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^{31}P NMR STUDIES ON THE MECHANISM OF ASYMMETRIC HYDROGENATION CATALYZED BY RHODIUM(I) COMPLEXES WITH CHIRAL PYRROLIDINODIPHOSPHINE LIGAND. EVIDENCE FOR EXTREMELY REGIOSELECTIVE COMPLEXATION OF PROCHIRAL SUBSTRATES

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^{31}P $\{^1H\}$ NMR studies on the key intermediate complex of asymmetric hydrogenation, $[(L^*L)Rh(S\text{-}S')]^+ClO_4^-$ (L^*L = pyrrolidinodiphosphine, BPPM and PPPM; S-S' = itaconic acid and α-acetamidoacrylic acid), revealed that the mode of the bidentated complexation of the prochiral substrate is extremely regioselective and stereoselective. A possible mechanism for chiral recognition of enantiofaces is proposed.

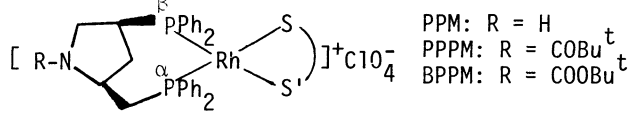
Recently, ^{31}P NMR spectroscopy has been successfully applied to the direct observation of intermediate rhodium complexes which are involved in asymmetric hydrogenations. For instance, Brown and Chaloner observed diastereomeric intermediate complexes with (Z)-α-benzamidocinnamic acid or its ester using DIOP[1] and DIPAMP,[2] and we reported in the previous paper the observation of "induced-fit" phenomena of a rhodium complex with a chiral pyrrolidinodiphosphine, BPPM, on coordinating with itaconic acid.[3] We wish to describe here evidence for the regioselective coordination of prochiral olefinic substrates with rhodium(I) complexes with pyrrolidinodiphosphines, and propose a possible mechanism of asymmetric induction based on ^{31}P NMR data, inspection of CPK models and the results of asymmetric hydrogenation.

As the most significant step for the chiral recognition of an enantioface of olefinic substrate has been shown to be the complexation of the olefin molecule to a chiral rhodium catalyst with cis chelating diphosphine under an atmospheric pressure of hydrogen,[4] it is extremely important to look into directly the behavior of the substrate-chiral rhodium complex in solution.

Although a chiral rhodium complex having a potential C_2 axis, e.g., $[(DIOP)Rh(CH_3OH)_n]^+BF_4^-$ and $[(DIPAMP)Rh(CH_3OH)_n]^+BF_4^-$, shows only one averaged signal as doublet in its ^{31}P NMR spectrum,[1,2] the rhodium complexes with pyrrolidinodiphosphines show a set of two distinct signals arising from non-equivalent phosphorus nuclei. This feature has a great advantage for looking at the mode of olefin complexation because there is a strong trans effect of the coordinated olefin on the chemical shift of these two phosphorus nuclei of the rhodium complex which has a square-planar configuration. Thus, in principle, one can determine how the olefinic substrate occupies the possible coordination sites on the basis of ^{31}P NMR spectra of the substrate-rhodium complex. Actually, the chemical shifts of the phosphorus nuclei change dramatically by the sort of coordinated molecule in the trans position as shown in Table 1. For instance, the methanol complex of PPPM or BPPM showed ca. 25 ppm down field shift from the corresponding 1,5-cyclooctadiene (COD) complex, and a similar down field shift was observed for the acetone complexes. As Table 1 and Figure 1 show, the α-acetamidoacrylic acid complex of BPPM displays two siganls at +33.22 ($^{\alpha}P$) and +29.80 ppm ($^{\beta}P$) as double doublet for each phosphorus. By taking into account the remarkable change in the chemical shift of

each phosphorus signal caused by the trans ligand listed in Table 1, it is concluded that the olefin moiety occupies the trans position of $^{\alpha}P$ and the carbonyl oxygen does trans position of $^{\beta}P$ as depicted in Figure 2.[5] As is immediately seen from Figure 1, there is no trace of the other regioisomeric complex in which α-acetamidoacrylic acid coordinates in an opposite way: The result unambiguously indicates that the complexation of this substrate is extremely regioselective. The result using itaconic acid-rhodium complex bearing BPPM as ligand makes us come to the same conclusion. It should be noted that evidence for the extremely regioselective complexation of prochiral substrates to chiral rhodium catalysts is obtained for the first time by using ^{31}P NMR spectroscopy.

Table 1. ^{31}P NMR data for complexes (δ ppm)[a]



PPM: R = H
PPPM: R = $COBu^t$
BPPM: R = $COOBu^t$

Complex	$^{\alpha}P$	$^{\beta}P$	Temp.(K)
$[(PPM)Rh(COD)]^+ClO_4^-$	+39.87	+29.52	303
$[(PPPM)Rh(COD)]^+ClO_4^-$	+43.12	+12.12	303
$[(BPPM)Rh(COD)]^+ClO_4^-$	+41.41	+13.03	333
	a +41.05	a +13.19	303
	b +40.67	b +13.17	
	a +37.46	a +14.92	233
	b +35.03	b +15.48	
$[(PPPM)Rh(CD_3OD)_n]^+ClO_4^-$	+69.64	+42.54	303
$[(BPPM)Rh(CD_3OD)_n]^+ClO_4^-$	a +67.96	a +42.22	303
	b +67.56	b +43.33	
$[(PPPM)Rh(acetone\text{-}d_6)]^+ClO_4^-$[b]	+66.64	+42.54	303
$[(BPPM)Rh(acetone\text{-}d_6)]^+ClO_4^-$[b]	a +65.05	a +38.81	303
	b +64.77	b +38.32	
$[(BPPM)Rh(O{=}C(COOH){-}C{=}C(NH){-}Me)]^+ClO_4^-$[c]	+33.22	+29.80	303
$[(BPPM)Rh(O{=}C(COOH){-}C{=}C(CH_2){-}OH)]^+ClO_4^-$[d]	+37.69	+34.06	303
$[(PPPM)Rh(O{=}C(CH){=}C(CH_2){-}OH)]^+ClO_4^-$[d]	+38.15	+30.74	233

a Measured in methanol-d_4 unless otherwise noted. b Measured in acetone-d_6. c Three fold excess of the substrate was used. d Twenty fold excess of the substrate was used.

The results provide a crucial basis for the stereochemical inspection of the mechanism of asymmetric induction in the chiral coordination sphere. Namely, there remains only two possible modes for the complexation of the prochiral substrate to the chiral rhodium complex as depicted in Figure 2.

The asymmetric hydrogenation of α-acetamidoacrylic acid and itaconic acid catalyzed by $[(BPPM)Rh(COD)]^+ClO_4^-$ has been found to give (R)-N-acetylalanine with 98.5% e.e.,[6] and (S)-methylsuccinic acid with 94.8% e.e.,[7] respectively. Thus, the mode of the complexation of the substrates to the rhodium catalyst is exclusively determined to be Mode A in Figure 2.[8] However, we cannot determine whether the observed substrate-rhodium complex is the Mode A complex or the Mode B complex at this stage.

As for the assignment of $^{\alpha}P$ and $^{\beta}P$, we employed the data listed in Table 2. As Table 2 shows, i) considerable shielding effects by the anisotropy of nitrogen lone pair on the phosphorus nuclei would be operative in pyrrolidinodiphosphines like those of oxygen lone pairs in DIOP, and ii) shielding effects by carbonyl anisotropy are operative in PPPM and BPPM. In the case of PPPM- and BPPM-rhodium complexes, the carbonyl anisotropy causes a slight deshielding on $^{\alpha}P$ and a considerable shielding on $^{\beta}P$ as is seen from Table 1.

In the previous paper,[3] we assumed that the two species observed in the ^{31}P NMR spectra of $[(BPPM)Rh(COD)]^+ClO_4^-$ and $[(BPPM)Rh(CD_3OD)_n]^+ClO_4^-$ at ambient temperature might be assigned to the possible quasi chair and quasi boat conformers with regard to the seven membered ring. However,

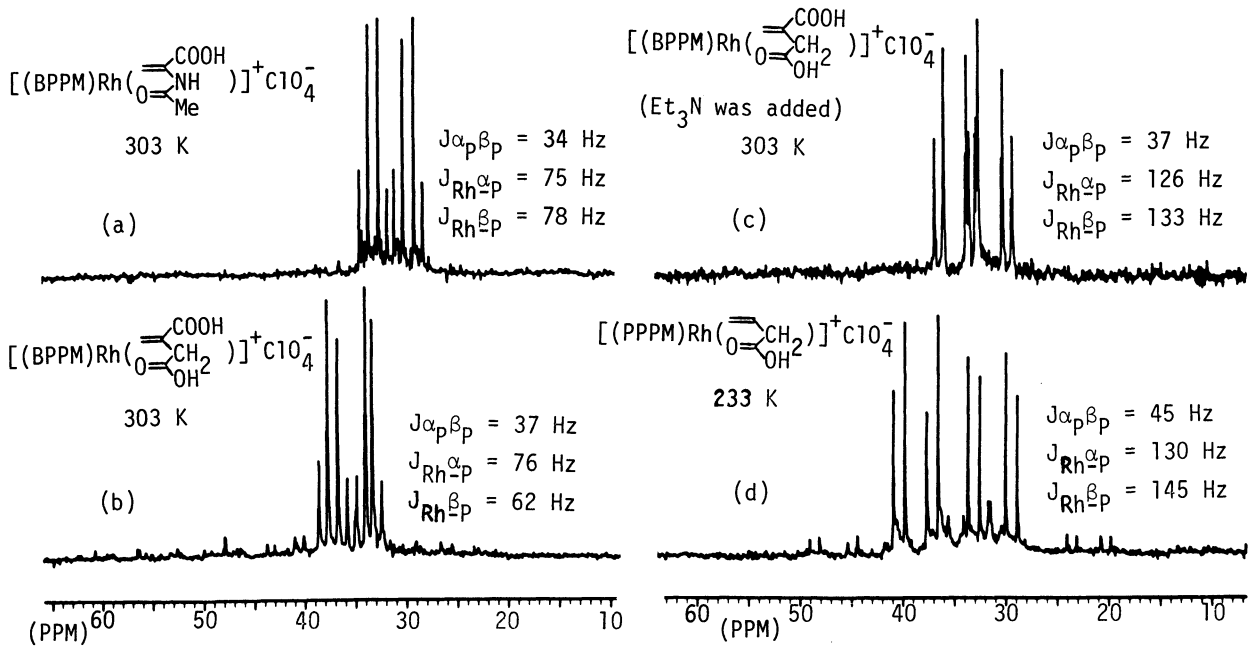


Figure 1. $^{31}P\ \{^{1}H\}$ NMR spectra of the substrate-chiral rhodium complexes in methanol-d_4.

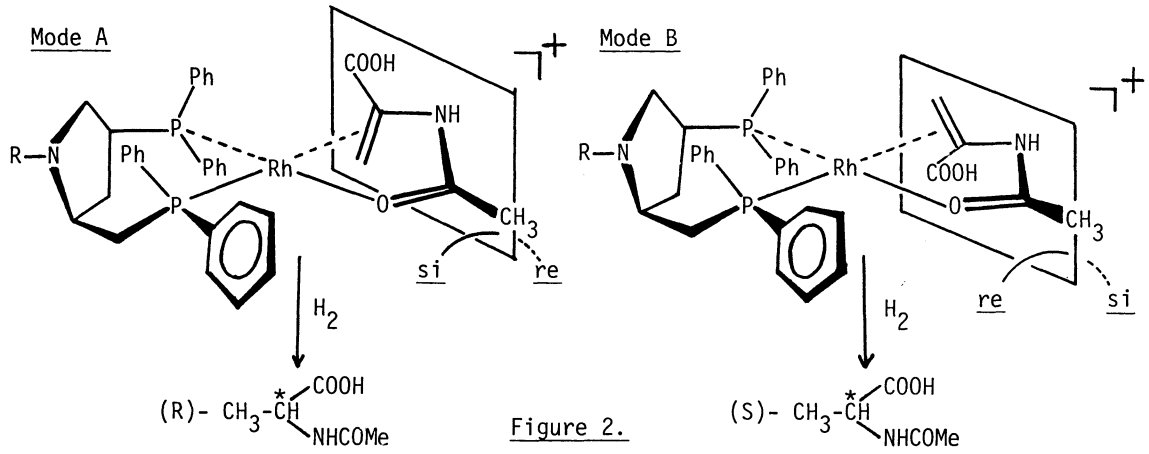


Figure 2.

it turns out that these are the conformers arising from the slow rotation around the N-C(O) bond of the BPPM moiety[9] since two species are also observed even in the spectrum of BPPM itself below the coalescence temperature (Tc 291 K) while only one species is observed for either PPPM or PPM in the temperature range 233-333 K (see Tables 1 and 2). The rotation of pivaloyl group around the N-C(O) bond in PPPM seems to be completely fixed because of its quite bulky t-butyl moiety. Accordingly, the quasi chair-boat interconversion of the seven membered ring would be easy like the case of the corresponding DIOP complex.[10] Nevertheless, inspection of CPK models clearly shows that the interconversion between the quasi chair and the quasi boat conformer is impossible once the chelating substrate comes into the coordination sphere to form the substrate-rhodium complex,

Table 2. ^{31}P NMR data for ligands (δ ppm)[a]

Ligand	α_P	β_P	(Temp. K)
PPM	-5.3	-21.9	303
PPPM	-10.9	-24.6	303
BPPM	-9.2	-23.6	303
	a -13.7 b -13.9	a -26.4 b -26.2	195
DIOP	-24.0		303
$Ph_2P\text{-}CH_3$	+28.1		(Ref. 11)
$Ph_2P\text{-}C_3H_7{}^n$	+17.6		(Ref. 11)
$Ph_2P\text{-}C_3H_7{}^i$	-0.2		(Ref. 11)
$Ph_2P\text{-}C_4H_9{}^t$	-17.1		(Ref. 11)
$Ph_2P\text{-}C_5H_9{}^c$	+3.9		(Ref. 11)
$Ph_2P\text{-}C_6H_{11}{}^c$	+4.4		(Ref. 11)
$(Ph_2P\text{-}CH_2\text{-})_2$	+13.2		(Ref. 11)

a Measured in methanol-d_4.

viz., only the quasi chair conformer is accessible for the complexation of the chelating substrate, which happens to correspond exactly to the X-ray structure of $[(PPPM)Rh(COD)]^+ClO_4^-$.[12]

It should be noted that even the rotation of the distal t-butoxycarbonyl group around the N-C(O) bond in BPPM is found to be fixed by the complexation of the prochiral substrate and this fixation is observed as the "induced-fit" of the chiral rhodium complex.

The studies along this line employing a variety of chiral diphosphines are actively underway.

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References and Notes

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5. As to the structure of the substrate-rhodium complex, the chelation is reasonably ascribed to that of the enamide moiety since the four membered ring chelate using the acrylic acid moiety is disadvantageous by steric reasons. To confirm the quasi five membered ring chelate formation, we employed vinylacetic acid and acrylic acid as substrate. The former complex displays a very similar spectrum as expected, as shown in Figure 1, whereas the latter does a complicated one. The corresponding BPPM complexes show a more complex pattern.
6. The reaction was run with 3.0 mmol of the substrate, 0.03 mmol of the catalyst, 0.06 mmol of triethylamine in 50 ml of methanol at 20°C and 1 atm of hydrogen for 6 hr. Without the amine the optical yield was 95.2% e.e.
7. The reaction was run with 3.0 mmol of the substrate, 0.015 mmol of the catalyst, 3.0 mmol of triethylamine in 6 ml of methanol-benzene (3:1) at 25°C and 1 atm of hydrogen for 12 hr. Without the amine, the optical yield was 91.3% e.e.
8. The difference in the configuration of the produced N-acetylphenylalanine and methylsuccinic acid is due to the sequence rule.
9. The barrier for the rotation ($\Delta G^{\ddagger}_{298}$) estimated by line shape analysis is 72 KJ/mol and Tc is 318 K for $[(BPPM)Rh(COD)]^+ ClO_4^-$.
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