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Observation of Unusual Kinetics in Heck Reactions of Aryl Halides: The Role of Non-Steady-State Catalyst Concentration

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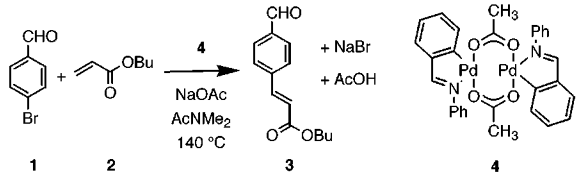
Transient behavior at the beginning of homogeneous catalytic reactions is a common phenomenon, since the active catalytic species is often formed under reaction conditions. If this process is slow, a significant number of turnovers of the catalytic cycle may occur before the catalytic species within the reaction network attain “steady-state”.[1] Induction periods have implications for the extraction of meaningful kinetic information from experimental data, especially when initial rate methods are employed. In situ techniques to monitor reaction progress can be helpful in identifying cases of transient behavior and can provide a valuable tool for assessing reaction complexity in general.[2−4]

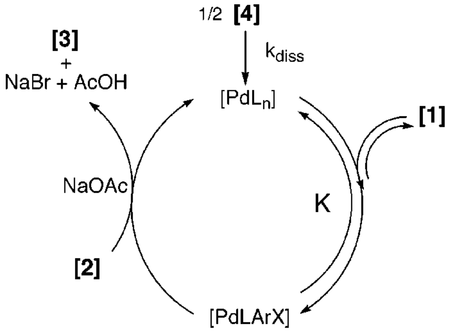
In the past few years, a number of reports have noted the high activity of dimeric Pd(II) complexes such as **4** in Heck olefinations of aryl halides.[3b,4,5] In the conventionally accepted reaction mechanism,[6] a four-coordinate aryl-Pd(II) intermediate is formed by oxidative addition of the aryl halide to a Pd^0 complex prior to olefin addition. This suggests that cleavage of the dimeric precursor complex, reduction of Pd^{2+}, and ligand dissociation combine to give a viable catalytic species. If these processes occur on a time scale comparable to that of the catalytic reaction, non-steady-state catalysis could occur while the active catalyst is forming.

We report here unusual kinetic behavior related to an induction period in the Heck olefination of *p*-bromobenzaldehyde (**1**) with butyl acrylate (**2**) using the dimeric palladacycle complex (**4**)[7] as a catalyst precursor (Scheme 1). In previous kinetic studies (carried out under conditions which included water in the range from greater than ca. 200 ppm up to 2 M), we observed saturation kinetics in **1** and first-order kinetics in **2**, suggesting that the oxidative addition product represented the resting state within the catalytic cycle.[4] This behavior was found to be general for Pd catalysts with different ligand types. We also reported that when the system contained <200 ppm of water, the overall rate was significantly suppressed and the reaction exhibited a prolonged induction period.

Scheme 1. Heck Reaction with Pd Precursor Complex **4**



Scheme 2. Reaction Mechanism According to Eq 2[10]



In this communication, we focus on the kinetics of the reaction under the dry conditions, using reaction calorimetry to monitor reaction progress.[4,8] An initially low reaction rate was observed to increase slowly until ca. 50% conversion of **1**. Analysis of the reaction progress after this induction period revealed an excellent fit to Michaelis−Menten kinetics in the aryl halide substrate **1**, according to eq 1. The constant V_m represents the maximum rate (incorporating the catalyst concentration), and the Michaelis constant K is the inverse binding constant of [**1**].

$$\text{rate} = \frac{V_m[\mathbf{1}]}{(K + [\mathbf{1}])} \qquad (1)$$

$$V_m = 0.302\ \text{M}\cdot\text{min}^{-1} \qquad K = 0.022\ \text{M}^{-1}$$

No dependence of reaction rate on the olefin **2** was observed. This most curious observation was in direct contrast to the first-order dependence we found previously.

We turned to a closer examination of the induction period to understand this apparently anomalous behavior. It is important to note that experimental procedures designed to extract concentration dependences and kinetic parameters, as well as mathematical models such as that shown in eq 1, implicitly require that the total amount of catalyst within the reaction network be constant. Processes which remove catalyst from the cycle, such as catalyst deactivation by precipitation of Pd, have been discussed, but less attention has been devoted to processes which may augment the active catalyst concentration during reaction.[9] However, if

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(1) The term “steady-state” refers in this context to a stable total concentration of catalytic species within the reaction cycle.

(2) For a detailed experimental examples of induction periods in asymmetric hydrogenation, see: (a) Heller, D.; Holz, J.; Borns, S.; Spannenberg, A.; Kempe, R.; Schmidt, U.; Börner, A. *Tetrahedron: Asymmetry* **1997**, *8*, 213−222. (b) Drexler, H.-J.; Baumann, W.; Spannenberg, A.; Fischer, G.; Heller, D. *J. Organomet. Chem.* **2001**, *621*, 89−102. (c) Börner, A.; Heller, D. *Tetrahedron Lett.* **2001**, *42*, 223−225.

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(7) Granell, J.; Sainz, D.; Solans, X.; Font-Alba, M. J. *Chem. Soc., Dalton Trans.* **1986**, 1785. Complex **4** was synthesized as described herein and purified by recrystallization from chloroform/heptane (see also: Schmees, N. Dissetration, University of Köln, 1998).

(8) Initial substrate concentrations in the range 0.16−0.24 M **1**, 1.67−2.5 equiv of **2**, and 10 μM **4** (ca. 0.01 mol % total Pd based on **1**).

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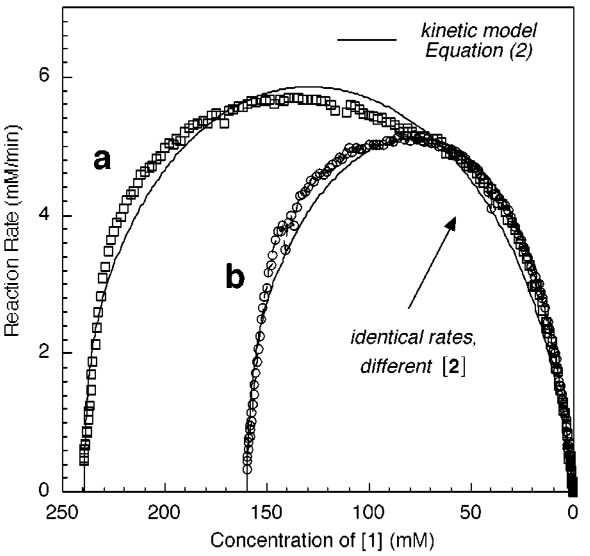

Figure 1. Reaction rate vs concentration of **1** for Heck reactions as shown in Scheme 1. Symbols represent experimental data: (a) [**2**]:[**1**] = 1.67; (b) [**2**]:[**1**] = 2.5. Solid lines represent the model fit to eq 2.

decomposition of the catalyst complex **4** to form PdL_n (see Scheme 2) is slow in the absence of water, the concentration of active catalyst species may increase as the reaction proceeds.

A simple model for decomposition of the dimeric Pd precursor assumes that complex **4** undergoes irreversible decomposition and combines the ill-defined steps which produce the zerovalent active species PdL_n into a single first-order process with rate constant k_{diss}. At any instant in time, *t*, the steady-state kinetic rate law given in eq 2 may then be used to describe the network shown in Scheme 2. Here we note that the form is similar to that of eq 1, except that the mechanism requires a first-order dependence on olefin concentration [**2**] in addition to the time dependence of catalyst concentration.

$$\text{rate} = \frac{V_m'[\mathbf{1}][\mathbf{2}](1 - \exp(-k_{diss}t))}{(K + [\mathbf{1}])} \qquad (2)$$

$$V_m' = 1.85\ \text{M}\cdot\text{min}^{-1} \qquad k_{diss} = 0.030\ \text{min}^{-1}$$

Figure 1 shows experimental data from two reactions exhibiting the pronounced induction period. Rate is plotted in the direction of decreasing concentration of the aryl halide substrate (increasing reaction time). At any given value of [**1**], [**2**] is different in the reactions shown in **a** and **b** in Figure 1. Thus the overlap of the two rate curves during the latter half of the reactions shows the region in which the reaction exhibits no apparent dependence on [**2**], following eq 1.

The solid lines in Figure 1 show that when the model of eq 2 is applied instead, an excellent fit is obtained for data over the *entire* course of the reaction. The fact that a single value of k_{diss} may be used to describe reactions carried out under different substrate concentrations provides strong support for the hypothesis that the slow addition of catalyst into the catalytic cycle leads to the pronounced induction period and the unusual subsequent kinetic behavior.

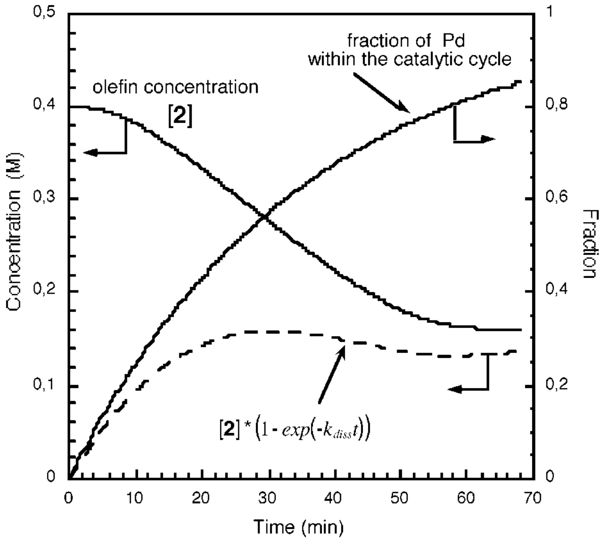

Figure 2. Concentrations of species calculated from the kinetic model of eq 2 applied to the experimental data from Figure 1a.

We may rationalize why a slow buildup of active catalyst manifests itself as zero-order kinetics in a substrate concentration as follows. The slow transformation of **4** to the active species PdL_n and its subsequent rapid reaction with **1** results in an increase in the concentration of the oxidative addition product PdLArX. Figure 2 shows that the rate at which new active catalyst species are introduced into the catalytic cycle becomes almost perfectly balanced by the rate at which [PdLArX] reacts with a decreasing concentration of **2**, thus reconciling eqs 1 and 2.

Hence anomalous kinetics may be observed when the rate-limiting step is not directly on the catalytic cycle. An analogous situation arises in gas−liquid reactions when the rate at which molecules of the gaseous reactant enter the solution is balanced by the rate at which they are consumed in the reaction, giving zero-order behavior in [substrate] often erroneously attributed to saturation kinetics.[11] The current example carries the added complexity that the limiting concentration is that of a catalyst and not a substrate.

This example may have implications for other cases where observations of unusual kinetics have been made. In a recent report concerning the mechanism of amination of aryl halides using $Pd(BINAP)_2$ catalysts, Hartwig and co-workers observed zero-order dependence on both ArX and amine substrates at high [ArX].[12] This might be rationalized by eq 2 if rate-limiting dissociation of a BINAP ligand *external* to the cycle resulted in a balance between the rate of new species entering the cycle and the rate of amination. This interpretation would obviate the need to invoke the concerted product release/ligand reassociation step required to regenerate $Pd(BINAP)_2$ if this species lies directly on the catalytic cycle as proposed in ref 12.

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[10] Scheme 2 represents a simplified version of the detailed mechanism presented in ref 4, retaining the important feature that [PdLArX] is the dominant intermediate species in the catalytic cycle.

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