# A novel chiral water-soluble phosphine ligand based on a water-soluble acrylic acid salt

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**(2*S*,4*S*)-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine reacts with poly(acrylic acid) to form a macro-ligand useful in biphasic chiral reductions.**

Extensive research in the field of homogeneous catalysis in biphasic media has been prompted by the prospect of facile recovery and reuse of the expensive metals and chiral ligands.[1] Although recent reports have demonstrated the use of the fluorous biphasic system (FBS)[2] much of the research in the field is still focused on aqueous/organic biphasic systems using water-soluble catalysts. The introduction of polar groups *e.g.* $NR_3^+$, $COO^-$, $SO_3^-$ as side-chain substituents on parent organo-soluble phosphine ligands, and the corresponding metal complexes, renders the solubility properties to change to its opposite. Sulfonation is the most frequently used method to achieve water solubility and by far the most well established ligand is trisulfonated triphenylphosphine (TPPTS).[3] A TPPTS complex of rhodium is currently commercially applied in the two phase propene hydroformylation process developed by Rhone-Poulenc/Rhur Chemie.[4] The method is not limited to triphenylphosphine, chiral bidentate ligands have also been converted to their water soluble analogues using the sulfonation methodology *i.e.* BINAP,[5] (*S*,*S*)-cyclobutanediop, (*S*,*S*)-BDPP, (*S*,*S*)-chiraphos and (*R*)-prophos[6] or the amination methodology *i.e.* BDPP, Chiraphos and DIOP.[7] Studies on the hydrogenation of (*Z*)-2-acetamidocinnamic acid or the corresponding methyl ester reported to date[8,6] using cationic rhodium complexes combined with such water-soluble chiral ligands as catalysts can be broadly summarized: Compared to the organo-soluble parent complex the activity of the water-soluble analogue is normally lower and the trend is the same with respect to chiral induction. However, a high ee (94%) in water has been reported for sulfonated chiraphos.[8]

Previous reports from this laboratory have demonstrated the preparation of two new water-soluble monodentate phosphine ligands based on the concept of binding functionalised triphenylphosphines to water-soluble polymers.[9] We now report an extension of this concept into the field of chiral ligands.

The secondary amine group contained in the chiral ligand (2*S*,4*S*)-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine (PPM)[10] can be acylated[11] thereby often giving enhanced chiral induction compared to catalysts based on the free amine.[10] PPM can be easily acylated in THF–$H_2O$ following standard procedures using polyacrylic acid (PAA) as the acylating agent and dicyclohexylcarbodiimine (DCC) as the coupling agent.† Work-up basic conditions afforded the sodium salt of the phosphinated polyacrylic acid. With respect to PPM the yield in the coupling reaction was virtually quantitative, so the expensive PPM ligand was effectively utilized. The phosphorus content (3.6%) and the water-solubility (115 mg ml$^{-1}$, [P] = 0.133 mol dm$^{-3}$) of the isolated product (PAA–PPM) can of course be varied by changing the selected ligand to carboxylate ratio in the synthesis. However, it is worth noting that an increased phosphorus loading is achieved at the expense of the water solubility which maximises the actual phosphine concentration that can be reached. To obtain a phosphine concentration in the range practical for catalytic applications a phosphine to carboxylate ratio of 1 : 5 was used throughout the present study. The $^{31}$P NMR spectrum of PAA–PPM displays two peaks at δ −7.55 and −21.27 and most importantly, no sign of phosphine oxide. Slow tumbling of the polymer aggregates causes a substantial line-broadening in the $^{31}$P NMR spectrum (halfline width of >500 Hz) thus limiting the information *i.e.* coupling constants in metal complexes, normally extractable by this method.

Reaction of an aqueous solution of PAA–PPM with $Rh(NBD)_2]^+CF_3SO_3$ in a 2 : 1 phosphorus to rhodium ratio afford, after work-up, an orange powder. This product **1** displays two broad resonances at δ 48.9 and 16.3 in the $^{31}$P NMR spectrum, in good agreement with data for the formation of the expected *cis* bisphosphine complex $[(PAA\text{–}PPM)Rh(NBD)]^+[CF_3SO_3]$ **1**. Stirring an aqueous solution of **1** under an atmosphere of hydrogen for 10 min results in a changed $^{31}$P NMR spectrum with two new peaks at δ 39.4 and 67.6, in line with a hydrogenation of the norbornadiene ligand and formation of the solvato complex $[(PAA\text{-}PPM)Rh(H_2O)_2]^+$. Aqueous solutions of the bis-aquo complex are remarkably stable and no colour change or in the $^{31}$P spectrum was observed when stored under $H_2$.

Selected results using complex **1** as catalyst in the hydrogenation of (*Z*)-2-acetamidocinnamic acid in water or water–ethyl acetate are displayed in Table 1. The solubility of the substrate acid in water is very low and consequently, attempts to carry out the reaction in neat water results in a rate of reaction which is governed by the rate of dissolution of the acid in the water-phase. Dissolving the acid in neat water by adjusting the pH

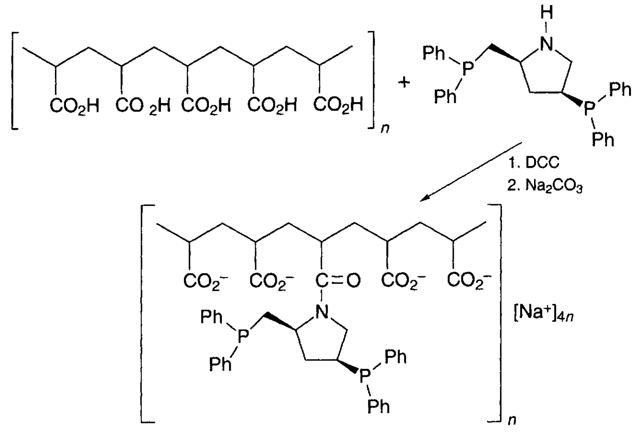
**Table 1** Hydrogenation of (Z)-2-acetamidocinnamic acid

| Entry | Solvent (ratio) | pH | Yield[d] (%) | ee[e] (%) | Rh : alkene | *t*/min | Reference |
|---|---|---|---|---|---|---|---|
| 1[a] | $H_2O$ | 8.26[b] | >97 | 56 (R) | 1 : 35 | 120 | this work |
| 2[a] | EtOAc/$H_2O$ (1 : 1) | 7.53[c] | >97 | 70 (R) | 1 : 80 | 45 | this work |
| 3[a] | EtOAc/$H_2O$ (1 : 1) | 7.00[c] | >97 | 74 (R) | 1 : 83 | 50 | this work |
| 4 | EtOH | | | 6 (S) | 1 : 100 | | ref. 10 |
| 5 | MeOH | | 100 | 93 (R) | 1 : 100 | | ref. 13 |

[a] (Z)-2-Acetamidocinnamic acid, $[Rh]_{aq}$ = 4 mmol dm$^{-3}$. [b] Adjusted with $NaHCO_3$. [c] $NaH_2PO_4$ buffer. [d] According to $H_2$ consumption and $^1$H NMR. [e] Calculated on the basis of reported values for the optically pure compounds *N*-acetyl-(*S*)-phenylalanine, $[\alpha]^{20}_D$ = + 46.0 (*c* 1, EtOH).

with $NaHCO_3$ (Table 1, entry 1), to obtain a homogeneous solution result in a rather low reaction rate and a low ee. In biphasic water–ethylacetate, however, the rate of reaction is comparable to that of the organo-soluble analogue in methanol solution. Although far from the best results obtained with the PPM-ligand[11,13] the optical yield in the biphasic reactions (Table 1, entry 2 and 3), are somewhat better than those observed earlier[11] using water soluble modified PPM. Whether the difference in reaction rate and optical yield between the different runs is an effect of pH differences or merely an effect of solvent is not clear and this line of research is currently being further investigated.

The present study show that the new concept of applying water soluble polymers to provide water soluble phosphines is also extendable to chiral phosphines. The PAA–PPM ligand is easily prepared and the corresponding cationic rhodium phosphine complexes catalyse the asymmetric hydrogenation of (*Z*)-2-acetamidocinnamic acid with moderate ees. Acidification of the water-solution precipitates the catalyst enabling an easy recovery of the catalysts.[‡]



**Scheme 1** Preparation of PAA–PPM.

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## Footnotes

† A flask containing a degassed water–THF mixture (1 : 5, 30 ml) is charged with poly(acrylic acid) (1.2 g, 63% aqueous solution) and PPM (600 mg in 7 ml THF). DCC (330 mg in 5 ml THF) is added over 30 min and the solution is stirred overnight. Dicyclohexylurea (DHU) precipitation is completed by evaporation of THF, addition of water (5 ml) and solid $NaHCO_3$ to pH 8. Removal of DHU by filtration followed by evaporation to dryness gives PAA–PPM as a white powder. Elemental analysis gives the P/N ratio (3.6/0.8 mass%). $^{31}$P NMR ($D_2O$) −7.55 (s) and −21.27 (s).

‡ Full account of recycling experiments will be given elsewhere.

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