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A new aspect of Heck catalyst formation

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Abstract The mechanism of the formation of the active Pd(0) complex from *trans*-dichlorobis(diethanolamine-*N*)palladium(II) complex in the presence of strong base was investigated by using density functional theory (M06 method). Our investigation shows that in the basic environment *trans*-dichlorobis(diethanolamine-*N*)palladium(II) complex undergoes abstraction of the alcoholic proton, and coordination of alkoxide oxygen to palladium. The intermediate complex, in which hydrogen is coordinated to Pd, undergoes reductive elimination of HCl, yielding the catalytically active low ligated Pd(0) complex.

Keywords Heck reaction · Reaction mechanism · Preactivation process · Catalytically active Pd(0) complex · Density functional theory

Introduction

The palladium-catalyzed arylation of olefins, known as the Heck reaction, is one of the most important methods for carbon–carbon bond formation in organic synthesis [1–4]. Because of its increasingly expanding use and importance, the Heck reaction attracts attention of both experimental [5–9] and theoretical chemists [10–22]. Owing to the significant synthetic versatility of palladium-catalyzed cross-coupling reactions, the Nobel Prize for chemistry for 2010 was awarded to Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki. On the basis of their methodologies, numerous fine chemicals and commercially available aromatic substrates were produced [23].

In spite of the fact that the Heck reaction has significant relevance in industry during the last two decades, the complex mechanism of this reaction has not been elucidated. Confusion arises, especially, when Pd(II) complexes are used as precatalysts, generating in situ Pd(0) active species [24]. Much effort has been devoted to the elucidation of the Heck reaction mechanism [10–12], including oxidative addition [15–21] and reductive elimination [22, 25]. On the other hand, very little is known about the mechanism of formation and molecular structure of Pd(0) complexes [13, 14] generally accepted as the catalytically active forms.

In our previous studies, the *trans*-dichlorobis(diethanolamine-*N*)palladium(II) complex (**1**), whose structure was reported earlier [13, 14, 26], has been used as a catalyst precursor in phosphine-free Heck reactions. The reactions between different olefins and aryl halides catalyzed with **1** have been studied in the presence of a weak base (diethanolamine), strong base (NaOEt) [13, 14], and ionic liquids (diethanolammonium acetate and diethanolammonium chloride) [27], where Pd(II) precatalyst was obtained in situ. Now we wish to report a new aspect of the preactivation reaction of the Heck catalyst precursor.

Results and discussion

Here we present the results of our investigation of the mechanism of formation of the Pd(0) catalyst in the presence of a strong base in acetonitrile as reaction medium. Acetonitrile was selected as solvent because it was used in

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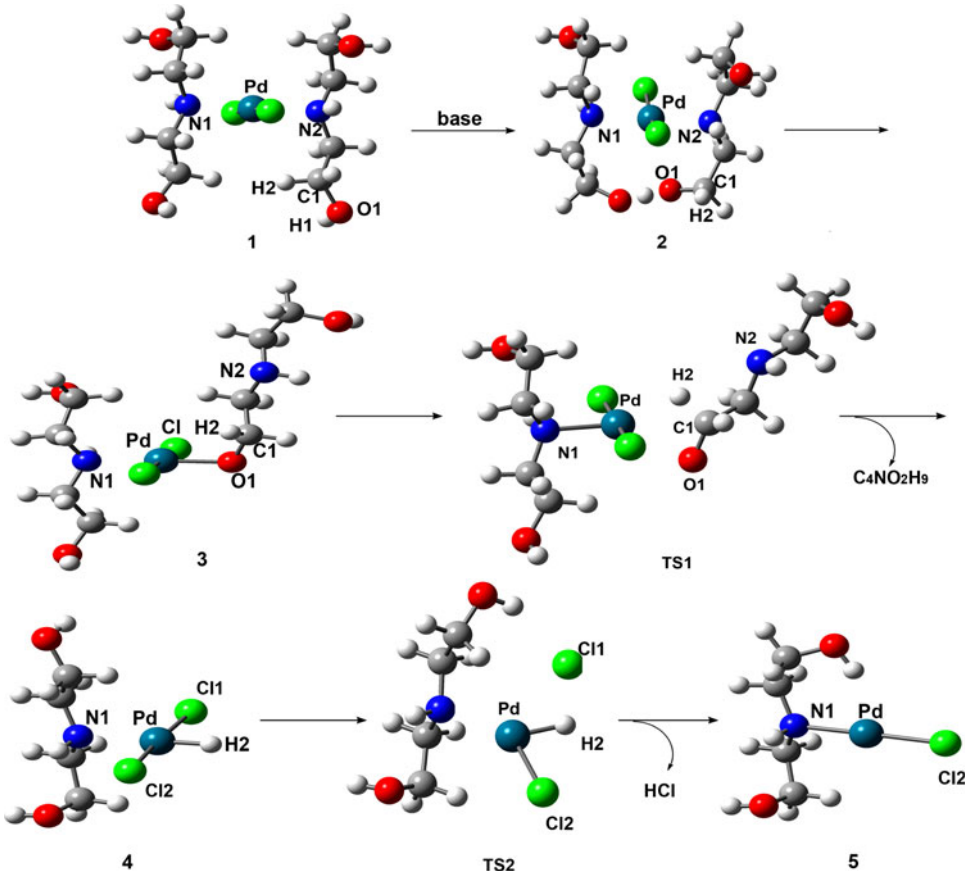

Fig. 1 Mechanistic pathway for the preactivation reaction of *trans*-dichlorobis-(diethanolamine-*N*)-palladium(II) complex (**1**)

our experiments on the Heck reaction [13, 21]. The computations performed under vacuum conditions are given in the Electronic Supplementary Material.

The proposed mechanism of the preactivation of **1** is presented in Fig. 1. First, the complex **1** undergoes abstraction of the alcoholic H1 proton in the basic environment, and coordination of O1 to Pd. Then, H2 coordinates to Pd and *N*-(2-hydroxyethyl)amino-acetaldehyde ($C_4NO_2H_9$) is liberated as a solvent molecule. Finally, the complex **4** undergoes reductive elimination, in which Pd(II) is reduced to Pd(0) yielding low ligated complex **5**. All relevant bond distances in transition states and intermediates are given in Table 1; the total energies, enthalpies, and free energies of all relevant species are provided in Table 1 of the Electronic Supplementary Material.

The earlier reported results of Muzart [28] showed that proton abstraction from the alcoholic group and oxygen coordination to Pd(II) is possible, even in a weakly acidic medium. Taking into account the fact that we consider the reaction mechanism in the presence of a strong base, we assume that H1 proton abstraction from alcoholic O1 and coordination of O1 to Pd is even more likely (Fig. 1). Our assumption was confirmed by revealing the structures **2**, formed by abstraction of H1 from O1, and **3** in which O1 is coordinated to Pd (Fig. 1).

Table 1 Selected bond distances (Å) in the investigated species for the mechanism of formation of the Pd(0) complex

	1	**2**	**3**	TS1	**4**	TS2	**5**
Pd–N1	2.11	2.10	2.14	2.08	2.28	2.38	2.18
Pd–N2	2.11	2.10	4.64	4.58	–	–	–
Pd–Cl1	2.38	2.41	2.42	2.39		2.40	2.98
Pd–Cl2	2.38	2.41	2.41	2.38	2.40	2.38	2.41
O1–H1	0.96	1.19	–	–	–	–	–
Pd–O1	4.66	3.05	2.01	2.52	–	–	–
C1–H2	1.10	–	1.11	1.10	1.17	–	–
Pd–H2	2.85	3.28	3.06	1.97	1.53	1.50	–
Cl1–H2	3.73	3.91	4.74	2.97	2.78	2.18	–

The calculations were performed for acetonitrile as the solvent

The natural bond orbital (NBO) analysis of **2** shows that p^2ds hybridized Pd forms covalent bonds with both chlorines and nitrogens. The *p* orbitals of the ligating atoms participate with over 80% in the bonds around palladium. Palladium bears positive charge (0.294), while the most negative charge is present on oxygen O1 (−0.838). The HOMO of **2** is delocalized among several atoms, with a

significant contribution coming from O1, while the LUMO shows that the most electron-deficient area is around Pd (Fig. 1 of Electronic Supplementary Material). All of these facts indicate possible coordination of O1 to Pd. As a result, we have revealed the structure **3** (Fig. 1).

The NBO analysis of **3** shows that the p^2ds hybridized Pd forms covalent bonds with O1 and both chlorines. The lone pair on N1 (sp^3 orbital) delocalizes into the σ^* antibonding Pd–O1 orbital, and into the formally empty p orbital of Pd. Each Pd–Cl bond delocalizes into the adjacent σ^* antibonding Pd–Cl orbital, whereas the Pd–O1 bond delocalizes into both σ^* antibonding Pd–Cl orbitals. As a consequence, the occupancies of all palladium bonds are low (about 1.90).

Our experience with the preactivation process of **1** [13, 14] shows that β hydrogens (in regard with Pd) have affinity to coordinate to Pd. As in **3** H2 has the most favorable position (Table 1), we supposed that a nucleophilic attack of H2 to palladium(II) is a plausible next step of the reaction. In agreement with this assumption is the shape of the HOMO of **3** (Fig. 2). Namely, the HOMO is delocalized over several atoms, but a significant contribution comes from H2. Our assumption was confirmed by revealing transition state TS1 (Fig. 1). The results of the intrinsic reaction coordinate (IRC) calculation for TS1 are presented in Fig. 2 of the Electronic Supplementary Material. The formation of TS1 requires an energy barrier of 160.1 kJ/mol. In TS1 the Pd–O1 bond is completely broken, while Pd–H2 bond is being formed, and C1–H2 bond is being broken (Table 1). It is worth pointing out that hydrogen is transferred from carbon to palladium as a hydride ion. This transfer leads to the formation of the intermediate **4** (Fig. 1) and a completely separated molecule (*N*-(2-hydroxyethyl)amino-acetaldehyde), which probably further acts as a solvent molecule. For this reason we excluded the *N*-(2-hydroxyethyl)amino-acetaldehyde molecule from further consideration.

The NBO analysis of **4** reveals that the intermediate complex exhibits a square-planar coordination, in which Pd forms covalent bonds with both chlorines and hydrogen. As for nitrogen, its almost pure p orbital donates density to the formally empty p orbital (with little s and d mixing) on Pd. The Pd–H2 orbital delocalizes into both σ^* antibonding Pd–Cl orbitals, and vice versa.

In the further course of the reaction **4** undergoes reductive elimination of HCl. Our investigation shows that this step of the reaction proceeds via early transition state TS2, which requires an activation energy of 86.7 kJ/mol. The results of the IRC calculation for TS2 are presented in Electronic Supplementary Material as Fig. 3. In TS2 the Pd–H2 and Pd–Cl1 bonds are being cleaved, whereas the Cl1–H2 bond is being formed (Table 1), implying that the HCl molecule leaves the reaction system. This process leads to the formation of the catalytically active Pd(0) complex, the final product of the preactivation process (**5** in Fig. 1).

The NBO analysis of **5** reveals that palladium is ps hybridized. The ligating atoms (chlorine and nitrogen) participate in bonds around palladium with more than 90%. The Pd–Cl2 bond delocalizes into the σ^* antibonding Pd–N1 orbital, and vice versa. Pd bears five lone pairs in the d orbitals. The HOMO map of **5** is in agreement with this fact, as it delineates that the most electron-sufficient area is palladium (Fig. 2). The electronic structure of **5** confirms our assumption that reduction of palladium(II) to palladium(0) is achieved in the preactivation reaction. This low ligated complex acts as a nucleophile in the further step of the Heck reaction, i.e., oxidative addition.

Our computations performed under vacuum conditions show that the formations of TS1 and TS2 require activation barriers of 174.4 and 101.8 kJ/mol (Table 2 of Electronic Supplementary Material). The applied solvation model (CPCM) slightly influences the structures of the investigated species (Table 3 of Electronic Supplementary Material), and lowers the activation energies. The obtained activation barriers are in agreement with the temperature regime of our experiments on the Heck reaction [13, 21, 27].

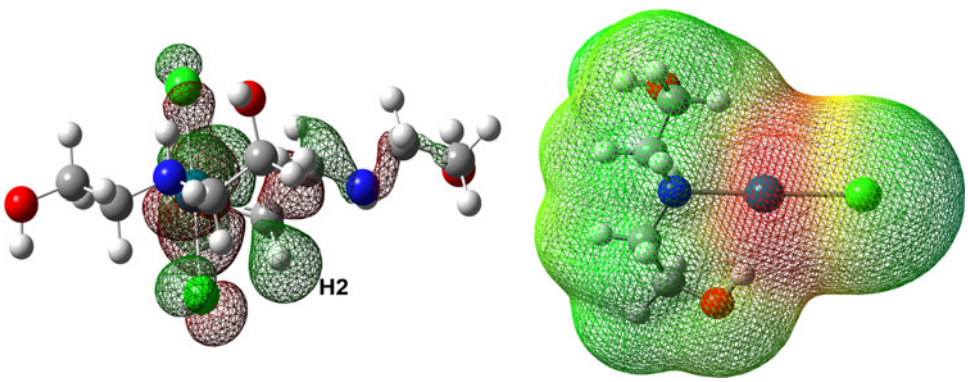

Fig. 2 HOMO of **3** and HOMO map of **5**. In the HOMO map of **5** the most electron-sufficient area is indicated in *red*. In the grayscale image, the darker region (around Pd) depicts the greatest values of the HOMO

Methods

All calculations were carried out using the Gaussian 09 program [29] using the M06 functional. The triple split valence basis set 6-311G(d, p) was used for C, H, O, N, and Cl, whereas LANL2DZ+ECP [30] was employed for the Pd centre. M06, a hybrid meta functional, is a functional with good accuracy "across-the-board" for transition metals, main group thermochemistry, medium-range correlation energy, and barrier heights [31]. The geometrical parameters of all stationary points and transition states were optimized for acetonitrile ($\varepsilon = 35.69$) as the solvent, using the conductor-like solvation model (CPCM) [32, 33]. All calculated structures were confirmed to be local minima (all positive eigenvalues) for ground state structures, or first-order saddle points (one negative eigenvalue) for transition state structures, by frequency calculations. The intrinsic reaction coordinates (IRCs), from the transition states down to the two lower energy structures, were traced by using the IRC routine in Gaussian in order to verify that each saddle point is linked with two putative minima. Evolution of relevant bonds along the reaction pathway was estimated by using the natural bond orbital analysis (Gaussian 09 version) [34].

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