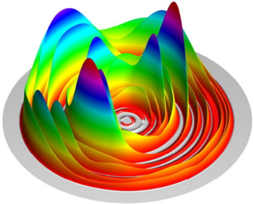
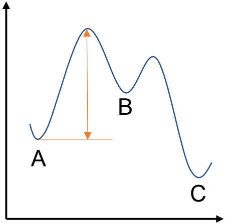
# RDS and Resting State



**Zepeng Yang**
Tongji University

# Rate Determining Step (RDS)

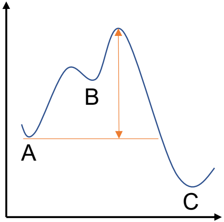
**RDS**: The elementary step whose rate predominantly determines the rate of product formation.



$$A \overset{\text{"slow"}}{\underset{\cancel{\dashleftarrow}}{\longrightarrow}} B \xrightarrow{\text{"fast"}} C$$

***RDS:*** A → B

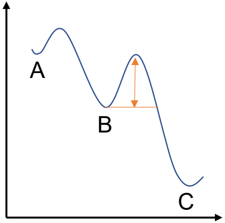
*resting state:* A



$$A \overset{\text{"fast"}}{\rightleftarrows} B \xrightarrow{\text{"slow"}} C$$

***RDS:*** B → C

*resting state:* A



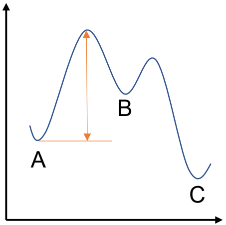
$$A \overset{\text{"fast"}}{\underset{\cancel{\dashleftarrow}}{\longrightarrow}} B \xrightarrow{\text{"slow"}} C$$

***RDS:*** B → C

*resting state:* B

# Rate Determining Step (RDS)

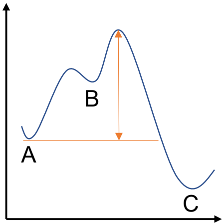
**RDS**: The elementary step whose rate predominantly determines the rate of product formation.



$$A \underset{\cancel{\dashleftarrow}}{\xrightarrow{\text{"slow"}}} B \xrightarrow{\text{"fast"}} C$$

***RDS:*** A $\longrightarrow$ B

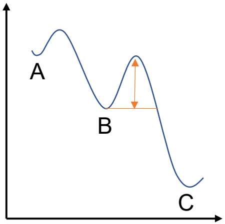
*resting state:* A



$$A \overset{\text{"fast"}}{\rightleftarrows} B \xrightarrow{\text{"slow"}} C$$

***RDS:*** B $\longrightarrow$ C

*resting state:* A



$$A \underset{\cancel{\dashleftarrow}}{\xrightarrow{\text{"fast"}}} B \xrightarrow{\text{"slow"}} C$$

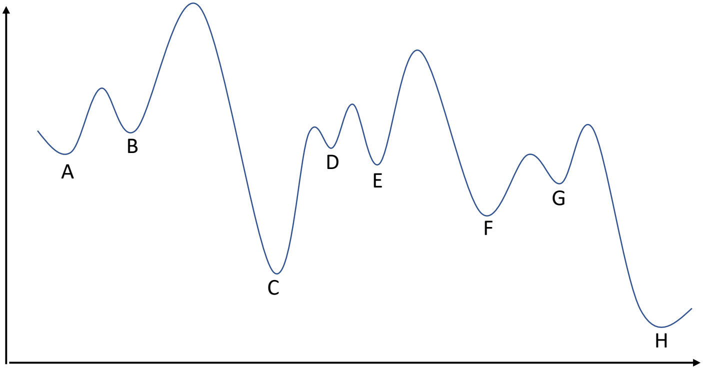
***RDS:*** B $\longrightarrow$ C

*resting state:* B

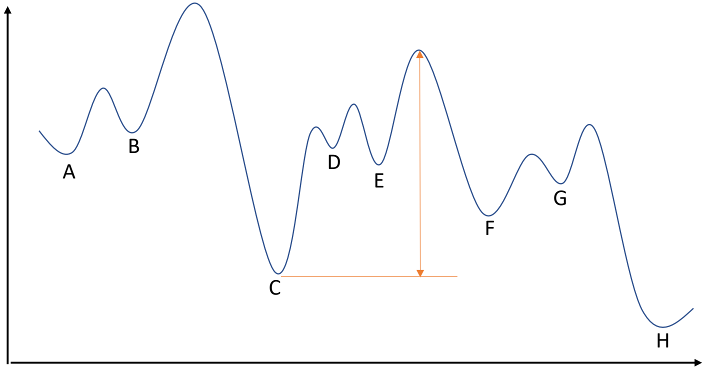
## How to locate the RDS:

Look for the highest barrier between the SM/any intermediate and a subsequent transition state.

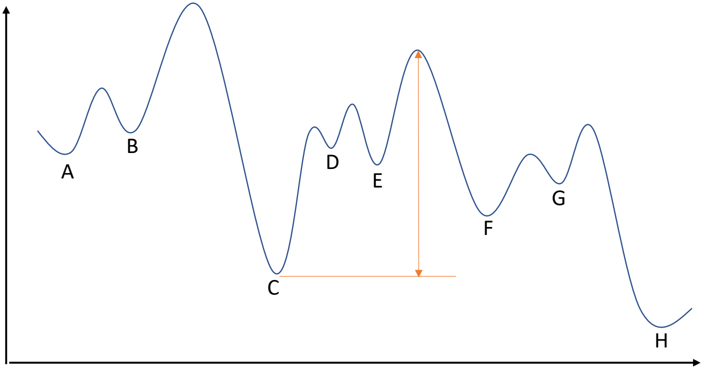
# RDS and Resting State



# RDS and Resting State

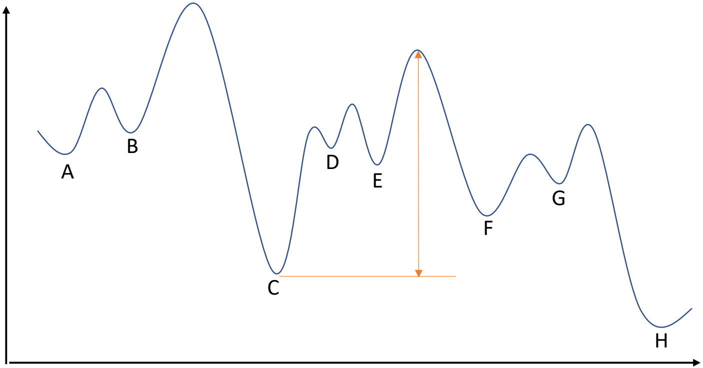


# RDS and Resting State



***RDS:*** E ⟶ F

# RDS and Resting State



***RDS:*** E ⟶ F

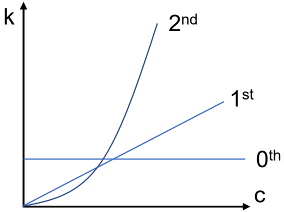
*C is the resting state of this reaction coordinate diagram*

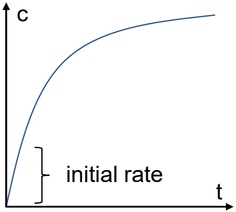
# Rate Law

$$A + B + C \longrightarrow \quad \longrightarrow P$$

$$d[P]/dt = k[A][B]^2 \quad \Longrightarrow$$

1st order in A
2nd order in B
0th order in C





**Initial-rate kinetics** (~10% conversion) are recommended due to the presence of significant competing pathways as the reaction proceeds.

# Rate Law

**What can/can't a rate law tell you:**

1) Only reaction steps that occur before and at the rate-determining step can be detected during a routine kinetic study.
2) Insight into composition of the T.S. of the RDS versus the resting state.
3) Does not always mean 1 A molecule, 2 B molecules and 0 C molecule in the T.S. of the RDS of the reaction

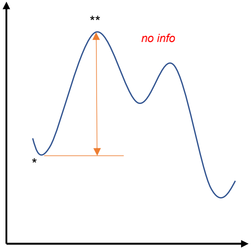
***rate law***: k[resting state][sub$^1$ (between resting state and T.S.)][sub$^2$ (between resting state and T.S.)]

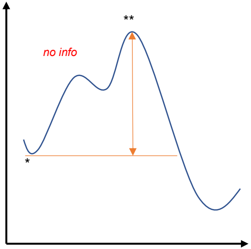
# Rate Law

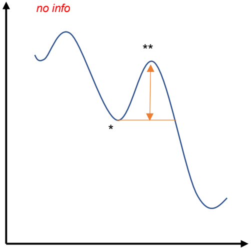
**What can/can’t a rate law tell you:**

1) Only reaction steps that occur before and at the rate-determining step can be detected during a routine kinetic study.
2) Insight into composition of the T.S. of the RDS versus the resting state.
3) Does not always mean 1 A molecule, 2 B molecules and 0 C molecule in the T.S. of the RDS of the reaction

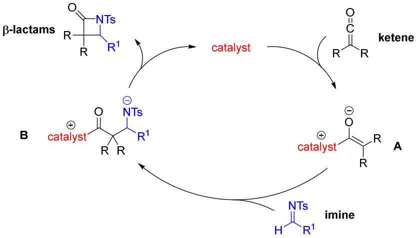
***rate law***: k[resting state][sub$^{1}$ (between resting state and T.S.)][sub$^{2}$ (between resting state and T.S.)]

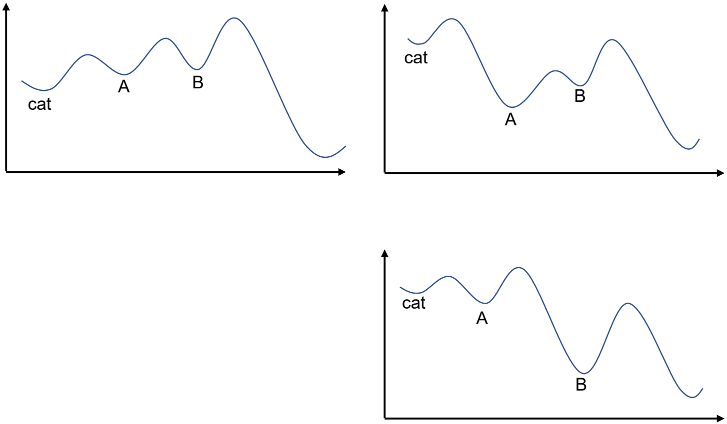




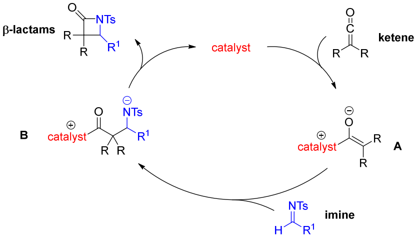


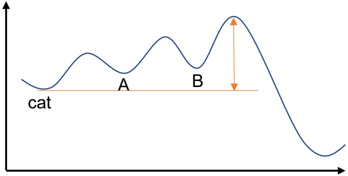
# Resting State: Case Study

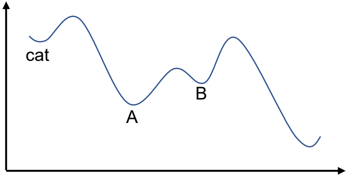


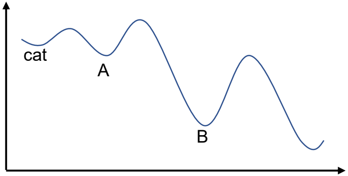


# Resting State: Case Study

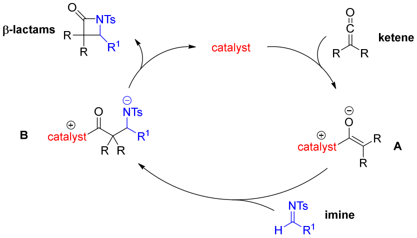


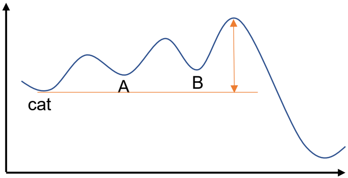




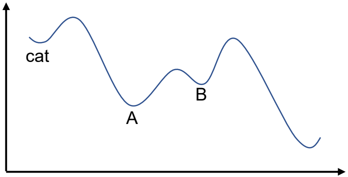


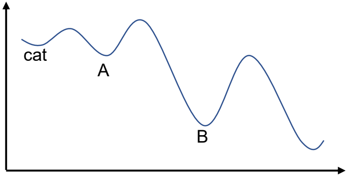
# Resting State: Case Study



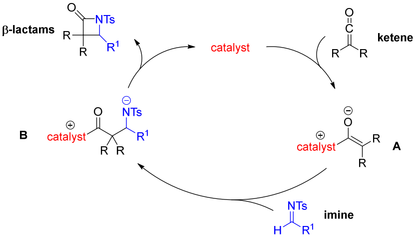


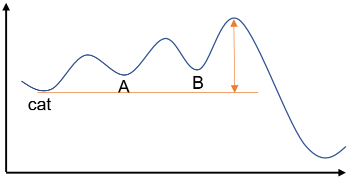
***resting state:** free catalyst*





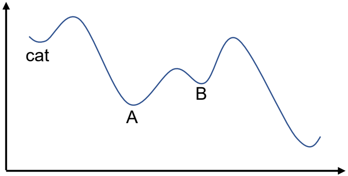
# Resting State: Case Study

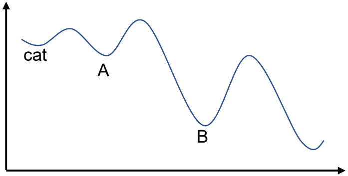




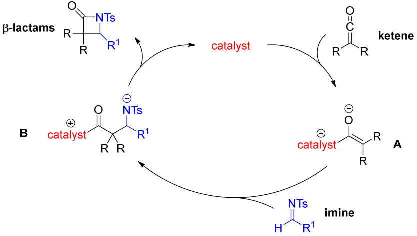
***resting state:*** *free catalyst*

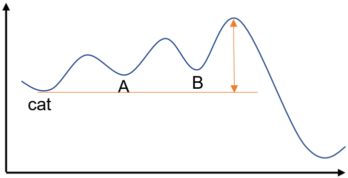
***rate law:*** *k[cat][ketene][imine]*





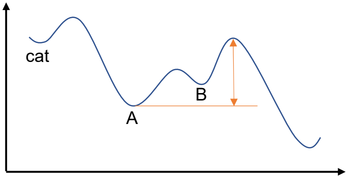
# Resting State: Case Study

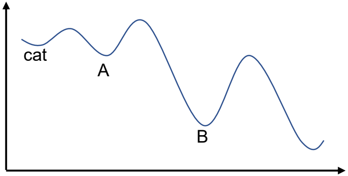




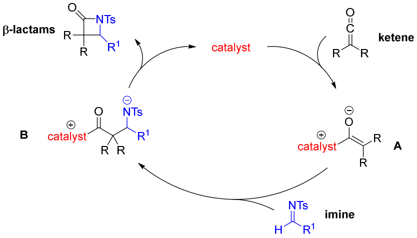
***resting state:*** *free catalyst*

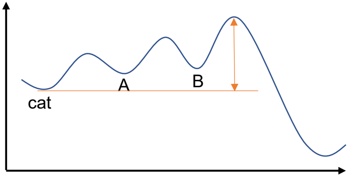
***rate law:*** *k[cat][ketene][imine]*





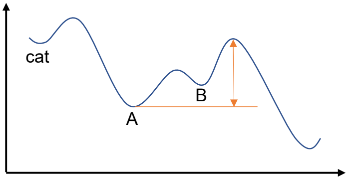
# Resting State: Case Study



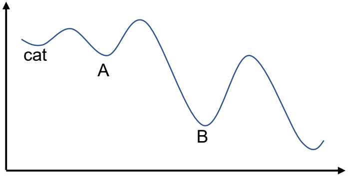


***resting state:*** *free catalyst*

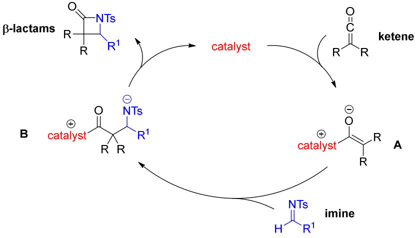
***rate law:*** *k[cat][ketene][imine]*

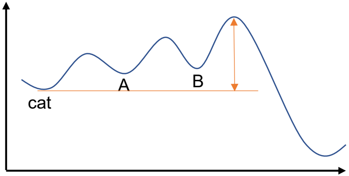


***resting state:*** *A*



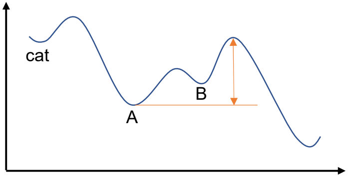
# Resting State: Case Study





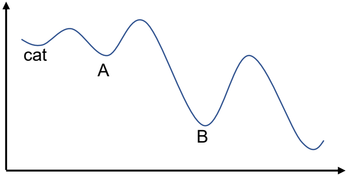
***resting state:*** *free catalyst*

***rate law:*** *k[cat][ketene][imine]*

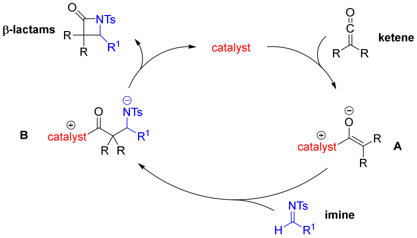


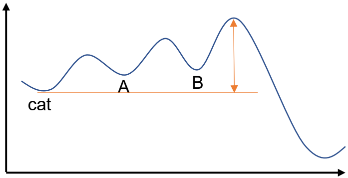
***resting state:*** *A*

***rate law:*** *k[cat][imine]*



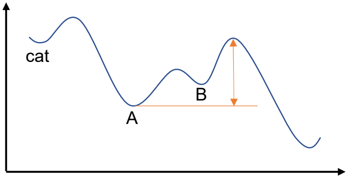
# Resting State: Case Study





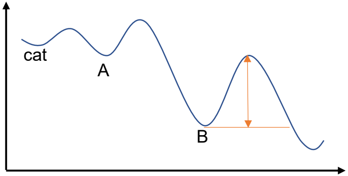
***resting state:*** *free catalyst*

***rate law:*** *k[cat][ketene][imine]*

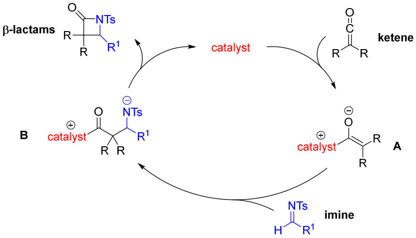


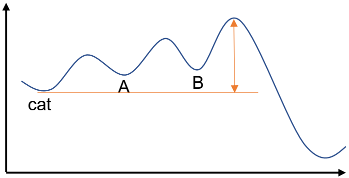
***resting state:*** *A*

***rate law:*** *k[cat][imine]*



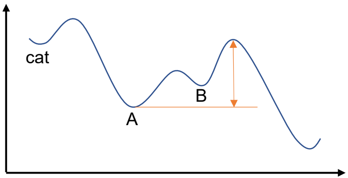
# Resting State: Case Study





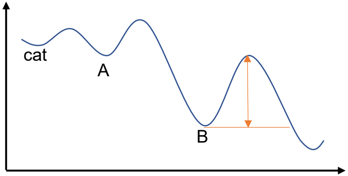
***resting state:*** *free catalyst*

***rate law:*** *k[cat][ketene][imine]*



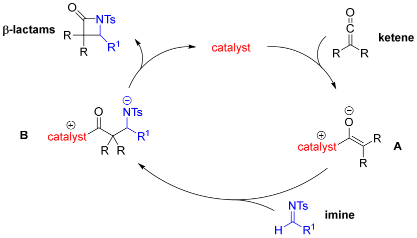
***resting state:*** *A*

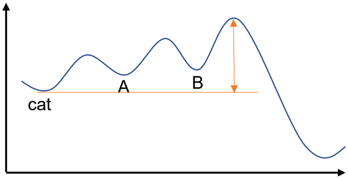
***rate law:*** *k[cat][imine]*



***resting state:*** *B*

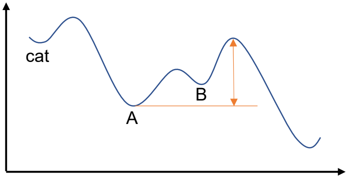
# Resting State: Case Study





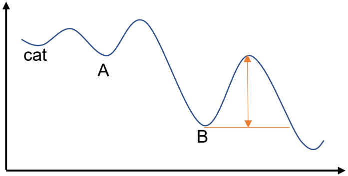
***resting state:*** *free catalyst*

***rate law:*** *k[cat][ketene][imine]*



***resting state:*** *A*

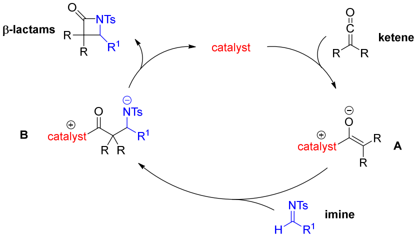
***rate law:*** *k[cat][imine]*

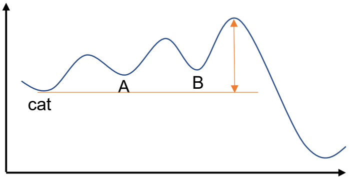


***resting state:*** *B*

***rate law:*** *k[cat]*

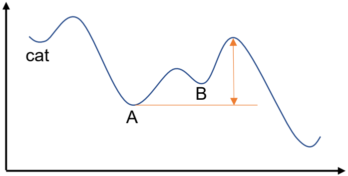
# Resting State: Case Study





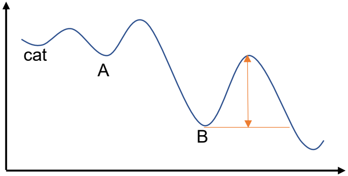
***resting state:*** *free catalyst*

***rate law:*** *k[cat][ketene][imine]*



***resting state:*** *A*

***rate law:*** *k[cat][imine]*

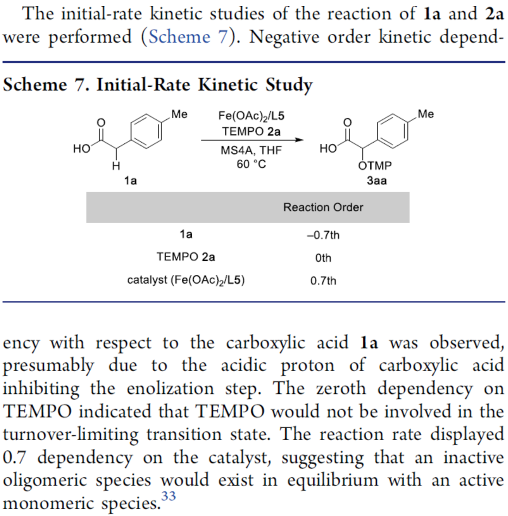


***resting state:*** *B*

***rate law:*** *k[cat]*

- RDS is B→product for all three scenarios. However, the resting state can be different depending on the potential energy surface.
- T.S. of the RDS is the same for all three scenarios, which contains the catalyst, ketene and imine. However, depending on the potential energy surface, the rate law does not necessarily reflect the composition of the T.S.

# Practice (I)



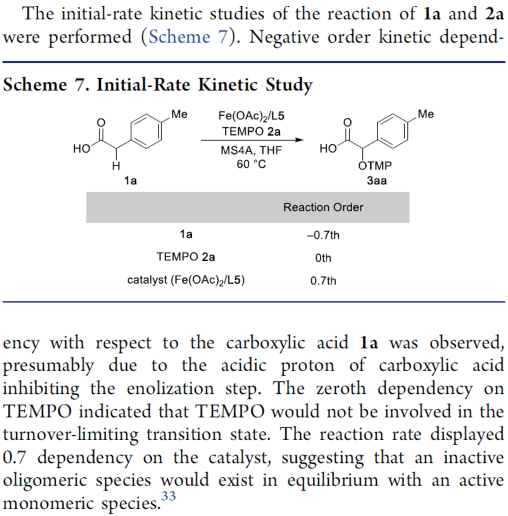
The initial-rate kinetic studies of the reaction of **1a** and **2a** were performed (Scheme 7). Negative order kinetic dependency with respect to the carboxylic acid **1a** was observed, presumably due to the acidic proton of carboxylic acid inhibiting the enolization step. The zeroth dependency on TEMPO indicated that TEMPO would not be involved in the turnover-limiting transition state. The reaction rate displayed 0.7 dependency on the catalyst, suggesting that an inactive oligomeric species would exist in equilibrium with an active monomeric species.[33]

**Scheme 7. Initial-Rate Kinetic Study**

| | Reaction Order |
|---|---|
| **1a** | –0.7th |
| TEMPO **2a** | 0th |
| catalyst ($Fe(OAc)_2$/**L5**) | 0.7th |

***Question:** is there any wrong conclusion drawn from their kinetic data?*

# Practice (I)



The initial-rate kinetic studies of the reaction of **1a** and **2a** were performed (Scheme 7). Negative order kinetic dependency with respect to the carboxylic acid **1a** was observed, presumably due to the acidic proton of carboxylic acid inhibiting the enolization step. The zeroth dependency on TEMPO indicated that TEMPO would not be involved in the turnover-limiting transition state. The reaction rate displayed 0.7 dependency on the catalyst, suggesting that an inactive oligomeric species would exist in equilibrium with an active monomeric species.[33]

**Scheme 7. Initial-Rate Kinetic Study**

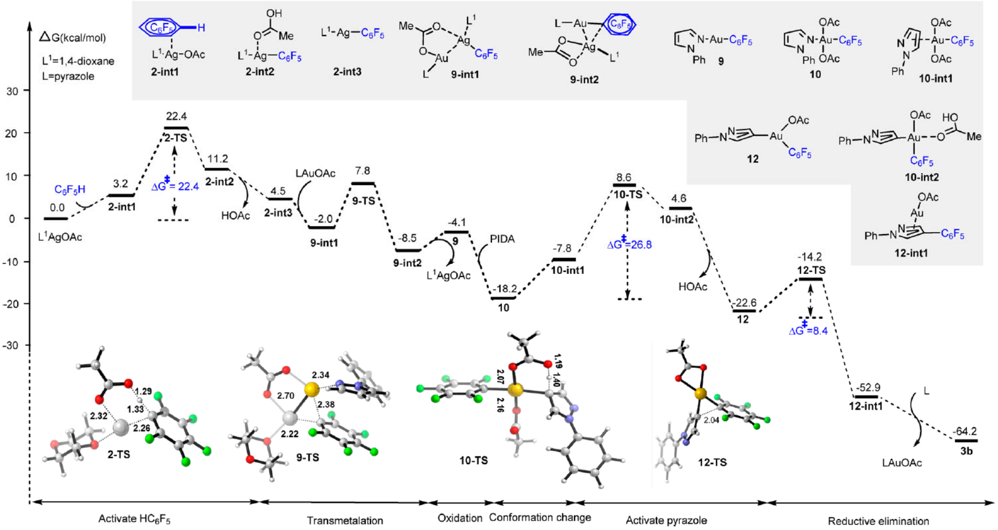
| | Reaction Order |
|---|---|
| **1a** | −0.7th |
| TEMPO **2a** | 0th |
| catalyst (Fe(OAc)$_2$/**L5**) | 0.7th |

***Question:*** *is there any wrong conclusion drawn from their kinetic data?*

Zeroth order on TEMPO **<u>does not</u>** indicate that TEMPO is not involved in the T.S. of RDS.

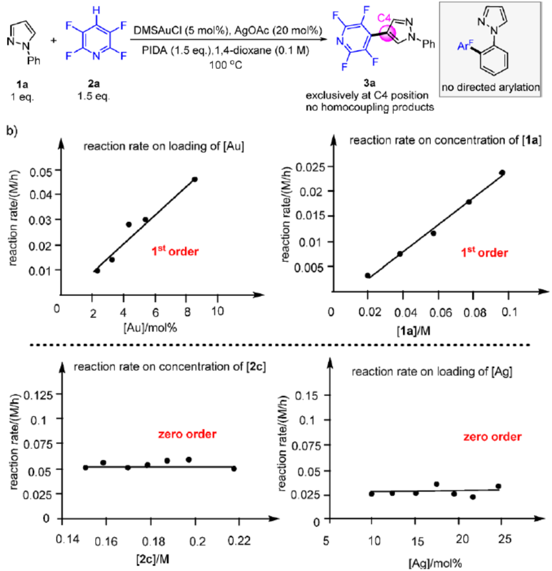
You can imagine a scenario where TEMPO is incorporated before the resting state, which will make TEMPO zeroth order even if it is in the T.S. of RDS.

# Practice (II)



Au: 1st order; 1a (pyrazole): 1st order; Ag: 0th order; $C_6F_5H$: 0th order

# Practice (II)



***Question:*** *is there anything wrong regarding the DFT calculations?*

Thanks for your attention!