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How Does Methanol Assist the Hydrogen Transfer in Pd-catalyzed Cyclocarbonylation of Allylic Alcohols? Insights from a DFT Study

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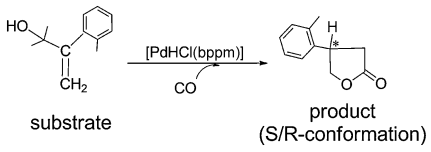
The carbonylation mechanisms of allylic alcohol catalyzed by [PdHCl(bppm)] complex were studied using a density functional theory (DFT) method. The results indicate that the catalytic cycle consists of three main steps: alkene insertion, CO insertion, and hydrogen transfer and product elimination. Pathways with a Pd(II) character are more favorable than that with Pd(IV) character. Methanol serves as the proton shuttle in carbonylation and reduces the energy barrier by 15.4 kcal mol^{-1} below that without methanol assistance.

The carbonylated allylic substrates catalyzed by transition-metal complexes are important precursors for the preparation of β,γ-unsaturated carboxylic acid derivatives.[1] Chiusoli et al. first reported the carbonylation of allylic halides under mild conditions using nickel tetracarbonyl as a catalyst.[2] Negishi and Alper made a breakthrough in Pd-catalyzed cyclocarbonylation with carbon monoxide, which is a useful method for the synthesis of cyclic ketones, lactones, and lactams.[3] Alper et al. have investigated the Pd-catalyzed cyclocarbonylation of allylic alcohols and first synthesized chiral γ-butyrolactones using this reaction (Scheme 1).[4] Recently, a theoretical investigation on β,γ-unsaturated acyl derivatives has been carried out by Bottoni et al. and they reported the mechanism of allyl halides with CO catalyzed by [$PdCl_2(PH_3)_2$].[5] This paper reports the mechanism of the carbonylation reaction catalyzed by [PdHCl(bppm)] (bppm: *tert*-butyl (2*S*,4*S*)-4-diphenylphosphino-2-[(diphenylphosphino)methyl]-1-pyrrolidinecarboxylate) complex using DFT method. As shown in Figure 1, the whole catalytic cycle consists of three main elementary steps: alkene insertion from **1** to **2**, CO insertion from **3** to **4**, and hydrogen transfer together with product elimination from **4** to **7**. The hydrogen-transfer step was found to proceed in two possible different paths according to involvement of Pd(II) or Pd(IV) intermediates (Path Pd(IV) and Path Pd(II)), and methanol-assisted effect has also been taken into consideration in Path Pd(II) (Path Pd(II) with methanol assistance). In Figure 1, Path Pd(IV), Path Pd(II), and Path Pd(II) with methanol assistance correspond to Path A, Path B, and Path B–OH, respectively. This paper shows details of the mechanism of Pd-catalyzed cyclocarbonylation of allylic alcohol and the important role of methanol solvent.



Scheme 1.

In the whole catalytic system, catalyst [PdHCl(bppm)] reported by experiment is simplified as [PdHCl{$H_2P(CH_2)_2$-PH_2}] in this study. The simplification for transition-metal complexes is reliable in our previous theoretical studies.[6] All the geometry optimizations, frequency analyses, and other properties of the model system were performed using B3LYP method[7] implemented in the Gaussian03 program package.[8] LANL2DZ basis set[9] is used for Pd and 6-31+G** basis set for the other atoms (denoted as BSI). Transition states are confirmed by existence of only one characteristic imaginary frequency mode in vibration analysis. Intrinsic reaction coordinates (IRC) calculations are performed in order to confirm the transition state connecting the intermediates. Solvent effects (methanol) were evaluated using polarizable continuum model (PCM) performing single-point calculations on gas-phase optimized geometries.

A general mechanism description is shown in Figure 1. In the alkene-insertion step (from **1** to **2**), H^1 of Pd transfers to C^1 of allylic alcohol to form **2** via **TS1-2**. The C^1–C^2 double bond is changed to a single one. In the CO-insertion step (from **2** to **4**), one CO molecule coordinates with Pd and inserts into the C^3–Pd bond via **TS3-4** with a three-membered ring of Pd–C^2–C^3. And then the Pd–C^2 bond is broken and **4** is formed. Rotation in **4** leads the hydroxy group to become closer to the Pd–C^3 bond and several conformations of **5** are formed with six-coordinated or four-coordinated structures with Pd center. In hydrogen transfer and product-elimination steps (from **4** to **7**), three possible pathways are proposed like Path A, Path B, and Path B–OH. In Path A, O^1–H^2 is broken first and H^2 is transferred to Pd center. The coordination number of **6** is six, this means Pd(IV) character in Path A. Then O^1 attacks C^3 of carbonyl group via **TS6-7** to complete the product elimination. In Path B, transfer of H^2 to Pd center, breaking of O^1–H^2 bond and attacking of O^1 to C^3 (nucleophilic attacking of O^1 of the OH group to C^3 of the acyl group) occur at the same time through a ring-closing transition state (**TS5-7**). In Path B–OH, the involvement of methanol solvent in Path B was considered. The coordination number of Path B and Path B–OH is always four from **5** to **7**, which corresponds to a Pd(II) character. Finally, the Pd catalytic species is regenerated and the substrate could coordinate with **7** to start another catalytic cycle.

The potential energy profiles of the catalytic reaction are shown in Figure 2. The barriers of alkene-insertion step and CO-insertion step are 3.9 kcal mol^{-1} from **1** to **2** and 11.1 kcal mol^{-1} from **3** to **4** respectively. In Path A and Path B, the rate-determining step is hydrogen transfer. In path A, the hydrogen-transfer step is endothermic with 51.5 kcal mol^{-1} in barrier from **5** to **6**. The product elimination process is only 7.2 kcal mol^{-1} via **TS6-7**. In path B, the hydrogen-transfer and product-elimination steps happen concomitantly and the barrier is

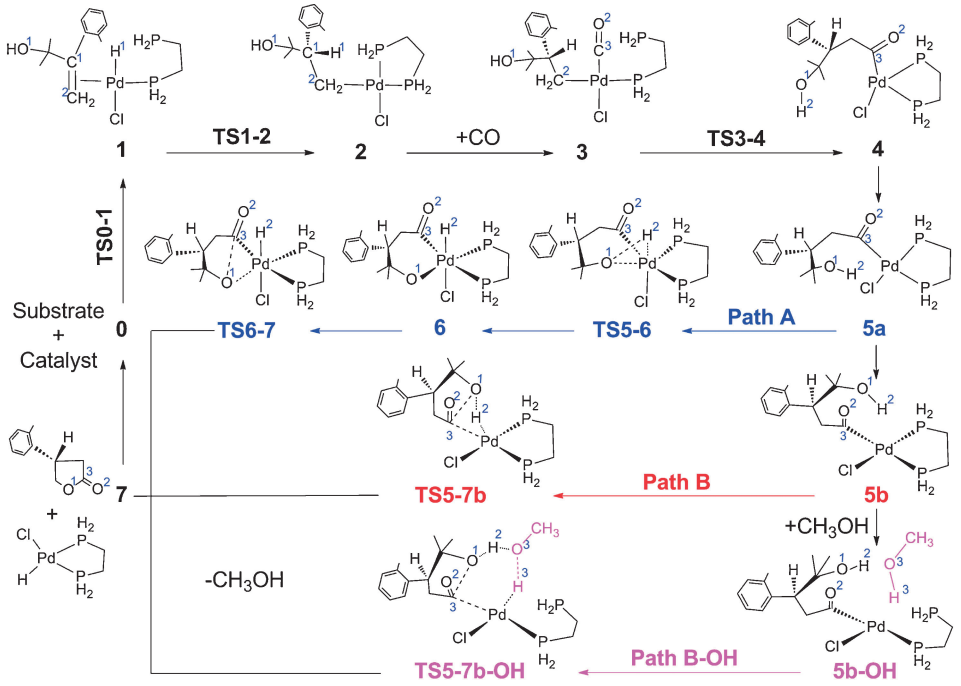


Figure 1. Mechanism of cyclocarbonylation of allylic alcohol catalyzed by Pd catalyst.

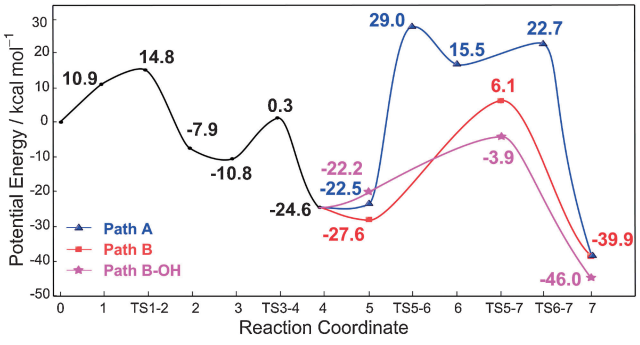


Figure 2. Potential energy profiles of catalytic cycle of Pd-catalyzed cyclocarbonylation of allylic alcohol.

33.7 kcal mol^{-1}. **TS5-7** has a four-member ring of Pd–C^3–O^1–H^2. The distances of O^1–H^2, Pd–C^3, O^1–C^3, and H^2–Pd bonds are 1.041, 2.931, 1.708, and 2.080 Å, respectively. It means the cleavage of Pd–C^3 bond and formation of O^1–C^3 and H^2–Pd bonds. It is obvious that Path B is more favorable than Path A, which implies that the pathway with a Pd(IV) character will lead to a higher reaction barrier of O^1–C^3 formation compared with that with a Pd(II) character. Solvent effect calculations indicate the solvent (methanol) does not change the trends presented in the potential energy surfaces (See Table S2 in Supporting Information[10]).

A lot of studies on the hydrogen transfer in the transition-metal catalysis suggest that the charge in H^2 is closely related to energy barrier of hydrogen transfer. The more positive charge of transferred hydrogen has, the lower energy barrier is. In complex **5** of Paths B and B–OH in which the hydrogen-transfer steps both possess the Pd(II) character, the APT (atomic polar tensor) charges of transferred hydrogen (Path B: H^2, Path B–OH: H^3) are 0.250 and 0.379, respectively. Path B–OH with more positive H^3 has lower barrier of hydrogen-transfer step than Path B. These calculated results agree with other studies on the hydrogen transfer in transition-metal catalysis.

Table 1. Bond lengths (unit: Å) of key structures in the catalytic cycle

State	O^1–H^2	Pd–H^2	O^1–C^3	O^3–H^3	H^2–O^3
5a	0.976	2.890	3.206	—	—
TS5-6	1.607	1.561	3.068	—	—
6	2.600	1.543	2.944	—	—
TS6-7	2.726	1.539	2.150	—	—
7	2.776	1.547	1.375	—	—
5b	0.971	2.700	3.003	—	—
TS5-7b	1.041	2.080	1.708	—	—
7	2.776	1.547	1.375	—	—
5b-OH	0.981	—	2.573	0.979	1.830
TS5-7b-OH	1.570	—	1.434	1.090	1.026
7b-OH	1.993	—	1.359	4.718	0.972

The energy barrier is still too high even for Path B with a Pd(II) character. Interestingly, methanol solvent is found to be of importance in the whole reaction. In Path B–OH, hydroxy transfers H to the methanol, the latter donates one proton to the Pd center and O^1 attacks C^3 at the same time. The bond lengths of O^1–H^2 and O^3–H^3 become longer and the distances of O^1–H^3 and H^3–Pd become closer via **TS5-7** (Table 1). Methanol acts like a bridge to accept hydrogen from O^1 and donate hydrogen to Pd center. A figure of three-dimensional structures with bond

lengths from **5** to **7** in three pathways is shown in Figure S1.[10] Finally, altogether with hydrogen transfer, the butyrolactone product is formed via the nucleophilic attacking of O^1 of the OH group to C^3 of the acyl group. It is obvious that the methanol assistance decreases the barrier of hydrogen transfer, which is 18.3 kcal mol^{-1} in Path B–OH. It is much lower than that of Path A (51.5 kcal mol^{-1}) and B (33.7 kcal mol^{-1}). Thus, the involvement of alcohol solvent is very important in the Pd-catalyzed cyclocarbonylation of allylic alcohol.

In summary, this paper investigated the carbonylation of allylic alcohol catalyzed by Pd catalyst using DFT method. The calculated results indicate that there are three possible pathways in hydrogen transfer. The pathways with Pd(II) character are more favorable than those with Pd(IV) character. Methanol assistance plays a very important role and effectively decreases the energy barrier of hydrogen transfer in Path B–OH.

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References and Notes

1 A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 433.
2 a) G. P. Chiusoli, *Angew. Chem.* **1960**, *72*, 74. b) E. J. Kuhlmann, J. J. Alexander, *Coord. Chem. Rev.* **1980**, *33*, 195. c) G. García-Gómez, J. M. Moretó, *J. Am. Chem. Soc.* **1999**, *121*, 878.
3 a) C. Copéret, S. Ma, E.-i. Negishi, *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2125. b) B. El Ali, K. Okuro, G. Vasapollo, H. Alper, *J. Am. Chem. Soc.* **1996**, *118*, 4264.
4 a) W.-Y. Yu, C. Bensimon, H. Alper, *Chem.—Eur. J.* **1997**, *3*, 417. b) B. El Ali, H. Alper, *Synlett* **2000**, 161.
5 M. A. Carvajal, G. P. Miscione, J. J. Novoa, A. Bottoni, *Organometallics* **2005**, *24*, 2086.
6 a) Y. Chen, Y. Tang, S. Liu, M. Lei, W. Fang, *Organometallics* **2009**, *28*, 2078. b) Z. Chen, Y. Chen, Y. Tang, M. Lei, *Dalton Trans.* **2010**, *39*, 2036. c) M. Lei, W. Zhang, Y. Chen, Y. Tang, *Organometallics* **2010**, *29*, 543.
7 a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372. b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785.
8 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09 (Revision B.01)*, Gaussian, Inc., Wallingford, CT, **2010**.
9 P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299.
10 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

