefins. By tailoring the structural features of a triphenylphosphine and a tris(ω-phenylalkyl)phosphines, it is clear that trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines, $P[C_6H_4(CH_2)_xC_6H_4SO_3Na]_3$, represent a desirable target for a surface active triarylphosphine.

The synthesis of these ligands is straightforward. The difficulty in the synthesis of *p*-(ω-phenylalkyl)phenyl chloride can be overcome by control of the different reactivity of bromo- and chloro- in the exchange reaction between *p*-chlorophenyl bromide and *n*-butyllithium.(Figure 2.2)

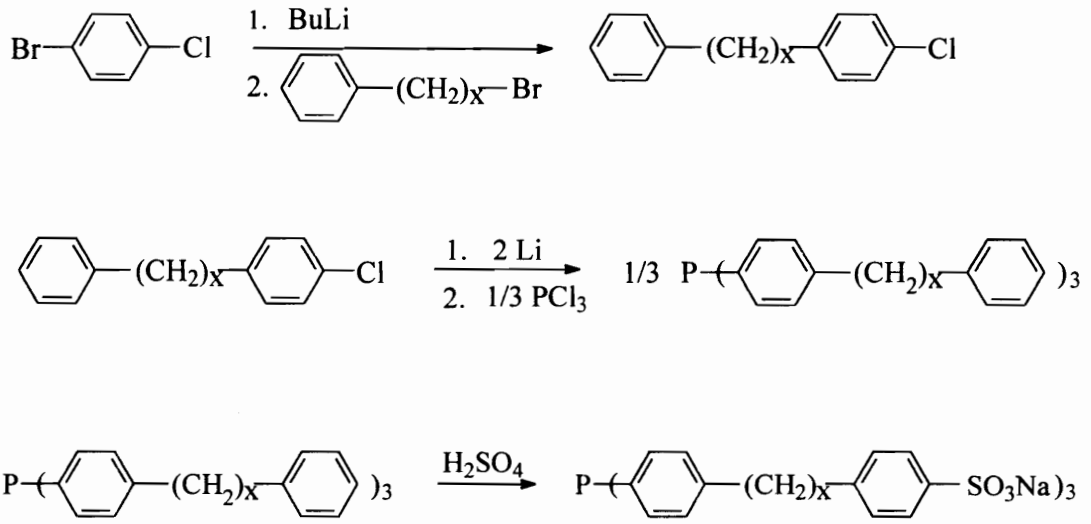


Figure 2.2 Synthesis of Trisulfonated Tris[*p*-(ω-phenylalkyl)phenyl]phosphines

The sulfonation of tris[*p*-(ω-phenylalkyl)phenyl]phosphines is extremely easy. It is accomplished simply by dissolving the phosphine into concentrated sulfuric acid. Trisulfonation is finished in several hours and the reaction produces no phosphine oxide which is commonly formed under normal sulfonation conditions.

2.2 The Synthetic Significance of the New Sulfonation Method

Traditional direct sulfonation method, as demonstrated by the sulfonation of triphenylphosphine, requires a mixture of oleum and concentrated sulfuric acid [7]. A high degree of sulfonation can only be achieved with long reaction time, usually several days. The reaction generates phosphine oxide which further complicates the purification.

Herrmann et al discovered that the addition of boric acid can significantly reduce the formation of phosphine oxide during direct sulfonation [48]. However long reaction times and the production of large amounts of salts are still associated with the sulfonation method.

The new phosphines, Tris[*p*-(ω-phenylalkyl)phenyl]phosphines, can be sulfonated by sulfuric acid without the presence of oleum. Trisulfonation is accomplished within several hours and there is no formation of phosphine oxide during the sulfonation process. The yield of sulfonation step alone is as high as 90% compared to 40-50% as a typical isolated yield of direct sulfonation of triphenylphosphine.

Based on ^{1}H and ^{13}C NMR spectra of sulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines, there is only tri-sulfonated product and sites of the sulfonation are exclusively the *para* positions of the outside phenyl rings. Specifically ^{1}H NMR spectra show typical non-first order splitting of aromatic proton signals for *para* substituted phenyl rings. ^{13}C NMR spectra give eight sets of aromatic carbon signals

whereas 10 or perhaps 12 are expected for *ortho* or *meta* sulfonation. The site and the degree of sulfonation are certain with this novel sulfonation method.

2.3 Surface Activity of Trisulfonated Tris[*p*-(ω-phenylalkyl)phenyl]phosphines

Although the surface activity of some sulfonated phosphines, such as mono-*meta*-sulfonated triphenylphosphine (TPPMS), has been noticed since the early investigation of these phosphines, quantitative determination of the extent of aggregation has never been done. Quantitative information on the aggregation of phosphines may be important for understanding observed hydroformylation reactivity and selectivity with these surface active ligands.

Aqueous solutions of trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines display several characteristics of a surfactant. For example, aqueous solution foams when shaken. Another qualitative test for the formation of micelles is the extent of dissolution of a poorly water soluble dye, such as Orange OT [93]. The dye dissolves more rapidly and to a greater extent in the solutions that contain micelles. Aqueous trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine solution dissolves Orange OT in a manner consistent with micelle formation. For comparison it is noted that aqueous solutions of TPPTS do not extract Orange OT into the aqueous phase.

Quantitative measurement of the hydrodynamic radius of micelles were done by dynamic light-scattering experiments in an attempt to elucidate the mechanism for increased reaction rate with surface active phosphines [94].

For an aqueous solution of trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine [PC(3)] at 0.05 M concentration the average hydrodynamic radius was consistently measured to be 7 Å. This value suggests that no aggregation of the ligand takes place under these conditions. At a NaCl concentration of 0.25 M the average hydrodynamic radius increases to 20 Å. The corresponding value for a sample of trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine [PC(6)] that may contain some Na_2SO_4 is 20 Å,. The hydrodynamic radius increases to 32 Å in 0.25 M aqueous NaCl. Aqueous solutions generated from $Rh(acac)(CO)_2$ and two equivalents of trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine showed the presence of aggregates with a hydrodynamic radius of 19 Å.

On the other hand, light-scattering experiments on aqueous solutions of TPPTS under the same conditions showed no evidence for uniform micelle formation at all concentrations of TPPTS (0.05-0.5M) and NaCl (0.25-1M) investigated.

The hydrodynamic radius of 7 Å observed for aqueous solution of trisulfonated tris-*p*-(3-phenylpropyl)phenylphosphine is consistent with isolated molecules of this ligand. The phosphine is comprised of three linear pendant groups terminated with a sulfonate group and linked at the hydrocarbon end by phosphorus. In the absence of added salt, electrostatic repulsions between the sulfonate groups are expected to define

the solution conformation. This generates a trigonal-planar arrangement of sulfonate groups with respect to the phosphorus atom. As solution ionic strength increases the electrostatic repulsions between sulfonate groups are expected to be lessened, thus aggregation of the phosphines apparently can take place upon addition of salt. If the relationship of the sulfonate groups to the phosphorus atom is pyramidal, then an octahedral array of six phosphines, with the phosphorus atoms comprising the hydrophobic core of a small micelle, fits the experimental hydrodynamic radius of 20 Å. (Figures 2.3 and 2.4) Although an aggregate of six phosphines fits the experiment data, aggregation numbers in the range of four to eight may be reasonable.

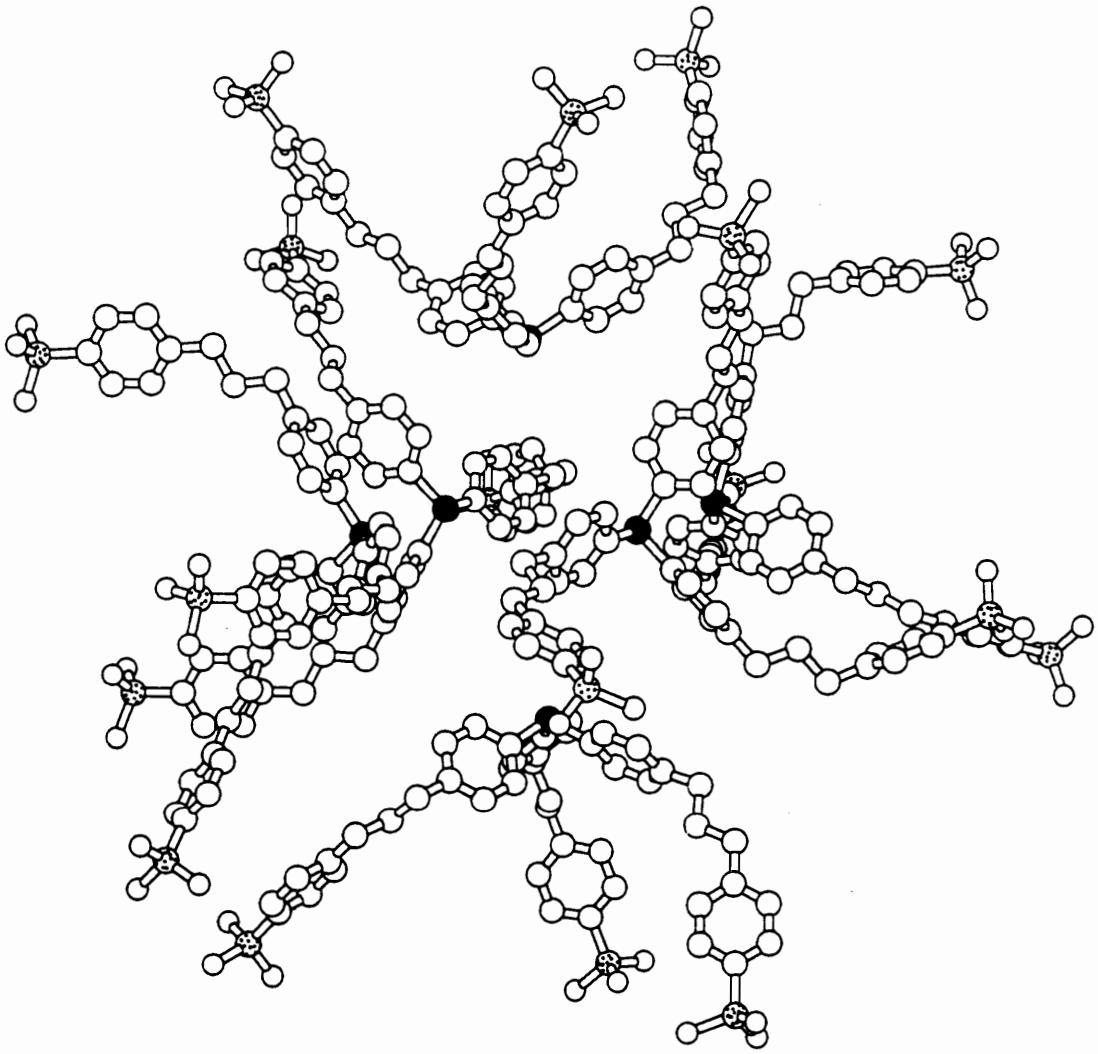
Formation of small aggregates is common for surfactants having unusually large or bulky hydrophobic groups. Significant rate enhancement has been observed for surfactants such as tatraalkylammonium halides when used as phase transfer catalysts. This suggests that tatraalkylammonium halides can function as normal surfactants in terms of increasing mixing even though formation of larger aggregates are precluded by their molecular structure. The sterically demanding phosphines with three pendant groups may behave just like tatraalkylammonium halides to form small micelle described above.

The results from dynamic light-scattering experiments demonstrate for the first time that surface active phosphines and their metal complexes aggregate in aqueous solution. This aggregation phenomenon can be used to explain the rate enhancement of two phase catalysis with these phosphines compared to Rh/TPPTS system (*vide infra*).

However, dynamic light-scattering results under catalytic conditions could not be obtained because of the limitation of available instrumentation. The fact that the catalytic systems with these surface active phosphines show rate enhancement with the addition of salts is consistent with micelle formation under catalytic conditions (*vide infra*).

Attempts were also made by ^{31}P NMR in order to confirm the formation of micelle. No change of chemical shift of trisulfonated tris-*p*-(3-phenylpropyl)phenylphosphine was observed upon addition of salt. The small chemical shift difference may not be observable because monomeric phosphines are in an equilibrium with aggregates of low concentration.

Figure 2.3 Aggregation of Six Trisulfonated Tri[*p*-(3-phenylpropyl)phenyl]phosphines



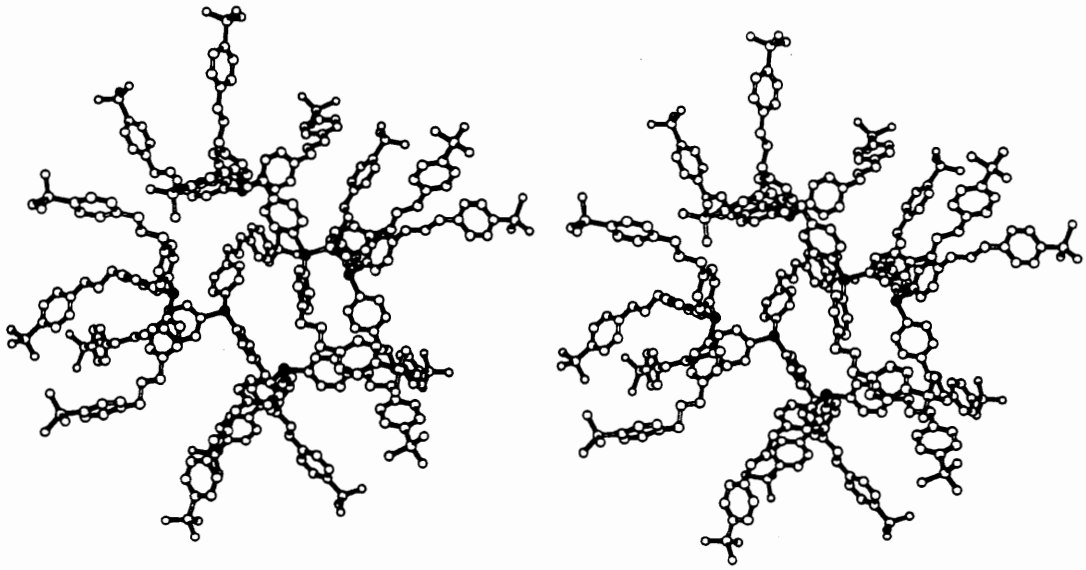


Figure 2.4 Stereoview of

Trisulfonated Tri[*p*-(3-phenylpropyl)phenyl]phosphine Aggregate

2.4 Influence of Solution Ionic Strength on the Dissociation of TPPTS From $HRh(CO)(TPPTS)_3$

Since it is evidenced that the addition of salt promotes the aggregation of water soluble phosphines and their metal complexes, it is interesting to see if the solution ionic strength has an influence on the relative stability of catalytic intermediates with sulfonated phosphines. Therefore the influence of salt addition on the dissociation of TPPTS from $HRh(CO)(TPPTS)_3$ is carried out. The activation energy (Ea) of the dissociation can be derived from the lineshape analysis of the dynamic NMR experiments [95]. In the slow exchange limit, the exchange rate (k) can be estimated from the linewidth ($1/t_2$) and natural linewidth ($1/t_{2(0)}$), by Equation 1.

$$k = \frac{1}{t_2} - \frac{1}{t_{2(0)}} \qquad \text{Equation 1}$$

Then the activation energy, Ea, can be determined from the slope of the plot ($ln\ k$ vs. 1/T) according to equation 2.

$$lnk = lnk_0 - \frac{E_a}{RT} \qquad \text{Equation 2}$$

The activation energies with different catalyst concentration and salt concentration are summarized in Table 2.1.

Table 2.1 The Influence of Ionic Strength on the Activation Energy of TPPTS Dissociation From $HRh(CO)(TPPTS)_3$

$HRh(CO)(TPPTS)_3$ [M]	TPPTS [M]	Na_2SO_4 [M]	Ionic Strength (μ)	Ea [kcal/mol]
0.01	0.18	0.0	1.5	22 ±1
0.01	0.18	0.1	1.8	26 ±1
0.10	1.80	0.0	15	31 ±1

The data clearly indicate that the activation barrier for exchange is dependent on the concentration of salt and the total concentration of reagents. An Ea of 22 ±1 kcal/mol which was obtained at relatively low concentrations of reagents and no additional salt approaches to the activation energy of PPh_3 dissociation from $HRh(CO)(PPh_3)_3$ in organic solvent (19 kcal/mol) [72]. The critical parameter appears to be the solution ionic strength since TPPTS, $HRh(CO)(TPPTS)_3$ and Na_2SO_4 are all strong electrolytes. The activation energy for the TPPTS dissociation increases with increasing ionic strength. The data reported by Horvath and co-workers, which gave an activation barrier of 30.2 kcal/mol, may have been collected at relatively high ionic strength since it is consistant with our data collected at high concentration of reagents [96].

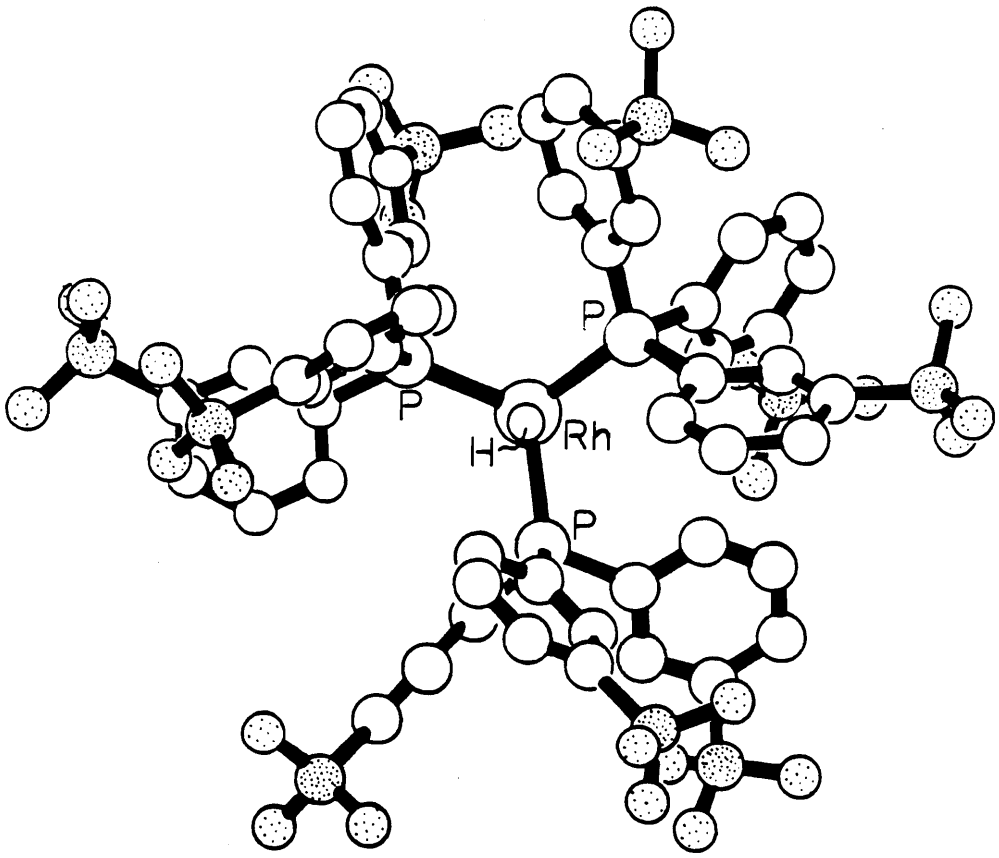
The rhodium complex, $HRh(CO)(TPPTS)_3$, can be thought of as a small molecular micelle (Figure 2.5). Dimensions for the TPPTS complex can be estimated from the crystal structure of the corresponding triphenyphosphine complex, $HRh(CO)(PPh_3)_3$ [97]. Using the atomic positions from this compound as a starting point one meta position on each of the nine phenyl groups was substituted by a sulfonate group.

Since there are two meta positions per phenyl ring and nine rings this leads to 2^9 possible conformations based on orientation of phenyl rings provided by the crystal structure; shown in Figure 2.5 is one possible conformer. It is derived from the orientation found in the solid state for $HRh(CO)(PPh_3)_3$ by substituting at the meta position and requiring the sulfonate groups to be as far apart on average as possible. No attempt was made to minimize the structure for rotation about the P-C bonds and the structure is meant only to give an estimate of the size of the molecule. The sulfonate groups can be considered to lie on the surface of a sphere of approximately 8 Å in diameter. This is quite compact for a "micelle" with a net charge of -9. The close proximity of nine sulfonate groups in this compound should promote ligand dissociation to minimize intramolecular electrostatic repulsions between sulfonate groups.

In the solid state it has been demonstrated that sodium cations plays an important role in coordinating sulfonate groups in the crystal of $Co_2(CO)_6(TPPTS)_2$ [86]. Sodium and other ions at relatively high concentration are likely to a similar role in minimizing electrostatic repulsion intramolecularly between sulfonate groups. Instead of the intramolecular hydrogen bonding model suggested by Horvath et al, it is more likely that the hydration sphere around $HRh(CO)(TPPTS)_3$ in aqueous solution is highly ordered and contains a high concentration of sodium cations to balance the charge on the rhodium TPPTS complex. High ionic strength of the solution stabilizes the hydration sphere by minimizing the electrostatic replusions between sulfonate groups. Loss of a TPPTS ligand would require considerable reorganization of the solvation sphere and is thus

unfavorable. It is expected to become even more unfavorable as the ionic strength of the solution increases.

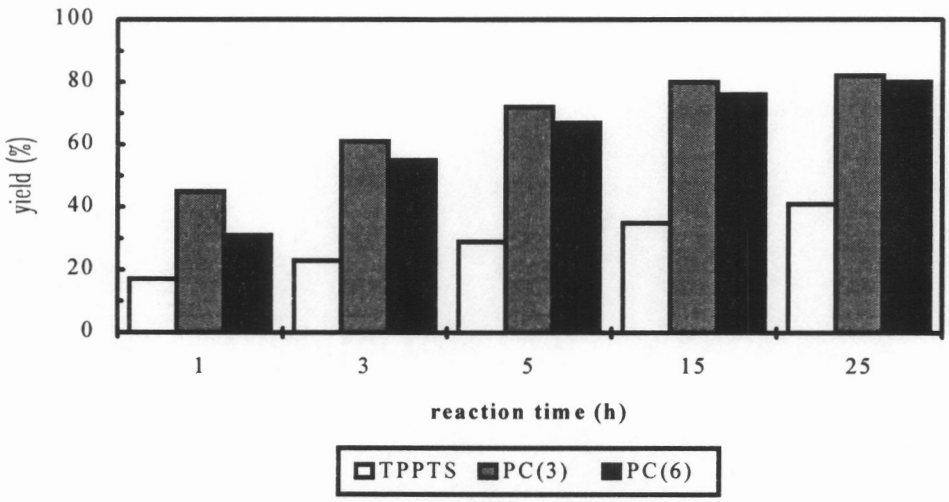
Figure 2.5 Molecular Micelle of $HRh(CO)(TPPTS)_3$



2.5 Two Phase Hydroformylation of 1-octene With Rhodium Complexes of Surface Active Phosphines

2.5.1 Catalytic Results With Methanol as a Co-solvent

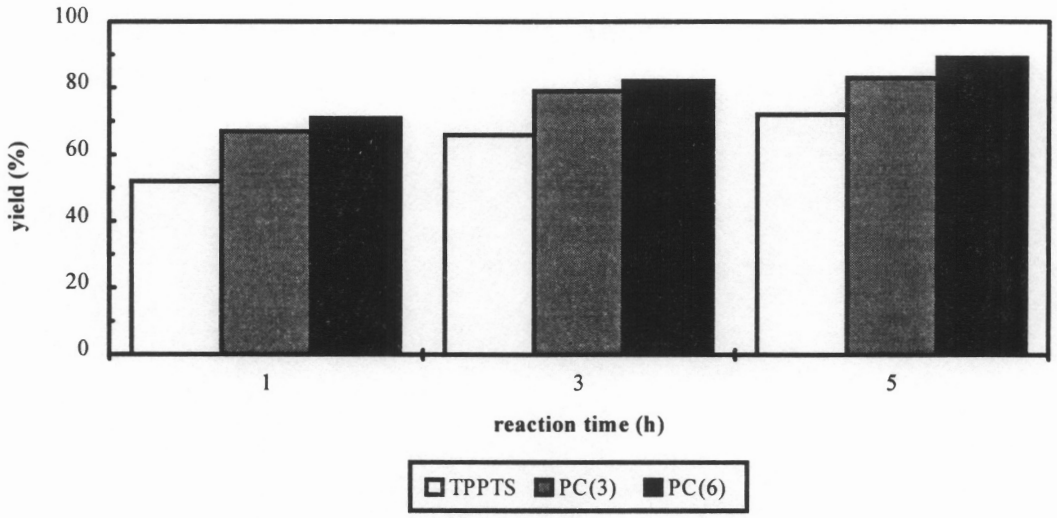
Catalytic results for the two phase hydroformylation of 1-octene with methanol as a cosolvent are summarized in Figures 2.6 and 2.7 at ligand /Rh ratios of 2 and 10 respectively. Significant activity for alcohol formation is seen at high conversion for all catalysts, as it has been observed elsewhere [61, 62, 68, 98]. The reaction yield refers to total products of aldehyde plus alcohols. The yield of nonanols represents up to 10% of the total products at conversions greater than 80%. To indicate the relative initial rate of reaction, the average turnover frequencies in the first 1 hour of reaction are presented in Table 2.2. Reaction selectivity at highest conversions, as normal to branched product ratios and the percentage of linear aldehyde (1-nonanal), is given in Table 2.3. Results for selectivity were obtained with the reaction yield from the same catalytic run.



reaction time (h)	yield (%)		
	with TPPTS	with PC(3)	with PC(6)
1	17 ±2	45 ±2	31 ±2
3	23 ±2	61 ±2	55 ±2
5	29 ±2	72 ±2	67 ±2
15	35 ±2	80 ±2	76 ±2
25	41 ±2	82 ±2	80 ±2

[a] [Rh] = 0.005 M; 1-octene/Rh = 500/1; volume of aqueous phase is 1.5 ml and volume of organic phase is 1.0 ml; pressure of CO/H_2 (1/1) is 19.5 atm; reaction temperature is 120°C; stirring rate is 260 rpm.

Figure 2.6 Reaction Yield as a Function of Time for the Ligands TPPTS, PC(3), PC(6) in the Rhodium Catalyzed Hydroformylation of 1-octene at L/Rh(acac)$(CO)_2$ Ratio of 2.[a]



reaction time (h)	yield (%)		
	with TPPTS	with PC(3)	with PC(6)
1	52 ±2	67 ±2	71 ±2
3	66 ±2	79 ±2	82 ±2
5	72 ±2	83 ±2	89 ±2

[a] [Rh] = 0.005 M; 1-octene/Rh = 500/1; volume of aqueous phase is 1.5 ml and volume of organic phase is 1.0 ml; pressure of CO/H_2 (1/1) is 19.5 atm; reaction temperature is 120°C; stirring rate is 260 rpm.

Figure 2.7 Reaction Yield as a Function 0f Time for the Ligands TPPTS, PC(3), PC(6) in the Rhodium Catalyzed Hydroformylation of 1-octene at L/Rh(Acac)$(CO)_2$ Ratio of 10.[a]

Table 2.2 Average Turnover Frequency[a] in the First 1 h of Reaction[b]

	L/Rh = 2	L/Rh = 10
TPPTS	90	260
PC(3)	225	335
PC(6)	160	360

[a] mol of aldehyde (mol of Rh)$^{-1}$h^{-1}.

[b] Conditions: reaction temperature, 120°C; initial pressure, 19.5 atm; [Rh] = 0.0005 M; stirring rate, 260 rpm.

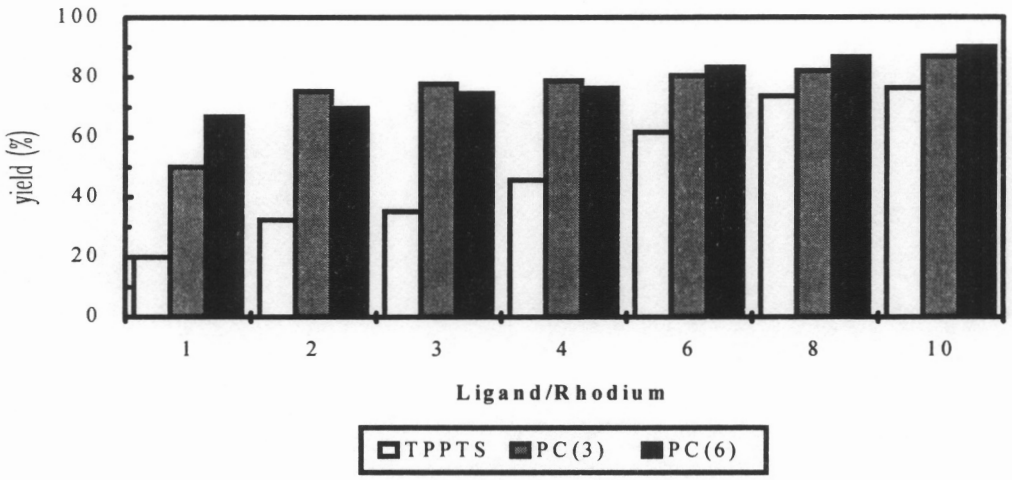
Table 2.3 Reaction Selectivity(n/b) at Highest Conversion[a]

	L/Rh = 2		L/Rh = 10	
	yield (%)	n/b (% of 1-nonanal)	yield (%)	n/b (% of 1-nonanal)
TPPTS	47 ±2	2.4 (71 ±2)	78 ±2	3.6 (78 ±2)
PC(3)	88 ±2	3.0 (75 ±2)	85 ±2	8.0 (89 ±2)
PC(6)	84 ±2	3.3 (77 ±2)	88 ±2	9.5 (90 ±2)

[a] Conditions: reaction temperature, 120°C; initial pressure, 19.5 atm; [Rh] = 0.0005 M; stirring rate, 260 rpm.

For a given ligand the turnover frequency in the first 1 h of reaction is faster at L/Rh = 10 than L/Rh = 2. This is true for TPPTS as well as for the trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines. The fact that the rates improve at higher ligand/rhodium ratio is in contrast to the case for Rh/PPh_3 homogeneous catalysts, in which reaction rate drops at high ligand concentration [68, 98]. The same trend was also observed in the ligand to rhodium ratio variation studies for both TPPTS and surface active phosphines(Figure 2.8). It has been suggested that catalysis under biphasic conditions with water soluble catalysts and water immiscible organic substrates is mass transfer limited [12]. Therefore it appears that the water-soluble phosphines not only serve to complex the rhodium but also facilitate the mixing of the immiscible phases.

Although the presence of methanol contributes to the solubility of 1-octene in water, the fact that higher activity, in terms of first 1 hour turnover frequency, was observed with trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines than with TPPTS still suggests the possibility of micelle formation under cataytic conditions. At a constant L/Rh ratio the rates improve on going from TPPTS to trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine and trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine. This may be explained by better mixing of the phases, since trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines are more likely to be surface active than TPPTS.



ligand/rhodium	yield (%)		
	with TPPTS	with PC(3)	with PC(6)
1	20 ±2	50 ±2	67 ±2
2	32 ±2	75 ±2	70 ±2
3	35 ±2	78 ±2	75 ±2
4	46 ±2	79 ±2	76 ±2
6	62 ±2	81 ±2	83 ±2
8	74 ±2	82 ±2	87 ±2
10	76 ±2	87 ±2	90 ±2

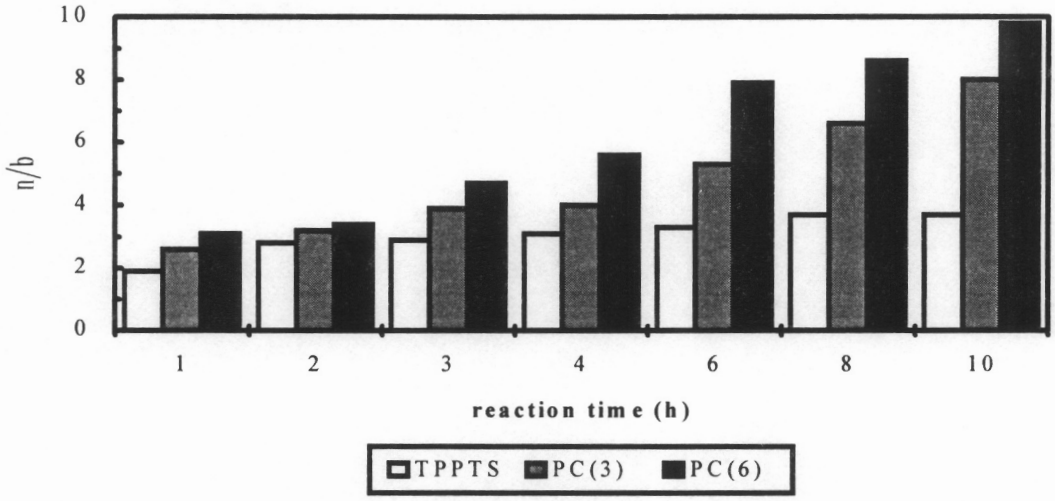
[a] Conditions: reaction time, 5h; reaction temperature, 120°C; initial pressure, 19.5 atm; [Rh] = 0.005 M; stirring rate, 260 rpm.

Figure 2.8 Reaction Activity as a Function of L/Rh(acac)$(CO)_2$ Ratio for the Ligands TPPTS, PC(3), PC(6) in the Rhodium Catalyzed Hydroformylation of 1-octene[a]

In all three cases the selectivity decreases as the yield of reaction increases. The same phenomenon has been observed elsewhere and explained mechanistically by hydroformylation of isomerization products at high conversion. On the other hand, selectivity, as evidenced by ligand to rhodium ratio variation studies (Figure 2.9), increases with the ligand concentration in both TPPTS and trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines. This is because that excess phosphine increases the concentration of $HRh(CO)L_2$ which is considered as the key intermediate for linear aldehyde formation [90]. However, selectivity of the catalyst with trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines is much higher than that with TPPTS at high ligand concentration in aqueous methanol, n/b = 3.7, 8.0, 9.8 for TPPTS, trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine and trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine respectively at L/Rh = 10. Much stronger influence of ligand concentration on hydroformylation selectivity with trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines than that with TPPTS may be due to the low solution ionic strength of aqueous methanol solution.

Compared to TPPTS the surface active phosphines, $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$ and $P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$, are significantly larger in the sense that the sulfonate groups are linked to the ends of three long aryl groups in the phosphines. The steric size of these surface active phosphines, as estimated by the Tolman cone angle, should be similar to PPh_3 and slightly smaller than TPPTS. In the solution of low ionic strength the

key catalytic intermediate for linear aldehyde formation, $HRh(CO)L_2$, when L is surface active phosphines, may still be the predominant catalytic species compared to $HRh(CO)_2L$, especially when ligand concentration is high. On the other hand, the same catalytically active species with TPPTS may not be present as the most available intermediate for catalytic hydroformylation in such a low ionic strength solution due to electrostatic repulsion between six sulfonate groups in close proximity. Therefore the catalytic cycle may be more likely to proceed via $HRh(CO)_2$TPPTS which in turn leads to a higher percentage of branched aldehyde products. This rationale can count for the higher n/b ratio observed with surface active phosphines, especially at high L/Rh ratio, compared to rhodium/TPPTS system in aqueous methanol solution which has a low ionic strength. $HRh(CO)L_2$ in all cases will be more favored without methanol as a co-solvent and the selectivity thus is expected to be higher in pure water than in aqueous methanol for each catalyst.



ligand/rhodium	selectivity n/b (% of 1-nonanal)		
	with TPPTS	with PC(3)	with PC(6)
1	1.9 (66 ±2)	2.6 (72 ±2)	3.1 (76 ±2)
2	2.8 (74 ±2)	3.2 (76 ±2)	3.4 (77 ±2)
3	2.9 (74 ±2)	3.9 (80 ±2)	4.7 (82 ±2)
4	3.1 (76 ±2)	4.0 (80 ±2)	5.6 (85 ±2)
6	3.3 (77 ±2)	5.3 (84 ±2)	7.9 (89 ±2)
8	3.7 (79 ±2)	6.6 (87 ±2)	8.6 (90 ±2)
10	3.7 (79 ±2)	8.0 (89 ±2)	9.8 (91 ±2)

[a.] Conditions: reaction time, 5h; reaction temperature, 120°C; initial pressure, 19.5 atm; [Rh] = 0.0005 M; stirring rate, 260 rpm.

Figure 2.9 Reaction Selectivity as a Function of L/Rh(acac)$(CO)_2$ Ratio for the Ligands TPPTS, PC(3), PC(6) in the Rhodium Catalyzed Hydroformylation of 1-octene[a]

2.5.2 Catalytic Result With Water as the Only Aqueous Solvent

The presence of methanol in the previous study is originated from the stock solution of $Rh(acac)(CO)_2$. Methanol as a co-solvent greatly enhances the activity of a two phase system. However, both the presence of methanol and the surface activity of trisulfonated tris[*p*-(ω-phenylalkyl)phenyl]phosphines may contribute to the water solubility of the olefin substrate. Since the solution ionic strength plays an important role in determining the reaction rate and selectivity of aqueous hydroformylation, it is necessary to investigate a system without methanol as a co-solvent. Also the dynamic light scattering results indicate that the addition of a salt promotes the aggregation of surface active phosphines. Therefore the salt addition may also have an influence on hydroformylation activity and selectivity. These effects are best studied in water alone as a solvent.

The results of two phase hydroformylation of 1-octene with and without added salt (Na_2HPO_4) are summarized in Tables 2.4, 2.5 2.6 for TPPTS, trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine and trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine respectively. The hydroformylation of 1-octene with $HRh(CO)L_3$ under two phase conditions in the absence of methanol proceeds slowly. However the selectivity in all three cases is higher than that with methanol as a co-solvent. It is postulated that this is due to higher solution ionic strength in the aqueous system.

Table 2.4 The Effect of Salt on the Activity and Selectivity

of Hydroformylation of 1-octene With TPPTS/Rh(acac)$(CO)_2$[a]

	TPPTS/Rh = 3			TPPTS/Rh = 10		
	μ[b]	Yield (%)	*n/b* (% of 1-nonanal)	μ[b]	Yield (%)	*n/b* (% of 1-nonanal)
TPPTS	0.22	10 ±2	4.0 (80 ±2)	0.44	19 ±2	12 (92 ±2)
TPPTS, 0.5 M Na_2HPO_4	1.7	4 ±2	8.4 (89 ±2)	1.9	8 ±2	24 (96 ±2)
TPPTS, 0.5 M SDS	—	—	—	0.94	43 ±2	9.4 (90 ±2)

[a] Reaction temperature, 120°C. Pressure at 120°C = 19.5 atm. Reaction time, 24 h. Rh/1-octene = 500. [Rh] = 0.005 M.

[b] Solution Ionic Strength

High ionic strength (μ = 1.7 and 1.9 with 0.5 M Na_2HPO_4 at TPPTS/Rh = 3 and 10 respectively) is anticipated to decrease the already low solubility of 1-octene in water. For this reason alone rates are expected to be lower in the catalytic reactions at high Na_2HPO_4 concentration. This is indeed observed with $HRh(CO)(TPPTS)_3$ as the catalyst. Even with excess TPPTS (TPPTS/Rh = 10) the catalytic activity drops as Na_2HPO_4 is added. This result is consistent with the observation from dynamic light scattering experiments. Specifically aggregates which could be expected to solubilize 1-octene in water are not formed in aqueous TPPTS solutions.

The fact that high solution ionic strength tends to stabilize the catalytic intermediates with relative high charge suggests that the high selectivity of aqueous hydroformylation reaction is expected when the solution is of high ionic strength. This is indeed observed as seen from the data reported in Table 2.4. The lower activity of the Rh/TPPTS catalyst in the presence of salt is consistent with diminished solubility of 1-octene in aqueous solution of high ionic strength. The selectivity however increases as the salt concentration increases. At a TPPTS/Rh ratio of 10/1 the selectivity to linear aldehyde is 96 % (n/b = 24) in the presence of Na_2HPO_4, compared to 92% linear (n/b = 12) in the absence of disodium phosphate. Since the conversion drops the difference in selectivity needs to be viewed with caution, however results observed with the surface active phosphines (Tables 2.5, 2.6) suggest that the selectivity enhancement is real. With no excess phosphine, Rh/TPPTS = 3, the same effect is observed with the addition of Na_2HPO_4. Compared to the data with the addition of Na_2HPO_4 the presence of a surfactant, SDS (sodium dodecylsulfate), increases the conversion but has little effect on the selectivity. The presence of the surfactant introduces the complication of poor phase separation when the reaction is terminated.

The results with Rh/surface active phosphine systems are quite different from those obtained with TPPTS. Specifically the reaction rate increases upon the addition of salt for the catalytic systems with trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine and trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine. (Table 2.5 and 2.6)

The increase in catalytic activity of Rh-surface active phsosphine catalysts with the addition of salt serves as an indirect evidence that these phosphines do have an ability to form aggregates under catalytic conditions. As noted previously aqueous solutions of trisulfonated tris[*p*-(3-phenylpropyl)phenyl]phosphine and trisulfonated tris[*p*-(6-phenylhexyl)phenyl]phosphine facilitate the dissolution of orange OT, a water insoluble dye (*vide supra*).

The reaction rates of hydroformylation of 1-octene with surface active phosphines are expected to increase with the salt concentrations since it has been demonstrated that , $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$ and $P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$ form aggregates in salt solution. Also a similar increase in selectivity with added salt was observed with $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$ and $P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$ respectively, as presented in Table 2.5 and Table 2.6.

Table 2.5 The Effect of Salt on the Activity and Selectivity

of 1-octene Hydroformylation With $Rh/P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$[a]

	L/Rh = 3			L/Rh = 10			L/Rh = 20		
	μ[b]	Yield (%)	*n/b* (%)[c]	μ[b]	Yield (%)	*n/b* (%)[c]	μ[b]	Yield (%)	*n/b* (%)[c]
no salt	0.22	13 ±2	3.6 (78 ±2)	0.44	15 ±2	9.7 (91 ±2)	0.74	15 ±2	13 (92 ±2)
0.5 M Na_2HPO_4	1.7	15 ±2	9.8 (91 ±2)	1.9	22 ±2	12 (92 ±2)	2.2	23 ±2	17 (94 ±2)
0.5 M Na_2SO_4	1.7	14 ±2	10 (91 ±2)	1.9	23 ±2	13 (93 ±2)	2.2	23 ±2	17 (94 ±2)

[a] L = $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$, Reaction temperature, 120°C. Pressure at 120°C = 19.5 atm. Reaction time, 24 h. Rh/1-octene = 500. [Rh] = 0.005 M.

[b] Solution Ionic Strength

[c] % of 1-nonanal

Table 2.6 The Effect of Salt on the Activity and Selectivity

of 1-octene Hydroformylation with $Rh/P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$[a]

	L/Rh = 3		
	μ[b]	Yield (%)	*n/b* (%,1-nonanal)
no salt	0.22	19 ±2	3.4 (77 ±2)
0.5 M Na_2HPO_4	1.7	24 ±2	8.6 (90 ±2)

[a] L = $P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$, Reaction temperature, 120°C. Pressure at 120°C = 19.5 atm. Reaction time, 24 h. Rh/1-octene = 500. [Rh] = 0.005 M.

[b] Solution Ionic Strength

There is little difference in reaction selectivity as the phosphine changes from $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$ to $P[C_6H_4(CH_2)_6C_6H_4SO_3Na]_3$. In the case of $P[C_6H_4(CH_2)_3C_6H_4SO_3Na]_3$ selectivity remains almost the same as ligand concentration increases from L/Rh = 10 to L/Rh = 20. This perhaps indicates that selectivity in this case is not sensitive to the increase of ligand concentration alone. Reaction selectivity improves upon the addition of Na_2HPO_4 to the catalytic systems with surface active phosphines, just as seen in the TPPTS case. However the improvement of selectivity in the surface active phosphine systems is not nearly as great as that observed in the TPPTS system. Addition of two different salts, Na_2HPO_4 and Na_2SO_4 shows no distinguishable effect on selectivity. Since both conversion and selectivity increase with two surface active ligands this leads to the conclusion that salt concentration has a real effect on reaction selectivity and activity in water soluble hydroformylation catalysts.

The fact that addition of salt has a stronger influence on the Rh/TPPTS system than the Rh/surface active phosphine systems is quite interesting. The TPPTS ligand is much more structurally compact than surface active phosphines. Thus three sulfonate groups on a TPPTS ligand are in close proximity and $HRh(CO)(TPPTS)_3$ for example has nine sulfonate groups sitting on the surface of a spherical molecule with a diameter of 8Å (*vide supra*). Electrostatic repulsions are therefore expected to be more pronounced in rhodium complexes with TPPTS than complexes with the surface active phosphines. An increase in solution ionic strength is then expected to have stronger influence on the stability of the Rh/TPPTS system compared to the Rh/surface active phosphine system.

2.6 The Effect of Spectator Cations on the Catalytic Selectivity of Aqueous Hydroformylation

The fact that the solution ionic strength influences the relative stability of catalytic intermediates suggests that the hydration sphere around a water soluble catalytic species is highly ordered and may contain a high concentration of cations to balance the charge and minimize the intramolecular electrostatic repulsion between sulfonate groups. The mechanism implies that reaction activity and selectivity may be dependent on the nature of the cation.

Different anions as noted with the added salt may have little effect on catalytic results. Na_2SO_4 and Na_2HPO_4 have almost identical effect on the reaction activity and selectivity of hydroformylation of 1-octene (*vide supra*).

2.6.1 The Influence of Metal Cation on the Hydroformylation of 1-hexene

In order to further elaborate the effect of solution ionic strength and investigate the role of the cations in determining reaction activity and selectivity, a systematic study of the effect of alkali metal sulfates on aqueous hydroformylation of 1-hexene with Rh/TPPTS catalyst was carried out. From the previous study of aqueous hydroformylation, it was noted that the conversion of 1-octene is low even with surface active phosphines. Therefore 1-hexene was chosen as the substrate for improved reaction rates compared to 1-octene in the two phase reactions.

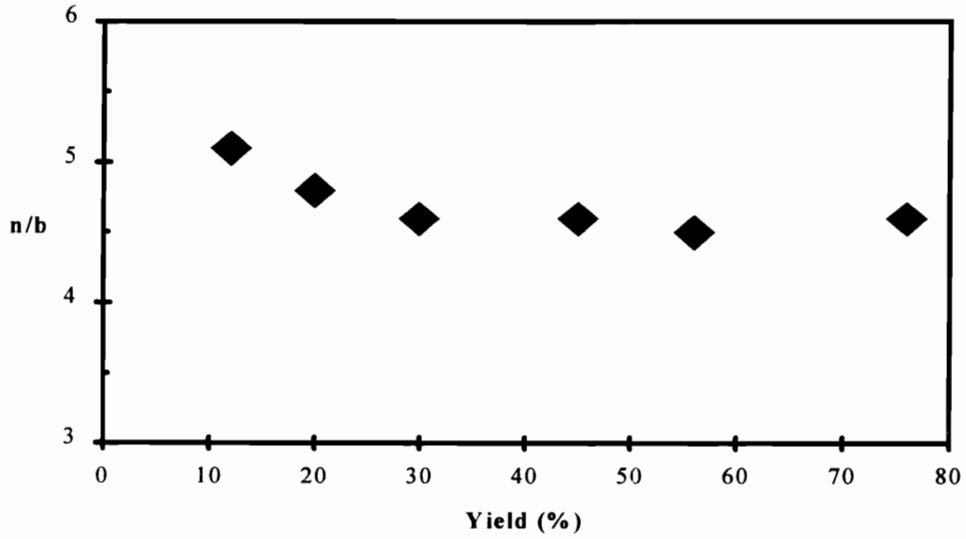
The results from the hydroformylation of neat 1-hexene with $HRhCO(TPPTS)_3$ in water without additional salt are shown in Figure 2.10. These data serve as a reference for the selectivity at certain conversion of olefin since n/b ratio usually is influenced by the conversion. At the stirring rate used the two-phase hydroformylation gives yields of up to 76% aldehyde in a 24 hour reaction period. Although the selectivity, as indicated by normal to branched (n/b) ratio, generally drops as the yield increases, it remained low in the whole range of yields under these condition; specifically the n/b ratio drops from 5.1 to 4.4 as the adehyde yield increases from 12% to 76%. This is indicative of some olefin isomerization, although in the present case internal olefins are not observed, nor is 2-ethylpentanal.

The effect of added Li_2SO_4, Na_2SO_4, and Cs_2SO_4 on the activity of the two-phase hydroformylation of hexene-1 is given in Figure 2.11. As expected the yield of aldehydes, as an indication of reaction activity, drops as the salt concentration increases from 0.0 M, to 0.5 M.

As noted earlier the addition of a water soluble salt to an aqueous solution increases solution ionic strength, and is expected to further diminish the limited the solubility of olefins in water. A drop in the yield of aldehydes then is expected when a salt is added to the aqueous catalytic solution. This effect is observed in all cases although it is not as pronounced as cation size increases.

The alkali metal salts, Li_2SO_4, Na_2SO_4, and Cs_2SO_4, have a significant influence on the reaction selectivity as shown in Figure 2.12. Specifically the normal to branched

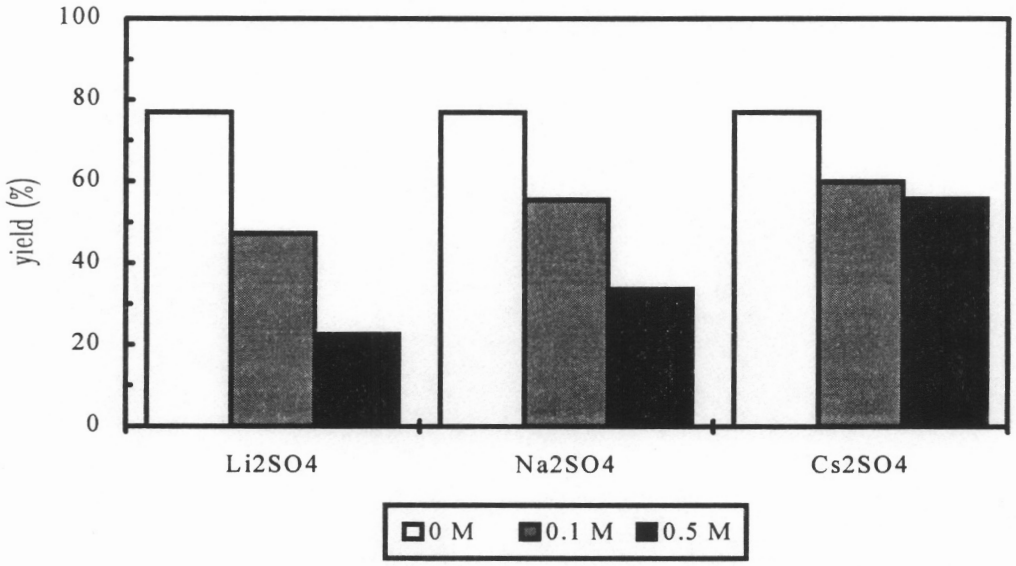
aldehyde ratio increased to 8.5 at 23% conversion, 8.0 at 34% conversion and 10 at 56% conversion with Li_2SO_4, Na_2SO_4, and Cs_2SO_4 respectively. Although these comparisons are made at different conversions, it is clear that the selectivities are improved compared to that obtained at low ionic strength, Figure 2.10.



yield (%)	12 ±2	20 ±2	30 ±2	45 ±2	57 ±2	76 ±2
n/b	5.1	4.8	4.5	4.5	4.3	4.4
(%, 1-heptanal)	(84 ±2)	(83 ±2)	(82 ±2)	(82 ±2)	(81 ±2)	(81 ±2)

[a] Reaction condition: $HRh(CO)(TPPTS)_3$ 0.005 M; 1-hexene/Rh = 500/1; Pressure = 20 atm; Temperature = 120°C; Stirring rate = 260 rpm.

Figure 2.10 Selectivity vs Yield in the Hydroformylation of 1-hexene with $HRh(CO)(TPPTS)_3$[a]

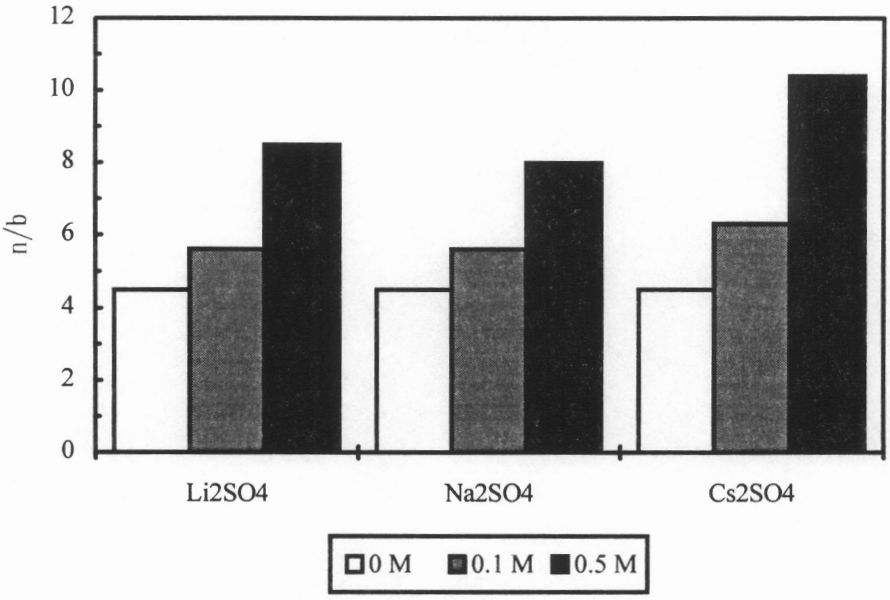


conc. of salt (M)	μ^b	yield (%) with Li_2SO_4	yield (%) with Na_2SO_4	yield (%) with Cs_2SO_4
0	0.23	76 ±2	76 ±2	76 ±2
0.1	0.53	47 ±2	56 ±2	60 ±2
0.5	1.7	23 ±2	34 ±2	56 ±2

[a.] Reaction condition: $HRh(CO)(TPPTS)_3$ 0.005 M; 1-hexene/Rh = 500/1; Pressure = 20 atm; Temperature = 120°C; Reaction time = 24 hours; Stirring rate = 260 rpm.

[b.] Solution Ionic Strength

Figure 2.11 The Effect of Alkali Metal Sulfates on the Reaction Activity of 1-hexene Hydroformylation[a]



conc. of salt (M)	μ^b	n/b (%, 1-heptanal) with Li_2SO_4	n/b (%, 1-heptanal) with Na_2SO_4	n/b (%, 1-heptanal) with Cs_2SO_4
0	0.23	4.4 (81 ±2)	4.4 (81 ±2)	4.4 (81 ±2)
0.1	0.53	5.6 (85 ±2)	5.6 (85 ±2)	6.3 (86 ±2)
0.5	1.7	8.5 (89 ±2)	8.0 (89 ±2)	10 (91 ±2)

[a.] Reaction condition: $HRh(CO)(TPPTS)_3$ 0.005 M; 1-hexene/Rh = 500/1; Pressure = 20 atm; Temperature = 120°C; Reaction time = 24 hours; Stirring rate = 260 rpm.

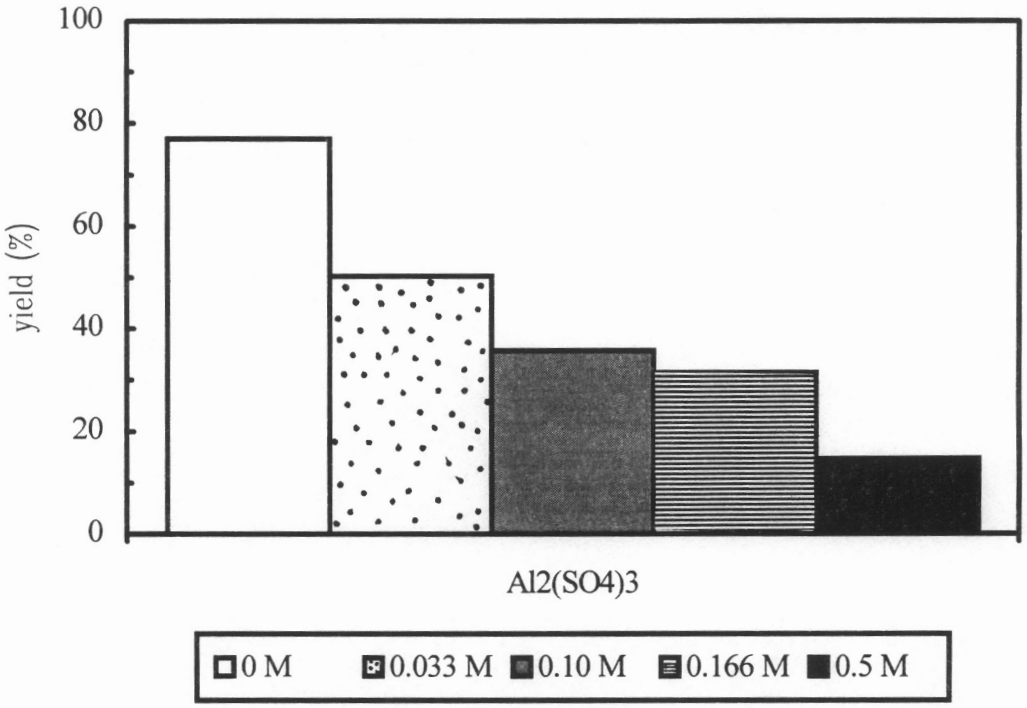
[b.] Solution Ionic Strength

Figure 2.12 The Effect of Alkali Metal Sulfates on the Reaction Selectivity of 1-hexene Hydroformylation [a]

The fine control of the normal to branched aldehyde ratio (n/b) is critical to the industrial application of high olefin hydroformylations. The aldehydes produced by hydroformylation are usually further used for generating alcohols or acids, therefore a high normal to branched aldehyde ratio is normally required for an acceptable viscosity index. Interestingly the "spectator" cation gives a measure of control on the reaction selectivity. By the rationale stated previously high solution ionic strength caused by addition of alkali metal sulfate generates a more selective catalyst. It is indeed observed here in Figure 2.12. The biggest increase of selctivity at the same ionic strength is always obtained with the addition of Cs_2SO_4. The reason is perhaps the relative large ionic radius of Cs^+ compared to Li^+ and Na^+.

In Figure 2.13, the effect of a trivalent cation, aluminum (III) in $Al_2(SO_4)_3$, on the reaction activity is presented. As in the case of the alkali metal sulfates the yield of aldehyde drops with increasing ionic strength. In order to make a meaningful comparison between a trivalent salt and monovalent salt, a broader range of $Al_2(SO_4)_3$ concentration was covered. No effort was made to control the pH of the catalyst that contained aluminum sulfate. At 0.5 M $Al_2(SO_4)_3$ prior to catalysis the pH was 4. No evidence for the formation of a precipitate in the aqueous phase was observed either prior to catalysis or after the catalytic runs.

Surprisingly the addition of $Al_2(SO_4)_3$ did not increase the reaction selectivity. As seen in Figure 2.14, the n/b ratio dropped slightly upon the addition of $Al_2(SO_4)_3$.

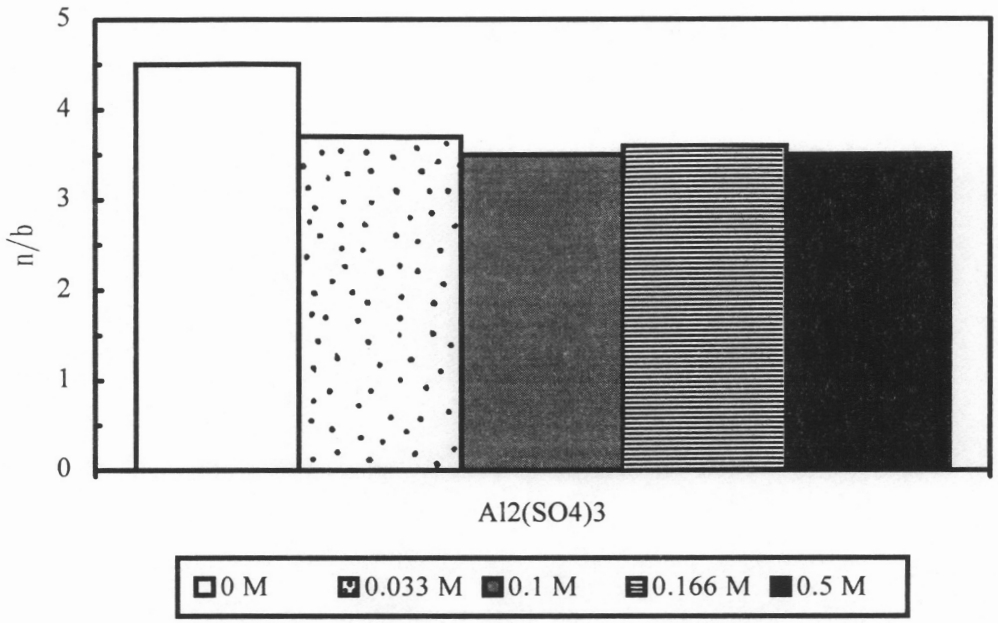


conc. $Al_2(SO_4)_3$ (M)	0	0.033	0.10	0.17	0.50
μ[b]	0.23	0.72	1.7	2.8	7.7
yield (%)	76 ±2	50±2	36±2	31±2	15±2

[a.] Reaction condition: $HRh(CO)(TPPTS)_3$ 0.005 M; 1-hexene/Rh = 500/1; Pressure = 20 atm; Temperature = 120°C; Reaction time = 24 hours; Stirring rate = 260 rpm.

[b.] Solution Ionic Strength

Figure 2.13 The Effect of $Al_2(SO_4)_3$ on the Reaction Activity of 1-hexene Hydroformylation [a]



conc. $Al_2(SO_4)_3$ (M)	0	0.033	0.10	0.17	0.50
μ^b	0.23	0.72	1.7	2.8	7.7
n/b (%. 1-heptanal)	4.4 (81 ±2)	3.7 (79 ±2)	3.5 (78 ±2)	3.6 (78 ±2)	3.5 (78 ±2)

[a.] Reaction condition: $HRh(CO)(TPPTS)_3$ 0.005 M; 1-hexene/Rh = 500/1; Pressure = 20 atm; Temperature = 120°C; Reaction time = 24 hours; Stirring rate = 260 rpm.

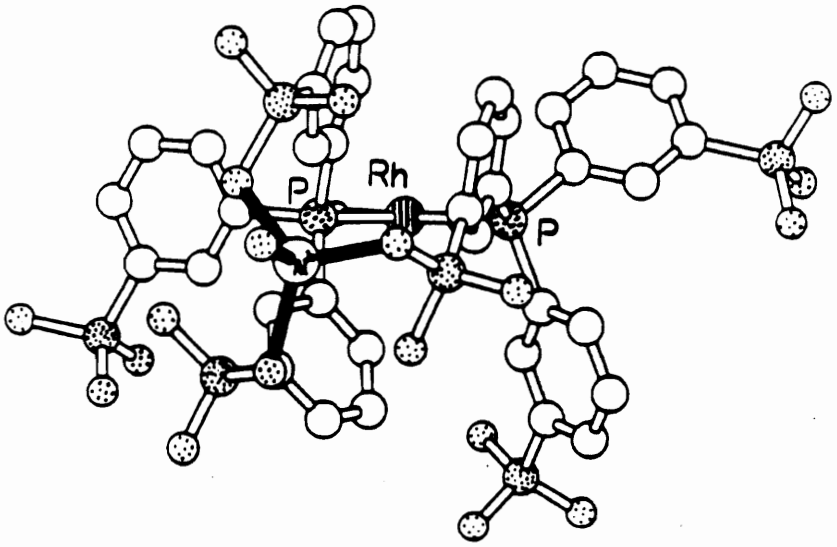
[b.] Solution Ionic Strength

Figure 2.14 The Effect of $Al_2(SO_4)_3$ on the Reaction Selectivity of 1-hexene Hydroformylation [a]

If the role of increased salt concentration is to stabilize intermediates that bear a large negative charge then $Al_2(SO)_4$ should behave similarly to M_2SO_4 at equivalent ionic strength. However reaction selectivity does not increase with added aluminum sulfate; in fact selectivity decreases slightly. We postulate that by stabilizing the negative charge on coordinated TPPTS aluminum cation alters either the effective dimension of the TPPTS ligand or the coordination geometry about rhodium. Two possibilities are illustrated in Figure 2.15. In Figure 2.15(a), a *cis* arrangement of phosphine at $HRh(CO)(TPPTS)_2$ is shown. It is possible that three sulfonate groups from two phosphines chelate the aluminum ion. This creates the situation where two TPPTS ligands form an effective chelate to rhodium. Rhodium catalysts with small chelates usually give poor selectivity in hydroformylation reactions [72]. Alternatively three sulfonate groups from a single phosphine can coordinate aluminum, as shown in Figure 2.15(b). Such an arrangement alters the configuration of the phosphine; it appears to be more compact when bound to aluminum. The role of a large cation then may be to increase the effective steric size of TPPTS. It was seen earlier that the addition of Cs_2SO_4 gives a relatively high n/b ratio.

Figure 2.15 (a) Possible Modes of Sulfonate Group Coordination to Aluminum Cation

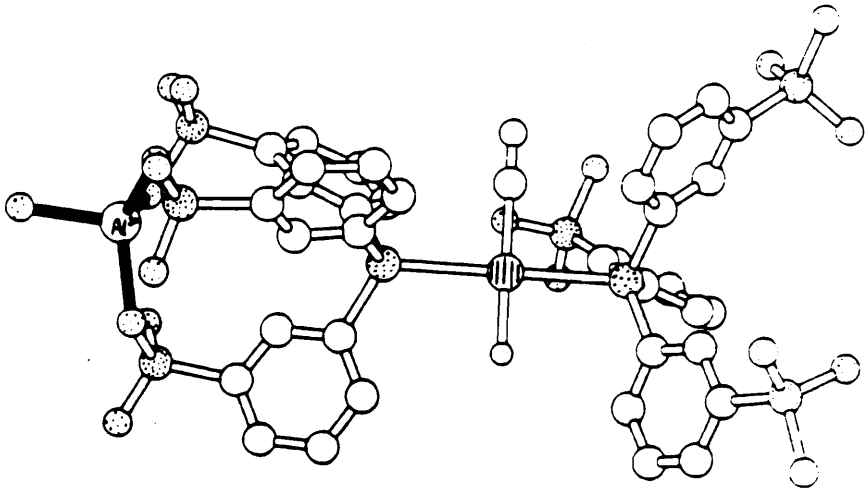
(a)



$HRhCO(TPPTS)_2$

Figure 2.15 (b) Possible Modes of Sulfonate Group Coordination to Aluminum Cation

(b)



$HRhCO(TPPTS)_2$

2.7 Summary of Salt Effects

Addition of a salt has a strong influence on the reaction activity and selectivity of aqueous hydroformylation. Hydroformylation activity usually decreases with the addition of salt since the presence of a salt increases solution ionic strength which further decreases the low solubility of water immiscible olefins. Surface active phosphines, on the other hand, aggregate in salt solution. Therefore higher activity of a Rh/surface active phosphine catalytic system is achieved as the water solubility of olefin substrates increases with the addition of an external salt.

Ionic strength of a solution affects the reaction selectivity by stabilizing certain catalytic intermediates which are responsible for the control of normal to branched aldehyde ratio. High salt concentration is normally in favor of the formation of $HRh(CO)L_2$ to $HRh(CO)_2L$, thus high selectivity is observed.

The size and the charge of cations in the solution also play a role in determining the selectivity. A relatively soft cation is desirable for high selectivity while a small and highly charged cation, such as Al^{3+}, results in poor n/b aldehyde ratio perhaps because of its capability of interacting with several sulfonate groups.

2.8 Experimental

2.8.1 Ligand Synthesis

All reactions and manipulations were carried out by standard Schlenk techniques under an atmosphere of purified nitrogen or Ar. All solvents were dried by standard method and distilled under nitrogen prior to use. Chemicals used in syntheses, such as *p*-chlorophenyl bromide, *n*-butyllithium, 1, 6-dibromohexane, 3-phenylpropyl bromide, 6-phenylhexyl bromide, trichlorophosphine, were purchased from Aldrich.

NMR measurements were done on a Bruker WP 200 at 200.133 Mhz for ^{1}H, 50.323 MHz for ^{13}C, and 81.015 MHz for ^{31}P. Key to NMR data: s, singlet; d, doublet; t, triplet; quart, quartet; quin, quintet; m, multiplet; br, broad; asterisk, pseudo.

2.8.1.a Synthesis of *p*-(3-phenylpropyl)phenylchloride

1-bromo, 4-chlorobenzene, 19.2 g (0.1 mol) and 200 ml of diethyl ether were placed into a 500 ml three-neck flask equipped with a reflux condenser, an equal-pressure dropping funnel and an Ar gas inlet. The flask was then placed in an ice-water bath. After the addition of 55.5 ml of 1.8 M BuLi (0.1 mol) in cyclohexane/diethylether the ice-water bath was removed and the reaction mixture was stirred at room temperature for an additional hour. A solution of 19.8 g (0.1 mol) 3-phenylpropylbromide in 50 ml diethylether was added dropwise and the reaction was then heated at reflux for 4 days. The LiBr precipitate was removed by filtration and solvent was removed by distillation.

The resulting viscous oil was vacuum distilled, and the fraction collected at 150-155°C and 5-6 Torr was *p*-(3-phenylpropyl)phenylchloride. Yield: 15 g, 65%.

Analytical data for *p*-(3-phenylpropyl)phenylchloride

Colorless oil, bp. 150-155°C (5 mmHg), ^{1}H NMR (in $CDCl_3$): 1.98 {m, 2H, (8)CH_2}; 2.67 {m, 4H, (7)CH_2 + (9)CH_2}; 7.12-7.46 {m, 9H, aromatic protons} (Appendix A-1). ^{13}C NMR (in $CDCl_3$): 32.85 {s, 1C, (8)C}; 34.79 {s, 1C, (9)C}; 35.33 {s, 1C, (7)C}; 125.87 {s, 1C, (13)C}; 128.64 {br.s, 6C, (5)C + (3)C + (15)C + (11)C + (14)C + (12)C}; 129.81 {s, 2C, (2)C + (6)C}; 131.51 {s, 1C, (10)C}; 140.73 {s, 1C, (4)C}; 142.08 {s, 1C, (1)C}.

2.8.1.b Synthesis of *p*-(6-phenylhexyl)phenylchloride

The synthesis of *p*-(6-phenylhexyl)phenylchloride is identical to the above procedure with the 6-phenylhexylbromide. 6-phenylhexylbromide is prepared by the method originally used by Hanson et al [28]. The yield of the reaction was 35% after distillation.

Analytical data for *p*-(6-phenylhexyl)phenylchloride

Colorless oil, bp. 178-183°C (5 mmHg), ^{1}H NMR (in $CDCl_3$): 1.38 {m, 4H, (9)CH_2 + (10)CH_2}; 1.59 {m, 4H, (8)CH_2 + (11)CH_2}; 2.60 {m, 4H, (7)CH_2 + (12)CH_2}; 7.09-7.43 {m, 9H, aromatic protons} (Appendix A-2). ^{13}C NMR (in $CDCl_3$): 28.88 {br.s, 2C, (9)C +(10)C}; 31.11 {br.s, 2C, (8)C +(11)C}; 35.09 {s, 1C, (12)C}; 35.77 {s, 1C, (7)C};

125.46 {s, 1C, (16)C}; 128.08 {br.s, 6C, (5)C + (3)C + (14)C + (18)C + (15)C + (17)C}; 129.58 {s, 2C, (2)C + (6)C}; 131.42 {s, 1C, (13)C}; 140.35 {s, 1C, (4)C}; 141.87 {s, 1C, (1)C}.

2.8.1.c The Synthesis of Tris-*p*-(3-phenylpropyl)phenylphosphine

Lithium metal, 1.4 g (0.2 mol) was chopped directly into 100 ml THF in a three 500 ml three-neck flask equipped with an equal-pressure dropping funnel under an Ar atmosphere. *p*-(3-phenylpropyl)phenylchloride (23.0 g, 0.1 mol) in 100 ml diethyl ether was added dropwise at 5°C. The color of the reaction mixture slowly changed to deep red and a grey precipitate of LiCl formed. The mixture was stirred at room temperature for 3 hours until nearly all the lithium disappeared. The solution was filtered to remove LiCl and unreacted lithium. The flask with the resulting deep red solution was chilled to 5°C by ice-water bath and 4.6 g (0.033mol) PCl_3 in 50 ml diethylether was added over a period of 1 hour. The ice-water bath was removed and the reaction mixture was stirred further for 10 hours. Dry ice (10 g) was added slowly to the mixture and the solution was filtered under Ar. The filtrate was pumped into dryness and redissolved in 100 ml diethyl ether. The solution was washed with 3× 50 ml degassed water and dried over $MgSO_4$. The diethyl ether was removed under reduced pressure to give 17.5 g (85%) tris-*p*-(3-phenylpropyl)phenylphosphine.

Analytical data for Tris-*p*-(3-phenylpropyl)phenylphosphine

Pale yellow viscous oil, ^{1}H NMR (in $CDCl_3$): 1.97 {*quint., $^{3}J_{H-H}$ = 7.5 Hz, 6H, (8)CH_2 }; 2.66 {*t., $^{3}J_{H-H}$ = 7.5 Hz, 12H, (7)CH_2 + (9)CH_2}; 7.0-7.4 {m, 27H, aromatic protons} (Appendix A-3). ^{13}C NMR (in $CDCl_3$): 32.74 {s, 3C, (8)C}; 35.26 {s, 3C, (9)C}; 35.47 {s, 3C, (7)C}; 125.82 {s, 3C, (13)C}; 128.38 { s, 6C, (12)C + (14)C}; 128.46 {s, 6C, (11)C + (15)C}; 128.67 {d, $^{3}J_{C-P}$ = 6.1 Hz, 6C, (3)C + (5)C}; 133.78 {d, $^{2}J_{C-P}$ = 20.8 Hz, 6C, (2)C + (6)C}; 134.76 {d, $^{1}J_{C-P}$ = 9.2 Hz, 3C, (1)C}; 142.14 {s, 3C, (4)C}; 142.86 {s, 3C, (10)C}. ^{31}P NMR (in $CDCl_3$): -7.20 (s)

2.8.1.d The Synthesis of Tris-*p*-(6-phenylhexyl)phenylphosphine

The synthsis of Tris-*p*-(6-phenylhexylyl)phenylphosphine was carried out by the identical method described above from *p*-(6-phenylhexyl)phenylchloride. The yield of the reaction was 80%.

Analytical data for Tris-*p*-(6-phenylhexyl)phenylphosphine:

Pale yellow viscous oil, ^{1}H NMR (in $CDCl_3$): 1.41 {m, 12H, (9)CH_2 + (10)CH_2}; 1.65 {m, 12H, (8)CH_2 + (11)CH_2}; 2.66 {*t., $^{3}J_{H-H}$ = 7.5 Hz, 12H, (7)CH_2 + (12)CH_2}; 7.14-7.31 {m, 27H, aromatic protons} (Appendix A-4). ^{13}C NMR (in $CDCl_3$): 29.12 {s, 6C, (9)C + (10)C}; 31.16 {s, 3C, (11)C}; 31.35 {s, 3C, (8)C}; 35.70 {s, 3C, (12)C}; 35.94 {s, 3C, (7)C}; 125.58 {s, 3C, (16)C}; 128.25 { s, 6C, (15)C + (17)C}; 128.36 {s, 6C, (14)C + (18)C}; 128.55 {d, $^{3}J_{C-P}$ = 5.9 Hz, 6C, (3)C + (5)C}; 133.64 {d, $^{2}J_{C-P}$ = 18.4 Hz, 6C,

(2)C + (6)C}; 134.61 {d, $^{1}J_{C\text{-}P}$ = 9.0 Hz, 3C, (1)C}; 142.79 {s, 3C, (4)C}; 143.34 {s, 3C, (13)C}. ^{31}P NMR (in $CDCl_3$): -6.85 (s)

2.8.1.e The synthesis of Trisulfonated Tris-*p*-(3-phenylpropyl)phenylphosphine [PC(3)]

Tris-*p*-(3-phenylpropyl)phenylphosphine 5 g (0.0081 mol) was placed into a 1000 ml flask under Ar at -78°C with a dry ice and acetone bath and 20 ml 96% H_2SO_4 was added. The mixture was then brought to room temperature with stir. The brown reaction mixture was neutralized by slow addition of 20% NaOH after 6 hours. The final pH was 9 and the final volume was about 120 ml. 720 ml methanol was added and the mixture was heated to reflux for 30 minutes. The mixture was then filtered and the precipitate was extracted with 200 ml hot methanol. Two filtrates were combined and the volume was reduced to about 45 ml. Acetone, 270 ml, was then added to precipitate trisulfonated tris-*p*-(3-phenylpropyl)phenylphosphine as a white solid. The precipitate was collected and dried. Yield: 6.9 g, 92%.

Analytical data for Trisulfonated Tris-*p*-(3-phenylpropyl)phenylphosphine:

White solid, solubility in water 200 mg/ml, ^{1}H NMR (in D_2O): 1.32 {br. s, 6H, (8)CH_2 }; 2.11 {br. s, 12H, (7)CH_2 + (9)CH_2}; 6.65 {br. s, 6H, aromatic H}; 6.73 {br. s, 6H, aromatic H}; 7.02 {br. s, 6H, aromatic H}; 7.50 {br. s, 6H, aromatic H} (Appendix A-5). ^{13}C NMR (in D_2O): 31.68 {s, 3C, (8)C}; 34.42 {s, 3C, (9)C}; 34.55 {s, 3C, (7)C}; 125.38 {s, 6C, (11)C + (15)C}; 128.43 { s, 6C, (12)C + (14)C}; 128.91 {d, $^{3}J_{C\text{-}P}$ = 4.5 Hz, 6C, (3)C + (5)C}; 133.60 {d, $^{2}J_{C\text{-}P}$ = 19.0 Hz, 6C, (2)C + (6)C}; 140.12 {s, 3C,

(10)C}; 142.97 {br. s, 3C, (4)C}; 145.49 {s, 3C, (13)C}; (1)C is not obverved. ^{31}P NMR (in D_2O): -8.41 (s)

Anal. Calcd for $C_{45}H_{42}Na_3O_9PS_3 \cdot 3H_2O$: C, 55.33; H, 4.92. Found: C, 55.19; H, 4.88.

2.8.1.f The Synthesis of Trisulfonated Tris-*p*-(6-phenylhexyl)phenylphosphine [PC(6)]

The method used for the preparation of Trisulfonated Tris-*p*-(6-phenylhexyl)phenylphosphine was identical with the method described for Trisulfonated Tris-*p*-(3-phenylpropyl)phenylphosphine. The yield of the sulfonation was 90%.

Analytical data for Trisulfonated Tris-*p*-(6-phenylhexyl)phenylphosphine:

White solid, ^{1}H NMR (in D_2O): 1.00 {br. s, 12H, (9)CH_2 + (10)CH_2}; 1.19 {br. s, 6H, (8)CH_2}; 1.27 {br. s, 6H, (11)CH2}; 2.20 {br. s, 6H, (7)CH_2}; 2.26 {br. s, 6H, (12)CH_2}; 6.81 {br. s, 6H, aromatic H}; 6.86 {br. s, 6H, aromatic H}; 7.10 {br. s, 6H, aromatic H}; 7.60 {br. s, 6H, aromatic H} (Appendix A-6). ^{13}C NMR (in D_2O): 28.89 {s, 3C, (9)C}; 29.19 {s, 3C, (10)C}; 30.70 {s, 3C, (8)C}; 30.92 {s, 3C, (11)C}; 35.27 {s, 6C, (12)C + (7)C}; 125.51 {s, 6C, (14)C + (18)C}; 128.24 { s, 6C, (15)C + (17)C}; 128.50 {br. s, 6C, (3)C + (5)C}; 133.16 {d, $^1J_{C\text{-}P}$ = 8.0 Hz, 3C, (1)C}; 133.58 {d, $^2J_{C\text{-}P}$ = 19.4 Hz, 6C, (2)C + (6)C}; }; 140.40 {s, 3C, (13)C}; 143.04 {s, 3C, (4)C}.145.61 {s, 3C, (16)C}. ^{31}P NMR (in D_2O): -7.96 (s). Anal. Calcd for $C_{54}H_{60}Na_3O_9PS_3 \cdot 3H_2O$: C, 58.80; H, 5.99. Found: C, 58.49; H, 5.97.

2.8.2 Dynamic Light Scattering Experiments

Molecules in solution are constantly moving. The speed of the moving molecule is a function of its radius. The dp-801 molecular size detector utilizes the principle of dynamic light scattering on molecules undergoing "Brownian Motion". The sample is illuminated by a solid state laser of 30 mV power and 780 nm wavelength. The photons scattered by the moving molecules in the flow cell are collected and transmitted via a fibre optic cable to an actively quenched solid state avalanche photodiod (APD). The APD counts photons and the time scale of the scattered light intensity fluctuation is automatically analyzed. The translational diffusion coefficient (D_T) of the molecules is then calculated. The hydrodynamic radius (R_H) of the molecules is derived from D_T.

The dynamic light-scattering experiments were done on a Biotage dp-801 molecular size detector [99]. The sample solutions were prepared in degassed, distilled, deionized water and filtered twice through a 0.1 μm syringe filter. Data were collected at ambient temperature (22°C) and atmospheric pressure.

2.8.3 Variable Temperature NMR Study

Variable temperature ^{31}P NMR spectra were recorded at 161.903 MHz on a Varian RU 400 spectrometer. All spectra were recorded with high power proton decoupling. The number of scans varied from 32 to 128; more scans were required for satisfactory signal to noise ratio at high temperature. The sample temperature was

controlled and measured by a Varian temperature controller. The temperature used in the analysis are those measured directly and are not corrected. At each temperature the sample was allowed to come to thermal equilibrium before data acquisition was initiated. This was judged to require 10 min after the temperature of the probe had been stabilized. The natural linewidth of $HRh(CO)(TPPTS)_3$ was estimated from the room temperature spectrum of the complex in the absence of excess TPPTS.

2.8.4 Two Phase Hydroformylation and Product Analysis

All reactions and manipulations were carried out by standard Schlenk techniques under an atmosphere of purified nitrogen or CO. Water was deoxygenated by distillation under nitrogen prior to use. Hexene-1, Octene-1 nonane and $Rh(acac)(CO)_2$ were purchased from Aldrich. The CO/H_2 (1/1) was received from Airco and used without further purification. TPPTS was prepared by direct sulfonation of triphenylphosphine as described previously [35].

The reaction products and starting material were analyzed by gas chromatography on a Varian 3300 chromatograph equipped with a HP1 column 25mx0.32mmx0.52μm, and FID detector; He was the carrier gas; the temperature program was from 50°C (2 min) to 220°C (1 min), at a heating rate of 10°C/min. The retention times were 8.2 min for linear nonanal, 6.8-7.5 min for the branched isomers of nonanal, 5.1 min for nonane, 7.0 min for 2-methylhexanal and 8.2 min for 1-heptanal.

All catalytic solutions within the same series were taken from the same stock solution for consistency. Catalytic runs were not repeated and the accuracy of this method, based on test runs with Rh/TPPTS system, was estimated within ±2%.

The octene-1 hydroformylation system consisted of an aqueous methanol layer and an organic layer. The catalyst was made in situ by mixing 0.76 ml 0.01 M $Rh(acac)(CO)_2$ in methanol and the required amount of 0.1 M aqueous solution of ligand in a 30 ml stainless steel reaction vessel. Water was added to adjust the total aqueous methanol volume to 1.5 ml. The substrate, 0.60 ml of 1-octene, was then transfered into the reaction vessel under positive pressure of CO. 0.34 ml of nonane was added as internal standard for gas chromatography analysis. 0.06 ml of toluene was used to adjust the total volume of organic phase as 1.0 ml. The Octene/Rh ratio was 500/1 in all catalytic runs. After the reaction vessel was loaded and pressurized with CO/H_2 to 19.5 atm, the reaction was initiated by placing the reaction vessel into a temperature bath preheated to 120°C. The reaction mixture was constantly stirred with a magnetic stir bar at 260 rpm. Catalytic reactions were terminated by removing the vessel from the oil bath and depressurizing when it had been cooled in an ice-water bath.

The product nonanals have no appreciable solubility in aqueous methanol as evidenced by the negative results from GC and NMR analysis of the aqueous layer. In all cases the organic layer was colorless and readily separated from aqueous layer after the

reaction. In a recycling test the organic layer recovered from a catalytic run showed no reactivity for the hydroformylation of 1-heptene.

In the case that the two phase hydroformylation was done without methanol as a cosolvent, the catalyst was made by dissolving $Rh(acac)CO_2$ into a aqueous solution of water soluble ligand under a positive pressure of H_2. All the catalytic conditions were the same as previously described for the system with methanol as a cosolvent.

Solution ionic strength is calculated according to Equation 3. Instead of activity of electrolytes, molar concentration is used in all cases.

$$\mu = 1/2\ \Sigma[a]Z_a^2 \qquad \text{Equation 3}$$

([a], molar concentration of ions; Z_a, the charge of ions)

The 1-hexene hydroformylation system consisted of an aqueous layer and an organic layer. The aqueous layer was a 1.5 ml solution 5 mM in $Rh(acac)(CO)_2$ and 15mM in TPPTS. The organic layer was 0.47 ml 1-hexene. The rhodium to 1-hexene ratio was 1:500 and the salts, Li_2SO_4 , Na_2SO_4, Cs_2SO_4 or $Al_2(SO_4)_3$ were added to adjust the salt concentration to either 0.1M or 0.5M. The catalysis was done in a 30 ml stainless steel reactor equipped with a pressure gauge. The reactor was charged with CO/H_2 (1:1) to 13.6 atm (200 psi) after all the reactants were added and then placed in a silicon oil

bath that had been preheated to 120°C. The stirring rate was 260 rpm. After 24 hours the reaction was terminated by cooling the reactor in a ice-water bath and then depressurized.

Side reactions, such as isomerization of olefin and hydrogenation of both olefin and aldehydes, were not observed. Neither hexane, hexene isomers, nor heptanol were detected by GC in any of the catalytic reactions. It is estimated that these products, if present, represent less than two percent of the total hexene charge.

Chapter 3

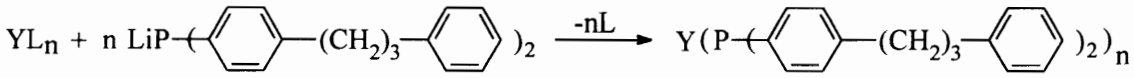
Preparation of a Surface Active Chiral Phosphine and Its Use in the Hydrogenation of Prochiral Olefins

3.1 The General Synthetic Method For the Preparation of Surface Active Chelating Phosphines

It has been demonstrated by the synthesis of trisulfonated tri[*p*-(ω-phenylalkyl)phenyl]phosphines (chapter 2) that the sulfonation of these phosphines can take place under remarkably mild sulfonation conditions to give *para,para,para* trisulfonated phosphines in very high yield. Complete sulfonation can be achieved within several hours without the presence of oleum. No phosphine oxide is generated by this mild sulfonation method. Sulfonation without oxidation is perhaps the most desirable feature which should find applications in the sulfonation of chiral phosphines.

It is possible synthetically to incorporate the di[*p*-(ω-phenylalkyl)phenyl]phosphino functional groups, for example di[*p*-(3-phenylpropyl)phenyl]phosphino group, to chelating phosphines for the purpose of easy sulfonation. Surface activity can also be achieved at the same time since dynamic light scattering experiments indicated aggregation of tri[*p*-(ω-phenylalkyl)phenyl]phosphines.

The proposed preparation method is shown in Figure 3.1.



L: leaving group Y: hydrocarbon backbone

Figure 3.1 General Synthetic Route for Chelating Phosphines

By this synthetic route, a class of novel chelating phosphines with several di[*p*-(3-phenylpropyl)phenyl]phosphino groups can be made. The catalytic properties of these ligands should be similar to their diphenylphosphino analogs since they are expected to have similar electronic and steric parameters. In order to demonstrate this method a bis-di[*p*-(3-phenylpropyl)phenyl]phosphino analog of (*S*, *S*)2, 4-bis-diphenylphosphinopentane was synthesized.

3.2 Experimental

All reactions and manipulations were carried out by standard Schlenk techniques under an atmosphere of purified nitrogen or Ar. All solvents were dried by standard method and distilled under nitrogen prior to use.

NMR measurements were done on a Bruker WP 200 at 200.133 MHz for ^{1}H, 50.323 MHz for ^{13}C, and 81.015 MHz for ^{31}P. Key to NMR data: s, singlet; d, doublet;

t, triplet; quart, quartet; quin, quintet; m, multiplet; br, broad; asterisk, pseudo. Carbon atoms in the phosphines are numbered as illustrated:

3.2.1 The Cleavage of Triarylphosphines

The first step of this synthesis is the cleavage of tri[*p*-(3-phenylpropyl)phenyl]phosphine. Triarylphosphines are readily cleaved by alkali metals under a variety of reaction conditions [100]. Mixed triarylphosphines, $PAr_{3-X}Ar'_X$ are reported to cleave at the most electron withdrawing aryl group [101]. However, analysis of cleavage products by ^{31}P NMR shows that in the case of Ar = Ph and Ar' = -*p*-$C_6H_4NMe_2$ cleavage does not go exclusively to the phenyl ring [102]. A similar test reaction between Li and $P[C_6H_5][C_6H_4(CH_2)_3C_6H_5]_2$ in THF gave a mixture of $LiP[C_6H_4(CH_2)_3C_6H_5]_2$ and $LiP[C_6H_5][C_6H_4(CH_2)_3C_6H_5]$. For this reason the triarylphosphine, $P[C_6H_4(CH_2)_3C_6H_5]_3$, rather than the mixed phosphine, $P[C_6H_5][C_6H_4(CH_2)_3C_6H_5]_2$, is used as the precursor to chiral chelating phosphines bearing $-P[C_6H_4(CH_2)_3C_6H_5]_2$. Cleavage of $P[C_6H_4(CH_2)_3C_6H_5]_3$ is accomplished with lithium metal in THF at room temperature (Figure 3.2). $LiC_6H_4(CH_2)_3C_6H_5$ which is also generated in the cleavage is selectively poisoned by the addition of *t*-BuCl. $LiP[C_6H_4(CH_2)_3C_6H_5]_2$ is then isolated as a red oil upon the addition of pentane at low temperature. The purpose for isolating the lithium phosphide is to remove the 1, 3-diphenylpropane. The oil is used directly in reactions with chiral ditosylates. Hydrolysis of an aliquot of $LiP[C_6H_4(CH_2)_3C_6H_5]_2$ with D_2O yields the corresponding deuterated

secondary phosphine $DP[C_6H_4(CH_2)_3C_6H_5]_2$ (^{31}P NMR [δ in THF] -43.06 ppm, $^1J_{D\text{-}P}$ = 32.7 Hz)

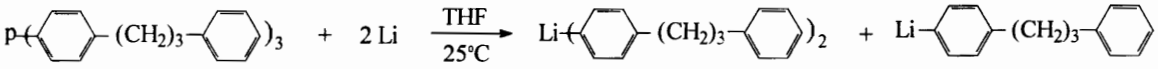


Figure 3.2 The Cleavage of $P[C_6H_4(CH_2)_3C_6H_5]_3$

3.2.2 Synthesis of (*S*, *S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPP)

The reaction of $LiP[C_6H_4(CH_2)_3C_6H_5]_2$ with (*R*, *R*)-2, 4-pentaneditosylate goes in high yield to form (*S*, *S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPP), a bisdiphenylphosphinopentane (BDPP) analog. (figure 3.3)

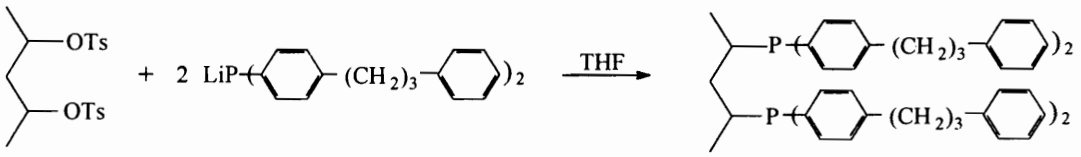


Figure 3.3 Synthesis of BDAPP

0.14 g (0.02 mol) fine chopped lithium was suspended in 10 ml dry THF and 6.2 g tris-*p*-(3-phenylpropyl)phenylphosphine (0.01mol) in 100 ml THF was added from a

dropping funnel in 10 minutes with vigorous stirring. The resulting deep red solution was stirred under room temperature for additional 2 hours. 0.93 g *t*-BuCl was then added and the reaction mixture was brought to reflux for 15 minutes. The volume of the solution was reduced to about 10 ml and 80 ml dry and degassed pentane was added. The reaction flask was placed in dry ice/acetone bath to yield a dark red viscous residue with a colorless solution. The solution was decanted and the residue was redissolved in 50 ml THF. 2.0 g (*S,S*) or (*R,R*) 2,4-pentanediol-ditosylate [103] in 10 ml THF was added. The solvent was pumped off after 10 hours to yield a pale yellow oil. The residue was redissolved in 40 ml diethyl ether and washed with 3× 10 ml water. The ether layer was dried over $MgSO_4$ and the volume was then reduced to about 10 ml. 30 ml methanol was added to yield a pale yellow oil. Yield: 3.2 g,71%.

Analytical data:

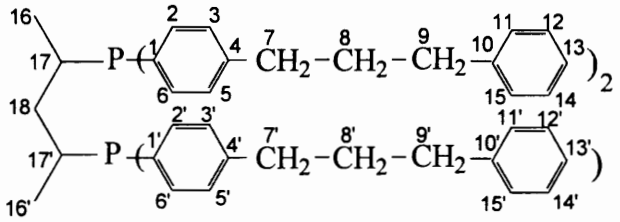
a) Lithium di[*p*-(3-phenylpropyl)phenyl]phosphide

^{31}P NMR δ (THF) -25.97 (s).

b) Deuterium di[*p*-(3-phenylpropyl)phenyl]phosphine

^{31}P NMR δ (THF) -43.06 (t, $^{1}J_{D\text{-}P}$ = 32.7 Hz).

c) (*S, S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPP)



Pale yellow oil, ^{1}H NMR δ ($CDCl_3$): 0.87 {d of d, $^{3}J_{H-H}$ = 6.7 Hz, $^{3}J_{H-P}$ = 15.4 Hz, 6H, (16) CH_3 + (16') CH_3}; 1.31 {*quin, $^{3}J_{H-H}$ + $^{3}J_{H-P}$ = 6.9 Hz, 2H, (18) CH_2}; 1.86 {m, 8H, (8) CH_2 + (8') CH_2}; 2.37 {m, 2H, (17) CH + (17') CH}; 2.53 {m, 16 H, (7) CH_2 + (7') CH_2 + (9) CH_2 + (9') CH_2}; 7.01-7.30 {m, 36 H, aromatic protons) (Appendix A-7). ^{13}C NMR δ ($CDCl_3$): 15.72 {d, $^{2}J_{C-P}$ = 12.1 Hz, 2C, (16) CH_3 + (16') CH_3}; 27.49 {*t, 2C, (17) CH + (17') CH}; 32.64 {s, 4C, (8) CH_2 + (8') CH_2}; 35.18 {s, 4C, (9) CH_2 + (9') CH_2}; 35.42 {s, 4C, (7) CH_2 + (7') CH_2}; 36.54 (br. s, 1C, (18) CH_2}; 125.72 {s, 4C, (13) CH + (13') CH}; 128.26 {s, 8C, (12) CH + (12') CH + (14) CH + (14') CH}; 128.38 {s, 8C, (11) CH + (11') CH + (15) CH + (15') CH}; 133.62 {d, $^{3}J_{C-P}$ = 21.1 Hz, 8C, (3) CH + (3') CH + (5) CH + (5') CH}; 142.51 { d, $^{2}J_{C-P}$ = 50.3 Hz, 8C, (2) CH + (2') CH + (6) CH + (6') CH}; (1)C, (4)C, (10)C are not observed. ^{31}P NMR δ ($CDCl_3$) -1.80 (s); δ (THF) -2.30 (s). MS(FB^{+}) 913 (M+1).

3.2.3 The Sulfonation of (*S,S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane

Sulfonation of (*S, S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane goes under similar conditions as the sulfonation of $P[C_6H_4(CH_2)_3C_6H_5]_3$ to produce tetrasulfonated (*S, S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPPTS) in high yield without the formation of phosphine oxide (Figure 3.4). Both ^{1}H and ^{13}C NMR are consistent with sulfonation in the *para* position of the outside phenyl rings.

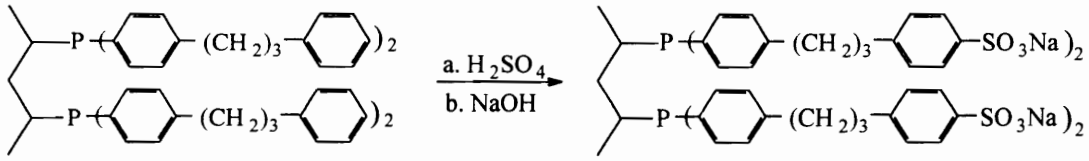
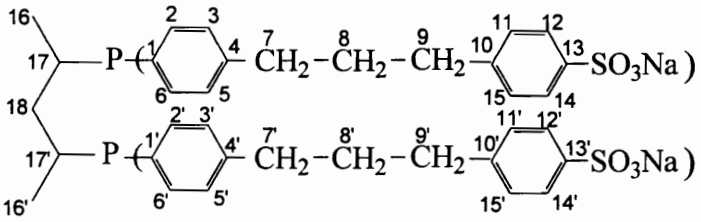


Figure 3.4 Direct Sulfonation of BDAPP

5 g (0.0055 mol) BDAPP was placed into a 1000 ml flask under Ar at -78°C with a dry ice and acetone bath and 20 ml 96% H_2SO_4 was added. The mixture was then brought to room temperature with stirring. The brown reaction mixture was neutralized by slow addition of 20% NaOH after 6 hours. The final pH was 9 and the final volume was about 120 ml. 720 ml methanol was added and the mixture was heated to reflux for 30 minutes. The mixture was then filtered and the precipitate was extracted with 200 ml hot methanol. Two filtrates were combined and the volume was reduced to about 45 ml. 270 ml acetone was then added to generate BDAPPTS as a white precipitate. The precipitate was collected and dried. Yield: 6.1 g, 84%.

Analytic data for Tetrasulfonated (*S, S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane



White solid, α_D^{25} = -38.9° {c = 10 mg/ml, CH_3OH}; ^1H NMR δ (CD_3OD): 0.82 {d of d, $^3J_{H-H}$ = 6.5 Hz, $^3J_{H-P}$ = 15.5 Hz, 6H, (16) CH_3 + (16') CH_3}; 1.17 {m, 2H, (18) CH_2}; 1.81 {m, 8H, (8) CH_2 + (8') CH_2}; 2.38 {m, 2H, (17) CH + (17') CH}; 2.52 {m, 16 H, (7) CH_2 + (7') CH_2 + (9) CH_2 + (9') CH_2}; 7.02 {m, 8H} + 7.24(m, 8H} {(12)CH + (12')CH + (14)CH + (14')CH + (11)CH + (11')CH + (15)CH + (15')CH}; 7.14 {m, 8H} + 7.64 (m, 8H} {(2)CH + (2')CH + (6)CH + (6')CH + (3)CH + (3')CH + (5)CH + (5')CH} (Appendix A-8). ^{13}C NMR δ (CD_3OD): 16.33 {d, $^2J_{C-P}$ = 17.9 Hz, 2C, (16) CH_3 + (16') CH_3}; 28.50 {*t, $^1J_{P-C}$ + $^3J_{P-C}$ = 8.4 Hz, 2C, (17) CH + (17') CH}; 33.98 {s, 4C, (8) CH_2 + (8') CH_2}; 36.10 {br. s, 8C, (9) CH_2 + (9') CH_2 + (7) CH_2 + (7') CH_2}; 36.97 {br. s, 1C, (18) CH_2}; 127.08 {s, 8C, (11) CH + (11') CH + (15) CH + (15') CH}; 129.35 {s, 8C, (12) CH + (12') CH + (14) CH + (14') CH}; 129.52 {d, $^3J_{C-P}$ = 7.7 Hz, 8C, (3) CH + (3') CH + (5) CH + (5') CH}; 134.78 { d of d, $^2J_{C-P}$ = 19.4 Hz, $^6J_{C-P}$ = 10.0 Hz, 8C, (2) CH + (2') CH + (6) CH + (6') CH}; 142.09 {s, 4C, (10) C + (10') C}; 143.89 {s, 4C, (4) C + (4') C}; 144.38 {d, $^1J_{C-P}$ = 4.2 Hz, 4C, (1) C + (1') C}; 146.10 {s, 4C, (13) C + (13') C}. ^{31}P NMR δ (CD_3OD) -1.11 (s). MS(FB^+) 1343 ($M+Na^+$). Elemental analysis: calcd. for the tetrahydrate: $C_{65}H_{74}Na_4O_{16}P_2S_4$: C, 56.05, H, 5.37; found: C, 55.63, H, 5.53.

3.3 Two Phase Asymmetric Hydrogenation of α-Acetamidocinnamic Acid Methyl Ester (AACA-Me) With BDAPPTS

Tetrasulfonated (*S*, *S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPPTS) is soluble in both methanol and water. This property offers an unique opportunity to compare the reaction activity and enantioselectivity under two different catalytic conditions. Homogeneously the catalysis was performed in methanol while ethylacetate and water were used for two phase asymmetric hydrogenation.

α-Acetamidocinnamic acid methyl ester(AACA-Me) is a common substrate for testing chiral ligands, including many chiral biphosphines which are structurally similar to BDAPPTS. Hydrogenation of AACA-Me is shown as Figure 3.5.

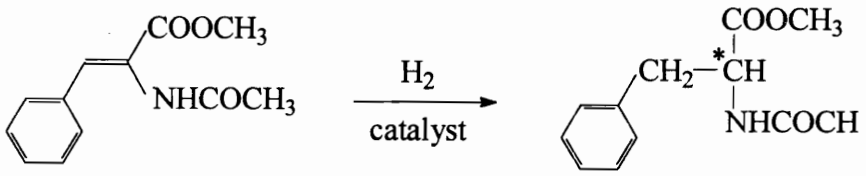


Figure 3.5 Asymmetric Hydrogenation of AACA-Me

The results from asymmetric hydrogenation in methanol are summarized in Table 3.1. For comparison the catalytic result with (S, S)-Bis-diphenylphosphinopentane (BDPP) is also listed [102]. It is well known that asymmetric hydrogenation is strongly substrate dependent and BDPP ligand is not the best for the of AACA-Me. A *para*-N, N-dimethylaminophenyl derivative of chiral BDPP gives similar enantioselectivity in the

asymmetric hydrogenation of AACA-Me [27]. With BDPP the maximum e.e. reported was 72 % with this substrate while with diphosphine derivatives of methyl-α-D-glucopyranosides (glup) and related compounds as the ligand, e.e.'s of ≥ 95% were obtained in the presence of non-chiral surfactants [104-107]. The substrate was chosen to determine if a two phase reaction environment could be modified with surface active chiral ligands to improve reaction activity and enantioselectivity. Potential improvement in enantioselectivity is best observed in a ligand and substrate system that begins with modest selectivity as was obtained with the BDPP ligand. From Table 3.1 it is clear that the new chiral diphosphine, BDAPPTS, performs just as well as its diphenylphosphino analog (BDPP).

Table 3.1 Asymmetric Hydrogenation of AACA-Me in Methanol [a]

exp	Ligand	Phase/ solvents	Pressure (atm)	Time (h)	Yield (%)	e.e. (%)
1	BDPP	one-phase methanol	1	0.20	100	72
2	BDAPPTS	one-phase methanol	1	0.75	100	75

[a] Reaction conditions: temperature: 25°C; [Rh] = [Ligand] = 0.0025 M; [AACA-Me]/[Rh] = 100. e.e. is determined by polarimetry method [108].

Comparison of two phase hydrogenation rate and enantioselectivity under various conditions between BDAPPTS and its closely related analog *m, m, m, m*-tetrasulfonated (S, S)-Bis-diphenylphosphinopentane (BDPPTS) is summerized in Table 3.2.

Although nearly identical hydrogenation results are observed with rhodium complexes of BDAPPTS and BDPP, when the reactions are done homogeneously in methanol, hydrogenation activity and enantioselectivity with BDAPPTS and BDPPTS under two phase conditions are substantially different. In EtOAc/H_2O 45% e.e. is obtained at 15 atm hydrogen pressure (exp. 6). The reaction rate with BDPPTS under two phase conditions is also relative slow; in EtOAc/H_2O only 32% conversion is observed after 20 h at 1 atm (exp. 7). In contrast, with the catalyst based on BDAPPTS an enantiomeric excess of 69% is observed in the EtOAc/H_2O two phase system (exp. 3). This value approaches that seen in methanol alone as the solvent. This is an improvement over the BDPPTS ligand in the same solvent system.

Reaction activity with BDAPPTS is greatly improved compared to that with BDPPTS; only 1.5 hours are required to reach 100% conversion with BDAPPTS in the two phase reaction (exp.3). Again this approaches the reaction time for homogeneously catalyzed hydrogenations(exp. 1 and 2)

Table 3.2 Two Phase Hydrogenation of AACA-Me with *BDAPPTS* and BDPPTS [a]

exp	Ligand	Phase/ solvents	Pressure (atm)	Time (h)	Yield (%)	e.e. (%)
3	*BDAPPTS*	two-phase EtOAc/H_2O	1	1.5	100	69
4[b]	*BDAPPTS*	two-phase EtOAc/H_2O + SDS	1	1.5	100	66
5[c]	*BDAPPTS*	two-phase EtOAc/H_2O + Na_2HPO_4	1	20	67	35
6(a)[d]	BDPPTS	two-phase EtOAc/H_2O	15	not reported	100	45
6(b)[e]	BDPPTS	two-phase EtOAc/H_2O	15	1.3	100	44
7	BDPPTS	two-phase EtOAc/H_2O	1	20	32	20
8[f]	BDPPTS	two-phase EtOAc/H_2O + SDS	1	20	36	18

[a] Reactions were carried out as following: T = 25°C, solvent EtOAc/H_2O = 1/1, the catalyst was prepared from $[Rh(COD)Cl]_2$ and water soluble ligand in water. [Rh] = [Ligand] = 0.0025 M; [AACA-Me]/[Rh] = 100. Optical purity was checked by optical rotation as described in [108].

[b] as in exp.3 plus 0.05 M SDS (sodium dodecylsulfate)

[c] as in exp.3 plus 0.05 M Na_2HPO_4

[d] previous work of Sinou [41]

[e] this work, repeat of experiment reported as exp.6(a)

[f] as in exp. 7 plus 0.05 M SDS.

Dynamic light scattering experiments on BDAPPTS show that aggregates of radius 25Å are formed in aqueous solution that is 0.01 M in BDAPPTS and 0.25 M in NaCl. Under two phase catalytic conditions the catalyst [(COD)Rh(BDAPPTS)]Cl may be viewed as a molecular micelle. This alone may increase the water solubility of AACA-Me which is critical for reaction rate. The formation of a molecular micelle is consistent with the observation of increasing catalytic activity with BDAPPTS compared to BDPPTS which is apparently not surface active. Further evidence comes from the result of BDAPPTS with the addition of Na_2HPO_4 (exp. 5). The negative effect on activity with the additon of a salt is not surprising, since there is no excess phosphine present to form micelles at high solution ionic strength. It has been observed in related systems that high ionic strength has the effect of decreasing catalytic activity in a two phase reaction with a poorly water soluble substrate in the absence of micelle. Addition of Na_2HPO_4 also decreases the enantioselectivity; the reason for this effect is not evident at this time. Although the results from Selke and co-workers suggested that the addition of surfactants can induce a modest increase in enantioselectivity as well as reaction activity in the hydrogenation of cinnamic acid derivative with the diphosphine derivatives of methyl-α-D-glucopyranosides (glup) ligands in water [104-107], there is no further improvement with the addition of SDS in BDAPPTS system (exp.4) over that with BDAPPTS alone as the catalyst (exp. 3). The reaction may not be mass tranfer

limited in the presence of [(COD)Rh(BDAPPTS)]Cl which might be surface active. Therefore addition of SDS has little effect on either reaction activity or selectivity.

3.4 The Significance of the Synthetic Method for Novel Water Soluble Chelating Phosphines

Chelating phosphines with biphenylphosphino functionalities account for the majority of chelating phosphines which are currently being investigated. By using this general synthetic method a new class of surface active phosphines can be made. The sulfonation conditions for chelates with di[*p*-(3-phenylpropyl)phenyl]phosphino groups is significantly milder than traditional sulfonation, and the reaction always goes in high yield. High yield with specific sulfonation site and degree is the virtue of this sulfonation method. The method is especially useful for introducing sulfonate groups to chiral phosphines, as demonstrated in the case of BDAPP. The sulfonated ligand, BDAPPTS, gives catalysts that show improved two phase reaction rate and enantioselectivity compared to its diphenyl analog, BDPPTS.

It is concluded that the incorporation of the easily sulfonated pendant group, di[*p*-(3-phenylpropyl)phenyl]phosphino, into other diphosphines will generally lead to chiral catalysts of improved activity under two phase reaction conditions. Reaction selectivity under these circumstances will be similar to that obtained with their non-water soluble analoges under homogeneous reaction conditions. Therefore with these novel surface active chiral phosphines, high activity and enantioselectivity which are usually offered by

homogeneous systems can be achieved along with the easy separation of catalyst from products which is the advantage of two phase catalysis.

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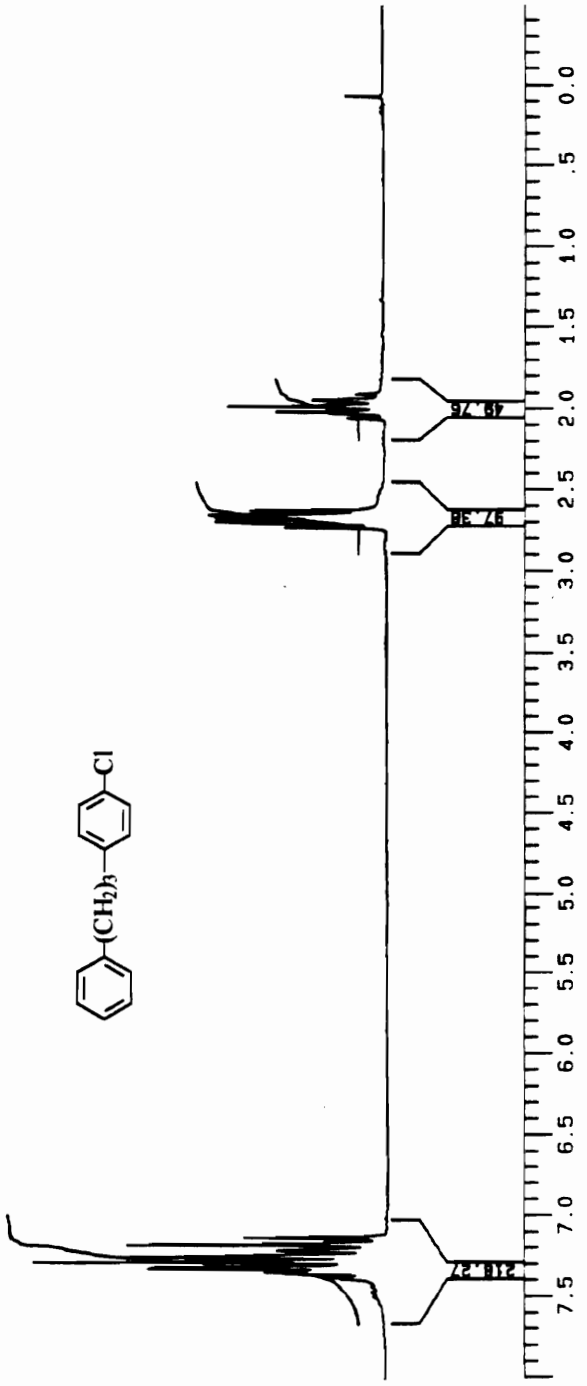
Appendix A-1

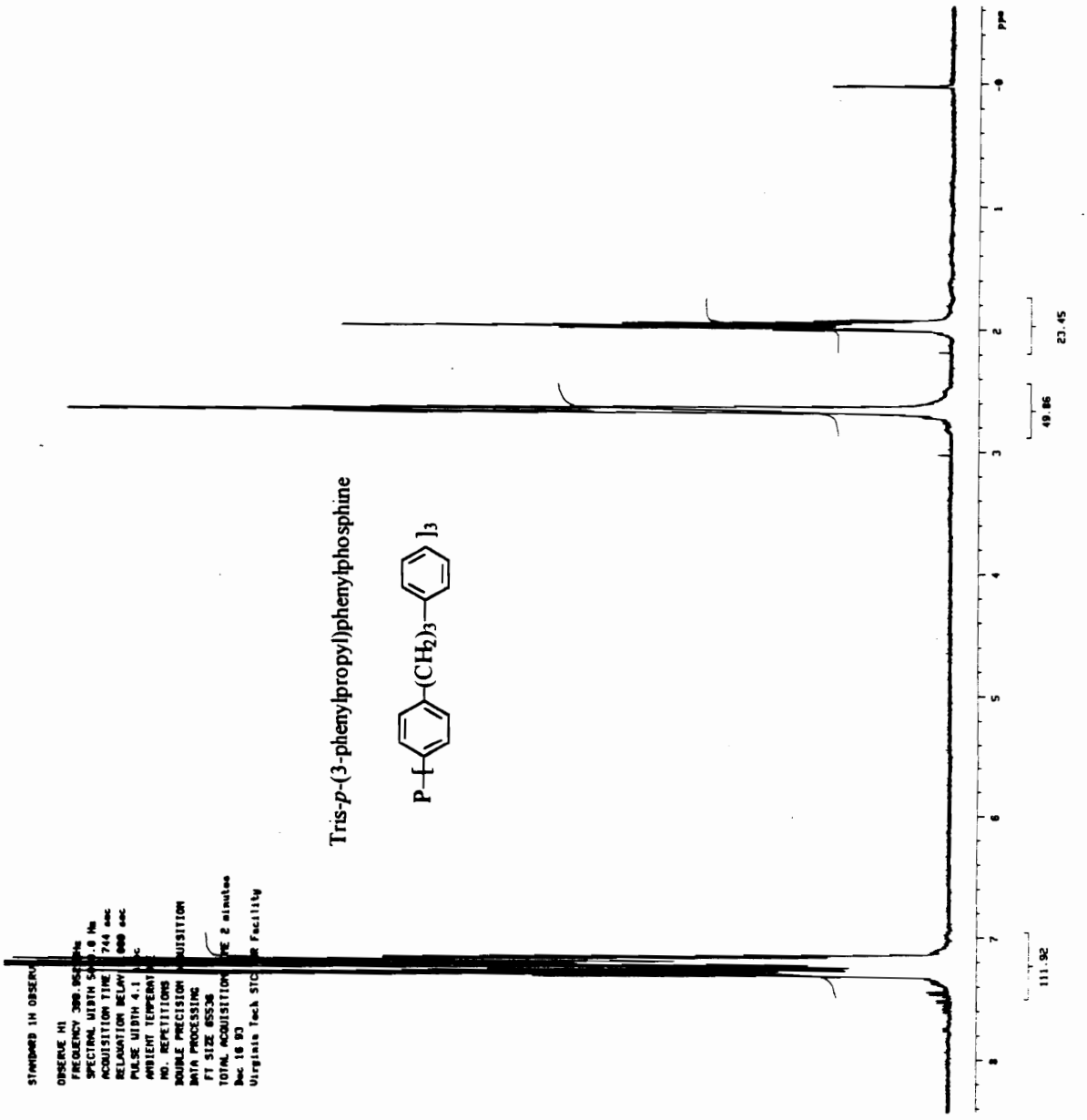
p-(3-phenylpropyl)phenylchloride



Appendix A-2

p-(6-phenylhexyl)phenylchloride

Appendix A-3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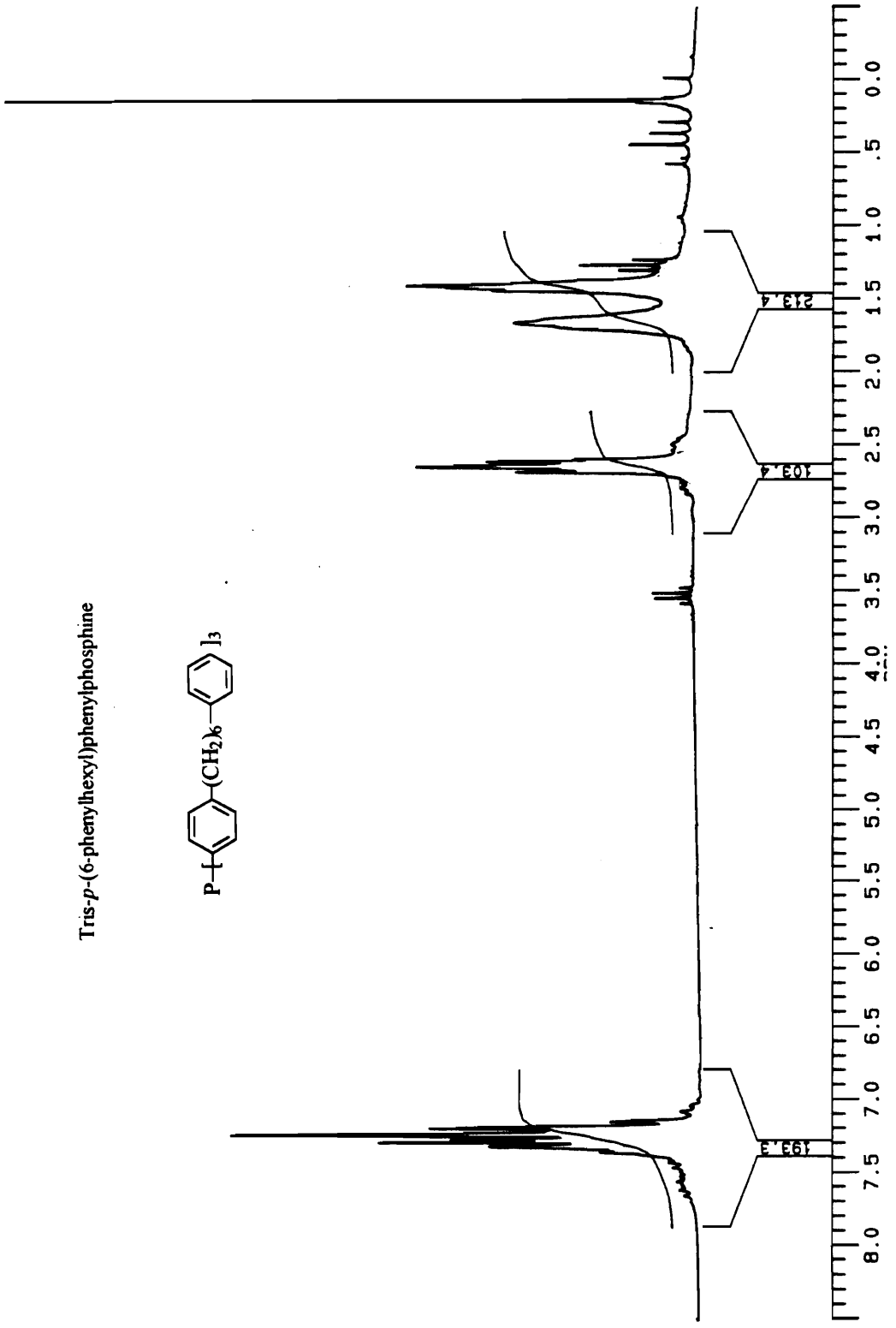
P
(CH2)3
3
111.92
49.86
23.45
ppm

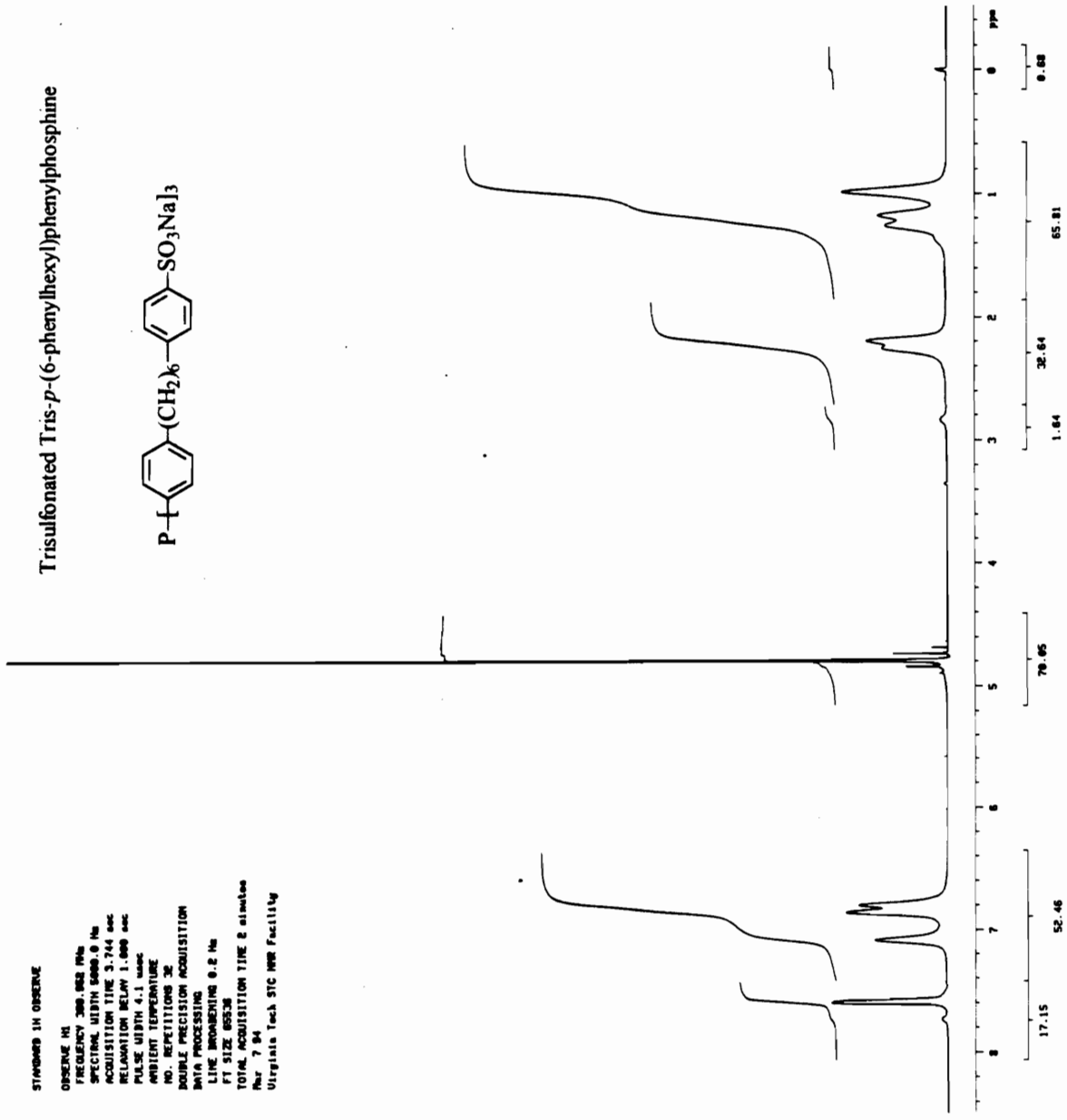
Appendix A-4


Tris-p-(6-phenylhexyl)phenylphosphine
P
(CH2)6
3
213.4
103.4
193.3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0

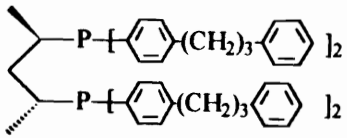
Appendix A-5

STANDARD 1H OBSERVE
OBSERVE H1
FREQUENCY 300.052 MHz
SPECTRAL WIDTH 5000.0 Hz
ACQUISITION TIME 3.744 sec
RELAXATION DELAY 1.000 sec
PULSE WIDTH 4.1 usec
AMBIENT TEMPERATURE
NO. REPETITIONS 32
DOUBLE PRECISION ACQUISITION
DATA PROCESSING
LINE BROADENING 0.3 Hz
FT SIZE 65536
TOTAL ACQUISITION TIME 2 minutes
Dec 22 93
Virginia Tech STC NMR Facility
Trisulfonated Tris-p-(3-phenylpropyl)phenylphosphine
P
(CH2)3
SO3Na]3
8
7
6
5
4
3
2
1
ppm
17.65
20.43
30.18
46.15
15.81

Appendix A-6

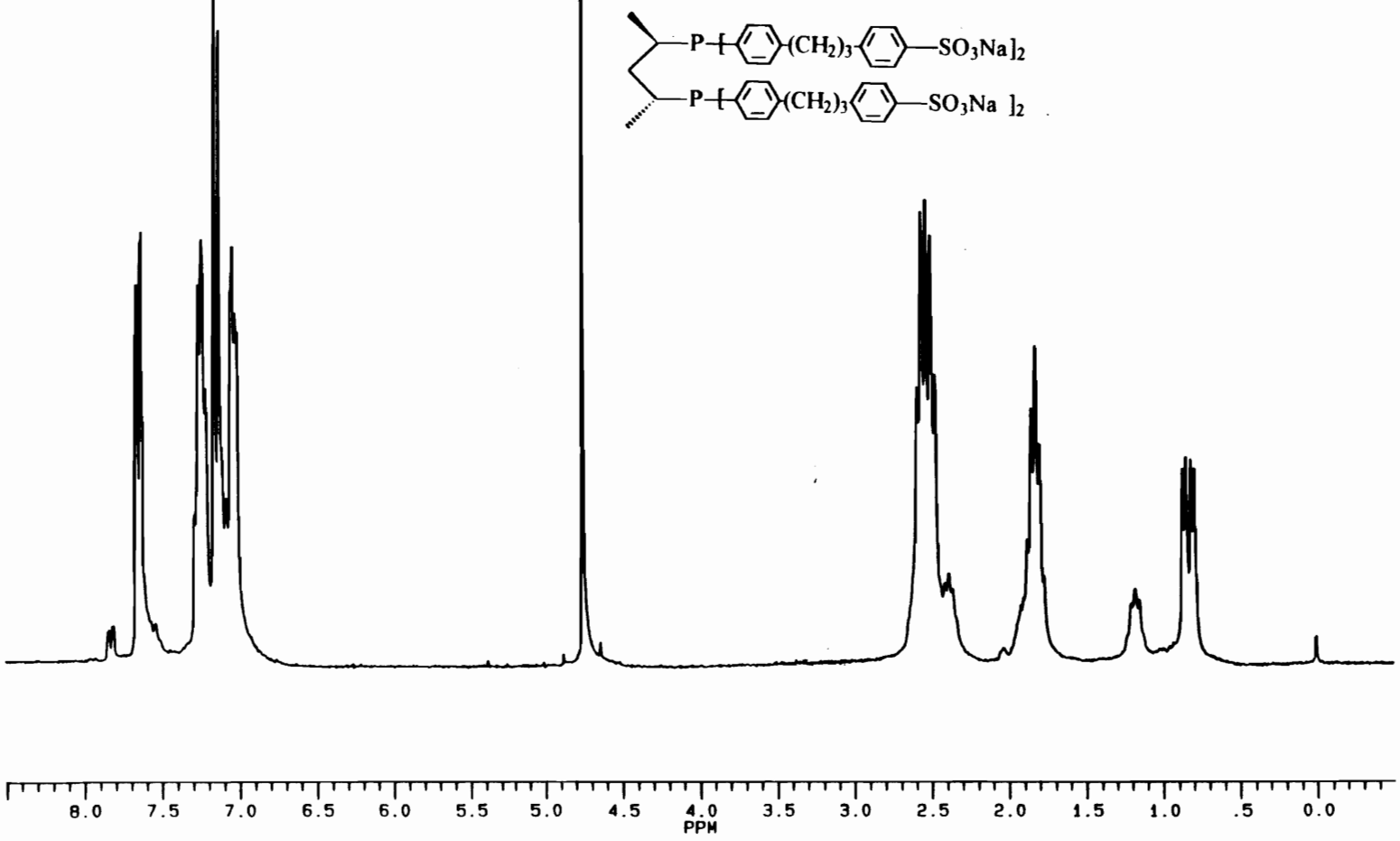

Trisulfonated Tris-p-(6-phenylhexyl)phenylphosphine
P
(CH2)6
SO3Na3
STANDARD 1H OBSERVE
OBSERVE H1
FREQUENCY 300.068 MHz
SPECTRAL WIDTH 5000.0 Hz
ACQUISITION TIME 3.744 sec
RELAXATION DELAY 1.000 sec
PULSE WIDTH 4.1 usec
AMBIENT TEMPERATURE
NO. REPETITIONS 32
DOUBLE PRECISION ACQUISITION
DATA PROCESSING
LINE BROADENING 0.2 Hz
FT SIZE 65536
TOTAL ACQUISITION TIME 2 minutes
Mar 7 04
Virginia Tech STC NMR Facility
17.15
52.46
70.05
1.84
32.64
65.81
0.88
PPM

(*S*, *S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane (BDAPP)



Appendix A-7

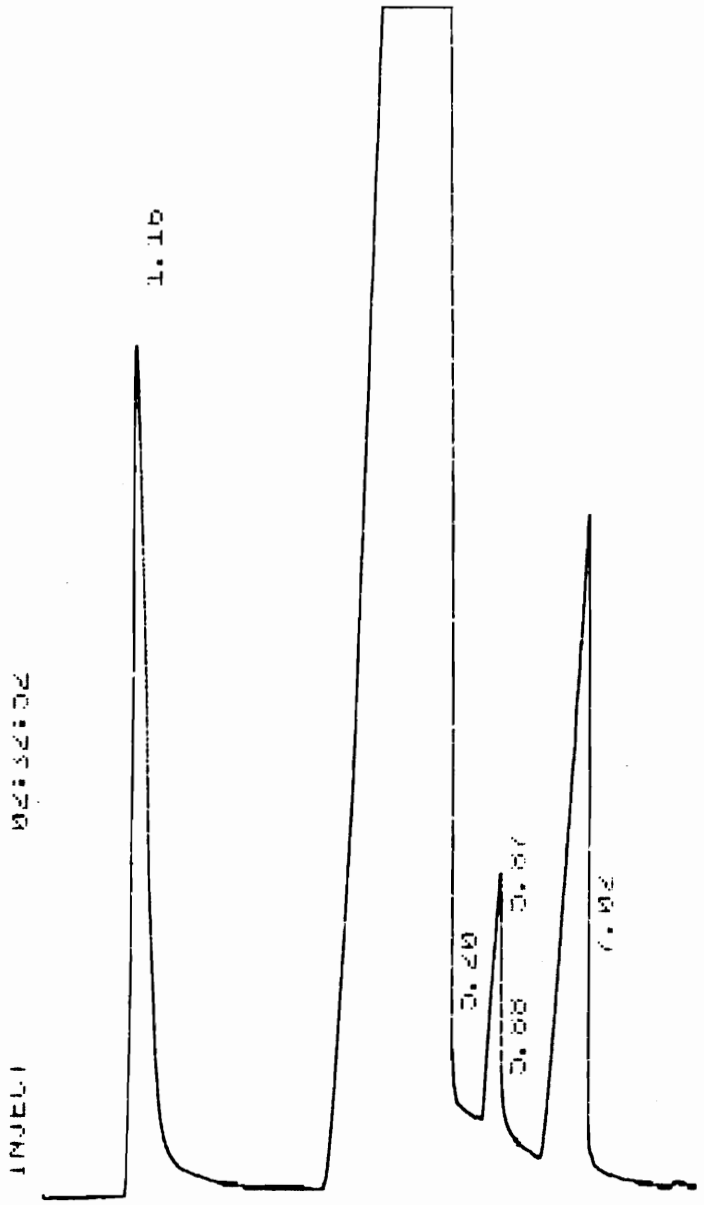
Tetrasulfonated (*S, S*)-2,4-Bis{di[*p*-(3-phenylpropyl)phenyl]phosphino}pentane
(BDAPPTS)



Appendix A-8

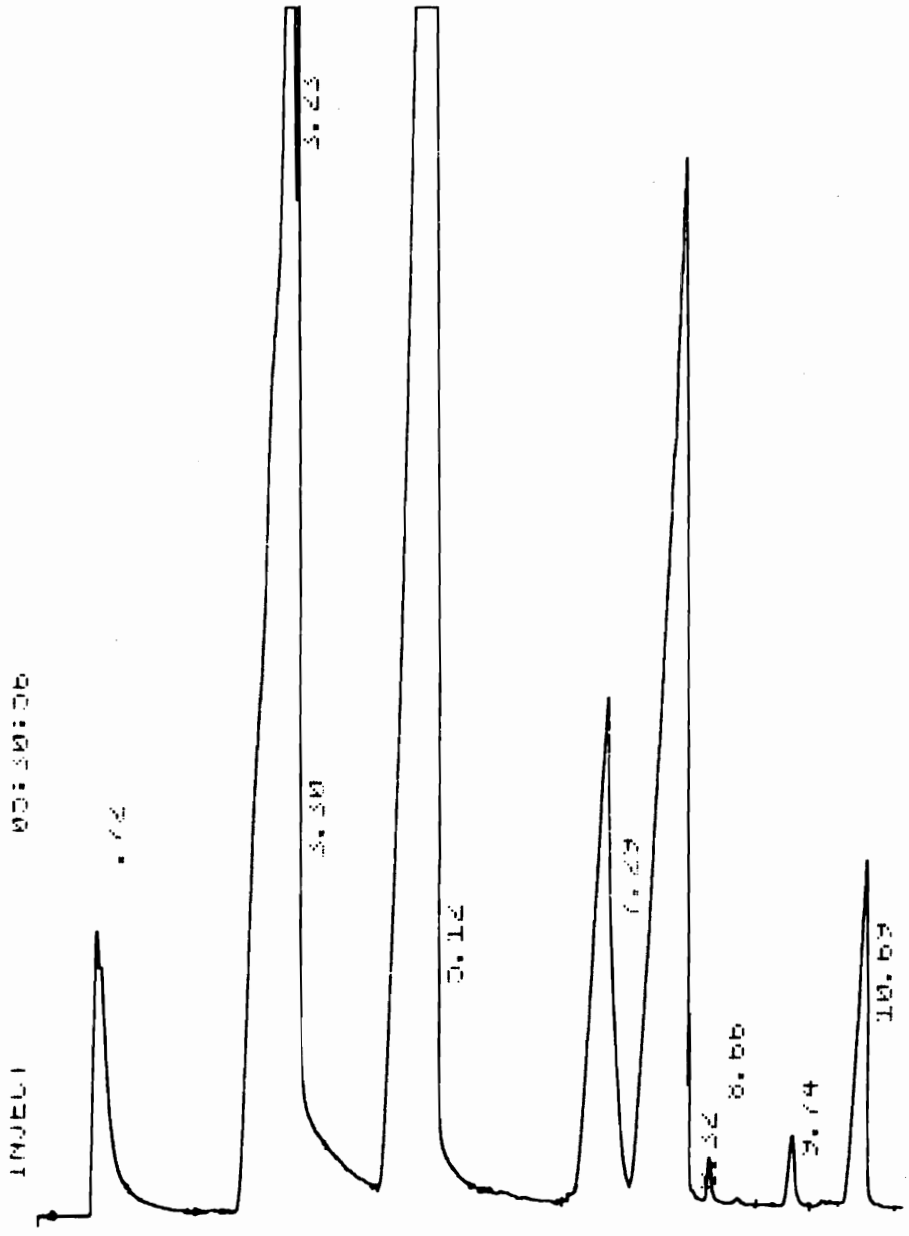
Appendix B

Typical Gas Chromatography of 1-hexene Hydroformylation Reaction Mixture



Appendix B

Typical Gas Chromatography of 1-octene Hydroformylation Reaction Mixture



Appendix C

Publication List

1. Hao Ding, Brian E. Hanson, Tamas Bartik, and Berit Bartik; "The Two-Phase Hydroformylation of Octene-1 with Rhodium Complexes of $P(C_6H_4\text{-}p\text{-}(CH_2)_x\text{-}C_6H_4\text{-}p\text{-}SO_3Na)_3$ x = 3, 6. Rate and Selectivity Enhancement with surface Active Phosphines"; **Organometallics, 13,** 3761 (1994).

2. Hao Ding, Brian E. Hanson and Thomas E. Glass; "The Effect of Salt on Selectivity in Water Soluble Hydroformylation Catalysts"; **Inorg. Chim. Acta**. (on the occasion of Professor F. A. Cotton's 65th birthday), **229**, 329 (1995).

3. Tamas Bartik, Hao Ding, Berit Bartik, and Brian E. Hanson; "Surface Active Phosphines for Catalysis in the Aqueous Phase. $P(Menthyl)((CH_2)_8C_6H_4\text{-}p\text{-}SO_3Na)_2$ and the Hydroformylation of Styrene"; **J. Mol. Catal., 98**, 117 (1995).

4. Elena Bonaplata, Hao Ding, Brian E. Hanson, and James E. McGrath; "Hydroformylation of Octene-1 by a New Rhodium-Polymer Complex Based on Poly(Arylene Ether Triaryl Phosphine)"; **Polymer,** *in press.*

5. Brian E. Hanson, Hao Ding, Tamas Bartik, and Berit Bartik; "New Water Soluble Phosphines for Organometallic Chemistry and Catalysis in the Aqueous Phase"; Proceedings of the NATO Advanced Research Workshop on Catalysis in Water, *Debrecen, Hungary* (1995).

6. Hao Ding and Brian E. Hanson; "Reaction Activity and Selectivity as a Function of Solution Ionic strength in 1-octene Hydroformylation with Sulfonated Phosphines"; **J. Chem. Soc., Chem. Commun.,** 2747, (1994).

7. Hao Ding and Brian E. Hanson; "Spectator Cations and Catalysis with Sulfonated Phosphines The Role of Cations in Determining Reaction Selectivity in the Aqueous Phase Hydroformylation of Olefins"; **J. Mol. Catal., 99,** 131 (1995).

8. Hao Ding and Brian E. Hanson; "Preparation of a Surface Active Chiral Phosphine and its Use in the Hydrogenation of Prochiral Olefins"; **Angew. Chem. Int. Ed. Engl., 34**, 1645 (1995).

9. Hao Ding, Barbara B. Bunn and Brian E. Hanson; "Sulfonated Phosphines"; **Inorganic Syntheses**, *submitted.*

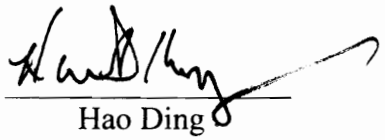
10. Brian E. Hanson and Hao Ding; "Complex Chemistry and Catalysis with Sulfonated Phosphines"; **Chem. Rev**., *to be submitted.*

Vita

Hao Ding was born on March 7, 1965 in Shanghai, China. He received a Bachelor of Science degree in Chemistry with an emphasis on analytical chemistry from Fudan University in 1988. He then began employment as a chemist at Johnson Wax in Shanghai.

On the second day after Christmas of 1991, he left Shanghai, the place where he had lived for twenty-seven years, and traveled to the United State for a Ph.D. degree in chemistry. The requirements for the degree were completed at Virginia Polytechnic Institute and State University in August, 1995.

During the Ph.D. program, he worked mainly as a graduate research assistant under the direction of Prof. Brian E. Hanson. Upon graduation he will continue his research project as a postdoctoral research associate at Virginia Tech.



Hao Ding