



Theoretical study on Pd-catalyzed reaction of aryl iodide with unsymmetrical alkyne

Yanan Tang, Siwei Bi*, Yuxia Liu, Congcong Liu, Haosheng Liang, Baoping Ling

School of Chemistry and Chemical Engineering, Qufu Normal University, Qufu 273165, PR China

ARTICLE INFO

Article history:

Received 2 July 2015

Received in revised form

7 December 2015

Accepted 11 December 2015

Available online 18 December 2015

Keywords:

Unsymmetrical alkyne

Reaction mechanism

Pd catalysis

DFT

ABSTRACT

With the aid of density functional theory (DFT) calculations, the Pd-catalyzed reactions of aryl iodide with unsymmetrical alkyne leading to two products containing C(sp³)–I bond (**P3** and **P4**) and one product containing a three-membered carbocyclic unit (**P5**), have been studied theoretically. It is found that both the alkyne insertion and the subsequent C=C bond insertion involved in the reaction are the major thermodynamic driving forces. The alkyne insertion instead of the C(sp³)–I reductive elimination is predicted to be rate-determinant. Similar barrier heights calculated for the two insertion modes of unsymmetrical internal alkyne (**TS₃₋₄** and **TS₃₋₄**) lead to the products **P3** (47.2%) and **P4** + **P5** (48.8%) having similar product yields. The intriguing formation of the product containing a three-membered carbocyclic unit (**P5**) was investigated in details. The second alkene insertion is found to be kinetically more favored than the C(sp³)–I reductive elimination, leading to product **P5** (39.0%) more productive than **P4** (9.8%). The remarkably thermodynamically favored β–H elimination is the key factor enabling formation of **P5**. Why significant bulky phosphine ligand such as P(t-Bu)₃ instead of small one such as P(Me)₃ was employed experimentally have also been rationalized based on our calculation results.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Generation of new carbon–carbon and carbon–heteroatom bonds by catalytic cross-coupling reactions is of significant importance. It has been demonstrated that transition metal complexes are powerful species in catalyzing cross-coupling reactions. Among transition metals, palladium proved to be the most commonly used because of its distinctive ability of catalyzing multiple redox reactions, and high functional group tolerance, such as the Mizoroki–Heck [1], Suzuki–Miyaura [2], Negishi [3], Sonogashira [4], Stille [5], and Kumada couplings [6]. Important studies related to C–I activation, carbopalladation of alkynes and cyclopropane formation have been reported [7]. The Lautens group have recently developed a novel type of Pd(0)-catalyzed *intramolecular* cross-coupling reactions to generate C–I bond [8]. Tong et al. also described interesting variants of this type of reactions towards the carbon–halogen bond generation frameworks [9,10] but this process requires higher temperatures and greater catalyst loading. Following these experimental advances, Houk and Lautens

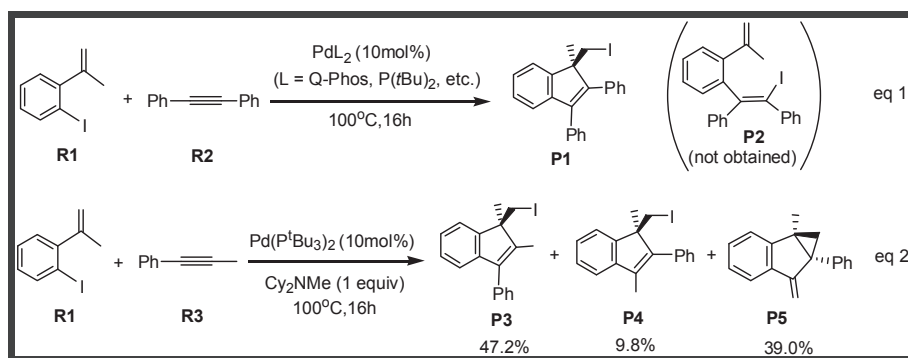
performed a theoretical study on the Pd(0)-catalyzed *intramolecular* carbohalogenation of alkenes, in which the mechanism and origins of reactivity and selectivity in the alkyl halide reductive elimination from Pd(II) species were specifically explored [11].

In 2012, the Lautens group reported the reactions of aryl iodides with internal alkynes leading to the generation of new C–C and C–I bonds [12]. In comparison with the carbohalogenation reactions mentioned above, this type of reactions was highlighted as an *intermolecular* process. Scheme 1 shows the reaction equations studied experimentally. Eq. (1) is the reaction of aryl iodide **R1** with symmetric internal alkyne **R2**, and Eq. (2) is the one with unsymmetrical internal alkyne **R3**. With the help of density functional theory (DFT) calculations, we have theoretically investigated in our previous work [13] the reaction mechanism of reaction Eq. (1) and elucidated why product **P1** could be obtained while the desired product **P2** could not.

Interestingly, when the internal alkyne employed in the experiments is unsymmetrical as shown in Eq. (2), product **P5** containing a three-membered carbocycle was produced, in addition to the two isomeric products **P3** and **P4** each containing a C–I bond. The X-ray crystal structure of **P5** was determined successfully. The cyclopropane unit is versatile in organic synthesis and commonly present in natural products, and thus growing interests have been attracted

* Corresponding author.

E-mail address: siweibi@126.com (S. Bi).



Scheme 1.

for developing synthetic methods of cyclopropane derivatives [14]. Clearly, the substituents attached on alkyne have a great influence on the intermolecular cross-coupling reactions. Electronic and steric effects of the substituents have been of special interest since these factors are crucial for efficiency, scope, and selectivity of the coupling reactions.

To the best of our knowledge, related theoretical study on the intermolecular coupling reactions with unsymmetrical alkyne to generate new C–C and C–I bonds is very limited [12], and in particular how the product containing a three-membered carbocycle is obtained has not been investigated theoretically. Insight into the reaction mechanisms is instructive and meaningful for more reasonable design of new related reactions. Prompted by these intriguing experimental results, we performed computational studies in this work to theoretically investigate the mechanism, influence of the substituents on alkyne, and the competing pathways of this novel reaction. Our theoretical studies, especially the analysis of influence of the substituents on alkyne, provide a detailed understanding of this novel reaction and helpful information for further related studies.

It can be seen from Scheme 1 that the C(sp³–I) bond is formed in both reactions, implying the C(sp³–I) reductive elimination is involved in the Pd(0)–catalyzed reaction mechanisms. The C(sp²–I) reductive elimination cannot be not involved due to the fact that **P2** was not obtained experimentally in Eq. (1). Previous theoretical [15] and experimental [16] studies have provided a thorough understanding of oxidative addition of aryl halides, the initial step in Pd(0)–catalyzed coupling reactions, which is mainly determined by the Ar–X bond strength [17,18]. In contrast, the opposite reaction, the aryl halide reductive elimination from Pd(II), is rarely studied due to the high endothermicity of this process. Only a few examples of aryl halide reductive elimination have been reported recently by the Buchwald [19], Hartwig [20], and Lautens [21] groups, all employing bulky and electron-rich spectator ligands such as P(*t*-Bu)₃. Recently, Houk, et al. presented a deep theoretical insight into the aryl halide reductive elimination from Pd(II) in catalytic *intramolecular* carbohalogenation of alkenes [11]. In this work, we mainly focus our attention on the intermolecular carbohalogenation of *unsymmetrical* alkynes, and the influence of substituents on the alkynes.

2. Computational details

The molecular geometries of the reactants, intermediates, transition states, and products were fully optimized via DFT calculations at the Becke3LYP level [22] without any constraints. The reliability of the chosen method has been verified by our previous work [13,23] and other theoretical studies of Pd-catalyzed reactions [24]. The M06 method has also been tested for the system studied

in this work by calculating some key steps. The selected steps are (1) the two alkyne insertion modes, which determines the regioselectivity of the reaction leading to **P3** vs (**P4** + **P5**), and (2) the C(sp³–I) reductive elimination vs the C=C insertion into Pd–C(sp³), which determines the regioselectivity of the reaction leading to **P4** vs **P5**. Our calculations indicated that both B3LYP and M06 give similar results. Detailed calculation results are given in the Supporting Information.

In the DFT calculations, the 6–31g(d,p) basis set was used for the C and H atoms, while the effective core potentials (ECPs) of Hay and Wadt with double- ζ valence basis set (LanL2DZ) [25] were chosen to describe the Pd, P and I atoms. Polarization functions were also added [26]: Pd(ζ_f) = 1.472, P(ζ_d) = 0.387 and I(ζ_d) = 0.289. Frequency analyses have been performed to obtain the Gibbs free energies and enthalpies and identify all of the stationary points as minima (zero imaginary frequency) or transition states (one imaginary frequency) on the potential energy surfaces (PES). Intrinsic reaction coordinate (IRC) calculations were also calculated for the transition states to confirm that such structures indeed connect two relevant minima [27]. The basis set at higher level, SDD, was also tested for a few key steps, and we found both LanL2DZ and SDD give similar calculation results. Related calculation results are given in the Supporting Information.

To obtain solvation-corrected relative free energies, we employed a continuum medium to do single-point energy calculations for all of the optimized species, using UAKS radii on the conductor-like polarizable continuum model (CPCM) [28]. Toluene was used as the solvent, corresponding to the experimental reaction conditions. Also, we calculated the solvation energy by optimizing the structures in solution, and found the optimized structures have no large difference from the single-point structures. The optimized structures and related solvation energies are given in the Supporting Information.

In all of the figures that contain potential energy profiles, solvation-corrected relative free energies and enthalpy energies (in parentheses) were presented. In this paper, the solvation-corrected relative free energies were used to analyze the reaction mechanism. All calculations were performed with the Gaussian 09 software package [29].

3. Results and discussion

Corresponding to the experiments, Pd(P^tBu₃)₂ is used as the catalyst in the computation. We first investigate the reaction mechanisms forming products **P3** and **P4** each containing a new formed C(sp³–I) bond and why the considerably bulky P^tBu₃ was employed in the experiments. Then we investigate the intriguing reaction mechanism accessing to product **P5** containing a three-

Download English Version:

<https://daneshyari.com/en/article/1322994>

Download Persian Version:

<https://daneshyari.com/article/1322994>

[Daneshyari.com](https://daneshyari.com)