The Study of Inorganic Systems by NMR Spectroscopy in Conjunction with Parahydrogen-Induced Polarisation

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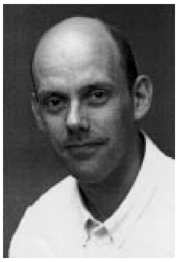
The study of reaction mechanisms by NMR spectroscopy normally suffers from limitations in sensitivity that result in substantial difficulties in the detection and characterisation of reaction intermediates. One technique that can circumvent this problem is the use of *para*-enriched hydrogen. Here, an overview of the developments in the study of chemical reactions using parahydrogen-assisted NMR spectroscopy is presented, with the characterisation of a number of new hydride complexes of iridium, rhodium, ruthenium and tantalum being described. A number of studies involving transition metal clusters and catalytic applications are also considered.

1. Introduction

An obvious aim in understanding the detailed mechanism of a chemical reaction is the unambiguous detection and characterisation of any associated reaction intermediates. Unfortunately, such species are often both transient in nature and present in low concentrations. Since this makes their direct detection difficult, indirect techniques, such as reaction kinetics or isotopic labelling, are often used to impart mechanistic information. However, there will always be a degree of ambiguity associated with a mechanism that is determined in this fashion.

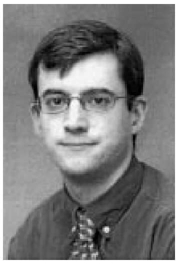
One technique that has found widespread use in the characterisation of compounds in all branches of chemistry is NMR spectroscopy. In many ways, NMR is an ideal technique for such studies since most important elements exhibit at least one NMR-active isotope, and isotopic labelling can be undertaken if greater sensitivity is required. The benefits of this approach when coupled with the wealth of available pulse sequences mean that it is often possible to determine molecular structures using NMR alone. Other factors, such as the ability to choose between solution and solid-state NMR and the possibility of monitoring slower dynamic processes, make this technique even more attractive for studying reactions. However, since NMR is inherently insensitive, its application in mechanistic studies has been somewhat limited.

In 1986 Bowers and Weitekamp proposed,[1] and later proved,[2] that greatly enhanced ^{1}H NMR signals could be obtained from molecules that were formed by the addition of hydrogen in the *para* spin-state. Since this report, the use of parahydrogen-enhanced NMR spectroscopy has revolutionised the study of reactions involving H_2 as a substrate by providing opportunities to study reaction intermediates directly by NMR for essentially the first time.



Simon Duckett (left) was born in Preston in England in 1965. He graduated with a B.Sc. degree in Chemistry from the University of York in 1986 and was awarded a D.Phil. from the same institution in 1990 (with Prof. R. N. Perutz). During 1990 he was a postdoctoral fellow with Prof. W. D. Jones at the University of Rochester and returned there in late 1991 to work as a postdoctoral fellow with Prof. R. Eisenberg on projects relating to parahydrogen. In 1993 he returned to the University of York to take up an appointment as Lecturer in Inorganic Chemistry and in 2001 he was promoted to Reader. He has authored 30 publications in the parahydrogen field and has research interests in using NMR to probe reaction mechanisms and help develop new catalysts.

Damir Blazina (right) was born in Zagreb, Croatia in 1977. He graduated with an MChem. degree in Chemistry from the University of York in 1999 and was awarded a Ph.D. from the same institution in 2003 (with Dr. S. Duckett and Prof. P. J. Dyson). He is currently a postdoctoral fellow in the same Department. He started working in the parahydrogen area on a project sponsored by Bruker UK in 1999 and has research interests in cluster-based catalysis and NMR spectroscopy.



MICROREVIEWS: This feature introduces the readers to the author's research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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2. Principles Behind the Parahydrogen Effect

The existence of two isomers of molecular hydrogen derives from the symmetrisation principle of quantum mechanics, which states that the overall wave function of fermions (such as protons) must be antisymmetric with respect to exchange of nuclei. Furthermore, since the product of rotational and nuclear wave functions has to be antisymmetric, it follows that antisymmetric rotational states (odd values of J) are associated with symmetric, or *ortho*, nuclear spin-states. Likewise, antisymmetric nuclear spin-states (called *para*) are reserved for symmetric rotational states (even values of J). Hydrogen therefore might be thought to consist of a 3:1 mixture of *ortho* and *para* isomers in accordance with the threefold degeneracy of the former state (spin configurations $\alpha\alpha$, $\alpha\beta+\beta\alpha$, $\beta\beta$) over the latter (spin configuration $\alpha\beta-\beta\alpha$). However, since these two forms have different rotational (internal) energies, their populations are temperature dependent, and since interconversion between the two isomers is forbidden, the isolation of pure parahydrogen is possible. This is readily achieved by cooling H_2 in the presence of a paramagnetic species. The degree of enrichment simply depends on the temperature of the catalyst; 50% enrichment is possible at 77 K.[3,4]

An important feature of parahydrogen (p-H_2) is that it is NMR silent. However, if it adds to a metal centre in such a way that two chemically distinct hydrides are formed, the energy level diagram shown in Figure 1 is obtained. Since parahydrogen selectively populates the $\alpha\beta$ and $\beta\alpha$ spin states of the product, the population difference between the states will approach unity. This reflects a substantial increase over the normal situation where populations are controlled by the corresponding energy level separations. Because the intensity of an NMR signal depends on this population difference, enhanced signals are observed in the spectra of parahydrogen-derived molecules. Furthermore, this novel population distribution results in two of the transitions occurring in the opposite sense to that which is normally seen and the associated resonances therefore have antiphase character. This process has been termed PASADENA (Parahydrogen And Synthesis Allow Dramatically Enhanced Nuclear Alignment)[2a] and PHIP (ParaHydrogen Induced Polarisation).[2b]

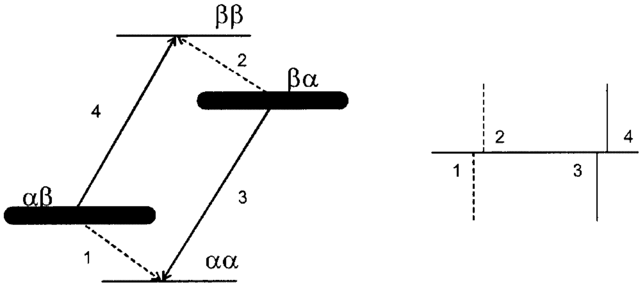
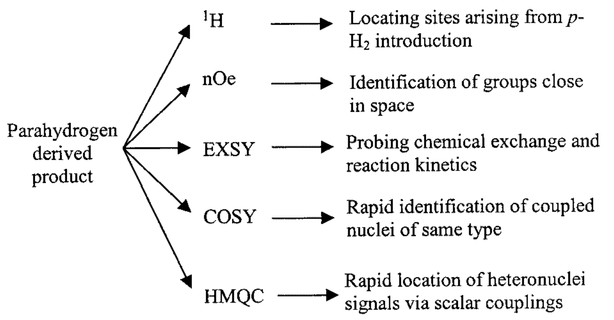


Figure 1. Idealised spin-state populations (represented by line thickness) and corresponding NMR signal patterns for an AX spin system, such as those found in $[(Me_2AsCH_2CH_2AsPh_2)Pt(H)_2]$, formed under parahydrogen-derived PASADENA conditions; the situation where $^2J_{H,H}$ is negative is illustrated

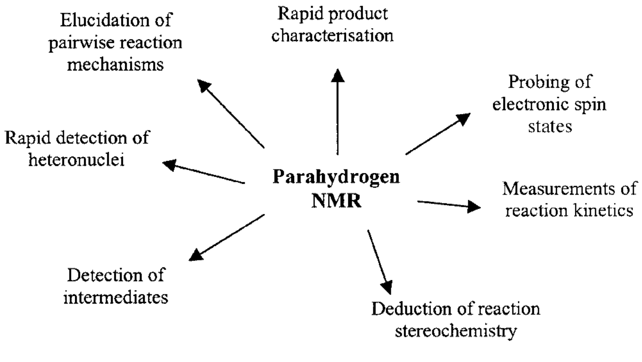
It is important to note that this situation corresponds to the chemical synthesis of an extreme spin-state, and that the system will subsequently re-establish the Boltzmann population distribution via relaxation. However, if a radio frequency pulse is applied prior to this point, the newly formed spin state can be interrogated and larger than normal coherences can be generated for detection. Scheme 1 summarises some of the ways that this approach has been harnessed in the literature.



Scheme 1. NMR approaches facilitated by parahydrogen

A different effect is observed if the reaction involving parahydrogen takes place in a weak magnetic field, such as outside the NMR spectrometer. This effect, called ALTADENA (Adiabatic Longitudinal Transport After Dissociation Engenders Net Alignment)[5] occurs because under such conditions, the coupling between the nuclei is large relative to the frequency difference between them. Consequently, the added parahydrogen nuclei selectively move from their initial spin state into either the $\alpha\beta$ or $\beta\alpha$ states of the AX system, depending on which is lower in energy. Only two enhanced transitions are therefore observed in the resulting NMR spectrum. The ALTADENA effect is transitory in nature; if the reaction is not complete outside the strong magnetic field of an NMR spectrometer, PASADENA and ALTADENA effects will compete in the early stages of the reaction. Any subsequent reaction in the strong magnetic field will result in the PASADENA effect being observed.

A number of articles have appeared that have reviewed the parahydrogen effect and its chemical applications (see Scheme 2).[6] This article focuses on inorganic reports since 1999.



Scheme 2. Chemical applications of parahydrogen NMR methodology

3. Applications of Parahydrogen to Mononuclear Transition Metal Complexes

If the parahydrogen effect is to be useful, it must make possible the detection of new species. For example, oxidative addition of H_2 to Vaska's Complex, *trans*-$[IrCl(CO)(PPh_3)_2]$,[7] and its many analogues has been the subject of much synthetic investigation and was accepted to proceed exclusively over the OC−Ir−Cl axis. Calculations by Sargent and Hall,[8] however, revealed that H_2 addition over the OC−Ir−Cl axis rather than the P−Ir−P axis is favoured by only 9.5 $kJ \cdot mol^{-1}$ in the case of $[IrCl(CO)(PMe_3)_2]$, and that increasing the π-accepting nature of the phosphane further favours H_2 addition across the P−Ir−P axis. Studying the oxidative addition of H_2 to Vaska's complex is therefore an ideal test of the *p*-H_2 approach, viz., is another isomer detectable? Figure 2a shows the resultant ^1H NMR spectrum, focusing on the hydride region, when *p*-H_2 adds to *trans*-$[IrCl(CO)(PPh_3)_2]$ at 295 K. The expected resonances for *cis-trans*-$[IrCl(H)_2(CO)(PPh_3)_2]$ are clearly visible, while those for a minor species are indeed detected.[9] In this case, the extra signals arise from a product with two chemically equivalent hydride protons that are magnetically distinct, i.e. *cis-cis*-$[IrCl(H)_2(CO)(PPh_3)_2]$. Further studies demonstrated that when PMe_3 was employed, a similar species could be observed, and when $AsPh_3$ was utilised, H_2 addition over the As−Ir−As axis was shown to be kinetically preferred, with slow isomerisation over the course of several days leading to the thermodynamic product *cis-trans*-$[IrCl(H)_2(CO)(AsPh_3)_2]$.

Evidence was also presented in this paper that the formation of trihydride complexes of the type $[Ir(H)_3(CO)_2(L)]$ was possible when CO and *p*-H_2 are warmed together in the presence of $[IrCl(CO)(L)_2]$ (L = PPh_3 and PMe_3). The trihydride product was shown to be formed via $[IrCl(H)_2(CO)_2(L)]$, which undergoes competitive HCl and H_2 elimination thereby accounting for the observation of $[IrH(Cl)_2CO(PPh_3)_2]$. The spectral features of the associated hydride resonances of $[Ir(H)_3(CO)_2(L)]$ are worthy of special comment (see Figure 2b) since they yield anti-phase components that have different frequency separations. This situation arises due to the internal cancellation of the central triplet feature in the unique IrH resonance.[10] Interestingly, a very different result was obtained when *trans*-$[IrCl(CO)(PPh_3)_2]$ was subjected to UV radiation while un-

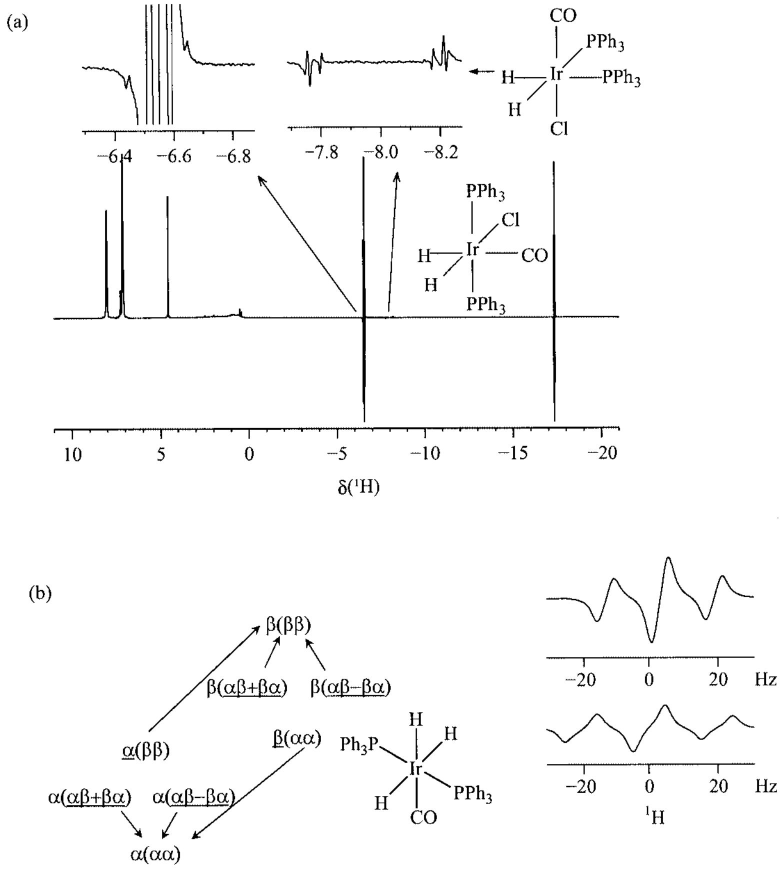
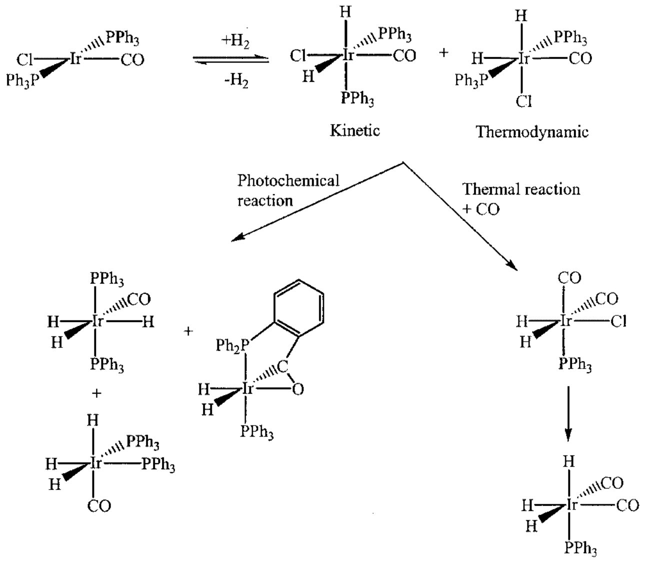


Figure 2. (a) 128 scan ^1H NMR spectrum obtained when a sample of $[IrCl(CO)(PPh_3)_2]$ reacts with *p*-H_2 in C_6D_6 at 295 K; enhanced hydride resonances for the major isomer (corresponding to addition over the Cl−Ir−CO axis) dominate the spectrum; insets illustrate how ^{13}C satellites and signals due to the minor product, corresponding to H_2 addition over the P−Ir−P axis, are visible; (b) energy level diagram for a *p*-H_2 derived metal trihydride complex containing two magnetically equivalent hydride ligands; the *p*-H_2 enhanced hydride resonances of the inset trihydride complex are illustrated (same scale) with the lower trace containing the resonance for the hydride that is *trans* to CO, for which the central feature is missing

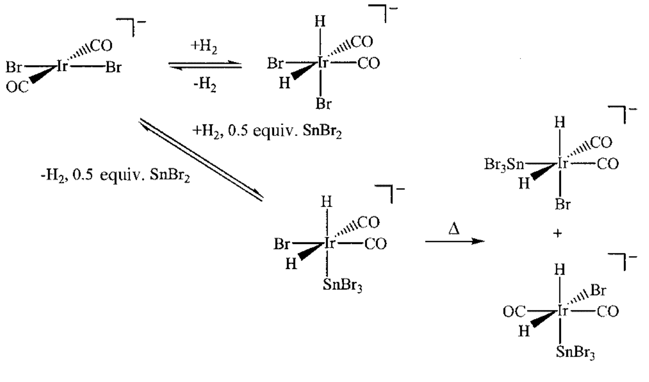
der an atmosphere of p-H_2. Now, a dihydride product corresponding to a species containing a five-membered Ir(CO-C_6H_4-P) ring was detected. This product was suggested to form by CO insertion into an unseen *ortho*-metallation product. The above reactions are summarised in Scheme 3.



Scheme 3. Reaction pathways for $[IrCl(CO)(PPh_3)_2]$ after H_2 addition as detected by p-H_2 NMR spectroscopy

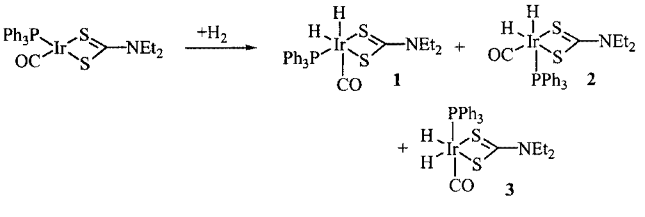
Another example of a complex that was purported not to react with H_2 directly is the 16-electron anion $[IrI_2(CO)_2]^-$ which features in the industrially significant CATIVA process. Oxidative addition of p-H_2 to the tetrabutylammonium salt of $[IrI_2(CO)_2]^-$ resulted in the detection of the all-*cis* $[Ir(H)_2I_2(CO)_2]^-$.[11] Kinetic studies employing EXSY methods resulted in the demonstration that this complex eliminates H_2 on the NMR timescale with the associated activation parameters being indicative of reductive elimination from the 18-electron $[Ir(H)_2I_2(CO)_2]^-$ rather than the 16-electron $[Ir(H)_2I(CO)_2]$. Isomerisation into a second product where the two hydride ligands are *trans* to iodide was found to proceed on a slower time scale via $[I]^-$ loss. Subsequently, these species were detected using normal NMR methods, albeit in a high pressure NMR cell.[12]

More recently, Permin et al. have employed p-H_2 to study the related complex $(Bu_4N)[IrBr_2(CO)_2]$ and its reactions with $SnBr_2$.[13] In the absence of $SnBr_2$, oxidative addition of p-H_2 yields the *all-cis* product $[Ir(H)_2Br_2(CO)_2]^-$, in an analogous manner to that for the iodide complex. However, the addition of 0.5 molar equivalents of $SnBr_2$ to this system results in the formation of the dibromostannyl complex $[Ir(H)_2Br(SnBr_3)(CO)_2]^-$ which isomerises at high temperatures into two other structural forms, as identified in Scheme 4. When a large excess of $SnBr_2$ is employed initially, insertion leads instead to *cis*, *trans*, *cis*-$[Ir(H)_2(SnBr_3)_2(CO)_2]^-$. By studying the relative intensities of the associated PHIP enhanced hydride signals, the authors determined that the presence of one $SnBr_3$ ligand facilitates H_2 addition due to the enhanced σ-donating effect of the new ligand, but that the presence of two such ligands deactivates the system.



Scheme 4. Formation of iridium tribromostannyl anions as detected by PHIP[13]

The utilisation of parahydrogen-induced polarisation to detect minor isomers of metal dihydrides thus clearly marks one of the most widespread successes of the parahydrogen approach. Indeed, when the related d^8 complex $[Ir(CO)(PPh_3)(Et_2dtc)]$ was examined with normal H_2, three dihydride complexes were rapidly formed and their concentrations were shown to rapidly equilibrate (Scheme 5). As expected, it proved a simple matter to assign product structures based on the coupling patterns of the hydride resonances.[14] When parahydrogen was utilised, the hydride resonances of **1** were estimated to be 40-fold enhanced at 298 K and the ratio of signals for **1**:**2** was about 170:1. This implied a kinetic selectivity of ca. 170:1 for the generation of isomer **1** compared with **2**. At 358 K, exchange peaks between the inequivalent hydrides resonances of **1** and **2** were observed with the exchange pathway shown to involve phosphane dissociation. Interestingly, the dominant reaction pathway corresponds to oxidative addition of H_2 over the axis of the starting square-planar complex that contains the CO ligand.



Scheme 5. Species formed by hydrogen addition to $[Ir(S_2CNEt_2)(CO)(PPh_3)]$

Since the parahydrogen approach relies on NMR characterisation, complexes of ^{103}Rh, where $I = 1/2$, have proven to be extremely valuable in establishing this technique. An early example is presented by the oxidative addition of p-H_2 to $[RhCl(PMe_3)_4]$ and $[RhCl(PMe_3)_3]$,[15] where the dihydride products were used to demonstrate that two-dimensional NMR techniques such as COSY, HSQC, HMQC and NOESY could be used with p-H_2. In addition, this study laid the groundwork for many subsequent investigations by showing that rapid chemical-shift detection of ^{31}P and ^{103}Rh nuclei was possible despite the inherent insensitivity of the latter (see Figure 3), that the magnitudes and relative sizes of heteronuclear coupling constants could be determined, and that NOESY methods could be used to probe ligand arrangements and monitor hydride ligand exchange.

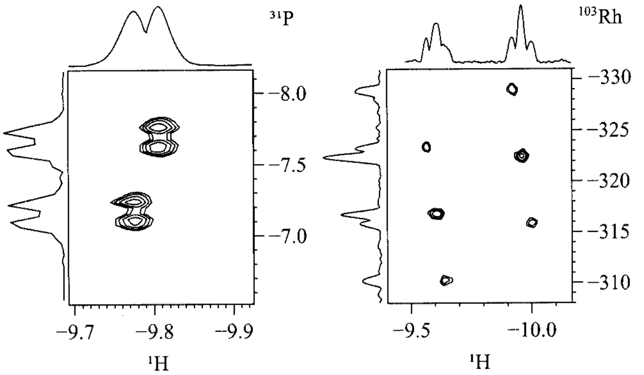


Figure 3. Selected cross-peaks (positive contours) and projections from ^{1}H-^{31}P (left) and ^{1}H-^{103}Rh (right) correlation spectra of $[Rh(H)_2Cl(PMe_3)_3]$ obtained with p-H_2 in CD_2Cl_2 at 313 K

As PHIP is still a relatively new NMR technique, an important part of work in this area consists of case studies that contribute to the understanding of the effect or extend its applications. One such discovery was the observation by Aime et al. that the oxidative addition of parahydrogen to a Rh^{I} centre containing a bound alkene resulted in the polarisation of the alkene protons.[16] Previously, such effects had been ascribed to exchange between the hydrides and the alkene protons.[17] However, isotopic labelling indicated that this was not the case here, and that the transfer of polarisation must occur via cross relaxation (NOE) between the hydrides and the alkene protons. This result has implications in catalytic studies since it means that it may be possible to detect unsaturated molecules bound to metal centres even in absence of hydrogenation or hydride exchange.

Recent work at York has involved extending the parahydrogen technique further via low temperature in-situ UV photolysis.[18] In this study, a 325 nm He-Cd continuous-wave laser was employed to irradiate $[Rh(\eta^5\text{-}C_5H_5)(C_2H_3SiMe_3)_2]$ at 203 K in the presence of p-H_2. Enhanced hydride resonances assigned to $[Rh(\eta^5\text{-}C_5H_5)(H)_2(C_2H_3SiMe_3)]$ were detected in the associated spectra (see Figure 4). This observation reflects an important result in this field since it overcomes the need for rapid thermally initiated H_2 cycling. In addition, it was concluded, on the basis of the photon flux and an estimate of the quantum yield, that the spectra illustrated the detection of 1 nmol of material.

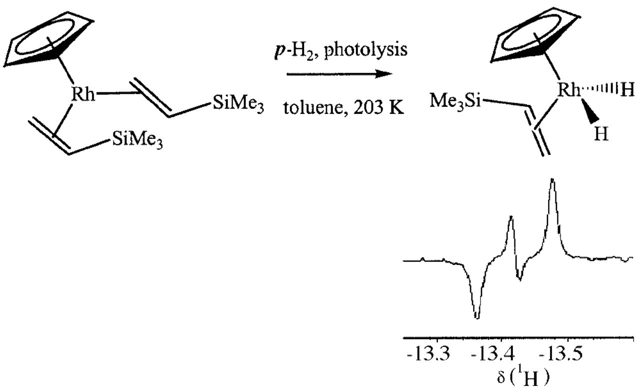


Figure 4. PHIP enhanced ^{1}H spectrum (bottom) showing hydride resonances of the inset dihydride complex obtained during concurrent UV irradiation according to the reaction illustrated

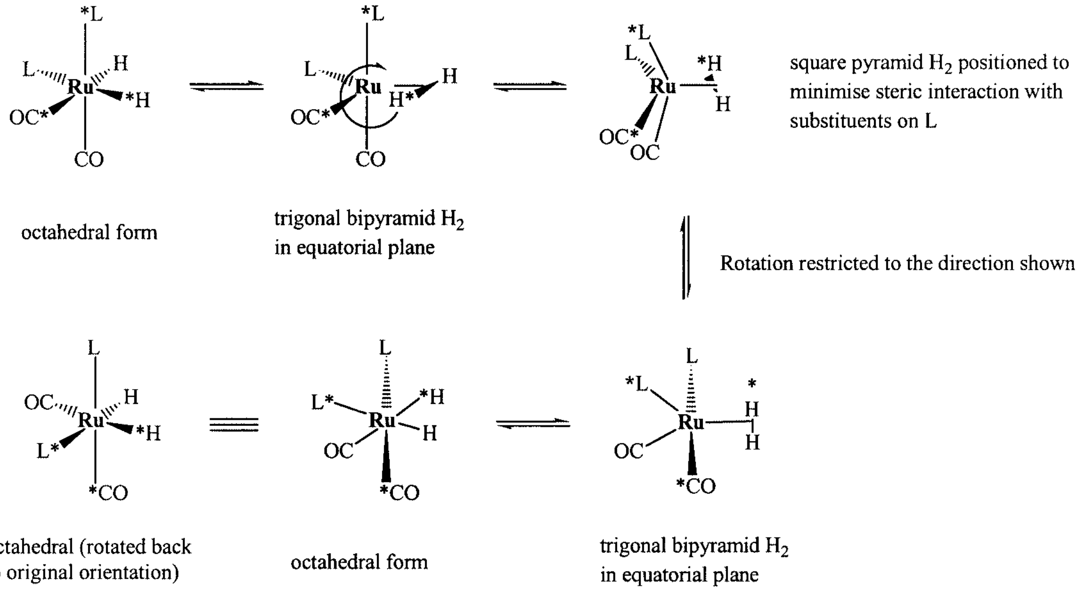
The reactions of stable 18-electron complexes of ruthenium have also been monitored using the PHIP methodology. Indeed, the value of p-H_2 as a mechanistic probe is well illustrated by the highly fluxional system $[Ru(H)_2(CO)_2(Ph_2PCH_2CH_2PPh_2)]$.[19] In this complex, exchange between the hydride ligands and exchange of the phenyl rings was monitored quantitatively by the EXSY approach. In addition, the complex was observed to readily undergo H_2 elimination. The utilisation of p-H_2 indicated that H_2 loss proceeds via a diamagnetic intermediate, since a paramagnetic one would quench any enhancement, and facilitated the elucidation of the mechanism for the exchange process, which was proposed to occur via a trigonal bipyramidal transition state containing an η^2-H_2 ligand (see Scheme 6). Since H-H and P-P interchange occurred at the same rate, a concerted rotation was indicated. When $[Ru(H)_2(CO)_2(dppe)]$ was generated by the in situ photolysis of $[Ru(CO)_3dppe]$, the observation of enhanced hydride resonances was taken to indicate that the intermediate $[Ru(CO)_2dppe]$ exists in a singlet electronic state.

The application of p-H_2 methods to the study of early transition metal complexes is currently much less common, with one recent study involving the preparation of the dimeric tantalum dinitrogen complex $[(Cp^*{}_2TaCl)_2(\mu\text{-}N_2)]$.[20] Upon H_2 addition, two isomers of the dihydride complex $[Cp^*{}_2Ta(H)_2Cl]$ are formed, which are shown in Scheme 7. Since only the asymmetric isomer was expected to show p-H_2 enhancement, PHIP provided a ready means of distinguishing between the two isomers.

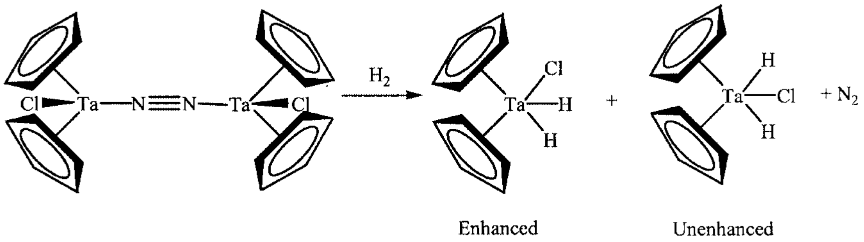
The oxidative addition of H_2 to the related complex $[Cp^*{}_2Ta(CH_2)(H)]$ has also been studied with parahydrogen.[21] This reaction leads to the formation of two enhanced products, $[Cp^*{}_2Ta(CH_3)(H)_2]$ and $[Cp^*{}_2Ta(H)_3]$. Isotopic labelling was used to show that, in both cases, the enhancement is due to two hydride ligands, and a mechanistic pathway involving the unsaturated methylene complex $[Cp^*{}_2Ta(CH_3)]$ was proposed.

4. Parahydrogen in the Study of Binuclear Complexes

Work at York has focused on extending the applications of PHIP methods by studying the reactions of the d^8-rho-



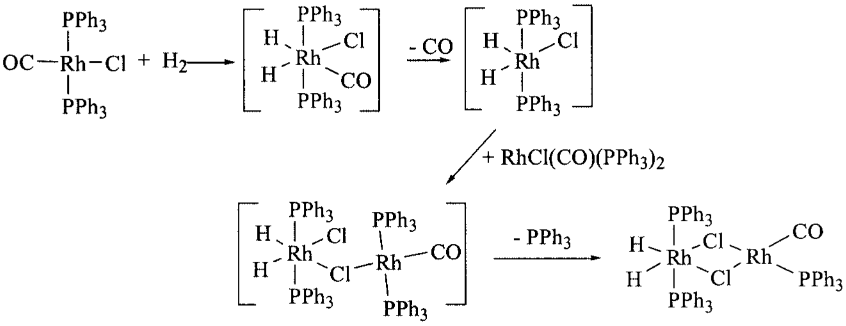
Scheme 6. Proposed mechanism of hydride ligand interchange in $[Ru(H)_2(CO)_2(L)_2]$



Scheme 7. Reaction of a dimeric tantalum dinitrogen complex with parahydrogen

dium complexes $[RhX(CO)(PR_3)_2]$ where X = Cl, Br, I and R = Ph, Me with p-H_2.[22] These complexes were previously not thought to react with hydrogen. In the case of $[RhX(CO)(PPh_3)_2]$, unexpected binuclear products of the general formula $[(H)_2Rh(PPh_3)_2(\mu\text{-}X)_2Rh(PPh_3)(CO)]$ were detected. Since the initial dihydrogen activation product $Rh(H)_2X(CO)(PPh_3)_2$ was not detected in these reactions, it was suggested that facile CO loss led to the generation of the unsaturated species $[Rh(H)_2X(PPh_3)_2]$. The proposed reaction mechanism is shown in Scheme 8.

Surprisingly, when the reaction of $[RhCl(CO)(PMe_3)_2]$ was monitored at 348 K under 3 atm of p-H_2, the major product corresponded to $[H(Cl)Rh(PMe_3)_2(\mu\text{-}H)(\mu\text{-}Cl)Rh(PMe_3)(CO)]$ with bridging and terminal hydride li-



Scheme 8. Suggested route to $[(H)_2Rh(PPh_3)_2(\mu\text{-}Cl)_2Rh(PPh_3)(CO)]$, formed in the reaction of $[RhCl(CO)(PPh_3)_2]$ with p-H_2

gands. However, when $RhI(CO)(PMe_3)_2$ was monitored, the reaction complexity increased still further and several new species were detected. A typical ^1H NMR spectrum from such a reaction is shown in Figure 5. Density functional theory indicated that all structural types correspond to reaction intermediates rather than transition states and Scheme 9 shows how they are formed.

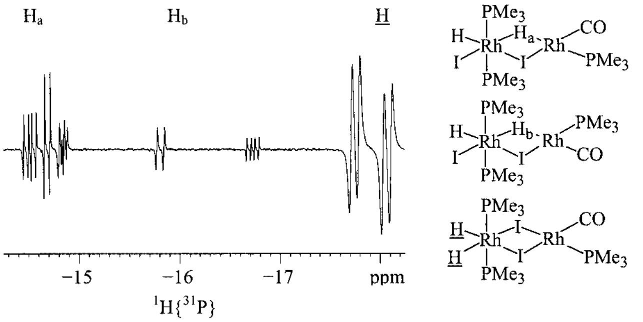


Figure 5. $^1H\{^{31}P\}$ NMR spectrum showing the hydride region after warming a sample of $[RhI(CO)(PMe_3)_2]$ with p-H_2 in C_6D_6 to 348 K; selected product resonances indicated by H_a, H_b and H are assigned according to the inset structures

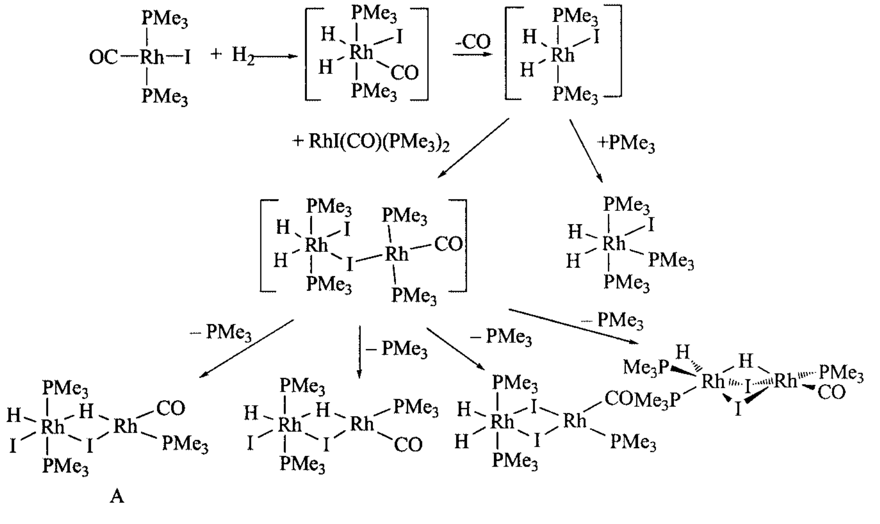
Significantly, when the reaction involving $[RhCl(CO)(PMe_3)_2]$ with p-H_2 was monitored in the presence of styrene, a dramatic increase in the hydride ligand's signal enhancement was observed. This facilitated the detection of $[(H)_2Rh(PMe_3)_2(\mu\text{-}Cl)_2Rh(CO)(PMe_3)]$ and $[HRh(PMe_3)_2(\mu\text{-}H)(\mu\text{-}Cl)_2Rh(CO)(PMe_3)]$ and demonstrated that a sacrificial alkene can dramatically extend the sensitivity of the parahydrogen method by promoting H_2 cycling through the system.[22]

Koch et al. have reported a number of similar complexes that were produced by studying the reactions of the binuclear complex $[RhCl(NBD)_2]_2$ with a range of phosphanes in-situ.[23] The authors noted that if the chloride ligand was replaced by TFA, only mononuclear complexes were observed. More importantly, this paper also described the construction of an apparatus designed to monitor reactions with p-H_2 in situ, by bubbling the gas through the NMR sample via a capillary prior to data acquisition. An NMR method was also reported that eliminated the interference of resonances from unpolarised spin systems. Furthermore, when $[RhCl(NBD)_2]_2$ was examined in methanol at low temperature and in the absence of substrate, an enhanced solvent complex was detected.[24] These techniques have also been used to investigate $SnCl_3$-activated rhodium dihydride complexes.[25] For example, oxidative addition of p-H_2 to the $[RhH(SnCl_3)_5]^{3-}/PR_3$ system (where PR_3 = PPh_3, $PEtPh_2$, PEt_3) in CD_3CN and to $[RhCl(CO)_2]_2/SnCl_2$ yielded enhanced hydride resonances in neutral complexes of the type $Rh(H)_2(PR_3)_3(SnCl_3)$, anions of the form $[Rh(H)_2(PR_3)_2(SnCl_3)_2]^-$, and cations of the form $[Rh(H)_2(PR_3)_3(CD_3CN)]^+$. The relative abundance of these products was found to depend crucially on the type of phosphane. These systems were shown to be active catalysts for the hydrogenation of phenylacetylene.

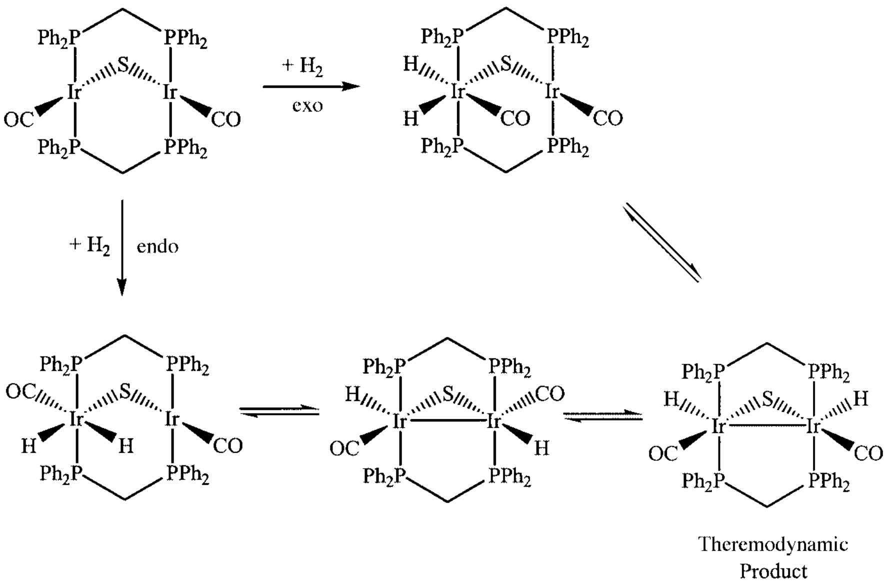
Another example of the use of parahydrogen in the study of binuclear complexes involved iridium, rhodium and mixed-metal A-frame complexes.[26] For $[Ir_2(\mu\text{-}S)(CO)_2(dppm)_2]$, where dppm = bis(diphenylphosphanyl)methane, reaction with hydrogen was found to proceed by two addition pathways corresponding to oxidative addition inside (*endo*) and outside (*exo*) the pocket of the A-frame complex. The previously unseen *exo* addition pathway yields a kinetically significant dihydride that is a key intermediate in the formation of the thermodynamic product of this reaction (Scheme 10).

5. Applications to Transition-Metal Clusters

Due to the presence of multiple metal atoms in transition-metal clusters, the potential reaction pathways of these species are much more complicated than those available to mononuclear complexes. The study of such species



Scheme 9. Reaction pathways available to $[RhCl(CO)(PMe_3)_2]$ that are detected due to the use of p-H_2; when I is replaced by Cl, only A is detected normally, but in the presence of an alkene the four other structural types are also visible in solution



Scheme 10. Hydrogen addition reactions involving an iridium A-frame complex detected by p-H_2

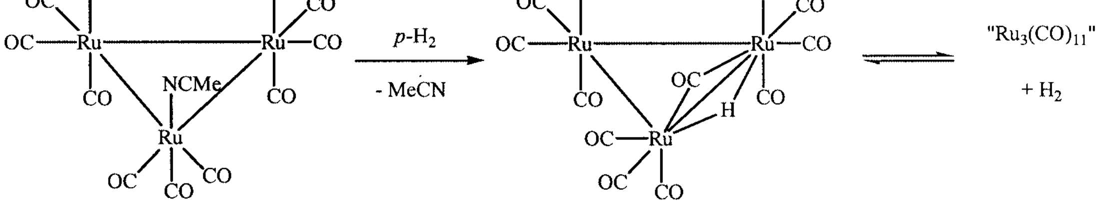
might therefore be expected to benefit greatly from the enhanced sensitivity afforded by p-H_2.

Aime et al. have utilised a triruthenium system to demonstrate that the transfer of polarisation from NMR-silent *para*-hydrogen to NMR-active *ortho*-hydrogen could be achieved via an intermediate with inequivalent hydrides, as shown in Scheme 11.[27] This phenomenon occurs because the symmetry of parahydrogen is broken in the intermediate, with subsequent H_2 elimination occurring rapidly relative to proton relaxation. Under such conditions, the eliminated H_2 molecule retains a "memory" of the intermediate and is consequently polarised. In practice, under these conditions, a strong emission signal is observed for the free hydrogen resonance.

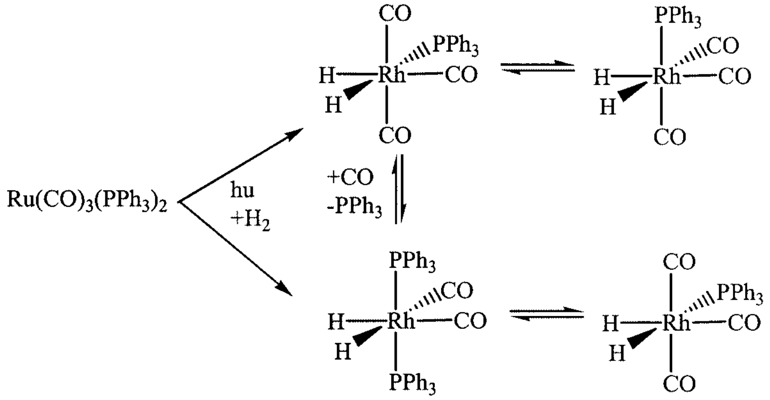
In York, our work in the area of cluster chemistry developed from the study of the reactions of $[Ru(H)_2(CO)_3(PPh_3)]$ and $[Ru(H)_2(CO)_2(PPh_3)_2]$ with p-H_2.[28] These complexes were prepared from $[Ru(CO)_3(PPh_3)_2]$, and two dihydride isomers were detected in both cases, as shown in Scheme 12. The former species was also generated by fragmentation of the trinuclear cluster $[Ru_3(H)(\mu\text{-}H)(CO)_9(PPh_3)_3]$.

Using the full repertoire of NMR approaches illustrated in this review, we have gained insights into the dynamic behaviour and catalytic activity of the triruthenium clusters $[Ru_3(CO)_{12-x}(PR_3)_x]$ (where PR_3 = PPh_3, PMe_2Ph, PMe_3, PCy_3; $x = 1-3$). Thus, when $x = 2$, oxidative addition of p-H_2 results in the formation of three isomers of $[Ru_3(H)(\mu\text{-}H)(CO)_9(PR_3)_2]$, which differ in the arrangement of their equatorial phosphanes: while one isomer contains both phosphanes on the same ruthenium centre, in the other two the phosphanes are located in different orientations on separate metal centres (see Figure 6).[29] These dihydride products were fully characterised in situ by ^1H, ^{13}C and ^{31}P NMR spectroscopy. Kinetic studies revealed the presence of intra- and inter-isomer hydride exchange processes, with activation parameters and solvent effects indicating the involvement of ruthenium−ruthenium bond heterolysis and CO loss in the respective rate-determining steps. When $x = 3$, reaction with H_2 proceeds to form identical products to those found with $x = 2$, although at a slower rate, while when $x = 1$ a single isomer of $[Ru_3(H)(\mu\text{-}H)(CO)_{10}(PR_3)]$ is formed.

The three isomers of $[Ru_3(H)(\mu\text{-}H)(CO)_9(PPh_3)_2]$ were shown to play a kinetically significant role in the hydrogenation of an alkyne substrate via initial CO loss (see Figure 7), with rates of H_2 transfer being explicitly determined for each isomer.[30] This was achieved by using EXSY to monitor the movement of parahydrogen-enhanced nuclei in complexes that are normally invisible. A less-significant



Scheme 11. Proposed mechanism for p-H_2 addition to $[Ru_3(CO)_{11}(NCMe)]$, yielding an enhanced emission resonance for free H_2



Scheme 12. Ruthenium dihydride complexes detected using parahydrogen

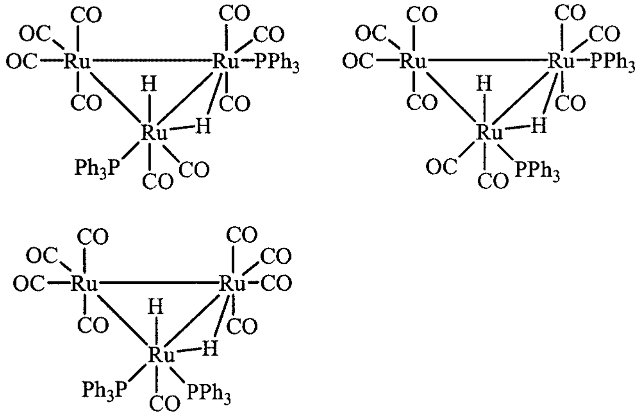
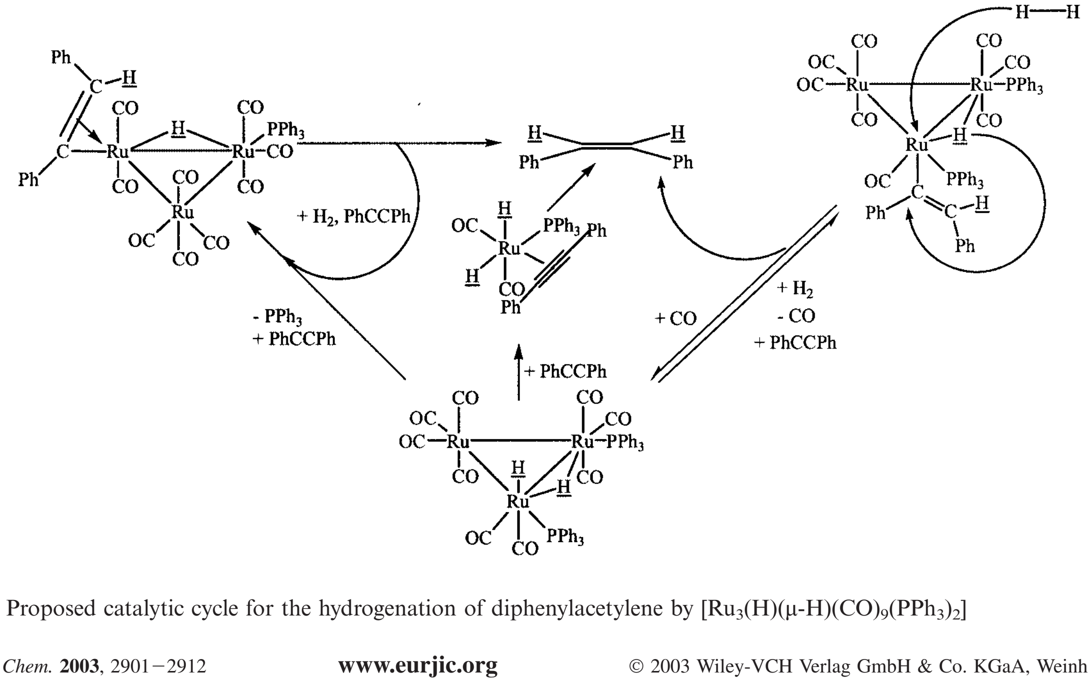


Figure 6. Isomers formed by H_2 addition to $[Ru_3(CO)_{10}(PPh_3)_2]$ detected via p-H_2

secondary reaction involving loss of L to yield a product containing both a pendant vinyl unit and a bridging hydride ligand was also observed, as were competing pathways involving fragmentation to form the less-active species $[Ru(H)_2(CO)_2(L)(alkyne)]$. The mechanism of catalytic hydrogenation is shown in Scheme 13. The abundance of the dihydride intermediates formed was shown to increase with the steric bulk of the phosphane, while their catalytic activity increased with the basicity of the phosphane, such that PPh_3 was the optimum phosphane for catalysis.[31] Significantly, polar solvents were found to facilitate catalysis by intact clusters while non-polar solvents led to increased cluster fragmentation. Furthermore, the activity of cluster-based intermediates was shown to be much greater than that of mononuclear fragments, a discovery with important implications for the study of catalysis by transition metal clusters.

A study of the hydrogenation of alkynes by the triosmium cluster $[Os_3(\mu\text{-}H)_2(CO)_{10}]$ led to the detection and characterisation of a range of vinyl hydride clusters.[32] Here, transfer of p-H_2 nuclei into the bound organic substrates was detected without alkene elimination. Parahydrogen has also been employed to support classical methods in the study of transition metal clusters during the investi-



Scheme 13. Proposed catalytic cycle for the hydrogenation of diphenylacetylene by $[Ru_3(H)(\mu\text{-}H)(CO)_9(PPh_3)_2]$

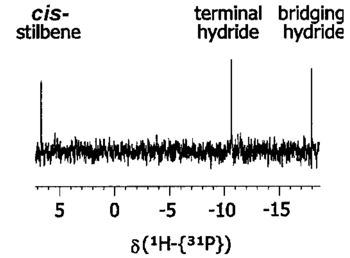


Figure 7. $^{1}H\{^{31}P\}$ EXSY spectrum obtained during the reaction of $[Ru_3(CO)_{10}(PPh_3)_2]$ with parahydrogen and diphenylacetylene in CD_3NO_2; the resonance corresponding to the terminal hydride of $[Ru_3(H)(\mu\text{-}H)(CO)_9(PPh_3)_2]$ was selectively excited; direct transfer of magnetisation into the bridging site on the cluster and into the hydrogenation product *cis*-stilbene are clearly evident after 700 ms

gations of hydride exchange in $[Os_3(\mu\text{-}H)_2(CO)_{10}]$.[33] Initially, studies using a mixture of H_2 and D_2 led to the proposal that the exchange proceeds via the formation of an $[Os_3(H)_2(D)_2(CO)_{10}]$ species, which is then able to undergo an H-D exchange prior to eliminating a hydrogen molecule as either H_2, HD or D_2. With the signal gain afforded by p-H_2, the existence of this process was confirmed and the tetrahydride intermediate was detected. In addition, a second pathway where H_2 dissociates from the cluster to yield a highly unsaturated $[Os_3(CO)_{10}]$ moiety was observed. This latter process results in no isotopic mixing. The rates for the two processes were determined via EXSY methods and subsequent kinetic simulations. It was found that the pathway involving initial hydrogen dissociation was much slower, but its efficiency and importance increased with temperature. More recently, a p-H_2 study involving triosmium μ_3-quinolyl trihydride clusters demonstrated that trihydride-containing clusters can be studied using this approach with all three hydride resonances showing polarisation due to fluxionality and cross polarisation effects.[34]

6. Catalytic Studies

Additional catalytic studies have been completed by Bargon et al., who have developed the DYPAS (DYnamic PASadena) method to measure reaction rates.[35] This method, based on the earlier ROCHESTER approach,[36] can be used to determine the rate of any process that involves the formation and decay of a parahydrogen signal. DYPAS involves the introduction of a variable delay between the addition of p-H_2 to the system and the 45° excitation pulse, yielding a plot of intensity versus time (see Figure 8). If the mechanistic scheme for the process is known, then the signal decay can be described by a series of differential equations, which can be solved to yield specific rate constants.

Hydrogenation reactions have also been studied using one-dimensional sequences involving the NOESY and ROESY effects. For example, in a study of styrene hydrogenation by $[Rh(dppb)]^{+}$, two sets of enhanced resonances were observed for the ethylbenzene hydrogenation product.[37] Using NOESY, it proved possible to determine that one of these signals corresponded to free ethylbenzene, while the other was due to ethylbenzene still bound to the Rh catalyst.

PHIP methodology has also been used to study stereoselective hydrogenation reactions. This approach relies on the difference between $^{2}J_{H,H}$ values for E and Z alkenes. For instance, Bargon et al. have shown that when $[Cp^{*}Ru(alkene)]^{+}$ was the catalyst, non-phenyl-substituted alkynes selectively formed the (E)-alkene while phenyl-substituted alkynes did likewise at low temperature, but increasingly favoured the (Z) isomer as the temperature was raised.[38] The same group has also reported several investigations into the homogeneous hydrogenation of dehydroamino acids using parahydrogen.[39] This work included the determination of the reaction mechanism and the quantification of the reaction rate. Interestingly, the intermediates detected in this reaction (see Figure 9) suggested that an initial agostic hydride species was formed (as evidenced by the ^{1}H resonance at the unusual δ value of -1.9 ppm, which exhibited a strong $^{1}J_{H,C}$ coupling of 86 Hz) that subsequently yielded an alkylhydride, which is the active species in hydrogenation.

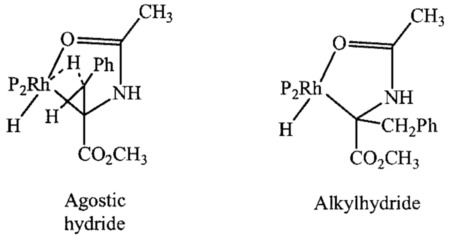


Figure 9. Intermediates detected during homogeneous hydrogenation of dehydroamino acids, where P_2 = PHANEPHOS

If a hydrogenation reaction is rapid, polarisation-transfer effects can be utilised to study secondary reactions and hence more complex catalytic transformations can be inves-

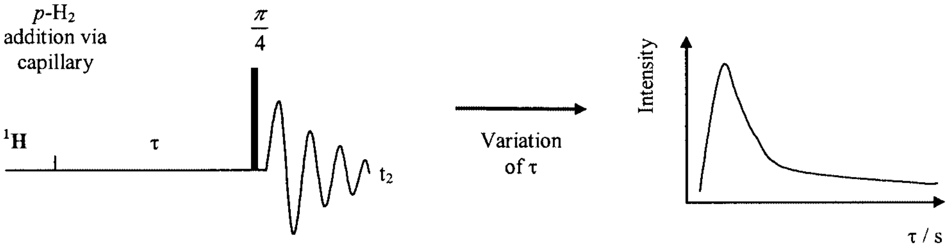
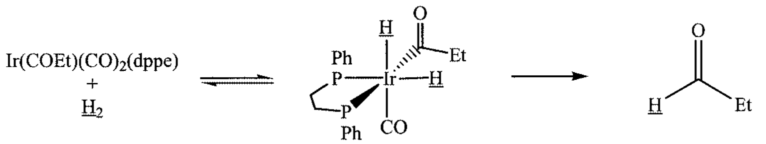


Figure 8. Pulse sequence and methodology of the DYPAS experiment



Scheme 14. System used by Eisenberg to detect one-hydrogen PHIP; the marked protons give rise to enhanced resonances

tigated. For instance, Koch et al. monitored the hydrogenation of 1-phenylpropyne by a Rh^{I} catalyst.[40] In the presence of parahydrogen, enhanced resonances for the product *cis*-1-phenylpropene are observed. If a dilute solution of bromine was added in situ, the subsequent alkane, 1,2-dibromo-1-phenypropane, proved also to be enhanced. This species has two chiral centres, and both diastereoisomers were detected.

This review has already illustrated how PHIP can be used to observe heteronuclei via radio frequency mediated polarisation transfer. However, if hydrogenation occurs in a weak magnetic field (i.e. outside the spectrometer), the resulting spin systems are strongly coupled and efficient polarisation transfer from ^{1}H to heteronuclei becomes possible via cross-relaxation and can be detected as the ALTADENA effect. A nice example of this result is provided by the hydrogenation of long-chain alkynes (4−8 carbon atoms), where polarisation of all the ^{13}C nuclei in the carbon chain of the alkene is observed.[41]

Very recently, a hydroformylation product containing a single parahydrogen atom has been successfully sensitised. This result was observed during the addition of p-H$_2$ to an acetone solution of *trans*-[PtCl(COEt)(PPh$_3$)$_2$] and SnCl$_2$ (see Scheme 14), as well as to [Ir(COEt)(CO)$_2$(dppe)]. These systems initially form dihydride products that subsequently eliminate propanal; this product appears with an enhanced aldehydic proton resonance.[42] This effect, termed OH-PHIP (one-hydrogen PHIP) was considerably weaker than regular PHIP and was attributed to the strong coupling that exists between the protons in the initial dihydride product.

7. Other Developments

In addition to the above examples, there have been a number of novel applications of the PHIP phenomenon that stand on their own. For example, Ulrich et al. have reported PHIP hydrogenation experiments in the presence of NMR shift-reagents.[43] The lanthanide shift-reagents cause resonance shifts due to their paramagnetic character, which unfortunately also quenches the parahydrogen enhancement. While small amounts of a racemic shift-reagent were sufficient to cause a substantial resonance shift without fully quenching the parahydrogen, the use of chiral shift-reagents yielded only a small perturbation. The authors concluded that the amount of shift-reagent required was too large to be tolerated by the parahydrogen and that optically active solvents would provide a better method to differentiate enantiomers using PHIP.

Parahydrogen has also been utilised to investigate colloidal catalysis.[44] The reaction of phenylacetylene with hydrogen using the colloidal palladium catalyst Pd$_x$[N(octyl)$_4$Cl]$_y$ was observed to yield enhanced signals in the product species. In another study, PHIP was used to study reversible H$_2$ adsorption on ZnO.[45] A prominent enhancement pattern was observed, which was attributed to p-H$_2$ chemisorbed on ZnO. Furthermore, parahydrogen has recently been employed in magnetic resonance imaging (MRI), where it was used to obtain enhanced ^{13}C resonances in vivo via initial polarisation transfer outside the strong field of the spectrometer, corresponding to the utilisation of ALTADENA.[46] Although only preliminary, these studies represent new opportunities for the PHIP effect.

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[1] C. R. Bowers, D. P. Weitekamp, *Phys. Rev. Lett.* **1986**, *57*, 2645−2648.

[2] [2a] C. R. Bowers, D. P. Weitekamp, *J. Am. Chem. Soc.* **1987**, *109*, 5541−5542. [2b] T. C. Eisenschmid, R. U. Kirss, P. A. Deutsch, S. I. Hommeltoft, R. Eisenberg, J. Bargon, R. G. Lawler, A. L. Balch, *J. Am. Chem. Soc.* **1987**, *109*, 8089−8091.

[3] S. B. Duckett, C. L. Newell, R. Eisenberg, *J. Am. Chem. Soc.* **1994**, *116*, 10548−10556.

[4] K. F. Bonhoeffer, P. Harteck, *Z. Phys. Chem.* **1929**, *B4*, 113.

[5] [5a] M. D. Pravica, D. P. Weitekamp, *Chem. Phys. Lett.* **1983**, *145*, 255−258. [5b] R. Eisenberg, T. C. Eisenschmid, M. S. Chinn, R. U. Kirss, *Adv. Chem. Ser. D* **1992**, *230*, 47−74.

[6] [6a] C. R. Bowers, D. H. Jones, N. D. Kurur, J. A. Labinger, M. G. Pravica, D. P. Weitekamp, *Adv. Magn. Reson.* **1990**, *14*, 269. [6b] R. Eisenberg, *Acc. Chem. Res.* **1991**, *24*, 110−116. [6c] J. Natterer, J. Bargon, *Prog. Nucl. Magn. Reson. Spectrosc.* **1997**, *31*, 293−315. [6d] S. B. Duckett, C. J. Sleigh, *Prog. Nucl. Magn. Reson. Spectrosc.* **1999**, *34*, 71−92.

[7] [7a] L. Vaska, M. F. Wernke, *Trans. N. Y. Acad. Sci.* **1971**, *33*, 80. [7b] R. Ugo, A. Pasini, S. Cenini, *J. Am. Chem. Soc.* **1972**, *94*, 7364−7370.

[8] A. L. Sargent, M. B. Hall, *Inorg. Chem.* **1992**, *31*, 317−321.

[9] [9a] S. K. Hasnip, S. B. Duckett, C. J. Sleigh, D. R. Taylor, G. K. Barlow, M. J. Taylor, *Chem. Commun.* **1999**, 1717−1718. [9b] S. K. Hasnip, S. A. Colebrooke, C. J. Sleigh, S. B. Duckett, D. R. Taylor, G. K. Barlow, M. J. Taylor, *J. Chem. Soc., Dalton Trans.* **2002**, 743−751.

[10] [10a] S. K. Hasnip, S. B. Duckett, D. R. Taylor, M. J. Taylor, *Chem. Commun.* **1998**, 923−924. [10b] S. P. Millar, D. L. Zubris,

J. E. Bercaw, R. Eisenberg, *J. Am. Chem. Soc.* **1998**, *120*, 5329−5330.

[11] S. K. Hasnip, S. B. Duckett, D. R. Taylor, G. K. Barlow, M. J. Taylor, *Chem. Commun.* **1999**, 889−890.

[12] R. Churlaud, U. Frey, F. Metz, A. E. Merbach, *Inorg. Chem.* **2000**, *39*, 4137−4142.

[13] A. Permin, R. Eisenberg, *Inorg. Chem.* **2002**, *41*, 2451−2458.

[14] G. Suardi, B. P. Cleary, S. B. Duckett, C. Sleigh, M. Rau, W. E. Reed, J. A. B. Lohman, R. Eisenberg, *J. Am. Chem. Soc.* **1997**, *119*, 7716−7725.

[15] B. A. Messerle, C. J. Sleigh, M. G. Partridge, S. B. Duckett, *J. Chem. Soc., Dalton Trans.* **1999**, 1429−1435.

[16] S. Aime, D. Canet, W. Dastru, R. Gobetto, F. Reineri, A. Viale, *J. Phys. Chem. A* **2001**, *105*, 6305−6310.

[17] [17a] A. Harthun, R. Selke, J. Bargon, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2505−2507. [17b] A. Harthun, R. Giernoth, C. J. Elsevier, J. Bargon, *Chem. Commun.* **1996**, 2483−2484.

[18] C. Godard, P. Callaghan, J. L. Cunningham, S. B. Duckett, J. A. B. Lohman, R. N. Perutz, *Chem. Commun.* **2002**, 2836−2387.

[19] D. Schott, C. J. Sleigh, J. P. Lowe, S. B. Duckett, R. J. Mawby, M. G. Partridge, *Inorg. Chem.* **2002**, *41*, 2960−2970.

[20] D. C. Bregel, S. M. Oldham, R. J. Lachicotte, R. Eisenberg, *Inorg. Chem.* **2002**, *41*, 4371−4377.

[21] D. C. Bregel, S. M. Oldham, R. Eisenberg, *J. Am. Chem. Soc.* **2002**, *124*, 13827−13832.

[22] [22a] P. D. Morran, S. B. Duckett, P. R. Howe, J. E. McGrady, S. A. Colebrooke, R. Eisenberg, M. G. Partridge, J. A. B. Lohman, *J. Chem. Soc., Dalton Trans.* **1999**, 3949−3960. [22b] S. A. Colebrooke, S. B. Duckett, J. A. B. Lohman, *Chem. Commun.* **2000**, 685−686.

[23] A. Koch, J. Bargon, *Inorg. Chem.* **2001**, *40*, 533−539.

[24] H. Heinrich, R. Giernoth, J. Bargon, J. M. Brown, *Chem. Commun.* **2001**, 1296−1297.

[25] [25a] A. Koch, C. Ulrich, J. Bargon, *Tetrahedron* **2000**, *56*, 3177−3179. [25b] C. Ulrich, A. Permin, V. Petrosyan, J. Bargon, *Eur. J. Inorg. Chem.* **2000**, 889−894.

[26] S. M. Oldham, J. M. Houlis, C. J. Sleigh, S. B. Duckett, R. Eisenberg, *Organometallics* **2000**, *19*, 2985−2993.

[27] S. Aime, W. Dastru, R. Gobetto, A. Russo, A. Viale, D. Canet, *J. Phys. Chem. A* **1999**, *103*, 9702−9705.

[28] C. J. Sleigh, S. B. Duckett, R. J. Mawby, J. P. Lowe, *Chem. Commun.* **1999**, 1223−1224.

[29] D. Blazina, S. B. Duckett, P. J. Dyson, B. F. G. Johnson, J. A. B. Lohman, C. J. Sleigh, *J. Am. Chem. Soc.* **2001**, *123*, 9760−9768.

[30] D. Blazina, S. B. Duckett, P. J. Dyson, J. A. B. Lohman, *Angew. Chem. Int. Ed.* **2001**, *40*, 3874−3877.

[31] D. Blazina, S. B. Duckett, P. J. Dyson, J. A. B. Lohman, *Chem. Eur. J.* **2003**, *9*, 1046−1061.

[32] R. Gobetto, L. Milone, F. Reineri, L. Salassa, A. Viale, E. Rosenberg, *Organometallics* **2002**, *21*, 1919−1924.

[33] [33a] S. Aime, W. Dastru, R. Gobetto, J. Krause, L. Matas, A. Viale, *Organometallics* **1996**, *15*, 4967−4970. [33b] S. Aime, W. Dastru, R. Gobetto, F. Reineri, A. Russo, A. Viale, *Organometallics* **2001**, *20*, 2924−2927.

[34] B. Bergman, E. Rosenberg, R. Gobetto, S. Aime, L. Milone, F. Reineri, *Organometallics* **2002**, *21*, 1508−1511.

[35] P. Hübler, R. Giernoth, G. Kümmerle, J. Bargon, *J. Am. Chem. Soc.* **1999**, *121*, 5311−5318.

[36] M. S. Chinn, R. Eisenberg, *J. Am. Chem. Soc.* **1992**, *114*, 1908−1909.

[37] P. Hübler, J. Bargon, *Angew. Chem. Int. Ed.* **2000**, *39*, 3701−3703.

[38] D. Schleyer, H. G. Niessen, J. Bargon, *New J. Chem.* **2001**, *25*, 423−426.

[39] [39a] R. Giernoth, H. Heinrich, N. J. Adams, R. J. Deeth, J. Bargon, J. M. Brown, *J. Am. Chem. Soc.* **2000**, *122*, 12381−12382. [39b] S. Wildschutz, P. Hübler, J. Bargon, *Chem. Phys. Chem.* **2001**, *5*, 328−331.

[40] A. Koch, J. Bargon, *Magn. Reson. Chem.* **2000**, *38*, 216−220.

[41] M. Stephan, O. Kohlman, H. G. Niessen, A. Eichhorn, J. Bargon, *Magn. Reson. Chem.* **2002**, *40*, 157−160.

[42] A. B. Permin, R. Eisenberg, *J. Am. Chem. Soc.* **2002**, *124*, 12406−12407.

[43] C. Ulrich, J. Bargon, *Prog. Nucl. Magn. Reson. Spectrosc.* **2000**, *38*, 33−37.

[44] A. Eichhorn, A. Koch, J. Bargon, *J. Mol. Catal. A: Chem.* **2001**, *174*, 293−295.

[45] P. J. Carson, C. R. Bowers, D. P. Weitekamp, *J. Am. Chem. Soc.* **2001**, *123*, 11821−11822.

[46] K. Golman, O. Axelsson, H. Johannesson, S. Mansson, C. Olofsson, J. S. Petersson, *Magn. Reson. Med.* **2001**, *46*, 1−5.

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