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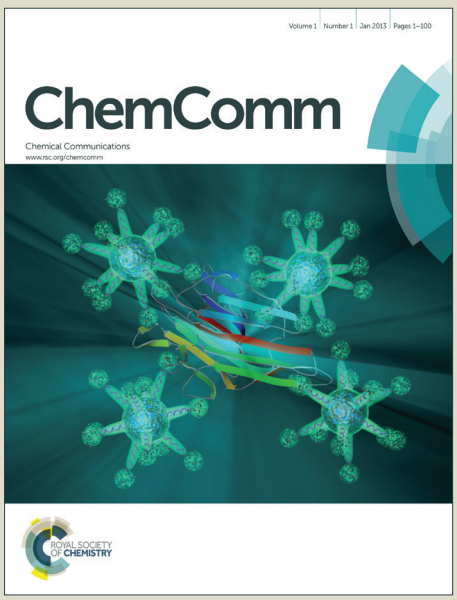

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Selective Catalytic Deuteration of Phosphorus Ligands using Ruthenium Nanoparticles. A New Approach to Gain Information on Ligand Coordination

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Phenyl rings in phenyl- or phenyl-alkylphosphines are selectively deuterated at the *ortho* position using Ru/PVP nanoparticles, while are fully reduced in the case of arylphosphine oxide derivatives and do no react in the case of arylphosphite. This different behavior provides information about the coordination mode of each ligand.

In the last decade, the application of metal nanoparticles in catalysis has developed due to their unique electronic properties, the mild reaction conditions required, and the high selectivity obtained.[1] Such nanocatalysts can be stabilized by polymers, surfactants or ligands, which allow the control of their size, shape and dispersion.[2] Furthermore, the choice of the appropriate stabilizer for the M-NPs is crucial since it usually has an important effect on NPs catalytic performances. For instance, phosphorus ligands have been employed as stabilizers of transition metal nanoparticles due to their excellent coordination properties.[3] Ru NPs stabilized by phosphorus ligands were shown to be excellent catalysts for various catalytic processes such as arene reduction,[4] and in particular, Ru NPs stabilized by triphenylphosphine were outstanding catalysts for selective hydrogenation reactions.[5]

The interaction of stabilizing ligands such as phosphines, carbenes and aromatic compounds with the nanoparticle surface has been an object of interest in the last years, with the aim of understanding how and where it takes place and its possible influence on NPs catalytic performance. Different techniques have been used for this purpose such as ^{1}H and ^{13}C MAS[6] (magic angle spinning) NMR spectroscopy,[7] and reactivity studies with CO.[8] All these studies contributed to better understand the influence of the ligands on the site selective hydrogenations. Other ligands such as secondary phosphine oxides[9] and 4-(3-phenylpropyl)pyridine[10] were also studied using these techniques.

Phosphines are ubiquitous ligands and reagents in organic and organometallic chemistry and the availability of labelled phosphines for mechanistic studies is of high interest. Several methods based on homogeneous or heterogeneous catalysis for H/D exchange have been reported.[11] There is only one example of deuteration using Ru nanoparticles stabilized by polyvinylpyrrolidone (PVP) and D_2,[12] applied to the selective deuteration of nitrogen containing compounds such as quinolines, indoles and amines by C-H activation. Ru/PVP nanoparticles are considered as "naked" particles that permit the coordination of the substrates to their surface. Using these NPs the exclusive deuteration of positions next to the nitrogen atoms were achieved, even in the presence of other electronegative elements such as oxygen atoms. Deuteration therefore appears as a powerful technique to get insights into the interaction between nanoparticles and molecules.

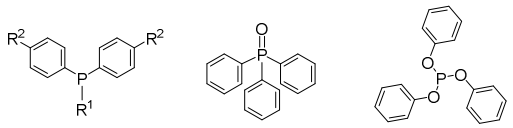

Fig. 1 Different phosphorus derivatives employed in deuteration reaction using Ru/NPs.

In this context, we envisioned that phosphorus ligands, previously reported to coordinate at the surface of nanoparticles, could be labelled using these nanoparticles as catalysts. Herein, we report a study on the use of Ru/PVP nanoparticles and D_2 for the deuteration of various phosphorus containing compounds, namely substituted phosphines, triphenylphosphine oxide and triphenylphosphite (Figure 1).

riphenylphosphine was initially used as a model substrate. The reaction was performed at 2 bar of D_2 and 55°C[12] (Scheme 1)

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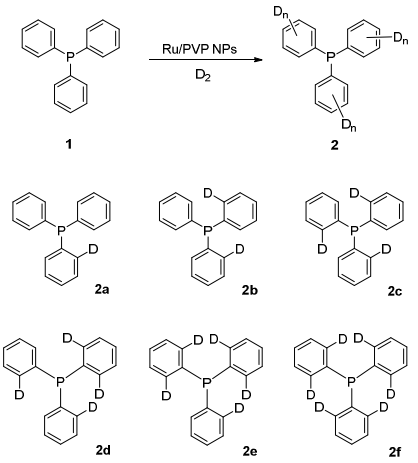
and monitored over time. Figures 2 and 3 show the $^{31}P\{^{1}H\}$ and $^{13}C\{^{1}H\}$ NMR spectra, respectively, at different reaction times (ii-v) compared with that of free triphenylphosphine (i). During the reaction, the deuteration products **2a-2f** were detected.



Scheme 1. Products detected during the deuteration of PPh_3 catalysed by Ru NPs.

Thus, when the reaction was monitored by ^{31}P NMR, after 16h, 6 new resonances located between -5.5 ppm and -6.2 ppm appeared together with the initial signal of triphenylphosphine at -5.55 ppm (Figure 2i, ii). At longer reaction times, the intensity of the signals at higher fields progressively increased (Figure 2, iii, iv). These 7 signals were shown to arise from PPh_3 and compounds **2a-f**. When the reaction was carried out for 48h at 80ºC, the signal at higher field (-6.2 ppm) corresponding to **2f** was almost exclusively observed, together with a small resonance at -6.1 ppm corresponding to compound **2e** (Figure 2v). It was therefore concluded that each added deuterium produced an isotopic shift of 0.11 ppm at higher fields and a broadening of the ^{31}P signal by 1 Hz, attributed to small P-D couplings. Mass spectrometry experiments confirmed the identity of these compounds. No signals of reduced aromatic rings were observed under these conditions.

Information about the evolution of the reaction can be also obtained by $^{13}C\{^{1}H\}$ NMR. Thus, after 16h, the signal corresponding to C2-D was detected at 134.4 ppm (td, $^{2}J_{C,P}$= 18 Hz, $^{1}J_{C,D}$=26 Hz) while C2-H remained unchanged as a doublet at 134.8 ppm ($J_{C,P}$= 19 Hz) (Figure 3, 3ii). This observation was in agreement with the partial deuteration of the *ortho* position of triphenylphosphine. The *ipso* carbon (137.3 ppm) was detected as a multiplet, as a result of the overlap of several doublets from the partially deuterated species.

When the reaction was carried out for 36h and 48h, or at 80ºC the ^{13}C NMR spectrum of the reaction product (Figure 3iii-v) clearly displayed an increase in intensity of the C2-D signal and the decrease of that of C2-H, as well as the evolution of C1 to a single doublet, due to the progressive and selective deuteration of *ortho* positions. Deuteration was >95%, measured by ^{31}P NMR. Only penta and hexadeuteraded phosphine were present in a ratio 0.08:1.

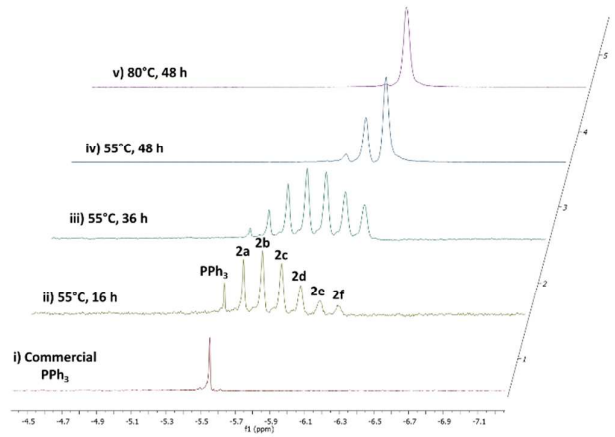


Fig. 2 Evolution of deuteration of PPh_3 (**1**) over time by ^{31}P-NMR.

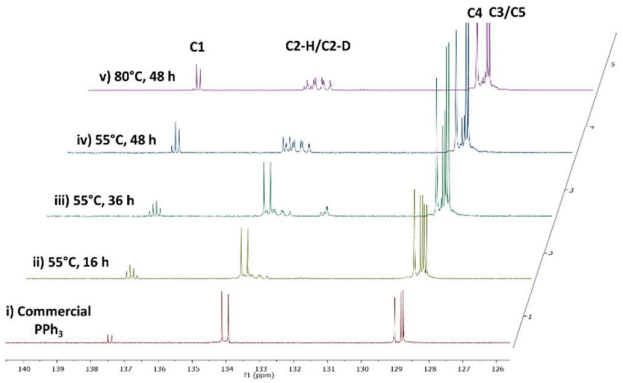
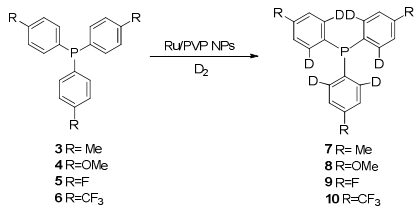


Fig. 3 Evolution of deuteration of PPh_3 (**1**) over time by ^{13}C NMR´

At this point, deuteration of various *para*-substituted triphenylphosphines was explored in order to investigate the effect of electron donating and electron withdrawing substituents (Scheme 2).



Scheme 2. Deuteration of *para*-substituted PPh_3 using Ru NPs.

In all cases, the selective deuteration of *ortho* positions of the aromatic rings of these ligands was observed. However, relevant differences in the rate of deuteration of these compounds were observed when compared with that of PPh_3. Indeed, the deuteration of phosphines **3**, **4** and **6** required heating of 80ºC for 88h for achieving levels of deuteration similar to PPh_3, while that of phosphine **5** was even slower and only 72% of labelling was achieved in similar reaction times.

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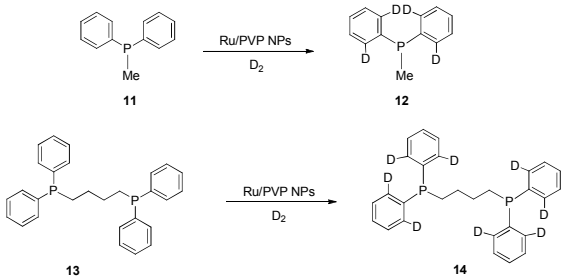
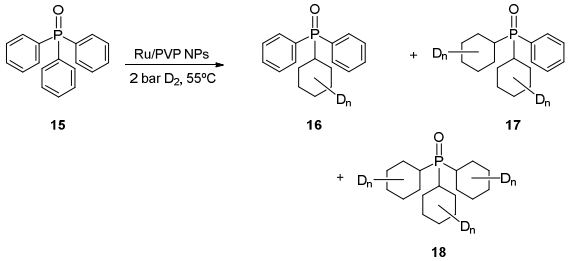
Mono (**11**) and bidentate (**13**) phosphine ligands containing aromatic and aliphatic substituents were also treated under similar reaction conditions. In these cases, only the selective deuteration of *ortho* positions of aromatic rings was observed to give **12** and **14**, respectively, whereas the methyl and methylene groups remained unaltered (Scheme 3.3).



Scheme 3. Deuteration of alkyl-containing phosphines **11**, **13** using Ru NPs.

It was therefore concluded that under these conditions, the Ru/PVP catalysts selectively deuterate the aromatic *ortho* positions and does not react with these aliphatic groups, in contrast to what has been observed with nitrogen containing compounds.[12]

We tested next deuteration of triphenylphosphine oxide (**15**), which was initially carried out under 2 bar of D_2 at 55ºC for 36 h. On the $^{31}P\{^1H\}$ NMR spectrum, the detection of signals at 45.6 and 51.4 ppm, corresponding to the dicyclohexyl-phenylphosphine oxide[13] (**17**) and tricyclohexyl phosphine oxide (**18**), respectively (Scheme 4), indicated that reduction of the substrate was taking place under these conditions (See Supplementary Information, Figure 43). The $^{13}C\{^1H\}$ NMR spectrum was much more complex than that of PPh_3 and an important number of signals were observed in the aliphatic zone, confirming the reduction of the phenyl rings. In the corresponding ^2D NMR spectrum, the presence of several broad signals in the aliphatic region, and the practical absence in the aromatic region, was also observed (See Supplementary Information, Figures 44, 46). But during the hydrogenation phase which must occur by arene coordination some additional incorporation of deuterium can result from H/D exchange.

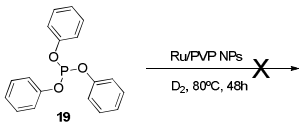


Scheme 4. Deuteration of $OPPh_3$ (**15**) using Ru NPs.

In order to avoid reduction of the substrate, the reaction time and the temperature were decreased. However, the reduced compounds **16** and **17** and/or starting material were again observed (See Supplementary information, Figures 45, 46).

These results were surprising since previous studies determined that in the presence of nanoparticles as catalysts, aromatic substrates with electron-donating groups are hydrogenated faster than compounds with electron-withdrawing groups,[14] although it should be mentioned that in some cases, no clear effects could be observed.[5] Here, despite that aryl rings of $O{=}PPh_3$ can be considered as electron poorer than those of the corresponding PPh_3, significant reduction of the aromatic rings was observed for the former while only H/D exchange was detected for the phosphine substrate. This fact was thus explained considering that the coordination of triphenylphosphine oxide to the nanoparticles involves π-interactions of the phenyl rings and, consequently, that reduction is favoured.

Finally, the deuteration of triphenylphosphite was attempted under the same reaction conditions but, surprisingly, no reaction was observed. Even when the reaction was performed at 80°C for 48 h, no deuteration was detected, and the starting material was recovered unaltered.[15]



Scheme 4. Deuteration of $P(OPh)_3$ using Ru-NPs.

Since phosphite ligands were previously reported to efficiently stabilise metal nanoparticles, it was concluded that the absence of deuteration or reduction of $P(OPh)_3$ resulted from the disposition of the phenyl groups of this ligand, which are probably pointing away from the surface of the Ru/PVP catalyst.

Although the reactivity of nanoparticles takes places in specific sites of the surface, the interest for the study of substrate/surface interactions has been limited. So far nanoparticles stabilized by ligands presenting very similar structures were shown to exhibit very distinct reactivities. Here we demonstrate that selective deuteration provides relevant information for the understanding of the surface chemistry of nanoparticles. The three types of structurally related ligands studied display very different reactivities which can be understood in terms of their coordination mode to the nanoparticle surface.

Thus, the phosphines **1**, **3-6** and the diphosphine **13** were selectively deuterated at the *ortho* positions of their aryl rings (but not in the alkyl groups), the phosphine oxide **15** gave reduction products and triphenylphosphite (**19**) remained unaltered under the same reaction conditions. These results suggest that phosphines coordinate to the nanoparticle surface through the phosphorus atom thus placing the *ortho* protons very close to the surface, which favours an H/D exchange (Figure 4). Similarly to what was proposed for nitrogen substrates, five membered-ring intermediates Ru-P-C-C-Ru' formed by oxidative addition are expected to produce this exchange.[16]

In contrast, the fact that for phosphine oxides, the phenyl rings are reduced can be explained considering that coordination to the

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nanoparticle takes place through the aromatic rings. The coordination through oxygen is unlikely, so the preferred coordination through the arenes occurs and leads to the reduction of the aromatic rings.

Triphenylphosphite was not labelled nor reduced, indicating that the presence of oxygen atoms may drive the aryl moieties away from the surface of the catalyst, impeding the H/D exchange. The five membered intermediate described for PPh_3 cannot be made in this case because coordination through oxygen atom and deuteration are disfavoured. An additional possible explanation of the behaviour of triphenylphosphite could be the strong bonding of phosphorus to the nanoparticle surface that prevents the ligand exchange and consequently the labelling of this species but it is unlikely that triphenylphosphite be more strongly coordinated to the Ru surface than triphenylphosphine.

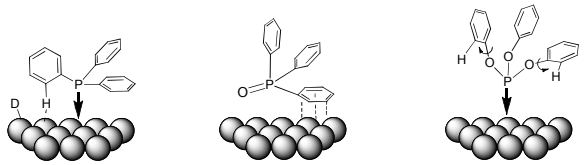

Fig. 4. Proposed coordination mode of the ligands studied to the Ru nanoparticle surface.

The results of isotopic labelling described above are compatible with the observed reduction of phosphines in catalytic processes under hydrogenation conditions, since in the presence of substrates and under drastic reaction conditions the mobility of the phosphines must increase allowing the coordination through faces and consequently the hydrogenation of the aromatic ring. However, it is remarkable that even at 80ºC for 88h no reduction of PPh_3 is observed under the 2 bar of D_2 pressure.

Important differences were observed between phosphine, phosphine oxide and phosphite. In the case of phosphine, the selective deuteration of C2 carbons indicates that the ligand is coordinated through the phosphorus atom, similarly to what has been previously observed for nitrogen donors and that the C-H bond can approach the NPs surface. This interaction allows, however, an exchange with additional ligands present in the solution so that deuteration of a macroscopic sample is possible.

In conclusion, the H/D exchange method described here allows the selective deuteration of phenyl rings in phenyl- or phenyl alkylphosphines, including diphosphines, using Ru/PVP nanoparticles and D_2, and enables the comprehension of how different phosphorus ligands coordinate to the nanoparticle surface.

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Selective Catalytic Deuteration of Phosphorus Ligands using Ruthenium Nanoparticles. A New Approach to Gain Information on Ligand Coordination

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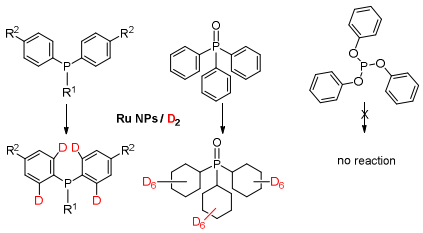

Selective deuteration of phenyl rings phenyl-alkyl phosphines, including diphosphines, was achieved using Ru/PVP nanoparticles and D_2, and enables the comprehension of how different phosphorus ligands coordinate to the nanoparticle surface.