

The NMR Study of the Mechanism of Alkene Arylation with Anhydrides of Aromatic Acids

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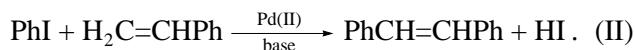
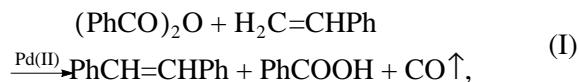
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Received February 13, 2001

Abstract—The main steps of the catalytic cycle of the alkene arylation reaction with the participation of anhydrides of aromatic acids as arylation agents were studied by ^{31}P NMR spectroscopy. In contrast to the mechanism proposed earlier, palladium complexes containing benzoate anions as acidoligands were not found in the reaction mixture. It was found that the catalytic cycle of the reaction includes the steps of oxidative addition of Pd(0) formed *in situ* to the anhydride of acid, the substitution of acidoligand, and the elimination of the CO molecule. Further transformations probably take place according to the usual steps of the Heck reaction. It was shown that CO elimination is a limiting step.

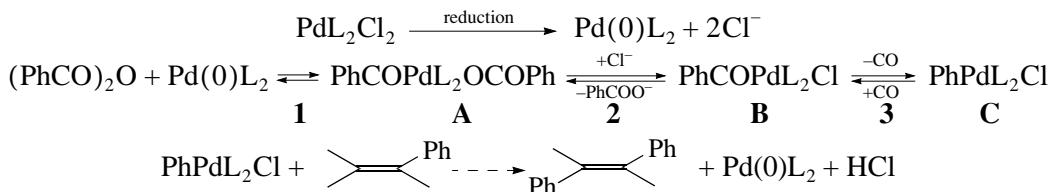
INTRODUCTION

A new method of alkene arylation with the anhydrides of aromatic acids (I) was proposed in [1]. In contrast to the traditional Heck reaction (II) [2], this method does not require the use of a base. Reaction (I) has some advantages: the reagents are readily available, the base is not present in stoichiometric amounts in the reaction mixture, and it is possible to reuse acid resulting from the reaction in anhydride synthesis.



Using regioselectivity and kinetic data for the reaction, a hypothetical mechanism of the reaction was proposed (Scheme 1) [3]. This mechanism includes the preliminary reduction of the initial Pd(II) complex, the step of oxidative addition of Pd(0) to the molecule of anhydride (1), the substitution of the chlorine anion for benzoate ligand (2), CO elimination (3), and a further reaction taking place in accordance with the usual steps of the Heck reaction [2]. In this case, it was suggested that catalyst activity is largely determined by the ability of palladium benzoyl complexes to eliminate CO (scheme 1, step 3).

The goal of this work was to study reaction (I) by ^{31}P NMR spectroscopy and to check the mechanism of the catalytic cycle proposed earlier [3] using kinetic data (Scheme 1).



Scheme 1. Hypothetical mechanism of reaction (I).

EXPERIMENTAL

Reaction (I) and the synthesis of palladium phosphine complexes were carried out under anaerobic conditions (in an argon atmosphere). All solvents and reagents were thoroughly degassed and stored in an argon atmosphere. ^{31}P NMR spectra were recorded using

Bruker WP-200SY (200 MHz) and Varian VXR-500S (500 MHz) spectrometers. Spectrometer stabilization was performed using the signal of deuterium in CDCl_3 (external standard); the chemical shifts are given with respect to the signal of 85% H_3PO_4 . The monitoring of reaction (I) was carried out by gas–liquid chromatogra-

phy (HP-4890 chromatograph, 15% polyphenylsilicon, 15 m, 100–200°C, flame-ionization detector; the internal standard was naphthalene). The purification of the reagent was performed using standard procedures.

*The Reaction of Styrene Phenylation
by Benzoic Anhydride*

Styrene (10 mmol) and benzoic anhydride (10 mmol) were dissolved in 10 ml of *N*-methyl pyrrolidone (**NMP**). This solution was introduced into a retort with PdCl_2 and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.16 mmol). The retort was kept at a constant temperature of 140°C and equipped with a magnetic stirrer. In some experiments, the reaction was carried out in the presence of LiCl (1.6 mmol). Reaction (I) occurred until product accumulation discontinued.

*The Preparation of $\text{PhCOPd}(\text{PPh}_3)_2\text{X}$
and $\text{PhPd}(\text{PPh}_3)_2\text{X}$ from Pd(II) Complexes*

For the preparation of $\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$, we added 10 mmol of $(\text{PhCO})_2\text{O}$ and 0.32 mmol of a reducing agent (NBu_3 or HCOONa) to 10 ml of an NMP solution containing 0.16 mmol of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$. The reaction mixture was stirred at 100°C until the signal of initial $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ completely disappeared (~40 min) and a signal at 20.19 ppm probably corresponding to $\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$ appeared. The same signal was observed under analogous conditions when $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ reacted with PhI and a reducing agent in a CO atmosphere. The exchange of chloride with the benzoate ligand was carried out at room temperature by the interaction of the complex with the equivalent amount of AgOCOPh . The AgCl precipitate was decanted. The reaction of decarbonylation of the complex was carried out at 100°C in a flow of argon (~120 min).

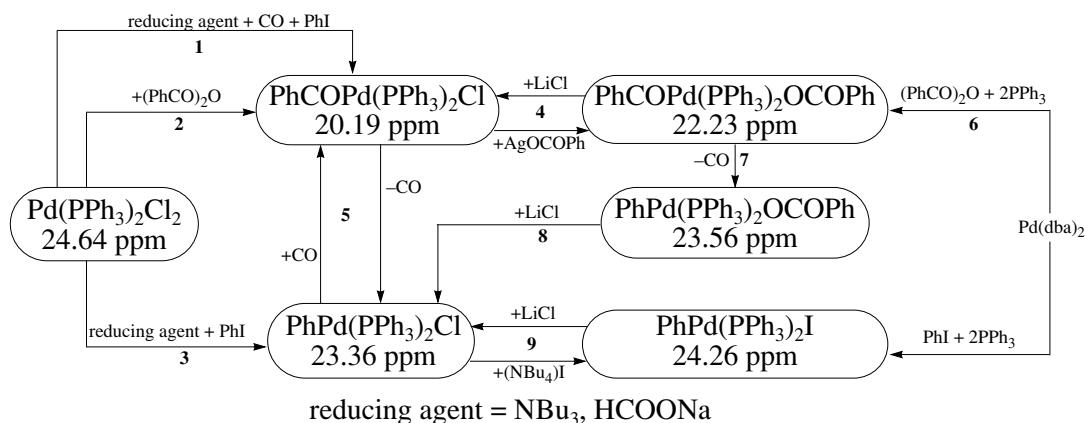
$\text{PhPd}(\text{PPh}_3)_2\text{Cl}$ was obtained under analogous conditions by the addition of 10 mmol of PhI and 0.32 mmol of a reducing agent to the $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ solution. The process was carried out until the complete conversion of the initial complex and the appearance of a signal at 23.36 ppm. The chloride ligand in the complex was exchanged with the iodide ligand at room temperature in a 20-fold excess of $(\text{NBu}_4)_2\text{I}$. The reaction of carbonylation of the complex was carried out in a CO atmosphere at room temperature (~30 min).

*The Preparation of $\text{PhCOPd}(\text{PPh}_3)_2\text{X}$
and $\text{PhPd}(\text{PPh}_3)_2\text{X}$ from Pd(0) Complexes*

$\text{PhCOPd}(\text{PPh}_3)_2\text{OCOPh}$ (22.23 ppm) and $\text{PhPd}(\text{PPh}_3)_2\text{I}$ (24.26 ppm) were prepared by analogy with the known procedures [4, 5] using the reaction of oxidative addition of $\text{Pd}(\text{dba})_2$ (0.16 mmol) (dba is *trans-trans*-dibenzylideneacetone) to $(\text{PhCO})_2\text{O}$ (10 mmol) and PhI (10 mmol), respectively, in the presence of PPh_3 (0.32 mmol). The ratio of reactants and the conditions of decarbonylation and ligand exchange were identical to the parameters described above.

RESULTS AND DISCUSSION

To verify the mechanism presented in Scheme 1, we studied the composition and structure of intermediate palladium complexes formed in reaction (I) in the presence of two equivalents of PPh_3 by ^{31}P NMR spectroscopy. Preliminarily, we obtained complexes that could be formed in the reaction mixture according to the mechanism (Scheme 1, complexes **A**, **B**, and **C**). For all complexes, the values of chemical shifts (Scheme 2) in NMP solvent were measured (parameters of the ^{31}P NMR spectra of these complexes in NMR were not published earlier). We also studied the reactivity of these complexes. These complexes were synthesized by two methods: using Pd(II) compounds and using a conventional method [4–6] from Pd(0) complexes (Scheme 2).



Scheme 2. The formation, chemical shifts, and reactions of palladium phosphine complexes.

(PhCO_2O , PhI , or PhI in the presence of CO (1 atm) began to react with $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ only if a reducing agent was present in the system (Scheme 2, steps 1, 2, 3). We used a twofold excess of HCOONa or NBu_3 as a reducing agent (the ability of NBu_3 to efficiently reduce $\text{Pd}(\text{II})$ complexes was demonstrated in [7]). The reaction formed σ -benzoyl ($\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$) and σ -phenyl ($\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$) complexes with a yield close to 100%. The ^{31}P NMR spectra of these complexes contain only one singlet. This indicates that phosphine ligands have *trans*-configuration. The presence of a chlorine atom and benzoyl fragment in $\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$ is confirmed by the reversible ligand exchange in the presence of AgOCOPh and LiCl (Scheme 2, step 4), by the reaction of CO elimination (heating at 100°C in an argon flow), and by reverse carbonylation (Scheme 2, step 5). These reactions are typical of the complexes of the $\text{ArCOPd}(\text{PR}_3)_2\text{X}$ type [5, 6]. It is necessary to note that the reaction of decarbonylation required a higher temperature and is much slower than carbonylation.

The oxidative addition of anhydrides of acids to $\text{Pd}(0)$ complexes was observed for the first time in [4]. The formation of $\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$ from $(\text{PhCO})_2\text{O}$ and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ in our case is evidence for the feasibility of this step under the conditions of catalytic reaction (I) when the $\text{Pd}(0)$ complexes are generated *in situ*. Alkene most probably is a reducing agent in reaction (I) as in the usual Heck reaction (II) [2, 7]. The formation of chloride complexes instead of benzoate complexes observed in [4] can be due to the higher strength of a $\text{Pd}-\text{Cl}$ bond or with the occurrence of the reaction via intermediate anionic complexes of $\text{Pd}(0)$ as in [6].

σ -Benzoyl and σ -phenyl complexes with the benzoate anion can be obtained from $\text{Pd}(0)$ compounds using the reaction of their oxidative addition to anhydride, as was observed in [4], and the subsequent elimination of CO (Scheme 2, steps 6 and 7). As was supposed above, the chlorine anion in these complexes can easily substitute for the benzoate anion in the interaction with LiCl (Scheme 2, steps 4 and 8). The same process is also typical of the complex with the iodine anion (Scheme 2, step 9). In this process, complexes analogous to those obtained above from $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ were formed. The evidence for this is the coincidence of respective chemical shifts.

Analysis of samples taken during the catalytic process (I) showed that the reaction mixture does not contain complexes with benzoate ligands (Fig. 1a). In this process, up to 50% of palladium is found in a catalytically inactive form $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (table, experiment 1). This shows that the processes of $\text{Pd}(0)$ formation are not efficient enough. According to ^{31}P NMR data, the reaction is completed due to the transition of all palladium into this catalytically inactive form (table, experiment 2). Palladium oxidation in reaction (I) can be caused by side processes of PhH and $\text{Ph}-\text{Ph}$ formation. This is also typical of the conventional Heck reaction [7].

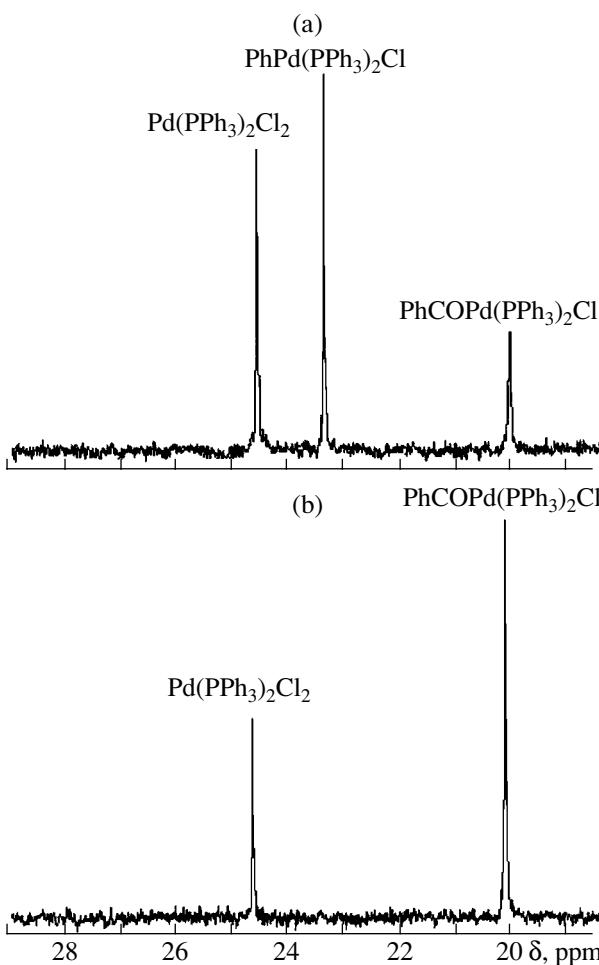


Fig. 1. ^{31}P NMR spectrum of the reaction mixture of reaction (I) at the instant of maximal catalytic activity (~20% conversion): (a) the reaction was carried out in the presence of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$; (b) PdCl_2 (PPh_3 was added immediately before recording the spectrum).

It was shown in [3] that the application of LiCl additives improves the catalytic activity. According to NMR spectroscopic data, the addition of LiCl is accompanied by the almost complete disappearance of the benzoyl complex in the reaction mixture (table, experiment 3). The high reactivity of benzoyl complexes in the presence of LiCl can be the reason for this phenomenon. Perhaps, this is due to a change in the palladium state in $\text{PhCOPd}(\text{PPh}_3)_2\text{Cl}$ because of the interaction of the Li^+ cation with chlorine (analogously to [6]) or oxygen atoms. Note that the nature of a cation of the added salt strongly affects catalyst activity in reaction (I) [3].

The presence of phosphine in the reaction mixture can understandably change the nature of the reaction and does not permit us to draw an unambiguous conclusion on the phosphine-free variant of the catalytic system, which was used in [1, 3]. Therefore, we carried out experiments where phosphine was added immediately before recording the spectrum and after fast cooling of

Relative signal intensities of palladium complexes in ^{31}P NMR spectra during reaction (I)

Experiment	Catalytic system	<i>J</i> , arb. units		
		Pd(PPh_3) ₂ Cl ₂	PhPd(PPh_3) ₂ Cl	PhCOPd(PPh_3) ₂ Cl
1	PdCl ₂ + 2PPh ₃	1.0	1.2	0.3
2	PdCl ₂ + 2PPh ₃ [*]	1.0	0	0
3	PdCl ₂ + 2PPh ₃ + 10LiCl	1.0	0.6	0
4	PdCl ₂ + 10LiCl**	1.0	0	2.7

* After reaction (I).

** PPh₃ was added after reaching 20% conversion in reaction (I).

the reaction mixture. In these experiments, it was supposed that palladium phosphine complexes are formed rapidly by the substitution of more labile ligands (solvent molecules or halogen anions). It was found that, in the moment of maximal activity of the catalyst during the reaction (I) in the reaction mixture, in addition to Pd(PPh_3)₂Cl₂, there is only PdCO(PPh_3)₂Cl (table, experiment 4, Fig. 1b). This agrees with the hypothesis that CO elimination is a limiting step, as suggested in [3] on the basis of the study of the kinetics and regioselectivity of reaction (I).

Thus, the results of the study of the kinetics and regioselectivity [3], as well as the NMR monitoring of reaction (I) show that the catalytic cycle of the reaction includes the steps of the oxidative addition of Pd(0) formed *in situ* to anhydride, the substitution of the halogen anion for the benzoate acidoligand, and the elimination of the CO molecule. The influence of halide additives on the catalytic activity is due to the substitution of the halogen anion for the benzoate acidoligand in the intermediate complexes of the catalytic cycle. One of the reasons for the activating influence of LiCl is the lower activity of benzoyl palladium complexes.

ACKNOWLEDGMENTS

This work was supported by the Russian Foundation for Basic Research (project no. 99-03-32090). The authors thank the German Service for Academic exchanges (DAAD) and personally Professor W. Keim (Technische Hochschule, Aachen, Germany) for the possibility to carry out some experiments.

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