

Influence of water on the deprotonation and the ionic mechanisms of a Heck alkynylation and its resultant E-factors

Chuntian Hu,^a Kevin H. Shaughnessy,^b and Ryan L. Hartman^{*a}

a. Department of Chemical and Biomolecular Engineering, New York University, Brooklyn, NY, 11201, USA.

Email: ryan.hartman@nyu.edu.

b. Department of Chemistry, The University of Alabama, Tuscaloosa, AL, 35487, USA

Supporting Information

Derivation of reaction kinetic expressions

Kinetic expressions, in the absence of transport limitations, derived from the cationic or the anionic mechanisms are readily available when their intermediate complexes react virtually as fast as they are formed (Pseudo-Steady-State-Hypothesis). Now let us consider the cationic mechanism of Fig. 2a. During the initial stages of the reactions, the substrate concentrations are high and far from equilibrium. The rate of disappearance of the aryl halide is derived as,

$$-r_{ArBr} = r_{ArR} = k_1 k_2 k_3 k_4 [ArBr][R-H][Base][L][Pd]_T \Lambda_1 \quad (S1)$$

where k_i are the rate constants of the reaction steps of Fig. 2a, and Λ_1 is defined by,

$$\Lambda_1 = \frac{1}{\left(k_2 k_3 k_4 [R-H][L][Base] + k_1 k_3 k_4 [ArBr][L][Base] + k_1 k_2 k_4 [ArBr][R-H][Base] \right. \\ \left. + k_1 k_2 k_3 [ArBr][R-H][L] + \frac{k_1 k_2 k_3 k_4}{k_5} [ArBr][R-H][L][Base] \right)}$$

(S2)

As one can anticipate, the rate expression (eqn (S1)) depends on the concentrations of all free species in the cationic mechanism. A similar analogy yields the rate expression, derived from first principles, for the anionic mechanism of Fig. 2b,

$$-r_{ArBr} = r_{ArR} = k_1' k_2' k_3' k_4' [ArBr][R-H][Base][L][Pd]_T \Lambda_2 \quad (S3)$$

where k_i' are the rate constants of the reaction steps of Fig. 2b, and Λ_2 is defined by,

$$\Lambda_2 = \frac{1}{\left(\begin{aligned} &k_2' k_3' k_4' [R-H][L][Base] + k_1' k_3' k_4' [ArBr][L][Base] + k_1' k_2' k_4' [ArBr][R-H][L] \\ &+ k_1' k_2' k_3' [ArBr][R-H][Base] + \frac{k_1' k_2' k_3' k_4'}{k_5'} [ArBr][R-H][L][Base] \end{aligned} \right)} \quad (S4)$$

Similarly, the kinetic expression for ionic mechanism can be derived as,

$$-r_{ArBr} = r_{ArR} = k_1'' k_2'' k_3'' k_5'' [ArBr][R-M][Base][L][Pd]_T \Lambda_3 \quad (S5)$$

where k_i'' are the rate constants of the reaction steps of Fig. 4, and Λ_3 is defined by,

$$\Lambda_3 = \frac{1}{\left(\begin{aligned} &k_2'' k_3'' k_5'' [R-M][L][Base] + k_1'' k_3'' k_5'' [ArBr][L][R-M] + k_1'' k_2'' k_5'' [ArBr][Base][L] \\ &+ k_1'' k_2'' k_3'' [ArBr][R-M][Base] + \frac{k_1'' k_2'' k_3'' k_5''}{k_4''} [ArBr][R-M][L][Base] \end{aligned} \right)} \quad (S6)$$

Both kinetic expressions (eqn (S1), (S3) and (S5)) are expected to hold under conditions when i) the rate of formation of the catalytically active PdL_n species **7** (or **7'**, or **7''**) are dominated by the catalytic cycle, ii) Pd colloid formation does not influence the kinetics, and iii) in reactors where the mass transfer rates are instantaneous relative to the reaction rates.

Calculation of ligand concentration

To identify the role of water on cationic and anionic mechanisms, quantitative assessments of the catalytically active intermediates of either Fig. 2a or 2b are necessary. The concentration of PdL_n can be calculated by performing mole balances on the number of Pd catalytic intermediates having n coordinated ligands (*i.e.*, **7**, **8**, **10** and **11** from Fig. 2a, or **7'**, **8'** and **11'** from Fig. 2b), as given in eqn (S7)¹,

$$[PdL_n] = \left(\frac{x-y}{nx}\right)(1-\theta)[L]_T \quad (S7)$$

where x is the total number of active transition metal intermediates and y is the number of metal intermediates with n coordinated ligands. The fraction of inactive Pd, θ , can be calculated from the difference between the free ligand concentration $[L]$ and the total ligand concentration $[L]_T$ (from Fig. 2a or b). Similarly, the concentration of PdL_{n-1} (Pd catalytic intermediates having $(n-1)$ coordinated ligands) can be derived as¹,

$$[PdL_{n-1}] = \left(\frac{x-z}{nx}\right)(1-\theta)[L]_T \quad (S8)$$

where z is the total number of intermediates with $(n-1)$ coordinated ligands. The concentration of free phosphine ligand $[L]$ can be determined by its stoichiometric relationship to the number of Pd intermediates (x , y , z , and n) and the total concentration of ligand $[L]_T$, as expressed in eqn (S9)¹,

$$[L] = \left[1 - (1-\theta)\left(\frac{y+nz}{nx}\right)\right][L]_T \quad (S9)$$

Quantitative understanding of the transition metal intermediates and free ligands makes the determination of intrinsic rate constants and Gibbs free energy possible.

Determination of intrinsic rate constants and Gibbs free energy

The intrinsic rate constant, k_i , derived as¹,

$$k_{i,n} = k_{i,fit} \left(\frac{x}{x-y}\right) \left(\frac{1}{1-\theta}\right) \quad (S10)$$

and,

$$k_{i,n-1} = k_{i,fit} \left(\frac{x}{x-z} \right) \left(\frac{1}{1-\theta} \right) \left(\frac{[L]_T}{[L]} \right) \quad (\text{S11})$$

where $k_{i,fit}$ is the measured apparent rate constant. Eqn (S10) describes k_i values of steps involving intermediates with n coordinated ligands (*i.e.*, **7**, **8**, **10** and **11** from Fig. 2a, or **7'**, **8'** and **11'** from Fig. 2b) and eqn (S11) describes k_i values of steps involving intermediates with $(n-1)$ coordinated ligands (*i.e.*, **9** from Fig. 2a, or **9'** and **10'** from Fig. 2b).

The relationship between Gibbs free energy (ΔG^{++}), intrinsic rate constant ($k_{i,n}$), the concentration of Pd catalytic intermediates with n coordinated ligands ($[PdL_n]$), and the free ligands concentration ($[L]$) is expressed by the Eyring-Polanyi equation¹,

$$\Delta G_{i,n}^{++} = -RT \ln \left(\frac{k_{i,n} [PdL_n]^{\nu} [L]^{\alpha} h}{k_B T} \right) \quad (\text{S12})$$

and for Pd catalytic intermediates having $(n-1)$ coordinated ligands, the Gibbs free energy is described as,

$$\Delta G_{i,n-1}^{++} = -RT \ln \left(\frac{k_{i,n-1} [PdL_{n-1}]^{\nu} [L]^{\alpha} h}{k_B T} \right) \quad (\text{S13})$$

where R is the gas constant ($8.3144 \text{ J mol}^{-1} \text{ K}^{-1}$), T is the absolute temperature, h is the Planck's constant ($6.62606957 \times 10^{-34} \text{ J s}^{-1}$), and k_B is the Boltzmann's constant ($1.3806488 \times 10^{-23} \text{ J K}^{-1}$). Here, $\nu = 1$ for reaction steps involving ligand association (otherwise $\nu = 0$), and $\alpha = 1$ for reaction steps having free ligands (otherwise $\alpha = 0$).

The Hatta modulus

The Hatta modulus (M_H) is defined as the ratio of the maximum possible conversion in the film and the maximum diffusional transport through the film, given as^{1, 2},

$$M_H^2 = \frac{k_i [L]^\alpha [R^1 X]^\beta [R^2 H]^\gamma [Base]^\delta x_0^2}{D}$$

(S14)

where k_i is rate constant of the fastest reaction step, D is the molecular diffusivity of the Pd intermediate through the solvent, and $\alpha, \beta, \gamma, \delta$ each separately equal to 1 if involving in the fast step, else equal to 0. M_H is useful to distinguish reaction rates from diffusive fluxes of substrates, catalytic intermediates, or products. In general, $M_H > 2$ indicates that the reaction occurs in the film, whereas $M_H < 0.02$ means infinitely slow reactions and diffusion does not control the reaction kinetics. If $0.02 < M_H < 2$, it is a transition region².

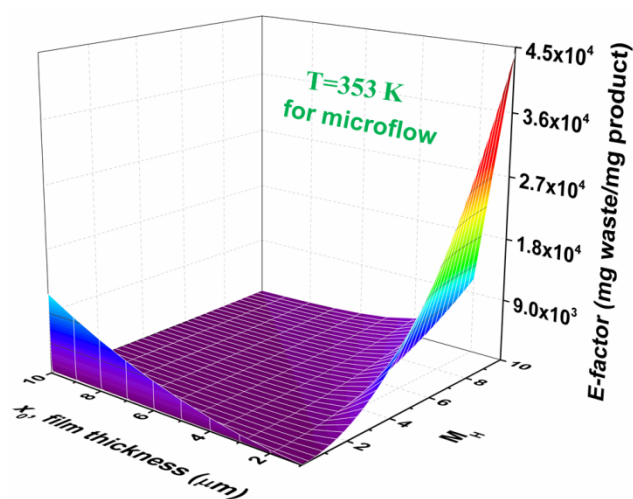


Fig. S1 E-factors at 353 K for M_H values from 0.01 to 10 and aqueous-organic film thicknesses (x_0) from 1 to 10 μm (linear axis).

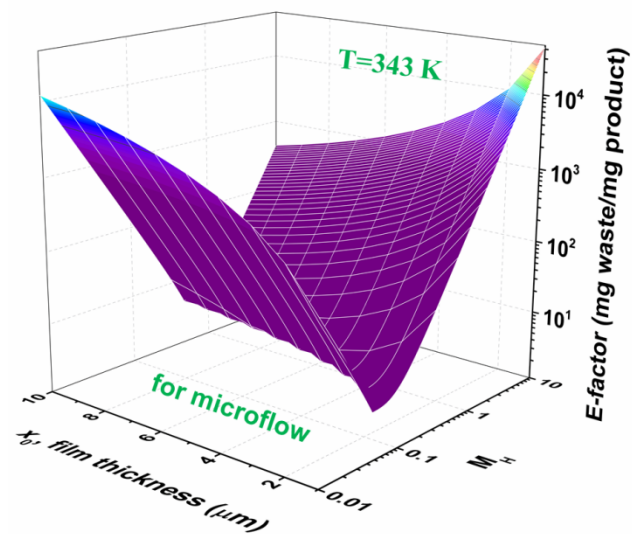


Fig. S2 E-factors at 343 K for M_H values from 0.01 to 10 and aqueous-organic film thicknesses (x_0) from 1 to 10 μm

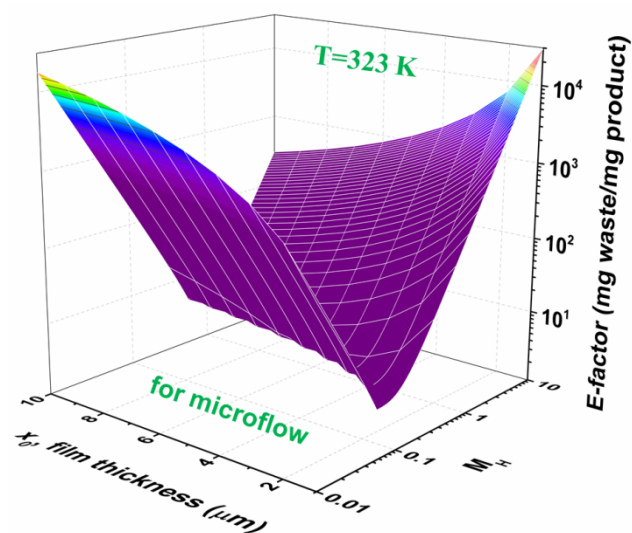


Fig. S3 E-factors at 323 K for M_H values from 0.01 to 10 and aqueous-organic film thicknesses (x_0) from 1 to 10 μm .

Symbols used

α	Reaction order with respect to the free ligand concentration, 0 or 1
β	Reaction order with respect to the aryl halide concentration, 0 or 1
γ	Reaction order with respect to the alkyne substrate concentration, 0 or 1
δ	Reaction order with respect to the base concentration, 0 or 1
θ	Fraction of stoichiometrically inactive <i>Pd</i>
ν	Reaction order with respect to <i>Pd</i> catalytic intermediate concentration, 0 or 1
$[ArBr]$	Aryl bromide concentration, mol L ⁻¹
<i>ArR</i>	Denotes alkyne product
$[Base]$	Base concentration, mol L ⁻¹
<i>D</i>	Binary molecular diffusivity, m ² s ⁻¹
$\Delta G_{i,n}^{++}$	Gibbs free energy for reaction steps involving <i>Pd</i> catalytic intermediates, kJ mol ⁻¹
<i>h</i>	Planck constant = 6.62606957 x 10 ⁻³⁴ J s ⁻¹
<i>i</i>	Denotes reaction species
k_B	Boltzmann constant = 1.3806488 x 10 ⁻²³ J K ⁻¹
k_i	Intrinsic cationic reaction rate constant of step <i>i</i> , min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
k_i'	Intrinsic anionic reaction rate constant of step <i>i</i> , min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
k_i''	Intrinsic ionic reaction rate constant of step <i>i</i> , min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
$k_{i,fit}$	Fitted cationic reaction rate constant of step <i>i</i> , min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
$k_{i,fit}'$	Fitted anionic reaction rate constant of step <i>i</i> , min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
$k_{i,n}$	Intrinsic reaction rate constant of step <i>i</i> having <i>n</i> coordinated ligands, min ⁻¹ , mol L ⁻¹ min ⁻¹ , or mol ² L ⁻² min ⁻¹
$[L]$	Free ligand concentration, mol L ⁻¹
$[L]_T$	Total ligand concentration, mol L ⁻¹

M_H	Hatta modulus
$[PdL_n]$	Concentration of Pd catalytic intermediates having n coordinated ligands, mol L ⁻¹
$[Pd]_T$	Total concentration of Pd, mol L ⁻¹
R	Gas constant = 8.3144 J mol ⁻¹ K ⁻¹
$-r_i$	Rate of disappearance of species i , mol min ⁻¹
$[R-H]$	Alkyne concentration, mol L ⁻¹
$[R-M]$	Phenylacetylide concentration, mol L ⁻¹
s^2	Least squares difference between measured and calculated concentrations, mol ² L ⁻²
T	Reaction temperature, K
X	Denotes halide
x_0	aqueous-organic thin film thickness, μm
x	Number of active transition metal intermediates in any catalytic cycle
y	Number of active transition metal intermediates having n coordinated ligands
z	Number of active transition metal intermediates having $n-1$ coordinated ligands

References

1. J. C. Sabio, R. C. Domier, J. N. Moore, K. H. Shaughnessy and R. L. Hartman, *Chem. Eng. Technol.*, 2015, DOI: 10.1002/ceat.201500117.
2. O. Levenspiel, *Chemical reaction engineering*, John Wiley & Sons: New York, NY, 3rd edn., 1999.