# New insights into the mechanism of asymmetric hydrogenation catalysed by monophosphonite–rhodium complexes

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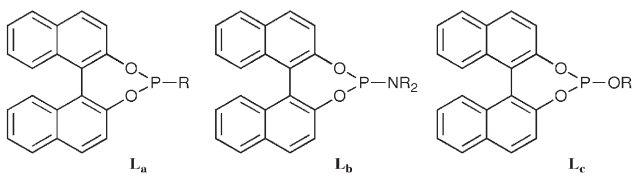
**The solvento complex $[Rh(L)_2(S)_2]^+$ where L = $^t$BuP(*R*-binaphthoxo) is shown to be in equilibrium with an η-arene dirhodium complex and only weak, monodentate binding of alkenes is observed; in addition, an intermediate Rh alkyl hydride complex containing two coordinated monophosphonites is unambiguously characterised by NMR.**

In 2000, the optically active, monodentate P-donors $\mathbf{L_{a–c}}$ (monophos ligands) were discovered and found to surpass their bidentate analogues in terms of the enantioselectivity of their rhodium complexes in asymmetric hydrogenation catalysis.[1–3]




This was unexpected because it had often been asserted that the stereocontrol offered by chelating ligands was a prerequisite for high enantioselectivity although many years earlier, catalysts featuring the monophosphine CAMP had been shown to give ees of over 90%.[4] One great advantage of monophos ligands $\mathbf{L_{a–c}}$ is that they can be readily made in one step and, in some cases, high throughput methods have been used to generate libraries of chiral ligands which facilitate the tailoring of the ligand R groups to a particular substrate.[5] Most impressively, this approach has already led to commercialisation of an asymmetric hydrogenation process based on monophos ligands $\mathbf{L_b}$ by DSM.[6] In view of the academic and industrial interest in this topic, it is surprising that intermediates in the asymmetric hydrogenation cycle catalyzed by the Rh–monophos complexes have not been conclusively characterized. This situation contrasts sharply with the widely explored chemistry of the intermediates in asymmetric hydrogenation catalyzed by Rh–diphos complexes.[7] de Vries, Feringa *et al.*[8] detected, by ESI MS spectrometry, weak signals corresponding to RhL(substrate) and $RhL_2$(substrate) complexes but the most intense peaks corresponded to $RhL_3$ and $RhL_4$ complexes which are not suggested to be part of the asymmetric hydrogenation catalytic cycle. At present the evidence for the intuitively attractive idea of the solvento complexes $[RhL_2(S)_2]^+$ carrying the flux of the asymmetric hydrogenation comes mainly from the observed non-linear effects[9,10] that exclude the possibility of the 1 : 1 complex being a significant component of the catalyst.[10] Here we describe the first characterization of a solvento species generated from hydrogenation of $[Rh(\mathbf{L})_2(cod)]^+$ (cod = 1,5-cyclooctadiene, $\mathbf{L} = \mathbf{L_a}$ where R = t-Bu)[1] as well as experiments on alkene substrate binding and subsequent hydrogenation which have led to revealing mechanistic conclusions.

When a solution of $[Rh(\mathbf{L})_2(cod)]^+$ (**1**) in $CH_2Cl_2$ was hydrogenated for 20 minutes at ambient temperature, only traces of the $^{31}$P NMR signals for the starting complex were present (Fig. 1(b)) and the $^1$H and $^{13}$C NMR spectra of the product showed that the hydrogenation of the coordinated cod was essentially complete. The broad $^{31}$P signals observed for the hydrogenated complex at 298 K sharpened at lower temperatures

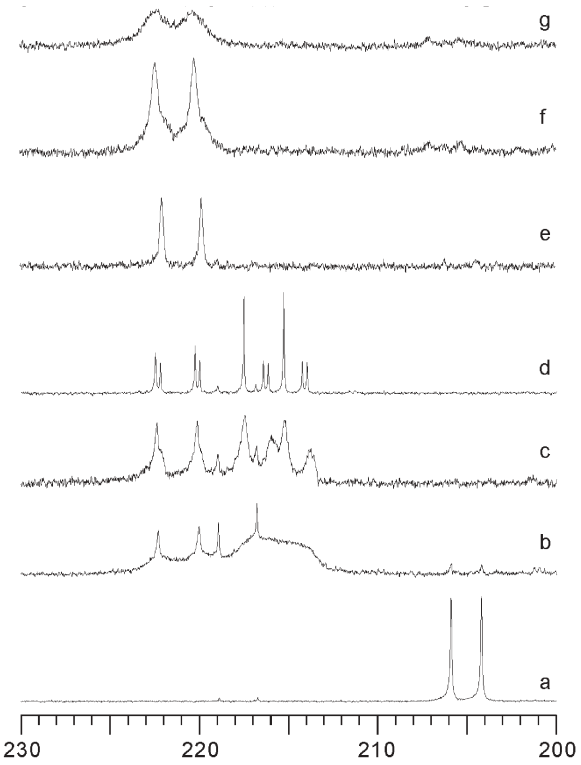



**Fig. 1** $^{31}$P NMR spectra (122 MHz, $CD_2Cl_2$) of the sample initially containing complex **1**: (a) starting spectrum, 298 K; (b) after hydrogenation for 20 min at ambient temperature, 298 K; (c) same sample at 273 K; (d) same sample at 233 K; (e) after 2 equiv. of substrate **4** added, 298 K; (f) same sample at 193 K; (g) additional 3 equiv. of substrate **4** added, 193 K.

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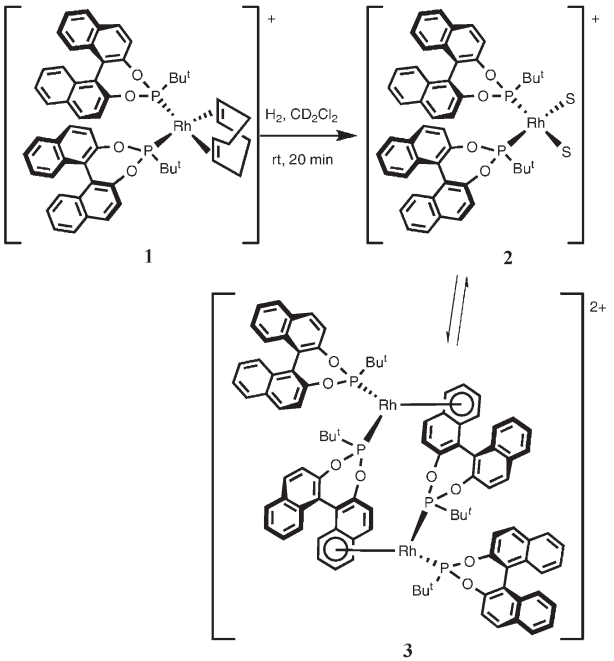



**Scheme 1** Hydrogenation of precatalyst **1**.

(Fig. 1(c)) and were resolved into two sets of sharp signals at 233 K (Fig. 1(d)) with the following parameters: a doublet at 216.4 ($J_{PRh}$ 272 Hz), and two doublets of doublets at 215.3 ($J_{PRh}$ 265 Hz, $J_{PP}$ 32 Hz) and 221.2 ($J_{PRh}$ 269 Hz, $J_{PP}$ 32 Hz). The $J_{PRh}$ values in both species are large (compared to the $J_{PRh}$ 208 Hz for **1**) which is characteristic of the formation of solvento complexes. The reversible lineshape changes in the $^{31}$P NMR spectrum in the temperature interval 203–290 K indicated that the two species are in dynamic equilibrium. Upon concentration of the sample, the amount of the component with two non-equivalent phosphorus atoms increased, which is consistent with the reversible dimerization of the solvento complex **2** to give an η-arene coordinated dirhodium complex **3** (Scheme 1) analogous to the η-arene species previously observed in Rh–dppe and Rh–BINAP complexes.[7b,11] The assignment of structure **3** was further supported by the $^1$H NMR spectrum at −40 °C which showed 6 signals in the region $\delta$ 4.5–6.5, characteristic of the protons in an η-arene ring (Fig. 2).

The prochiral substrate, methyl *Z*-(α)-acetamidocinnamate (**4**) is known[12] to form strong chelate complexes when reacted with various [Rh(diphos)(S)$_2$]$^+$. As can be seen from Fig. 1(e), addition of a 2-fold excess of **4** to **2** (and **3**) led to a suppression of the $^{31}$P signals for the binuclear **3** leaving only a doublet with parameters

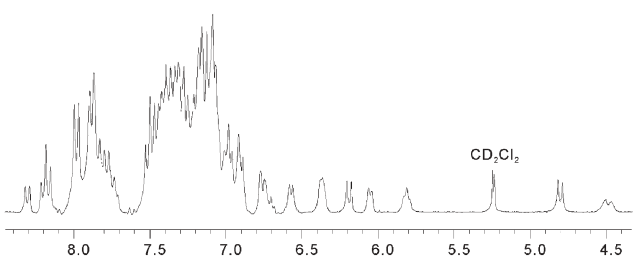
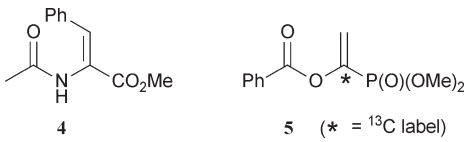



**Fig. 2** Section plot of $^1$H (300 MHz, $CD_2Cl_2$, −40 °C) NMR spectrum of **3** showing the signals of an η-arene ring.

(221.4, $J_{PRh}$ 267 Hz) similar to those for **2**. The colour of the solution remained amber upon addition of **4** whereas solutions of chelate complexes of the type [Rh(diphos)(**4**)]$^+$ are invariably intensely dark red.[12] Furthermore, there were no indications from the $^{31}$P, $^1$H or $^{13}$C NMR spectra for the formation of a chelating substrate complex. Adding a further 3 equivalents of **4** did not change the appearance of the $^{31}$P NMR spectrum at ambient temperature. Nevertheless, the reversible broadening of the signal observed at decreased temperatures (Fig. 1(f)) became more pronounced with the larger excess of **4** (Fig. 1(g)). Thus, the NMR data indicated that the binding of **4** to the Rh is extremely weak and we are unable to characterise further the nature of the binding of **4** to Rh.




To get a deeper insight into the substrate binding properties of **2**, its $CD_2Cl_2$ solution was treated with a 2-fold excess of methyl α-benzoyloxyethenephosphonate (**5**) which forms strongly chelating substrate complexes when added to [Rh(diphos)(S)$_2$]$^+$.[13] The α-$^{13}$C labelled phosphonate **5** was used to enable the unambiguous determination of the coordination mode of the prochiral alkene. As can be seen from Fig. 3, the evidence from the multinuclear NMR study indicates that a small equilibrium concentration of catalyst–substrate complex **6** is formed upon addition of phosphonate **5** to the solution containing **2**. At 203 K the equilibration is slow on the NMR timescale which allowed us to draw definitive conclusions on the character of the substrate binding in **6**. The C=C is apparently not coordinated in complex **6** because the olefinic protons in the $^1$H NMR spectrum are only slightly down-field of the non-coordinated **5**, whereas a significant up-field shift is characteristic of chelating **5**.[13] Moreover, the chemical shift of the α-carbon in the $^{13}$C NMR spectrum of **6** differs only slightly from that of **5** and does not have any additional couplings, while in [Rh(diphos)(**5**)]$^+$ complexes, the α-carbon is shifted approximately 60 ppm to lower frequency and

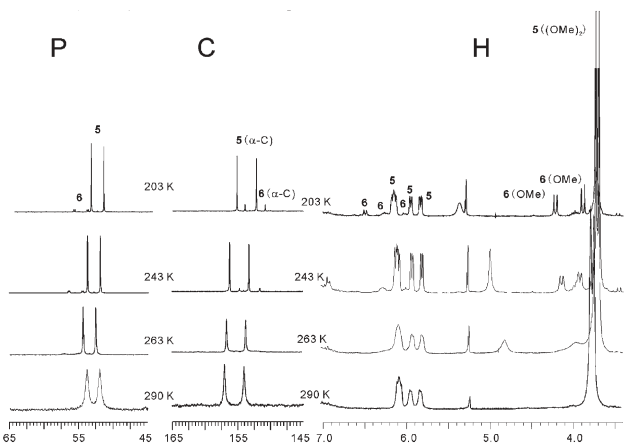
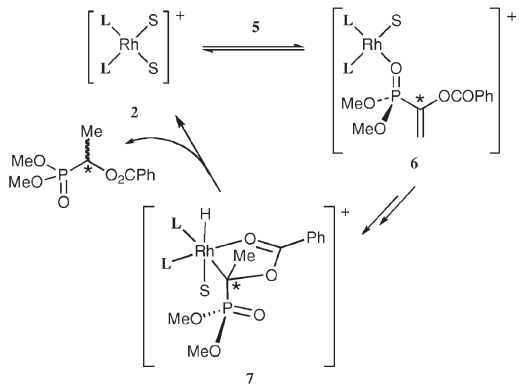



**Fig. 3** Section plots of $^{31}$P (121 MHz, $CD_2Cl_2$), $^{13}$C (75 MHz, $CD_2Cl_2$) and $^1$H (300 MHz, $CD_2Cl_2$) NMR spectra of the sample obtained by addition of a 2-fold excess of the α-$^{13}$C labelled complexes **2** and **3** in $CD_2Cl_2$.



**Scheme 2** Coordination and hydrogenation of methyl α-benzoyloxyethenephosphonate (**5**) where * denotes the $^{13}C$ label.

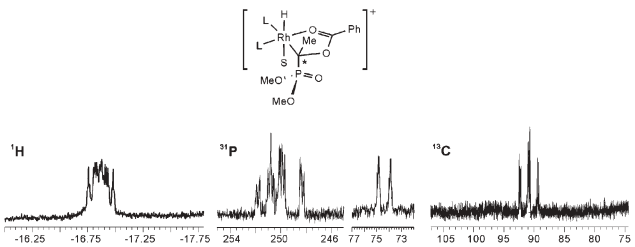



**Fig. 4** Characterization of the monohydride intermediate **7** by multinuclear NMR. $^1H$ NMR (300 MHz, $CD_2Cl_2$, −40 °C): −16.88 (m, 1H, Rh–H; $J$ = 3, 15, 18, 22, 26 Hz); $^{31}P$ NMR (121 MHz, $CD_2Cl_2$, −40 °C): 74.4 (dm, P=O, $^1J_{PC}$ = 16 Hz), 249.1 (ddd, $P_{cis}$, $^3J_{PP}$ = 9 Hz, $^2J_{PP}$ = 27 Hz, $^1J_{PRh}$ = 82 Hz), 250.8 (ddd, $P_{trans}$, $^2J_{PP}$ = 27 Hz, $^2J_{PC}$ = 109 Hz, $^1J_{PRh}$ = 136 Hz); $^{13}C$ NMR (75 MHz, $CD_2Cl_2$, −40 °C): 90.7 (ddd, α-$^{13}C$, $^1J_{CRh}$ = 21 Hz, $^2J_{PC}$ = 109 Hz, $^1J_{PC}$ = 116 Hz).

has characteristic couplings with rhodium and two phosphorus atoms.[13] There are two $^1H$ NMR signals for the diastereotopic methoxy groups of the $OP(OMe)_2$ and the $^{31}P$ signal for this group shows coupling with the *trans*-phosphorus on the Rh. Overall, the NMR evidence accords with the structure of **6** depicted in Scheme 2 in which the substrate is weakly monocoordinated *via* the phosphoryl oxygen.†

Low-temperature hydrogenation of the sample containing the equilibrium mixture of **2** and **6** resulted in the detection of a monohydride intermediate **7** with the α-carbon atom bonded to Rh (Scheme 2). The structure of **7** was elucidated by comparing its NMR data (Fig. 4) with those known for several monohydrides derived from $[Rh(BisP^*)(\mathbf{5})]^+$.[13] Thus, although the binding properties of the substrates are very different, the later intermediates in the catalytic cycle of **2** are quite normal.

We have shown that hydrogenation of the monophos catalytic precursor $[Rh(\mathbf{L})_2(cod)]^+$ leads to an equilibrium mixture of solvento complex $[Rh(\mathbf{L})_2(S)_2]^+$ (**2**) and η-arene coordinated dirhodium complex **3**, behaviour related to that of BINAP–Rh complexes. However, in contrast to the BINAP–Rh system, the binding of **5** to the $RhL_2^+$ is weak and monodentate. Since enamides and derivatives of itaconic acid are known to give even weaker catalyst–substrate complexes,[14] it is clear that the strength and manner of the substrate binding to $RhL_2^+$ has no bearing on the enantioselectivities obtained with monophos catalyst **1**.[1,2] We have identified an intermediate of the type $[RhH(alkyl)\mathbf{L}_2]^+$ which conclusively establishes that two monophos ligands are coordinated to the Rh during the catalysis.

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## Notes and references

† Phosphonate complexes of Rh have been previously reported as part of a chelate, for example see refs. 15,16.

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