

Mechanistic insight into the preactivation of a modern palladium catalyst precursor in phosphine-free Heck reactions

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Received: 28 May 2008 / Accepted: 2 July 2008 / Published online: 17 September 2008
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Abstract The use of well-defined *trans*-dichlorobis(diethanolamine-*N*)palladium(II) complex (*trans*-[PdCl₂(DEA)₂]) as a new, modern, and effective Heck precatalyst is reported. The mechanism of the key, initial steps of the reaction, i.e., the formation of the Pd(0) complex, is examined using density functional theory.

Keywords Reaction mechanism · Pd(II) precatalyst · Amino alcohol · Quantum chemical calculations

Introduction

The palladium-catalyzed arylation of olefins, known as the Heck reaction, deserves considerable attention due to its synthetic versatility [1]. In the past decade, phosphine-free Pd complexes have been introduced as a less complicated and environmentally more desirable alternative to original Pd–phosphine catalysts [2]. However, nitrogen- and sulfur-based palladacycles [3, 4], Pd complexes of *N,S*-based carbenes and *N*-heterocyclic compounds [5–7] have been associated with high-cost multistep syntheses and considerable sensitivity of the ligands towards air and moisture. In addition, very little is known about the molecular structure of Pd(0) complexes, which have been generally accepted as the catalytically active form [8, 9].

Amino alcohols and amino acids have been widely used as *O,N*-ligands for the synthesis of different metal-organic compounds and catalysts [10–16]. Triethanolamine has proved to be an efficient base and reaction medium for

phosphine-free Heck reactions [17]. The recently synthesized *trans*-dichlorobis(diethanolamine-*N*)palladium(II) complex (*trans*-[PdCl₂(DEA)₂], **1**) [14] contains both the necessary amine (diethanolamine, DEA) and Pd(II). For this reason we assume that it can be used as a precatalyst in phosphine-free Heck reactions in the presence of strong and weaker bases. Herein, we report the use and a preliminary mechanistic study of the preactivation step of **1**. More precisely, we investigate the possible intramolecular reduction of Pd(II) to Pd(0) using experimental and computational methods.

Results and discussion

When a reaction is performed in the presence of a strong base, it can be expected that a proton of the OH group will be abstracted from **1** (Fig. 1). In this way, the anion **2** would be formed. We assume that a hydrogen bonded to the carbinol C atom can be coordinated to Pd(II) [9, 18], thus forming **4** via transition state **3** (Fig. 1). This transformation can be followed by the reductive elimination of HCl, producing **5**. Complex **5** contains Pd(0), and so it should be a catalytically active species in the Heck reaction. To confirm our assumptions, we performed preliminary computational and experimental investigations.

The optimized geometries of **2** and **3** are presented in Fig. 2, whereas some crucial bond distances for structures **1–5** are given in Table 1.

Our calculation of **1** yields a structure with bond distances and angles consistent with the crystallographic experimental data (Table 1) [14]. Following the considerations presented above (Fig. 1), H1 is removed from **1** as a proton, and the structure thus obtained is optimized (**2** in Fig. 2). The atomic polar tensor (APT) [19] charge

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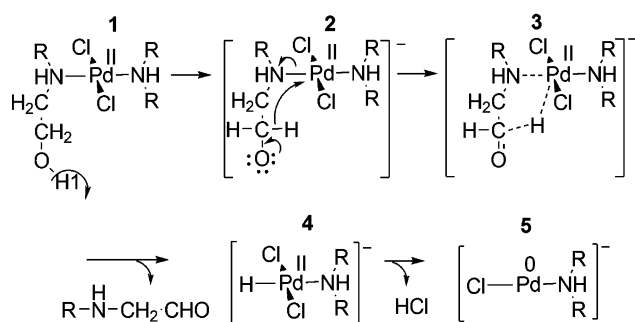


Fig. 1 Proposed mechanism of the preactivation process of *trans*-[PdCl₂(DEA)₂] precatalyst. R = -CH₂CH₂OH

distribution of **2** shows that positive charge is distributed among palladium (0.765), carbons, and some hydrogens, whereas negative charge is distributed among all other atoms. The C1-H2 and C1-H3 bonds become particularly polarized, with the APT charges on C1, H2, and H3 of 0.700, -0.127, and -0.231, respectively. In addition, the greatest contributions to the HOMO of **2** come from O1, H2, and H3 (Fig. 2). Thus, one can expect that H2 will perform a nucleophilic attack on palladium, because its position is the most favorable. This attack leads to the formation of transition state **3** (Fig. 2), with an energy barrier of 83.0 kJ/mol. Here, the C1-H2 and Pd-N1 bonds are being broken whereas the Pd-H2 bond is being formed (Table 1). The negative charge on H2 is slightly increased (-0.167). Subsequently in the reaction, H2 coordinates with palladium as a hydride ion (**4** in Fig. 1; Table 1). The Pd-N1 and C1-H2 bonds are completely broken, implying that dehydrogenated DEA is eliminated. In the basic environment, **4** undergoes reductive elimination, thus forming **5**.

If a strong base is not present in the reaction mixture, then the initial abstraction of a proton from an alcoholic OH group does not occur. Our calculations show that a transformation of **1** involves the formation of **4** and

Table 1 Selected bond distances for the species under consideration

Dist. (nm)	1	2	3	4	5
Pd-C11	0.2376	0.2405	0.2396	0.2392	0.2385
Pd-C12	0.2376	0.2408	0.2396	0.2408	-
Pd-N1	0.2116	0.2111	0.2453	-	-
Pd-N2	0.2116	0.2123	0.2247	0.2325	0.2191
C1-H2	0.1098	0.1117	0.1201	-	-
Pd-H2	0.2866	0.2603	0.2056	0.1536	-

iminium ion ($\text{HOCH}_2\text{CH}=\text{NHCH}_2\text{CH}_2\text{OH}$)⁺, via a transition state which requires significantly higher activation energy. The complete reaction path, as well as solvent effects, will be reported elsewhere.

Our predictions, obtained by means of DFT calculations, were confirmed by performing Heck reactions catalyzed with **1** in the presence of a weak and a strong base. The results of our experiments are presented in Table 2.

At first, the reactions are performed with the equimolar ratio of the reactants in the presence of DEA as a weak base and 1 mol% of complex **1** (synthesized according to the recently established procedure [14]), at 110 °C. In order to increase the reaction rate, NaOEt is used instead of DEA. It is established that the use of this strong base significantly decreases the reaction time from 8 to 4 h for iodobenzene, and from 11 to 6 h for bromobenzene. The desired coupling products are obtained in good yield (Table 2).

The considerable stability of complex **1** towards air and moisture and the simplicity of the reaction procedure make the investigated reactions desirable alternatives to original reactions catalyzed with Pd-phosphine. The obtained reaction products confirm that **1** really acts as an effective precatalyst in the examined Heck reactions. In addition, our experimental results show that the formation of the new C-C bond between the aromatic ring and olefins does

Fig. 2 Optimized geometries of crucial participants in the preactivation process of *trans*-[PdCl₂(DEA)₂]: **2** with the depicted HOMO (left), and **3** (right)

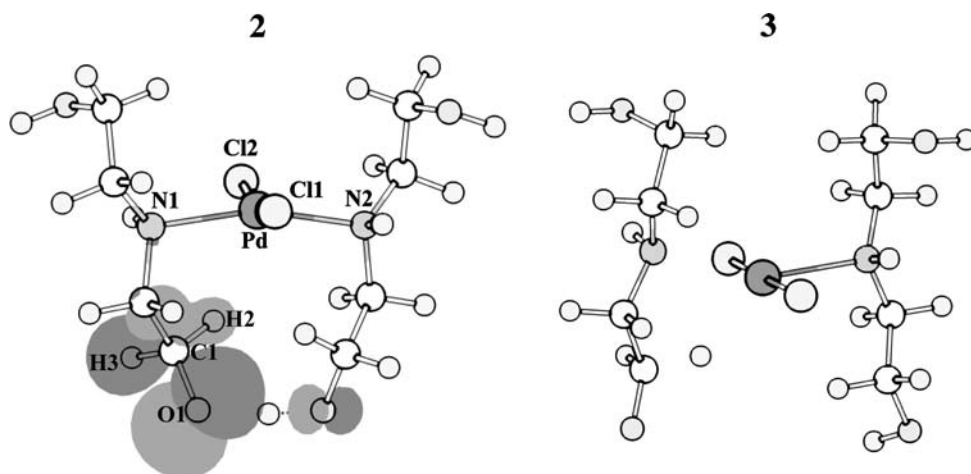


Table 2 Reactions between olefins and aryl halides catalyzed by *trans*-[PdCl₂(DEA)₂]
$$\text{C}_6\text{H}_5\text{X} + \text{CH}_2 = \text{CHR} \xrightarrow[\text{base}]{\text{trans-[PdCl}_2\text{(DEA)}_2\text{]} 1\text{mol}\%} \text{C}_6\text{H}_5\text{CH} = \text{CHR}$$

6: R = C₆H₅; 7: R = COOCH₃; 8: R = COOC₂H₅; 9: R = COOC₄H₉

Entry	Organic halide	R	Base	Time (h)	Yield (%) ^c
1	C ₆ H ₅ I	C ₆ H ₅	DEA ^a	8	75
2	C ₆ H ₅ I	C ₆ H ₅	NaOEt ^b	4	72
3	C ₆ H ₅ I	COOCH ₃	DEA	8	75
4	C ₆ H ₅ I	COOCH ₃	NaOEt	4	71
5	C ₆ H ₅ I	COOC ₂ H ₅	DEA	8	80
6	C ₆ H ₅ I	COOC ₂ H ₅	NaOEt	4	76
7	C ₆ H ₅ I	COOC ₄ H ₉	DEA	8	81
8	C ₆ H ₅ I	COOC ₄ H ₉	NaOEt	4	80
9	C ₆ H ₅ Br	C ₆ H ₅	DEA	11	82
10	C ₆ H ₅ Br	C ₆ H ₅	NaOEt	6	81

^a DEA (0.25 mmol) at 110 °C^b NaOEt (0.2 mmol) at 100 °C^c Isolated yield; only the *trans* product was detected by ¹H NMR

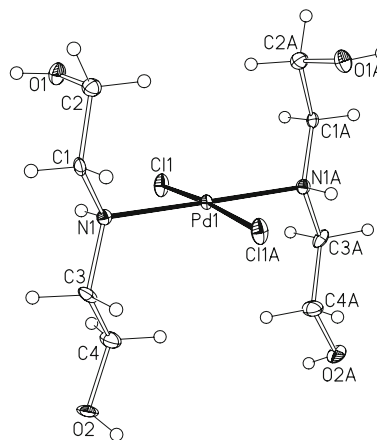
indeed occur faster in the presence of the strong base, which is in agreement with our theoretical and computational predictions.

Materials and methods

GC analyses were performed with an Agilent (Palo Alto, CA, USA) 6,890 N (G 1,530 N) instrument (Serial# CN10702033), with a capillary apolar column. ¹H and ¹³C NMR spectra were run in CDCl₃ on a Varian Gemini 200 MHz spectrometer. IR spectra were recorded on a PerkinElmer (Waltham, MA, USA) Spectrum One FT-IR spectrophotometer. Silica gel 60 (Merck, Darmstadt, Germany; particle size 0.063–0.200 mm) was used for column chromatography. The compounds: PdCl₂, DEA, aryl halides and olefins were obtained from Aldrich Chemical Co. (St. Louis, MO, USA).

The reactions of olefins and aryl halides in the presence of *trans*-[PdCl₂(DEA)₂] were performed in the following way. To a magnetically stirred solution of 1 mol% of PdCl₂ in 2 cm³ of ethanol, 2 mol% of diethanolamine at room temperature is added. Stirring is continued at 50–60 °C for half an hour. After the evaporation of EtOH in vacuo, the orange complex **1** is obtained. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre. Copies of the information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk or URL: <http://www.ccdc.cam.ac.uk>), quoting the deposition number CCDC299671.

The crystal structure determination of *trans*-[PdCl₂(DEA)₂], as well as selected bond distances, bond angles and hydrogen bonds, are presented in [14].



Aryl halide (1 mmol), activated olefin (1 mmol) and 0.026 g DEA (0.25 mmol) are then added to the same reaction flask. The reaction mixture is stirred and heated at 110 °C for 8 h in the case of iodobenzene, and 11 h in the case of bromobenzene. After cooling the reaction mixture to room temperature, CH₂Cl₂ (7.0 cm³) is added to extract the product. The organic phase is washed with water, and the aqueous layer is extracted with dichloromethane (2 × 10 cm³). The combined organic layers are dried over anhydrous sodium sulfate, and then the solvent is evaporated in vacuo. When reactions are performed in the presence of strong base, equimolar ratios of aryl halide (1 mmol) and activated olefin (1 mmol), 1 mol% *trans*-[PdCl₂(DEA)₂], and 0.20 mmol NaOEt are mixed. The reactions are performed at 100 °C, in CH₃CN as solvent (1 cm³), for a duration of 4 h for iodobenzene, and 6 h for bromobenzene.

The reactions were monitored and analyzed with GC chromatography and ¹H NMR spectroscopy. Reaction products were purified with column chromatography (silica gel; ethylacetate:dichloromethane = 1:1). The known coupling products were analyzed and characterized on the basis of their spectroscopic data, and by comparing these data to the spectra of the commercially available compounds.

All calculations were conducted using Gaussian03 [20] with the B3LYP hybrid functional [21, 22]. The 6–31G(d) basis set was used for C, H, O, N, and Cl, and LANL2DZ + ECP [23] was employed for the Pd center. Geometrical parameters of all investigated species were optimized in vacuum. All calculated structures were verified as being local minima (all positive eigenvalues) for ground-state structures or first-order saddle points (one negative eigenvalue) for transition-state structures by frequency calculations.

Acknowledgments This work is supported by the Ministry of Science and the Environment of Serbia, project No. 142013 B.

References

1. De Vries JG (2001) *Can J Chem* 79:1086
2. Heck R (1979) *Acc Chem Res* 12:146
3. Alonso DA, Nájera C, Pácheo MC (2000) *Org Lett* 2:1823
4. Consorti CS, Zanini ML, Leal S, Ebeling G, Dupont J (2003) *Org Lett* 5:983
5. Wang R, Twamley B, Shreeve JM (2006) *J Org Chem* 71:426
6. Jin CM, Twamley B, Shreeve JM (2005) *Organometallics* 24:3020
7. Cui X, Li J, Zhang ZP, Fu Y, Liu L, Guo QX (2007) *J Org Chem* 72:9342
8. Amatore C, Jutand A (2000) *Acc Chem Res* 33:314
9. Cabri W, Candiani I (1995) *Acc Chem Res* 28:2
10. Emmerson DPG, Hems WP, Davis BG (2006) *Org Lett* 8:207
11. Lu G, Li X, Zhou Z, Chan WL, Chan ASC (2001) *Tetrahedron Asymm* 12:2147
12. Wu X, Li X, McConville M, Saidi O, Xiao J (2006) *J Mol Catal A* 247:153
13. Patti A, Pedotti S (2003) *Tetrahedron Asymm* 14:597
14. Petrović ZD, Djuran MI, Heinemann FW, Rajković S, Trifunović S (2006) *Bioorg Chem* 34:225
15. Cui X, Li Z, Tao CZ, Xu Y, Li J, Liu L, Guo QX (2006) *Org Lett* 8:2467
16. Cui X, Qin T, Wang JR, Liu L, Guo QX (2007) *Synthesis* 3:393
17. Hong JL, Wang L (2006) *Eur J Org Chem* 22:5099
18. Jensen DR, Schultz MJ, Mueller JA, Sigman MS (2003) *Angew Chem Int Ed* 42:3810
19. Marti J (2001) *Chem Phys* 265:263
20. Gaussian Inc. (2003) Gaussian 03, revision E.01-SMP. Gaussian Inc., Pittsburgh, PA
21. Lee C, Yang W, Parr RG (1988) *Phys Rev B* 37:785
22. Becke AD (1993) *J Chem Phys* 98:5648
23. Hay PJ, Wadt WR (1985) *J Chem Phys* 82:270