

C–H activation and C–C coupling of 4-methylpyridine using palladium supported on nanoparticle alumina

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Abstract

The C–H activation and C–C coupling of 4-methyl pyridine to 4,4'-dimethyl-2,2'-bipyridine was studied over palladium catalysts supported on nanoparticle alumina [nano- $\text{Al}_2\text{O}_3(+)$]. Even though Pd/ Al_2O_3 catalysts are traditionally poor catalysts in this reaction, the Pd/nano- $\text{Al}_2\text{O}_3(+)$ catalysts prepared via the precipitation method give the highest yield observed to date for this reaction system. The catalytic activity is very dependent on the catalyst preparation as Pd/nano- $\text{Al}_2\text{O}_3(+)$ catalysts prepared via the wet impregnation method exhibit poor activities in the reaction. Additionally, a catalyst prepared using another nanoparticle alumina with larger particle sizes [nano- $\text{Al}_2\text{O}_3(-)$] does not have a significant activity. It was shown that using a commercial bimodal γ - Al_2O_3 support can result in an active catalyst if prepared via the precipitation method, but compared to the best performing catalyst, Pd/nano- $\text{Al}_2\text{O}_3(+)$, the yields obtained from Pd/bimodal- γ - Al_2O_3 are lower and less reproducible. Pd surface area measurements indicate that the reaction is structure sensitive as there is no correlation between the Pd surface area and the catalytic activity. The reaction is also very sensitive to reactant quality and the 4-methyl pyridine must be distilled over KOH to ensure reproducible yields. Additional experiments indicate that this reaction requires a solid phase for catalysis.

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Keywords: Pd/ Al_2O_3 ; Nanoparticle oxide; Pyridine; C–H activation; Aromatic coupling

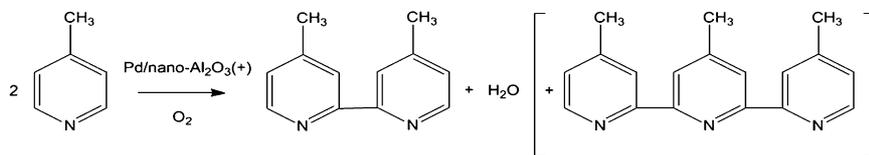
1. Introduction

Bipyridines are receiving increasing attention in the literature due to their ability to coordinate to transition metal cations and form complexes with interesting properties [1]. The importance of metal complexes containing bipyridine ligands has been revealed in several reviews that have been published in the past fifteen years on the synthesis of bipyridines, as well as on properties of metal-bipyridine complexes and their applications [2–6]. Of the transition metals, bipyridine complexes of ruthenium are by far the most commonly studied systems [2,5]. This is due to their unique photo- and electrochemical properties. Ruthenium-bipyridine complexes can absorb photons in the visible light region and have unique redox properties that can lead to electron transfer and chemiluminescence, which make them suitable for application in solar energy conversion (e.g. in solar cells and artificial photosynthesis systems [6,7]), in organic light-

emitting diodes [8] and in chemiluminescence detection systems [9]. Bipyridines are also commonly used as ligands to metals in various catalyst systems. For example, many copper-based atom transfer radical polymerization (ATRP) catalysts contain bipyridine units [10]. Iron and cobalt complexes of bi- or terpyridines have been shown to catalyze the reduction of CO_2 and O_2 [11]. Palladium bipyridine complexes have been used as catalyst in several reactions, such as oxidative carbonylation [12], the Kumada-Corriu reaction [13], and the Suzuki cross-coupling reaction [14]. Of the bipyridines, 4,4'-dimethyl-2,2'-bipyridine is of particular interest, since this compound can easily be modified by reactions with the methyl groups in the 4-positions. However, due to the poor yields in the coupling reaction of 4-methylpyridine, the production of 4,4' dimethyl-2,2'-bipyridine is prohibitively expensive for large scale processes. A kilogram quantity sells for more than \$4,500 [15], while smaller quantities sell for significantly higher prices per unit weight.

Bipyridines can be formed via a number of pathways. Some include building the second pyridine ring from a substituted pyridine, while other methods rely on the coupling of halogenated pyridines using transition metal catalysts [16–18].

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Scheme 1. Oxidative coupling of 4-methylpyridine using a palladium catalyst.

The disadvantages with these processes are the low yields of multi-step processes, the cost of the halogenated precursors and the environmental impact of the waste streams of halide salts and other byproducts that result from these reactions. Furthermore, these processes require a high level of subsequent purification for applications that are sensitive to halogens, such as catalysis. Consequently, a one-step process in which the bipyridine is formed directly from the pyridine reactant is desirable. The oxidative coupling of 4-methylpyridine to 4,4'-dimethyl-2,2'-bipyridine using palladium on carbon as the catalyst meets this criterion (Scheme 1). This reaction requires only a catalyst plus the reactant and the only by-products of the reaction are water and the terpyridine (Scheme 1). Furthermore, compared to its halogenated derivatives (the most active bromo-derivative is available through reaction with commercially available 2-amino-4-methylpyridine at ~\$200/kg [18,19]), 4-methylpyridine is relatively inexpensive (less than \$40/kg [20]) with lower environmental impact. The disadvantages of this reaction are the slow reaction rate and the deactivation of the catalyst [21].

Early research has shown that 2,2'-bipyridines can be formed via coupling of pyridine derivatives over catalysts such as Raney nickel and palladium on carbon (Pd/C) [22–25]. The results from these early experiments reveal that while palladium on carbon is a reasonable catalyst in the coupling reaction of pyridine derivatives, palladium on alumina exhibits poor activity [22]. No explanation as to why alumina is an inferior support has been given in the literature. The early research also indicated that low-valent palladium is the active form of the Pd/C catalysts. However, more recent results revealed that the active catalyst actually contains a Pd(II) species [21] and that the variation in catalytic activity between batches of Pd/C catalysts could be reduced by simply oxidizing the catalyst before reaction. However, despite previous improvements of the catalyst, the reaction is slow and suffers from catalyst deactivation. One of the major limitations of the reaction appears to be reox-

idation of Pd in these solution experiments, since the catalyst after exposure to the reaction conditions is in a reduced form [21]. The maximum isolated yield reported for a 5% Pd/C is ~2 g product per gram of catalyst, i.e. 40 g/g Pd [26]. However, yields of 1.5–2 g/g for a 10% Pd/C catalyst are more common [21,27,28]. Comparing these product yields to reactions using a homogeneous catalyst complex or halogenated precursors in solution is difficult. The yields reported as converted reactant tend to be higher for reactions in solution with halogenated precursors [17,18,29], while the yield per gram of palladium generally is higher in reactions where 4-methylpyridine is the reactant and no solvent is used (See summary of literature yields in Table 1). The higher conversion of reactant for the reactions using solvent and halogenated precursors can be outweighed by the lower yields per gram of palladium, the formed byproducts (halide salts) and the use of solvent. Furthermore, the unreacted 4-methylpyridine can easily be recovered in the reactions with no solvent and a heterogeneous catalyst, and there is a potential for recycling and regeneration of the heterogeneous catalyst. Therefore, there are significant advantages of synthesizing 4,4'-dimethyl-2,2'-bipyridine using a heterogeneous catalyst and no solvent, particularly if the yields can be increased. Naturally, the converted reactant yield can also be increased in reactions with no solvent by simply increasing the catalyst-to-reactant ratio, although more terpyridine byproduct will be formed in these cases.

Our hypothesis is that palladium supported on nanoparticle oxide supports has potential to be a very efficient catalyst. This hypothesis is based on the fact that nanoparticles have a large surface area compared to their bulk analogues. Furthermore, nanoparticles have a high degree of low coordination sites, such as corners and edges [30]. These low coordination sites may cause a stronger interaction between the support oxide and the active metal deposited onto the nanoparticles compared with more conventional supports. In addition to potentially higher dispersions of the active metal, these interactions may result in

Table 1
Reported literature yields for 4,4'-dimethyl-2,2'-bipyridine forming reactions

Starting material	Amount reactant (mol)	Catalyst	Amount catalyst (g)	Yield (%)	Yield (g/g Pd)	Reference
2-Br-4-methylpyridine	2×10^{-3}	5% Pd/C, Zn	0.3	19	2.3	[17]
2-Br-4-methylpyridine	2×10^{-3}	5% Pd/C, Zn	0.11	19	6.6	[17]
2-Br-4-methylpyridine +	23×10^{-3}	Pd(PPh ₃) ₄	0.95	67	32.5	[18]
2-SnBu ₃ -4-methylpyridine	27×10^{-3}					
2-Br-4-methylpyridine	5×10^{-3}	NiBr ₂	0.07	47	10.5 [Ni]	[29]
2-Br-4-methylpyridine	5×10^{-3}	NiBr ₂	0.3	93	4.9 [Ni]	[29]
4-Methylpyridine	1.03	10% Pd/C	4	7	17.3	[27]
4-Methylpyridine	2.06	5% Pd/C	8.93	9	40.0	[26]
4-Methylpyridine	7.19	10% Pd/C	28	6	14.3	[28]
4-Methylpyridine	75×10^{-3}	5% Pd/C	0.7	26	52	This work

unique catalytic properties. It is possible that this is the reason for the high activity observed at low temperatures in the palladium-catalyzed oxidation of methane when nanoparticle oxides are used as supports [31]. Consequently, not only the large surface area, but also the intrinsic properties of nanoparticle oxides can result in unique catalytic activities of nanoparticle-supported catalysts.

The main objective in this work is to determine if palladium supported on nanoparticle alumina can be an efficient catalyst in the coupling of pyridines despite previous research showing that commercial palladium on alumina is a poor catalyst in this reaction. Part of the objective is also to determine the effects of catalyst preparation on the catalytic activity and if the active species is likely to be a dissolved homogeneous complex instead of heterogeneous palladium surface species.

2. Experimental

2.1. Catalyst preparation

The catalysts were prepared using commercially available alumina nanoparticles [32]. Two catalyst preparation methods were used; wet impregnation and precipitation. In the wet impregnation method the support powders were dispersed in an aqueous solution of palladium nitrate (Fluka or Alfa Aesar). The water was then boiled off until a paste consistency was achieved. This paste was dried in a muffle furnace at 105 °C overnight. The dried samples were ground and then calcinated at 450 °C for 3 h to decompose the palladium nitrate and form palladium oxide on the support.

In the precipitation method, the support was dispersed into a solution of palladium nitrate. The mixture was then titrated with a NaOH solution, which formed Pd(OH)₂ on the support [33]. The amount of NaOH used in these experiments corresponds to 50% stoichiometric excess. The resulting mixture was aged overnight at room temperature before it was filtered. The recovered catalyst was rinsed by stirring in water overnight, followed by another filtration. As for the catalysts prepared via the wet impregnation method, the precipitated samples were dried over night at 105 °C and calcinated at 450 °C for 3 h.

Several commercial catalyst supports and catalysts were also used for catalyst preparation or used as received, and tested for activity in the coupling reaction of 4-methylpyridine. These include 5% Pd/C (Alfa Aesar, surface area (SA): 695 m²/g), 5% Pd/Al₂O₃ (Alfa Aesar Pd/γ-alumina, SA: 155 m²/g), γ-Al₂O₃ (Alfa Aesar high surface area bimodal, SA: 260 m²/g) and activated carbon (Calgon F 400, SA: 765 m²/g).

2.2. Reaction conditions

The 4-methylpyridine (Aldrich or Across) was distilled over KOH or NaOH prior to use. In a typical reaction run 1 g of catalyst was placed in a round bottom flask along with 10 g of the distilled 4-methylpyridine. The reaction mixture was evacuated and an oxygen atmosphere introduced before it was heated to the boiling point (145 °C). The reaction proceeded

under reflux for 72 h. After a complete reaction the flask contents were filtered using a glass micro-fiber filter and washed with chloroform to dissolve the product. The chloroform, water and unreacted 4-methylpyridine were removed using a rotary evaporator.

Selected samples were purified via sublimation. These experiments indicate that at least 75% of the raw yield is the desired product. This, however, is a low number since only about 85% of the original sample mass is recovered in the sublimate and residue due to the difficulty in removing the product from the sublimation apparatus. Consequently, the yields are reported as raw yields in the paper. The sublimate, residue, and raw products were characterized using NMR. The only significant product found was the bipyridine. The residue did not redissolve well into the chloroform. The soluble fraction of the sublimation residue showed little evidence of organic compounds other than the product. Based upon NMR it is likely that the major portion of the non-sublimated impurities is inorganic residues from the catalysts.

2.3. Catalyst characterization

Brunauer–Emmett–Teller (BET) surface area measurements were performed on a Quantachrome NOVA 1200 instrument. Fresh catalysts were outgassed under vacuum for 3 h at room temperature before the measurements. Catalysts that had been stored for longer times were outgassed at 105 °C for at least 1 h before the BET analysis. The N₂ adsorption was performed over five isotherms, which gave roughly linear fits.

To determine the dispersion of Pd on the catalysts carbon monoxide chemisorption experiments were performed using a ChemBET 3000 instrument. The fresh catalysts were reduced for 2 h at 170 °C using a 5% hydrogen in nitrogen gas mixture. The samples were then out-gassed for 1 h in helium before the pulse titration experiments with CO at 25 °C and 1 atm. The low reduction temperature was used to avoid excessive sintering or spalling of the Pd particles during the reductive treatment and was chosen to be close to reaction temperature.

3. Results and discussion

3.1. Effects of catalyst preparation method

In the first set of experiments 10% (by weight) of palladium was deposited onto the Nanoactive aluminum oxide plus support [Pd/nano-Al₂O₃(+)] using the wet impregnation method. This catalyst was tested for activity in the coupling reaction of 4-methylpyridine. As expected for a palladium on alumina catalyst, this nano-particle supported catalyst did not exhibit any significant activity in the reaction (Table 2, entry 1). When the precipitation method was used, however, a 10% Pd/nano-Al₂O₃(+) catalyst yielded a significant amount of the 4,4'-dimethyl-2,2'-bipyridine (Table 2, entries 2 and 3). In fact, the 20–25 g product per g of palladium corresponds to 2–2.5 g product per gram of catalyst, which is equal to or higher than the maximum yield reported from a palladium on carbon catalyst [21]. It was also shown that the Pd content can be reduced

Table 2
Product yields and catalyst surface areas of various catalysts prepared and tested in the coupling reaction of 4-methylpyridine

Entry	Catalyst description ^a	4-Methyl-pyridine ^b	Raw product (g/g Pd) ^c	Specific surface area (m ² /g)
1	10% Pd impregnated on nano-Al ₂ O ₃ (+)	1	<1 ^d	155
2	10% Pd precipitated on nano-Al ₂ O ₃ (+)	1	25.4	205
3	10% Pd precipitated on nano-Al ₂ O ₃ (+)	1	20.0	165
4	5% Pd precipitated on nano-Al ₂ O ₃ (+)	1	48.6	180
5	5% Pd/C commercial	1	16.4	695
6	5% Pd/Al ₂ O ₃ commercial	1	2.6 ^d	155
7	5% Pd impregnated on nano-Al ₂ O ₃ (+)	2	1.4 ^d	170
8	5% Pd precipitated on nano-Al ₂ O ₃ (+)	2	18.2	170
9	5% Pd/C commercial	2	7.6	695
10	5% Pd/Al ₂ O ₃ commercial	2	2.4 ^d	155
11	5% Pd precipitated on nano-Al ₂ O ₃ (+)	3	52.6	165
12	5% Pd/C commercial	3	14.4	695
13	5% Pd precipitated (KOH) on nano-Al ₂ O ₃ (+) ^e	3	55.2	165
14	5% Pd precipitated on nano-Al ₂ O ₃ (-)	3	8.2	155
15	5% Pd precipitated on commercial γ -Al ₂ O ₃ ^f	3	4.2	200
16	5% Pd Precipitated on activated carbon	3	2.4	
17	5% Pd Impregnated on nano-Al ₂ O ₃ (+) + KOH ^g	3	2.6	
18	5% Pd Precipitated on nano-Al ₂ O ₃ (+) (Alfa) ^h	4	14	
19	5% Pd Precipitated on nano-Al ₂ O ₃ (+)	4	44	
20	5% Pd Precipitated on nano-Al ₂ O ₃ (-)	4	5.8	
21	5% Pd Precipitated on Commercial γ -Al ₂ O ₃ ^f	4	24	
22	5% Pd precipitated on activated carbon	4	15.1	
23	5% Pd impregnated on activated carbon	4	6.6	
24	5% Pd precipitated on commercial γ -Al ₂ O ₃ ^f	4	34	
25	5% Pd/C commercial	5	36	
26	5% Pd precipitated on nano-Al ₂ O ₃ (+)	5	52	
27	5% Pd Precipitated on nano-Al ₂ O ₃ (+) + H ₂ O ⁱ	5	31	

Reaction conditions are given in the Section 2 (Experimental section).

^a Nano-Al₂O₃(+): nanoparticle alumina (Nanoactive aluminum oxide plus), nano-Al₂O₃(-): nanoparticle alumina (Nanoactive aluminum oxide). Unless otherwise stated the palladium(II) nitrate source is Fluka.

^b 4-Methylpyridine distillates: 1: 4-methylpyridine distilled over KOH, 2: 4-methylpyridine distilled over NaOH, 3: 4-methylpyridine treated with KOH over night before distilling over the same KOH, 4 and 5: 4-methylpyridine treated with KOH over night then decanted and distilled over fresh KOH.

^c Product: 4,4'-dimethyl-2,2'-bipyridine. Raw yield contains a small amount of the terpyridine: 4,4',4''-trimethyl-2,2',6',2''-terpyridine as the only byproduct.

^d There is very little 4,4'-dimethyl-2,2'-bipyridine product in these runs. The solids recovered appear to be mostly catalyst and organic byproducts.

^e Catalyst prepared via precipitation using KOH instead of NaOH.

^f Alfa Aesar high surface area bimodal γ -alumina.

^g 0.09 g of KOH was added to the reaction mixture.

^h Palladium(II) nitrate source was Alfa Aesar not Fluka.

ⁱ 0.3 g of H₂O was added to the reaction mixture.

to 5% Pd on alumina without substantially reducing the product yield (Table 2, entry 4). In other words, the yield per gram of palladium can be doubled by going from a 10% to a 5% Pd/nano-Al₂O₃(+). Consequently, a yield of 50 g raw product per gram palladium can be obtained with this catalyst. The 5% Pd/nano-Al₂O₃(+) catalyst is more active than the commonly used Pd/C catalyst despite the inactivity reported for commercial Pd/Al₂O₃ catalysts. It is also interesting to note that the catalytic activity is very dependent on the catalyst preparation method. While the precipitation method yields a catalyst with the highest observed catalytic activity to date, the impregnation technique results in a very low activity or an inactive catalyst. Both the impregnated and the precipitated catalysts have specific surface areas in the range of 150–200 m²/g (Table 2, entries 1–4). Therefore, the support surface areas cannot explain the differences in activities between these catalysts. As can be seen in Table 2, the results are reproducible (entries 4, 11 and 26). In fact, the yields obtained from different preparations of precipitated Pd/nano-Al₂O₃(+)

catalysts are more reproducible than the yields obtained from different runs on the same batch of commercial Pd/C (Table 2, Entries 5 and 25). This is likely due to variations in the PdO concentration on the “as received” Pd/C catalysts [21]. Since our catalysts are calcined in air and not reduced before reaction, the amount of PdO on the Pd/nano-Al₂O₃(+) catalysts is almost certainly more constant compared to the commercial “Pd(0)"/C.

To test whether or not the differences in the catalytic activity between catalysts prepared by the impregnation and precipitation methods only applies to alumina supports, impregnated and precipitated palladium on activated carbon catalysts were prepared. The precipitated catalyst gave a modest yield (15.1 g/g Pd, entry 22, Table 2), which is comparable to the commercial Pd/C catalyst, while the impregnated Pd/C catalyst gave a low yield (6.6 g/g Pd, entry 23, Table 2). This indicates that the precipitation method is superior to the impregnation method regardless of the support used, although the difference is more drastic for the nanoparticle alumina support.

Table 3
BET surface areas of the supports used in the catalyst preparations

Catalyst support	Surface area (m ² /g)
Nanoactive alumina plus	695
Nanoactive alumina	275
Commercial γ -alumina bimodal (Alfa Aesar)	260
Activated carbon (Calgon F 400)	765

3.2. Catalyst support effects

As expected, the commercial 5% Pd/Al₂O₃ catalyst exhibited poor activity and resulted in little, if any, product under the reaction conditions of the experiments. This is most likely due to the fact that the commercial 5% Pd/Al₂O₃ catalyst consists mainly of Pd(0), in contrast to commercial Pd/C catalysts which appear to have a relatively high, albeit varying, surface Pd(II) content. The yield of the commercial 5% Pd/C catalyst agrees with previous results [21]. It is lower than the highest yield observed using this catalyst, due to the fact that the catalyst was used as received without oxidation treatment. To determine if it is the nature of the nanoparticle alumina support or the preparation method that is responsible for the high catalytic activity, a 5% Pd/Al₂O₃ catalyst was prepared with a commercial alumina support using the precipitation method. The yield for this catalyst varied widely (Table 2, entries 15, 21 and 24). On average the catalyst does exhibit a fair activity, but it is not as active as the nanoparticle-supported Pd/Al₂O₃ catalyst. Another catalyst was prepared using the precipitation method and a second nanoparticle alumina sample [Nanoactive aluminum oxide, nano-Al₂O₃(–)] as support. The surface area of this alumina sample (275 m²/g) is lower than the Nanoactive aluminum oxide plus sample (695 m²/g), but on the same order as the commercial γ -alumina support (260 m²/g) (see Table 3). The catalytic activity of this catalyst is significantly lower than that obtained on the commercial Pd/C catalyst and the palladium on the Nanoactive aluminum oxide plus or commercial γ -alumina supports. Consequently, there is a significant difference in the catalytic activities of the catalysts prepared with the two Nanoactive aluminum oxide supports. It is interesting to note that the catalyst supported on the nano-Al₂O₃(–) gives a lower yield than the catalyst prepared using the commercial γ -

alumina despite the fact that the surface areas of these supports are similar. The catalysts prepared via precipitation onto these three alumina supports all have surface areas between 150 and 205 m²/g. These results indicate that neither the surface area of the bare support nor the final surface area of the prepared catalysts is the sole determining factor of the catalytic activity.

A further indication that the initial support surface area is not the main factor in determining the catalytic activity can be seen when comparing alumina and carbon supported catalysts. While a catalyst prepared via precipitation of palladium onto Nanoactive aluminum oxide plus (695 m²/g, Table 3) gives a product yield of ~50 g/g Pd, a catalyst prepared using the same method but with an activated carbon support (surface area: 765 m²/g, Table 3) only gives a yield of 15 g/g Pd. Thus, despite the slightly higher surface area of the activated carbon it does not result in a catalyst as active as the one supported on nano-Al₂O₃(+).

Aside from giving the best activity of any of the supports tested, the nano-Al₂O₃(+) catalysts exhibited better reproducibility than any of the catalysts including the commonly used commercial palladium on carbon. The only major activity variations seen for the catalysts supported on nano-Al₂O₃(+) can be attributed to reactant quality.

3.3. Palladium surface areas

The palladium surface areas were determined after reduction of the PdO on the catalyst surfaces using CO adsorption and the volume of adsorbed CO is given in Table 4 for selected catalysts. Performing CO titration measurements on reduced catalysts do not necessarily result in a good measure of the catalytically active surface area since the active phase on these catalysts is PdO and not Pd metal. This is particularly the case when the catalyst before reduction consists of Pd metal or a mixture of PdO and Pd, as in the case of the commercial Pd/C and Pd/Al₂O₃ catalysts. However, in cases where the original catalysts consist solely of PdO (as is the case for the nanoparticle-supported catalysts), if the same mild reduction conditions are used for all catalysts, it should be possible to observe trends and obtain qualitative results from the Pd surface area measurements. CO chemisorption measurements on supported Pd catalysts are further complicated by the dependence of the Pd:CO stoichiometry on the dispersion since CO can adsorb in linear, bridge and hol-

Table 4
Results from CO chemisorption measurements of selected catalysts prepared and tested in the coupling reaction of 4-methylpyridine

Catalyst	CO adsorbed (μ l/g cat)	Pd surface area ^a (m ² /g catalyst)	Product yield (g/m ² Pd)
Nano-Al ₂ O ₃ (+)	0	0	N/A
10% Pd precipitated on nano-Al ₂ O ₃ (+)	8480	29.4	0.08
5% Pd precipitated on nano-Al ₂ O ₃ (+)	4550	15.8	0.17
5% Pd impregnated on nano-Al ₂ O ₃ (+)	1530	5.3	0.06
5% Pd precipitated on nano-Al ₂ O ₃ (–)	280	1.0	0.29
5% Pd/Al ₂ O ₃ commercial	1880	6.5	0.02
5% Pd/C commercial	2530	8.8	0.20
5% Pd precipitated on activated carbon	310	1.1	0.68
5% Pd Impregnated on activated carbon	240	0.8	0.41
5% Pd precipitated on commercial γ -Al ₂ O ₃ ^f	140	0.5	3.4

^a The Pd surface area has been calculated assuming a Pd:CO stoichiometry of 2:1 and a surface atom density of 1.42×10^{15} atoms/cm².

low binding modes on the surface [34]. Literature data indicate that a stoichiometry of two Pd surface atoms per CO molecule adsorbed is appropriate for high dispersions and a surface atom density (C_m) of $1.42 \times 10^{15} / \text{cm}^2$ based on the cubo-octahedral geometry is reasonable for small Pd crystallites [35]. While the exact Pd:CO stoichiometry may deviate slightly from the 2:1 ratio used here, the assumptions made in calculating the Pd surface area should give sufficient accuracy for comparisons between the different catalysts in the study, particularly considering that the active phase is PdO rather than Pd on these catalysts.

The 5% precipitated nano- $\text{Al}_2\text{O}_3(+)$ has a very high Pd surface area compared to the other catalysts in this study (Table 4). In fact, the Pd surface area of this catalyst is more than two times that of the commercial 5% Pd on activated carbon catalyst, which is the commercial catalyst with the highest Pd surface area. The commercial 5% Pd/ Al_2O_3 catalyst also has a high dispersion but, as mentioned, this catalyst exhibits a low activity due to a low PdO concentration rather than a lack of Pd surface area. The 5% impregnated nano- $\text{Al}_2\text{O}_3(+)$ has a surprisingly high Pd dispersion considering its low activity. The high yields per Pd surface area for the impregnated palladium on carbon and the palladium precipitated on nano-alumina(–) catalysts are likely an artifact of impurities in the product and the low dispersions of the catalysts. For low yields (~ 0.1 g for 0.7 g catalyst or 2.9 g/g Pd) trace impurities from the reactant and catalyst can be a significant portion of the raw product mass, and due to the nanoparticle supports used, it is difficult to separate these impurities from the products. Even though the same is partly true for the precipitated palladium on carbon catalyst, i.e. the reported yield per surface area is unrealistically high it appears that this catalyst does give a decent yield despite the low dispersion. The Pd surface areas of the precipitated Pd/C and Pd/nano- $\text{Al}_2\text{O}_3(-)$ are on the same order, but the yield is higher for the Pd/C catalyst. In fact, the data suggest that the palladium on the surface of the precipitated Pd/C catalyst is more active than the palladium on the surface of the commercial Pd/C. Comparing the data in Tables 2 and 4 it is evident that the modest yields obtained from the precipitated Pd/nano- $\text{Al}_2\text{O}_3(-)$ and the precipitated and impregnated Pd/C catalysts can be explained in part by low dispersions. Another surprising result is the relatively high Pd surface area of the 10% precipitated nano- $\text{Al}_2\text{O}_3(+)$. It has roughly twice the metal surface area of the 5% catalyst but exhibits no increase in yield. The most striking result, however, is that the Pd surface area of the 5% Pd precipitated on commercial γ - Al_2O_3 is very low despite the relatively good yield. The low dispersion of this catalyst is the main reason for the very high yield reported per palladium surface area. These results strongly indicate a structure sensitive reaction, i.e. only a portion of the surface Pd atoms are active. Consequently, the catalytic activity does not correlate with the measured Pd surface areas. This can be a result of the fact that the surface areas are determined on reduced catalysts, while the active catalyst is the unreduced form. While the support is important to give catalysts with high Pd surface areas, it is evident that this is not a sufficient criterion for an active catalyst. The Pd, or rather PdO, on the surface must also have the correct structure.

3.4. Impact of reactant quality

As mentioned, the catalysts prepared using the nanoparticle alumina(+) support for the most part exhibited good reproducibility. There were slight variations in the specific surface areas and yields for repeated samples as seen in Table 2 (Entries 4, 11, 13 and 26). However, the results are very sensitive to the quality of the 4-methylpyridine used. The 4-methylpyridine must be distilled over KOH (Distillates 1 and 3–5 in Table 2) to give good results, preferably doubly distilled. The product yields obtained with a reactant that had been distilled over a small amount of NaOH (Distillate 2) were markedly lower than the yields for reactants distilled over KOH (compare entries 8 and 11 in Table 2). It was noticed that distillate 2 discolored more quickly over time compared with the other distillates. In addition, distillate 3, which was treated with KOH over night and then distilled over the same KOH, turned cloudy or turbid over time. This may explain the lower yields obtained for entries 15 and 16 in Table 2, since those were the last two runs using distillate 3. The best and most reproducible results are obtained if the 4-methylpyridine is treated with KOH over night then decanted and distilled over fresh KOH. This treatment results in a clear liquid, which will not discolor or turn opaque over a reasonable time (on the order of months). These results tend to indicate that an impurity is present in the lower quality reactants (distillate 2 and 3) and that this impurity inhibits the reaction. As the primary purpose of adding KOH to the sample during distillation is for drying, it seems possible that water is the impurity. To test this hypothesis, parallel reactions were run with the same catalyst preparation [5% Pd precipitated onto nano- $\text{Al}_2\text{O}_3(+)$] and the same reactant distillate. To one of these reactions 0.3 g of water per gram of catalyst was added to the reactant. The water-free specimen gave a typical yield of 52 g/g Pd (entry 26, Table 2). The sample with the added water yielded 31 g/g catalyst (entry 27, Table 2). While this reveals that water exhibits an inhibiting effect on the reaction, it does not explain the considerably lower yields (18.2 g/g Pd) obtained from distillate 2 (cf entries 8 and 27 in Table 2). Furthermore, at a product yield of 50 g/g Pd the amount of water formed is slightly lower than the added 0.3 g/g catalyst. Consequently, the presence of water cannot be solely responsible for the inhibiting effects seen in the lower quality distillates.

The palladium nitrate source also had an effect on the catalytic activity. Catalysts prepared using the palladium nitrate from Fluka resulted in higher catalytic activities than catalysts prepared using the palladium nitrate from Alfa Aesar. During the catalyst preparation it was observed that the palladium nitrate from Alfa Aesar did not dissolve as well in the deionized water as the Fluka $\text{Pd}(\text{NO}_3)_2$. In fact, the residual solids from the Alfa Aesar palladium nitrate did not dissolve even after addition of acid (HNO_3 to a pH of 1.0). XRD analysis of both materials indicated the presence of a palladium oxide or related phase in the palladium nitrate from Alfa Aesar. The Fluka $\text{Pd}(\text{NO}_3)_2$ did not contain these phases. Consequently, it is important to check the catalyst precursor quality before preparing supported palladium catalysts.

3.5. Homogeneous versus heterogeneous catalysis

With palladium–pyridine systems there is a natural question of whether supported catalysts are truly heterogeneous, or if the actual active species is dissolved into the solution. Palladium(II) ions coordinate easily to the nitrogen of 4-methylpyridine and perhaps even more strongly to the bipyridine product formed in the reaction. Consequently, it is possible that the surface palladium is simply a precursor, or a source, to active palladium ions in solution. Other palladium-catalyzed coupling reactions, such as the Heck reaction, do exhibit palladium leaching when heterogeneous catalysts are used [36,37], and there is still a debate as to whether these heterogeneous palladium catalysts are active catalysts or simply precursors to a dissolved active species [38]. Therefore, a set of experiments was designed to probe if a dissolved palladium species is active in this reaction. If palladium is dissolved into the reaction mixture and this palladium is catalytically active, it would be expected that the reaction proceed after the heterogeneous catalyst (support) has been removed. One reaction was taken out of the oil bath after 24 h and the reaction mixture was filtered hot to remove the solid catalyst. The filtrate was then returned to reflux under oxygen for an additional 72 h. The product yield recovered from a 24 h experiment is lower than the product yield after a 72 h reaction (17 g/g Pd versus 50 g/g Pd, entry 1, Column 3 in Table 5). This reveals a slow reaction rate and the need for a 72 h reaction time. Furthermore, the product recovered after 24 h with solid catalyst plus 72 h without solid catalyst (i.e. after returning the filtrate to the reaction conditions) is very close to the yield of a 24 h reaction (22 g/g Pd). This is evidence that the reaction is heterogeneous, or at least that the presence of a heterogeneous catalyst is necessary for the reaction to proceed.

A set of similar experiments was run by reacting a catalyst-reactant mixture for 24 h and then use the recovered catalyst in a subsequent reaction. The recovered catalyst from a 24 h reaction was washed with chloroform, dried and then reloaded with fresh 4-methylpyridine. After 72 h at the reaction conditions, 24 g of product was recovered per gram of the reloaded catalyst [Pd/nano-Al₂O₃(+), entry 1, Column 4 in Table 5].

This is significantly less product compared to a fresh catalyst, however, the combined product yield from the 24 h and the 72 h reactions is consistent with an uninterrupted 72 h experiment (there is very little product formed after the initial 72 h at the reaction conditions). While the results clearly show that a recovered catalyst is still active, it is evident that the recovered catalyst has a lower activity compared to a fresh catalyst. One of the main reasons for the lower activity of a catalyst after exposure to the reaction conditions for 24 h or more, is probably reduction of the active Pd(II) species. However, it is also possible that some leaching does occur, even though any palladium in solution does not appear to be an active catalyst. From the experiments on commercial Pd/C it is evident that the 24 h product yield is higher (~30 g/g Pd) than for the Pd/nano-Al₂O₃(+) catalyst (~20 g/g Pd), even though the 72 h yield is considerably higher for the nano-Al₂O₃(+) supported catalyst. However, the recovered catalyst is much less active (Table 5). This indicates that the reaction is faster on Pd/C, but the catalyst also deactivates faster than the Pd/nano-Al₂O₃(+) catalyst.

Even though the above results imply that no catalytically active species is present in solution, there are indications of palladium leaching from the support. Previous results have indicated that the palladium surface concentration is lower after reaction [21]. In these reaction runs a palladium mirror could be observed in some experiments. However, generally the active Pd/nano-Al₂O₃(+) catalyst prepared via precipitation displayed little or no Pd mirror on the reaction flask after a completed reaction. In contrast, significant Pd mirrors were seen on several of the poorly performing catalysts, such as the Pd/nano-Al₂O₃(+) catalyst prepared via impregnation. Some mirroring was observed also in the commercial Pd/C catalyst. If the catalytic action of these catalysts was reliant solely upon a dissolved palladium species, it might be expected that palladium mirroring (which is evidence of palladium leaching from the support) would accompany a significant catalyst activity. In contrast, palladium dissolution is observed mainly for catalysts with poor activity. Thus, this can be taken as another indication that the active species is on the surface of the heterogeneous catalyst and not dissolved into the solution.

Table 5

Results from experiments at different reaction times to probe homogeneous vs. heterogeneous catalysis

Entry	Catalyst description ^a	Raw yield (g/g Pd) ^b 1st-day	Raw yield (g/g Pd) ^b 4th-day
Recovered catalyst ^c			
1	5% Precipitated Pd/nano-Al ₂ O ₃ (+) (1st-day and 4th-day)	17	24
2	5% Pd/C Commercial (1st-day and 4th-day)	32	5
Recovered reactant mixture ^d			
3	5% Precipitated Pd/nano-Al ₂ O ₃ (+) (1 day with and 3 days without catalyst)	N/A	22
4	5% Pd/C commercial (1 day with and 3 days without catalyst)	N/A	30

^a Nano-Al₂O₃(+): nanoparticle alumina (Nanoactive aluminum oxide plus).

^b Raw yield of 4,4'-dimethyl-2,2'-bipyridine, which contains a small amount of the terpyridine: 4,4',4''-trimethyl-2,2',6'2''-terpyridine as the only byproduct.

^c The 1st-day yield is the product recovered during filtration after the first 24 h. The 4th-day yield is the product obtained from a recovered 1st-day catalyst after reaction with fresh 4-methylpyridine for three additional days.

^d Reaction was run for 24 h with catalyst. The reaction mixture was filtered and the catalyst removed. The filtrate was then returned to the reaction conditions for an additional 72 h.

3.6. Precipitation base

NaOH or KOH were used as the base to force palladium precipitation onto the support. Both these bases resulted in highly active catalysts with similar yields (entries 11 and 13, Table 2). To determine if the presence of trace amounts of base was responsible for the activity of the precipitated samples, KOH was added to a reaction with an impregnated catalyst. This catalyst system showed no significant increase in activity. If the base is crucial for the activity it is possible the Na or K is required in the deposition stage, i.e. a closer interaction between the Pd and the Na or K is necessary.

4. Conclusions

While the palladium impregnated on nano- $\text{Al}_2\text{O}_3(+)$ exhibits little or no activity in the coupling reaction of 4-methylpyridine, nano- $\text{Al}_2\text{O}_3(+)$ supported catalysts prepared via the precipitation method give significant yields. Despite the fact that commercial Pd/ Al_2O_3 is not an active catalyst in this reaction, the nano- $\text{Al}_2\text{O}_3(+)$ was shown to be a viable support for the coupling reaction. The yield obtained from the palladium precipitated onto nano- $\text{Al}_2\text{O}_3(+)$ is significantly higher, the highest reported for this reaction system, and more reproducible compared to the yields obtained from commercial Pd/C catalysts, which are the commonly used catalysts in this reaction. Additionally, it was found that traditional alumina supported catalysts could be active for this reaction if prepared by precipitation. However, the yields are not as reproducible or as high as those obtained for the nano- $\text{Al}_2\text{O}_3(+)$ support. The sensitivity to catalyst preparation indicates that the activity of this catalyst is not based solely upon the surface area of the support. The lack of correlation between the measured Pd surface and the catalyst yields strongly suggests a structure sensitive reaction. Furthermore, experiments reveal that the differences in activities between catalysts prepared via precipitation and impregnation is not due to the presence of bases (NaOH or KOH) in the reaction mixture. To ensure high product yields the 4-methylpyridine must be distilled over KOH. Purification by sublimation followed by NMR measurements verifies that the product is 4,4'-dimethyl 2,2'-bipyridine and that the raw yields are at least 75% or more of the desired product. Experiments also reveal that a heterogeneous phase is necessary for the reaction to proceed at a significant rate.

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