Parahydrogen-Induced Polarization: A New Spin on Reactions with H_2

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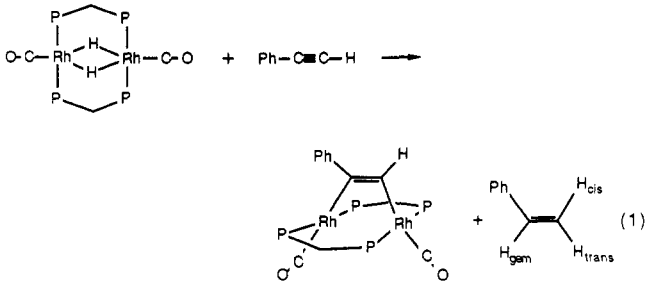
Received September 10, 1990 (Revised Manuscript Received January 7, 1991)

This Account focuses on a new and fascinating NMR phenomenon that has been the object of intense scrutiny in my laboratory over the past five years. It is also a story of how science is sometimes done, a detective story of sorts, with twists and unexpected turns, a story of how hypotheses are made and tested, of how they are reformulated, and of how sometimes the model on which the hypotheses were based fails. It is a story of quality experimentation by my co-workers, persistent testing of hypotheses, and a fair amount of head-scratching by the author.

Exploring. In April 1985 we were studying the reaction of the binuclear complex $Rh_2H_2(CO)_2(dppm)_2$ (1) (dppm = bis(diphenylphosphino)methane) with phenylacetylene shown in eq 1. The rich color changes that



(1)

accompanied the reaction led to the suggestion that radicals might be involved in the hydrogenation step, and on the basis of little more than a hunch, we examined the sample at very early reaction times, looking for evidence of the phenomenon known as chemically induced dynamic nuclear polarization or CIDNP.[1-4] An affirmative observation set us on the path leading to this Account.

Because of the relative instability of 1 under N_2 and the fact that 1 could be stabilized against decomposition under H_2, the reactions of 1 with alkynes were conducted under a hydrogen atmosphere. We quickly obtained excellent polarization and found that other alkynes led to similar polarization when hydrogenated by 1.[5] The results of eq 1 are illustrated in Figure 1 with polarization seen in the H_{trans} and H_{gem} resonances of the product styrene. The former exists as an absorption/emission or A/E doublet while the latter appears as an unusual A/E/A/E pattern. After 5 min, virtually all of the polarization is gone. Figure 1 and related results led to the conclusion that we were observing multiplet-effect CIDNP (vide infra). We also established through the use of deuterated substrates and D_2 that, in the reaction, hydrogen was added to substrate in a cis manner and that polarization occurred mainly in the added protons.

Attempts to observe polarization using olefinic substrates with 1 yielded marginal success until fully deuterated substrates were tried, based on the notion that longer T_1's for protons in the saturated products would make polarization observable. The striking result for the hydrogenation of styrene-d_8 is shown as part of Figure 2. The only two protons in the ethylbenzene-d_8 product originated as H_2 and occur as A/E doublets. Similarly, propylene-d_6 and 1 yielded CD_3CDHCD_2H with A/E polarization, while ethylene-d_4 gave totally unexpected polarization in the CD_2HCD_2H product.

With the establishment of polarization as a general phenomenon in the hydrogenation of unsaturated substrates by 1, we turned attention to the basis of the phenomenon. What did its occurrence mean from a mechanistic standpoint? To address this question, we touched briefly on the theory of CIDNP developed by Closs and Kaptein in 1969.[2,3] Previous Accounts and other references describe in more detail the basis of CIDNP first observed in 1967.[1,3,4] According to Closs and Kaptein, CIDNP arises in reactions proceeding through a radical-pair (RP) mechanism in which (1) a RP forms by dissociation of a molecule A–B or by encounter of A• and B• radicals; (2) the electron spins are weakly correlated so that the RP spin states are singlet and triplet with near degeneracy between them; (3) mixing of singlet and triplet states takes place on a time scale similar to that of reaction of the RP; (4) the RP possesses several different reaction channels such as geminate recombination and diffusion apart; and (5) one of these reaction channels is spin selective, for example, geminate recombination via the singlet state only.

With regard to item 3, there are two different mixing mechanisms which yield fundamentally different CIDNP effects. The first requires that the two radicals comprising the RP have different g values and leads to the more dominant *net effect*, in which individual

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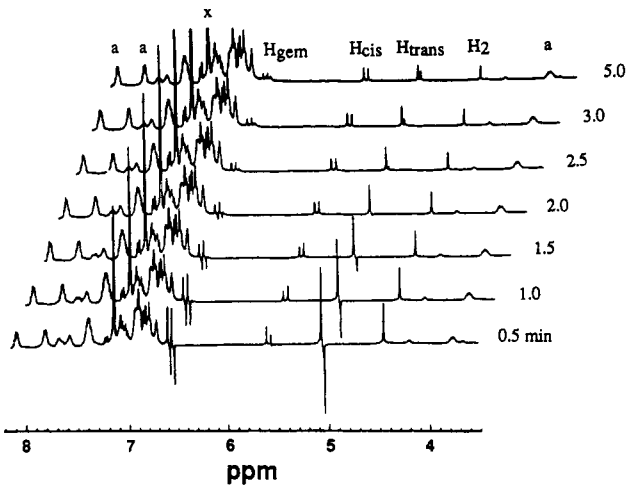


Figure 1. ^{1}H NMR spectra for eq 1 in C_6D_6 under para H_2. The resonances marked a are due to the metal complex product while the resonance marked x is due to benzene-d_5.

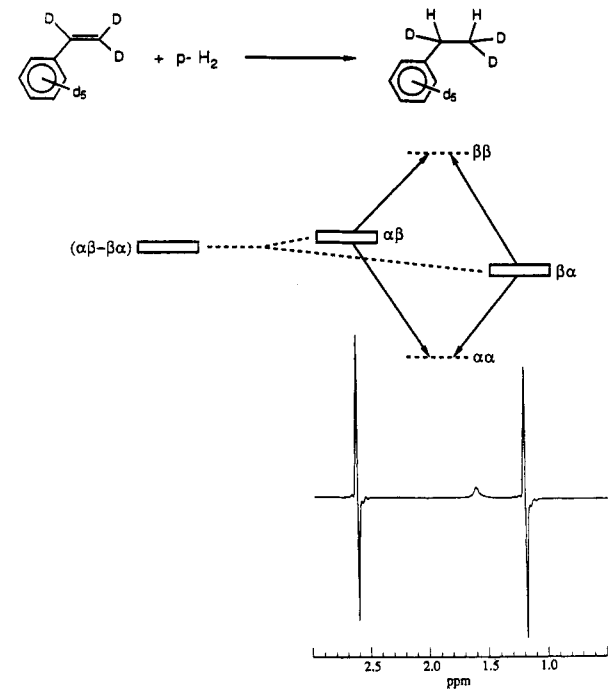
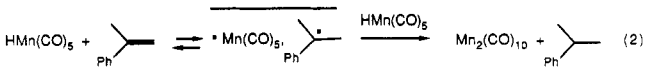


Figure 2. Diagram for generating multiplet polarization in the hydrogenation of styrene-d_8 using para H_2. The spin states for ortho H_2 are not shown.

resonances exhibit enhanced absorption *or* emission. The second achieves singlet/triplet mixing through hyperfine interaction involving coupled protons and produces the *multiplet effect*, in which coupled resonances show both absorption and emission similar to the A/E polarization shown in Figure 2. A key point is that seeing a pure multiplet effect means that the two radicals of the RP have the same *g* value, which for a series of reactions showing the multiplet effect means that the two radicals of the RP are identical. In other words, the RP is symmetrical, i.e., $\overline{A^\bullet,A^\bullet}$ and not $\overline{A^\bullet,B^\bullet}$.

Examples of CIDNP based on transition-metal hydrides in hydrogenation reactions have been reported by a number of authors.[6-9] In the earliest study, eq 2 was found to proceed via a RP composed of $\overline{Mn(CO)_5^\bullet,\text{cumyl}^\bullet}$ formed by H atom transfer from $HMn(CO)_5$ to α-methylstryene.[6] This system generated



net-effect CIDNP consistent with different *g* values of the radical-pair components. In contrast, our results exemplified by Figures 1 and 2 showed multiplet type polarization and could not be accommodated by the H atom transfer mechanism of eq 2. Our results demanded a different mechanism.

Within the framework of CIDNP, the multiplet polarization we were witnessing required a symmetrical radical pair, and this in turn colored our thinking for nearly two years. Of the two types of RPs possible, i.e., $\overline{R^\bullet,R^\bullet}$ and $\overline{M^\bullet,M^\bullet}$, the former was the easier to test and led to some difficult labeling studies. The strategy was to employ ^{13}C-labeled substrates and look for polarization due to ^{13}C in the resultant CIDNP. If this was observed, then organic radicals $R^\bullet$ were the components of the RP. Through experiments using 1 and $Ph^{13}C{\equiv}CH$, $PhC{\equiv}^{13}CH$, and $C_6D_5{}^{13}CD{=}CD_2$, no polarization due to ^{13}C was observed although product protons clearly showed coupling to ^{13}C.[5,10] The results were unambiguous that organic radicals did not comprise the RP.

If $\overline{R^\bullet,R^\bullet}$ was eliminated easily once the ^{13}C-labeled substrates were used, the same was not true of $\overline{M^\bullet,M^\bullet}$, which appeared to be our last refuge. To his credit, G. L. Closs found the $\overline{M^\bullet,M^\bullet}$ radical pair within a binuclear complex objectionable, but like others had no alternative explanation of the phenomenon.[11] By this time, other metal complexes were also found to produce polarization including the dpam or arsine analogue of 1 and $Pd_2Cl_2(dppm)_2$.[10,12] In addition, Bergman had reported a hydrogenolysis of $Co_3(CO)_9(\mu_3\text{-}CCH_2R)$ with similar polarization which was ascribed to CIDNP.[13] All of the systems were bi- or polynuclear and capable of generating a symmetric $\overline{M^\bullet,M^\bullet}$ radical pair.

Upon learning of Balch's trinuclear complex $[Rh_3Cl_2H_2(CO)_2((Ph_2PCH_2)_2PPh)_2]^+$ (2),[14] we reasoned that this might provide a test of our model since it would generate an unsymmetrical metal centered biradical (i.e., a species having two adjacent but different $Rh^\bullet$ centers) which would yield a net (or partial net) effect. To conflicting delight and dismay, the polarization obtained by using 2 was both truly impressive and perfectly multiplet. Our model, which predicted net or partial net polarization, failed, and within the radical-pair model for CIDNP, our results could not be accommodated. At this point other problems with out experiments were surfacing without explanation. Specifically, polarization was not uniformly good, it varied widely with seemingly identical samples, and it appeared sensitive to factors not immediately obvious.

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The Denouement: Weitekamp's Proposal. In June 1987, during final preparation of a talk about our "CIDNP" studies for the Sheffield meeting on the chemistry of the platinum group elements, J. Bargon and R. Lawler, with whom we had been in contact, called to tell of a different means of polarization published by D. Weitekamp of Caltech a few months earlier.[15] It was based on parahydrogen and would necessitate a complete reinterpretation of our now puzzling results. It also meant that proof and a new title for the talk would be needed, quickly and desperately.

At ambient temperatures, normal hydrogen is composed of an approximately 3:1 mixture of ortho and para H_2, reflecting the 3-fold degeneracy of the nuclear spin functions of the former ($\alpha\alpha$, $\beta\beta$, and $\alpha\beta + \beta\alpha$) and the nondegeneracy of the latter ($\alpha\beta - \beta\alpha$; the nuclear "singlet").[16] While the ratio of ortho:para H_2 at 298 K is virtually statistical (3:1), an energy difference between these two forms makes para H_2 increasingly favorable as the temperature is lowered.[16,17a] At 80 K, the equilibrium Boltzmann distribution is 51.61% ortho and 48.39% para; at 20 K, it is 0.18% ortho and 99.82% para. Despite the smallness of the energy difference between ortho and para H_2, interconversion requires a catalyst and does not occur readily in its absence.[16,17b] Paramagnetic solids are the most effective catalysts, but other materials and compounds, especially having metal atoms, work as well.

For polarization to occur, hydrogen enriched in the para form is required. According to Weitekamp,[15] polarization can arise if para H_2 is transferred pairwise to a substrate to yield a product in which the two transferred protons are magnetically distinct. If the reaction occurs fast relative to proton relaxation, the transferred protons will initially reflect the nuclear spin populations of the starting dihydrogen. This is shown in Figure 2 for hydrogenation of styrene-d_8 with para H_2. Since only the $\alpha\beta$ and $\beta\alpha$ states of the product ethylbenzene-d_8 correlate with the nuclear spin function of para H_2, these states will be overpopulated relative to a normal Boltzmann distribution and give rise to polarized A/E or E/A transitions similar to a CIDNP multiplet effect.

But how did *we* come to a parahydrogen-induced polarization when all we were studying was the reaction chemistry of metal hydride complexes with organic substrates? The answer, in retrospect, is simple. After samples were prepared during the day for NMR runs at night, they were stored in liquid N_2 baths at which temperature the only thing happening in the system was the slow conversion of ortho to para H_2 catalyzed by the frozen solution of the metal complex. By the time samples were thawed, a para-enriched-H_2 atmosphere had been generated, and upon shaking of the sample, reaction commenced with para-enriched H_2.

Within 10 days and in time for Sheffield, we confirmed that this was indeed the case.[18] Identical samples gave different polarization depending on the type of hydrogen employed. Addition of para-enriched H_2 just prior to reaction yielded polarization identical with earlier results whereas addition of normal H_2 did not, despite the occurrence of hydrogenation.

While Weitekamp's initial report had been theoretical, he also demonstrated parahydrogen-induced polarization experimentally using the well-known hydrogenation catalyst $RhCl(PPh_3)_3$ and acrylonitrile as the substrate.[19] More recently, Bargon and co-workers have reported that similar enhanced absorption/emission patterns can be observed by using ortho H_2, which must be separated by low-temperature chromatography from the para form, although the effect is not as strong and the sense of polarization is reversed (i.e., E/A rather than A/E).[20]

The question of what to call this new phenomenon has been discussed and we have opted for the innocuous acronym PHIP for *para*hydrogen-*i*nduced *p*olarization rather than alternatives derived from "*p*arahydrogen-*i*nduced *m*ultiplet *p*olarization" and Weitekamp's "*p*arahydrogen *a*nd *s*ynthesis *a*llow *d*ynamically *e*nhanced *n*uclear *a*lignment". Of more scientific substance, PHIP is relatively short-lived, decaying in virtually all systems within 10 min. The decay in most cases follows simple first-order behavior although it is clear that a number of factors contribute to it. By far, the dominant factor is dipolar relaxation as measured by T_1's of the protons added in the hydrogenation reaction. However, since polarization lasts substantially longer than T_1's, newly polarized material is produced in the probe as relaxation occurs in previously synthesized product. This factor relates directly to the rate of the hydrogenation reaction. Another contributor to PHIP decay is relaxation of the para H_2 pool in solution *prior* to hydrogenation. This may come about from simple H_2 oxidative addition/reductive elimination to the catalyst without hydrogenation. A final element in this analysis is gas/solution mixing of para-enriched H_2, which in an NMR tube is slower than the other factors and is demonstrated by the fact that shaking a sample after 15 min regenerates PHIP, often impressively.

From a reaction mechanism standpoint, the observation of PHIP means that the two H atoms added during the hydrogenation reaction must originate from the same H_2 molecule. Mechanisms for homogeneous catalysts such as $RhCl(PPh_3)_3$ and Rh(chiraphos)(diene)$^+$ support this notion,[21,22] but for monohydride catalysts such as $RhH(CO)(PPh_3)_3$ and $RuHCl(PPh_3)_3$, the proposed mechanisms have the two added hydro-

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(17) (a) From the Pauli exclusion principle, the symmetry of the nuclear spin functions determines the symmetry of the rotational states of the H_2 molecule: para H_2 has only even rotational states and ortho H_2 odd. While the nuclear spin functions determine symmetry, the energy difference is due mainly to allowed rotational states. For molecular H_2, the rotational constant B is 60.864 cm^{-1}. (b) Transitions between symmetric and antisymmetric spin functions are forbidden so that, in the absence of a catalyst, normal H_2 can be viewed as a 3:1 mixture of two different and *stable* species that happen to be chemically identical!

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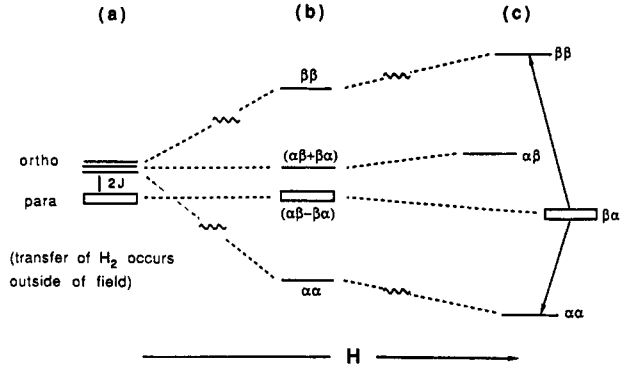

Figure 3. Correlation diagram leading to a *net* effect in an HH′ spin system. (a) Energy levels for the protons transferred from para-enriched H_2 to substrate at zero magnetic field (the labels ortho and para indicate the origin of the spin wave functions). Under increasing magnetic field, energy levels change with $\nu_a - \nu_b \ll J$ for part b and $\Delta\nu \gg J$ for part c. Only the $\beta\alpha$ product spin state is overpopulated by adiabatic movement into the field.

gens coming from different H_2 molecules.[23,24] Consequently, the latter systems cannot have spins of the added H atoms correlated and should not show PHIP.

Net Polarization and Magnetic Field Effects. Early in our studies, polarizations were observed that differed greatly from multiplet PHIP and were not explained by the proposal of Figure 2. These polarizations were more characteristic of a CIDNP net effect in which coupled resonances of the transferred protons appeared in *either* enhanced absorption or emission, but with the *absence* of a component line of each resonance. For example, while the hydrogenation of propylene-d_6 catalyzed by 1 in CD_2Cl_2 yielded A/E PHIP for the methyl and methylene resonances of propane-d_6, the same hydrogenation in C_6D_6 gave an enhanced absorption for –C*H*D– and an emission for –C*H*D_2 with a separation between lines equal to the chemical shift difference $\Delta\delta$ in hertz *plus* the coupling constant *J*. This meant that the upfield component of the –CHD– doublet and the downfield component of the –CHD_2 doublet were absent in the polarized spectrum in C_6D_6. Interestingly, the net polarization appeared more intense and decayed more quickly than the corresponding multiplet polarization.

The basis of net polarization was explained in 1988 by Weitekamp, who observed the effect independently.[25] It was proposed that para H_2 adds to substrate *prior* to placement of the sample into the magnetic field of the NMR spectrometer. If the hydrogenation with para H_2 takes place without loss of spin correlation while outside the magnetic field, the *product* protons are characterized by the $(\alpha\beta - \beta\alpha)$ spin state even though the symmetry of the H_2 molecule no longer holds. As the sample is lowered into the spectrometer, the energy levels change as shown in the correlation of Figure 3. A key element in achieving net polarization is that the sample is moved into the field adiabatically, meaning that the overpopulation of the $(\alpha\beta - \beta\alpha)$ state is transferred solely to the lower of the $\alpha\beta$ and $\beta\alpha$ product states. Thus only one of the protons in the AB system can undergo enhanced absorption while the other is limited to emission.

This proposal explained our net polarization observations mentioned above. Whereas the sample of propylene-d_6 + 1 in CD_2Cl_2 was introduced into the probe at ca. −50 °C, leading solely to reaction in the probe and *multiplet* polarization, the same system in C_6D_6 was warmed outside the probe until thawing at 5 °C, yielding hydrogenation *prior* to sample placement in the spectrometer and consequent *net* polarization. Signal enhancement for net polarization can be truly impressive. To date, an enhancement for this hydrogenation of over 200-fold has been achieved although this is still well below the 10^3–10^4 factor theoretically possible when a 1:1 mixture of ortho and para H_2 is used.[19]

Since net polarization results from hydrogenation before the sample is introduced into the spectrometer, it can serve as a qualitative indicator of relative rate. For example, $RuH_4(PPh_3)_3$-promoted hydrogenation of PhC≡CH in C_6D_6 yields only net polarization,[26a] whereas the same reaction promoted by $Rh_2H_2(CO)_2(dppm)_2$ (1) leads to a multiplet effect. This suggests that hydrogenation proceeds more rapidly under the reaction conditions using the former catalyst than the latter. The relative reactivity of substrates can be assessed analogously.

PHIP in Hydrogenation Reactions. With the basis of PHIP in hand, the scope of the phenomenon was probed by examining different homogeneous hydrogenation catalysts. While $RhCl(PPh_3)_3$ and $Rh(COD)(dppe)^+$ both function by pairwise H_2 transfer, they follow different mechanistic paths.[21,22] The former proceeds by reversible H_2 addition followed by olefin binding and insertion, whereas the latter reversibly binds olefin first, followed by H_2 addition leading irreversibly to product. Since reversible H_2 addition is a means of relaxing para enrichment of H_2, $RhCl(PPh_3)_3$ would be expected to show PHIP that was weaker and less able to be regenerated than the $Rh(dppe)^+$ system. This was indeed the case,[26b] confirming an earlier study by Brown using para H_2 and Raman spectroscopy.[22g]

The ruthenium catalysts examined merit additional comment. The tetrahydride species $RuH_4(PPh_3)_3$, which readily exchanges H_2 and is a dihydrogen complex,[27] produces strong PHIP. For styrene-d_8 as the substrate, multiplet polarization was found with a first-order rate for decay of 0.044 s^{-1}. During this period, the broad hydride resonance of $RuH_4(PPh_3)_3$ at δ −7.52 ppm remained unchanged. When hydrogenations were performed in halogenated solvents ($CDCl_3$ and CD_2Cl_2), the magnitude of PHIP decreased dramatically, the solution turned purple-red, and the hydride resonance changed to that found in $RuHCl(PPh_3)_3$-catalyzed hydrogenation. Thus in halogenated solvents, the $RuH_4(PPh_3)_3$ catalyst system changed to that of $RuHCl(PPh_3)_3$.

An unanticipated result was the observation of PHIP, albeit weak, in $RuHCl(PPh_3)_3$-promoted hydrogenations

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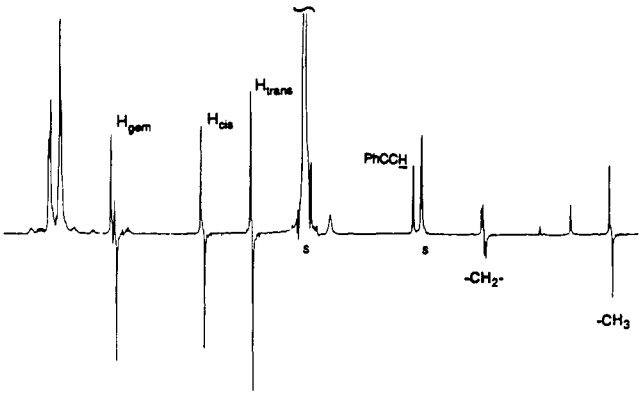
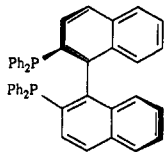


Figure 4. PHIP in hydrogenation of PhC≡CH with para H_2 catalyzed by $Ru(BINAP)(OAc)_2$ in CD_3OD at 53 °C. Peaks marked s are from dissolved ortho H_2 and methanol-d_3.

because this well-known catalyst system was thought to function by a nonpairwise H_2-transfer mechanism.[24] Observation of the hydride resonance of $RuHCl(PPh_3)_3$ under various conditions gave insight into the nature of this catalyst system.[26a] While loss of the hydride resonance occurred readily under D_2, it was found that under catalytic conditions (298–320 K and 1–3 atm of H_2) the resonance remains sharp and virtually identical with that seen under N_2 alone. Moreover, when the hydrogenation of styrene-d_8 was performed under D_2, there was no reduction of the hydride resonance for up to 2 h. These results were unexpected and indicate that $RuHCl(PPh_3)$ is not the active catalyst in styrene hydrogenation nor is it connected to the active catalyst by an equilibrium that is rapid on the NMR time scale. A species capable of yielding PHIP is $RuH_2(PPh_3)_3$, which forms readily from $RuH_4(PPh_3)_3$ and can be generated by dehydrohalogenation from $RuHCl(PPh_3)_3$ under H_2, as has been proposed previously.[28] We suggest that, even in halogenated solvents, a small amount of $RuH_2(PPh_3)_3$ is present as an active catalyst if PHIP is observed. The qualitative differences in the magnitudes of PHIP, large for $RuH_4(PPh_3)_3$ catalysis in C_6D_6 and weak for $RuHCl(PPh_3)_3$ in halogenated solvents, support this notion.

Hydrogenation using Noyori's asymmetric hydrogenation catalyst $Ru(BINAP)(OAc)_2$[29] was also examined using PHIP. While prochiral substrates reacted

(S)-BINAP =



too slowly under 1–3 atm of para-enriched H_2 to show any NMR polarization in the products, a number of simpler olefins and alkynes yielded PHIP.[30] For example, very short-lived multiplet polarization was observed in the hydrogenation of methyl acrylate. When PhC≡CH was used as the substrate in either CD_2Cl_2 or CD_3OD, the resultant PHIP contrasted significantly

(28) (a) Strathdee, G.; Given, R. *Can. J. Chem.* **1975**, *52*, 106. (b) Hampton, C.; Dekleva, T. W.; James, B. R.; Cullen, W. R. *Inorg. Chim. Acta* **1988**, *145*, 165.

(29) (a) Noyori, R.; Ohta, M.; Hsiao, Y.; Kitamura, M.; Ohta, T.; Yakaya, H. *J. Am. Chem. Soc.* **1986**, *108*, 7117. (b) Ohta, T.; Takaya, H.; Noyori, R. *Inorg. Chem.* **1988**, *27*, 566.

(30) (a) Eisenberg, R.; Eisenschmid, T. C.; Chinn, M. S.; Kirss, R. U. *Adv. Chem. Ser.*, in press. (b) Eisenschmid, T. C. Ph.D. Dissertation, University of Rochester, 1989.

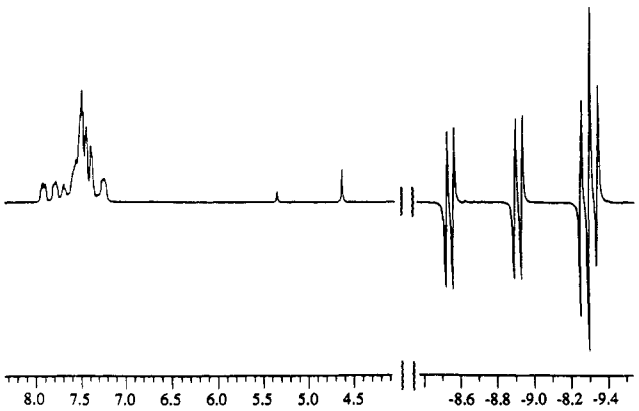
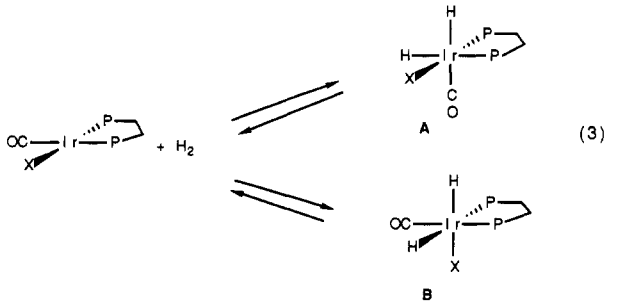


Figure 5. PHIP of $IrH_2Br(CO)(dppb)$ (A) formed in eq 3 at 48 °C 40 s after thawing from −196 °C.

with that found for this hydrogenation with other catalysts discussed above. Figure 4 shows the spectrum observed ~35 s after thawing and insertion into the spectrometer probe at 53 °C. The striking features are (1) nearly equal A/E polarizations of the trans and cis protons of the styrene product, (2) a simple A/E pattern for the gem proton (cf. Figure 1), (3) long-lasting polarization with non-first-order decay, and (4) significant PHIP in the secondary hydrogenation product, ethylbenzene.

The differences in PHIP for PhC≡CH hydrogenation indicate mechanistic differences for the various catalyst systems examined. For **1**, hydrogenation takes place by cis addition across the triple bond, giving strongly polarized H_{trans} and an A/E/A/E pattern for H_{gem} in the styrene product. In contrast, for $Ru(BINAP)(OAc)_2$, the results indicate that hydrogenation proceeds nonstereoselectively. One of the protons originating on the para H_2 molecule adds to the geminal position while the other ends up nearly equally in *either* the cis or trans position of the product styrene.

Oxidative Addition Reactions. In the hydrogenation reactions described above, the polarization was observed in the organic product. Because H_2 oxidative addition is a fundamental step in homogeneous hydrogenation, several complexes with well-understood H_2 addition chemistry were examined to see if PHIP could occur in metal hydride resonances. The best studied of these systems is of the type IrX(CO)(P–P), where P–P = $Ph_2PCH_2CH_2PPh_2$ (dppe), *cis*-$Ph_2PCH{=}CHPPh_2$ (dppv), *o*-$(Ph_2P)_2C_6H_4$ (dppb), and $Ph_2PCH(Me)CH(Me)PPh_2$ (chiraphos), and the reaction of interest is shown in eq 3.[31] The Ir(III) cis dihydride



(3)

product A of eq 3 forms stereoselectively and under kinetic control, while at longer reaction times, conver-

(31) (a) Johnson, C. E.; Eisenberg, R. *J. Am. Chem. Soc.* **1985**, *107*, 3148. (b) Johnson, C. E.; Fisher, B. J.; Eisenberg, R. *J. Am. Chem. Soc.* **1983**, *105*, 7772.

sion to a thermodynamically preferred isomer, B, takes place. However, in the context of PHIP only the former is of importance.

The reaction of IrBr(CO)(dppb) in CD_2Cl_2 solution with para-enriched H_2 yields the ^1H NMR spectrum shown in Figure 5.[32] This spectrum, taken after 1 min of reaction, shows polarized resonances at δ −8.73 and −9.32 corresponding respectively to the hydride trans to P and the hydride trans to CO of the kinetic isomer. In this spectrum, each of the ^{31}P-coupled lines exists as an E/A doublet with a splitting between the emission minimum and absorption maximum of 3.7 Hz corresponding to normally unresolved coupling between the hydrides. From the phase of the doublets as E/A rather than A/E, the sign of J_{H-H} can be assigned as negative. At 23 °C, PHIP due to these hydrides lasts for up to 5 min and the magnitude of signal enhancement achieved to date is ~10–15-fold. Only multiplet polarization is seen, indicating that reaction yielding the polarized product is occurring within the magnetic field of the spectrometer. This is consistent with the rapid reversibility of eq 3. Since A forms immediately upon shaking of the sample, any net polarization decays too quickly to be seen. This is supported by independent T_1 measurements of the hydrides which were found to be 1.49 s for H trans to P and 0.73 s for H trans to CO.

Oxidative addition–reductive elimination is known to equilibrate ortho and para forms of H_2. By raising the temperature for eq 3 to 48 °C, the rate of this process is increased, decreasing the duration of PHIP to less than 3 min. However, gas–solution mixing in an NMR tube and hence the relative enrichment of para H_2 *over* the solution are little affected on this time scale, and PHIP may be reestablished by simply shaking the sample tube and reinserting it into the spectrometer.

Because of signal enhancement, PHIP may allow observation of metal hydride intermediates during hydrogenation catalysis. This has indeed been accomplished by Weitekamp,[19] who saw polarization in $RhH_2Cl(PPh_3)_3$ during hydrogenation of acrylonitrile, and by us in the $RuH_4(PPh_3)_3$-catalyzed hydrogenation of PhC≡CH.[30b]

Dipolar Relaxation and Polarization Transfer to Other Nuclei. The notion of dipolar relaxation together with the establishment of nonequilibrium ^1H spin populations through chemical means using para H_2 suggested the possibility that these spin populations could be transferred to other nuclei such as ^{13}C and ^{31}P, resulting in polarization and signal enhancement in their resonances. Initial studies in this regard have examined whether the oxidative addition of para H_2 would lead to polarization in the ^{31}P NMR resonances of dihydride A.[32]

As seen in trace a of Figure 6 for the dppb system, polarization transfer does indeed occur. The two ^{31}P resonances show antiphase polarization with a signal enhancement of ~7 relative to the normal spectrum of $IrH_2Br(CO)(dppb)$, trace b, taken several minutes later. The ^{31}P polarization decays over a period of ~3 min, similar to the decay of ^1H polarization in the hydride resonances discussed above.[32]

For P trans to one hydride and cis to the other, phosphorus–proton coupling yields a doublet of doublets, or if $J_{PH^{cis}}$ is unresolved, a doublet of broad resonances. Trace a of Figure 6 shows that this resonance at δ 21.3 ppm exhibits strong E/A polarization with a peak separation corresponding to the sum of $^2J_{PH^{trans}}$ + $^2J_{PH^{cis}}$ (148.0 and 14.8 Hz). The two inner lines of this doublet of doublets are not observed, and an explanation for their absence and the observed polarization has been described elsewhere.[32] The other ^{31}P resonance at δ 34.2 ppm for the phosphorus cis to both hydrides exists as a weaker E/A pattern with a separation of 34 Hz or ca. twice $^2J_{PH^{cis}}$. In this multiplet polarization, only the outer lines of the expected triplet are seen, with the central line absent. However, its duration is very short-lived (less than 1 min after thawing), possibly because the phosphorus cis to both hydrides relaxes more rapidly, leading to quicker loss of any nonequilibrium spin population.

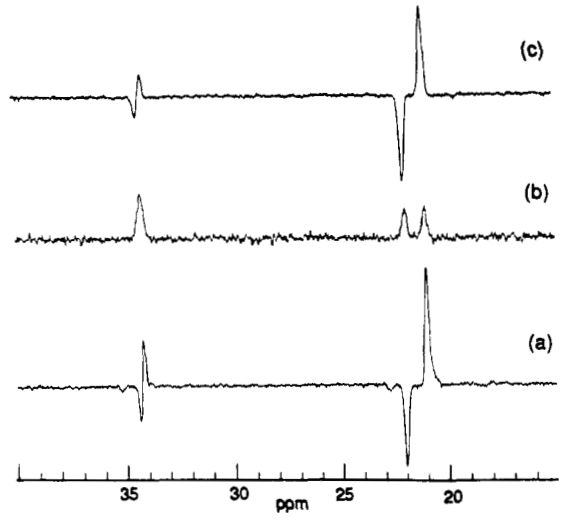


Figure 6. ^{31}P NMR spectra of $IrH_2Br(CO)(dppb)$ (A) formed in eq 3 at 48 °C: (a) 42 s after thawing from −196 °C, 16 scans; (b) 2 min later, 16 scans; (c) INEPT of the same sample with normal H_2, 64 scans with $1/(4J)$ delay of 1.7 ms.

For the other $IrH_2Br(CO)(P–P)$ complexes formed by oxidative addition of para H_2, polarization transfer to ^{31}P yields similar results.[32] All examples show an E/A phase in P trans to H, a peak separation of $^2J_{PH^{trans}}$ + $^2J_{PH^{cis}}$, and an estimated signal enhancement of 6–10-fold. Experimentally, the spectrum generated by using para H_2 (Figure 6, trace a) can be duplicated by using the INEPT pulse sequence (Figure 6c). In INEPT,[33] the hydride nuclear spin populations are inverted through a pulse sequence, while with PHIP the ^1H populations are perturbed chemically with the population differences transferred to ^{31}P by dipolar relaxation. The polarization for P trans to H has been explained in greater detail elsewhere.[32]

These experiments with iridium phosphine complexes show that PHIP can be used to polarize and enhance NMR signals of less sensitive nuclei. The conditions necessary for this enhancement are that (1) the less sensitive nucleus have a positive nuclear Overhauser effect (NOE) with a proton that was originally part of a para H_2 molecule and (2) the para H_2 molecule undergo pairwise addition without loss of spin correlation. Positive preliminary results with ^{13}C nuclei have also

(32) Eisenschmid, T. C.; McDonald, J.; Eisenberg, R.; Lawler, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 7267.

(33) (a) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760. (b) Derome, A. E. *Modern NMR Techniques for Chemistry Research*; Pergamon Press: Oxford, 1987.

been obtained in hydrogenation reactions using α-^{13}C-labeled styrene-d_8.[30b]

Concluding Comments. Is PHIP a valuable new tool for the mechanistic chemist or an interesting but idle curiosity? The developments of the next few years will answer this question. Certainly, its occurrence is unequivocal in establishing the pairwise nature of H_2 addition and transfer reactions, and this can be used to probe reactions such as heterolytic addition of H_2 and asymmetric hydrogenation. Quantitation of the magnitude and decay of PHIP may provide a facile and valuable means of obtaining kinetic data for reactions of interest. In addition, polarization transfer to ^{13}C, ^{31}P, and other nuclei may prove a convenient means for signal enhancement of these nuclei in appropriate reactions.

The story of PHIP has also been educational about doing science. For the talk at Sheffield, a new analysis of two years' worth of results was given after the audience was instructed to disregard the title and interpretive comments of the published abstract. The response was favorable. If experiments are done honestly and properly, reanalysis and reinterpretation, while not recommended every day, reaffirm the vitality of science.

I want to thank my co-workers Tom Eisenschmid, Sven Hommeltoft, Rein Kirss, Don Berry, and Mitch Chinn for their excellent and tireless efforts. I gratefully acknowledge the National Science Foundation (CHE 86-03055 and 89-06090 and instrumentation grant CHE 89-11868) and the donors of the Petroleum Research Fund, administered by the Americal Chemical Society, for their support and the Johnson Matthey Co., Inc., for loans of precious metal salts. Finally, I want to thank Professors R. G. Lawler and J. Bargon for their interest and help as the story of PHIP was developing and Professors A. Balch and R. Noyori for catalyst samples and helpful discussions.