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Review

Parahydrogen-based NMR methods as a mechanistic probe in inorganic chemistry

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Abstract

The study of reactions by NMR spectroscopy is normally limited by the poor detection limits offered by the method. An overview is presented of how chemical reactions can be studied using parahydrogen-assisted NMR spectroscopy, where detected signals can have strengths that exceed those normally available by factors that approach 31,000.

Keywords: NMR; Parahydrogen; Mechanism; Photochemistry; Hydrogenation; Catalysis

1. Introduction

Many metal complexes react with molecular hydrogen, forming complexes with either discrete η^2-H_2 moieties or 'classical' metal-hydride ligands. NMR spectroscopy is often a convenient way to monitor these reactions and characterise their products because the ^{1}H nuclei of these ligands generally resonate in a characteristically high field region of the NMR spectrum. However, if the hydrogen addition reaction is unfavourable, or if the product is rapidly consumed in a subsequent reaction, then the species will exist only in low concentration. This situation might be expected if the metal–hydrogen species is predicted to act as an intermediate in a catalytic process. Under these conditions, the low concentration of the metal–hydrogen species would render the NMR approach less effective as a tool for characterisation, due to the inherent insensitivity of the NMR technique. While kinetic evidence plays in important role in determining the mechanisms of such catalytic processes, and theoretical methods may predict the existence and structure of the associated reaction intermediates, the detection and characterisation of these intermediate species remains essential. For this reason, any method by which the sensitivity of NMR spectroscopy can be increased is potentially significant. One such method is the use of parahydrogen (p-H_2), molecular hydrogen

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enriched in the *para* nuclear spin state. This review summarises the ways in which parahydrogen-enhanced NMR methods (often referred to as ParaHydrogen Induced Polarisation, or PHIP) have contributed to our understanding of reactions with molecular hydrogen, with particular emphasis being placed on illustrating how the technique has contributed to the elucidation of reaction mechanisms.

The initial prediction [1] and demonstration [2] of this phenomenon was made by Bowers and Weitekamp in the late 1980's. Since the inception of this field of enquiry, the chemical [3–7] and theoretical [8,9] concepts that underpin the phenomenon have been periodically reviewed.

1.1. The existence of spin-isomers of hydrogen

Molecular hydrogen exists as two isomers, termed *para*- and orthohydrogen, which differ in their nuclear spin configurations. The existence of these isomers derives from the Pauli principle, which requires that the overall wavefunction describing fermions (a class of particle to which protons belong) is antisymmetric with respect to the exchange of nuclei. The overall wavefunction of hydrogen is composed of electronic, translational, vibrational, rotational and nuclear contributions; since the electronic, translational, and vibrational components are all symmetric, it follows that the product of the rotational and nuclear contributions must be antisymmetric. Thus, symmetric nuclear configurations are restricted to antisymmetric rotational states (with $J = 1, 3, 5, \ldots$), and antisymmetric nuclear configurations are restricted to symmetric rotational states (with $J = 0, 2, 4, \ldots$). In the case of molecular hydrogen, the αα, ββ, and αβ + βα nuclear configurations are symmetric, and are collectively termed orthohydrogen, while the αβ–βα nuclear configuration is antisymmetric, and is termed parahydrogen. The difference in rotational states accessible to the two isomers leads to a difference in energy—parahydrogen is more stable than orthohydrogen, as it can access a lower energy rotational state. This difference in energy leads to a Boltzmann distribution among the isomers, with a greater equilibrium concentration of parahydrogen favoured by lower temperatures. Interconversion between the *ortho* and *para* isomers is forbidden, but can occur in the presence of paramagnetic material. *Para*-enriched hydrogen can therefore be prepared by cooling hydrogen gas in the presence of a suitable interconversion catalyst; isolation of the gas from the catalyst preserves the low-temperature equilibrium, even as the hydrogen returns to ambient temperature. In this way, essentially pure parahydrogen can be prepared by cooling to 20 K (Fig. 1); alternatively, 50% *para*-enriched hydrogen can be prepared in any well-equipped laboratory by cooling hydrogen gas in a bath of liquid nitrogen (*vide infra*, Section 1.3). It is also possible to prepare *ortho*-enriched hydrogen, by exploiting the preferential adsorption of orthohydrogen on diamagnetic surfaces at low temperatures [10].

1.2. Parahydrogen-enhanced NMR

When dihydrogen reacts with a molecular species in a *spin-correlated* manner, the initial spin configurations of the hydrogen nuclei are often preserved in the product. In this way, the use of parahydrogen as a reactant can selectively populate the αβ and βα spin states of the product; in other words, the product has been synthesised in a specific nuclear spin state. Perhaps the easiest way to visualise this effect is in terms of an AX spin system, such as that which would be formed from the oxidative addition of dihydrogen to a metal centre that creates two chemically inequivalent hydride ligands; this situation is represented in Fig. 2.

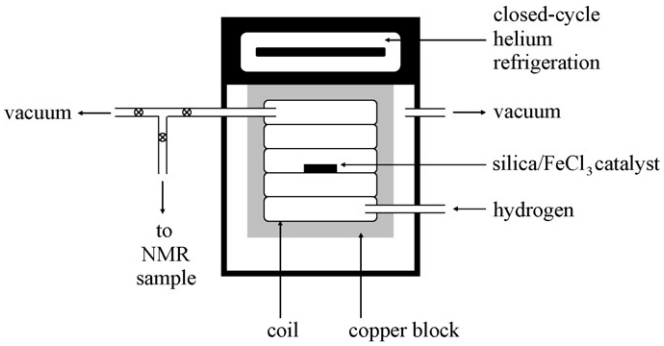

Fig. 1. Apparatus used to generate pure parahydrogen.

It can be seen from Fig. 2 that the use of *para*-enriched hydrogen in a reaction of this type should lead to much greater population differences between transitions than when 'normal' hydrogen is used. Since the intensity of the NMR signals is critically dependent on this difference in population, the parahydrogen-derived distribution (Fig. 2b) gives rise to much more intense signals than are observed with the standard Boltzmann-derived distribution (Fig. 2a); these signals also exhibit a characteristic antiphase profile because of the inverted sense of the population difference associated with these transitions. If the reaction with parahydrogen occurs in the Earth's relatively weak magnetic field, and the sample is subsequently transferred into the strong magnetic field of the NMR spectrome-

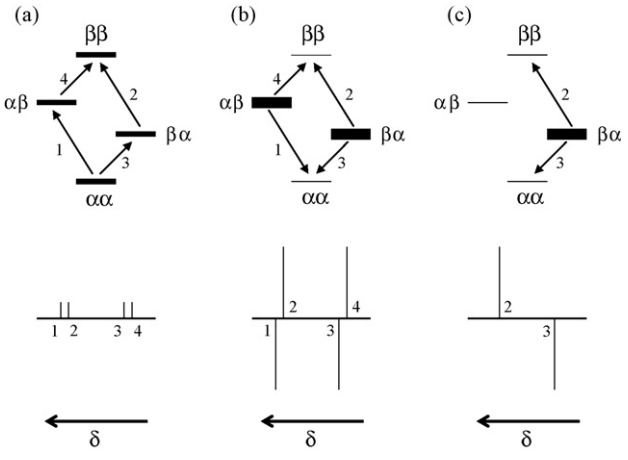

Fig. 2. The energy levels of an AX spin system, with the population of each spin state represented by line thickness. The transitions between energy levels and the corresponding NMR signals are shown, for a negative value of J_{AX}: (a) standard Boltzmann-derived population distribution; (b) parahydrogen-derived population distribution; (c) population distribution under parahydrogen-derived ALTADENA conditions.

ter, a related effect termed ALTADENA may occur (Fig. 2c); this arises from selective population of only one of the product spin states, giving rise to two antiphase NMR signals [11,4]. Since the ALTADENA effect can only be observed for a relatively short time its application in mechanistic studies is relatively limited, although it has been involved in providing some significant observations (*vide infra*, Section 2.2). It should also be noted that the use of *ortho*-enriched hydrogen as a reactant also leads to enhanced product resonances (with opposite phases to the parahydrogen-derived signals) *via* selective population of the product spin states. However, the signal enhancement in the orthohydrogen case is necessarily of lower magnitude than that arising from the use of parahydrogen, and it has consequently found less widespread use in the literature [10].

1.3. Experimental considerations

In addition to the enrichment of hydrogen in the *para* spin state, there are a number of other requirements which must be fulfilled in order to observe parahydrogen enhancement. First, as described above, in order for there to be a selective population of the αβ and βα spin states of the product, the reaction with parahydrogen must proceed in a spin-correlated fashion. In practice, this means that both parahydrogen nuclei must be transferred into the same product molecule, while maintaining their spin-spin coupling throughout the reaction. Furthermore, in order for enhanced signals to be observed, it is also necessary for the symmetry of the parahydrogen molecule to be broken at some stage during the addition process. Upon the fulfilment of these two conditions, it should be possible to observe enhanced proton resonances; however, if the relaxation rate of the former parahydrogen nuclei is fast relative to the rate of parahydrogen addition, the hydrogen spin states will equilibrate before they can be interrogated. A final condition, then, is that the rate of relaxation of the product ^{1}H nuclei is relatively slow. For this reason, the parahydrogen approach is generally unsuitable for the examination of dihydrogen complexes, although Bargon and co-workers have succeeded in polarising the protons of organic molecules when they are hydrogenated by a dihydrogen complex [12].

If a system fulfils the physical requirements for exhibiting parahydrogen enhancement, it is possible to observe the PHIP effect by NMR spectroscopy using certain pulse sequences. In general, standard pulse sequences for the detection of ^{1}H resonances are inappropriate for this purpose; the pulse sequences used have generally been designed specifically or adapted from existing sequences. For instance, in a simple ^{1}H NMR experiment, the maximum proton enhancement is achieved by the application of a $\pi/4$ (45°) pulse, instead of the conventional $\pi/2$ (90°) pulse. This, along with the other modifications necessary for more complex parahydrogen NMR studies, is described extensively in existing literature reviews, and in the original published reports of the pulse sequences [2,13–24]. Among the advances detailed in these reports, it is particularly worth noting that methods have been developed which allow the parahydrogen-derived enhancement to be transferred to other nuclei by the use of appropriate NMR experiments, so that the characterisation of species by this approach is by no means restricted to ^{1}H nuclei alone.

In addition, Bargon and co-workers [25] demonstrated, and Golman et al. have exploited [26], spontaneous polarisation transfer from *para*-H_2 to heteronuclei such a ^{13}C or ^{19}F in saturated molecules that are formed from unsaturated counterparts during rapid hydrogenation reactions in low field. Aime et al. have published an elegant explanation of the mechanism of polarisation transfer to X in AA′X and $A_2A_2'X$ spin systems that results from the hydrogenation of a double bond (where A is ^{1}H and X is ^{13}C) [9].

An idiosyncrasy of the parahydrogen NMR approach is that, unlike in conventional methods, it is not necessary to wait for the nuclei to relax between pulses in order to derive the maximum signal. This is because, once a set of enhanced former parahydrogen nuclei have been interrogated, they relax to the normal Boltzmann distribution of spin states, thereby ceasing to be enhanced. In this way, each nucleus will only exhibit enhancement once. Therefore, in order to maintain enhancement, it is necessary to keep creating new enhanced nuclei in the system, by reacting new molecules of parahydrogen. This can be achieved by transmitting *para*-enriched hydrogen to an NMR sample tube, already in place in the NMR spectrometer, by means of a capillary [2,27–29]. A simpler system was developed by Eisenberg and co-workers, in which *para*-enriched hydrogen is generated separately, then introduced to a suitably degassed NMR sample by transfer on a high vacuum line [3,7]. One disadvantage of this approach is that it generates a fixed atmosphere of *para*-enriched hydrogen in the sample, which is gradually consumed as the reaction progresses; in order to regenerate the enhancement, the sample must be periodically removed from the spectrometer, degassed and refilled. While this is adequate for the study of many chemical reactions, and sufficiently simple that it can be implemented using standard equipment in any moderately well-equipped research laboratory, the systems which produce a continuous purge of *para*-enriched hydrogen offer advantages when dealing with catalytic reactions in which the parahydrogen is rapidly consumed.

In the case of the fixed atmosphere technique, the chemical system can often be induced to exchange with fresh parahydrogen, thus maintaining the degree of enhancement, by raising the temperature of the sample. Of course, this may have the effect of consuming the parahydrogen too quickly, as well as affecting the stability and dynamics of the chemical system under investigation. If necessary, the rate of parahydrogen depletion can be reduced by lowering the concentration of the sample; this may increase the longevity of the enhancement phenomenon, resulting (somewhat counter-intuitively) in signals of greater magnitude over the course of a long NMR experiment. For these reasons, careful choice of sample concentration and temperature are essential. It is also necessary that the NMR glassware used in these studies is clean, and that samples are rigorously degassed/purged, since the presence of a small quantity of paramagnetic material (such as oxygen) will catalyse the interconversion of the hydrogen spin isomer back to thermal equilibrium, thus quenching the enhancement before the sample has been examined.

Despite these stipulations, parahydrogen-enhanced NMR spectroscopy has emerged as a powerful spectroscopic tool. The theoretical maximum possible enhancement depends on the magnetic field strength of the NMR spectrometer (the inverse Boltzmann factor), corresponding to an enhancement factor of approximately 31,000 at 9.4 T [7]. Enhancement factors have recently been quantified which approach this magnitude, albeit under somewhat idealised conditions [30,31]. Enhancement factors between 10^2 and 10^3 are more commonly observed: these enhancements translate directly into reductions in the amount of instrument time required to perform an experiment, or (more usually) greatly increased signals arising from low concentration species, that may be undetectable using standard NMR experiments. The lower than theoretical signal amplifications that are observed arise from effects that include the results of relaxation once the reaction products are formed, the dead-time overhead associated with the NMR measurement, and the routine use of a 45° excitation pulse.

1.4. The scope of this review

For a technique offering unprecedented signal enhancements of ^{1}H nuclei derived from molecular hydrogen, it is perhaps unsurprising that the parahydrogen approach has been primarily applied to the study of transition metal hydrides, and catalytic reactions involving hydrogen such as hydrogenation and hydroformylation. These aspects will be considered separately, although there is of course a certain degree of overlap between them. It is not our intention for this review to be exhaustive: selected highlights of the pre-2004 literature will be presented, followed by a more thorough examination of the most relevant recent publications in the field. In addition, the use of *in situ* photochemistry to initiate and study parahydrogen-based reactions will also be explored in detail. Other developments, such as the use of parahydrogen-derived systems in quantum information processing and Magnetic Resonance Imaging, fall outside the scope of this review.

2. The use of parahydrogen in inorganic chemistry

The first correctly characterised demonstration of the parahydrogen effect was in the catalytic hydrogenation of acrylonitrile by $RhCl(PPh_3)_3$, Wilkinson's catalyst, in which large, antiphase signals were observed for propionitrile, the hydrogenation product [2]. Weakly enhanced, broad resonances matching those expected for $RhCl(H)_2(PPh_3)_3$ were observed in the high-field region of the spectrum, supporting the assertion that this species acts as an intermediate in the hydrogenation reaction; this species was to be examined in more detail on several occasions (*vide infra*). The parahydrogen enhancement effect had been observed previously by Eisenberg and co-workers, during a study of the reaction of $Rh_2(H)_2(CO)_2(dppm)_2$ with phenylacetylene, but attributed to CIDNP rather than parahydrogen enhancement [32]. These events are detailed in Eisenberg's early review [3].

2.1. The detection and investigation of metal hydride species

The first detailed study of metal hydrides with parahydrogen was reported by Eisenberg and co-workers [33], who examined the addition of parahydrogen to $IrBr(CO)(PPh_3)_2$ and $Ir(CN)(CO)(PPh_3)_2$ as part of their investigations into the stereoselectivity of dihydrogen oxidative addition [34]. The hydride resonances of the corresponding H_2 addition products showed substantial enhancement. Subsequent reports extended these investigations by varying the ligand sphere, and demonstrated that the heteronuclei ^{31}P and ^{13}C could also be enhanced through the parahydrogen effect [13,14]. These studies also detailed preliminary experiments into the reaction of $IrCl(CO)(PPh_3)_2$ with parahydrogen, which was subsequently to be examined in greater detail (*vide infra*).

These iridium complexes, such as Vaska's complex and its analogues, are very well suited for study with parahydrogen. In the case of $IrCl(CO)(PPh_3)_2$, the complex is easy to synthesise, and the reaction with H_2 proceeds to completion at room temperature. It is instructive to consider this system in more detail. The addition of parahydrogen yields the well-known complex $IrCl(H)_2(CO)(PPh_3)_2$, indicated by the ^{1}H NMR resonances at δ −7.02 and δ −17.6. These signals appear as triplets of antiphase doublets, with triplet couplings of 18.8 and 13.7 Hz, respectively; these arise from the mutually *trans*-oriented phosphine ligands, which resonate at δ 8.4 in the ^{31}P NMR spectrum. The 5.7 Hz antiphase doublet coupling, which gives the resonances their characteristic appearance, arises from the coupling between the two hydride nuclei. The hydride resonances show an enhancement for around 90 seconds at 298 K, but if the sample temperature is raised to 343 K, at which temperature the oxidative addition of hydrogen is reversible, the resonances remain enhanced for many minutes. This system therefore provides a good starting point from which to explore the parahydrogen effect, and optimise the NMR methods which are employed.

The reaction of $RhCl(CO)(PPh_3)_2$ with parahydrogen has also been investigated [35]. This system was considered interesting because the addition of hydrogen to the complex had not been previously observed, unlike its well-known iridium analogue. The resultant enhanced resonances, and those of the bromide and iodide analogues, indicated the formation of dihydride halide-bridged dinuclear rhodium species in these reactions (Fig. 3). Comparable results were obtained with the PMe_3 analogue, although in this case one of the hydride ligands was observed to bridge two rhodium centres [36]. Indeed, when the related complex $RhI(CO)(PMe_3)_2$ was reacted with parahydrogen, five different products were observed [37]. These species were characterized *via* PHIP enhanced methods and served to illustrate that complex reactions yielding previously unseen species can be detected using this approach. A more detailed account of the hydrogen addition chemistry of these species was subsequently published, including activation parameters for hydride exchange, a general formation mechanism, and DFT calculations of related species [38]. These observations complemented the contemporary research into catalytic hydro-

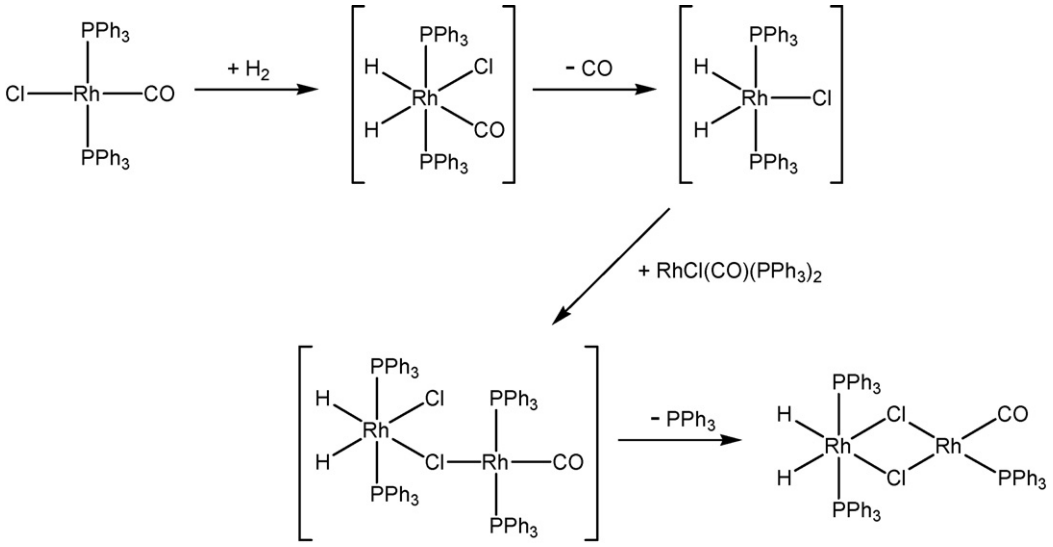

Fig. 3. Suggested route to the dinuclear rhodium species observed in the reaction of $RhCl(CO)(PPh_3)_2$ with parahydrogen.

genation of alkenes by $RhCl(PPh_3)_3$, in which related dinuclear rhodium species were observed (*vide infra*, Section 2.2).

Initial examinations of the reactivity of $IrCl(CO)(PPh_3)_2$ with parahydrogen had demonstrated that, at 343 K and 3 atm, conditions under which the addition reaction is reversible, the hydride resonances of the well-known product $IrCl(H)_2(CO)(PPh_3)_2$ are polarised. The reaction of $IrCl(CO)(PPh_3)_2$ and the related complex $IrCl(PPh_3)_3$ with parahydrogen was investigated further by 2D NOESY methods [20,21]. These experiments revealed that, at 343 K, the intermolecular exchange of hydride ligands with free hydrogen was much more rapid in the case of $IrCl(PPh_3)_3$ than for $IrCl(CO)(PPh_3)_2$. Repeating the experiments on $IrCl(PPh_3)_3$ with increasing concentrations of free PPh_3 yielded some intriguing results: small increases caused the intramolecular hydride-hydride exchange peaks to increase, and the intermolecular hydride-hydrogen exchange peak to decrease. However, further increases in the PPh_3 concentration had the effect of decreasing the intramolecular hydride-hydride exchange peaks. This was interpreted to mean that the loss of a PPh_3 ligand produces $IrCl(H)_2(PPh_3)_2$, which can then either recoordinate PPh_3 or eliminate H_2. The suppression of intramolecular hydride exchange at high PPh_3 concentrations was interpreted as evidence that the two hydride ligands of the intermediate $IrCl(H)_2(PPh_3)_2$ retain distinct identities (Fig. 4), implying that the intermediate adopts a square pyramidal structure in solution, comparable with that of $IrCl(H)_2(P^tBu_2Ph)_2$ [39].

Subsequent investigations into the reactivity of $IrCl(CO)(PPh_3)_2$ revealed that, when the initial addition of parahydrogen was conducted at 298 K, a second hydride-containing product was observed in addition to the usual product, which was only observable because of the enhancement afforded by the parahydrogen methodology [40]. This second product was revealed to be the product of hydrogen addition over the P–Ir–P axis of $IrCl(CO)(PPh_3)_2$, rather than the usual addition over the Cl–Ir–CO axis, resulting in the formation of a previously unknown isomer of $IrCl(H)_2(CO)(PPh_3)_2$ containing mutually *cis* phosphines (Fig. 5). The hydride ligands of this complex appear as a second-order resonance at δ −9.10 in the ^1H NMR spectrum. By using a pulse sequence which suppressed all non-enhanced resonances, the authors were able to directly compare the enhanced signals of both isomers, and thereby estimate the difference in the free energy of activation between the two hydrogen addition pathways. This estimate showed that hydrogen addition over the Cl–Ir–CO axis was favoured by 11 kJ mol^{-1} at 295 K, which is in good agreement with the value of 9.5 kJmol^{-1} calculated for the closely related complex $IrCl(CO)(PMe_3)_2$ [41]. These results were complemented by further studies on the PMe_3 and $AsPh_3$ analogues [42]. In general, the observations made on the reaction of parahydrogen with $IrCl(CO)(PPh_3)_2$ support its use as a test system; observation of the minor isomer of H_2 addition indicates that the sensitivity of the experimental set-up is adequate.

A more recent study on this system focused on the reaction of $IrCl(CO)(PPh_3)_2$ with parahydrogen in the presence of low concentrations of nitrogen donor molecules such as pyridine [43]. These experiments yielded transient, well-enhanced hydride signals for the products, with the general structure shown in Fig. 6. It was reported that, in approximately one minute of instrument time, diagnostic signals could be detected at concentrations of 0.1 μM, corresponding to the detection of 50 pmoles of the N-donor substrate. The degree of enhancement in this system was great enough to allow the detection of the ^{15}N chemical shift of the coordinated N-donor, at natural abundance, in less than 15 min of instrument time. The methodology was also extended to include molecules of biological relevance, such as purine and adenine; in these cases, several different isomers of each product were detected, corresponding to coordination *via* different nitrogen atoms in the substrate.

The same authors performed NMR studies with parahydrogen and $Ru(H)_2(CO)_2L_2$ (L = PMe_3, PMe_2Ph, and $AsMe_2Ph$), which revealed that these species actually exist in three geometries, *ccc*, *cct*-L and *cct*-CO, in contrast to earlier literature

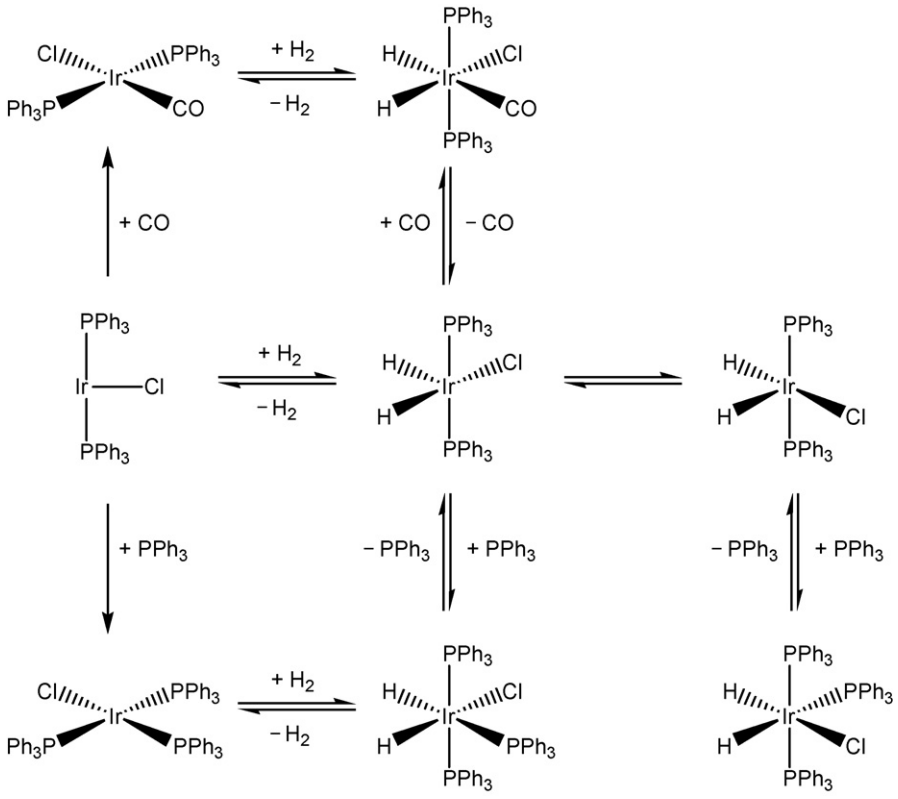

Fig. 4. The proposed reaction pathways for $IrCl(CO)(PPh_3)_2$ and $IrCl(PPh_3)_3$ in the presence of hydrogen and PPh_3.

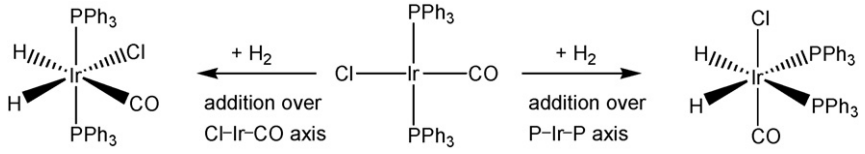

Fig. 5. The two isomeric products of hydrogen addition to $IrCl(CO)(PPh_3)_2$.

reports [44–46]. Thus when $L = PMe_3$, the *ccc* form is only visible when parahydrogen is used to amplify its spectral features. In contrast, when $L = AsMe_2Ph$, the *ccc* and *cct*-L isomers are present in similar quantities. These complexes were found to undergo a number of dynamic processes, which were investigated using magnetisation transfer methods. Where L_2 = dppe = 1,2-bis(diphenylphosphino)ethane, interchange of hydride positions within the *ccc* isomer was shown to be accompanied by synchronised CO and phosphorus centre exchange. The authors also asserted that, since the reactions led to complexes with polarised resonances, the $[Ru(CO)_2L_2]$-type intermediates in these reactions must have singlet electronic configurations, since a triplet configuration would have the effect of equilibrating the H_2 to its statistical mixture of *ortho* and *para* isomers. This contrasts with the comparable iron systems, which were shown in subsequent investigations to produce normal (i.e. non-enhanced) resonances, implying that the intermediate in this system has a triplet electronic configuration. This account was later followed by a detailed investigation of the photochemical reactivity of $Fe(CO)_3(dppe)$ and $Ru(CO)_3(dppe)$ with parahydrogen (*vide infra*, Section 2.4) [47].

Following on from their investigations of stereoselectivity at Ir(I) centres, Eisenberg and co-workers investigated the reaction of parahydrogen with the square planar complex $Ir(S_2CNEt_2)(CO)(PPh_3)$ [48]. This reaction led to three isomeric iridium dihydrides; the two products with chemically inequivalent hydrides both exhibited PHIP effects, with one of the isomers enhanced over the other by a factor of 170. This differential enhancement was interpreted in terms of kinetic selectivity, demonstrating that the activation barrier for H_2 addition over the S–Ir–CO axis is significantly lower than that for H_2 addition over the S–Ir–P axis.

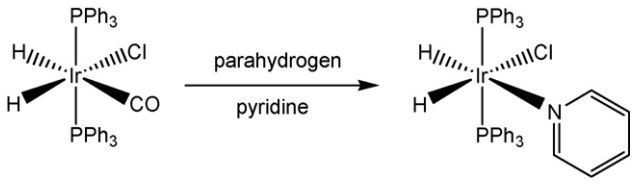

Fig. 6. The product of the reaction of $IrCl(CO)(PPh_3)_2$ with parahydrogen and pyridine. Products of similar geometry are formed with purine and adenine.

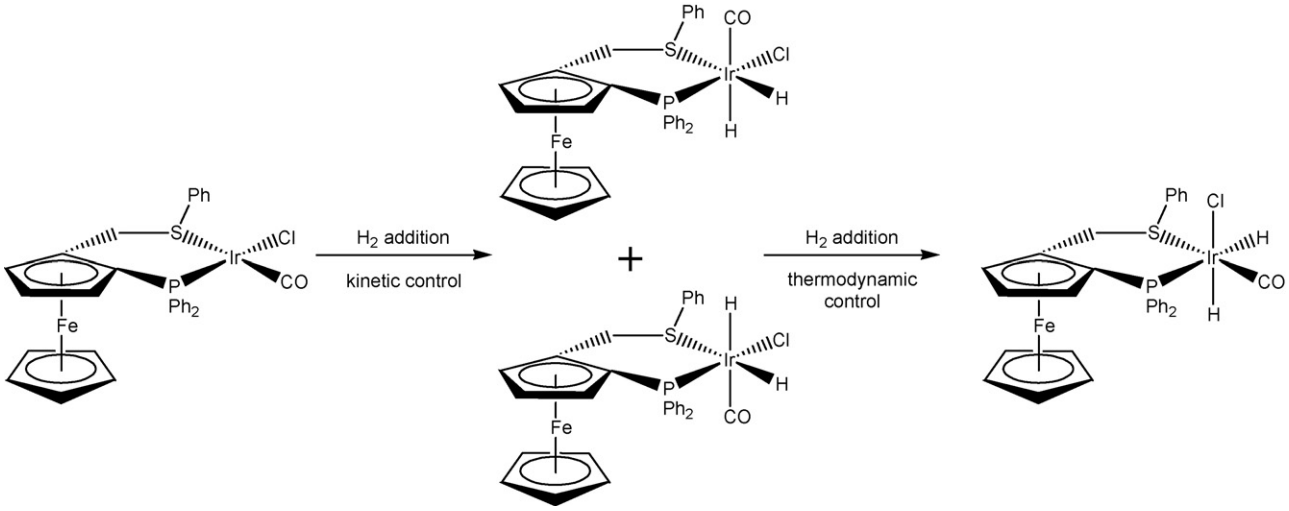

Fig. 7. The kinetic and thermodynamic products of parahydrogen addition to IrCl(CO)(CpFe(η^5-$C_5H_3(PPh_2)CH_2SPh$)).

Aime et al. studied the addition of hydrogen to a tri-osmium cluster species, $Os_3(CO)_{10}(NCCH_3)_2$, using PHIP methods [49]. The authors observed that the cluster reacted with parahydrogen, yielding an unexpectedly enhanced resonance for the chemically and magnetically equivalent bridging hydride ligands of the product $Os_3(CO)_{10}(H)_2$. It was proposed that this enhancement arises from the intermediacy of another dihydride cluster, in which the two former parahydrogen nuclei are magnetically inequivalent and therefore polarised; this intermediate then converts rapidly into the observed product, with the effect that the two equivalent hydrides retain a 'memory' of their inequivalence, which manifests itself in their enhancement. The same group made similar observations on the reversible addition and elimination of hydrogen at a tri-ruthenium cluster species, $Ru_3(CO)_{11}(NCCH_3)$, in which the molecular hydrogen resonance in the resultant ^{1}H NMR spectrum appears as a strongly enhanced emission signal [50]. The authors proposed that this occurred *via* the intermediacy of a cluster species with two inequivalent hydride ligands; the rate of hydrogen elimination from this species is fast relative to the ^{1}H relaxation times, resulting in the eliminated dihydrogen molecule retaining a degree of polarisation. In a subsequent investigation, the authors used PHIP methods and isotopic substitution to delineate the mechanisms of hydrogen exchange in $Os_3(CO)_{10}(H)_2$, identifying a previously unobserved tetrahydride intermediate [51].

While conducting parallel studies into alkene and alkyne hydrogenation by tri-ruthenium clusters (*vide infra*, Section 2.2), Duckett and co-workers investigated mechanisms for cluster isomerisation using parahydrogen methods [52]. These investigations, conducted on the tri-ruthenium clusters $Ru_3(CO)_{10}(PMe_2Ph)_2$ and $Ru(CO)_{10}(PPh_3)_2$, used EXSY experiments to monitor the interconversion of the three isomers of each cluster; the activation parameters of these processes were measured, and their solvent dependency was also investigated. Similar processes in a series of μ_3-quinolyl tri-osmium clusters were studied by Aime and co-workers [53].

The industrially significant complexes $[Rh(CO)_2I_2]^-$ and $[Ir(CO)_2I_2]^-$ were previously thought not to react with hydrogen directly. Studies with parahydrogen demonstrated that both complexes react with hydrogen to form *ccc*-$[Rh(CO)_2(H)_2I_2]^-$ and *ccc*-$[Ir(CO)_2(H)_2I_2]^-$, respectively. The latter complex was found to undergo H_2 elimination, for which the activation parameters ($\Delta H^{\neq} = 106 \pm 10$ kJ mol^{-1}, $\Delta S^{\neq} = 60 \pm 6$ J K^{-1} mol^{-1}) were determined by magnetisation transfer experiments [54]. These studies were complemented by those of Permin and Eisenberg, who employed parahydrogen to study the related complex $[Ir(CO)_2Br_2]^-$ and its reactions with $SnBr_2$ [55].

Duckett and co-workers determined the activation parameters for hydrogen site exchange in the reaction of rhodium phosphine complexes with parahydrogen and pyridine [56]. In this investigation, complexes of the type $RhCl(PR_3)_2L$ (L = phosphine, alkene) were shown to react with parahydrogen and pyridine, to yield mono- and di-nuclear pyridine complexes. While not exhibiting enhancement under normal conditions, hydrogen cycling in the system was promoted by the addition of 1-phenyl-1-propyne as a sacrificial hydrogenation substrate, thus rendering the complexes enhanced. Diffusion-ordered spectroscopy and isotopic labelling studies were used to confirm the identities of the products.

Duckett and co-workers returned to the subject of stereoselectivity of dihydrogen addition to square planar iridium systems in a more recent study [57]. In this investigation, IrCl(CO)(CpFe(η^5-$C_5H_3(PPh_2)CH_2SR$)) [R = Ph and ^{t}Bu], containing a κ^2: P, S ligand, was shown to undergo H_2 addition across the S–Ir–CO axis under kinetic control to form two distinct diastereoisomeric products. These products were then shown to rearrange *via* sulfur dissociation to ultimately form a single diastereoisomer, the thermodynamic product as shown in Fig. 7.

A related study focused on the reactivity towards dihydrogen of two chiral iridium complexes, IrI(CO)(R-BINAP) and $[Ir(CO)_2$(R-BINAP)$][SbF_6]$ [58]. These reactions show high levels of selectivity in both their kinetic and thermodynamic products. For IrI(CO)(R-BINAP), the kinetic H_2 addition product is formed by addition across the P–Ir–CO axis, yielding two diastereomers, which convert to two related thermody-

namic isomers that can be formed *via* oxidative addition across the P–Ir–I axis. The presence of C_2 symmetry in $[Ir(CO)_2$(R-BINAP)$][SbF_6]$ again leads to two diastereomers in the reaction with H_2. In both complexes, only the kinetic products showed any polarisation when parahydrogen was used.

2.2. Studies of catalytic hydrogenation with parahydrogen

The initial study by Bowers and Weitekamp [2] of the hydrogenation of acrylonitrile by $RhCl(PPh_3)_3$ was followed by a report by Eisenberg and co-workers into the action of $Ru(H)_2(H_2)(PPh_3)_3$ as a hydrogenation catalyst [59]. In the reaction of d_4-ethene and d_8-styrene, large enhanced antiphase ^{1}H resonances were observed for the hydrogenated products. However, when methyl acrylate or phenylacetylene were used as substrates, significantly different results were obtained: the product resonances were still polarised, but they each appeared either entirely with 'emission' character or 'absorption' character. Other alkynes exhibited the same phenomenon. These observations of 'net polarisation' were interpreted in terms of the ALTADENA effect previously discussed by Pravica and Weitekamp [11], and arising as a consequence of the hydrogenation occurring in the Earth's weak magnetic field rather than inside the spectrometer. This was regarded as evidence that the latter substrates were hydrogenated at a much higher rate, as the reactions effectively occurred before the sample could be examined.

Kirss and Eisenberg then investigated the catalytic hydrogenation of phenylacetylene by three different rhodium complexes, $RhCl(PPh_3)_3$, $[Rh(COD)(PPh_3)_2]^+$ and $[Rh(COD)(dppe)]^+$ [60]. In the reaction with $RhCl(PPh_3)_3$, the product styrene exhibited weakly enhanced ^{1}H signals for its *gem* and *trans* protons, with the enhancement dwindling over a few minutes. The authors interpreted this as evidence that, along with the catalytic hydrogenation, a competing reaction is occurring, in which the parahydrogen molecules undergo rapid, reversible oxidation to the rhodium centre. Since this promotes parahydrogen/orthohydrogen equilibration, the *para*-enriched hydrogen is depleted, leading to weak, short-lived polarisation. This is consistent with the established reversible H_2 addition to $RhCl(PPh_3)_3$ [61]. When the two cationic catalysts were tested under the same conditions, the resultant product resonances were strongly enhanced and relatively long-lived, indicating that the rate of hydrogenation under these conditions is much greater than the rate of *para*/*ortho* equilibration.

Bargon et al. made significant observations on the hydrogenation of dihydrofuran by $RhCl(PPh_3)_3$ [62]. In the hydrogenation of 2,5-dihydrofuran, polarised resonances were observed for both the α and β protons of the product THF molecule; this was rationalised as a consequence of scalar coupling between the protons, although polarisation transfer *via* nOe was also cited as a possible explanation. The group conducted similar work into the rhodium-catalysed hydrogenation of 1,4-dihydro-1,4-epoxynaphthalene to 1,4-epoxytetralin, using $RhCl(PPh_3)_3$ and $[Rh(COD)(Ph\text{-}\beta\text{-glup-OH})]^+$ as catalysts [63]. The different catalysts produced different polarisation patterns in the ^{1}H NMR spectra of the hydrogenation products. The authors demonstrated that these features could be interpreted in terms of different degrees of singlet/triplet mixing which occurred during the course of each reaction, and could be computationally modelled as a function of how long the former parahydrogen ^{1}H nuclei spent occupying magnetically inequivalent positions on the catalyst [64,65]. The action of these catalysts in the hydrogenation of an allene species, 1-methoxypropa-1,2-diene, was also investigated, in which the magnitudes of the enhanced resonances were used as a probe for regioselectivity in the reaction [66]. Further rhodium-catalysed hydrogenation reactions with parahydrogen were also reported by this group [67,68].

Eisenberg and co-workers used the parahydrogen effect as a mechanistic probe in the study of the hydrogenation of phenylacetylene to styrene by $Ru(BINAP)(OAc)_2$ [4]. Previous work had shown that, when this reaction was effected by the dimeric species $Rh_2(CO)_2(dppm)_2(H)_2$, the polarisation in the product styrene resonances was distributed equally between the *gem* and *trans* protons, with any weak polarisation at the *cis* proton arising from cross-relaxation; this is the expected result from simple *cis*-addition of hydrogen across the phenylacetylene triple bond. In the $Ru(BINAP)(OAc)_2$-mediated system, the *cis* and *trans* protons appeared equally enhanced, while the *gem* proton appeared better enhanced than either. The authors concluded that the reaction does not proceed exclusively by simple *cis*-addition.

Chinn and Eisenberg subsequently used the parahydrogen effect as a means of quantifying the rate of catalytic hydrogenation of the prochiral alkene ethyl (*Z*)-α-acetamidocinnamate by $[Rh(NBD)(chiraphos)]BF_4$ [69]. The polarisation of the product proton resonances was monitored over time, and the decay of the enhancement was modelled to determine the rate of hydrogenation. Data collected in this way matched that obtained using standard methods, confirming that parahydrogen methods can yield quantitative rate information.

Eisenberg and co-workers also conducted a detailed investigation into the mechanism of alkene hydrogenation by $RhCl(PPh_3)_3$ [70,71]. In the course of these studies, using a wide range of alkene substrates, a previously unobserved dinuclear rhodium alkene dihydride species was characterised (Fig. 8). In the reaction with styrene, enhanced resonances consistent with a mononuclear rhodium alkene dihydride were observed, which were attributed to a catalytic intermediate. Subsequent studies into the dinuclear rhodium species, and related systems, revealed direct evidence for their activity as hydrogenation catalysts: parahydrogen-modified EXSY methods were used to observe magnetisation transfer from parahydrogen, through a dinuclear intermediate, and into the hydrogenated product [24,72].

Bargon and co-workers reported an investigation into the reversibility of hydrogen transfer in catalysis [73]. In this study, $[Rh(COD)(Ph\text{-}\beta\text{-glup-OH})]BF_4$ was used to catalytically hydrogenate itaconic acid, a substituted alkene, with parahydrogen. Polarised signals were observed for the two *gem* protons of the alkene starting material, as well as for the hydrogenated product; this was interpreted as evidence that, in addition to the expected alkene hydrogenation reaction, hydrogen exchange with the *gem* protons was occurring. Similar results were observed in the hydrogenation of styrene [74]. In their study of the hydrogenation of cyclooctadiene by the same catalyst,

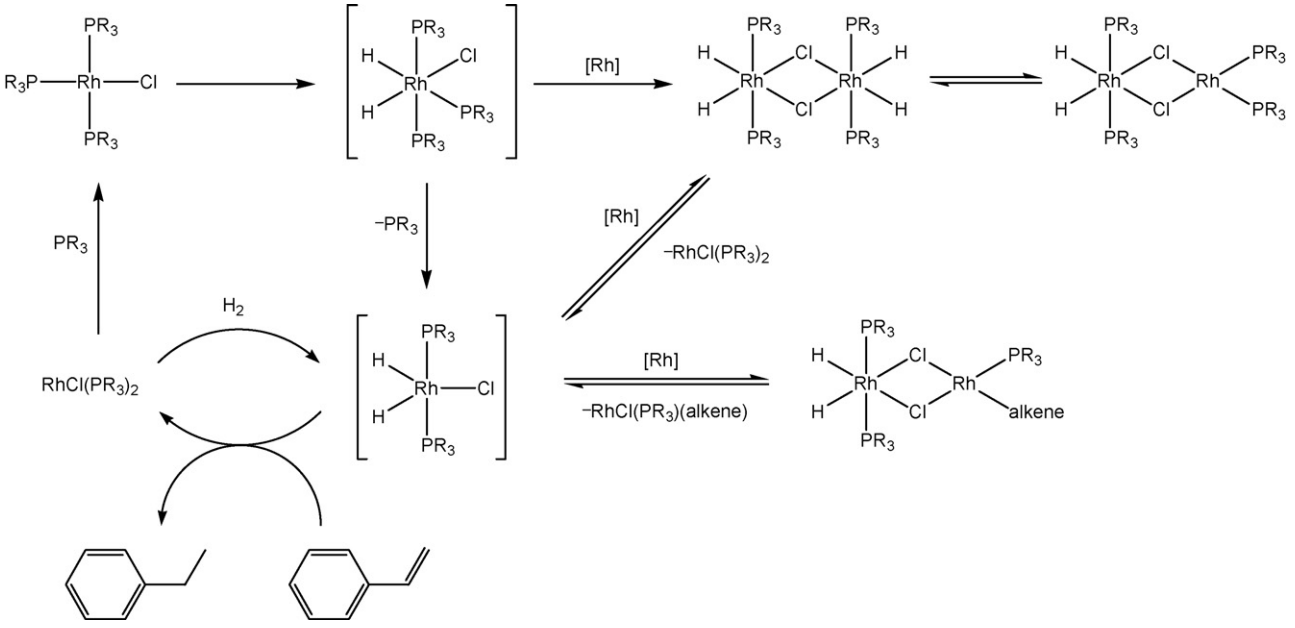

Fig. 8. Products observed in the reaction of $RhCl(PPh_3)_3$ with parahydrogen and styrene.

Aime et al. observed the same *gem*-enhancement, but found that conducting the reaction with D_2 did not result in deuterium incorporation in the product [75]. They concluded that the enhancement arises from polarisation transfer from the parahydrogen-derived hydride ligands to the alkene *via* the nuclear Overhauser effect.

Significant observations were made by Bargon and co-workers on the hydrogenation of styrene by $[Rh(COD)(dppb)]BF_4$, in which an intermediate catalyst–product complex was characterised [76]. Addition of styrene to the precatalyst in the presence of parahydrogen gave rise to the expected enhanced proton resonances for the hydrogenated product ethylbenzene, and another set of enhanced proton resonances with identical coupling characteristics, appearing at higher field. These were attributed to the ethyl protons of the catalyst–ethylbenzene complex, still enhanced from their formation from parahydrogen, but coordinated to the metal centre *via* the arene functionality (Fig. 9). More evidence for

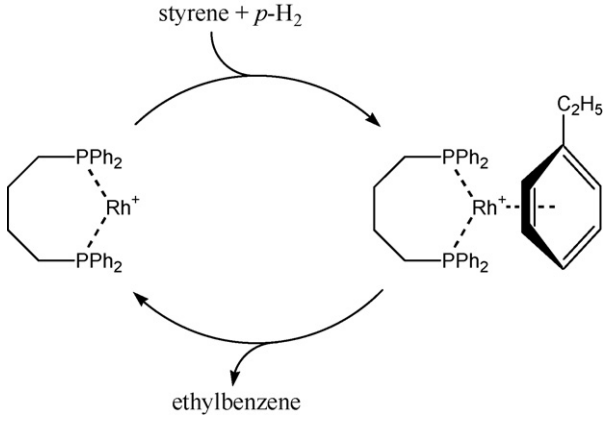

Fig. 9. Simplified mechanism for the hydrogenation of styrene by $[Rh(COD)(dppb)]^+$, showing the catalyst–product complex.

the structure was obtained from NOESY experiments [77]. The authors also investigated the kinetics of the reaction [22].

Another significant set of observations was reported by Blazina et al. [78]. In this study, the tri-ruthenium clusters $[Ru_3(CO)_{12-x}(PPh_3)_x]$ ($x = 1,2$) were used to hydrogenate alkynes and alkenes using parahydrogen. Kinetic studies using EXSY methods revealed that the hydrogen addition products of the clusters can interconvert, and catalyse hydrogenation at different rates. Changing the solvent from chloroform to benzene had the effect of inducing some cluster fragmentation, resulting in the observation of a mononuclear ruthenium species. This species was also observed to be catalytically active; EXSY methods were then used to directly compare the hydrogenation rates of the tri-ruthenium clusters with that of the mononuclear ruthenium fragment (Fig. 10). The system was investigated in more detail by varying the composition of the cluster.

A report of the use of parahydrogen as a mechanistic probe was made by Elsevier and co-workers [28]. In their study of the semi-hydrogenation of several alkynes by a highly active palladium catalyst, they observed that in each case the major product, the (*Z*)-alkene, gave rise to enhanced ^1H resonances in the NMR spectrum, while the minor product, the (*E*)-alkene, did not. The authors concluded that the hydrogenation reaction proceeds *via* a pairwise addition of the two hydrogen atoms of H_2 to the substrate, and furthermore, that the (*E*)-alkene product does not arise from direct hydrogenation but from isomerisation of the (*Z*)-alkene product. The relatively modest enhancement of these species was interpreted as a consequence of the proposed mechanism, which involves heterolytic activation of dihydrogen.

Recent reports have demonstrated that the parahydrogen effect can be used to enhance organic ligands within the coordination sphere of a metal atom. Duckett and co-workers initially demonstrated that, in the catalytic hydrogenation of diphenylacetylene by $Pd(bcope)(OTf)_2$, enhanced resonances could

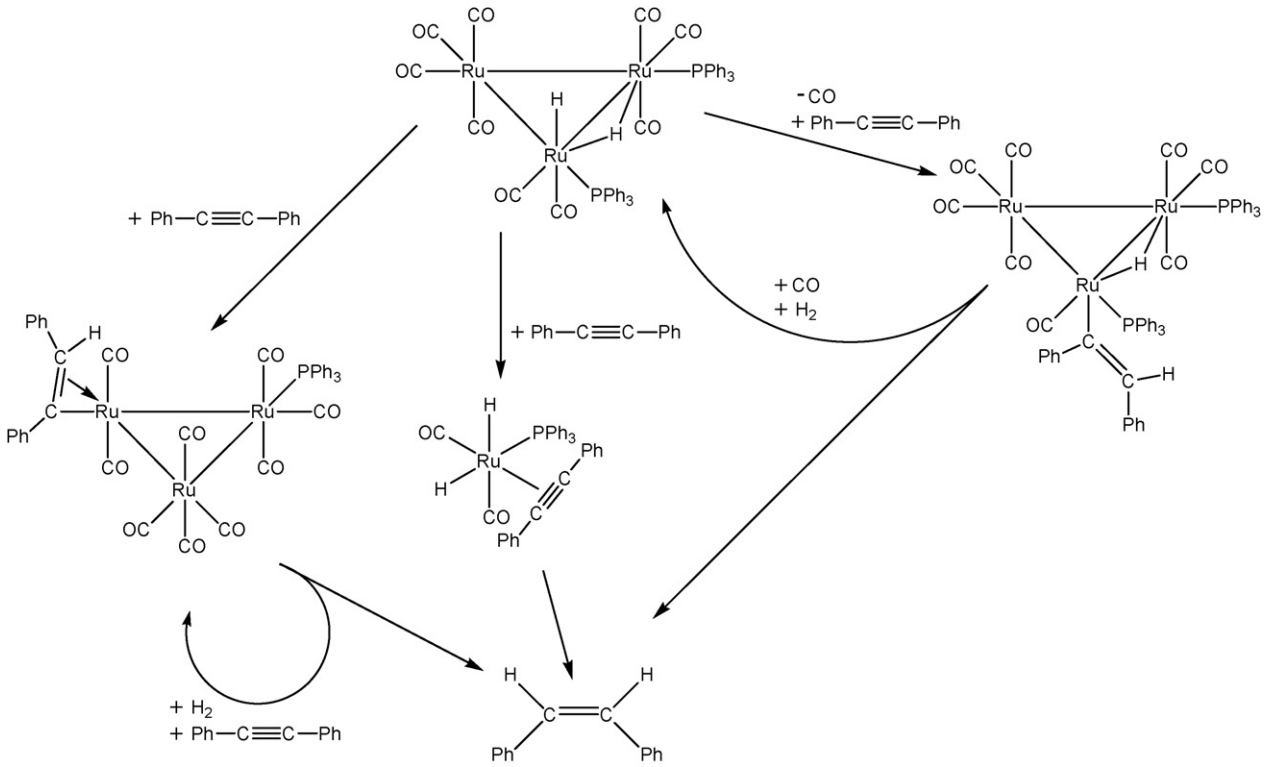

Fig. 10. Proposed catalytic cycle for the hydrogenation of diphenylacetylene by $Ru_3(H)(\mu\text{-}H)(CO)_9(PPh_3)_2$ taken from references [79,80].

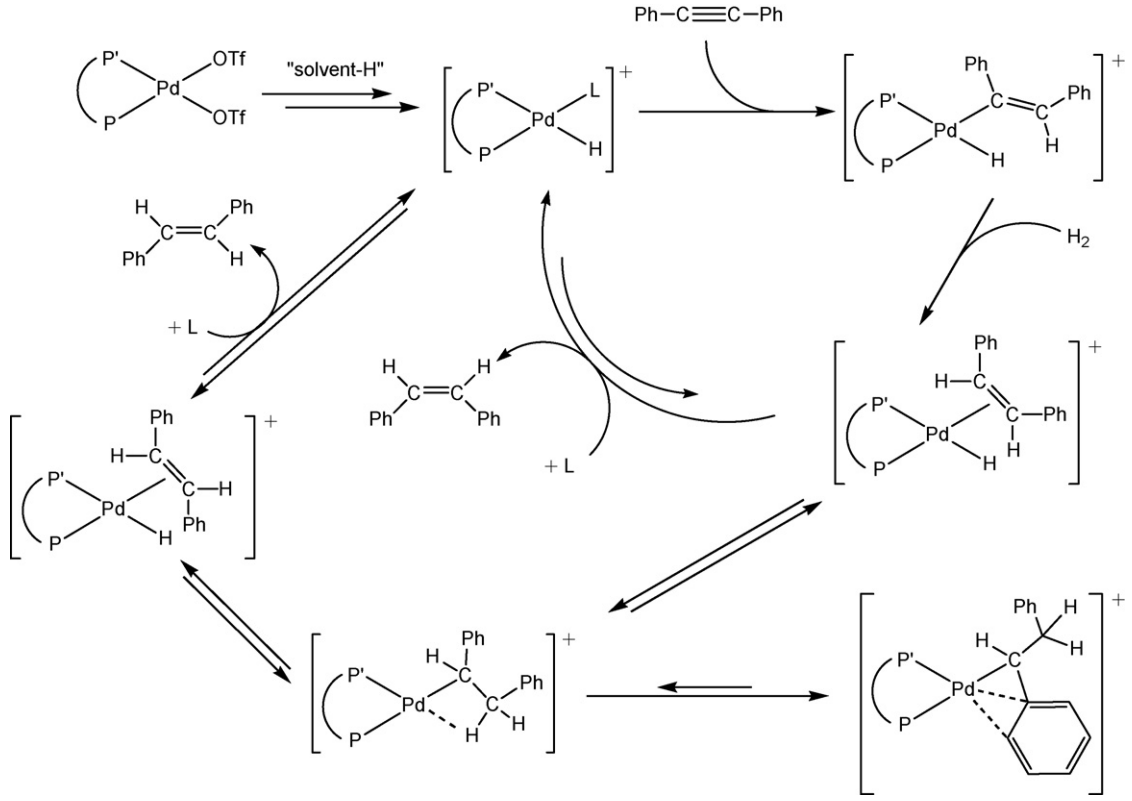

Fig. 11. Mechanism of alkyne hydrogenation by $Pd(bcope)(OTf)_2$, showing alkene formation and isomerisation.

be observed for intermediate species containing alkyl ligands derived from the hydrogenation of the alkyne substrate, but not containing discrete hydride ligands [81]. While the key intermediate was initially formulated as a palladium alkyl hydride species, subsequent experiments demonstrated it to be a cationic palladium alkyl species, stabilised by an additional interaction between the metal centre and the aromatic moiety of the coordinated substrate [82]. In this later report, Duckett and co-workers used isotopically labelled alkyne substrate to delineate the species involved in the catalytic hydrogenation. The observation and characterisation of solvent-stabilised, cationic palladium hydride and alkenyl species was interpreted as evidence that the catalysis occurred through a cationic route (Fig. 11). However, upon altering the bidentate phosphine to the unsymmetrical ^{t}bucope, a neutral palladium dihydride species was observed, indicating that a neutral reaction pathway may also be accessible. These conclusions were supported by an earlier report detailing experimental observations and DFT calculations on the hydrogenation of alkynes by the related complex $Pd(PEt_3)_2(OTf)_2$ [83].

2.3. Studies of catalytic hydroformylation with parahydrogen

The first report of parahydrogen enhancement in hydroformylation was made by Permin and Eisenberg, in which *trans*-$PtCl(COEt)(PPh_3)_2$, activated with $SnCl_2$, was reacted with parahydrogen [84]. The resultant ^{1}H NMR spectrum revealed that propanal was produced, with all of the resonances appearing normal except that of the aldehydic proton, which appeared as an enhanced emission signal. This was especially significant, as it was the first observed incidence of enhancement occurring from the transfer of only one proton to the product. Similar results were observed when the related complex *cis*-$PtCl_2(CO)(PPh_3)$-$SnCl_2$ was used to catalytically hydroformylate 1-hexene. The occurrence of this one-proton enhancement was rationalised as a result of the parahydrogen undergoing oxidative addition to the metal centre, forming an intermediate in which the two former parahydrogen nuclei are strongly coupled; this must occur immediately prior to the elimination of the aldehyde product containing only one of the former parahydrogen nuclei, in the aldehydic position. The postulated platinum intermediate was not observed, but a comparable intermediate was observed in the study of Ir(COEt)(CO)(dppe), a hydroformylation model system, which also exhibited one-proton enhancement under appropriate conditions. In a subsequent report, Eisenberg and co-workers isolated several similar iridium complexes with the large bite angle bidentate phosphine xantphos as a supporting ligand [85]. The use of parahydrogen allowed the observation of the proprionyl dihydride complex $Ir(H)_2(COEt)(CO)$(xantphos), a key intermediate in the hydroformylation reaction.

Another use of parahydrogen enhancement in monitoring hydroformylation was reported by Godard et al., in which allyl complexes such as $Ir(\eta^3\text{-}C_3H_5)(CO)(PPh_3)_2$ were used as catalyst precursors [86]. In the presence of a mixture of parahydrogen and carbon monoxide, two significant intermediates were detected *via* their enhanced signals, corresponding to an acyl dihydride complex and an alkyl dihydride complex. The parahydrogen enhancement, in conjunction with extensive ^{13}C labelling experiments, allowed these intermediates to be fully characterised, and their reaction pathways determined. The authors also reported a similar study into hydroformylation using $Co(\eta^3\text{-}C_3H_5)(CO)_2(PCy_3)$, in which cobalt acyl intermediates with both linear and branched acyl substituents were detected, in addition to the corresponding aldehydes [87]. The enhancement provided by the parahydrogen was found to be transferred into the organic ligand framework, thus allowing the characterisation of intermediates which do not contain discrete hydride ligands, mirroring the contemporary development reported by Duckett et al. in the field of hydrogenation catalysis (*vide supra*, Section 2.2). This allowed a detailed investigation of the reaction to be accomplished.

2.4. In situ photochemistry with parahydrogen

The characterisation of unstable complexes by NMR spectroscopy is normally limited by the warming effect of the air stream that is utilised to lower samples into the NMR probe. Various research groups, including those of Ball and Duckett, have demonstrated that UV photolysis of samples within the NMR probe can be used to generate species that may then be characterised using conventional methods [88], while others have used photo-CIDNP to determine kinetic parameters [89,90]. Duckett and co-workers refined this approach to allow irradiation of the NMR tube using a 325 nm 25 mW He-Cd cw laser on pressurised samples at low temperature, initially using this method to study the reaction of $CpRh(C_2H_3SiMe_3)_2$ with parahydrogen [91]. Under these conditions, PHIP-enhanced resonances are observed for the hydride ligands of the product $CpRh(H)_2(C_2H_3SiMe_3)$.

Building on the prior studies on $Ru(H)_2(CO)_2L_2$-type species [44,45], Duckett et al. investigated the photochemically induced generation of $Ru(H)_2(CO)_2$(dppe) from $Ru(CO)_3$(dppe) and parahydrogen [47]. The observation of enhanced hydride resonances was interpreted as definitive evidence that the intermediate [$Ru(CO)_2$(dppe)] exists in a singlet electronic state, as detailed previously (*vide supra*, section 2.1). This was confirmed by the observation that, when a mixture of $Ru(CO)_3$(dppe) and $Fe(CO)_3$(dppe) was examined, only the signals for $Ru(H)_2(CO)_2$(dppe) were polarised. Using the *in situ* irradiation methods allowed the chemical reaction between $Ru(CO)_3(L_2)$ (where L_2 = dppe or dpae, 1,2-bis(diphenylarsino)ethane) with pure parahydrogen to be monitored in a very precise way, such that the scale of the parahydrogen effect could be quantified. These experiments showed that the spin state of the hydride nuclei in $Ru(H)_2(CO)_2$(dppe) had a purity of $89.8 \pm 2.6\%$ (from 12 measurements) [31,92]. Amazingly, to achieve comparable results by cooling would require a temperature of 6.6 mK, which is unmanageable in the liquid state, or an impractical magnetic field of 0.44 MT at room temperature. In contrast, when $Ru(CO)_3$(dpae) was examined, the corresponding dihydride product spin state purity was determined to be $106 \pm 4\%$

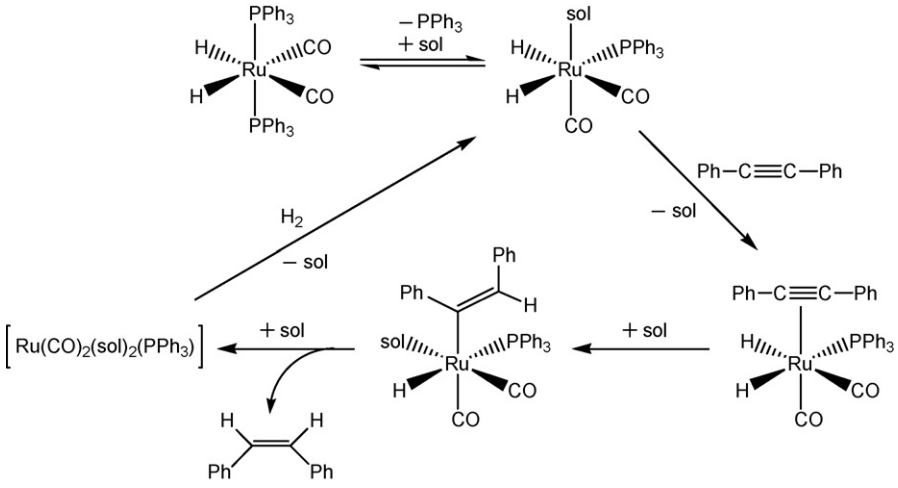

Fig. 12. Proposed catalytic cycle for the hydrogenation of diphenylacetylene, after photolysis of $Ru(CO)_3(PPh_3)_2$, where sol = pyridine.

of the theoretical maximum. In other words, the state prepared using $Ru(CO)_3$(dpae) as the precursor was indistinguishable from a pure spin state.

More recent studies involving *in situ* UV irradiation of solutions containing parahydrogen and $Ru(CO)_3L_2$, where L = PPh_3, PMe_3, PCy_3 and P(p-tolyl)$_3$, have been described [93]. In this case, two reactions are involved. The first involves loss of CO, and results in the formation of the *cis–cis–trans*-L isomer of $Ru(H)_2(CO)_2L_2$. In the second reaction, the formation of the complexes *cis–cis–cis* $Ru(H)_2(CO)_2L_2$ and $Ru(H)_2(CO)_2$(L)(solvent) (solvent = toluene, THF, pyridine) is indicated. In the case of L = PPh_3, the normally invisible species *cis–cis–trans*-L $Ru(H)_2(CO)_2L_2$ was shown to be an effective hydrogenation catalyst with rate-limiting phosphine dissociation proceeding at a rate of 2.2 s^{-1} in pyridine at 355 K (Fig. 12). Both experimental observations and theoretical calculations demonstrated that H_2 addition to the $[Ru(CO)_2L_2]$ moiety proceeds to form *cis–cis–trans*-L $Ru(H)_2(CO)_2L_2$ as the major product *via* addition over the OC–Ru–CO axis. In a related paper the reactivity of $Ru(CO)_2(PPh_3)$(dppe) towards hydrogen has been described. Thermally, this complex undergoes PPh_3 loss to form $Ru(H)_2(CO)_2$(dppe) while photochemically CO loss occurs and products of the type $Ru(H)_2(CO)(PPh_3)$(dppe) are detected [94].

3. Conclusions

Parahydrogen studies of inorganic reactions have produced a number of important observations. These include the detection of minor H_2 addition products, the observation of true reaction intermediates, and the probing of the kinetic significance of these species. The approach has also made a significant contribution to the study of cluster-based catalysis, where it has enabled the differentiation and direct comparison of intact and fragmentation-based reaction pathways. More recent advances have included the observation of one proton PHIP [84], studies of surface adsorption of hydrogen [95], applications in Magnetic Resonance Imaging where transfer to heteronuclei has been effected [26]. Further studies in the field of quantum information processing [96] and the use of parahydrogen enhancement to facilitate the detection of low concentrations of biological substrates [43] will doubtless all encourage other researchers to use and develop this field yet further. For those that are interested in taking up this challenge, starting out with Vaska's complex is likely to prove the easiest route to come to grips with this interesting phenomenon.

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References

[1] C.R. Bowers, D.P. Weitekamp, Phys. Rev. Lett. 57 (1986) 2645.
[2] C.R. Bowers, D.P. Weitekamp, J. Am. Chem. Soc. 109 (1987) 5541.
[3] R. Eisenberg, Accounts Chem. Res. 24 (1991) 110.
[4] R. Eisenberg, T.C. Eisenschmid, M.S. Chinn, R.U. Kirss, Adv. Chem. Ser. (1992) 47.
[5] S.B. Duckett, C.J. Sleigh, Prog. Nuclear Magn. Reson. Spectrosc. 34 (1999) 71.
[6] S.B. Duckett, D. Blazina, Eur. J. Inorg. Chem. (2003) 2901.
[7] D. Blazina, S.B. Duckett, J.P. Dunne, C. Godard, Dalton Trans. (2004) 2601.
[8] J. Natterer, J. Bargon, Prog. Nuclear Magn. Reson. Spectrosc. 31 (1997) 293.
[9] D. Canet, C. Aroulanda, P. Mutzenhardt, S. Aime, R. Gobetto, F. Reineri, Concepts Magn. Reson. Part A 28A (2006) 321.

[10] J. Bargon, J. Kandels, K. Woelk, Zeitschrift Fur Physikalische Chemie—Int. J. Res. Phys. Chem. Chem. Phys. 180 (1993) 65.
[11] M.G. Pravica, D.P. Weitekamp, Chem. Phys. Lett. 145 (1988) 255.
[12] A. Thomas, M. Haake, F.W. Grevels, J. Bargon, Angew. Chem.—Int. Ed. English 33 (1994) 755.
[13] T.C. Eisenschmid, J. Mcdonald, R. Eisenberg, R.G. Lawler, J. Am. Chem. Soc. 111 (1989) 7267.
[14] S.B. Duckett, C.L. Newell, R. Eisenberg, J. Am. Chem. Soc. 115 (1993) 1156.
[15] J. Barkemeyer, M. Haake, J. Bargon, J. Am. Chem. Soc. 117 (1995) 2927.
[16] S.B. Duckett, G.K. Barlow, M.G. Partridge, B.A. Messerle, J. Chem. Soc.-Dalton Trans. (1995) 3427.
[17] J. Barkemeyer, J. Bargon, H. Sengstschmid, R. Freeman, J. Magn. Reson. Ser. A 120 (1996) 129.
[18] H. Sengstschmid, R. Freeman, J. Barkemeyer, J. Bargon, J. Magn. Reson. Ser. A 120 (1996) 249.
[19] M. Haake, J. Natterer, J. Bargon, J. Am. Chem. Soc. 118 (1996) 8688.
[20] C.J. Sleigh, S.B. Duckett, B.A. Messerle, Chem. Commun. (1996) 2395.
[21] B.A. Messerle, C.J. Sleigh, M.G. Partridge, S.B. Duckett, J. Chem. Soc.-Dalton Trans. (1999) 1429.
[22] P. Hubler, R. Giernoth, G. Kummerle, J. Bargon, J. Am. Chem. Soc. 121 (1999) 5311.
[23] P. Hubler, J. Bargon, Angew. Chem.—Int. Ed. 39 (2000) 3701.
[24] S.A. Colebrooke, S.B. Duckett, J.A.B. Lohman, Chem. Commun. (2000) 685.
[25] T. Jonischkeit, U. Bommerich, J. Stadler, K. Woelk, H.G. Niessen, J. Bargon, J. Chem. Phys. (2006) 124.
[26] K. Golman, O. Axelsson, H. Johannesson, S. Mansson, C. Olofsson, J.S. Petersson, Magnetic Resonance In Medicine 46 (2001) 1.
[27] J. Bargon, J. Kandels, P. Kating, J. Chem. Phys. 98 (1993) 6150.
[28] A.M. Kluwer, T.S. Koblenz, T. Jonischkeit, K. Woelk, C.J. Elsevier, J. Am. Chem. Soc. 127 (2005) 15470.
[29] M. Ahlquist, M. Gustafsson, M. Karlsson, M. Thaning, O. Axelsson, O.F. Wendt, Inorg. Chim. Acta 360 (2007) 1621.
[30] M.S. Anwar, D. Blazina, H.A. Carteret, S.B. Duckett, J.A. Jones, Chem. Phys. Lett. 400 (2004) 94.
[31] D. Blazina, S.B. Duckett, T.K. Halstead, C.M. Kozak, R.J.K. Taylor, M.S. Anwar, J.A. Jones, H.A. Carteret, Magn. Reson. Chem. 43 (2005) 200.
[32] S.I. Hommeltoft, D.H. Berry, R. Eisenberg, J. Am. Chem. Soc. 108 (1986) 5345.
[33] T.C. Eisenschmid, R.U. Kirss, P.P. Deutsch, S.I. Hommeltoft, R. Eisenberg, J. Bargon, R.G. Lawler, A.L. Balch, J. Am. Chem. Soc. 109 (1987) 8089.
[34] P.P. Deutsch, R. Eisenberg, Chem. Rev. 88 (1988) 1147.
[35] S.B. Duckett, R. Eisenberg, J. Am. Chem. Soc. 115 (1993) 5292.
[36] S.B. Duckett, R. Eisenberg, A.S. Goldman, J. Chem. Soc.-Chem. Commun. (1993) 1185.
[37] P.D. Morran, S.A. Colebrooke, S.B. Duckett, J.A.B. Lohman, R. Eisenberg, J. Chem. Soc.-Dalton Trans. (1998) 3363.
[38] 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.
[39] M. Ogasawara, S.A. Macgregor, W.E. Streib, K. Folting, O. Eisenstein, K.G. Caulton, J. Am. Chem. Soc. 117 (1995) 8869.
[40] S.K. Hasnip, S.B. Duckett, C.J. Sleigh, D.R. Taylor, G.K. Barlow, M.J. Taylor, Chem. Commun. 1999 (1717).
[41] A.L. Sargent, M.B. Hall, Inorg. Chem. 31 (1992) 317.
[42] 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.
[43] N.J. Wood, J.A. Brannigan, S.B. Duckett, S.L. Heath, J. Wagstafft, J. Am. Chem. Soc. 129 (2007) 11012.
[44] S.B. Duckett, R.J. Mawby, M.G. Partridge, Chem. Commun. (1996) 383.
[45] D. Schott, C.J. Sleigh, J.P. Lowe, S.B. Duckett, R.J. Mawby, M.G. Partridge, Inorg. Chem. 41 (2002) 2960.
[46] J.M. Bray, R.J. Mawby, J. Chem. Soc.-Dalton Trans. (1987) 2989.
[47] D. Schott, P. Callaghan, J. Dunne, S.B. Duckett, C. Godard, J.M. Goicoechea, J.N. Harvey, J.P. Lowe, R.J. Mawby, G. Muller, R.N. Perutz, R. Poli, M.K. Whittlesey, Dalton Trans. (2004) 3218.
[48] G. Suardi, B.P. Cleary, S.B. Duckett, C. Sleigh, M. Rau, E.W. Reed, J.A.B. Lohman, R. Eisenberg, J. Am. Chem. Soc. 119 (1997) 7716.
[49] S. Aime, R. Gobetto, D. Canet, J. Am. Chem. Soc. 120 (1998) 6770.
[50] S. Aime, W. Dastru, R. Gobetto, A. Russo, A. Viale, D. Canet, J. Phys. Chem. A 103 (1999) 9702.
[51] S. Aime, W. Dastru, R. Gobetto, F. Reineri, A. Russo, A. Viale, Organometallics 20 (2001) 2924.
[52] D. Blazina, S.B. Duckett, P.J. Dyson, B.F.G. Johnson, J.A.B. Lohman, C.J. Sleigh, J. Am. Chem. Soc. 123 (2001) 9760.
[53] B. Bergman, E. Rosenberg, R. Gobetto, S. Aime, L. Milone, F. Reineri, Organometallics 21 (2002) 1508.
[54] S.K. Hasnip, S.B. Duckett, D.R. Taylor, G.K. Barlow, M.J. Taylor, Chem. Commun. (1999) 889.
[55] A. Permin, R. Eisenberg, Inorg. Chem. 41 (2002) 2451.
[56] R.R. Zhou, J.A. Aguilar, A. Charlton, S.B. Duckett, P.I.P. Elliott, R. Kandiah, Dalton Trans. (2005) 3773.
[57] R. Malacea, J.C. Daran, S.B. Duckett, J.P. Dunne, C. Godard, E. Manoury, R. Poli, A.C. Whitwood, Dalton Trans. (2006) 3350.
[58] A.C. Atesin, S.B. Duckett, C. Flaschenriem, W.W. Brennessel, R. Eisenberg, Inorg. Chem. 46 (2007) 1196.
[59] R. Eisenberg, R.U. Kirss, T. Eisenschmid, Abstracts Of Papers Of The American Chemical Society, 195 (1988) 294.
[60] R.U. Kirss, R. Eisenberg, J. Organomet. Chem. 359 (1989) C22.
[61] J.M. Brown, L.R. Canning, A.J. Downs, A.M. Forster, J. Organomet. Chem. 255 (1983) 103.
[62] J. Bargon, J. Kandels, P. Kating, A. Thomas, K. Woelk, Tetrahedron Lett. 31 (1990) 5721.
[63] P. Kating, A. Wandelt, R. Selke, J. Bargon, J. Phys. Chem. 97 (1993) 13313.
[64] M. Haake, J. Barkemeyer, J. Bargon, J. Phys. Chem. 99 (1995) 17539.
[65] G. Buntkowsky, J. Bargon, H.H. Limbach, J. Am. Chem. Soc. 118 (1996) 8677.
[66] A. Harthun, J. Bargon, R. Selke, Tetrahedron Lett. 35 (1994) 7755.
[67] A. Harthun, J. Barkemeyer, R. Selke, J. Bargon, Tetrahedron Lett. 36 (1995) 7423.
[68] A. Harthun, K. Woelk, J. Bargon, A. Weigt, Tetrahedron 51 (1995) 11199.
[69] M.S. Chinn, R. Eisenberg, J. Am. Chem. Soc. 114 (1992) 1908.
[70] S.B. Duckett, C.L. Newell, R. Eisenberg, J. Am. Chem. Soc. 116 (1994) 10548.
[71] S.B. Duckett, C.L. Newell, R. Eisenberg, J. Am. Chem. Soc. 119 (1997) 2068.
[72] S.A. Colebrooke, S.B. Duckett, J.A.B. Lohman, R. Eisenberg, Chem.-A Eur. J. 10 (2004) 2459.
[73] A. Harthun, R. Selke, J. Bargon, Angew. Chem.—Int. Ed. English 35 (1996) 2505.
[74] A. Harthun, R. Giernoth, C.J. Elsevier, J. Bargon, Chem. Commun. (1996) 2483.
[75] S. Aime, D. Canet, W. Dastru, R. Gobetto, F. Reineri, A. Viale, J. Phys. Chem. A 105 (2001) 6305.
[76] R. Giernoth, P. Huebler, J. Bargon, Angew. Chem.—Int. Ed. 37 (1998) 2473.
[77] P. Hubler, J. Bargon, S.J. Glaser, J. Chem. Phys. 113 (2000) 2056.
[78] D. Blazina, S.B. Duckett, P.J. Dyson, J.A.B. Lohman, Angew. Chem.—Int. Ed. 40 (2001) 3874.
[79] D. Blazina, S.B. Duckett, P.J. Dyson, J.A.B. Lohmann, Chem.-A Eur. J. 9 (2003) 1046.
[80] T.G. Prestwich, D. Blazina, S.B. Duckett, P.J. Dyson, Eur. J. Inorg. Chem. (2004) 4381.
[81] J.P. Dunne, S. Aiken, S.B. Duckett, D. Konya, K.Q.A. Lenero, E. Drent, J. Am. Chem. Soc. 126 (2004) 16708.
[82] J. Lopez-Serrano, S.B. Duckett, S. Aiken, K.Q.A. Lenero, E. Drent, J.P. Dunne, D. Konya, A.C. Whitwood, J. Am. Chem. Soc. 129 (2007) 6513.
[83] J. Lopez-Serrano, S.B. Duckett, A. Lledos, J. Am. Chem. Soc. 128 (2006) 9596.
[84] A.B. Permin, R. Eisenberg, J. Am. Chem. Soc. 124 (2002) 12406.
[85] D.J. Fox, S.B. Duckett, C. Flaschenriem, W.W. Brennessel, J. Schneider, A. Gunay, R. Eisenberg, Inorg. Chem. 45 (2006) 7197.

[86] C. Godard, S.B. Duckett, C. Henry, S. Polas, R. Toose, A.C. Whitwood, Chem. Commun. (2004) 1826.
[87] C. Godard, S.B. Duckett, S. Polas, R. Tooze, A.C. Whitwood, J. Am. Chem. Soc. 127 (2005) 4994.
[88] G.E. Ball, C.M. Brookes, A.J. Cowan, T.A. Darwish, M.W. George, H.K. Kawanami, P. Portius, J.P. Rourke, Proc. Natl. Acad. Sci. U.S.A. 104 (2007) 6927.
[89] A.S. Kiryutin, O.B. Morozova, L.T. Kuhn, A.V. Yurkovskaya, P.J. Hore, J. Phys. Chem. B 111 (2007) 11221.
[90] M. Goez, I. Kuprov, K.H. Mok, P.J. Hore, Mol. Phys. 104 (2006) 1675.
[91] C. Godard, P. Callaghan, J.L. Cunningham, S.B. Duckett, J.A.B. Lohman, R.N. Perutz, Chem. Commun. (2002) 2836.
[92] M.S. Anwar, D. Blazina, H.A. Carteret, S.B. Duckett, T.K. Halstead, J.A. Jones, C.M. Kozak, R.J.K. Taylor, Phys. Rev. Lett. (2004) 93.
[93] J.P. Dunne, D. Blazina, S. Aiken, H.A. Carteret, S.B. Duckett, J.A. Jones, R. Poli, A.C. Whitwood, Dalton Trans. (2004) 3616.
[94] D. Blazina, J.P. Dunne, S. Aiken, S.B. Duckett, C. Elkington, J.E. Mcgrady, R. Poli, S.J. Walton, M.S. Anwar, J.A. Jones, H.A. Carteret, Dalton Trans. (2006) 2072.
[95] P.J. Carson, C.R. Bowers, D.P. Weitekamp, J. Am. Chem. Soc. 123 (2001) 11821.
[96] M.S. Anwar, L. Xiao, A.J. Short, J.A. Jones, D. Blazina, S.B. Duckett, H.A. Carteret, Phys. Rev. A (2005) 71.