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Following Palladium Catalyzed Methoxycarbonylation by Hyperpolarized NMR Spectroscopy: A Parahydrogen Based Investigation

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$Pd(OTf)_2$(bcope) is shown to react in methanol solution with diphenylacetylene, carbon monoxide and hydrogen to produce the methoxy-carbonylation product methyl 2,3 diphenyl acrylate alongside *cis*– and *trans*–stilbene. In-situ NMR studies harnessing the parahydrogen induced polarization effect reveal substantially enhanced ^{1}H NMR signals in both protic and aprotic solvents for a series of reaction intermediates that play a direct role in this homogeneous transformation. Exchange Spectroscopy (EXSY) measurements reveal that the corresponding CO adducts are less reactive than their methanol counterparts.

1. Introduction

The alkoxycarbonylation of vinyl acetate reflects an important step in the production of alkyl lactate that is subsequently used to prepare a range of hydroxypropionic acid esters. Importantly, esters of this type form biodegradable polymers and their production therefore reflects a green solution to waste disposal.[1] High molecular weight thermoplastics, and the production of methylpropanoate[2], reflect other high value products that are formed on an industrial scale via this reaction, which is most clearly illustrated by Lucite's Alpha process, one of the many successes of palladium catalysis. In addition, the alkoxycarbonylatyion of 1-alkynes finds a further role in the formation of unsaturated carboxylic acids that feature as building blocks in a range of situations.[3, 4] Consequently, these developments illustrate just how critical early studies on the mechanism of the methoxycarbonylation of alkenes,[2, 5] and more generally the palladium catalysed hydroformylation of alkenes[6, 7] were for the development of an array of new clean technologies.[3]

For a number of years, the *para*hydrogen (p–H_2)[8] induced polarization (PHIP)[9, 10] effect has been used to yield mechanistic insight into a range of catalytic hydrogenation and hydroformlyation reactions besides monitoring the formation of metal hydride based products.[11, 12] These studies employ the PHIP effect to increase the ^{1}H NMR signal strengths of reaction products that contain protons which were originally located in a molecule of p–H_2 to achieve this goal. The potential signal improvement on a 400 MHz NMR spectrometer, the workhorse of many academic and industrial facilities is dramatic at 32,000-fold and while it has only been reached for one system[13], when more widely applied the signal gains have still allowed the detection of true reaction intermediates that exist in such low concentrations as to preclude their detection by traditional NMR methods.[11, 14, 15] In addition, as PHIP enables the analogous detection of scalar coupled heteronuclei through polarisation transfer, the reliable characterisation of such species is possible[16] and when this approach is coupled with Exchange Spectroscopy (EXSY) experiments their kinetic significance can be determined.[17-20] Workers have also used this method to examine not only a range of heterogeneous reactions[21-25] but some that don't involve a metal centre.[26-29] The PHIP approach has therefore developed substantially from the early starting point of Weitekamp,[30, 31] Eisenberg[32, 33] and Bargon,[34, 35] as illustrated in several reviews.[11, 12]

In order to understand the physical basis of PHIP, p–H_2 needs to be recognised as simply dihydrogen that exists in the anti-symmetric magnetic state that is represented by the nuclear wave function $\Psi_{\{\alpha\beta-\beta\alpha\}}$.[36] It is easy to prepare, and when a molecule of it is introduced into a reaction product, in high magnetic field, if the two newly formed hydrogen nuclei become chemically distinct then, in the absence of relaxation, they exist initially in two equally populated, and coupled, $\alpha\beta$ and $\beta\alpha$ states.[8] Consequently when such a reaction is probed by NMR spectroscopy, a non-Boltzmann spin distribution is created across their NMR addressable energy levels. Hence, if these nuclei correspond to those of a dihydride product, with two distinct hydride resonances, ^{1}H NMR signals result that are

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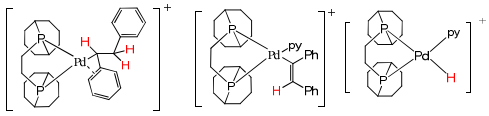
of dramatically enhanced amplitude, with anti-phase components that are separated by their mutual scalar coupling.[11, 30] In contrast, when a monohydride complex is formed indirectly from such a dihydride species it has proven possible to detect its single hydride resonance as an enhanced–emission signal as a consequence of the related One–Proton–PHIP effect described by Eisenberg.[37] Furthermore, when such a reaction is monitored in conjunction with the Only Parahydrogen SpectroscopY (OPSY) approach it is possible to harness the magnetic state of the two *p*–H_2 derived protons to readily separate their signals from those of other protons that arise from what would be referred to, as normal, or thermally polarised resonances.[38, 39]

We seek here to harness the unique properties of PHIP to demonstrate that it is possible to extend the range of reactions that are amenable to study using this approach whilst adding to our understanding of the role that the metal plays in an important industrial reaction. We have selected the palladium catalysed methoxy-carbonylation of an alkyne for this purpose, a reaction that has been widely studied, and hence provides a good background from which to work.[2, 40-44] This study therefore builds on the earlier elegant work of Clegg and others on the alkoxycarbonylation of alkenes.[2, 5, 45] Such studies traditionally use a combination of low temperatures and high pressures,[44] in this case in conjunction with a phosphine such as 1,2–$(CH_2PBu^t_2)_2C_6H_4$ (d^tbpx), to detect a range of intermediates such as Pd(d^tbpx)(H)(MeOH)$^+$, Pd(d^tbpx)(H)(CO)$^+$, Pd(d^tbpx)(Et)(MeOH)$^+$ and Pd(d^tbpx)(COEt)(THF)$^+$, each with a $CF_3SO_3^-$ counter ion. Van Leeuwen has completed a range of studies on this reaction as a function of phosphine[40, 46] with Claver completing related studies on vinyl arenes.[43] The alkoxycarbonylation of alkynes by palladium has also been examined.[47, 48] However, it must be borne in mind that highly active palladium nanoparticles can play a role.[49-51] We are therefore seeking to detect active reaction intermediates in this process, which contrasts with the situation faced in some of the earlier *p*-H_2 based studies of the hydroformylation reaction where a series of resting states were detected.[52, 53]

From the perspective of this paper, we harness the known NMR parameters of these previously reported palladium complexes to support the speciation enunciated here and build on the fact that PHIP-NMR has already been shown to facilitate the detection of a number of related intermediates during studies of palladium catalysed hydrogenation under mild conditions. For example when chelating[17,54, 55] or monodentate phosphines[56] are used as ligands a range of reaction intermediates are detected. In the case of Pd$(OTf)_2$(PP') (**1**, where PP' = bcope, which is 1,2-P,P'-bis(9-phosphabicyclo[3.3.1]nonyl)ethane)) strong signals for [Pd(CHPhCH_2Ph)(bcope)]OTf (**2**) were detected with diphenylacetylene and *p*-H_2. The addition of the Lewis base pyridine (py) enabled the trapping, and hence detection, of vinyl containing [Pd(CPh=CHPh)(bcope)(py)]OTf (**3**–**py**) and the monohydride [Pd(H)(bcope)(py)]OTf (**4**–**py**) of Scheme 1.[20] These complexes then undergo slow pyridine loss such that the system maintains hydrogenation activity. A DFT study considered the role of neutral versus cationic pathways within this reaction and supported a cationic route that is based around a monohydride intermediate in accordance with experimental results.[57]

Related reactions involving the aqua adduct, [Pd(bcope)$(OH_2)_2$]$(OTf)_2$, with H_2 and CO, have also been reported by Baya, et *al*.[58] They saw the formation of the mixed hydrido carbonyl complex [[(bcope)Pd]$_2$(μ–H)(μ–CO)][OTf] (**5**), alongside the dimer [Pd_2(bcope)$_2(CO)_2$]$(OTf)_2$. In contrast, the trimer [Pd_3(bcope)$_3(\mu_3–H)_2$]$(OTf)_2$ proved to form upon reaction with H_2 alone. These products form as a direct result of the low stability of the corresponding palladium monohydride species.[46]



Scheme 1: Reported reaction intermediates detected through PHIP-NMR spectroscopy during the hydrogenation of diphenylacetylene by **1** and *p*-H_2 with the red labels indicating which signals provide an enhanced response.[20]

In this study, we use Pd$(OTf)_2$(bcope) (**1**) to drive the methoxycarbonylation of diphenylacetylene, and both ^{13}CO and C_6D_5–^{13}C≡C–C_6D_5 are employed to aid in the characterization of a series of reaction intermediates that are seen through the use of *p*–H_2 under mild conditions. A series of 1D–EXSY studies are completed to probe, directly, the reactivity of these species, with GC/MS measurements being used to confirm the identity of the organic reaction products. As a consequence we improve on our understanding of the role these species play in this important industrial reaction.

Experimental

General Conditions and Materials: All manipulations were carried out under an inert atmosphere, using standard Schlenk or high vacuum techniques. Solvents were obtained from Fisher and $PdCl_2$ from Acros Organics. The phosphine ligands were provided by Shell. [Pd$(OTf)_2$(bcope)] (**1**) was prepared according to a literature methods[17] and its identity confirmed by NMR. Ph–^{13}C≡C–Ph was prepared as described previously.[17] NMR spectra were collected on Bruker DRX 400, and Avance 500 spectrometers. The deuterated solvents methanol–d_4 and dichloromethane–d_2 used in this study were obtained from Sigma Aldrich. The reported shifts are temperature and solvent sensitive, all spectra are calibrated and the chemical shifts quoted refer to those detected under the conditions indicated. The authentic methoxycarbonylation product, α-phenyl-cinnamic ester, **6** was prepared independently by the reaction of the corresponding carboxylic acid with methanol.

NMR samples: For a typical NMR sample, *ca.* 1 mg of **1** and 2 mg of diphenylacetylene (*ca*. 10 fold excess) were dissolved in 0.6 ml of the specified deuterated solvent in a 5 mm NMR tube, which was equipped with a Young's valve. When a carbonylation reaction was being explored, the sample was

degassed and an appropriate mixture of CO and *p*–H_2 added (typically a 1:2 ratio, in order to reach a total pressure of 3 bar).

Key NMR data, organic reaction products:

PhHC=C(Ph)COOMe (**6**), $CDCl_3$, 298 K, ^{1}H NMR: δ 7.84 (s, 1H, C*H*Ph, $^1J_{CH}$ = 156.0 Hz, $^2J_{CH}$ = 3.5 Hz; $^3J_{CH}$ = 7.5 Hz), δ 3.82 (s, 3H, OCH_3), δ 7.06 (t, 2H, J_{HH} = 7.5 Hz, *o*-H of *Ph*C), δ 7.18 (t, 2H, J_{HH} = 7.5 Hz, *m*-H of *Ph*C), δ 7.65 (t, 1H, J_{HH} = 7.5 Hz, *p*-H of *Ph*C), δ 7.21 (t, 2H, J_{HH} = 7.5 Hz, *o*-H of *Ph*C), δ 7.38 (t, 2H, J_{HH} = 7.5 Hz, *m*-H of *Ph*CH), δ 7.52 (t, 1H, J_{HH} = 7.5 Hz p-H of *Ph*CH); $^{13}C\{^1H\}$ NMR: δ 140.5 (s, 1H, $^1J_{CH}$ = 156.0 Hz, *C*HPh), δ 132.6 (s, 1H, $^2J_{CH}$ = 3.6 Hz, *C*Ph), δ 168.0 (s, 1H, $^3J_{CH}$ = 7.5 Hz, *C*O), δ 130.6, 129.8 (C*Ph*), δ 129.1, 127.9, 126.7 (CH*Ph*).

PhHC=C(Ph)COOEt, $CDCl_3$, 298 K, ^{1}H: δ 7.74 (s, 1H, C*H*Ph, $^3J_{CH}$ = 7.4 Hz), δ 4.32 (quart, 2H, $^3J_{CH}$ = 7.13 Hz, OCH_2), δ 1.34 (t, 3H, $^3J_{CH}$ = 7.13 Hz, CH_3); $^{13}C\{^1H\}$: δ 163.9 (s, 1H, $^3J_{CH}$ = 7.4 Hz, *C*O).

PhHC=C(Ph)CO(OTf), CD_2Cl_2, 308 K, ^{1}H: δ 7.69 (C*H*Ph)

Key NMR data, reaction intermediates:

[Pd(CHPhCH$_2$Ph)(bcope)]OTf (**2**), CD_2Cl_2, 313 K, ^{1}H NMR: δ 4.95 (m, J_{HH} = –4.3 Hz, 11.2 Hz, C*H*Ph), δ 3.10 (dd, CH_2Ph, J_{HH} = –4.3 Hz, 15.0 Hz) and δ 2.93 (dd, CH_2Ph, J_{HH} = 11.2, 15.0 Hz); $^{31}P\{^1H\}$ NMR: δ 32.2 (d, J_{PP} = 90.2 Hz, P *trans* to alkyl), δ 42.1 (d, J_{PP} = 90.2 Hz, P *cis* to alkyl); $^{13}C\{^1H\}$ NMR: δ 35.2 (dd, J_{CP} =16.2 Hz, 5.4 Hz, *C*H_2Ph), δ 62.3 (dd, J_{CP} = 54.0 Hz, 16.2 Hz, *C*HPh).

[Pd(CPh=CHPh)(bcope)(CD$_3$OD)]OTf (**3–CD$_3$OD**), CD_3OD, 313 K, ^{1}H NMR: δ 6.77 (dd, J_{PH} = 13.6 and 6.8 Hz, 1H, =C*H*Ph); $^{31}P\{^1H\}$ NMR: δ 21.8 (m, J_{PH} = 13.6 Hz, P *trans* to vinyl), 39.0 (m, J_{PH} = 6.8 Hz, P *cis* to vinyl); $^{13}C\{^1H\}$ NMR: δ 162.1 (*C*Ph), δ 130.1 (CHPh).

[Pd(C(Ph)=CHPh)(bcope)(CO)]OTf (**3–CO**), CD_3OD, 308 K, ^{1}H NMR: δ 6.90 (br, 1H, PhC*H*).

[PdH(bcope)(CO)]OTf (**4–CO**), CD_2Cl_2, 313 K, ^{1}H NMR: δ –4.64 (dd, J_{PH} = 190.0 Hz, 29.0 Hz, hydride); $^{31}P\{^1H\}$ NMR: δ 46.0 (d, J_{PH} = 190.0 Hz, P *trans* to hydride).

[[(bcope)Pd]$_2$(μ–H)(μ–CO)]OTf (**5**), CD_3OD, 308 K, ^{1}H NMR: –5.34 (quint, J_{PH} = 47.2 Hz, 1H, hydride); $^{31}P\{^1H\}$: δ –20.9 (d, J_{PH} = 47.2 Hz).

[Pd(H)$_2$(μ^1–bcope)(μ^2–bcope)]OTf (**7**), CD_3OD, 308 K, ^{1}H NMR: δ –8.59 (ddt, J_{PH} = 105.4 Hz, 44.2 Hz, 10 Hz, J_{HH}= –10 Hz, H_a), δ –8.61 (ddt, J_{PH} = 105.4 Hz, 44.2 Hz, 10 Hz, J_{HH}= –10Hz, H_b); $^{31}P\{^1H\}$ NMR: δ 48.9 (m, J_{PH} = 105.4 Hz, 44.2 Hz, J_{PP} = 29.4 and 12.6 Hz, P *trans* to H_a), δ 48.2 (m, J_{PH} = 105.4 Hz, 44.2 Hz, J_{PP} =29.4 and 12.6 Hz, P *trans* to H_b), 19.2 (t, J_{PH} = 10 Hz, J_{PP} = 12.6 Hz).

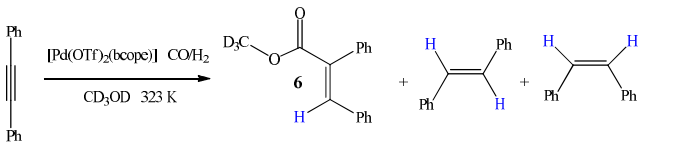
[Pd[COC(Ph)=CHPh(bcope)(CO)]OTf (**8**), CD_2Cl_2, 313 K, ^{1}H NMR: δ 7.89 (dd, J_{PH} = 22.0 Hz, 3.5 Hz, $^1J_{CH}$ = 156.2 Hz, $^2J_{CH}$ = 3.5 Hz, 1H, vinyl H); $^{31}P\{^1H\}$ NMR: δ 36.0, (m, J_{PH} = 22.2 Hz, P *trans* to vinyl), δ 43.2, (m, J_{PH} = 3.5 Hz, P *cis* to vinyl); $^{13}C\{^1H\}$ NMR: δ 137.2 (d, J_{CH} = 156.2 Hz, *C*HPh), δ 137.8 (d, J_{CH} = 3.4 Hz, CPh).

[Pd(MeOOCPhC=CHPh)(bcope)] (**9**), CD_3OD, 333 K, ^{1}H NMR: δ 5.08 (m, J_{PH} = 7.0 Hz, J_{PH} = 7.0 Hz, $^3J_{CH}$ = 7.5 Hz, PhC*H* = 151 Hz). $^{13}C\{^1H\}$ NMR δ 35.6 (CHPh).

[Pd(*cis*–PhCH=CHPh)(bcope)(CO)](OTf)$_2$ (**10**), CD_3OD, 333 K, ^{1}H NMR: δ 4.26 (m, J_{PH} = 13.0 Hz, 3.7 Hz, $^1J_{CH}$ = 133.5 Hz, $^2J_{CH}$ = 3.3 Hz, PhC*H*=C*H*Ph); $^{13}C\{^1H\}$ NMR: δ 59.5 (*C*HPh).

Results and Discussion

$Pd(OTf)_2$(bcope) (**1**) readily catalyzes the conversion of diphenylacetylene and H_2 in methanol solution into *cis*- and *trans*-stilbene, and diphenylethane.[20] The addition of CO to the H_2 feed (1:2 ratio) proved to change this product mix, with the methyl-ester C(Ph)(H)=C(Ph)CO_2CD_3 (**6**) of Scheme 2 also being formed according to gas chromatographic analysis. Furthermore, when a series of $^{31}P\{^1H\}$ NMR spectra are recorded while this reaction is taking place the signal for **1** at δ 74.0 is slowly replaced by a δ 51.9 resonance that is due to $[Pd_2(bcope)_2(CO)_2](OTf)_2$.



Scheme 2: Summary of the organic products detected during the reaction of diphenylacetylene with CO and H_2 in the presence of **1** in methanol–d_4; the blue labels reflect atoms that show the PHIP effect.

Detection of PhHC=C(Ph)COOMe (6) in methanol-d_4 solution. The identity of the new organic product, **6**, was further confirmed by comparing appropriate NMR data with those of the authentic compound. The vinyl proton's ^{1}H NMR signal of **6** appears at δ 7.84, and its carbonyl resonance appears at δ 168.0 and is associated with a 7.5 Hz coupling to the vinyl proton. Furthermore, when Ph–^{13}C≡C–Ph is used, the vinyl proton signal splits again through the addition of 1- and 2-bond ^{1}H–^{13}C couplings of 156 Hz and 3.5 Hz. GC-MS analysis of this mixture yields a molecular ion at m/z 242 for **6** when it is formed in methanol–d_4, which falls to m/z 239 when the reaction is completed in methanol–h_4 and increases further to 252 when d_{10}–Ph–C≡C–Ph rather than Ph–C≡C–Ph is employed. Consequently we deduce that the alcohol is the source of the esters methyl substituent rather than CO. In a typical NMR study with **1** at 298 K, the yield of ester proved to be 70 %. However, with 100 bar of CO and 20 bar of H_2, the selectivity of this reaction approaches 99 %.

Effect of employing p-H_2. A study was then undertaken where the *normal*–H_2 gas used in these studies was replaced with *p*–H_2. Now, in methanol–d_4, PHIP enhanced ^{1}H NMR signals are evident as shown in Figure 1 at temperatures around 306 K.

These enhanced resonances can be divided into those that originate from the organic products, *cis*- and *trans*-stilbene, **6**, and those that are palladium based which include signals for the previously reported intermediates [Pd(CHPhCH$_2$Ph)(bcope)]OTf (**2**) and [Pd(CPh=CHPh)(bcope)(methanol)]OTf (**3–CD$_3$OD**) alongside those for newly seen, [Pd(CPh=CHPh)(bcope)(CO)]OTf, **3–CO**. The three alkyl proton signals of **2** are enhanced through PHIP, whilst those of the vinyl protons of **3–CD$_3$OD** and **3–CO**, which contain a single *p*-H_2 derived proton, exhibit the One–Proton–PHIP effect described by Eisenberg.[37] In this case, this is a result of their formation from a monohydride complex, such as [Pd(H)(bcope)(CO)]OTf (**4-CO**, see later), which is formed after stilbene loss from **2**. The signals for **3-CD$_3$OD** and **3-CO** are broad, and coalesce when the temperature is raised, or a lower [CO] is present in a process that is [CO] dependent.

The signal at around δ 7.6 that is enhanced belongs to the η^3-Ph[59] group of the alkyl ligand of **2**. The aromatic protons of

the phenyl group of the PdCHPh group therefore couple to those of the PHIP-enhanced CH proton. In low field, the result is SABRE type magnetization transfer which is visible when the sample is interrogated at high field.[60]

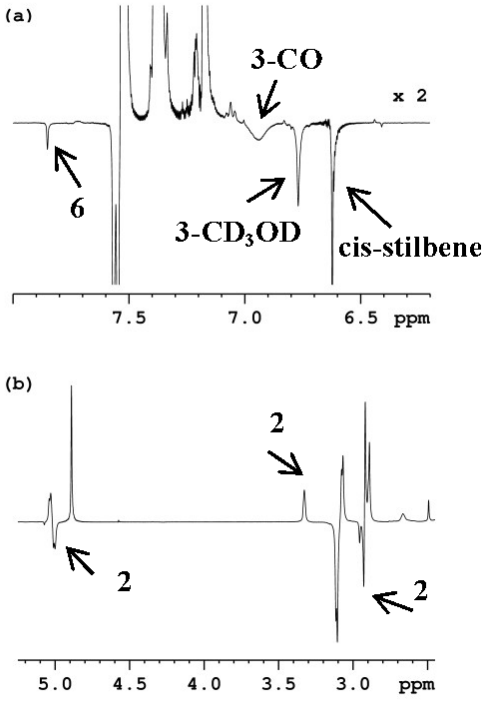


Figure 1: Two sections of a $^1H\{^{31}P\}$ NMR spectrum, recorded in methanol-d_4 during the reaction of **1**, diphenyl acetylene, CO and *p*-H_2 showing (a) the one-proton PHIP enhanced signals of **6**, **3-CD$_3$OD**, **3-CO** and (b) the PHIP enhanced signals of cis-stilbene and **2**, attributed according to the labels of Scheme 1.

Role for 2 in the hyperpolarisation step. The effect that leads to the detection of PHIP enhanced resonances in **2** plays a vital role in this work. Previous studies have shown that this complex is formed by the reaction of [Pd(H)(bcope)]OTf with Ph–C≡C–Ph and H_2. When such a study is completed with *p*-H_2, this process leads to the generation of **2** where two of the alkyl protons originate from this reagent.[20] However, **2** reacts further on the NMR timescale in a number of ways, forming *cis*- and *trans*-stilbene and [Pd(H)(bcope)]OTF through reversible β-H transfer. These processes act to place *p*-H_2 derived protons in all sites and result in the hydride signal of [Pd(H)(bcope)]OTF appearing in emission through the one-proton PHIP effect throughout these measurements. When this polarized monohydride precursor reacts with Ph–C≡C–Ph, the vinyl complexes **3-CO** and **3-CD$_3$OD** are detected through a hyperpolarized response as exemplified by Figure 1. While **1** has been shown previously to react with methanol or H_2 to yield [Pd(H)(bcope)]OTF when *p*-H_2 is used its hydride signal remains unpolarised in the absence of Ph–C≡C–Ph[20]; the formation of palladium monohydride cations under such condition is well established.[61-63]

Route to 6 According to the independent work of Leeuwen[40] and Iggo[64] the key intermediate that is predicted to be involved in the formation of **6** is [Pd(COCPh=CHPh)(bcope)(methanol)]OTf rather than [Pd(COCPh=CHPh)(bcope)(CO)]OTf, with rapid inner sphere nucleophilic attack of the associated alcohol/alkoxide ligand leading to the ester, alongside the formation of [[(bcope)Pd]$_2$(μ–H)(μ–CO)]OTf (**5**) which is evident as a weak signal in the NMR spectrum shown Figure 2. PHIP therefore allows the detection of a number of predicted species under the mild reaction conditions described here but fails in showing any direct evidence for [Pd(COCPh=CHPh)(bcope)(methanol)]OTf.

Catalyst degradation. In the hydride region of this methanol-d_4 sample, signals for the previously unseen catalyst degradation product [Pd(H)$_2$(μ^1–bcope)(μ^2–bcope)] (**7**) are visible, as detailed in Figure 2. **7** actually exhibits two overlapping hydride signals at δ –8.59 and δ –8.61 that appear in a 1:1 ratio and are separated by less than 10 Hz on a 500 MHz spectrometer (Figure 2). These hydride signals are visible for several minutes at 308 K and can be regenerated by adding fresh *p*–H_2 to the solution. They also remain visible in a double quantum filtered OPSY–NMR experiment in accordance with their dihydride origin. The three ^{31}P NMR signals of this product were located at δ 48.9, 48.2 and 19.2 in the corresponding PHIP enhanced heteronuclear multiple quantum correlation (HMQC) measurement. We note that the related complex (^{t}BuCOPE)Pd(H)$_2$ has been seen previously in dichloromethane–d_2 solution.[17]

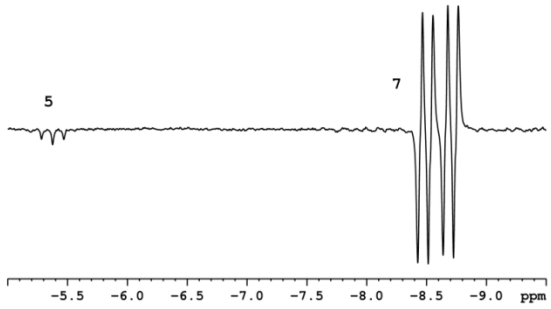


Figure 2: ^1H NMR spectrum showing the hydride signals for **5** and **7** that are visible through the PHIP effect.

Utilisation of dichloromethane–d_2 to detect [Pd(CO-CPh=CHPh)(bcope)(CO)]OTf (8). These observations change when dichloromethane–d_2 is used as the solvent instead of methanol. Now, at 298 K PHIP enhanced signals are readily seen for **2** and **3**–**CO**. In this case, the δ 3.13 and 2.93 signals of the CH_2Ph group of [Pd(CHPhCH_2Ph)(bcope)]OTf (**2**) are strongly polarised, whilst that for its CHPh resonance, at δ 4.96, is barely visible. This dramatic change in relative polarisation level from the 1:4 ratio of Figure 1, in methanol–d_4, will be discussed later. We note that the emission peak for **3-CO** appears at δ 6.89, and is still very broad in appearance, having 17 times lower area than the δ 3.13 signal of **2**. While it sharpens on phosphorus decoupling, a series of 2D spectra

that were recorded to locate the two expected ^{31}P coupling partners were unsuccessful. However, a series of selective ^{1}H{^{31}P} NMR experiments, where the ^{31}P decoupling frequency was varied systematically, suggested the presence of two signals at *ca*. δ 45 and 30. Broad features for such species at 298 K are not unexpected given the high reactivity of these systems.[65]

Upon warming to 305 K, these signals all roughly double in intensity in accordance with an increase in reaction turnover. This simple change, however, also allows the NMR signals for a number of further species to be detected. First, in the organic region, a weakly polarized doublet of doublets appears at δ 7.89 as shown in Figure 3. This emission signal collapses into singlet on ^{31}P decoupling and is therefore metal based. Phosphorus couplings in this resonance were measured at 22 Hz and 3.5 Hz, with the associated ^{31}P resonances occurring at δ 36.0 and δ 43.2 respectively. Furthermore, when mono–^{13}C labelled Ph–^{13}C≡C–Ph was used, further ^{13}C couplings of 156 Hz and 3 Hz were observed on this proton signal. This new product is therefore assigned to the acyl intermediate [Pd(CO-CPh=CHPh)(bcope)(CO)]OTf (**8**) whose formation is implicated in the earlier methanol-d_4 reaction. The formulation of **8** as a CO adduct is consistent with results presented in the literature for related systems.[64]

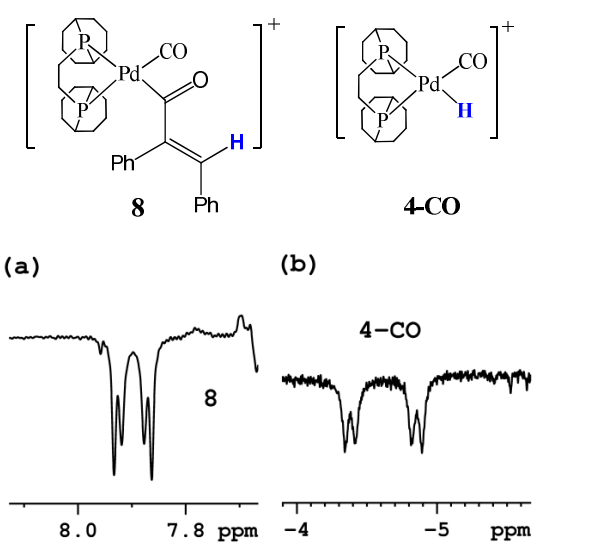


Figure 3: Upper: Structures of monohydride **4-CO** and acyl **8**. Lower: (a) PHIP enhanced ^{1}H NMR signal of **8** (blue atom) and (b) corresponding NMR signal for **4-CO** (blue atom).

Detection of PhHC=C(Ph)CO(OTf). A further, weak singlet is observed as an emission signal at δ 7.69 which we attribute to the corresponding trifluromethane sulfonate ester (see ESI). We note that an enhanced signal is also seen at δ 9.52 for HOTf in these NMR spectra and that neither of these signals are seen in methanol-d_4 itself, or when a single equivalent of CH_3OH is added to this CD_2Cl_2 solution as both signals are replaced by an enhanced peak at δ 7.84 for **6**. The formation of this triflic acid product is consistent with the promotion of this reaction with added acid.[40]

Detection of CO stabilised [Pd(H)(bcope)(CO)]OTf (4-CO). The hydride region of this 305 K NMR spectrum is further complicated by the detection of a new monohydride complex, as an emission signal, at δ –4.64, with doublet of doublets multiplicity which simplifies into a singlet on ^{31}P decoupling (Figure 3). The corresponding ^{31}P couplings exhibited by this resonance are 189 Hz and 29 Hz and require a palladium centre with magnetically inequivalent phosphine ligands that are *trans* and *cis* the hydride ligand respectively. Although this hydride signal is only observed in the presence of CO, the use of ^{13}CO failed to change its appearance. However, its chemical shift and splitting pattern are very similar to that of [Pd(H)(d^{t}bpx)(CO)]OTf reported by Clegg et *al*.[2] and it is therefore assigned to [Pd(H)(bcope)(CO)]OTf (**4-CO**). A further and much weaker hydride signal appears at δ –5.34 after 10 minutes due to **5**.[40, 58] Complexes of this type have been shown to exhibit carbonylation activity but are thought to be off-loop and have been proposed to form via the reaction of [(bcope)Pd] with **4-CO**.[40, 64]

Upon warming this sample to 310 K, these two hydride signals both grow in size, with the difference in relative hydride peak areas falling to 4 : 1. Additionally, in the organic region of this ^{1}H NMR spectrum, the enhanced signals of **3-CO** and **8** now appear in a 1: 1.7 intensity ratio thereby suggesting an increase in the rate of CO insertion. Further warming of this sample to 315 K results in the δ 2.93 signal that is seen for the C*H*Ph group of **2** becoming more strongly polarised, such that there is a 1:8 intensity ratio when compared to the CH_2Ph signals and this difference reduces further to 1:4 at 320 K and 1:1.2 at 323 K. Additionally, at 315 K, hyperpolarised *cis*-stilbene becomes readily visible as a signal at δ 6.66 with the signals for **3-CO** and **8** now appearing in a 1:8 ratio.

Rationalising the change in alkyl proton signal intensities observed in 2. This difference in intensity is readily apparent in the corresponding ^{1}H-OPSY NMR spectra and confirms that the kinetically dominant addition of *para*hydrogen places two protons on the δ 3.10 and δ 2.93 derived sites of **2**. Hence the mechanism of formation of **2** must therefore involve a reaction which shows a level of selectivity for geminal substitution which reduces as the temperature is raised, presumably because of alkene rotation in the resulting Pd(H)(PhCH=CHPh) containing reaction intermediate. We note that similar selectivity has been reported previously by Bargon et *al*.[66]

It is noteworthy that warming also results in a fall in the hydride signal strength of **4-CO** with that of [(bcope)Pd]$_2$(μ–H)(μ–CO)]OTf (**5**) gaining intensity. The emission signal of **5** now appears clearly with a quintet multiplicity that simplifies into a singlet on ^{31}P decoupling. It proved possible to dramatically increase the size of the hydride signal for **5** by adding 1μl of D_2O or H_2O to this sample and the corresponding acid C(Ph)(H)=C(Ph)CO_2H is now produced as a carbonylation product, revealed through an enhanced signal at δ 7.96 with signals for **7** being seen, centred on δ -8.65, and **10** at δ 4.26 (see later). Interesting, the free H_2 peak also proved to be enhanced in these NMR traces, with the corresponding HD signals also appearing in emission as detailed in Figure 4. The observation of a hyperpolarised H_2 response has been

commented on before.[67] Increasing the level of water to 5 μl, proved to suppress the signals for both **3-CO** and **4-CO** whilst further enhancing that for **5** alongside that of the acid product.

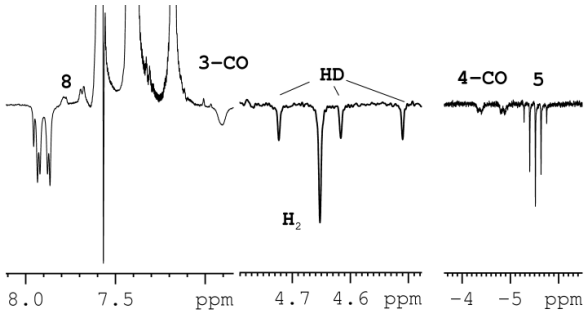


Figure 4: Three sections of a ^{1}H NMR spectrum recorded during the palladium catalysed reaction of diphenylacetylene with CO, D_2O and H_2 in CD_2Cl_2 solution are presented. The formation of C(Ph)(H)=C(Ph)CO_2H is indicated by the emission signal at δ 7.96 (left panel). Hyperpolarised H_2 and HD is created (middle panel) alongside **4-CO** and **5** (right panel).

Minor reaction products detected in methanol-d_4 solution. We now return to the methanol-d_4 spectra in order to build on the earlier observations by incorporating the dichloromethane–d_2 based information. We note, that the intensity of the resulting PHIP enhanced NMR signals are again strongly temperature sensitive, and at 304.4 K signals for **3**–**CH_3OH** and **3-CO** are visible alongside those of a new species, **9**, at δ 5.08. Upon warming to 306.6 K the signals for **3**–**CH_3OH** and **3-CO** reduce in size with those of the ester **6** appearing at δ 7.84 alongside that of **9**. The hyperpolarised resonance of **9** also appears in emission, but surprisingly exhibits a triplet multiplicity where J_{PH} = 7.0 Hz, and upon ^{31}P decoupling it changes into a singlet. Furthermore, when ^{13}CO is used this resonance exhibits a further 7.5 Hz splitting which is similar in size to that exhibited by **6**. When ^{13}CO and C_6D_5–^{13}C≡C–C_6D_5 are used, additional ^{1}H–^{13}C splittings of 150.1 and 6.6 Hz are detected and a ^{13}C signal for an alkene CH resonance is located at ~36 ppm. This product therefore contains **6** as a ligand and we assign it to species **9** of Figure 5. It is predicted to form via **8** after CO loss and reaction with methanol which leads to ester **6** and DOTf. This process involves the coordination of **6** to neutral Pd(bcope) and could proceed in a concerted manner within the coordination sphere of the metal or within the solvent cage. As the temperature is raised further the signals for **6** dominate.

In addition, a further weak and polarised emission signal also becomes visible at δ 4.26 due to **10**. ^{31}P decoupling simplifies the appearance of this resonance into a doublet of doublets by removing J_{PH} couplings of 13.5 and 4.1 Hz, and when ^{13}C labelled diphenylacetylene is employed additional $^{1}J_{CH}$ and $^{2}J_{CH}$ couplings of 133.5 Hz and 3.3 Hz are visible and a weak alkene CH signal at ~60 ppm. Now, however, the addition of ^{13}CO provides no further splitting, although we note that this product is only detected in the presence of CO and its intensity is largest when a strong PHIP-signal is seen for *cis* stilbene.

When looking at the appearance of these additional ^{1}H NMR signals, we need to consider the impact of J_{PP} on their appearance. For conditions where the phosphines are inequivalent, and $J_{PP}>J_{PH}$, we will see a virtual triplet regardless of the individual J_{PH} values while if $J_{PP}<J_{PH}$ then a doublet of doublets would be expected. Glueck et *al*. reported a number of Pd(0) *bis*-phosphine *trans*-stilbene complexes yield ^{13}C signal for the alkene at around 60 ppm, with the connected ^{1}H signal appearing at ca. 5 ppm but they yield small J_{PH} couplings of just 2 Hz and J_{PP} couplings of between 20 and 27 Hz.[68] Interesting, the corresponding ^{31}P coupling increases to around 70 Hz in related hexadiene based complexes.[69] In the case of related Pd(II) *bis* phosphine complexes containing H and MeOH ligands couplings of 16-30 Hz are typical and so a virtual triplet would be expected for the alkenic protons in both of these types of product if such large couplings are retained.[2, 70]

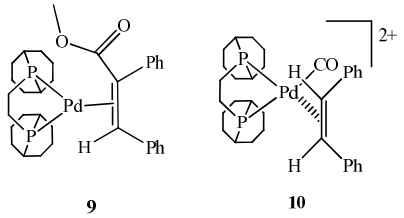


Figure 5: Structures of **9** and **10.**

We therefore suggest in **10** that CO binding to the fourth site occurs, and that the palladium centre is charged, which means that an out-of-plane *cis*-stilbene ligand is indicated (Figure 5). The signals of **10**, alongside those of **2** and *cis*–stilbene itself, become more evident as the samples temperature is raised and overtime, the enhanced hydride signal of **5** appears in the associated NMR spectra. Studies by Parker et *al*. have suggested that the alkenes of such species could be labile and it is therefore not surprising that complexes of this type are only detected here through a hyperpolarised response.[71]

Exchange Spectroscopy measurements in dichloromethane rationalise the failure to detect [Pd(COCPh=CHPh)(bcope)(methanol)]OTf. A series of 1D exchange spectroscopy (EXSY) experiments were used to probe magnetization transfer in **8** and **4-CO** in dichloromethane solution at 300 K. When the signal at δ 7.89 for the acyl complex **8** was selectively excited, magnetisation transfer into the δ 7.69 signal of the triflate ester, alongside weaker transfer into the δ 4.99 of **2** is readily observed, with even weaker transfer into the signal for *trans*–stilbene being evident. We estimate that the relative rates for these conversions are 0.73 s^{-1}, 0.03 s^{-1} and 0.006 s^{-1} respectively. Analysis of these data requires that the triflate ester reacts to reform **8** with a rate constant of 3.4 s^{-1}. In confirmation of this, when the signal at δ 7.69 for the triflate ester is probed in a similar way, rapid transfer into the δ 7.89 signal of **8** is seen at an identical rate, within error, to that predicted from the observations based on the excitation of **8**.

In addition, when the hydride signal of **4-CO** at δ –4.64 is selected, magnetization transfer into signals at δ 7.89 (**8**), δ

7.69 (triflate ester) and δ 4.66 (H_2) is seen. The ratio of the resulting signal intensities for **8** and the triflate ester that result from magnetisation transfer via **4-CO** are 1 : 6.25, and differ from the predicted ratio of 4.6 : 1 that comes from the earlier rates constants. This observation suggests the existence of a second, concentration dependent route to the triflate ester involving **4–CO** that does not involve **8**. Logically, this involves [Pd(CO-CPh=CHPh)(bcope)(OTf)], formed by the competitive trapping of 16-electron [Pd(CO-CPh=CHPh)(bcope)]OTf by $^{-}$OTf rather than CO. This is in direct agreement with literature predictions[40] which predict a role for [Pd(COCPh=CHPh)(bcope)(methanol)]OTf in the formation of **6**.

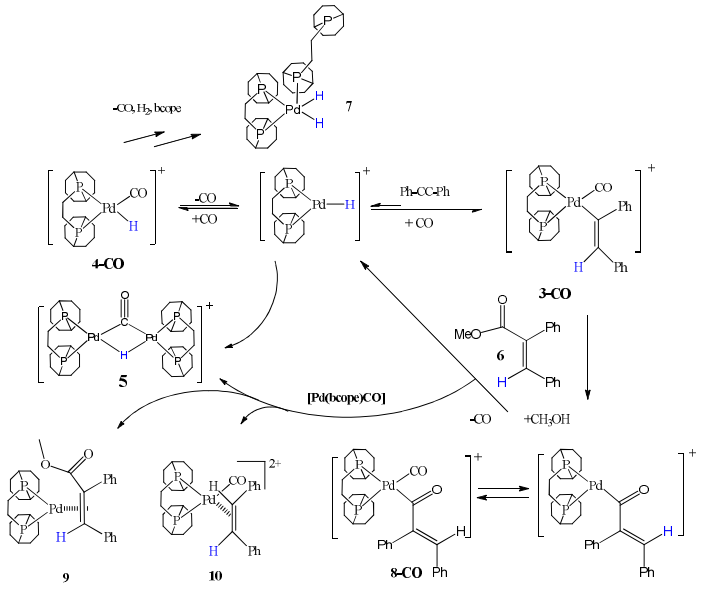
Conclusions

In summary, the methoxycarbonylation of diphenylacetylene has been studied with *p*–H_2 and a number of reaction intermediates have been identified through the use of the PHIP effect in methanol and dichloromethane solution. This reaction is initiated by the conversion of **1** into the monohydride complex [Pd(H)(bcope)(OTf)] which is readily observed as its CO adduct, through the hyperpolarised response of [Pd(H)(bcope)(CO)]OTf (**4-CO**), as detailed in Scheme 3. **4-CO** has been shown to play a direct role in the methoxycarbonylation process according to Scheme 3, where the detection of an enhanced NMR signal for the vinyl product **3–CO** is augmented by those of the ester **6**. Logically these form sequentially in agreement with the analogous reactions described in the introduction.

6 is most readily formed when methanol intercepts the acyl product [Pd(CO-CPh=CHPh)(bcope)]OTf, rather than CO which leads to [Pd(bcope)] and DOTf. The [Pd(bcope)] that is formed in this process can then be trapped to form products **5** and **9** according to Scheme 3. **9** is predicted to form by a simple ligand rearrangement within the coordination sphere of the metal after MeOD attack leads to **6**, but **5** requires a reaction with **4-CO**. Baya et *al.* and others have suggested that **5** forms via the combination of [Pd(bcope)CO] and $[Pd(H)(bcope)]^+$ which would also be expected to be present under these conditions.[40, 64]

In addition, signals for the dihydride based deactivation product **7** are seen in these NMR spectra because of the PHIP effect. This reflects the fact that its hydride ligands are magnetically distinct. As a consequence, **7** must undergo the reductive elimination of H_2 which provides a route to [Pd(μ^1–bcope)(μ^2–bcope)] under conditions where H_2 is present. This neutral species might be expected to undergo phosphine loss to form [Pd(bcope)] and hence a second route to **5** is possible. We note that the dihydride $[Pd(H)_2(bcope)]$ would be PHIP active because of the second order nature of its hydride ligands.[72] Hence, as it is not detected, we can conclude that it is either too reactive to be seen, which is unlikely given the previous observation of (^{t}BuCOPE)Pd$(H)_2$ or that the contribution of a dihydride based reaction pathway is minimal in agreement with earlier literature predictions.[57, 73]

We conclude therefore that PHIP reflects an ideal platform from which to study this methoxycarbonylation reaction and thereby establish its potential to follow a wider range of catalytic processes than was previously thought possible. Furthermore, the observation of the enhanced NMR signals for these reaction intermediates under our mild reaction conditions confirms a high level of intermediate turnover during catalysis. This deduction is based on the fact that hyperpolarised signals are only expected to retain a visible signal enhancement for 3 T_1 periods unless the molecules that provide these signals are continually replenished. This time will range from 1-10 seconds, according to whether we are dealing with a PdH or CH based signal, and further confirms the importance of these intermediates in the catalytic cycle. By using EXSY methods we have also established a direct role for **3** and **4** in this process which is clearly homogeneous in nature.



Scheme 3: Structures of the reaction intermediates that are detected through PHIP when hyperpolarized **4-CO** converts diphenylacetylene into **6** and related products.

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