

# Mechanism of Pd(NHC)-Catalyzed Transfer Hydrogenation of Alkynes

Peter Hauwert, Romilda Boerleider, Stefan Warsink, Jan J. Weigand, and

Cornelis J. Elsevier

*J. Am. Chem. Soc.* **2010**, *132* (47), pp 16900–16910.

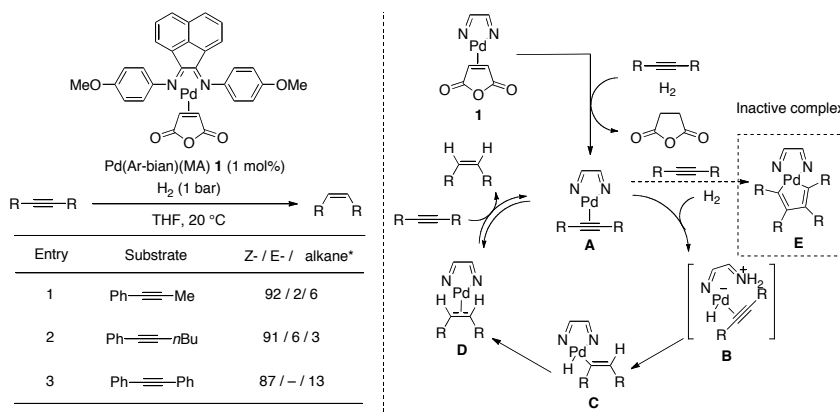
## 1. Introduction

- The partial hydrogenation of alkynes to *cis*-alkenes is a very important transformation.
- Heterogeneous catalyst (Lindlar catalyst) has been used for the reaction.
- => Problem: *cis/trans*-isomerization and over-reduction
- Some homogeneous catalyst that chemo- and stereoselectively hydrogenate alkyne were reported.<sup>1</sup> However, the reaction mechanism has not been well studied.

### 1.1. The Authors' Previous Work<sup>2</sup>

- The authors found that complex [Pd(Ar-bian)(MA)] **1** is able to homogeneously hydrogenate alkynes to form the *Z*-alkenes, and studied the reaction mechanism.
- The catalyst still has problems; low reproducibility, instability of the catalyst, considerable over-reduction for arylalkynes.

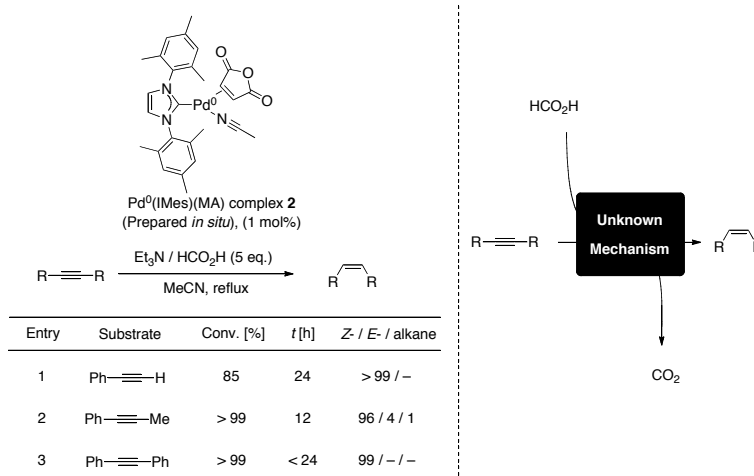
**Scheme 1.** Semihydrogenation of alkyne with homogeneous Pd catalyst.



### 1.2. This work<sup>3</sup>

- The authors found another complex suitable for the reaction; Pd(NHC) catalyst **2** (Scheme 2).
- In the case of **2**, over-reduction was fully inhibited when TEAF (triethylammonium formate) was adopted.

**Scheme 2.** Semihydrogenation of alkyne with Pd (NHC)-catalyst using formic acid as a hydrogen donor.



– Aim of this work

(1) To reveal the mechanism of the Pd(NHC)-catalyzed hydrogen transfer using formic acid

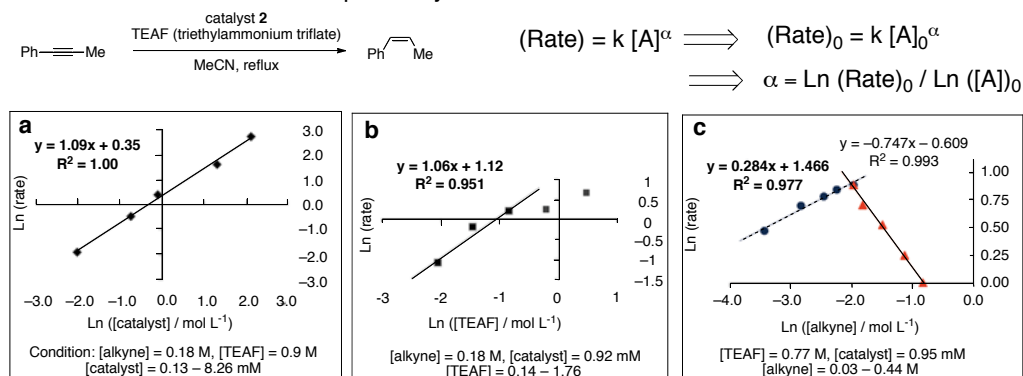
(2) To understand the reason for inhibition of over-reduction

## 2. Results and Discussion

### 2.1. Kinetic Studies

#### 2.1.1. Determination of Rate Equation by Initial Rate Method (Scheme 4)

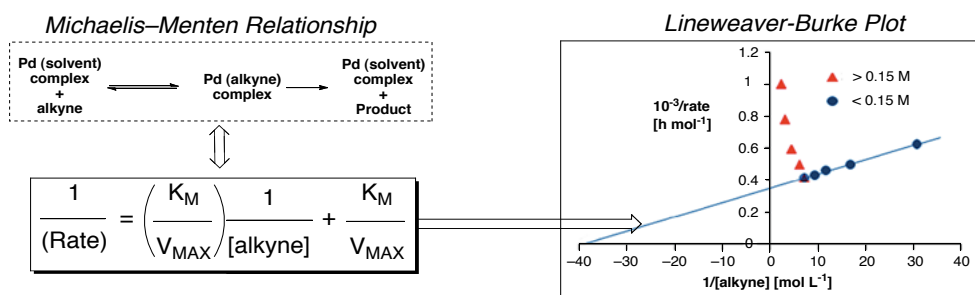
**Scheme 4.** Determination of Rate Equation by Initial Rate Method.



$$\implies \frac{d(\text{substrate})}{dt} = -k_{\text{cat}} \cdot [\text{alkyne}]^{0.28} \cdot [\text{TEAF}] \cdot [\text{catalyst}] \quad ([\text{substrate}] < 0.15 \text{ M}) \quad (\text{eq. 1})$$

- Substrate and formate coordinate to Pd before rate-determining step (eq. 1).
- Catalyst and alkyne satisfy Michaelis-Menten relationship when alkyne concentration is low (< 0.15 M); There is an equilibrium between alkyne and catalyst (scheme 5).

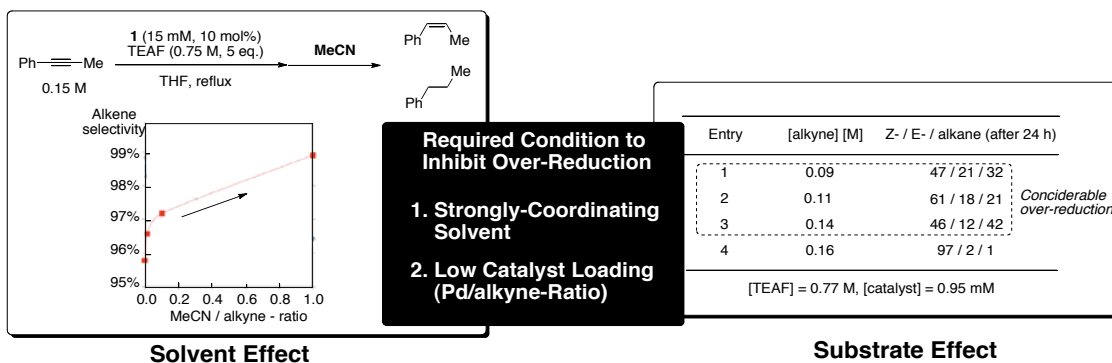
**Scheme 5.** Michaelis-Menten Relationship between Alkyne and Catalyst.



- When alkyne concentration is high (> 0.15 M, triangle), the reaction is possibly inhibited by formation of inactive complex (cf. scheme 1, palladacyclopentadiene E).

#### 2.1.2. The key factor for over-reduction

- The effects of solvent and substrate are the key factor of over-reduction.

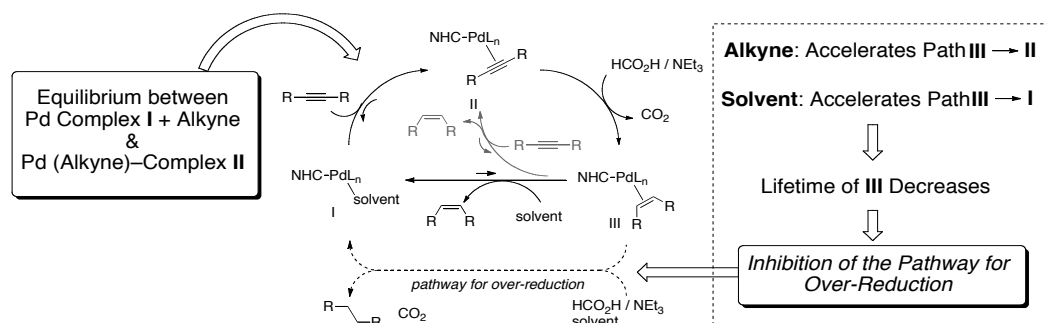


**Figure 1.** Effect of Strongly-Coordinating Effect and Substrate on Over-Reduction.

### 2.1.3. Simplified Reaction Mechanism

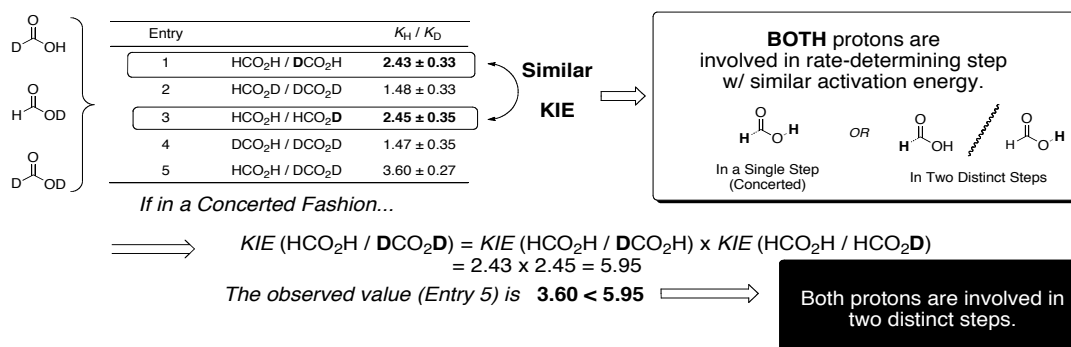
– A simplified mechanism is proposed based on the observations discussed above.

**Scheme 5.** Simplified reaction mechanism focusing on competition between alkyne, solvent, and Pd (alkene)-complex.



### 2.2. Isotopic Labeling of the Hydrogen Donor

– The role of the two hydrogens of formic acid was investigated by D-labeling of formic acid.



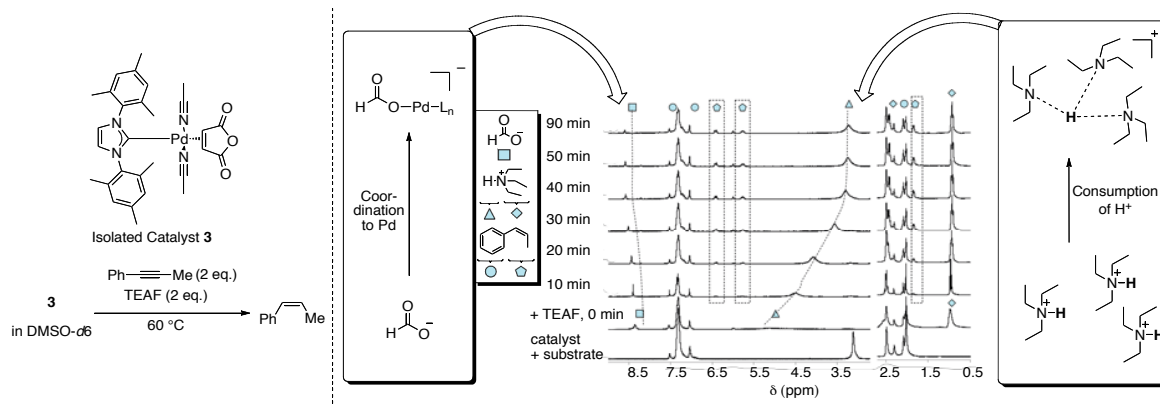
**Figure 2.** Kinetic Isotopic Effect of Two Protons of Formic Acid.

### 2.3. NMR Studies

#### 2.3.1. $^1\text{H}$ NMR study of the reaction catalyzed by isolated catalyst 3.

– The reaction was monitored by  $^1\text{H}$  NMR to gain more insight into the species present, using catalyst 3, which had been isolated from solution of 1 in MeCN.

**Scheme 6.**  $^1\text{H}$  NMR Study of the reaction with isolated catalyst 3 in DMSO- $d_6$ .



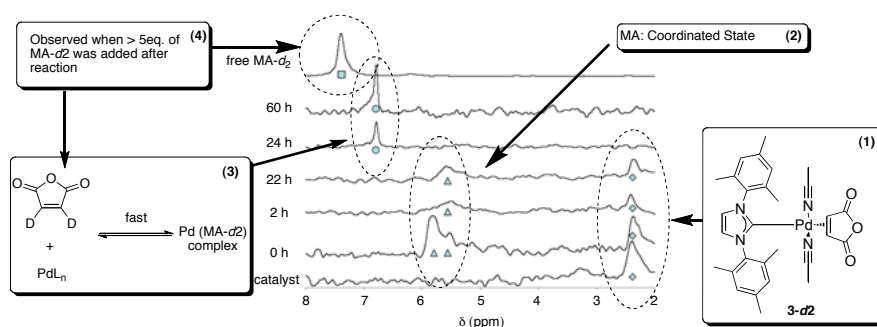
– As the reaction proceeds, positive charge is distributed over more than one amine.

– Formate anion coordinates to Pd species.

### 2.3.2. $^2\text{H}$ NMR study of labeled catalyst 3-d2.

– Aim of this study; to know the state of MA(maleic anhydride) in the reaction

– 3-d2 (catalyst with labeled MA) is used in the reaction (DMSO-d6, 25 °C) to observe spectrum.



**Figure 3.**  $^2\text{H}$  NMR Study of Labeled Catalyst 3-d2.

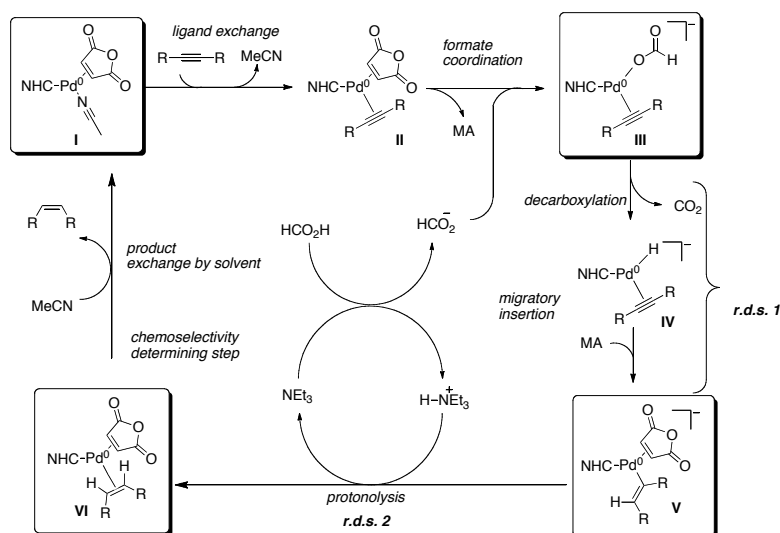
– Part of MA is clearly coordinated to Pd catalyst (cf. previous case, scheme 1)

### 2.4. Proposed Catalytic Cycle.

– On the basis of the results described above, the catalytic cycle is proposed (scheme 6.)

- (1) A Pd(formate) is involved. (2.3.1.).
- (2) Two rate-determining steps with similar activation energy (2.2.)
- (3) Substrate and formate are coordinated to Pd before the rate-determining steps (2.1.).
- (4) Coordination of solvent and alkene affects alkene-selectivity (2.1.).

**Scheme 6.** Proposed Catalytic Cycle for Transfer Hydrogenation of Alkynes to Z-Alkenes, Catalyzed by Complex 2 with TEAF as Hydrogen Donor.



### 3. Conclusion

- The mechanism of Pd<sup>0</sup>(IMes)-catalyzed transfer hydrogenation of alkynes has been elucidated .
- Over-reduction of alkyne is inhibited by strong competition between substrate and solvent for a Pd(alkene) intermediate occurring in the reaction.

### 4.Reference

- 1) Werner, H. et.al. *J. Am. Chem. Soc.* **1989**, *111*, 7131–7437.
- 2) Elsevier, C. J. et. al. *J. Am. Chem. Soc.* **2005**, *44*, 2026–2029.
- 3) Elsevier, C. J. et. al. *Angew. Chem. Int. Ed.* **2008**, *47*, 3223–3226.