

Investigation of the palladium catalyzed aromatic coupling of pyridine derivatives

Helena Hagelin^{a,1}, Björn Hedman^a, Ida Orabona^a, Torbjörn Åkermark^a,
Björn Åkermark^a, Christopher A. Klug^{b,*}

^a Department of Chemistry, Organic Chemistry, Royal Institute of Technology, S-10044 Stockholm, Sweden

^b Department of Chemical Engineering, Stanford University, Stanford, CA 94305-5025, USA

Received 30 March 2000; received in revised form 17 July 2000; accepted 17 July 2000

Abstract

The coupling reaction of 4-methylpyridine to form 4,4'-dimethyl-2,2'-bipyridine using a carbon-supported palladium catalyst was studied. Whereas previous research indicated that the reaction is catalyzed by palladium(0), we have found evidence that the reaction is catalyzed by palladium(II). Although oxygen can be used as the oxidative agent, the reaction is ultimately limited by catalyst deactivation. The major source of deactivation is most likely depletion of the palladium(II) oxide. The catalyst is reduced during the reaction and in the case of the oxygen-treated catalyst a small amount of palladium appears to be dissolved. In an investigation of the catalyst using X-ray photoelectron spectroscopy (XPS) and solid state nuclear magnetic resonance (NMR) it was found that deactivation is also caused by poisoning, the poison being either the product and/or the by-product. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Palladium; Catalysis; Aromatic coupling; NMR; XPS

1. Introduction

Transition metal complexes of bipyridine derivatives are important due to their chemical reactivity and photochemical properties [1,2]. For example, photons can induce electron and energy transfer in ruthenium(II) complexes of bipyridines [3]. These complexes are, therefore, commonly used as photosensitizers in artificial photosynthesis systems [4]. Several transition metals with bipyridine ligands have

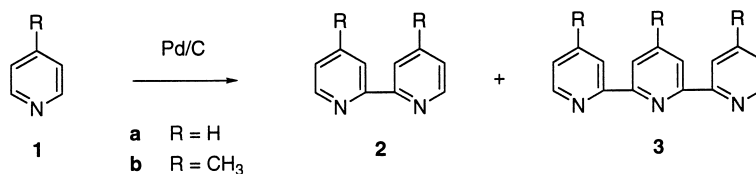
been used in catalysis. Iron and cobalt complexes of bi- or ter-pyridine substrates have been shown to catalyze the reduction of CO₂ and O₂ [5] and palladium(II) with bipyridine ligands can be used as a catalyst precursor in the carbon monoxide and styrene copolymerization reaction [6]. In addition, complexes of chiral bipyridine derivatives with rhodium, iron, zinc, and nickel have been used in asymmetric reductions [7].

Several methods of synthesizing bipyridine derivatives start with a substituted pyridine and require the building of the second pyridine ring, while other methods involve the transition metal catalyzed coupling of halogenated pyridines [8]. A simple one-step route to bipyridine derivatives that eliminates the use of halogens, like the palladium catalyzed oxidative coupling of aromatic compounds to biaryls or polycyclic systems [9–13], would be preferred. However, the cou-

* Corresponding author.

E-mail addresses: hagge@kth.se, hhagelin@che.ufl.edu (H. Hagelin), klug@chemeng.stanford.edu (C.A. Klug).

¹ Co-corresponding author. Present address: Department of Chemical Engineering, University of Florida, Gainesville, FL 32611, USA.



Scheme 1. Palladium-catalyzed coupling of 4-methylpyridine.

pling of heterocyclic aromatics differs from the coupling of aromatic compounds that do not contain heteroatoms [14]. For example, the coupling of electron poor heterocyclic aromatics, like the pyridines, has been found to require low valent metal catalysts, such as Raney nickel and palladium on activated carbon [15,16], while the coupling of aromatics, e.g. benzenes, requires palladium(II) [9–13]. Metals other than palladium and nickel have also been investigated, as well as different supports, but Raney nickel and palladium on activated carbon were shown to be the most efficient catalyst systems for the pyridine coupling reaction [17]. This reaction was first reported in 1967 and although several modifications of the reaction conditions have been made, they have lead only to small increases in yield [18–23].

The focus of this study is the palladium catalyzed coupling of 4-methylpyridine to form 4,4'-dimethyl-2,2'-bipyridine (**2b** of Scheme 1). This reaction has been investigated in detail and it was shown that the reaction proceeds best under reflux of 4-methylpyridine using a degassed catalyst under an inert atmosphere [24]. The reaction was not very sensitive to catalyst loading and the only by-product observed was 4,4',4''-trimethyl-2,2':6,6''-terpyridine (**3b**). Following the reaction, the catalyst can be filtered off and the starting material recovered by distillation. While the remaining crude product is fairly pure, containing only a small amount of terpyridine which can be removed by sublimation, the 4,4'-dimethyl-2,2'-bipyridine can be further purified by recrystallization in ethyl acetate. The yield based on consumed starting material is good, up to about 90%. However, the yield calculated per gram of catalyst is poor due to catalyst deactivation: the maximum yield is approximately 2 g/g catalyst. With a typical catalyst to starting material ratio of 1:10 this corresponds to 20% conversion of the starting material, but the yield was observed to be very dependent on catalyst preparation [25].

The ultimate goal in studying this reaction is to increase the yield and also to extend the reaction to include other heterocyclic systems. However, before this can be accomplished detailed knowledge about this reaction is required. Our objective in this study was therefore to obtain more information about the active catalyst and the reaction mechanism and also to determine the cause of the catalyst deactivation, which leads to low conversions.

2. Experimental

2.1. Experimental reaction conditions

The catalyst, palladium 10% on carbon, and 4-methylpyridine were purchased from Lancaster Synthesis Inc. The catalyst was used as received, while the 4-methylpyridine was distilled over KOH prior to use. In a typical reaction run 1 g (0.94 mmol Pd) of catalyst was weighed in a reaction flask and 10 g (107.4 mmol) of 4-methylpyridine was added. The system was evacuated three times while stirring, introducing the new atmosphere, either argon, nitrogen, or oxygen at atmospheric pressure. The reaction mixture was then heated to the boiling point and left for 72 h under reflux. After complete reaction the catalyst was filtered off and washed several times with either ethyl acetate, chloroform, or both. The solvent was rotary evaporated and the unreacted starting material was removed under vacuum. The crude product was recrystallized from ethyl acetate.

2.2. XPS details

The X-ray photoelectron spectra were obtained on a Surface Science Model 150 XPS spectrometer equipped with an Al K α source, quartz monochromator, concentric hemispherical analyzer, and a multi-channel detector.

2.3. NMR details

All NMR experiments were carried out at 9.40T using a Chemagnetics console (Fort Collins, CO). The static ^{13}C spin echo pulse experiments were carried out with homebuilt probes with either a 5 mm diameter coil (^{13}C π pulse of 9 μs) or a 10 mm diameter coil (^{13}C π pulse of 18 μs). The CP/MAS experiments were performed using a Chemagnetics double resonance probe with a ceramic stator and 7.5 mm outside-diameter zirconia rotors fitted with boron nitride spacers and Kel-F drive and end caps. Power levels, ^{13}C and ^1H , were set at 50 kHz during CP contact with a proton decoupling of 60 kHz.

3. Results and discussion

Little is known about the nature of the active sites of the catalyst. In general, the commercial palladium on carbon catalysts are not well defined, particularly with respect to the dispersion, the fraction of metal atoms occupying surface sites. (We were unable to perform surface area measurements on our catalysts due to the fine-powdered carbon support.) Furthermore, in the initial stages of our work we found that there was a large variation in the activities of catalysts from different suppliers and even between batches from the same supplier and several attempts at modifying the reaction conditions in order to increase the yield failed. However, in these earlier experiments palladium metal was believed to be the active catalyst whereas in the present study we have found that the active catalyst is probably palladium oxide.

3.1. Reaction conditions

The highest yields (2 g/g catalyst) were obtained at reflux (145°C) of 4-methylpyridine (no solvent was used in the reactions). We observed no significant yield at room temperature. The reaction could be run under atmospheric pressure of argon, nitrogen, or oxygen without affecting the yield to any appreciable extent, though in some cases, oxygen gave inferior results, particularly with catalysts obtained from suppliers other than Lancaster. Running under oxygen also gave a small amount of an orange colored by-product. This

is believed to be a palladium(II) complex of the product or a complex with the by-product, the terpyridine.

One reaction was run at 180°C and an increased argon pressure of 2 atm, but this did not improve the yield. In the case of oxygen under increased pressure (2–4 atm) no 4,4'-dimethyl-2,2'-pyridine could be observed — instead an orange-brown colored product was formed. Solution ^1H NMR of this compound did not allow a positive identification of the product.

The reaction worked well without solvent, especially if the catalyst to reactant ratio was kept low (<0.10). At higher catalyst concentrations the amount of terpyridine by-product formed was quite high, increasing from a few percent to 40% if the catalyst to reactant ratio was increased from 0.03 to 0.20. This implies that the formation of by-product is limited by the concentration of the product in the reactant mixture. To reduce the amount of terpyridine formed we have found that toluene is a good solvent for the reaction [26]. The reaction in toluene is clean with no detectable by-product formation. However, the yield calculated based on starting material (using the same amount of catalyst) is lower than for reactions run without solvent. Using a 1:1 ratio of 4-methylpyridine to toluene, the yield was decreased by one-half, consistent with a simple dilution effect.

Addition of up to 0.3 eq. (based on 4-methylpyridine) of water to the reaction mixture did not reduce the yield significantly, but the product from these reactions did contain a small amount of the orange by-product. Heating the catalyst to 145°C under slight vacuum prior to reaction had a negative effect. During this heat treatment, desorption of water was observed. The presence of a small amount of water thus has a positive effect on the reaction.

Catalyst pretreatment by reduction with hydrogen and then degassing at 18 Torr and 140°C for 3 h decreased the yield considerably. Only about a third of the yield of an untreated catalyst was obtained for this reduced catalyst.

An attempt with palladium black as catalyst gave no measurable yield. The low metal surface area could have been the limiting factor in this case.

To increase the amount of palladium oxide on the surface of the supported palladium catalyst, it was heated under an oxygen atmosphere. The temperature was kept below 200°C at all times, to avoid unwanted side effects, such as sintering of the metal particles

and oxidation of the support. Using this oxidized catalyst under an inert atmosphere gave the same yield as an untreated catalyst. Running under oxygen instead, keeping the other reaction conditions the same, led to a significant increase in the yield when compared to the untreated catalyst under an inert atmosphere. More of the orange colored by-product was formed in this case, but it is a small amount of strongly colored product that cannot be detected by solution NMR of the crude product. All attempts to isolate and identify the by-product failed.

To probe the efficiency of palladium(II) as catalyst, palladium(II) acetate with 4-methylpyridine-*N*-oxide as the oxidative agent was tested, but it turned out to be ineffective as a catalyst. Palladium(II) trifluoroacetate under an oxygen atmosphere did not show any formation of the desired product either.

The catalyst can be reused, but not regenerated to its original activity. Washing the catalyst with hot (close to the boiling point) pyridine and hot 4-methylpyridine did dissolve additional products, in this case more 4,4',4''-trimethyl-2,2':6',6''-terpyridine than 4,4'-dimethyl-2,2'-bipyridine. The activity of this regenerated catalyst was about a third of the original activity of the fresh catalyst. The inability to regenerate the catalyst to the original activity indicates that either the catalyst is dissolved or the catalyst is poisoned by some species that cannot be washed away.

3.2. Different substrates and catalysts

Pyridine could also be coupled to the 2,2'-bipyridine using palladium on carbon, but the yield was about half of that for 4-methylpyridine.

Following the procedure of Haginawa and Higuchi, which uses 4-methylpyridine and 4-methylpyridine-*N*-oxide in a ratio of 1:1 [18], attempts to form cross-coupling products were carried out by mixing pyridine-*N*-oxide and 4-methylpyridine or 4-methylpyridine-*N*-oxide and pyridine. Mainly starting material was recovered in these reactions. In the case of pyridine-*N*-oxide and 4-methylpyridine, a considerable amount of pyridine together with a small amount of the 4,4'-dimethyl-2,2'-bipyridine was observed. This together with results from a pyridine treated catalyst indicates that pyridine coordinates more strongly to palladium than 4-methylpyridine and acts as a poison for the coupling of the latter.

2,4-, 2,5-, and 3,5-dimethylpyridine were also treated with pyridine- or 4-methylpyridine-*N*-oxide in the presence of palladium on activated carbon, but only starting material together with some reduced *N*-oxide were recovered in these reactions. The additional methyl group, especially in the 2-position, probably resulted in severe steric interactions with the catalyst surface.

4-Isopropyl pyridine gave about the same yield as 4-methylpyridine, while the starting material was recovered in the reaction of 4-*tert*-butylpyridine. Steric factors are thus clearly very important.

In the reaction of 4-methoxypyridine a palladium mirror was formed on the reaction flask, resulting in an ineffective catalyst system. 4-*N,N*-Dimethylamino pyridine did not give any coupled product, which is probably due to coordination of the amino-nitrogen to palladium instead of the pyridine-nitrogen.

Platinum on carbon did not give any detectable amount of product under the reaction conditions used here and neither did homogeneous platinum(0) with norbornene ligands.

A few homogeneous palladium(0) catalysts were also studied, using ligands such as dibenzylidene acetone, bipyridine and fumaronitrile, and 2,9-dimethyl-1,10-phenantroline and fumaronitrile, but rapid catalyst decomposition occurred without product formation irrespective of the atmosphere, oxygen or argon.

Copper(II) acetate and nickel(II) acetate were not active catalysts for this reaction.

3.3. XPS measurements

3.3.1. Reference catalyst

The XPS survey spectrum obtained from the reference catalyst, as used in the reactions, is shown in Fig. 1a. Only peaks due to carbon, oxygen, and palladium are present. The high resolution XPS spectrum of the palladium 3*d* peaks for the reference catalyst is shown in Fig. 2a. Two states of palladium can readily be distinguished on the surface (see dashed lines in Fig. 2). The higher binding energy peaks are consistent with a palladium(II) oxide [27]. Based on peak areas about 50% of the total amount of palladium is palladium(II). However, this percentage ranged from 50 to 67% for different runs on reference catalysts obtained from the same batch. Since the XPS mea-

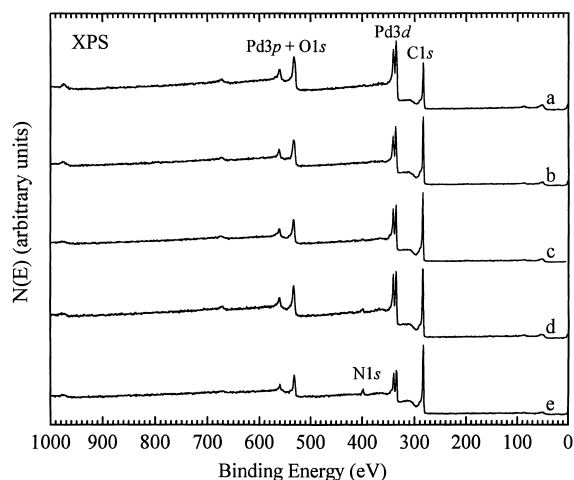


Fig. 1. XPS survey spectra of (a) reference catalyst, (b) oxygen pretreated catalyst, (c) heat-treated catalyst, (d) deactivated catalyst, and (e) oxygen-treated deactivated catalyst.

measurements probe several atomic layers, the true oxide content of the surface could be higher than this ratio would imply. The surface, and the near surface region, of the palladium on carbon catalyst, therefore, consist of a considerable amount of oxidized palladium.

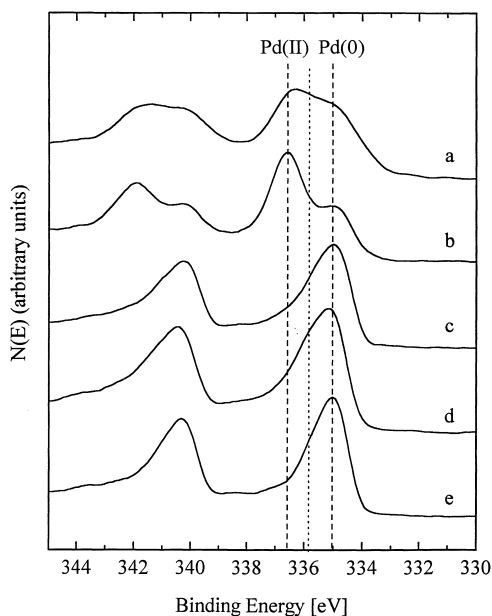


Fig. 2. XPS palladium 3d peaks from (a) reference catalyst, (b) oxygen pretreated catalyst, (c) heat-treated catalyst, (d) deactivated catalyst, and (e) oxygen-treated deactivated catalyst.

3.3.2. Oxidized catalyst

The amount of the higher oxidation state of palladium could be increased (up to about 75%) by oxygen treatment (200°C and oxygen at atmospheric pressure) as can be seen in Fig. 2b. The palladium to carbon ratio is attenuated after the catalyst is treated with oxygen (cf. Fig. 1a and b), most likely due to sintering of the palladium particles. Sintering results in larger palladium particles and consequently a reduction in the surface area of palladium. Since this catalyst runs better under an oxygen atmosphere, compared to untreated catalyst under an inert atmosphere, the large variation in catalytic activity between catalyst batches and suppliers may be the result of varying initial amounts of palladium oxide on the surface of these catalysts. The palladium oxide is, therefore, most likely the active species rather than palladium metal. The belief that palladium metal is the catalyst may have impeded attempts to improve the yield in earlier work. This could be the reason why only small increases in the yield have been reported since 1967. The smaller palladium to carbon ratio does not seem to affect the catalytic activity.

3.3.3. Heat-treated catalyst

Heating the reference catalyst to 150°C under slight vacuum removed almost all of the higher oxidation state. Only a small shoulder due to palladium(II) can be seen in the XPS spectrum (Fig. 2c). The lower activity for this catalyst is consistent with the higher oxidation state being the active state. The XPS survey spectrum from this heat-treated catalyst also showed that the palladium to carbon ratio is reduced, when compared to untreated catalyst (Fig. 1c and a, respectively).

3.3.4. Deactivated catalysts

XPS measurements were performed on the deactivated catalysts that were filtered off after a complete reaction, washed with hot ethyl acetate and dried in vacuo at 20 mTorr overnight. The survey spectra of the catalysts after the reaction (normal treatment: Fig. 1d and oxygen pretreated: Fig. 1e) showed the presence of a small amount of nitrogen, most likely adsorbed surface species. The nitrogen peak appears more pronounced on the deactivated catalyst that had been exposed to oxygen at elevated temperature prior to reaction. No nitrogen could be detected on

the fresh catalyst (Fig. 1a). As for the oxygen and heat-treated catalysts, the palladium to carbon ratio is lower on the deactivated catalysts than on the fresh catalyst (cf. Spectra a and d, or b and e of Fig. 1). This reduction could, as mentioned, be due to sintering of the palladium particles, to palladium being covered by adsorbed carbon species, to a small amount of palladium being dissolved from the surface, or to a combination of these effects. The reduction in palladium to carbon ratio is larger for the oxygen pretreated catalyst run under oxygen when compared to the reference catalyst run under an inert atmosphere, which suggests that more palladium is dissolved from the surface of the oxygen-treated catalyst, or that the palladium is covered by a higher amount of carbon containing species, or both. There is evidence for both effects in the current data. The removal of palladium from the surface is corroborated by the observed orange by-product in the case of the catalyst treated with oxygen, while a higher coverage of adsorbed molecules (either starting material or product) is consistent with the higher intensity of the nitrogen peak when comparing the oxygen-treated and reference catalysts. More significant is that most of the palladium(II) oxide is removed from the surface regardless of whether the catalyst had been pretreated in or run under oxygen (Fig. 2, spectra d and e). Nevertheless, multiple states of palladium are still left on the surface. This can be seen as a shoulder on the palladium 3d peak in spectra d and e, Fig. 2 (see dotted line). The peak area of the higher energy state comprises about 30% of the total peak area and the binding energy of this state is in between that of palladium metal and palladium(II) oxide. This could correspond to a palladium species with a coordinated, bonded, or even decomposed 4-methylpyridine derivative.

The depletion of palladium(II) oxide is probably the main reason for catalyst deactivation and explains why the oxygen pretreated catalysts work better under oxygen than under an inert atmosphere. However, the formed palladium metal is difficult to reoxidize to palladium(II) and consequently, atmospheric pressure of oxygen is not a sufficiently good oxidative agent.

3.4. NMR measurements

3.4.1. Background

Solid state NMR has proven to be a useful tool for studying heterogeneous catalysts in general and

surface species on supported metal catalysts in particular [28]. There are several options as to which nuclei in this system to observe: ^{105}Pd , ^1H , ^{15}N , ^{14}N , and ^{13}C . Given that both the reactant and product contain nitrogen, ^{15}N NMR was initially considered. However, the low natural abundance, 0.365%, and low sensitivity of ^{15}N require the use of a reactant isotopically enriched in ^{15}N . Attempts at synthesizing 4-methylpyridine from ^{15}N -labeled starting materials were unsuccessful. Our second option was to observe ^{13}C , which has a higher sensitivity and higher natural abundance (1.108%) — again attempts at synthesizing 4-methylpyridine from ^{13}C -labeled starting materials were unsuccessful. We, therefore, focused on natural abundance ^{13}C NMR. The most significant difficulty associated with this approach was the large background signal from the carbon support. We used two methods for suppression of this ^{13}C background signal. The first method exploits the large observed difference in the spin-lattice relaxation times: the ^{13}C nuclei in the activated carbon have a very long spin-lattice relaxation time T_1 , on the order of minutes, while the species adsorbed on the metal surface have much shorter spin-lattice relaxation times, on the order of seconds. (This observation was not unexpected as previous NMR studies have shown that metal effects often lead to shorter spin-lattice relaxation times of adsorbed species [29].) We used short repetition rates of the spin echo pulse sequence to suppress signals from ^{13}C nuclei with long T_1 's. Comparison of data obtained for a deactivated catalyst with that for the clean catalyst allowed further isolation of the signal from surface species. The second approach relied on the expectation that the only hydrogen-containing species in our sample were deposited as a result of the reaction. We used standard cross-polarization combined with magic angle sample spinning to selectively observe those species containing hydrogen. To avoid effects due to water adsorbed on the support, the catalysts were dried under vacuum (20 mTorr, overnight) prior to analysis. Finally, it should be noted that neither approach unambiguously allows for the separation of signals from surface species on the metal and surface species on the support, i.e. they do not identify surface species spilled over onto the support itself.

There are additional difficulties associated with the NMR study of catalysts with activated carbon supports. The conductivity of the support due to unpaired

electrons (dangling bonds) leads to a lowering in the quality factor Q of the probe coil, a reduction in the maximum radiofrequency power levels and difficulties in magic angle sample spinning. In these experiments, the samples were diluted with nine parts of sulfur to one part of catalyst by weight which, although spinning and tuning then worked satisfactorily, reduced the net amount of sample used in the measurements, and lead to long acquisition times. The presence of unpaired electrons also affects the NMR signals leading to significant line broadening and short spin-lattice relaxation times for those carbon nuclei coupled to the electrons [30]. In extreme situations no NMR signal is observable. However, in our experiments ^{13}C NMR signals are clearly observed and we make the assumption that the observed signals are representative of all the carbon nuclei in the sample, i.e. that the unpaired electrons and adsorbed surface species are uniformly distributed.

3.4.2. Reference and deactivated catalysts

A ^{13}C spectrum obtained for an untreated catalyst, as used in the reactions, using a spin echo pulse sequence under non-spinning conditions is shown in Fig. 3. The chemical shift anisotropy agrees qualitatively with previous work on pure carbon [31], although clearly we have significant additional broadening due to the conductivity of the sample.

A catalyst from a reaction with 4-methylpyridine at reflux (145°C) for 72 h under a nitrogen atmosphere was prepared as for the XPS measurements (vide supra). The ^{13}C spectrum for this deactivated catalyst obtained using fast repetition rates reveals several features not evident in the spectrum for the raw catalyst (Fig. 4a).

The two most prominent new features occur at approximately 20 and 125 ppm corresponding to methyl and protonated aromatic carbon nuclei, respectively (The pure starting material and product, run under the same experimental conditions, both give features at 150, 125, 20 ppm. Signals from the by-product, 4,4',4''-trimethyl-2,2':6',6''-terpyridine, are also expected close to these values.) The absence of a clear feature at 150 ppm, which corresponds to the carbon next to the pyridine nitrogen, suggests significant broadening and/or shift for this carbon, consistent with either direct coordination to palladium (as a result of a C–H insertion) or coordination

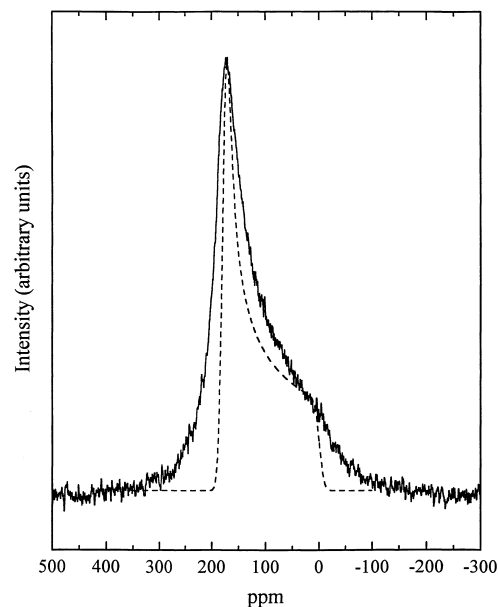


Fig. 3. ^{13}C NMR spectra of fresh catalyst. The spectrum was obtained using a homebuilt probe with a 10 mm coil. The dashed curve is a broadened spectrum calculated using the chemical shift parameters from [31].

of the pyridine-nitrogen to palladium(II). (The signal for this carbon would shift to higher ppm values and it is thus possible that it is masked by the support signal). In an attempt at improving the overall signal-to-noise ratio for the deactivated catalyst sample, the experiments were repeated at low temperature (77 K). However, this approach was unsuccessful as no clearly resolvable signals other than from the support were observed. One possible explanation is that the signals observed at room temperature were due to mobile species and that this mobility was frozen out at 77 K, thus leading to broad features, which were not resolvable from the background. Another possible explanation is that the difference in spin-lattice relaxation times became significantly smaller at 77 K and thus the background support signal overwhelmed the signal from the adsorbed species.

3.4.3. Room temperature treated catalyst

A second catalyst was stirred for 72 h with 4-methylpyridine at room temperature under a nitrogen atmosphere. Filtration, washing with ethyl acetate, and drying at room temperature was done as

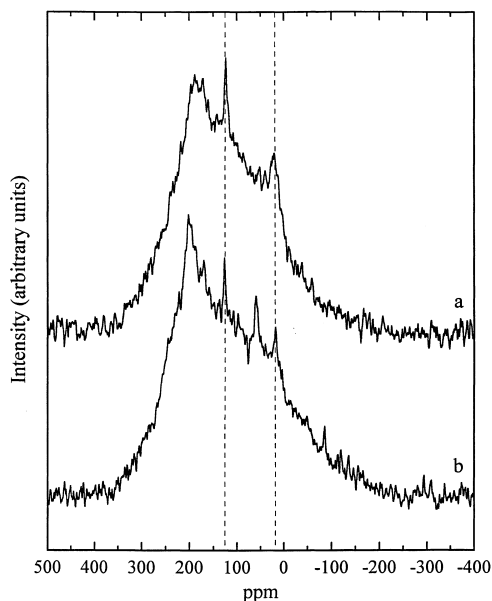


Fig. 4. ^{13}C NMR spectra of treated catalysts obtained using a homebuilt probe with a 10 mm coil. (a) Spectrum of deactivated catalyst after 18 h of signal averaging with a spin echo pulse sequence repetition rate of 10 ms. (b) Spectrum of catalyst treated with 4-methylpyridine at room temperature obtained using the same repetition rate.

for the deactivated catalysts. The ^{13}C spectrum obtained for this catalyst is shown in Fig. 4b. Again, a sharp feature due to protonated aromatic carbon nuclei is observed at roughly 125 ppm. The signal from the methyl group of the 4-methylpyridine can be seen at 20 ppm while the amino-carbon cannot be distinguished from the background signal. An additional feature, most likely due to residual ethyl acetate, is observed at roughly 60 ppm. Additional pumping significantly reduced the intensity of this peak. The observation of the 125 ppm feature suggests that the starting material is strongly adsorbed and cannot be removed under vacuum (*vide infra*). The feature could also be due to a small amount of formed product that cannot desorb from the catalyst at this temperature. The product in this case would stay on the surface and, consequently, cannot be detected after work-up since it is filtered off with the catalyst. The strong adsorption of 4-methylpyridine was confirmed by an NMR measurement on a catalyst that was not washed with ethyl acetate after reaction. Instead the catalyst was washed with hot 4-methylpyridine. Even after

pumping at 20 mTorr for 55 h the signal from the starting material was not reduced.

3.4.4. Heat-treated deactivated catalyst

In an attempt at catalyst regeneration, the deactivated catalyst was heated under vacuum (85 mTorr) to 150°C and left at this temperature for 28 h. Carbon-13 NMR spectra obtained for this catalyst showed that while some surface species have been removed by this treatment, a significant fraction remains. The activity of this catalyst was lower by a third when compared to the original catalyst. Therefore, heating under vacuum is a more efficient way of regeneration than washing with hot pyridines, which lead to a two-thirds reduction in activity (*vide supra*). However, it may not be possible to completely regenerate the catalyst by increasing the temperature even further due to the risk of damaging the catalyst.

3.4.5. Picoline-treated support

As a further reference sample, activated carbon was treated with 4-methylpyridine under the experimental conditions (reflux under oxygen for 72 h). Only starting material was recovered after filtering off the carbon. The NMR spectrum of the carbon after normal catalyst treatment (washing with ethyl acetate and drying overnight at 20 mTorr) did not show any significant features due to 4-methylpyridine or 4,4'-dimethyl-2,2'-bipyridine. The signals from the deactivated catalysts should therefore not be due to any reactant species that are adsorbed on the support.

3.4.6. Cross-polarization and magic angle spinning (CPMAS)

Fig. 5a shows the ^{13}C CPMAS spectrum obtained for the deactivated catalyst after 55 h of signal averaging. No background signal from the support is evident. For comparison, the spectrum obtained for 4,4'-dimethyl-2,2'-bipyridine, run at the same conditions, is shown in Fig. 5b. The similarities between these two spectra are again consistent with the presence of either the reactant or one of the products. Returning to the spectra shown in Fig. 4 which were obtained using fast repetition rates under non-spinning conditions without proton decoupling suggests that the relatively narrow feature observed at 125 ppm in the non-spinning experiments may be due to mobile surface species for which cross polarization is not

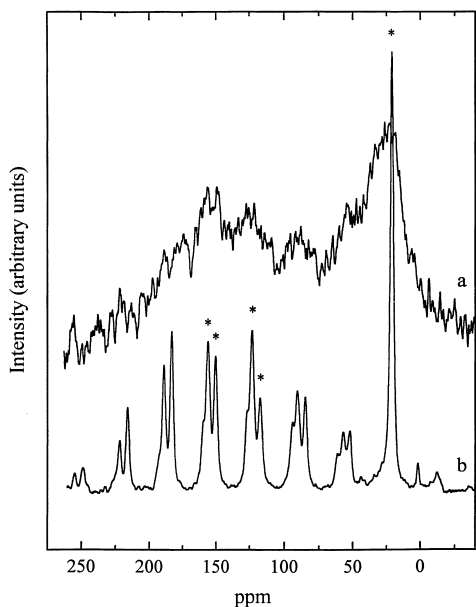


Fig. 5. CP/MAS spectra of (a) deactivated catalyst and (b) product. The spectrum in (a) was obtained with a pulse sequence repetition rate of 2 s and a spinning speed of 3.3 kHz. The asterisks mark the positions of the centerbands (156, 150, 126, 123, and 21 ppm).

very efficient. However, results obtained for the pure solid product under similar conditions suggest that we may be observing a sharp discontinuity in the full chemical shift anisotropy pattern which is further distorted by the absence of proton decoupling and anisotropic relaxation.

In summary the NMR results show that (i) the reactant does not strongly interact with the support alone; (ii) the reactant adsorbs strongly on the catalyst; (iii) the deactivated catalyst gives NMR signals in both non-spinning and CPMAS experiments consistent with reactant, product, and/or by-product; (iv) complete regeneration of the catalyst (i.e. removal of surface species) is difficult under reasonable treatment conditions.

4. Conclusions

The studies of the palladium catalyzed coupling of 4-methylpyridine to 4,4'-dimethyl-2,2'-bipyridine showed some very interesting results. We discovered, in contrast to earlier findings, that the reaction works

better under oxygen if the catalyst is pretreated under oxidative conditions. This reduces the dependence of catalytic activity on catalyst preparation. The active catalyst was consequently found to be a palladium oxide rather than palladium metal, as believed earlier. The coupling of pyridines therefore requires, as is the case for other palladium-catalyzed aromatic coupling reactions, a palladium(II) rather than a palladium(0) catalyst. Since pyridines are fairly unreactive in electrophilic reactions, palladium trifluoroacetate is not sufficiently active. However, the palladium oxide surface, where the only ligand for palladium is O^{2-} apparently has sufficient electrophilic activity.

Depletion of palladium(II) together with poisoning are the most probable reasons for the decrease in catalytic activity with time. The palladium(II) is reduced to palladium(0) during the reaction and the formed palladium metal is difficult to reoxidize to palladium(II), which explains the presence of palladium(0) even under oxidizing conditions. The formation of the colored product in the reactions under oxygen also indicates that at a small portion of the palladium is dissolved from the surface by forming a complex with the product (or the by-product). This is consistent with the slightly smaller palladium to carbon ratio in the XPS measurements. The XPS data showed the presence of nitrogen containing surface species on the deactivated catalyst and this poison is most probably, as shown by the NMR data, either the product or the by-product, which both bind very strongly to palladium(II). Using a different washing procedure after the normal treatment did dissolve more 4,4',4''-trimethyl 2,2':6',6''-terpyridine than 4,4'-dimethyl-2,2'-bipyridine, which may indicate that the more severe poison is the by-product. From studies in homogeneous phase, using palladium(II) as catalyst, it was shown that pyridine and bipyridine inhibit the aromatic coupling of 4-methylpyridine.

With the information acquired in this work we will try to modify the conditions to improve the yield for future industrial synthesis and also try to develop a more general procedure that will work for other similar substrates. More insight into the reaction mechanism is needed and solid state NMR methods will continue to be used. The use of ^{15}N and/or ^{13}C labeled starting materials will give enhanced signal-to-noise and lead to further insights, particularly with respect to binding of the surface species. (A parallel series of ex-

periments on ^{15}N -enriched pyridine is underway to probe the binding and subsequent reactions of this molecule.) Work to synthesize the necessary compounds is underway.

Acknowledgements

Financial support from the Royal Institute of Technology for establishing collaboration with Stanford University and from the Carl Trygger Foundation is gratefully acknowledged. CAK gratefully acknowledges support via a Terman Fellow award from Stanford University. H.H. also wishes to thank the Ernst Johnson foundation for a scholarship.

References

- [1] W. Śliwa, B. Mianowska, *Transition Met. Chem.* 13 (1988) 161.
- [2] W. Śliwa, *Transition Met. Chem.* 14 (1989) 321.
- [3] K. Kalyanasundaram, *Photochemistry of Polypyridine and Porphyrin Complexes*, Academic Press, London, 1992.
- [4] V. Balzani, A. Juris, M. Venturi, S. Campagna, S. Serroni, *Chem. Rev.* 96 (1996) 759.
- [5] D.L. Feldheim, C.J. Baldy, P. Sebring, S.M. Hendrickson, C.M. Elliott, *J. Electrochem. Soc.* 142 (1995) 3366.
- [6] B. Milani, A. Anzilutti, L. Vicentini, A. Sessanta o Santi, E. Zangrando, S. Geremia, G. Mestroni, *Organometallics* 16 (1997) 5064.
- [7] G. Chelucci, *Gazz. Chim. Ital.* 122 (1992) 89.
- [8] L.A. Summers, *Adv. Heterocycl. Chem.* 35 (1984) 281.
- [9] R. van Helden, G. Verberg, B. Balder, *Recl. Trav. Chim. Pays-Bas* 84 (1965) 1263.
- [10] J.M. Davidson, C. Triggs, *J. Chem. Soc. A* (1968) 1324.
- [11] H. Iataaki, H. Yoshimoto, *J. Org. Chem.* 38 (1973) 76.
- [12] F.R.S. Clarke, R.P.C. Norman, C.B. Thomas, J.S. Willson, *J. Chem. Soc., Perkin Trans. 1* (38) (1974) 1289.
- [13] B. Åkermark, L. Ebersson, E. Jonsson, E. Pettersson, *J. Org. Chem.* 40 (1975) 1365.
- [14] L.S. Hegedus, *Transition Metals in the Synthesis of Complex Organic Molecules*, University Science Books, Mill Valley, CA, 1994.
- [15] G.M. Badger, W.H.F. Sasse, *J. Chem. Soc.* (1956) 616.
- [16] H. Rapoport, R. Iwamoto, J.R. Tretter, *J. Org. Chem.* 25 (1960) 372.
- [17] G.D.F. Jackson, W.H.F. Sasse, C.P. Whittle, *Aust. J. Chem.* 16 (1963) 1126.
- [18] J. Haginawa, Y. Higuchi, *Yakugaku Zasshi* 93 (1973) 144.
- [19] G. Sprintschnik, H.W. Sprintschnik, P.P. Kirsch, D.G. Whitten, *J. Am. Chem. Soc.* 99 (1977) 4947.
- [20] P.K. Ghosh, T.G. Spiro, *J. Am. Chem. Soc.* 102 (1980) 5543.
- [21] P.A. Adcock, F.R. Keene, R.S. Smythe, M.R. Snow, *Inorg. Chem.* 23 (1984) 2336.
- [22] K. Sumi, M. Furue, S.-I. Nozakura, *J. Polym. Sci.* 22 (1984) 3779.
- [23] G.A. Mines, M.J. Bjerrum, M.G. Hill, D.R. Casimiro, I.-J. Chang, J.R. Winkler, H.B. Gray, *J. Am. Chem. Soc.* 118 (1996) 1961.
- [24] P.E. Rosevear, W.H. Sasse, *Patent App. No.* 40930/72, 1973, p. 1.
- [25] P.E. Rosevear, W.H.F. Sasse, *J. Heterocycl. Chem.* 8 (1971) 483.
- [26] E.C. Constable, personal communication.
- [27] C.D. Wagner, W.M. Riggs, L.E. Davis, J.F. Moulder, G.E. Muilenberg (Eds.), *Handbook of X-Ray Photoelectron Spectroscopy*, Perkin-Elmer, Eden Prarie, MN, 1978.
- [28] A.T. Bell, A. Pines (Eds.), *NMR Techniques in Catalysis*, Marcel Dekker, New York, 1994.
- [29] J.-P. Ansermet, P.-K. Wang, C.P. Slichter, J.H. Sinfelt, *Phys. Rev. B* 37 (1988) 1417.
- [30] R. Blinc, D. Arcon, P. Cevc, I. Posic, M. Koos, Z. Trontelj, Z. Jaglicic, *J. Phys. Condens. Matter* 10 (1998) 6813.
- [31] H.A. Resing, D.C. Weber, M. Anderson, G.R. Miller, M. Moran, C.F. Poranski Jr., L. Mattix, *Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem.* 23 (1982) 101.