Optimisation of Palladium-Based Supported Liquid-Phase Catalysts in the Heck Reaction

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Abstract:

Heck reactions using sulphonated triphenylphosphine palladium complexes have been carried out using a supported liquid-phase catalysis system in a batch reactor. The catalyst complex is held in solution in a polar, hydrophilic film supported upon porous glass beads whilst reactants and products are restricted to a nonmiscible solvent phase. Several factors in the preparation of the supported catalyst were investigated with the aim of ensuring good assembly, distribution, and immobilisation of the catalyst complex across the surface of the beads. The thickness of the hydrophilic film upon the porous glass beads was varied. The hydrophilic nature of the ligand complex was studied using mono- and trisulphonated sodium and lithium salts of triphenylphosphine. The effects of level of catalyst loading and ligand/catalyst ratio upon leaching and activity were also examined. These factors have been examined to develop a better understanding of the catalysis occurring in supported liquid-phase systems.

Introduction

The synthesis of a wide variety of fine chemicals and pharmaceuticals is accomplished using homogeneous platinum- or palladium-based catalytic systems.[1,2] However, homogeneous systems often demand expensive separation of the catalyst from the desired product.[3] This is particularly necessary and required by legislation for compounds to be used in drug fabrication or for human consumption. To avoid this separation stage, efforts have been made to immobilise homogeneous catalysts upon suitable porous carriers. The aim is to maintain the activity and selectivity of a homogeneous system whilst avoiding or minimising the leaching of the catalyst into the product. The advantages of a successful process would be to enhance economic potential whilst reducing possible toxicity from transition metals in a synthetic procedure.[4] Techniques that have been used to separate products from catalyst include distilling the products

from the reaction medium; coordinating the metal to a functionalised organic polymer or inorganic support; or using a semipermeable membrane.[3] Generally, these systems lack the combined activity/selectivity of their homogeneous counterparts at low temperatures.[5,6]

Another technique is to include a nonmiscible solvent.[1–4,6] One such approach is supported aqueous-phase (SAP) catalysis, described by Davis et al. and demonstrated for use in the hydroformylation of higher alkenes.[7–9] The system is based upon a water-soluble organometallic catalyst complex, $HRh(CO)(TPPTS)_3$, being dissolved in a polar, hydrophilic film supported upon high surface area glass beads whilst reactants and products are restricted to a nonmiscible solvent phase. The approach assumes that interaction between the substrates and the catalyst complex occurs at the interface between the two phases. Hence, the high surface area afforded by the porous silica support maintains the activity that would be associated with reactions within a homogeneous system whilst reducing the potential for heavy metal contamination in the product. The technique has also been extended to reactions such as asymmetric hydrogenation, Wacker oxidation, and hydroformylation of α,β-unsaturated esters.[9–11]

More recently, work has been carried out by this group upon palladium-catalysed allylic alkylations using SAP catalysts made using palladium(II) acetate and trisodium tris-(*m*-sulphonatophenyl)phosphine (Na-TPPTS).[12,13] The catalysts were shown to be active, though less so than their homogeneous counterparts. Palladium complexes are extremely useful for C–C bond coupling reactions. They are commonly used to carry out vinylation of organic halides, refluxing under nitrogen in common organic solvents, to give

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excellent yields. The Heck reaction is a well-known example of such a coupling. The reaction can typically be carried out by heating the halide with 1 mol % palladium(II) acetate or palladium(II) chloride, 2 mol % triphenylphosphine (TPP), a slight excess of tertiary amine (triethylamine), and alkene in acetonitrile. The palladium(II) compound is reduced to palladium(0) by the phosphine or triethylamine base during the catalytic cycle.[2] The use of aqueous conditions in such reactions has been studied using a number of homogeneous biphasic systems. These techniques, however, are often limited by the solubility of the ethylene in the catalyst or substrate phase.[14,15] Recently, the arylation of methyl acrylate with iodobenzene was studied using heterogeneous catalysts upon modified silica supports. Promising results were obtained for a range of precursors screened for conversion, activity, and stability.[16]

This article describes the preparation and use of the supported aqueous-phase system of catalysis and the efforts made to optimise and expand upon its use for palladium-based catalysis. It is a continuation of the work that has been carried out by groups on using this system for rhodium hydroformylation and asymmetric hydrogenation, with the target of easy separation of active catalysts from products in chemical processes. Water-soluble sulphonated triphenylphosphine ligands complexed with palladium(II)chloride, dissolved in hydrophilic ethylene glycol, are shown being used to facilitate the Heck coupling of the above substrates in an SAP-type system.[13] Sodium and lithium sulphonated triphenylphosphine ligands were investigated, as were the loading of the catalyst complex, the ligand-to-catalyst ratio, and the level of hydrophilic phase loading to establish optimum activity and leaching.[11,17]

Experimental Section

Materials. Iodobenzene (98%), methyl acrylate (99%), palladium(II) chloride (99%), triphenylphosphine (99%), palladium AAS standard solution (1000 μg/mL in 5 wt % HCl), ethylene glycol (99.8%), and phosphorus trichloride (98%) were used as purchased from Aldrich. Hexane (95+%), ethyl acetate (99.8%), tetrahydrofuran (99.9+%), diphenylphosphine chloride, and diethyl ether (99.8% anhydrous) were purchased with the lowest level of water content from Aldrich. Oleum and n-butyllithium solutions (titrated prior to use with 1,3 diphenyl-2-propanone-p-toluene sulphenyl hydrazone) were purchased from Fluka. The lithium salt of benzenesulphonic acid was prepared as described in the literature.[18] In all operations requiring water, Millipore deionised water was used. Aqua regia was prepared as required (3:1 concentrated HCl/HNO$_3$).

Davisil 300 Å 653XWP (pore diameter, D_p = 300 Å; surface area, SA = 160 m^2/g) was purchased from Supelco Inc. Controlled pore glasses (CPG Inc.), CPG-120B (D_p = 128 Å; SA = 141 m^2/g), CPG-240B (D_p = 239 Å; SA = 82

m^2/g), CPG-290B (D_p = 290 Å; SA = 132 m^2/g), CPG-350B (D_p = 348 Å; SA = 62 m^2/g), CPG-410B (D_p = 410 Å; SA = 96 m^2/g), CPG-500B (D_p = 513 Å; SA = 51 m^2/g), and CPG-700B (D_p = 697 Å; SA = 39 m^2/g), were obtained from Cambio Limited and donated by Glaxo-Wellcome.[19] All porous silicas were vacuum-dried overnight at 200 °C before use to remove residual moisture.

Preparation of Mono- and Trisulphonated Triphenylphosphines. Monosodium mono(m-sulphonatophenyl)-diphenylphosphine (Na-TPPMS) was prepared by dropwise addition of 0.5 mL of oleum (25% sulphur trioxide in sulphuric acid) to triphenylphosphine (80 g, 305 mmol) suspended in 36 mL of concentrated sulphuric acid.[20] A further 165 mL of oleum was added to the cooled solution, and the mixture was stirred at room temperature for 3 h before being poured onto ca. 2 kg of stirred ice. The emulsion was stirred for 5 min and extracted with 2 × 500 mL of ethyl acetate. It was then extracted with 150 mL of 6% aqueous sodium hydroxide solution. The extract was neutralised with concentrated sulphuric acid and evaporated to give a white solid, which was dried and then refluxed in 750 mL of methanol. This was hot filtered, reduced to 200 mL, and cooled. The resulting slurry was filtered and washed with 3 × 20 mL of methanol. ^{31}P NMR δ_p (DMSO-d_6, 160 MHz, −6 ppm) suggested product was >99% pure (yield 25.4 g, 23%) after single recrystallisation from water. Mass spectroscopy suggested that the impurity is the disodium salt.

Trisodium tris(m-sulphonatophenyl)phosphine (Na-TPPTS) was prepared by slow addition of triphenylphosphine (10 g, 38.1 mmol) to 100 mL of oleum at 0 °C. After the solution was allowed to warm to room temperature, the reaction was continued for ca. 150 h. It was then neutralised at 0 °C with 20% aqueous sodium hydroxide and the volume reduced to 200 mL. This was refluxed with 1000 mL of methanol and filtered hot. The solid was further extracted with 500 mL of hot methanol, and the combined extracts were reduced to 200 mL in volume. Addition of 800 mL of acetone precipitated the product (75−85% purity, the main impurity being Na-TPPTS oxide). A number of techniques were available for purification. This was achieved by extraction with 300 mL of acetone/methanol/water (10:5:1), followed by repeated dissolution, reprecipitation, and extraction.[21] After two repetitions, 97% purity (yield 14.2 g, 66%) was determined by ^{31}P NMR δ_p (D$_2$O, 80 MHz, −5.14 ppm).

Monolithium mono(o-sulphonatophenyl)diphenylphosphine (Li-TPPMS) was prepared from the lithium salt of benzenesulphonic acid (1.804 g, 11 mmol) in 15 mL of tetrahydrofuran. The solution was cooled to 0 °C, and then n-butyllithium (8 mL, 12 mmol, 1.5 M solution in hexanes) was added, and the mixture was allowed to stir for 20 min. Diphenylphosphine chloride (1.79 mL, 10 mmol) was added dropwise, and the reaction was allowed to warm to room temperature and stirred for 1 h. The product was poured

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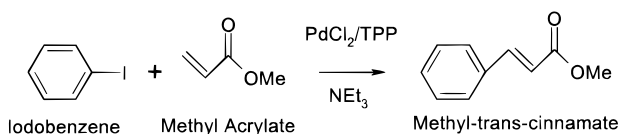(18) Figuly, G. D.; Martin, J. C. *J. Org. Chem.* **1980**, *45*, 3728.

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Scheme 1. Arylation of methyl acrylate in a homogeneous system[a]

Iodobenzene + Methyl Acrylate → Methyl-trans-cinnamate (PdCl₂/TPP, NEt₃)

[a] Reaction conditions: PdCl$_2$ (1 mol %), triphenylphosphine (2 mol %). Carried out in acetonitrile at 100 °C under nitrogen atmosphere.

onto 100 mL of water and 200 mL of light petroleum ether (bp 40−60 °C). The water was washed with 100 mL of diethyl ether, and the aqueous layer was then evaporated at 150 °C by Kugelrohr to dryness (bp diphenylphosphine chloride ca. 135 °C at 1 mmHg). Purity was determined by ^{31}P NMR δ_p (D$_2$O, 90 MHz, −7.24 ppm) to be >90% (yield 1.9 g, 55%).

Trilithium tris(*o*-sulphonatophenyl)phosphine (Li-TPPTS) was prepared from the lithium salt of benzenesulphonic acid (3.936 g, 24 mmol) in 30 mL of tetrahydrofuran. The solution was cooled to 0 °C, and then *n*-butyllithium (17.6 mL, 26.4 mmol, 2.7 M solution in heptane) was introduced, and the mixture was allowed to stir for 25 min. Next, phosphorus trichloride (0.348 mL, 4 mmol) in 6 mL of tetrahydrofuran was added, and the mixture was stirred for 1 h. The reaction mixture was filtered through cotton wool, and solvent was removed in vacuo to give the yellow powdered product of >90% purity (yield 1.4 g, 67%) by ^{31}P NMR δ_p (D$_2$O, 90 MHz, −9 ppm).[22]

Heck Reaction. Methyl acrylate (5.49 mmol) was added to iodobenzene (1.88 mmol) in the presence of triethylamine (5.49 mmol) at 100 °C (Scheme 1). The coupling was performed in a 5-mL solvent mixture of hexane/ether (4:1). The dry palladium sulphonated triphenylphosphine complex supported upon silica was resolved with hydrophilic phase mixed with the reaction solvent prior to the reaction. Sulphonated phosphine ligands were chosen for their excellent solubility in water (e.g., ∼80 g L^{-1} for Na-TPPMS and ∼1100 g L^{-1} for Na-TPPTS).[3] Palladium levels in the reaction supernatant were determined prior to and at the end of reactions.

Conversion of the iodobenzene starting material to the methyl *trans*-cinnamate product was monitored by gas liquid chromatography at regular intervals during the course of the experiment over 12 h. Yields in excess of 90% were obtained after completion. It is interesting to note that the reaction displayed pseudo-first-order kinetics with respect to the methyl acrylate substrate being present in excess. Activities quoted were obtained from linear conversions graphs of $\ln[(M - X_A)/M(1 - X_A)]$ against time. $M = C_{B0}/C_{A0}$, C_{A0} being the initial concentration of substrate A and C_{B0} being the initial concentration of substrate B. For the fractional conversion of substrate A, $X_A = (N_{A0} - N_A)/N_{A0}$, N_{A0} being the initial number of moles of A whilst N_A is the number of moles of A at any given time. Similar observa-

tions have been made in reactions with a triphase catalysis system.[23]

Apparatus and Instrumentation. All Heck couplings were performed under an atmosphere of nitrogen. Batch reactions were carried out at 100 °C in 25-mL round-bottomed flasks fitted with condensers. The flasks were heated in an oil bath upon a stirrer/hotplate with automatic temperature control. Sampling for gas liquid chromatography and atomic absorption spectrometry was via a Teflon/glass sample probe fitted with an in-line Millipore filter and syringe.

BET-N$_2$ adsorption/desorption analysis carried out on porous glasses was performed on a Micromeritics ASAP2000, outgassing to 10 mPa at 22 °C. Palladium atomic absorption analysis of reaction filtrates was performed on a Perkin-Elmer 1100B spectrometer. Filtered samples were evaporated at 400 °C and extracted into deionised water with a few drops of aqua regia. Flame (sensitivity, 250 ppb fuel lean flame) and graphite furnace (sensitivity, 100 ppb) techniques were employed using an S+S Juniper palladium hollow cathode lamp, HGA700 graphite furnace, and AS70 autosampler. The extent of reaction was monitored on a Pye Unicam series 304 gas chromatograph and a Perkin-Elmer GC8700, with FID and Supelco S*P*2330 vitreous silica column, using iodobenzene and methyl *trans*-cinnamate internal standards. An Edwards Modulyo Pirani 10 freeze-drier was used in the preparation of the supported catalysts.

Results and Discussion

Analysis of Silica Pore Size Distribution, Surface Area, Pore Volume, and Adsorption Isotherm. BET-N$_2$ adsorption/desorption analysis was carried out on the porous silicas to confirm reported pore size distribution, surface area, and pore volume. It was found that the porous glasses typically gave type IV isotherms with characteristic HI hysteresis loops associated with porous materials known to consist of uniform spheres in a fairly regular array with narrow distributions of pore size.[24]

The controlled pore glasses (CPGs) were shown to possess narrow pore size distributions but also displayed many microsize pores (<2 nm). However, CPGs with greater average pore diameter, CPG-500 and CPG-700, exhibited greater deviations in pore size. This is illustrated by their proximity to the horizontal in the pore size distribution diagram, especially in the case of CPG-700, which appears indistinguishable from the baseline (Figure 1). The porous silica, CPG-350, was chosen for study. It displayed deviation in pore size similar to that of Davisil 300, which is an inexpensive viable alternative for future large-scale operations. The two silicas also have similar average pore diameter (350 and 300 Å, respectively). The properties of catalysts supported upon them were very similar despite the large difference in surface area. A previous study has shown pore diameter to be of greater importance in influencing these properties.[11]

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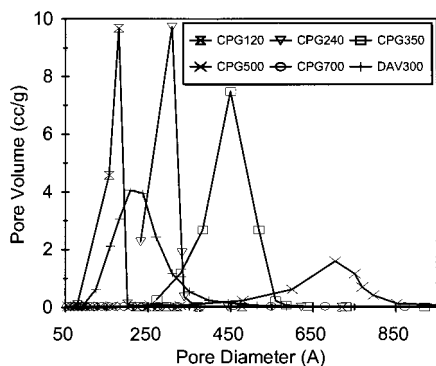
Figure 1. Comparative graph of pore size distributions for silicas CPG-120, CPG-240, CPG-250, CPG-350, CPG-500, CPG-700, and Davisil 300. Data points are calculated from BET-N$_2$ adsorption/desorption analysis.

Immobilisation of Palladium Complex onto Porous Silica. Several techniques were explored in order to optimise the assembly and immobilisation of the catalyst complex onto the porous glass beads. These different techniques of dried supported liquid-phase catalyst preparation were seen to produce variations in activity and leaching. The dried supported catalysts were resolvated with ethylene glycol/water (0.5 mL) added to the organic phase by stirring for 1 h prior to reaction. The level of solvation with hydrophilic phase, expressed in terms of the degree of pore filling, $\delta = 2$, was calculated by dividing the volume of the coating added (5×10^{-7} m^3) by the total pore volume of the solid ($V_p = 2.5 \times 10^{-7}$ m^3) in these experiments. The amount of silica and hydrophilic phase used was determined by comparison with work done previously by this and other groups. All manipulations were performed under nitrogen atmosphere or a vacuum. Palladium(II) chloride (6.6 mol % with respect to iodobenzene) and Na-TPPMS ligand (14.6 mol %) were used in each preparation. The complexes were supported onto 250 mg of CPG-350.

Initially, a relatively cumbersome multistep procedure was used, involving separate formation of the palladium complex by stirring the palladium(II) chloride with ligand for 3 h at 60 °C in excess hydrophilic solvent, followed by introduction of silica which had been "wetted" by stirring in excess hydrophilic solvent for 3 h at room temperature. Further stirring was used to facilitate good distribution of the complex across the support over 3 h before the solvent was removed overnight by freeze-drying, produced a catalyst which exhibited poor activity (1.9×10^{-3} min^{-1}) and high levels of palladium leaching after reaction (10.3 ppm). A more convenient procedure was developed which gave a significant reduced level of leaching (1.0 ppm) with greater activity (3.4×10^{-3} min^{-1}). Water had been substituted with ethylene glycol, as it was seen to have a detrimental effect upon the complexation of the catalytic species. This tripled the activity of the supported catalyst and halved the level of palladium leached after reaction. The preparation involved the palladium(II) chloride and ligand being stirred for 3 h at 60 °C in 0.5 mL of ethylene glycol. Dry CPG-350 and 0.5 mL of ethylene glycol were then introduced, and the mixture was stirred for a further 3 h at room temperature before being freeze-dried until constant mass.
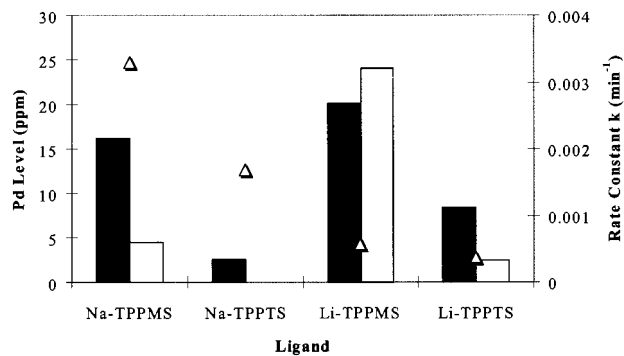

Figure 2. Effect of ligand hydrophilicity upon activity and level of palladium leached in supported liquid-phase catalysts. The reaction was carried out using PdCl$_2$ (5.9 mol %) and CPG-350 (250 mg) hydrated with ethylene glycol ($\delta = 2$) and ligand (Na-TPPMS, monosodium mono(m-sulphonatophenyl)diphenylphosphine; Na-TPPTS, trisodium tris(m-sulphonatophenyl)-phosphine; Li-TPPMS, monolithium mono(o-sulphonatophenyl)-diphenylphosphine; or Li-TPPTS, trilithium tris(o-sulphonato-phenyl)phosphine) (14.6 mol %). Black bars, Pd level before reaction; white bars, Pd level after reaction. △, Rate constant.

The procedure gave the lowest level of palladium leaching from the supported catalyst preparation coupled with a reasonable activity and was, thus, used in proceeding studies. Comparison of the palladium levels present in the supernatant before and after reaction revealed an active uptake of the palladium onto the supported liquid-phase catalyst; i.e., self-assembly of the supported catalyst was occurring.

Hydrophilic Nature of Ligand. Alternative sulphonated triphenylphosphine ligands were used in the catalyst preparation to determine whether the hydrophilicity of the ligand could be used as a tool for manipulating the efficiency of the catalyst system. Each reaction was carried out using palladium(II) chloride (5.9 mol %) and CPG-350 (250 mg) hydrated with ethylene glycol ($\delta = 2$). To each was added ligand (Na-TPPMS, monosodium mono(m-sulphonato phenyl)diphenylphosphine; Na-TPPTS, trisodium tris(m-sulphonato phenyl)phosphine; Li-TPPMS, monolithium mono(o-sulphonato phenyl)diphenylphosphine; or Li-TPPTS, trilithium tris(o-sulphonato phenyl)phosphine) (14.6 mol %).

It was evident from the study that the tris(sulphonatophenyl) phosphine ligands gave reduced levels of palladium leached from the supported liquid-phase catalyst, compared to the mono(sulphonato phenyl)diphenylphosphines, but markedly reduced the activities observed in the reactions (Figure 2). Also, when carrying out the reaction with the lithium analogues of the ligands, there was a significant decrease in reactivity whilst leaching of the palladium from the support was observed to increase. These observations can be explained in terms of the interaction between the hydrophilic moiety of the catalyst complex and the molecules of the hydrophilic phase. The more hydrophilic tris-(sulphonatophenyl)phosphine ligands (Na-TPPTS and Li-TPPTS) are more strongly held in this interaction. This slows the reaction, as seen in heterogeneous systems, and reduces leaching. Also, with the lithium ligands, the sulphonato group is more hindered as it is *ortho*-substituted. This makes the lithium ligand complex less soluble in the hydrophilic phase and can disrupt the catalyst system across
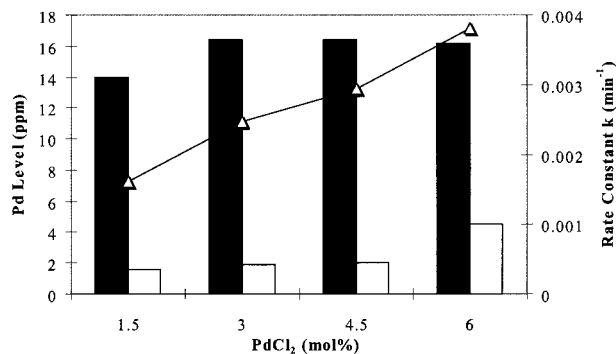
Figure 3. Effect of PdCl$_2$ catalyst loading upon activity and leaching in supported liquid-phase catalysts. The reaction was carried out using Na-TPPMS (2.5 molar equiv) and ethylene glycol ($\delta = 2$) upon CPG-350 (250 mg). Black bars, Pd level before reaction; white bars, Pd level after reaction. $\triangle$, Rate constant.

Figure 4. Effect of excess Na-TPPMS ligand upon activity and palladium leaching in supported liquid-phase catalysts. PdCl$_2$ (4.5 mol %), CPG-350 (250 mg), and ethylene glycol ($\delta = 2$) were used in each reaction. Black bars, Pd level before reaction; white bars, Pd level after reaction. $\triangle$, Rate constant.

the phase interface. The higher levels of palladium in the organic phase coupled with low activity in reaction are evidence of this.

Catalyst Loading. Having decided that the Na-TPPMS ligand gave the best compromise between hydrophilicity, activity, and leaching, the optimum loading of the catalyst onto the support was sought. This served to demonstrate the efficiency of the support in limiting leaching. To this end, experiments using Na-TPPMS (2.5 molar equiv with respect to catalyst) were carried out with varying amounts of palladium(II) chloride (1.5, 3, 4.5, and 6 mol %). These studies used standard conditions of ethylene glycol ($\delta = 2$) upon CPG-350 (250 mg).

There was a linear increase in activity with the level of palladium(II) chloride loading onto the support (Figure 3). It is suggested that there is a direct relationship between the activity observed and the level of palladium present in the reaction solvent at the end of the reaction. It was suspected that the activity could derive from homogeneous palladium complexes. The supernatant was filtered at different stages during the reaction and allowed to continue reacting whilst comparing it with an unfiltered duplicate. It was established that greater than 85% of the activity was derived from organic-soluble palladium complexes during the course of the reaction. The palladium level throughout the reaction profile mirrors the level of activity of the catalyst in reaction (rate of conversion to the product). This suggests that the reaction is predominantly homogeneous. However, there was uptake of palladium during the course of the reaction. The low levels attained after reaction was completed demonstrate that the system is potentially very useful. The final level of palladium leached was independent of the initial level observed. The filtered supernatant after reaction was not seen to be active to fresh substrate, as has been reported in past works.

Catalyst/Ligand Ratio. Having determined the level of palladium upon silica which gave sufficient activity without contributing to leaching, the amount of ligand used in reactions was varied. This was done to assess whether this was a factor that could be successfully used to limit the level of catalyst leaching during the reaction. Palladium(II) chloride (4.5 mol %) with CPG-350 (250 mg)
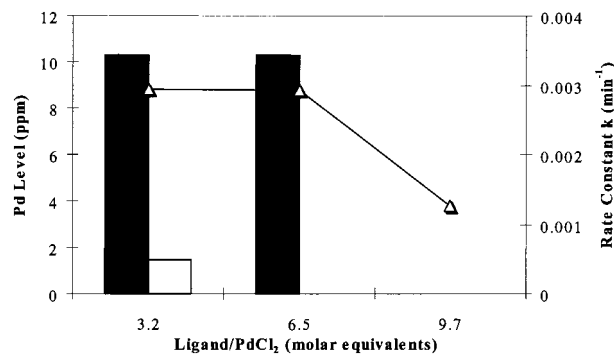
and ethylene glycol ($\delta = 2$) was used in each reaction. The amount of Na-TPPMS added was varied in each case (3.2 molar equiv with respect to catalyst, 6.5 molar equiv, and 9.7 molar equiv).

Excess ligand significantly retarded the reaction at 9.7 molar equiv of Na-TPPMS to palladium(II) chloride (Figure 4). However, it was seen that addition of 6.5 molar equiv of ligand eliminated the palladium leaching from the silica observed after reaction. This would be of vital significance for any proposed industrial process.

Catalyst Recycling. It was necessary to determine how robust the supported catalyst was to degradation; thus, experiments were carried out to study the viability for recycling and reuse of the catalyst in an industrial process. In this study, palladium(II) chloride (4.5 mol %) was used with Na-TPPMS (29.2 mol %), CPG-350 (250 mg), and ethylene glycol ($\delta = 2$). Filtered aliquots (0.3 mL) of reaction supernatant were removed at the initial stages of and after each reaction for palladium level determination. After each reaction, the supported catalyst was rinsed with reaction solvent (2 × 5 mL) and the reactor recharged with substrates. The coupling was repeated three times using the same preparation of catalyst.

It was observed that the activity of the supported liquid-phase catalyst decreased significantly after recycling (Figure 5). As reactions were repeated, decreasing levels of palladium were observed in the solvent prior to use, suggesting gradual leaching of the palladium from the support. However, there was no detectable level of palladium present in the supernatant after reaction or in the solvent rinse prior to reaction; therefore, there could be no major loss of catalyst. High levels of nonactive oxidised phosphine were observed, suggesting catalyst deactivation, coupled with interaction between the deactivated complex and the support, leading to decreased leaching. The reappearance of palladium in the supernatant when reaction solvent and substrate were recharged into the vessal was quite unexpected. The addition of fresh substrate, particularly iodobenzene, in subsequent reactions is evidently drawing palladium off the support at the beginning of couplings by the formation of a less polar intermediate in the catalytic cycle. As this substrate is consumed during reaction, we again see total uptake of the palladium onto the support. This may appear surprising, but
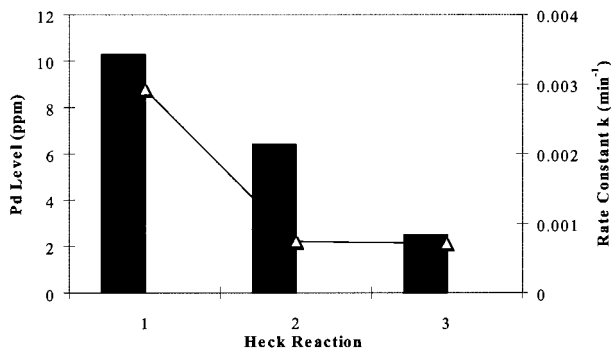
Figure 5. Effect of recycling upon activity and palladium leaching from supported liquid-phase catalysts in consecutive Heck reactions. The reaction was carried out using $PdCl_2$ (4.5 mol %), Na-TPPMS (29.2 mol %), and ethylene glycol ($\delta = 2$) upon CPG-350 (250 mg). Black bars, Pd level before reaction; white bars, Pd level after reaction. $\triangle$, Rate constant.

Table 1. Degree of pore filling with hydrophilic phase, ethylene glycol, onto CPG-350 (250 mg, total $V_p = 0.25$ cm³, SA = 15.5 m²)[a]

ethylene glycol loading (mL = ×10⁻⁶ m³)	degree of pore filling, δ	theoretical thickness of phase coating (Å)
0.01	0.04	6.5
0.02	0.08	13
0.025	0.1	16
0.035	0.14	23
0.05	0.2	32
0.1	0.4	65
0.25	1.0	160
0.5	2.0	320

[a] Calculation of film thickness is based upon a perfectly flat surface area.

further work carried out by this group has shown that the characteristic solubilities of the substrates, including bases, can interfere with the phase separation in supported liquid-phase catalysts resulting in temporary leaching.

Hydrophilic Phase Loading. Before using the porous silicas, the level of residual water was thermogravimetrically determined. It was found that up to 3 wt % water was present in the pores. Therefore, silicas were oven-dried (200 °C) for 6 h before use. The influence of the level of hydrophilic phase, ethylene glycol, loading onto the catalyst upon activity and leaching was studied. The thickness of the coating would determine the mobility of the catalyst complex in the system and, therefore, be significant in controlling activity of the supported catalyst. Prior to these experiments, the degree of pore filling, $\delta = 2$, had been used in the catalyst preparations. In this study, Na-TPPMS (29.2 mol %) and palladium(II) chloride (4.5 mol %) were used with CPG-350 (250 mg) (Table 1).

The effect of the level of solvation of the supported liquid-phase catalyst upon activity proved to be significant. Maximum activity was repeatedly attained at a degree of pore filling of $\delta = 0.1$ (theoretical film thickness = 16 Å) (Figure 6). At very low pore filling, i.e., $\delta = 0.04$, no activity was observed, indicating the lack of mobility of the catalyst complex within a 6.5-Å film. Above $\delta = 0.1$, analysis of the graph suggested that the activity decreased as the pores were being filled, due to diminishing interfacial
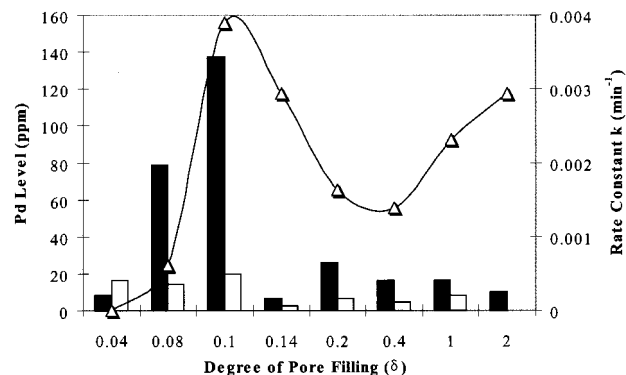

Figure 6. Effect of degree of pore filling with ethylene glycol upon activity and palladium leaching in supported liquid-phase catalysts. Na-TPPMS (29.2 mol %) and $PdCl_2$ (4.5 mol %) were used upon CPG-350 (250 mg). Black bars, Pd level before reaction; white bars, Pd level after reaction. $\triangle$, Rate constant.

area. It then increased again as the thickness of the coating around the silica increased, thereby increasing the area of the interface.

Molecular modeling of the Na-TPPMS catalyst complex ascertained that the average diameter of the catalyst structure was 11 Å (largest diameter, 15 Å; total volume, 590 Å³). It can thus be assumed that the thickness of the coating at a pore filling of $\delta = 0.1$ (16 Å) is adequate for a monolayer of the catalyst complex. Prior to this level of loading, it was observed that leaching prior to reaction increased. At low levels, the coating across the surface was likely to be discontinuous, resulting in leaching of both unsolvated palladium and catalyst dissolved in micelles of ethylene glycol from the silica. As more glycol was added up to a certain level, instead of increasing the film thickness, its surface tension served to spread the film further across the surface, resulting in actual thinning of the film.

Conclusions

The Na-TPPMS ligand offers low levels of leaching without retarding catalyst activity. Therefore, the combination of Na-TPPMS (29.2 mol %) and palladium(II) chloride (4.5 mol %) supported upon CPG-350 (250 mg) solvated with ethylene glycol (0.025 mL; $\delta = 0.1$) produces a supported liquid-phase catalyst with optimum activity whilst eliminating leaching to the limits of detection. However, this does pose the question of whether all the prior conclusions are valid under these optimised conditions. Future work will focus on establishing this.

The method developed for preparation of the supported liquid-phase catalysts, and outlined earlier, is a convenient procedure for producing large quantities for reaction. The catalyst thus prepared is stable and can be stored dry for a number of weeks. Ethylene glycol as a coating would not be an ideal choice for an industrial process. Its viscosity and poor mass-transfer properties result in comparatively low activity, as witnessed in this supported liquid-phase system compared to an equivalent homogeneous catalyst system. In a biphase system, i.e., without the high surface area silica support, we see a significantly reduced activity for the catalyst, compared to that in a single-phase homogeneous system, as it is insoluble in the substrate phase. Water would

be preferable for solvating the supported catalyst. However, as this method is seen to degrade the catalyst complex and has also been shown in the past to leach from the silica, it carries with it its own disadvantages.[7,11,25] A more suitable solvent to solvate the catalyst and the application of the system to more effective solvent systems (e.g., aceto-nitrile) have been explored, and the results will be disclosed soon.

With the supported liquid-phase system described in these studies, <0.3 wt % of palladium used was observed to have leached into the solvent after reaction (10 ppm in 5 mL). The optimisation that has been carried out can be used successfully to reduce this down to a traceable level of 250 ppb. This is a remarkable reduction when compared with the levels of heavy metal contamination seen in homogeneous systems. The convenience offered by this system of catalysis for heavy metal separation is very significant. The catalyst can simply be filtered away from the reaction solvent. With regard to the nature of the catalysis occurring within the system, evidence suggests that the catalysis is predominantly homogeneous via the formation of organic-soluble catalyst complex. The high surface area interface between the support coating and the bulk reaction solvent facilitates efficient removal of the heavy metal complex after completion of the reaction.

The recycling of the catalyst must be made efficient if it is to have any likelihood of competing with homogeneous systems on a commercial scale. To this end, the nature and cause of the deactivation are to be further investigated. Impurities in starting materials may be responsible for the observed poisoning. The system is currently being studied in continuous-flow reactions. Theoretically, as the supported catalyst is exposed to a much higher level of stabilising phosphines, the catalyst complex should be much more robust than that in the homogeneous system. In addition to this, the phosphines in themselves are very hydrophilic; therefore, there is no risk of the product being contaminated with leached phosphine. This was confirmed by atomic absorption spectrometry. Other such uses will be sought for this technology and work done to expand upon our under-standing of the nature of the catalysis in such systems with the aim of achieving a highly active, selective, and reusable system of catalysis for large-scale reactions.

(25) Horvath, I. T. *Catal. Lett.* **1990**, *6*, 43.