ORGANOMETALLICS

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Mechanistic Study of the L_2Pd-Catalyzed Reduction of Nitrobenzene with CO in Methanol: Comparative Study between Diphosphane and 1,10-Phenanthroline Complexes

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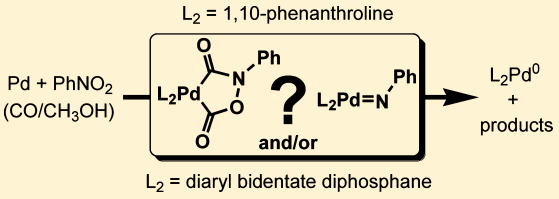
Supporting Information

ABSTRACT: The catalytic activity of Pd^{II} compounds supported by 1,10-phenanthroline (phen) or the bidentate diarylphosphane ligand L4X has been studied in the reaction of nitrobenzene with CO in methanol. Both systems are ~70% selective for azoxybenzene and azobenzene but also produce carbonylation products (methyl phenyl carbamate (MPC) and *N,N′*-diphenylurea (DPU)) and hydrogenation products (aniline and DPU). The Pd^{II}(L4X) system also produces methanol oxidation products (dimethyl carbonate, dimethyl oxalate, water). Upon the addition of a catalytic amount of acid, the coupling reaction is suppressed in favor of either the carbonylation reaction (for Pd^{II}(phen)) or of both the carbonylation and hydrogenation reaction (for Pd^{II}(L4X)). The palladacycle $L_2PdC(O)N(Ph)OC(O)$ (**C7**) and palladium−imido species $L_2Pd{=}NPh$ (**C3**) were considered as possible carbonylation product-releasing species, where L_2 is phen or the diphosphane ligands L4X and L3X. A ligand exchange experiment of phen-**C7** with L4X and L3X, ESI-MS analysis of L3X-**C7** and phen-**C7**, and a DFT study of nitrobenzene deoxygenation intermediates to $L_2Pd{=}NPh$ all suggest that **C7** is not the major product-releasing intermediate; all data suggest that the barrier for **C7** decarbonylation (−CO) is lower than that for decarboxylation ($-CO_2$). **C7** is thus thought to be part of an "NPh reservoir" consisting of palladacycles that are mutually accessible through carbonylation/decarbonylation. Under *acidic conditions* the decarboxylation barrier is lowered; for phen-**C7** apparently to the point where decarboxylative alcoholysis is favored relative to decarbonylation, but for L4X-**C7** the decarbonylation barrier still seems lowest due to the destabilizing effect that this bulkier ligand has on such palladacycles. It is thus concluded that the $L_2Pd{=}NPh$ complex **C3** is the prime "NPh" product-releasing intermediate and only under acidic conditions and in an alcoholic environment may **C7**—for phenanthroline—become the predominant carbamate product releasing intermediate.



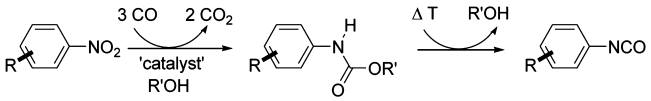
1. INTRODUCTION

Studies in homogeneous catalysis are often motivated by financial and/or ecological incentives. One process in which both motivators are in play is the synthesis of aromatic isocyanates[1,2] such as the polymer precursors MDI and TDI,[3,4] which are produced on a megaton scale per year. These use respectively nitrobenzene and dinitrotoluene as the ultimate feedstocks, while the highly toxic[5,6] and corrosive[2] phosgene is employed as the carbonylating reagent.

Phosgene can in principle be replaced by the less toxic carbon monoxide as the carbonylating reagent, whereby CO also acts as the reductant/deoxygenating agent for nitrobenzene; this process is known to proceed in the presence of a transition-metal catalyst.[7] When this reductive carbonylation of nitrobenzene with carbon monoxide is conducted in a protic medium such as an alcohol, a carbamate is obtained which can be pyrolyzed to the isocyanate with the recovery of the alcohol (Scheme 1).

It was disclosed already in the early 1980s that reasonably active (~500 turnover numbers) palladium-based catalysts for this carbonylation reaction are obtained when the Pd center is stabilized by bidentate N or P ligands.[8] Use of the ligand 1,10-phenanthroline (phen) yielded the most active catalytic systems

Scheme 1. Alternative Route To Make Aromatic Isocyanates by Carbonylation Followed by Pyrolysis



(in the presence of an acid cocatalyst), which resulted in the focus of the scientific community on this Pd/phen/H^+/CH_3OH catalytic system.[7−16] Although a very active catalytic system has been reported (with ~10^5 turnover numbers),[13] a clear-cut and generally agreed upon mechanism for this reaction involving common intermediates has yet to emerge.

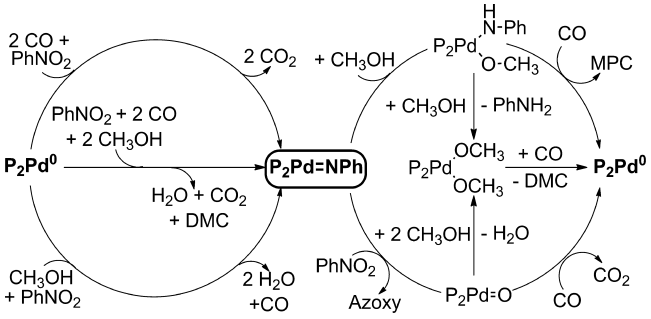
We have recently reported on our mechanistic studies of this carbonylation reaction in methanol, using bidentate diarylphosphane ligands in combination with a source of palladium.[17,18] During these studies, it became clear that for this catalytic system there is a catalytic connection between nitrobenzene reduction chemistry (forming methyl phenyl carbamate (MPC), *N,N′*-diphenylurea (DPU), azoxybenzene,

Received: September 21, 2011
Published: May 31, 2012

   dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

aniline, and water) and methanol oxidation chemistry (forming dimethyl carbonate (DMC), dimethyl oxalate (DMO), methyl formate (MF), aniline, water, and carbon monoxide).[17] This experimental observation has far-reaching implications for the underlying mechanisms. Thus, we proposed a stepwise deoxygenation of nitrobenzene, wherein only CO, only methanol, or CO and methanol act as the reductant for nitrobenzene to yield a diphosphane ligand supported palladium–imido complex ($P_2Pd{=}NPh$, left-hand side of Scheme 2).[17] In a methanolic environment, this imido complex

Scheme 2. Working Hypothesis of the Interrelated Catalytic Cycles Operating in the P_2Pd-Catalyzed Reaction of Nitrobenzene with CO in Methanol, Rationalizing the Genesis of All the Products Observed[17]

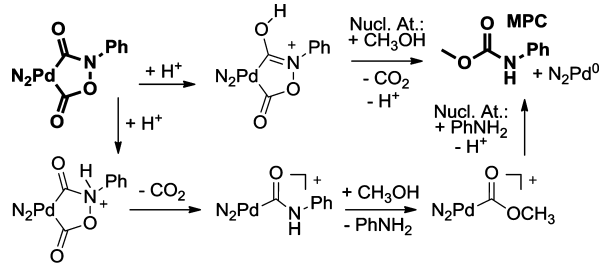


can readily form the anilido–methoxido palladium species $P_2Pd(NHPh)(OCH_3)$ and dimethoxido species $Pd_2Pd(OCH_3)_2$ with the coproduction of aniline. Under a CO atmosphere, these anilido–methoxido type palladium complexes naturally will convert into a kinetic mixture of palladium anilido–carbomethoxylates (e.g., $P_2Pd(C(O)NHPh)OCH_3$, $P_2Pd(C(O)OCH_3)OCH_3$, and $P_2Pd(C(O)OCH_3)_2$) that respectively produce MPC, DMC, and DMO upon reductive elimination.[17,18] It is thus our current thinking that the genesis of nitrobenzene carbonylation products such as MPC follows a pathway very similar to and competing with the formation of DMC and DMO: i.e., via a net hydromethoxycarbonylation of the palladium–imido intermediate. The $P_2Pd{=}NPh$ intermediate can also rationalize the genesis of products such as azoxybenzene by a [2 + 2′] cycloaddition type reaction with nitrobenzene; this places azoxybenzene formation within our overall mechanistic proposal as well (see right-hand side of Scheme 2). We have thus constructed a hypothesis centered around the palladium–imido intermediate that allows rationalization of the catalytic formation of *all* products observed in nitrobenzene carbonylation experiments using diphosphane-supported palladium catalysts. We were also able to directly apply this hypothesis to understand alterations in product selectivity patterns that were induced by the structure of the ligand or the choice of additives and reaction conditions employed.[17,18] Although the intermediacy of palladium–imido complexes has been postulated in earlier reports, mechanistic details and experimental evidence have not been put forth to justify these speculations.[7,9,10,19]

Our mechanistic proposal deviates significantly from those postulated by others, which are mainly based on phen-supported palladium catalyst systems. The most recent hypothesis for the mechanism of the Pd/phen-catalyzed carbonylation of nitroarenes in methanolic media—using large molar excesses of phen (up to 300) and acid (up to 1300) on Pd—comes from the Ragaini group.[16] They proposed that carbamates and ureas are formed as the final carbonylation products from initially formed isocyanates involving a direct carbonylation of the corresponding amine. It is speculated that the direct carbonylation of the amine to the corresponding isocyanate involves a five-coordinated $(phen)Pd(CO)(C(O)OCH_3)_2$ catalyst species together with a proposed Pd–carbenoid type intermediate. The main reasons for this mechanistic proposal lie in the observed cocatalytic effect of amine and the observation that carbonylation of a d_5-labeled nitrobenzene in equimolar amounts of aniline produces a significant amount of unlabeled urea.

In contrast, a more common rationalization of carbamate formation for the $Pd/phen/CH_3OH(/H^+)$ system, prior to the proposal of Ragaini et al., involves a palladacyclic intermediate as the central product-releasing intermediate (top left in Scheme 3). This palladacycle can be synthesized and isolated by

Scheme 3. Palladacycle (Top Left) Proposed To Be the Key Intermediate MPC (Top Right) Product-Releasing Species in the $Pd/phen/CH_3OH(/H^+)$ Catalytic System via a Pathway Adapted from a Proposal by Osborn et al. (Top)[11] and van Leeuwen et al. (Bottom)[9] [a]



[a] N_2 = 1,10-phenanthroline.

exposing a Pd/phen mixture in an alcoholic nitrobenzene medium to mild carbonylation conditions.[11,20–22] This palladacycle is thermally very stable and only decomposes to yield 0.2 equiv of isocyanate when heated to 170 °C under 20 bar of CO in an aprotic medium.[11] Addition of 1.6 equiv of a weak acid (2,4,6-trimethylbenzoic acid) leads to a 3-fold increase in isocyanate formation, while in the presence of acid and ethanol as solvent, carbamate/urea formation already proceeds smoothly at 90 °C with more than 90% isolated yield.[11] Osborn et al. proposed (Scheme 3, top) that protonation of the palladacycle at the carbonyl O may lower the barrier of CO_2 extrusion by nucleophilic attack of the alcohol on the amide carbonyl to produce the carbamate directly.[11] Van Leeuwen et al.[9] postulated (Scheme 3, bottom) that protonation occurs on the ring N atom, followed by CO_2 extrusion and $[PdC(O)NHPh]^+$ formation. In a subsequent transesterification event with methanol, aniline is thought to be formed together with the carbomethoxy cation $[PdC(O)OCH_3]^+$; nucleophilic attack of aniline on this intermediate then leads to MPC formation.

The question naturally arises as to the relationship between the diphosphane- and phen-based catalytic systems and to the relationship between proposed palladium–imido and palladacyclic intermediates.

The aim of the present study is therefore to gain crucial additional catalytic and organometallic data to understand the differences and similarities between the two systems. In particular, the relative importance of the proposed palladium–imido and palladacycle intermediates was considered.

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142–4156

Because we found that the product distribution of the aryl-containing nitrobenzene reduction products is remarkably similar (especially for azoxybenzene) when employing the N-donor ligand phen (Figure 1, left) or the P-donor ligand L4X

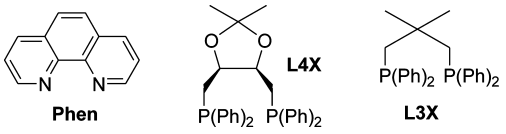


Figure 1. N-donor ligand phen and P-donor ligands L4X and L3X used in this study.

(Figure 1, middle), these ligands have mainly been used for the catalytic experiments in this study; the ligand L3X (Figure 1, right) was mainly used for insight supporting (organometallic) experiments.

2. RESULTS

2.1. General Considerations. In most catalytic reactions, the catalyst precursor was formed in situ from 0.05 mmol of $Pd(OAc)_2$ and a certain amount of ligand; testing the catalytic activity of preformed complex gave identical results. By thorough drying of the reagents it was ensured that the reaction conditions were strictly anhydrous (<100 ppm of H_2O).[17]

The products that were observed in the catalytic reactions are shown in Scheme 4. The aryl-containing reduction products of nitrobenzene can be grouped into the carbonylation products (NCO) methyl phenyl carbamate (MPC) and *N*,*N*′-diphenylurea (DPU), the coupling products (N═N) azobenzene (Azo) and azoxybenzene (Azoxy), and the hydrogenation products (NH) aniline ($PhNH_2$) and also DPU (derived from aniline).[23]

Azo and Azoxy are frequently reported side products, as are aniline and DPU.[7] Azo and Azoxy are only derived from nitrobenzene, but for the formation of aniline and DPU H atoms are required. We have shown that these H atoms originate from methanol oxidation, resulting in the oxidative carbonylation products dimethyl carbonate (DMC) and dimethyl oxalate (DMO) and in the oxidative dehydrogenation products methyl formate (MF) and carbon monoxide.[17]

At reaction temperatures (110−130 °C) DPU in methanol is involved in a reversible transesterification reaction yielding MPC and aniline;[24] therefore, DPU and MPC should be considered together as carbonylation products and aniline and DPU together as hydrogenation products. The coupling products Azo and Azoxy were almost always detected; Azoxy is always the major product and Azo the minor product (<2% selectivity).

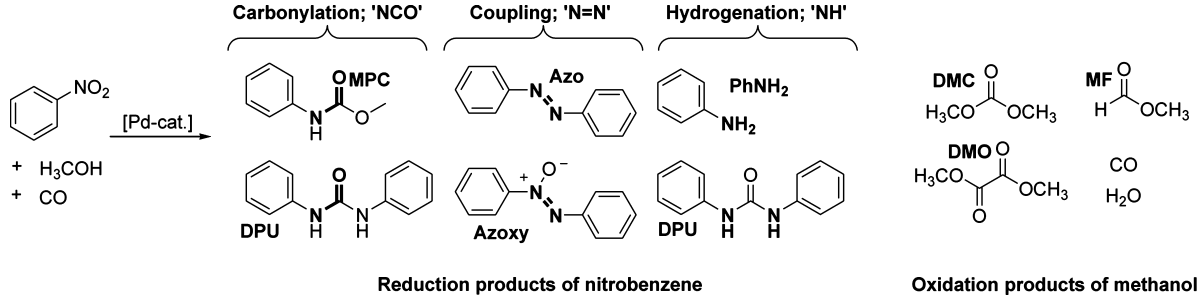
2.2. Catalytic Experiments. *2.2.1. Reactivity without Additives or Cocatalysts.* Using GLC analysis of the reaction mixtures all products could be quantified with calibration lines made from authentic samples. Selected data are given in Table 1; full analytical details of all reactions are given as Supporting Information (Table S1). The mass balance of phenyl-containing products is excellent, showing that all important products have indeed been identified and quantified (column $\sum_{\varnothing}$ in Table 1).

When the Pd^{II}(phen) system was employed at a reaction temperature of 110 °C (entry 1), only 17% conversion was reached, whereas at a reaction temperature of 130 °C (entry 2), 56% nitrobenzene was converted. This conversion at 130 °C is similar to that of the Pd^{II}(L4X) catalytic system at 110 °C (52%, entry 3). Both catalytic systems are about equally selective for the coupling product Azoxy (∼70%); Pd^{II}(phen) is more selective toward carbonylation (20%), while Pd^{II}(L4X) is more selective toward hydrogenation (20%). Notably, using Pd^{II}(L4X), large quantities of oxidation products of methanol are coproduced, whereas these products are hardly formed when using Pd^{II}(phen).

2.2.2. Effects of the Initial Nitrobenzene Concentration. The similar selectivity for reductive coupling products (yielding predominantly Azoxy) with Pd^{II}(phen) and Pd^{II}(L4X) catalyst systems is quite remarkable, given the different structural characteristics of these catalyst systems. Intrigued by an observed higher order formation kinetics in nitrobenzene, in particular with Pd catalyst supported by larger backbone (C4) diphosphane ligands,[17] we investigated the effect of the initial concentration of the nitrobenzene on product yields. It appears that the relative ratio of carbonylation (NCO) and hydrogenation (NH) products over coupling (N═N) products decreases significantly with increasing nitrobenzene concentrations (Supporting Information, Figure S1 and Table S1). These data suggest that also for Pd^{II}(phen) catalysts the formation of Azo(xy) coupling products from nitrobenzene involves a step competing with carbonylation and hydrogenation, with higher order kinetics in nitrobenzene.

2.2.3. Effects of Acid Addition. It has been reported that (over)stoichiometric amounts of acid are beneficial for the MPC selectivity of the Pd^{II}(phen) system.[9,12,14] We therefore decided to investigate the effects of the addition of acid for Pd^{II}(phen) and Pd^{II}(L4X) catalyst systems under our reaction conditions. Thus, some experiments were conducted wherein (sub)stoichiometric amounts (on Pd) of *p*-toluenesulfonic acid

Scheme 4. Overview of the Different Products That Are Formed in the Palladium-Catalyzed Reaction of Nitrobenzene with CO in Methanol



dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

Table 1. Reactions of Nitrobenzene with CO in Methanol, Using $Pd^{II}(phen)(OAc)_2$ or $Pd^{II}(L4X)(OAc)_2$ as Catalyst Precursor[a]

					selectivity (%)			amt (mmol)		
entry	ligand	temp (°C)	conversn (%)[b]	$\sum_o$	NCO[c]	N=N[d]	NH[e]	MF	H_2O	DMC/O
1	phen	110	17	24.7	23	71	6	0.0	0.0	0.0
2	phen	130	56	24.3	22	71	7	0.2	0.3	0.5
3	L4X	110	52	24.4	8	73	19	0.2	10.1	8.2

[a]Reaction mixtures were heated for 4 h at the indicated temperature in 25.0 mL of dry and degassed methanol under 50 bar of CO. The catalyst was generated in situ from 0.05 mmol of $Pd(OAc)_2$. Mole ratios are as follows: $Pd(OAc)_2$:ligand:nitrobenzene = 1:1.5:488. All reactions were performed in quadruplicate, and the relative standard deviation of all analytes was <5% in all cases. [b]Conversion = $(\sum_{aryl\ converted})/24.4 \times 100\%$. [c]Selectivity toward carbonylation products = $(MPC + DPU)/\sum_{aryl\ converted} \times 100\%$. [d]Selectivity toward coupling products = $(2 \times Azo + 2 \times Azoxy)/\sum_{aryl\ converted} \times 100\%$. [e]Selectivity toward hydrogenation products = $(PhNH_2 + DPU)/\sum_{aryl\ converted} \times 100\%$.

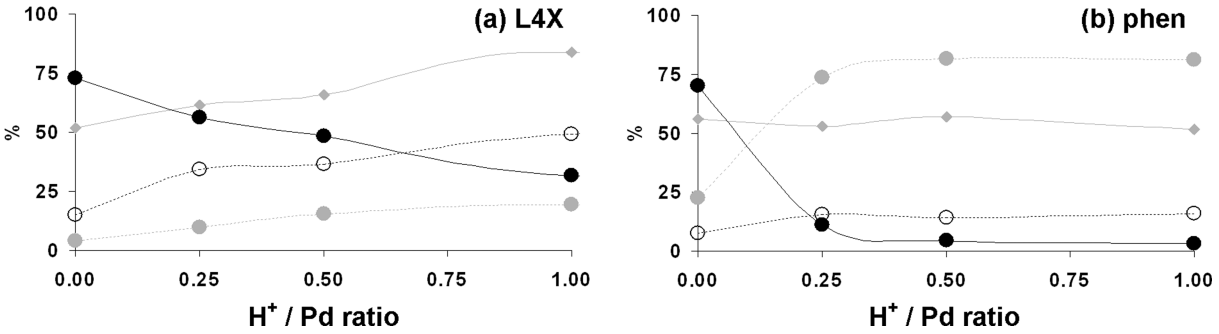


Figure 2. Plot of the conversion (◆) and selectivity toward coupling products (●, Azo(xy)), hydrogenation products (○, DPU + $PhNH_2$), and carbonylation products (●, MPC + DPU) as a function of the amount of *p*-toluenesulfonic acid added (relative to Pd), when using the ligands L4X at 110 °C (a) and phen at 130 °C (b). The lines are added as a guide for the eye.

(HOTs) were added, using our standard experimental conditions (110 °C for $Pd^{II}(L4X)$ and 130 °C for $Pd^{II}(phen)$).

As shown in Figure 2a for the $Pd^{II}(L4X)$ system, the conversion increases with the addition of more HOTs, whereas for the $Pd^{II}(phen)$ catalytic system (Figure 2b), the conversion is more or less constant. Interestingly, in both systems the coupling reaction is significantly suppressed already when adding substoichiometric amounts of HOTs. The change in selectivity, however, is drastically different for the two catalysts: for $Pd^{II}(L4X)$ both the hydrogenation and carbonylation reactions become more important, whereas for $Pd^{II}(phen)$ the carbonylation reaction becomes highly dominant. This observed difference in selectivity change upon addition of acid indicates that dissimilar reaction mechanisms are operative for the two systems.

2.2.4. Nitrosobenzene as Intermediate toward Azo or Azoxy? It has been suggested that, in the $Pd^{II}(phen)$ catalytic system, nitrobenzene is first reduced to "free" nitrosobenzene, which then would react further to form mainly Azoxy and some Azo.[10,15] We have investigated whether elevated amounts of Azo and Azoxy are detected upon addition of 2.5 mmol of nitrosobenzene *during* a catalytic run. However, when either $Pd^{II}(L4X)$ or $Pd^{II}(phen)$ is employed, both the conversion and selectivity are nearly identical with those in a "normal" catalytic experiment (see Figure S2 in the Supporting Information); no significant increase in the selectivity for Azo and Azoxy is observed. Nitrosobenzene is not detected after the catalytic run, while a significant amount of nitrobenzene is still present. This confirms that nitrosobenzene is more prone to reductive carbonylation reactions[25] than nitrobenzene, which is consistent with the observation of only traces of nitrosobenzene in ordinary catalytic experiments.

2.2.5. Azo or Azoxy as Intermediate toward MPC, DPU, or Aniline? We investigated if the coupling products Azo and Azoxy could perhaps also be intermediates to products such as MPC, DPU, and/or aniline in our catalytic system. The intermediacy of Azo and Azoxy has been suggested by Mestroni et al. for the Pd/phen/H^+ system at 155 °C[26] but was disputed by Ragaini et al.[14] When 2.5 mmol of Azo or Azoxy is added to the $Pd^{II}(phen)$ catalytic system under our standard reaction conditions, the same amount (plus the amount formed in a normal run) is detected after the catalytic run, even when 1 equiv of HOTs and 2.5 mmol of Azoxy are used (Table S2, Supporting Information). This means that Azo and Azoxy are stable reaction products and are not intermediates toward MPC, DPU, or aniline employing our standard reaction conditions of 130 °C and 50 bar of CO.

2.2.6. Is Aniline Directly Carbonylated to Isocyanate for MPC? Ragaini et al.[16] proposed that nitrobenzene, at least with their catalytic precursor system, $[Pd(phen)_2](BF_4)_2$ with an excess of the ligand phen (300 equiv), diphenylphosphinic acid ($Ph_2P(O)OH$, 1300 equiv), and drying agent (2,2′-dimethoxypropane, 4200 equiv), is first fully reduced to aniline. Aniline is then carbonylated to phenyl isocyanate (via a five-coordinate $(phen)Pd(C(O)OCH_3)_2CO$ complex), which in turn forms MPC in the prevailing methanolic environment.[16] To verify such a scenario with our catalytic system, one could think of adding labeled aniline (e.g., toluidine) during a catalytic run to see whether its corresponding carbamate is produced. However, such an experiment cannot yield meaningful results, as transesterification and transamidation reactions occur readily under typical reaction temperatures (i.e., 170 °C employed by Ragaini et al.). Already at 80 °C, DPU and MPC in methanol are involved in a reversible transesterification reaction.[24] Also, a labeled aromatic amine and DPU will be involved in a reversible transamidation reaction; we found that transamidation between 3-methylaniline and DPU occurs to a significant extent already at 70–80 °C.[27]

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142–4156

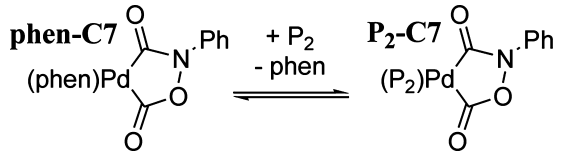
It is well-documented that when aniline is used instead of methanol as the nucleophilic reactant−solvent to yield DPU, significantly milder reaction conditions (90−120 °C) can generally be applied for both phen and diphosphane-based systems.[28−35] With our experimental setup and using preformed (phen)Pd(OAc)$_2$ as catalyst precursor at 110 °C, in aniline 76% of nitrobenzene was converted into DPU (53%) and Azo/Azoxy (47%) (in comparison to the 17% conversion in methanol at 110 °C, entry 1 in Table 1), but this system appears to be inactive below 80 °C. On the other hand, nearly all the Pd/diphosphane catalysts tested in this solvent reach (nearly) full conversion typically within 1−4 h at 110 °C.[36] The catalyst precursor (L3X)Pd(OAc)$_2$ proved to be particularly active, reaching full conversion after 4 h at 60 °C. Thus, the experiment was repeated, using 3-methylnitrobenzene as the substrate and a large excess of unsubstituted aniline as the nucleophilic reagent and solvent.[37] Full conversion of 3-methylnitrobenzene was reached; GLC-FID analysis surprisingly revealed the presence of 3-methylaniline (24.4 mmol) as the only liquid-phase reaction product, while ^{1}H and ^{13}C NMR analysis of the solid revealed that symmetric, *unsubstituted* DPU was produced with 90% selectivity, with the remaining 10% being diphenyl oxalamide (DPO, verified by ESI-MS). The formation of large quantities of DPU (and 3-methylaniline) is in qualitative agreement with reported results by Ragaini et al.[16] of an experiment with equimolar quantities of d_5-deuterated nitrobenzene in aniline.

2.3. Considering Two Possible Palladium Intermediates. *2.3.1. Attempted Synthesis of a Palladacyclic Complex and DFT Calculations.* The five-membered-ring palladacycle with phen as the supporting ligand—often proposed to be a key intermediate in the title reaction (i.e., phen-**C7** in Scheme 3)[7,11,22,26]—is readily obtained using a literature procedure.[11,22] When the same procedure is applied for L4X as the ligand, however, the anticipated L4X-**C7** could not be obtained, nor could an asymmetric complex attributed to this palladacycle be observed in ^{31}P NMR spectra of the resulting reaction mixture. One explanation for the apparent lack of L4X-**C7** formation is that the steric constraints in the plane of coordination, opposite to the ligand, of such species lead to its destabilization. The steric constraints are, of course, influenced by the ligand bite angle, which is much smaller for the ligand phen (∼78°) than for bidentate diarylphosphane ligands with a butylene backbone (96°). Indeed, when the above experiment was conducted with the smaller bite angle ligand L3X (92°), an asymmetric complex was clearly observed (two doublets in the ^{31}P NMR spectrum around 3.8 and 5.8 ppm, J = 30 Hz), but this species decomposed during workup. DFT calculations of the palladacyclic complexes supported by L4X and L3X (see section S1 of the Supporting Information for details) indeed suggest that the used phosphane ligands significantly (ca. 15 kcal mol^{-1}) destabilize the palladacyclic compound relative to the phen analogue.

*2.3.2. Ligand Exchange Experiment of phen-**C7** with L4X and L3X.* As our attempts to isolate P$_2$−palladacycle complexes were unsuccessful, we subsequently considered monitoring phenanthroline ligand exchange for L4X or L3X of the phen−palladacycle complex phen-**C7** (Scheme 5).[11,22]

In the case of L4X, the anticipated asymmetric palladacyclic species L4X-**C7** could not be detected with ^{31}P NMR spectroscopy, but the final product of the reaction, namely [Pd^0(L4X)$_2$] as well as "free" phen, clearly evolved (see section S2 of the Supporting Information for details). This suggests

Scheme 5. Envisaged Ligand Exchange for phen-C7 with L4X or L3X (P$_2$) To Form P$_2$-C7



that ligand exchange indeed took place but that the resulting product is highly unstable.

In an attempt to slow down the supposed decomposition reaction, the ligand exchange experiment was repeated, but now with ligand L3X. Five equivalents of the ligand L3X (dissolved in deuterated nitrobenzene) was added to 1 equiv of the complex phen-**C7**. The yellow suspension was measured with ^{31}P{^{1}H} NMR, showing initially the resonance of ligand L3X around −25.1 ppm and traces of a new complex around 4−6 ppm (Figure 3a), which was also observed in the reaction

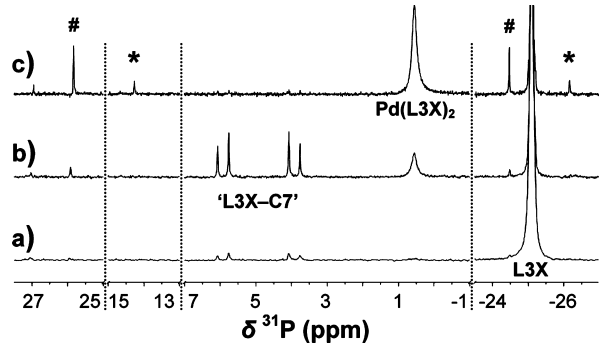


Figure 3. ^{31}P{^{1}H} NMR spectra for a solution containing complex phen-**C7** and 5 equiv of L3X under an argon atmosphere in nitrobenzene: (a) before heating; (b) after heating to 60 °C for about 1 min and then cooling to room temperature; (c) after standing for an additional 2 h at room temperature. # denotes the monoxide of L3X, and * denotes the monophosphazene of L3X.

mixture of our attempt to synthesize L3X-**C7** directly via nitrobenzene carbonylation. After gentle heating to about 60 °C for about 1 min, a clear solution was obtained which was cooled to room temperature (∼25 °C) and measured with ^{31}P{^{1}H} NMR. As can be seen in Figure 3b, an unsymmetric diphosphane complex was formed, characterized by two doublets centered around 3.8 and 5.8 ppm (J = 30 Hz). In the ^{1}H NMR spectrum of this solution a resonance is observed around 9.1 ppm, characteristic for uncoordinated phen, suggesting successful ligand exchange. Assuming that L3X replaces phen as ligand while keeping the palladacycle intact, the two doublets can thus reasonably be assigned to the unsymmetric complex L3X-**C7**.

The two doublets disappear in about 2 h at room temperature, while a new broad resonance around 0.5 ppm appears. This resonance belongs to the neutral bis-ligand complex [Pd^0(L3X)$_2$], as verified by in situ synthesis of [Pd^0(L3X)$_2$] from [Pd$_2$(dba)$_3$] (dba = dibenzylideneacetone) and 10 equiv of L3X in nitrobenzene (Figure S5, Supporting Information). Resonances due to some mono-oxidized ligand (P═O; 25.8 and −24.5 ppm) and some dioxidized ligand (O═PP═O′; 27.0 ppm) are present as well (Figure 3); two additional resonances are observed around 14.3 and −26.2 ppm (marked with * in Figure 3c). These resonances grow equally

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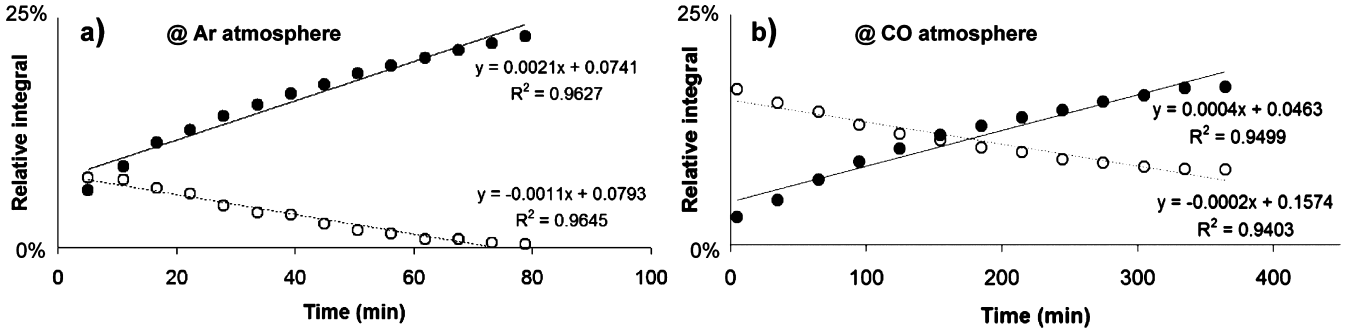


Figure 4. Plots of the $^{31}P\{^1H\}$ NMR integrals (relative to the ligand and the appearing and disappearing compounds) for the resonances of $[Pd^0(L3X)_2]$ around 0.5 ppm (●) and palladacycle L3X-**C7** around 5 ppm (○) as a function of time: (a) under an argon atmosphere; (b) under an atmosphere of CO.

fast, indicating that they belong to the same species. These signals cannot arise from a divalent palladium complex; $[Pd^{II}(L3X)(OAc)_2]$ is characterized by a sharp singlet around 16 ppm, and $[Pd^{II}(L3X)_2](OTs)_2$ exhibits a broad resonance around 5 ppm, as do related complexes.[38,39] This leaves as the only likely option the formation of a phosphazane (P═NPh), which must be formed during the decomposition of the initially formed unsymmetric complex L3X-**C7**. The presence of such a phosphazene was also observed with electron spray ionization mass spectroscopy (vide infra).

*2.3.3. Ligand-Exchange Experiment of phen-**C7** with L3X under a CO Atmosphere.* The ligand-exchange experiment was repeated under an atmosphere of carbon monoxide. The kinetic data of this experiment are shown in Figure 4b, while the kinetic data for the reaction under argon are shown in Figure 4a. The rate of appearance of the resonance assigned to $[Pd^0(L3X)_2]$ (0.5 ppm, 0.0021 and 0.0004 min^{-1}) is about twice the rate of the disappearing signals at 3.8 and 5.8 ppm (−0.0011 and −0.0002 min^{-1}), which is consistent with the assignment of the disappearing resonances to a compound containing one diphosphane ligand (two P atoms, probably L3X-**C7**), and the appearing signal to $[Pd^0(L3X)_2]$ (four P atoms). The decomposition of the presumed L3X-**C7** is approximately 5 times slower for the reaction under a carbon monoxide atmosphere (−0.0002 min^{-1}) in comparison to the reaction in argon (−0.0011 min^{-1}). Under a CO atmosphere less $[Pd^0(L3X)_2]$ is formed during the initial ligand exchange reaction (the intercept is 0.046 (CO) versus 0.074 (Ar)).

The apparent stabilization by CO suggests that the initial step in the decomposition of L3X-**C7** proceeds via a *reversible* decarbonylation/carbonylation process. Apparently, extrusion of CO_2 from L3X-**C7** has a higher barrier than decarbonylation, as can be also concluded from the fact that only traces of isocyanate are formed (vide infra).

2.3.4. Ligand Exchange Experiment with 1 equiv of L3X. In an attempt to prevent or slow down the decomposition of L3X-**C7** to $[Pd^0(L3X)_2]$, which possibly could be accelerated by the presence of an excess of L3X, and in order to detect possible intermediate species in the decomposition of L3X-**C7**, the ligand exchange experiment was repeated with only 1 equiv of L3X. The resulting spectra are shown in Figure 5.

The $^{31}P\{^1H\}$ NMR spectrum (Figure 5b) of the reaction mixture after heating to 60 °C and cooling shows the resonances of the anticipated unsymmetric species around 5.0 ppm, the signal of $[Pd^0(L3X)_2]$ around 0.5 ppm, and two additional weak doublet signals around 23.9 and −7.1 ppm which evolved at the same rate and have an identical coupling

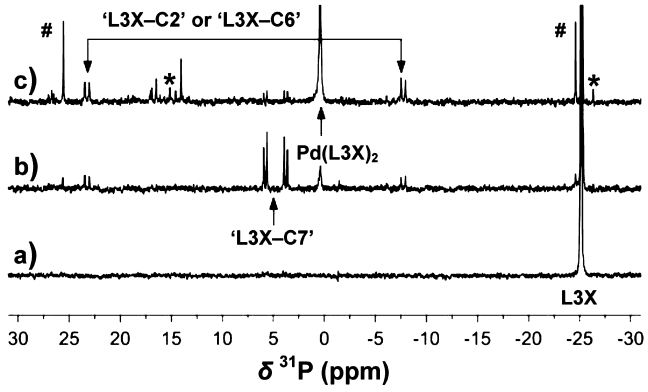


Figure 5. $^{31}P\{^1H\}$ NMR spectra for a solution containing phen-**C7** and 1 equiv of L3X in nitrobenzene: (a) before heating; (b) after heating to 60 °C for about 1 min and cooling to room temperature; (c) after standing for an additional 180 min at room temperature. # denotes the monoxide of L3X, and * denotes the monophosphazene of L3X.

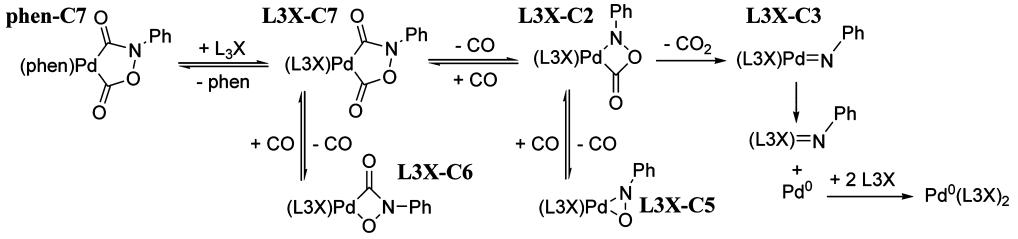
constant (J = 42 Hz). These doublets are indicative of the formation of another unsymmetric monochelate palladium complex, which may well be one of the decarbonylated four-membered-ring complexes L3X-**C2** and L3X-**C6** shown in Scheme 6 (see section 2.3.5). The large difference in chemical shift (31 ppm) between the two phosphorus nuclei is more consistent with the complex L3X-**C2**, as the Pd−C(O)O moiety will cause severe deshielding (23.9 ppm), while the Pd−N(Ph) moiety will cause significant shielding (−7.1 ppm).

After the solution was allowed to stand at room temperature for an additional 180 min (Figure 5c), the resonances assigned to complex L3X-**C7** largely disappeared, while the presumed four-membered-ring complex L3X-**C2** is still significantly present (~20% based on Pd;[40] see also Figure S6 in the Supporting Information). $[Pd^0(L3X)_2]$ has become the major species (33% based on Pd). Among the several unknown species that have evolved (resonances between 14 and 18 ppm; 25% based on Pd) the presence of the palladacyclic complex L3X-**C6** can neither be proven nor be ruled out. Some ligand monoxide is formed (P═O; 25.8 and −24.5 ppm), and some uncoordinated ligand (−25.1 ppm) is still present, suggesting that the ligand exchange reaction is not quantitative after 180 min; this is corroborated by ^1H NMR, showing that the complex phen-**C7** is also still present in approximately the same amount as uncoordinated L3X.[40]

2.3.5. ESI-MS Analysis of Ligand Exchange Experiment with 1 equiv of L3X. The ligand exchange experiment was

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

Scheme 6. Proposed Reaction Sequence of the Ligand Exchange between phen-C7 and the Diphosphane Ligand L3X, Followed by Decomposition of the Palladacycle L3X-C7



repeated, and after gentle heating the clear solution was analyzed with electron spray ionization mass spectroscopy (ESI-MS). In the resulting mass spectrum (Figure 6), the highest observed mass (m/z 986.2) originates from $[Pd(L3X)_2]^+$ (exact mass 986.3).

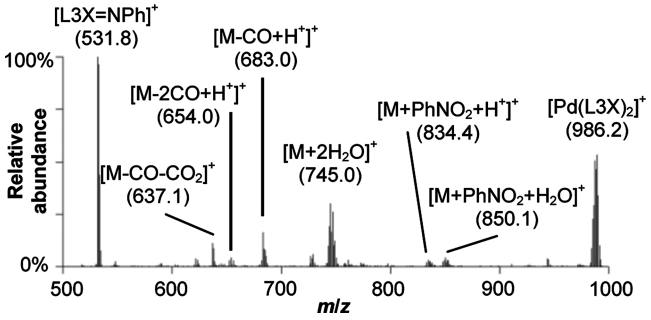


Figure 6. ESI mass spectrum of the reaction mixture taken directly after the ligand exchange of phen-**C7** with 1 equiv of L3X. M = L3X-**C7**.

The lower mass products observed are absent in an ESI-MS of pure $[Pd^0(L3X)_2]$ in nitrobenzene; these lower mass peaks must originate from other complexes formed in the exchange reaction. Although the exact mass (709.1) of the presumed palladacycle L3X-**C7** is not observed, various peaks and their isotope distributions are consistent with solvent adducts of L3X-**C7** (see Figure S7 in the Supporting Information).

A small peak is present with a mass corresponding to the decarbonylated palladacycle L3X-**C7** (i.e., L3X-**C2** or L3X-**C6**; $[M - CO + H^+]^+$ m/z 683.0), whereas the mass of decarboxylated L3X-**C7** ($[M - CO_2]^+$; exact mass 665.1) is not observed. The small peak at m/z 654.0 corresponds to $[M - 2CO + H]^+$: i.e., nitrosobenzene bound to $[(L3X)Pd^0]$, L3X-**C5**. Interestingly, the small feature at m/z 637.1 can be assigned to $[M - CO - CO_2]^+$, which corresponds to the imido complex (L3X)Pd═NPh (L3X-**C3**). The presence of (L3X)Pd(ONPh) and (L3X)Pd═NPh complexes as fragmentation products of L3X-**C7** may be reflecting its thermal decomposition pathway. The monophosphazene $[L3X═NPh]^+$ (m/z 531.8) is clearly present as well (see also $^{31}P\{^1H\}$ NMR above), while small quantities of aniline and nitrosobenzene are observed with GLC-MS.

These MS data are thus in agreement with the NMR data and suggest that the initially formed five-membered P_2–palladacycle L3X-**C7** may (at least partially) decompose to a L3X-**C3** imido species, via L3X-**C2**, as is shown in Scheme 6. The imido complex (L3X-**C3**) may, at least partially, decompose to form the observed phosphazene while liberating zerovalent palladium, which is trapped by uncoordinated L3X as $[Pd^0(L3X)_2]$.

2.4.6. Attempted Identification and Quantification of PhN-Containing Products. The integrals of L3X═NPh and $[Pd^0(L3X)_2]$ by the end of the ligand exchange experiment (Figure 3c) indicate that merely ~0.4 μmol of the initial amount of PhN present in the complex phen-**C7** (~10 μmol) ends up in the L3X-phosphazene.[41] Likely products that may contain the remaining ~9.6 μmol of the PhN fragment could be aniline, phenyl isocyanate, nitrosobenzene, and/or azo(xy)-benzene. Because the ^1H NMR resonances of all possible reaction products containing the PhN moiety are obscured by the resonances of the abundantly present nitrobenzene, L3X, and $[Pd^0(L3X)_2]$, the solution was analyzed with GLC-MS. However, using this technique we were only able to positively identify about 10% of the NPh fragment originally present in complex phen-**C7** as aniline, nitrosobenzene, phenyl isocyanate, and L3X═NPh.

To obtain more unambiguous information about the fate of the organic PhN moiety, the NMR experiment was repeated in non-aromatic solvents such as CH_3NO_2 and CD_2Cl_2 (see section 3.1 in the Supporting Information). Although these experiments strongly suggest the formation of various PhN-

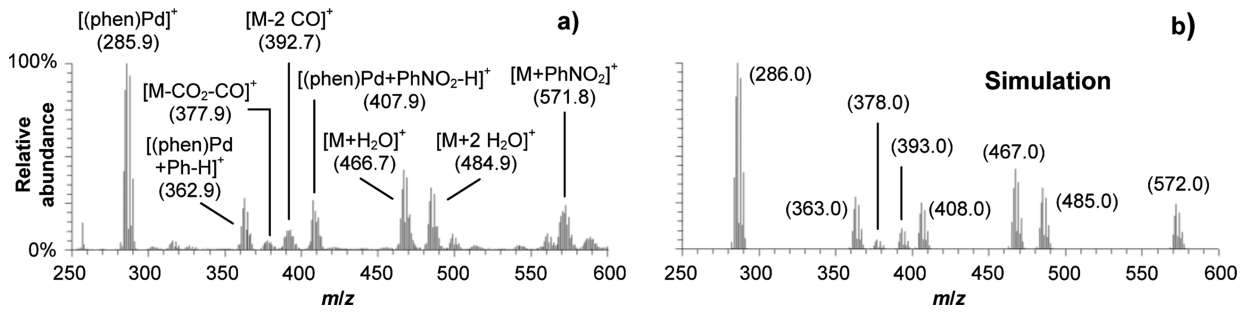


Figure 7. (a) ESI mass spectrum of a saturated solution of palladacycle phen-**C7** (=M) in nitrobenzene and (b) simulation of the most prominent peaks.

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containing products, neither a positive identification nor quantification could be achieved, mostly due to the interference of the aromatic resonances of L3X and $Pd^0(L3X)_2$. Experiments using a ligand with pentafluorophenyl groups were also inconclusive but again showed the formation of various PhN-containing products (see section 3.2 in the Supporting Information).

2.3.6. ESI-MS Analysis of phen-C7. The phen-**C7** complex was analyzed with ESI-MS in order to see whether it decomposes in a manner similar to that for L3X-**C7**. Due to the poor solubility of phen-**C7** in various common solvents, a saturated solution of this complex in nitrobenzene was introduced *directly* into the ESI source (instead of using an injector with an eluent). However, when using the same ionization conditions that were successful for measuring the fragmentation of L3X-**C7** (i.e., 3 kV and 300 °C), no clear mass spectrum could be obtained. Only when the ionization temperature was elevated to 450 °C could a proper mass spectrum be recorded. The mass spectrum of this experiment is shown in Figure 7a; a simulation of the most prominent peaks is given in Figure 7b.

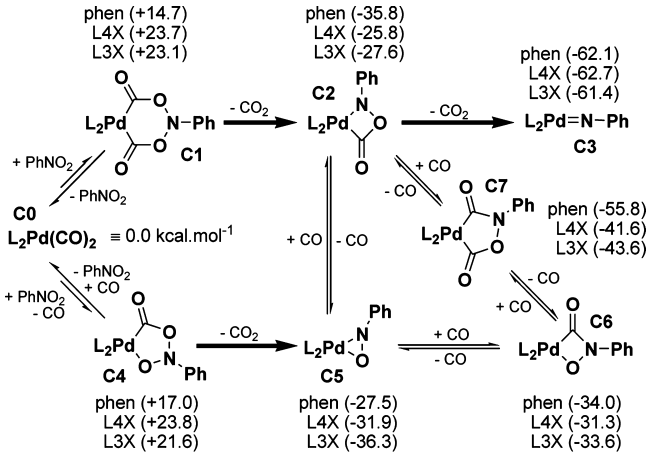
The $[M]^+$ peak of palladacycle phen-**C7** (exact mass 449.0) is not observed. The highest significant mass around m/z 571.8 is consistent with a nitrobenzene solvent adduct of the phen–palladacycle phen-**C7** (the exact mass is 572.0; the solid state structure of phen-**C7** also contains a nitrobenzene molecule in its lattice).[22] The mass and isotope distributions of the two features found around m/z 466.7 and 484.9 are in perfect agreement with $[M + H_2O]^+$ and $[M + 2\ H_2O]^+$, respectively (see Figure S15 in the Supporting Information). The H_2O in these adducts probably derives from trace amounts of water in the solvent nitrobenzene.

The monodecarbonylated fragment ($[M - CO]^+$, exact mass 421.0) is not observed, but the mass of the didecarbonylated fragment $[M - 2CO]^+$ (i.e., the nitrosobenzene complex phen-**C5**) is present around m/z 392.7 (exact mass 393.0). The most abundant mass observed is that of $[(phen)Pd]^+$ around m/z 285.9 (exact mass 286.0); a phenyl adduct of this species seems also to be present (m/z 362.9; $[(phen)Pd + Ph - H]^+$, exact mass 363.0). The feature around m/z 407.9 cannot be ascribed to the anticipated palladium-bound phenyl isocyanate (i.e., $[M - CO_2]^+$), as the exact mass of this species (405.0) differs by 3 units. As the experiment was performed in a nitrobenzene solvent matrix, the mass around 407.9 may be assigned to a nitrophenyl adduct of $[(phen)Pd]^+$: i.e., $[(phen)Pd + PhNO_2 - H]^+$ (exact mass 408.0). Interestingly, the mass of the very small peak around m/z 377.9 is in agreement with a $(phen)Pd^{II}{=}NPh$ complex (i.e., $[M - CO_2 - CO]^+$, exact mass 378.0).

The fragmentation pattern surprisingly suggests that phen-**C7** may decompose predominantly via an initial decarbonylation (−CO) instead of a direct decarboxylation ($-CO_2$) to palladium-bound phenyl isocyanate. After the first decarbonylation, a second decarbonylation may follow, yielding a palladium-bound nitrosobenzene compound, or CO_2 can be extruded to form the imido intermediate $(phen)Pd^{II}{=}NPh$. The latter compound may decompose further to $[(phen)Pd]^+$ that will give rise to the observed adducts thereof. Osborn et al. analyzed the fragmentation of phen-**C7** using the fast atom bombardment ionization technique and also observed the monodecarbonylated fragment at m/z 422.[11] Remarkably, a fragment at m/z 378 was also reported, but this was assigned to phen-**C7** with loss of CO + NCO instead of loss of CO + CO_2. However, they did not connect these observations with a suggestion that phen-**C7** preferentially decomposes via decarbonylation rather than decarboxylation and that an imido species (phen-**C3**) might be formed.

2.4. DFT Study of Nitrobenzene Deoxygenation with CO. The presented data suggest that palladacyclic species such as phen-**C7** and L3X-**C7** shown in Scheme 5 may decompose to the corresponding palladium–imido compounds **C3**. To relate these data to the actual catalytic process, the possible deoxygenation pathways of nitrobenzene to form the palladacyclic and/or palladium–imido complex were studied using DFT calculations. Because of computational limitations, attempts to estimate the reaction barrier from one complex to another were not undertaken. Instead, our approach was to estimate the Gibbs free energies for the relevant complexes (Scheme 7), via the methodology explained and validated in

Scheme 7. Possible Intermediates in Nitrobenzene Deoxygenation with CO as Reductant and Their Relative Energies As Computed with DFT for L_2 = phen (at 130 °C) and L_2 = L4X, L3X (Both at 110 °C)[a]



[a]Values are given in kcal mol^{-1} relative to complex **C0**.

sections S4 and S5 of the Supporting Information. The enthalpy differences were estimated using DFT calculations, and the changes in entropy were estimated at the relevant reaction temperature from literature data (standard molar entropy ($S°$) in J mol^{-1} K^{-1}). Hence, the data shown in Scheme 7 are the estimated Gibbs free energies at 110 °C for complexes containing L4X and L3X and at 130 °C for complexes containing phen as the supporting ligand.

The starting compound for the nitrobenzene reduction process is the zerovalent complex $L_2Pd(CO)_2$ (**C0**), which is therefore defined as 0.0 kcal mol^{-1}. The oxidative coupling of CO with nitrobenzene at **C0** can proceed via either **C1** or **C4**. No preference can be given, as **C1** and **C4** are similar in energy for phen, L4X, and L3X. The irreversible CO_2 extrusions **C1** → **C2** and **C4** → **C5** are both about equally exothermic (ca. −50 kcal.mol^{-1}), thereby completing the first deoxygenation step of nitrobenzene.

Complexes **C2** and **C5** differ in energy only ∼8 kcal mol^{-1}; they may thus very well interconvert into each other via a reversible carbonylation/decarbonylation process, possibly at equilibrium under carbonylation reaction conditions. Likewise, the reactions **C2** ⇆ **C7**, **C5** ⇆ **C6**, and **C6** ⇆ **C7** are all likely to be reversible carbonylation/decarbonylation reactions,

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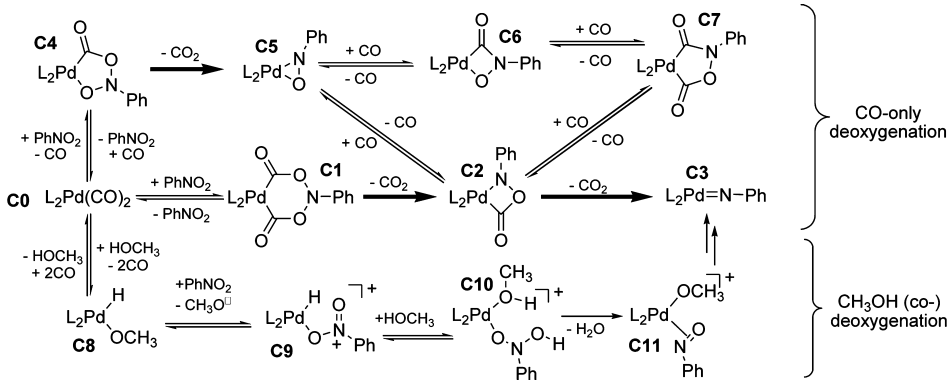
Scheme 8. Schematic Overview of the Possible Intermediates for the Formation of the Palladacyclic Intermediate C7 (Top) and the Pd−Imido Intermediate C3 (Center and Bottom) in the Deoxygenation of Nitrobenzene



meaning that **C2**, **C5**, **C6**, and **C7** are probably all interconvertible and possibly at equilibrium. Similar reversible interconversions are ubiquitous in carbonylation reactions. For instance, carbonylation−decarbonylation equillibria are known to exist during the carbonylation of olefins; the carbonylation step of Pd−alkyl and Pd−O-alkyl intermediates generally is almost thermoneutral or only slightly exothermic and is generally fully reversible with a low activation barrier.[42] Note that the palladacycle **C7** is the most stable complex of these (presumably) CO equilibrated species for all three ligands. The oxidative coupling of nitrosobenzene with CO (i.e., **C5** ⇆ **C2** and **C5** ⇆ **C6**) is exothermic by ca. −8 kcal mol^{-1}, whereas the oxidative coupling of nitrobenzene with CO is endothermic (i.e., **C0** ⇆ **C1** and **C0** ⇆ **C4**) by ca. +20 kcal mol^{-1}; this is in line with our finding (vide supra) and literature data[7,25] that nitrosobenzene is more easily reduced than nitrobenzene.

The second deoxygenation of nitrobenzene can only occur by the irreversible CO_2 extrusion from **C2** to the imido complex **C3**, which is thermodynamically also the most stable complex (ca. −62 kcal mol^{-1}). The palladacycles that are formally Pd^{II} species and are sterically crowded in the equatorial positions of Pd (i.e., **C1**, **C2**, **C4**, and **C7**) are all destabilized by ca. 10 kcal mol^{-1} by the bulkier L3X and L4X ligands relative to phen. The formally zerovalent palladium−nitrosobenzene complex **C5** is more stable when L4X or L3X is the supporting ligand, due to the increased acidity of palladium, as induced by the increased π-back-bonding from Pd to P.

These data thus suggest that it is likely that complexes **C2**, **C5**, **C6**, and **C7** exist in mutual carbonylation/decarbonylation equillibria, as is indeed also experimentally suggested for L3X-**C7** ⇆ L3X-**C2**/L3X-**C6** (section 2.3.3).

3. DISCUSSION

3.1. Molecular Mechanism of Nitrobenzene Deoxygenation. *3.1.1. Deoxygenation with Diphosphane-Based Catalysts.* We have shown that the fraction of nitrobenzene that is deoxygenated with only CO or with methanol depends on the characteristics of the catalyst employed, as determined by the properties of the supporting ligand; for the catalytic system based on L4X the CO-only deoxygenation route contributes merely 9%.[17] Our current understanding of the molecular basis underlying the deoxygenation of nitrobenzene in methanol for catalysts with phosphanes as the supporting ligand (L_2) is summarized in Scheme 8.[17] The CO-only deoxygenation route starts with an oxidative coupling of nitrobenzene and CO at $L_2Pd^0(CO)_2$ (**C0**) to form **C1** or **C4**, followed by an irreversible decarboxylation step (i.e., **C1** → **C2** or **C4** → **C5**). As argued above, it is likely that carbonylation−decarbonylation reversible steps connect species **C2**, **C5**, **C6**, and **C7**, which all likely act merely as temporary reservoirs of the PhN fragment; none of these is expected to be a product-releasing species. Palladacycle **C7** should also not be considered as such, as the ligand exchange and ESI-MS experiments with L3X suggest that the barrier for decarboxylation (CO_2 loss) is higher than the barrier for decarbonylation (CO loss) of **C7**.

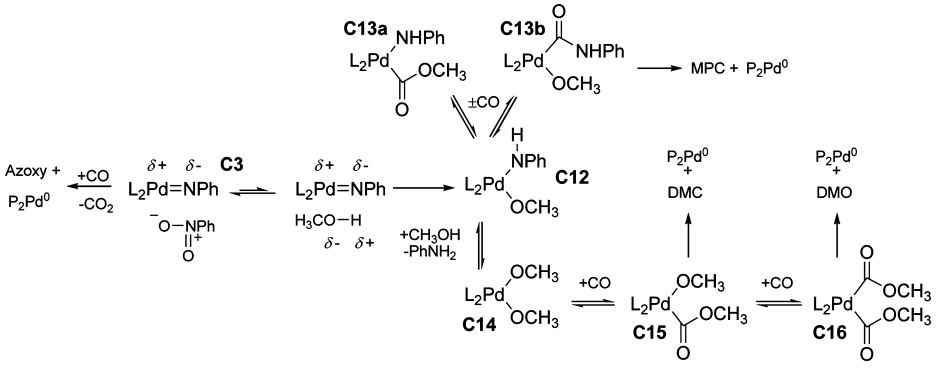
The methanol-assisted deoxygenation routes are thought to start with oxidative addition of methanol on $L_2Pd^0(CO)_2$ to **C8** (possibly assisted by coordinated CO)[43,44] and most likely proceed via palladium−hydride chemistry (**C8** ⇆ **C9** ⇆ **C10** → **C11**). Eventually the same palladium−imido intermediate **C3** will be formed, as is discussed in more detail elsewhere.[17,18] The nitrosobenzene generated in compound **C11** may re-enter the catalytic cycle by binding to **C0**, forming species **C5**. The diphosphane−Pd−imido complex **C3** is thought to be the sole PhN-containing, product-releasing species (i.e., ultimately producing MPC, DPU, $PhNH_2$, and Azo(xy)).[17]

3.1.2. Deoxygenation with phen-Based Catalysts. When the more basic phen is used as the supporting ligand, the CO-only deoxygenation pathway contributes more than 95%, which means that the oxidation of methanol is almost completely suppressed (see section S6 in the Supporting Information for details). An increased basicity (electron density) of the Pd center is generally thought to be favorable for oxidative processes at Pd and thus would be expected to promote *both* oxidative coupling of CO with nitrobenzene *and* oxidative addition of methanol. Apparently, the oxidative coupling of CO with nitrobenzene at Pd is significantly more sensitive to Pd basicity than oxidative addition of methanol, presumably because of increased electron back-donation of the filled dπ orbitals of Pd into the antibonding π^* orbitals of CO in $L_2Pd(CO)_2$. While increased back-donation from Pd to CO apparently makes CO more susceptible for attack by the nitro group, it makes the CO less susceptible for attack by a methoxide anion possibly necessary for facilitating the oxidative addition of methanol.

On the basis of on the ESI-MS fragmentation pattern of phen-**C7**, the ligand exchange experiments of phen-**C7** with L4X and L3X, the dependence of the Azo(xy) selectivity on the nitrobenzene concentration, and our DFT results, we propose that the molecular mechanism of the CO-only deoxygenation shown in Scheme 8 is also valid for the Pd/phen catalytic system. We furthermore propose that phen-**C7**—commonly

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

Scheme 9. Schematic Overview of the Possible Intermediates of L_2Pd^{II}=NPh (C3) Reduction to L_2Pd^0 and the Various Aryl-Containing Nitrobenzene Reduction Products



thought to be the direct carbonylation product releasing species—is *not* the (main) product-releasing species under normal (acid-free) catalytic carbonylation conditions. Instead, phen-**C7** merely is part of a network of reversible carbonylation−decarbonylation steps, connecting species (**C2**, **C5**, and **C6**) that together act as temporary PhN reservoir. This explains why phen-**C7** can be synthesized and isolated under mild carbonylation conditions (60 °C, ethanol);[11] phen-**C7** is the thermodynamically most stable of the CO-connected species and is therefore thought to be an important resting state of the catalyst. At elevated temperatures, phen-**C7** may be decarboxylated to phenyl isocyanate (and thus MPC and DPU), but judging from the product distribution of the reaction under acid-free conditions, this is not the dominant reaction pathway; merely 20% MPC but 70% Azoxy is produced. This must mean that the reaction barrier for phen-**C7** decarboxylation (to PhNCO) is higher than that of its decarbonylation (to phen-**C2** and/or phen-**C6**). Irreversible decarboxylation of phen-**C2** to phen-**C3** then removes the catalyst from the CO-connected PhN reservoir.

The different temperatures required when phen (130 °C) or diphosphanes such as L4X (110 °C) are used as the supporting ligands in catalytic nitrobenzene carbonylation may be ascribed to the destabilizing effect that the bulkier phosphane ligands have on palladacycles such as **C7** (as indicated by DFT). Both the decarbonylation barriers (e.g., **C7** ⇆ **C2**) and the barrier for decarboxylation of **C2** → **C3** will be lowered, thus allowing the PhN fragment to escape the temporary reservoir more easily and thus also allowing the application of milder reaction temperatures.

3.2. Molecular Mechanism of Reactions of the Pd^{II}=NPh Intermediate. *3.2.1. Azo- and Azoxybenzene Formation.* Once the imido intermediate **C3** has been formed, it can undergo a disproportionation reaction with nitrobenzene and CO to produce azoxybenzene and CO_2 as the stable end products (Scheme 9, left).[17]

Because formally one N−O bond in nitrobenzene is fully polarized, nitrobenzene is thought to associate more strongly to the (also polarized and sterically quite accessible) Pd=N bond in **C3** (more strongly than the relatively weakly polarized and charge-neutral methanol). As a result, the disproportionation reaction dominates, resulting in the high selectivity toward Azoxy (70%) for both the phen and L4X catalyst systems. The observed dependence of the Azoxy selectivity on the nitrobenzene concentration confirms that the formation of Azo(xy) coupling products from nitrobenzene involves a step competing with carbonylation and hydrogenation, but with higher order kinetics in nitrobenzene. It has been proposed that Azoxy stems from a reaction between free nitrosobenzene and free nitrene (PhN)[9,10] or from a condensation reaction of nitrobenzene with aniline.[15] We have shown, however, that adding extra nitrosobenzene during a catalytic run does not result in the formation of more Azoxy. Nitrosobenzene is more easily reduced than nitrobenzene, which is suggested by our DFT studies and finds support in the literature as well.[7,10,25,45,46] The condensation of aniline and nitrosobenzene to azobenzene has been reported to occur under reaction conditions much more forcing than those employed by us (hot glacial acetic acid;[47] very basic conditions[48]). Furthermore, it is known that Azoxy cannot be formed by a condensation reaction of aniline and nitrobenzene during catalysis, as a carbonylation experiment with deuterated nitrobenzene and undeuterated aniline gave only fully deuterated Azoxy when working with the Pd/phen catalytic system.[32]

The observed similarity in selectivity for Azoxy when using both phen and L4X as the supporting ligands can be understood by considering the electronic and steric effects that these ligands will have on the proposed imido intermediate. For phen, the increased basicity is thought to render the imido complex more polar, thus increasing its *association* with nitrobenzene and hence the portion of PhN that is involved in the disproportionation reaction. L4X, on the other hand, is far less basic, but here the steric bulk in the plane of coordination is thought to expedite the reaction with associated nitrobenzene. Indeed, when the less sterically demanding ligand L3X is used, hardly any Azoxy is formed, as detailed elsewhere.[17]

3.2.2. Formation of Carbonylation Products (MPC, DPU, DMC, DMO). As an alternative to the disproportionation reaction, the imido intermediate **C3** can be protonated by methanol to produce $PhNH_2$ and/or MPC (Scheme 9, right). Direct carbonylation of the highly polarized imido intermediate with CO to form (palladium-bound) isocyanate is not likely to occur in a protic environment and also conflicts with our experimental data using a labeled substrate, 3-methylnitrobenzene in aniline (see below). Protonation of **C3** by methanol gives **C12**, which may undergo carbonylation to **C13a** via an associative displacement of CH_3O^- by the smaller and charge-neutral CO. This is then followed by nucleophilic attack of nearby CH_3O^- on coordinated CO and reductive elimination to produce MPC. Likewise, **C13b** may be generated, followed by MPC genesis. DPU may be produced via a similar process in which aniline replaces methanol as the nucleophilic reagent. As an alternative to MPC or DPU formation, **C12** may be

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

protonated to **C14** with liberation of aniline. **C14** will then be carbonylated once or twice via associative displacement of methoxide by CO and subsequent nucleophilic attack on coordinated CO by methoxide to give **C15** and **C16**, from which reductive elimination will produce DMC and DMO, respectively. The strong similarity of the chemistry for formation of MPC with that of DMC/DMO is an attractive point for the proposal of a $L_2Pd{=}NPh$ intermediate in nitrobenzene carbonylation chemistry. All carbonylation intermediates, **C12**–**C16**, are considered as being involved in reversible reactions and are possibly at mutual equilibrium. MPC-, DPU-, DMC-, and DMO-releasing reactions likely involve irreversible and possibly rate-determining reductive elimination reactions, thus reproducing a zerovalent palladium complex. As detailed elsewhere with P_2Pd catalysts, an increase of CO pressure generally leads to an increase in *absolute* productivity of *all* carbonylation products (DMC, DMO, MPC, DPU).[17] This suggests indeed that all intermediate carbonylation complexes in Scheme 9 under the reaction conditions are interconvertible via CO (de)insertions. The relative productivity of MPC/DPU vs DMC/DMO depends on the ligand properties and thus on the exact position of the equilibria with the particular ligand. With phen as supporting ligand, only small quantities of DMC/DMO are formed, implying only a small quantity of H atom production and therefore of aniline; this could be either a consequence of the equilibrium position of phen-**C15** and phen-**C16** in the reaction mixture or a consequence of a low rate of reductive elimination of DMC/DMO from these respective complexes (which are smaller than **C13**).

As it appears from our data, carbonylation of **C12** is favored when phen is the supporting ligand (20% MPC), whereas protonation of **C12** is favored in case of L4X (20% $PhNH_2$) with accompanying formation of DMC/DMC (see Table S1 in the Supporting Information). This effect can be understood by the difference in basicity of both ligands; the more basic phen will destabilize the $Pd{-}OCH_3$ bond in **C12**, thus facilitating the associative displacement by CO leading to MPC (via **C13**).

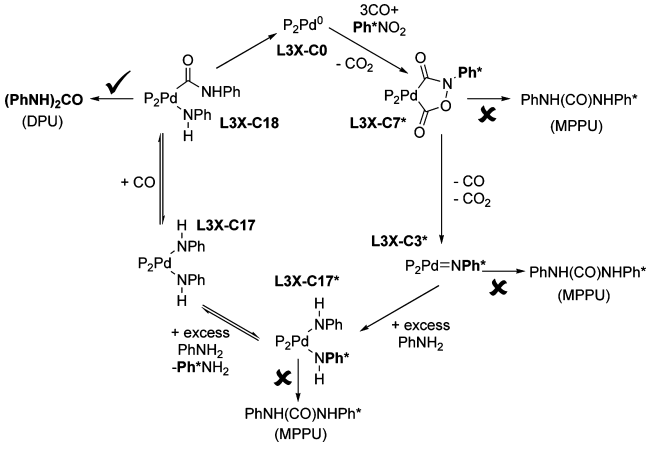
Our mechanistic proposal for the formation of MPC is somewhat related to that recently proposed by Ragaini and coworkers.[15,16] Their hypothesis apparently involves first full reduction of nitrobenzene to aniline while forming a five-coordinated (phen)Pd(dicarbomethoxy)carbonyl intermediate species ((phen)$Pd(C(O)OCH_3)_2CO$), via an unspecified mechanism.[49] It is noteworthy that the (phen)$Pd(C(O)OCH_3)_2$ complex is equal to **C16** in our mechanism, but as a direct precursor to DMO and *not* to MPC. The CO moiety in the five-coordinate (phen)$Pd(C(O)OCH_3)_2(CO)$ species is proposed to be involved in nucleophilic attack by aniline to ultimately yield phenyl isocyanate via proton transfer from the aniline moiety via a (hypothetical) five-coordinate palladium–carbenoid complex. The carbamate then evolves upon reaction of the isocyanate with solvent methanol.[15,16] This proposal leans heavily on the observed cocatalytic role of added aniline (as initially reported by the van Leeuwen group)[10] and the observation of the formation of significant amounts of unlabeled DPU in an experiment with d_5-deuterated nitrobenzene in aniline.[16]

Our mechanistic proposal, however, is distinctly different in that the precursor for aniline formation (the palladium–imido intermediate **C3**) itself is hydromethoxycarbonylated to ultimately form MPC (see below). The observed cocatalytic role of aniline can simply be rationalized on the basis of our proposed carbonylation mechanism, as depicted in Scheme 9. The increased nucleophilicity of aniline relative to methanol favors urea formation over carbamate formation, by competing directly with the **C3** → **C12** → **C13** (Scheme 9) reaction, which thus leads to a higher overall carbonylation rate, as is indeed observed in aniline. At temperatures above 120 °C DPU transesterifies rapidly with methanol to give MPC and aniline.[24] As the experiments of Ragaini et al. as well as those of van Leeuwen et al. were carried out above 130 °C (respectively 170 and 135 °C), transesterification of initially formed DPU to MPC will surely occur. The transesterification of DPU to MPC will become rate determining at high aniline concentration, such that the rate of carbonylation (=rate of nitrobenzene conversion) becomes at a constant level very similar to that in pure aniline; this also explains the flattening profile of the aniline-promoting role at high aniline concentrations as reported by van Leeuwen et al.[10] and Ragaini et al.[16] We have observed that when P_2Pd systems are applied as catalysts in reactions with aniline as nucleophile only, carbonylation rates (giving DPU) even at temperatures below 70 °C can be 100-fold higher relative to that of carbamate formation.[36]

Of crucial importance, also in this context, are our experiments conducted with (L3X)$Pd(OAc)_2$ in aniline as (excess) solvent using 3-methylnitrobenzene as the substrate and working *below* the transamidation temperature (i.e., at 60 °C). Surprisingly, the asymmetric *N*-(3-methylphenyl)-*N*′-phenylurea (MPPU) and symmetric *N*,*N*′-bis(3-methylphenyl)-urea (DMPU) are not observed, whereas a stoichiometric amount of 3-methylaniline is formed. As transamidation of MPPU and/or DMPU with solvent aniline cannot occur at the temperature used, this must mean that the N-aryl groups derived from 3-methylnitrobenzene at some stage have been exchanged by those derived from aniline *via a mechanism other than a transamidation*. The 3-methylnitrobenzene must interact with the catalyst in order to be deoxygenated. As indicated above, the CO-only deoxygenation route will proceed via species L3X-**C7*** (Scheme 10).

As proposed above, L3X-**C7*** cannot be the direct isocyanate product releasing intermediate, as the *un*symmetric MPPU should then be formed predominantly (which is the very reason that Ragaini et al. propose a direct *aniline carbonylation* to

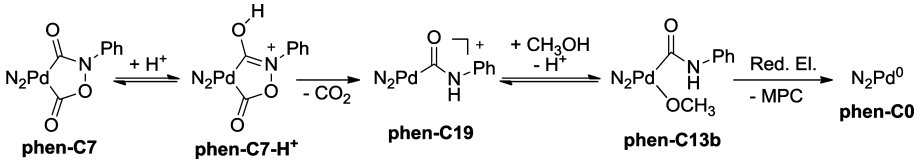
Scheme 10. Proposed Mechanism for the Formation of DPU in the Pd/Diphosphane-Catalyzed Reduction of 3-Methylnitrobenzene (Ph*NO_2) in Aniline[a]



[a] P_2 = L3X.

dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142–4156

Scheme 11. Proposed Mechanism for MPC Genesis under Acidic Conditions for the Pd/phen, Starting with Protonation and Decarboxylation of phen-C7[a]



[a] N_2 = phen.

isocyanate).[16] Decomposition (through initial decarbonylation) of L3X-**C7*** will give L3X-**C3***. L3X-**C3*** will, in analogy to our hypothesis in a methanolic medium (Scheme 9), *not* be carbonylated to isocyanate (as no MPPU was observed) but rapidly react with solvent aniline to produce the dianilido−palladium complex L3X-**C17***. At this point there will be a competition between CO insertion (and formation of MPPU) and anion exchange with the solvent aniline to liberate the observed 3-methylaniline (L3X-**C17*** + (excess) $PhNH_2$ ⇆ L3X-**C17** + Ph^*NH_2). Clearly this anion exchange reaction must be faster than the ultimate formation of the urea, as otherwise the unsymmetrical MPPU would be formed. From L3X-**C17** DPU is formed by a CO insertion (L3X-**C17** + CO ⇆ L3X-**C18**) followed by a reductive elimination (L3X-**C18** → L3X-**C0**) to return palladium in the catalytic cycle, which explains why only DPU (and some DPO) was observed. The appeal of this proposed reaction sequence is that it is analogous to the evolution of the methanol carbonylation products DMC (and DMO) and the nitrobenzene carbonylation product MPC when methanol is the nucleophilic solvent (i.e., **C3** → **C12** ⇆ **C14** ⇆ **C15** → **C0** and **C3** → **C12** ⇆ **C13** → **C0** in Scheme 9).

Our mechanistic understanding of nitrobenzene reductive carbonylation in a CO/CH_3OH environment with diphosphane-stabilized palladium complexes thus translates directly to the mechanism of this reaction for the phen-supported catalysts, as well as to the mechanism of this reaction in aniline as the nucleophilic reactant/solvent.

3.3. Effect of Added Acid. With our current understanding of the mechanism detailed above, it can be rationalized why the addition of (sub)stoichiometric amounts (on Pd) of acid has such a dramatically different effect on the selectivity of the Pd^{II}(phen) (producing more MPC) and the Pd^{II}(L4X) (producing more $PhNH_2$) catalytic systems. Under acid-free conditions, the palladacycle **C7** (with either phen or diphosphane ligands such as L4X) is not a (main) product-releasing species due to the high barrier for decarboxylation relative to that of decarbonylation. When an acid is added, however, the decarboxylation barrier is significantly lowered, we believe by protonation at the amide carbonyl O of the palladacycle, as suggested by Osborn (top of Scheme 3);[11] in the case of phen-**C7** this apparently occurs to the point where CO_2 extrusion is favored over decarbonylation. As a result, in acidic media phen-**C7** becomes the main product-releasing species, selectively producing MPC. As is shown in Scheme 11, we believe the mechanism of this decarboxylative methanolysis proceeds via intermediate **C13b** (see also Scheme 9).

The imido-intermediate phen-**C3** will thus, under acidic conditions, only scarcely be formed, explaining the strongly decreased azoxybenzene selectivity (from 71 to ∼15%). This is in agreement with the findings of Osborn and co-workers, who reported that phen-**C7** is thermally very stable but in the presence of an added acid (catalyst) it smoothly decomposes to form ethyl phenyl carbamate with high yield, when heated in ethanol at just 90 °C.[11] It is worth mentioning that decarboxylative aminolysis, with aniline replacing methanol as shown in Scheme 11, also rationalizes the observed formation (at low conversion) of predominantly symmetrical *undeuterated* ureas when equimolar amounts of deuterated nitrobenzene and undeuterated aniline are reacted under acidic conditions with the Pd/phen catalytic system,[16] similar to our observation for the Pd/L3X system under acid-free conditions in aniline with 3-methylnitrobenzene as the substrate (vide supra). Whereas the direct pyrolysis of phen-**C7** to isocyanate would result in the *unsymmetrical* urea, its decarboxylative aminolysis delivers the **C13b** anilide analogue that can be involved in rapid $C_6D_5NH^-$ anion exchange with undeuterated aniline, while at the same time being involved in fast decarbonylation−carbonylation equilibration reactions. This is in complete analogy to the equillibria **C12** ⇆ **C13**, **C12** ⇆ **C14** ⇆ **C15** (Scheme 9, in methanol, acid free) and L3X-**C17*** ⇆ L3X-**C17** ⇆ L3X-**C18** (Scheme 10, in aniline, acid free), producing respectively MPC, DMC, and DPU.

Our proposed mechanism shown in Schemes 9 and 10 is also consistent with the formation of fully deuterated azo(xy)-benzene ($C_6D_5N{=}N(O)C_6D_5$) side products of reductive carbonylation of deuterated nitrobenzene in aniline.[32] *Irreversible* Azo(xy) benzene formation (**C3*** + Ph^*NO_2 + CO → P_2Pd^0 + $Ph^*N{=}N(O)Ph^*$ + CO_2) and *irreversible* addition of **C3*** + $PhNH_2$ → **C17*** directly compete for **C3***, *prior* to the anilido group exchange and equilibrating carbonylation steps, ultimately delivering DPU (Scheme10).

For the Pd^{II}(L4X) system the barrier for L4X-**C7** decarboxylation is most probably also lowered by the addition of acid. However, the barrier for L4X-**C7** decarbonylation apparently is still relatively lower, which is most likely due to the fact that L4X-**C7** is relatively less stable than phen-**C7**, as suggested by DFT. As a consequence, L4X-**C3** will still be formed, remaining the main product-releasing species. The lower azoxybenzene production upon the addition of acid in favor of the carbonylation *and* hydrogenation reactions can be rationalized by an acid-assisted protonation of **C3** to **C12**, thereby competing with the disproportionation reaction. Why in the Pd/L4X/H^+ system the hydrogenation is promoted somewhat more than the carbonylation reaction can easily be understood; protonation of the [$PhNH^-$] anion in **C12** to form aniline will be facilitated by the acid, at the expense of the associative replacement of the [CH_3O^-] ligand in **C12** by CO. It is important to note that, in line with this mechanism, upon addition of an acid to the Pd^{II}(phen) system, the amount of DMC + DMO produced *decreases* (from 0.5 to 0.2 mmol), whereas for the catalytic system based on Pd^{II}(L4X) the amount of DMC + DMO *increases* (from 8.2 to ∼13 mmol, see Table S1 in the Supporting Information for details).

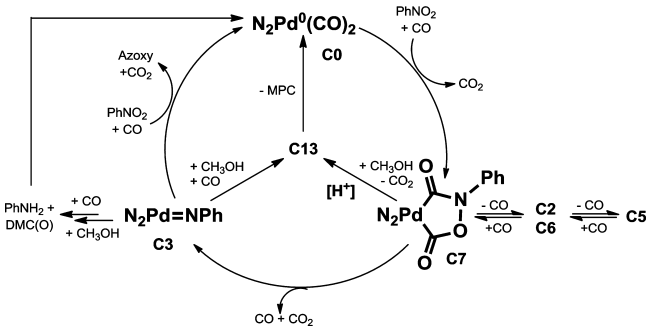
dx.doi.org/10.1021/om200882p | *Organometallics* 2012, 31, 4142−4156

4. CONCLUSIONS

The palladium−imido species $L_2Pd{=}NPh$ (**C3**) and the palladacycle $L_2PdC(O)N(Ph)OC(O)$ (**C7**) were considered as possible carbonylation product releasing species for both phen- and diphosphane-based catalytic systems. The results of catalytic experiments, supported by ligand exchange experiments of phen-**C7** with L4X and L3X, spectroscopic (ESI-MS and NMR) evidence, and a DFT study, suggest that the palladacyclic compound **C7** in the absence of acid is not a major product-releasing intermediate. Thus, in the absence of acid, our proposed mechanism for Pd/diphosphane catalysts (Schemes 2 and 8)[17,18] applies directly to the Pd/phen catalytic system. Indeed, **C7** is thought to be part of a family of CO-equilibrated palladacycles that together act as temporary PhN reservoirs (i.e., **C7** ⇆ **C2** ⇆ **C5** ⇆ **C6** ⇆ **C7**). It is our understanding that this PhN fragment is only released via the imido complex $L_2Pd{=}NPh$ (**C3**), which is thus thought to be the central product-releasing species, producing mainly the coupling product Azoxy with phen- and L4X-based systems.

On the other hand, *in the presence of acid* the palladacyclic complex phen-**C7** becomes the major product-releasing species, resulting in the selective formation of the nitrobenzene carbonylation product MPC. Our mechanistic conclusion for the carbonylation of nitrobenzene in methanol, catalyzed by the palladium−phenanthroline system, is illustrated in Scheme 12.

Scheme 12. Summarizing Scheme for the Connecting Catalytic Processes in the Palladium-Catalyzed Reductive Carbonylation Reactions of Nitrobenzene when 1,10-Phenanthroline (N_2) is the Supporting Ligand



Osborn et al. already proposed a palladacycle such as phen-**C7** as the intermediate for direct isocyanate formation.[11] However, here we propose a crucial modification involving acid-catalyzed decarboxylative alcoholysis of phen-**C7** to produce intermediates capable of anilide anion exchange to fully rationalize our catalytic and organometallic observations. Our mechanistic proposal is also in full agreement with observations reported by the groups of Ragaini et al. and van Leeuwen et al.

5. EXPERIMENTAL SECTION

5.1. General Remarks. All solids were purchased from Acros Organics and used as received. Methanol, nitrobenzene, and aniline were all of analytical reagent purity and were distilled under an argon atmosphere over the appropriate drying agent.[50] After the distillation, these liquids were saturated with argon. We ensured that no water was present using an analytical reaction with trimethyl orthoformate according to a literature procedure.[51] Carbon monoxide (>99% pure) was purchased from Lindegas Benelux BV and used as received.[52] The compound phen-**C7** was synthesized according to a literature procedure;[11,22] the analytical data are given in section S7 of the Supporting Information.

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX300 (300 MHz) or a Bruker DMX400 (400 MHz) instrument. A Finnigan Aqua mass spectrometer (MS) with electrospray ionization (ESI) was used to record mass spectra. Samples were directly introduced into the ESI source, which was heated at 300 or 450 °C. The voltage of the capillary and the voltage for the aquamax were set at 3 kV and 50 V, respectively. High-pressure experiments were conducted in stainless steel autoclaves (100 mL) equipped with two inlet/outlet valves, a burst disk, a pressure sensor, and a thermocouple. The autoclaves were heated by an HEL polyBLOCK electrical heating system. Temperatures and pressures were measured with probes connected to a computer interface, making it possible to record these parameters throughout the course of the reaction.

5.2. Catalytic/High-Pressure Reactions. In a typical catalytic experiment, 0.05 mmol of $Pd(OAc)_2$ and 0.075 mmol of the ligand (and, if relevant, another additive) were weighed and transferred into an autoclave, together with a magnetic stirring rod. The autoclave was tightly closed and subsequently filled with argon using a Schlenk system that was connected to the one of the valves of the autoclave. Through the other valve was added 2.50 mL (24.4 mmol) of dried and degassed nitrobenzene, under a continuous flow of argon. In a similar fashion, 25.0 mL of dried and degassed methanol was then added. This reaction mixture was stirred at 500 rpm for about 15 min to ensure that complex formation was complete.[38] The autoclave was then inserted into the heating block and put under 50 bar of carbon monoxide gas. The reaction mixture was heated to 110 or 130 °C (within 30 min) with stirring at 500 rpm. After it stood for 4 h at a certain temperature, the autoclave was cooled to room temperature in about 1 h. The autoclave was then slowly vented to atmospheric pressure, and the reaction mixture was analyzed as described elsewhere.[17] To ensure reproducibility, some standard catalytic reactions were performed in quadruplicate, and the relative standard deviation was always less than 5% for each analyte.

5.3. Adding Nitrosobenzene during a Catalytic Run. The experiment was first started as a normal high-pressure experiment. A stainless steel hollow pipe (10 mL), sealed with two valves on each side, was then put under an argon atmosphere, and nitrosobenzene (2.5 mmol in 5 mL methanol) was transferred into the hollow pipe using standard Schlenk techniques. The bottom valve of the hollow pipe was then mounted onto one of the valves of the autoclave, connected to the CO supply, and pressurized to about 5 bar above the pressure inside the autoclave. After about 1 h reaction time, nitrosobenzene was added to the reaction mixture by opening the two valves between the autoclave and the hollow pipe. The reaction was then allowed to run for the remaining reaction time and treated as any other catalytic experiment.

5.4. NMR Experiments. A 4.50 mg amount (10 μmol) of phen-**C7**[11,22] was weighed into an NMR tube and put under argon. In another tube, the appropriate amount of phosphane ligand was dissolved in 1 mL of nitrobenzene(-d_5) under an argon atmosphere. Of this solution, 0.5 mL was added to the phen-**C7** complex using a 1 mL syringe, which was dry and flushed with argon. The yellow suspension thus obtained (20 mM phen-**C7**) was thoroughly mixed using a vortex mixer and measured. After the first measurements, the reaction mixture was carefully heated to about 60 °C, resulting in a clear yellow-orange solution. This solution was monitored with ^1H and $^{31}P\{^1H\}$ NMR spectroscopy, over a period of 14 h. For the proton measurements, the number of free inductive decays (FIDs) was 16, and for the phosphorus NMR spectra, the number of FIDs was 40. The same procedure was applied for the experiment under a CO atmosphere, but nitrobenzene was first saturated with CO gas, the NMR tube was put under a CO atmosphere, and the 1 mL syringe was flushed with CO.

5.5. DFT Studies. Calculations were done with the SPARTAN '04 package (Wavefunction, Inc.; www.wavefun.com), using density functional theory (DFT)[53,54] with the Becke and Perdew (BP) functional.[55,56] Geometry optimizations were carried out using Pople's 6-31G*(d,p) basis set for H, C, O, and P atoms[57] and the LANL2DZ effective core potential for palladium.[58−60] All of the geometrical parameters were fully optimized. No constraints to bonds, angles, or

dx.doi.org/10.1021/om200882p | Organometallics 2012, 31, 4142−4156

dihedral angles were applied in the calculations, and all atoms were free to be optimized. Cartesian coordinates and raw energies (in hartrees) are collected in an .xls file in the Supporting Information, along with .mol2 files of all optimized structures **C0**−**C7**.

■ ASSOCIATED CONTENT

Supporting Information

An Excel file giving Cartesian coordinates and raw energies, .mol2 files giving all optimized structures C0-C7, and tables, figures, and text giving additional details of the experiments and calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research has been financially supported by the Council for Chemical Sciences of The Netherlands Organisation for Scientific Research (CW-NWO). This work has been performed under the auspices of the joint NIOK Research Graduate School of Leiden University and six other Dutch Universities. Dr. Andreas Ehlers (Vrije Universiteit Amsterdam) is kindly acknowledged for his assistance with the DFT calculations. We thank the reviewers for critical reading of the paper, which has resulted in significant improvements in the clarity of our message.

■ REFERENCES

(1) Richter, R. H.; Priester, R. D. In *Kirk-Othmer Encyclopedia of Chemical Technology*; Kroschmitz, J. L., Howe-Grand, M., Eds.; Wiley: New York, 1995; Vol. *14*.
(2) Ulrich, H. *Ullmann's Encyclopedia of Industrial Chemistry*; VCH: New York, 1989; Vol. *A14*.
(3) Ryan, A. J.; Stanford, J. L. In *Comprehensive Polymer Science*; Allen, G., Bevington, J. C., Eds.; Pergamon: New York, 1989; Vol. *5*.
(4) Weisermel, K.; Arpe, H. J., *Industrielle Organische Chemie*, VCH Verslagsgesellschaft GmbH, Weinheim, Germany, 1988.
(5) *Registry of Toxic Effects of Chemical Substances (RTECS, online database)*; United States Department of Health and Human Services (National Toxicology Information, National Library of Medicine), Bethesda, MD, 1993.
(6) Weast, R. C., Ed. *Handbook of Chemistry and Physics*, 58th ed.; CRC Press: Cleveland, OH, 1977−1978; p D-110.
(7) Paul, F. *Coord. Chem. Rev.* **2000**, *203*, 269.
(8) Drent, E.; van Leeuwen, P. W. N. M., EU 0086281A1, 1982.
(9) Wehman, P.; Borst, L.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Mol. Catal. A: Chem.* **1996**, *112*, 23.
(10) Wehman, P.; Borst, L.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Chem. Ber.-Recl.* **1997**, *130*, 13.
(11) Leconte, P.; Metz, F.; Mortreux, A.; Osborn, J. A.; Paul, F.; Petit, F.; Pillot, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1616.
(12) Drent, E.; van Leeuwen, P. W. N. M. EU 86281, 1981.
(13) Ragaini, F.; Cognolato, C.; Gasperini, M.; Cenini, S. *Angew. Chem.* **2003**, *42*, 2886.
(14) Ragaini, F.; Gasperini, M.; Cenini, S. *Adv. Synth. Catal.* **2004**, *346*, 63.
(15) Ragaini, F. *Dalton Trans.* **2009**, 6251.
(16) Ragaini, F.; Gasperini, M.; Cenini, S.; Arnera, L.; Caselli, A.; Macchi, P.; Casati, N. *Chem. Eur. J.* **2009**, *15*, 8064.
(17) Mooibroek, T. J.; Schoon, L.; Bouwman, E.; Drent, E. *Chem. Eur. J.* **2011**, *17*, 13318.
(18) Mooibroek, T. J.; Bouwman, E.; Drent, E. *Eur. J. Inorg. Chem.* **2012**, 1403.
(19) Akazome, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1994**, *59*, 3375.
(20) Paul, F.; Fischer, J.; Ochsenbein, P.; Osborn, J. A. *Organometallics* **1998**, *17*, 2199.
(21) Paul, F.; Fischer, J.; Ochsenbein, P.; Osborn, J. A. *C. R. Chim.* **2002**, *5*, 267.
(22) Santi, A. S. o; Milani, B.; Mestroni, G.; Zangrando, E.; Randaccio, L. *J. Organomet. Chem.* **1997**, *546*, 89.
(23) Note that DPU can be formed not only by the reaction of nitrobenzene, CO, and (in situ generated) aniline but also by the transesterification of MPC with aniline. In both cases, aniline is formed first and DPU is thus derived from aniline.
(24) When 6 mmol DPU was heated for 4 h in methanol under 50 bar of CO, significant amounts of MPC were found: 3.2 mmol (110 °C), 1.5 mmol (100 °C), 1.0 mmol (90 °C), 0.4 mmol (80 °C).
(25) Lund, H. In *Organic Electrochemistry. An Introduction and a Guide*, 3rd ed.; Lund, H., Baizer, M. M., Eds.; Marcel Dekker: New York, 1991; p 411.
(26) o Santi, A. S.; Milani, B.; Zangrando, E.; Mestroni, G. *Eur. J. Inorg. Chem.* **2000**, 2351.
(27) Already at about 70−80 °C a significant (3−7%) conversion was observed when 6 mmol of DPU was heated in 25 mL of 3-methylaniline under 50 bar of CO for 2 h.
(28) Kim, H. S.; Kim, Y. J.; Lee, H.; Park, K. Y.; Lee, C.; Chin, C. S. *Angew. Chem.* **2002**, *41*, 4300.
(29) Lee, S. M.; Cho, N. S.; Kim, K. D.; Oh, J. S.; Lee, C. W.; Lee, J. S. *J. Mol. Catal.* **1992**, *73*, 43.
(30) Lee, C. W.; Lee, J. S.; Lee, S. M.; Kim, K. D.; Cho, N. S.; Oh, J. S. *J. Mol. Catal.* **1993**, *81*, 17.
(31) Lee, C. W.; Lee, S. M.; Oh, J. S.; Lee, J. S. *Catal. Lett.* **1993**, *19*, 217.
(32) Gasperini, M.; Ragaini, F.; Remondini, C.; Caselli, A.; Cenini, S. *J. Organomet. Chem.* **2005**, *690*, 4517.
(33) Wang, X. F.; Li, P.; Yuan, X. H.; Lu, S. W. *J. Mol. Catal. A: Chem.* **2006**, *253*, 261.
(34) Tafesh, A. M.; Weiguny, J. *Chem. Rev.* **1996**, *96*, 2035.
(35) Dieck, H. A.; Laine, R. M.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 2819.
(36) Mooibroek, T. J. Ph.D. Thesis, Leiden University, Leiden, The Netherlands, 2011; Chapter 7.
(37) These reactions were performed using the same procedure as our standard carbonylation experiments (see the Experimental Section), but using 2.5 mL (22.9 mmol) of dry and degassed 3-methylnitrobenzene as the substrate, 25.0 mL (274.3 mmol) of dry and degassed aniline as solvent, and 0.05 mmol of (L3X)Pd(OAc)$_2$ as the catalyst precursor.
(38) Mooibroek, T. J.; Bouwman, E.; Lutz, M.; Spek, A. L.; Drent, E. *Eur. J. Inorg. Chem.* **2010**, 298.
(39) Mooibroek, T. J.; Lutz, M.; Spek, A. L.; Bouwman, E. *Dalton Trans.* **2010**, *39*, 11027.
(40) After 180 min, the solution contained 17% of phen−palladacycle and 83% phen (^{1}H NMR), meaning that only 83% of the initially added palladium can end up as the L3X complex. The percentage of a specific L3X-Pd complex (relative to palladium) can thus be calculated by: $\sum\int_{\text{L3X complex}}/\sum\int_{\text{all L3X complexes}} \times 83\%$. Thus, the species detected with ^{31}P{^{1}H} NMR that were assigned to Pd-containing species are as follows (δ ($\int$; assignment; percentage based on Pd)): 1.0 (1.00; Pd^0(L3X)$_2$; 33); 5.0 (0.06; L3X−palladacycle; 4); 13−20 (0.33; unknown Pd complexes; 22); 24/−7 (0.32; decarbonylated L3X−palladacycle; 21); 35 (0.05; unknown Pd complex; 3); $\sum\int$ = 1.76. The solution also contained L3X (−25 ppm, $\int$ = 0.33) and L3X═O (26/−24 ppm, $\int$ = 0.30), which is (0.33 + 0.30)/1.76 × 100% = 26% of the initially added L3X. Hence, 74% of L3X is thus bound to palladium; this is indeed roughly 1 equiv with respect to the 83% Pd complex, computed on the basis of ^{1}H NMR.
(41) $\int_{0.5\text{ ppm}}$ = 100 (Pd^0(L3X)$_2$ = 4P); $\int_{14.3+(-26.2)\text{ ppm}}$ = 2.2 (L3X═NPh, 2P). Hence, 2.2/(100/2 + 2.2) × 100% = 4.2% and 4.2% of 10 μmol (the amount of phen−palladacycle present) is ∼0.4 μmol.

(42) Haras, A.; Michalak, A.; Rieger, B.; Ziegler, T. *J. Am. Chem. Soc.* **2005**, *127*, 8765.
(43) Aberg, J. B.; Nyhlen, J.; Martin-Matute, B.; Privalov, T.; Backvall, J. E. *J. Am. Chem. Soc.* **2009**, *131*, 9500.
(44) We thank one of the reviewers for suggesting a catalytic role of CO in the net oxidative addition of methanol on palladium. For example, a quite conceivable scenario is that coordinated CO at the $Pd^0(CO)_2$ center will be initially attacked by $CH_3O^-H^+$ to generate a $[Pd(CO)C(O)OCH_3]^-H^+$ ion pair. This increases both the acidity of the proton and the nucleophilicity of the Pd center, thus facilitating the protonation of the Pd center to provide $H-Pd(CO)CO(O)CH_3$, which upon decarbonylation results in **C8**, i.e. a CO-assisted net oxidative addition of methanol to a Pd^0 center. Interestingly, some methyl formate, with more at the higher CO pressure, is always formed, which at least partially may originate from reductive elimination of $HCOOCH_3$ from the $HPdCO(O)CH_3$ intermediate.
(45) Ragaini, F.; Cenini, S.; Fumagalli, A.; Crotti, C. *J. Organomet. Chem.* **1992**, *428*, 401.
(46) Zuman, P.; Fijalek, Z.; Dumanovic, D.; Suznjevic, D. *Electroanalysis* **1992**, *4*, 783.
(47) Ueno, K.; Akiyoshi, S. *J. Am. Chem. Soc.* **1954**, *76*, 3670.
(48) Dalmagro, J.; Yunes, R. A.; Simionatto, E. L. *J. Phys. Org. Chem.* **1994**, *7*, 399.
(49) Note that, in the formation of this complex from CO/methanol, two hydrogen atoms must have been produced; in our view, these can only be transferred to nitrobenzene, giving aniline via a nitrene (Pd═NPh) moiety, as we propose.
(50) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Elsevier: Amsterdam, 2003.
(51) Chen, J.; Fritz, J. S. *Anal. Chem.* **1991**, *63*, 2016.
(52) customer.linde.com/FIRSTspiritWeb/linde/LGNL/media/datasheets/NL-PIB-0024.pdf, April 2012.
(53) Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2000.
(54) Eichkorn, K.; Treutler, O.; Ohm, H.; Haser, M.; Ahlrichs, R. *Chem. Phys. Lett.* **1995**, *240*, 283.
(55) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
(56) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822.
(57) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.
(58) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270.
(59) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.
(60) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284.