Catalysis

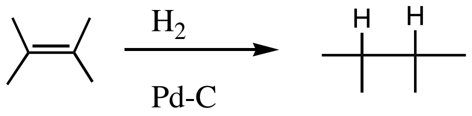
A **Catalyst** is a compound that takes part in a reaction but is not consumed in the reaction, and it increases the rate of the reaction

The **turn-over number** is the average number of reactants that a catalyst acts on befor ethe catalyst loses its activity

Since catalysts affect rate-determining steps, they may be involved in the rate law, but their concentration doesn't change

$$\mathbf{A} + \mathbf{Cat} \xrightarrow{k} \mathbf{B} + \mathbf{Cat}$$

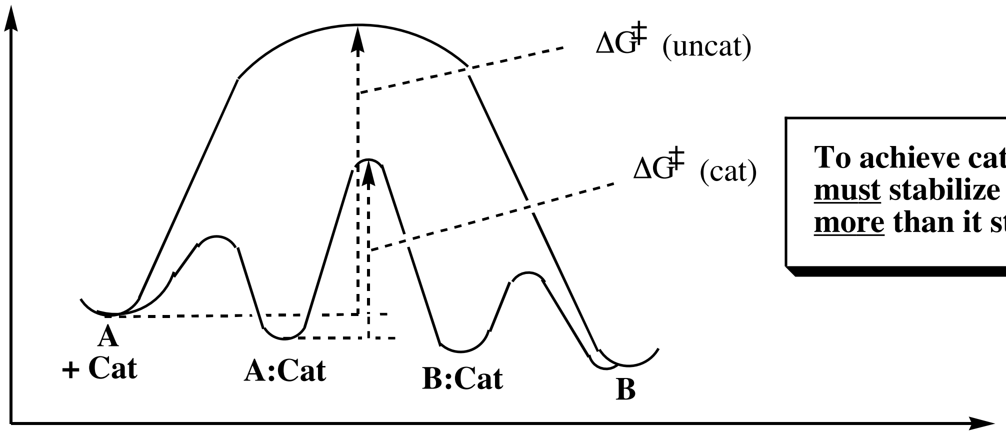
A **Heterogeneous Catalyst** is one that does not dissolve in solution and hence the catalysis takes place in a separate phase from the solution. Example:



A **Homogenous Catalyst** is one that dissolves in solution to perform the catalysis: acid or base catalyst

For rate to be increased, the activation energy of the rate-determining step must be lowered; in many cases this means a mechanism change:

$$\mathbf{A} + \mathbf{Cat} \rightleftharpoons \mathbf{A{:}Cat} \xrightleftharpoons{\text{rds}} \mathbf{B{:}Cat} \rightleftharpoons \mathbf{B} + \mathbf{Cat}$$

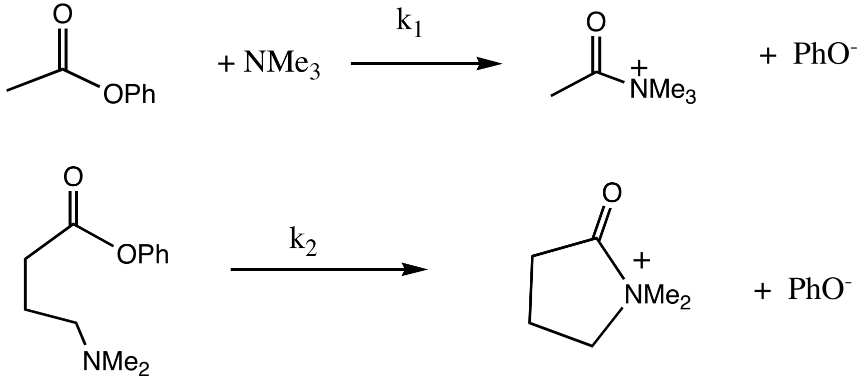


To achieve catalysis, the catalyst must stabilize the transition state more than it stabilizes the ground state

Forms of Catalysis: Proximity Effects

Going from a second order process to a first order process: if the reactants are bound together , much of the energy cost in reducing the entropy of the reactants (loss of rotational and translational degrees of freedom) has been paid

Example: a $T\Delta S^{\ddagger}$ difference of 4.6 kcal/mol @ 25°C corresponds to a $2\text{x}10^{3}$ rate enhancement for intramolecular vs. intermolecular processes.



$k_2/k_1 = 1200$

Effective Molarity is defined as the ratio of the first order to the second- order rate constants for analogous reactions

$$\mathbf{E.M.} = k_{1storder}/k_{2ndorder} \qquad \textbf{units of molarity}$$

The **EM** tells us the concentration of one of the reactants that would be needed to make the intermolecular reaction have a pseudo first-order rate constant identical to the first-order rate constant for the intramolecular reaction.

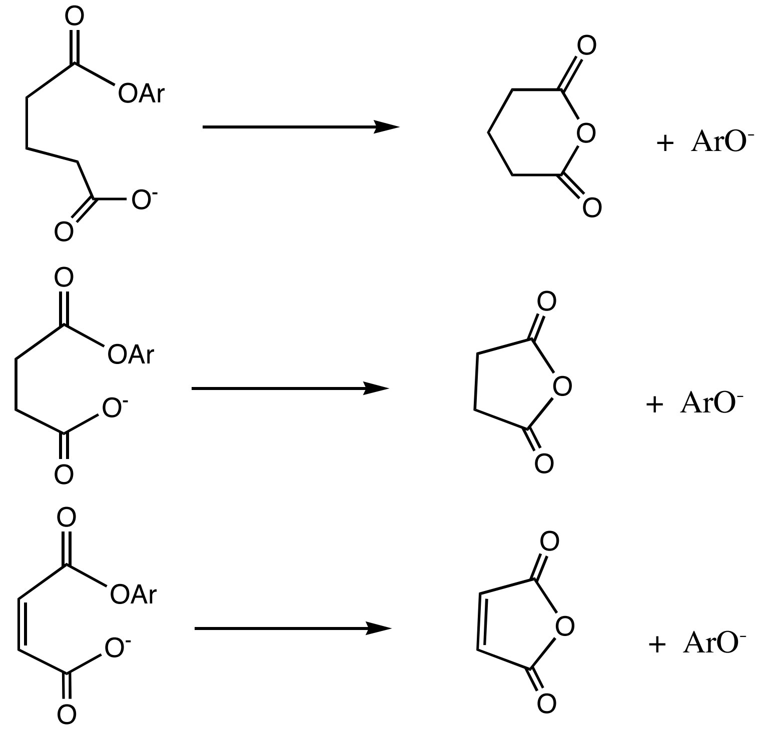
Usually , EM concentrations are impossible to achieve

EM tells us the **effective concentration** of one of the components in the intramolecular reaction

Relative Rates of Intramolecular Cyclizations

relative rate

Ar=4-Br-Ph



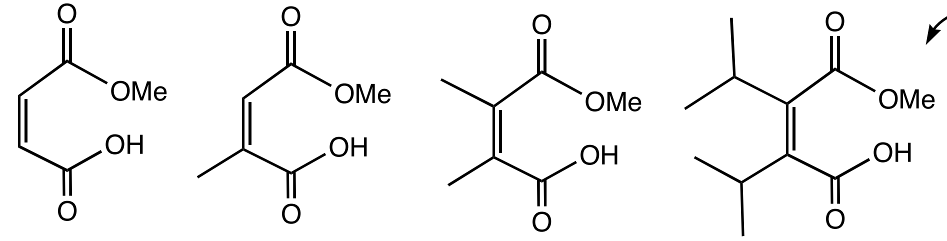
1

230

10,300

rotation already frozen- no penalty to restrict rotational degrees of freedom in T.S.

Effective Molarities for cyclizations



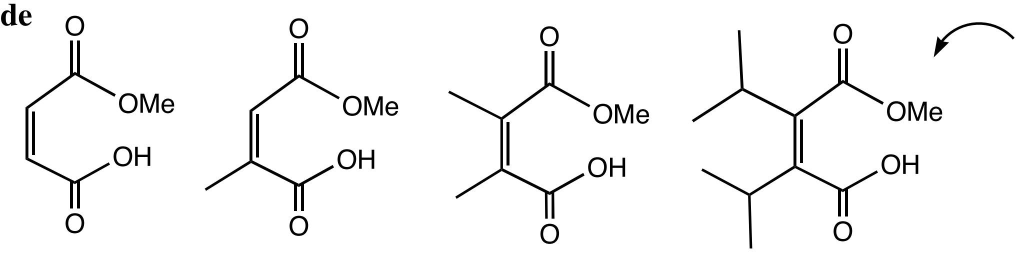
Relief of strain in T.S. for cyclization

E.M. $3x10^{9}$ $6x10^{10}$ $4x10^{12}$ $5x10^{12}$

Steric Compression in Substrate Enhances Cyclization Rates

Methyl groups push electrophile and nucleophile closer together in transition state:

Cyclic Anhydride Formation

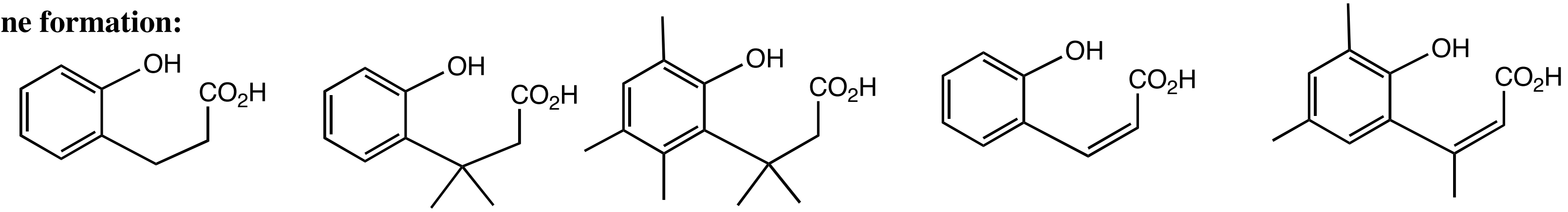


Relief of strain in T.S. for cyclization

Reactant Structure Pushed toward that of the transition state

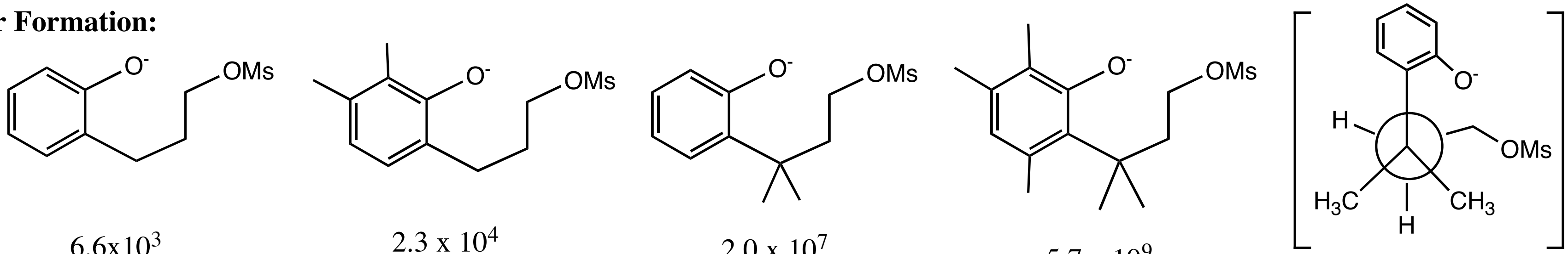
E.M.	3×10^{9}	6×10^{10}	4×10^{12}	5×10^{12}

Lactone formation:



E.M.	4×10^{4}	7×10^{6}	2.3×10^{7}	3.7×10^{11}	2×10^{13}

Ether Formation:

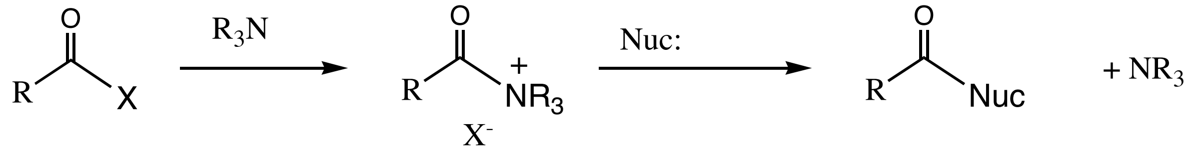


E.M.	6.6×10^{3}	2.3×10^{4}	2.0×10^{7}	5.7×10^{9}	**preferred**

Steric compression caused by geminal methyl groups leading to enhanced cyclization rates is termed the "Thorpe-Ingold Effect" or the "gem-dimethyl" effect

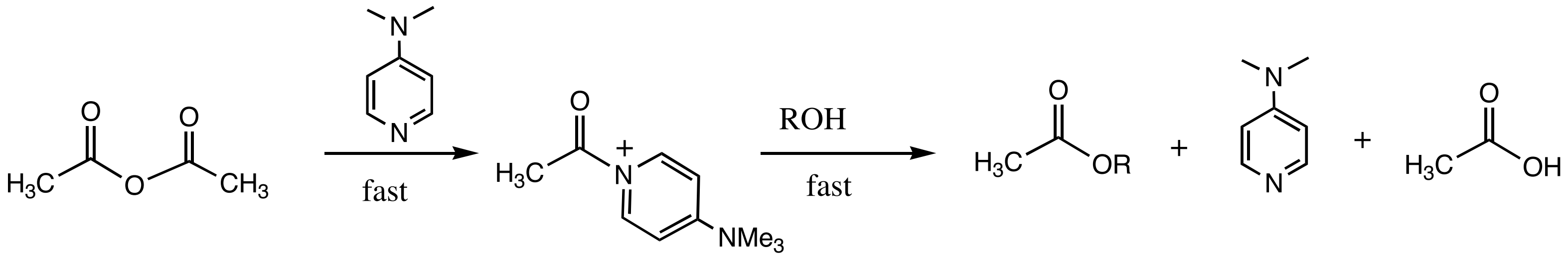
Nucleophilic Catalysis and Covalent Catalysis

3° amines are good nucleophiles and often function as acylation catalysts:



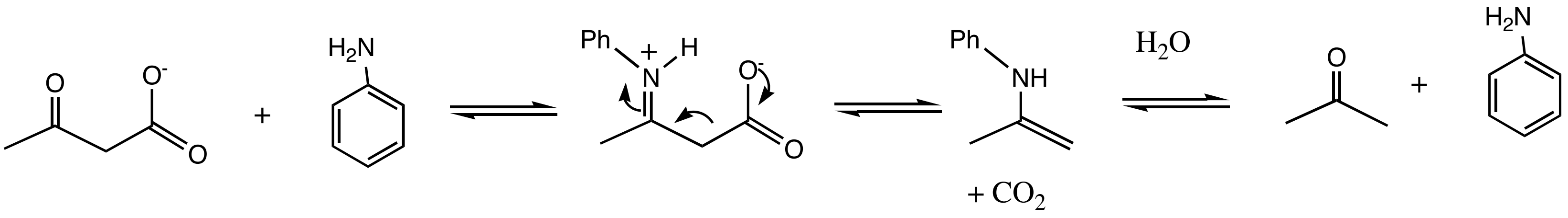
acyl ammonium ion - a superior electrophile
when compared to the starting material!

Classic Example: DMAP catalysis of alcohol acylation by an anhydride



acylpyridinium ion
powerful electrophile!

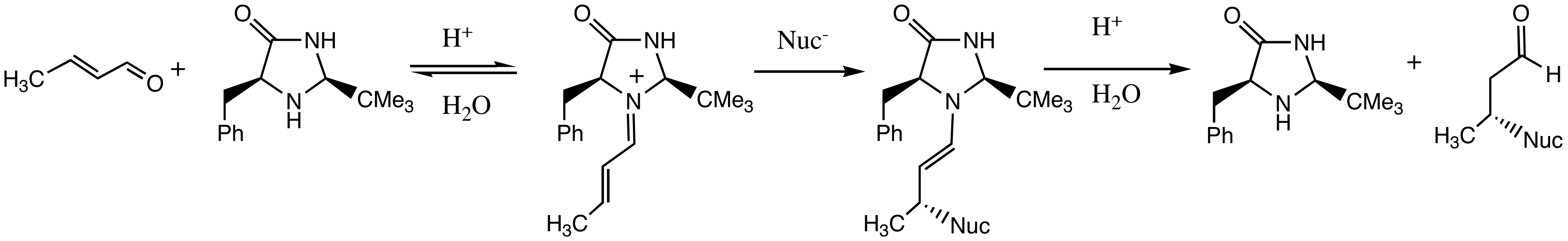
Covalent Catalysis: the catalyst forms full covalent bonds with the substrate
Aniline catalyzes decarboxylations:



Organocatalysis

Chiral organic catalysts for enantioselective reactions - do not have as high turn-over numbers as transition-metal catalysts but are air and water stable and environmentally benign

MacMillan Catalyst - especially effective for Diels-alder and Michael additions



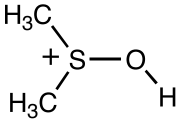
Formation of iminium ion creates a much lower lying LUMO relative to that found in the starting enone

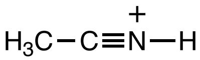
JACS**,** 124**, 1172** (2002).

Acid-Base Catalysis

Specific Catalysis

<u>A Specific Acid</u> is defined as the protonated form of the solvent in which the reaction is being performed:



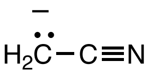


$H_3C-C\equiv\overset{+}{N}-H$

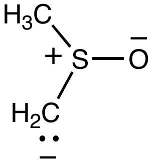
H_3O^+

<u>A Specific Base</u> is defined as the conjugate base of the solvent:

HO^-



$H_2\overset{-}{\ddot{C}}-C\equiv N$



<u>Specific Acid Catalysis</u> refers to a process in which the reaction rate depends upon the specific acid, not upon other acids in solution. <u>In Specific acid catalysis, substrate protonation or proton transfer occurs before the rate-determining step</u>

<u>Specific Base Catalysis</u> referes to a process in which the reaction rate depends upon the specific base, not upon other bases in solution. <u>In Specific base catalysis, substrate deprotonation or proton transfer occurs before the rate-determining step</u>

Specific Acid Catalysis : Scenario

$$R \underset{\text{fast}}{\overset{H_3O^+}{\rightleftharpoons}} RH^+ \xrightarrow{\text{slow}} PH^+ \xrightarrow{\text{fast}} P + H_3O^+$$

$d[P]/dt = k\,[RH^+]$

$[RH^+] = [H_3O^+][R]/K_{aRH^+}$

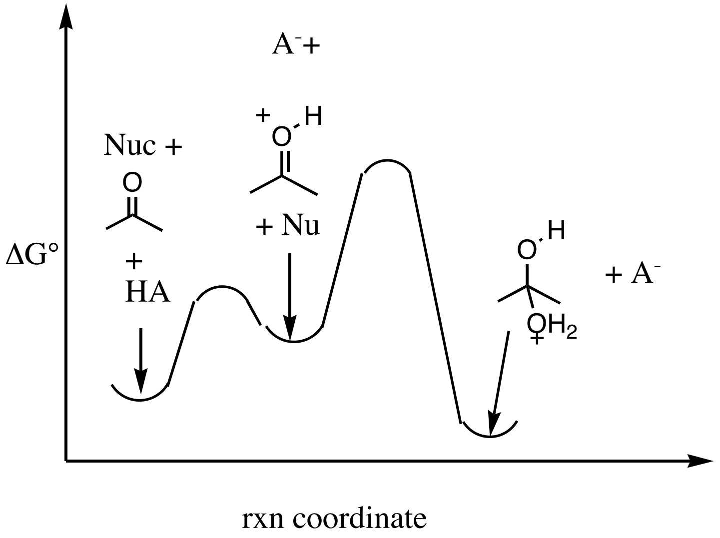
$[RH^+]$ depends on pH and pKa_{RH^+}
not on [HA]

$d[P]/dt = k\,[R][H_3O^+]/K_{aRH^+}$

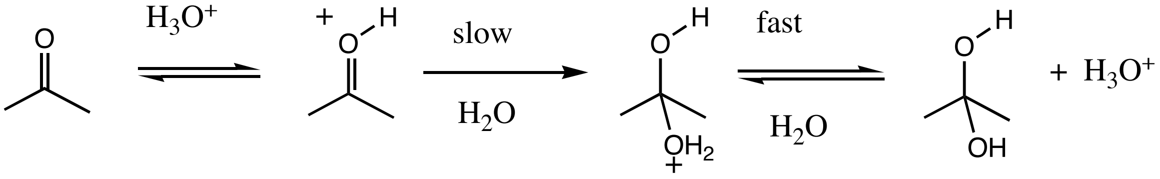
$d[P]/dt = k_{obs}[R]$

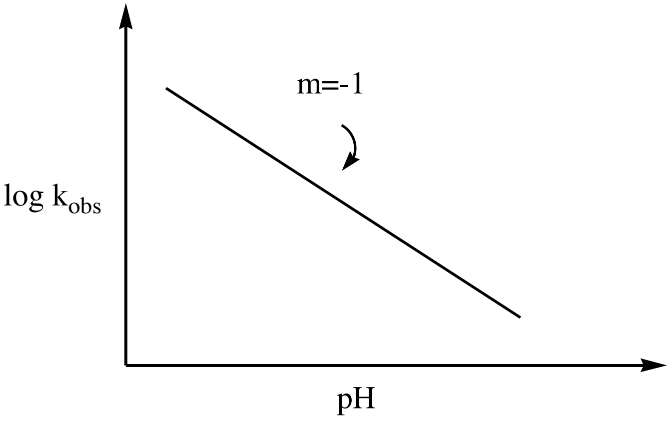
where $k_{obs}=k[H_3O^+]/K_{aRH^+}$

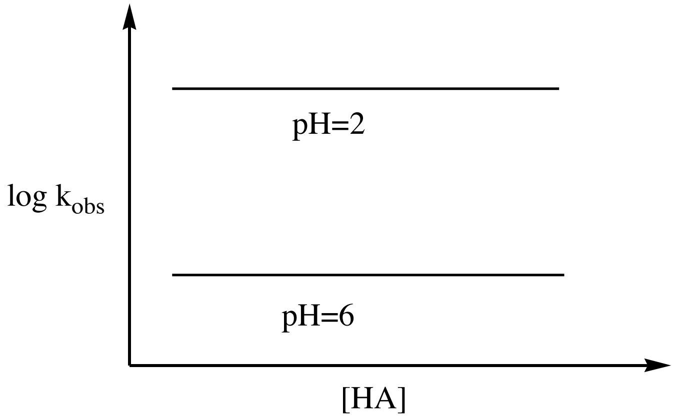
poor electrophile, poor nucleophile



Example:







General Catalysis

When an acid is involved in the rate-determining step, General Acid Catalysis is observed

When a base is involved in the rate-determining step, General Base Catalysis is observed

Any acid or base present in solution can participate in general acid catalysis

Scenario:

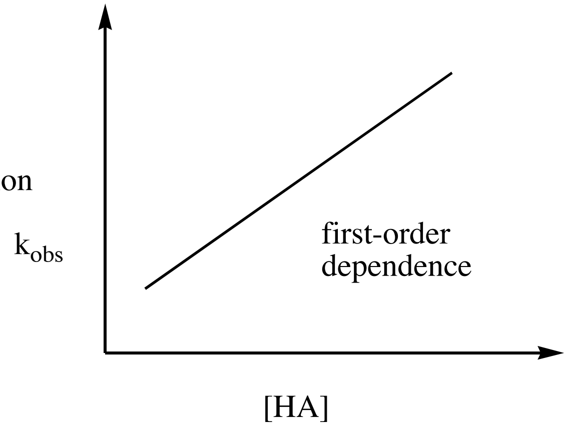
$$HA + R + H_2O \xrightarrow{\text{slow}} HR(H_2O)^+ + A^- \xrightarrow{\text{fast}} P + HA$$

$d[P]/dt = k[HA][R]$ the concentration of HA effects rate of reaction

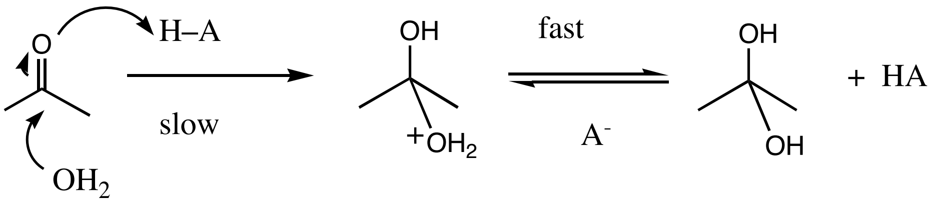
$[HA] = [H_3O^+][A^-]/K_a$ a constant, since HA is a catalyst

$d[P]/dt = k[H_3O^+][A^-][R]/K_a$

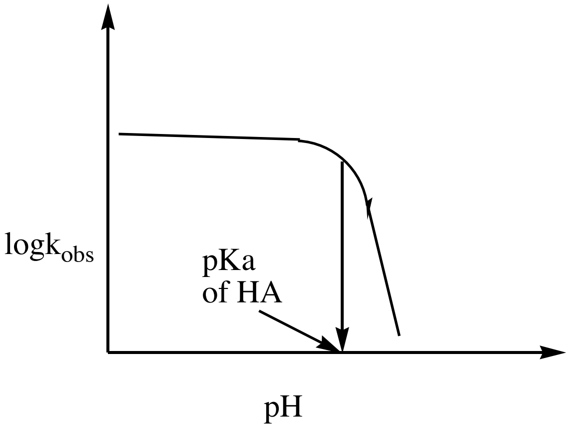
$d[P]/dt = k_{obs}[R]$ where $k_{obs} = k[H_3O^+][A^-]/K_a$



Example:



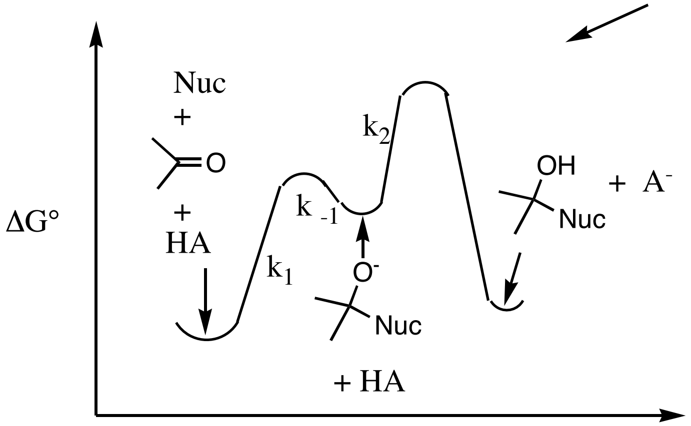
"concerted" or "enforced"



General Catalysis

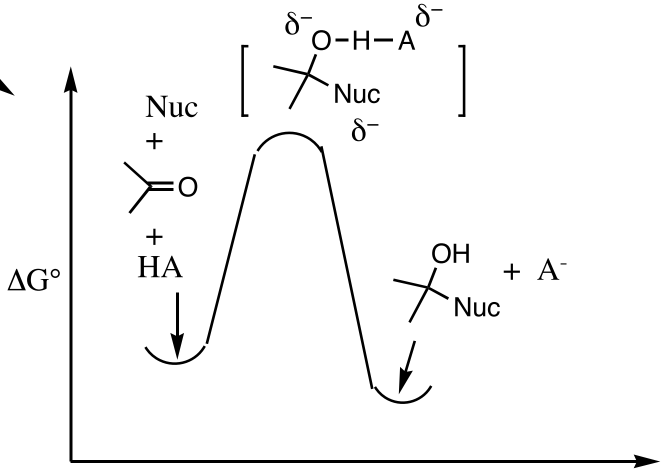
Weak Nucleophile
and/or weak electrophile

Enforced



protonation in RDS, intermediate has a short lifetime, can revert to carbonyl

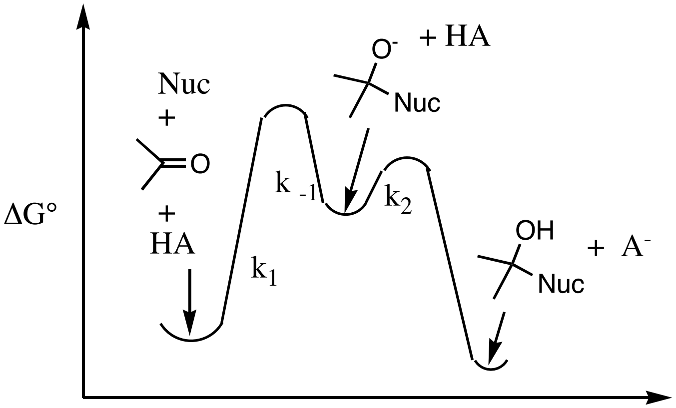
Concerted



simultaneous protonation/nucleophilic attack

No Acid Catalysis

Very Strong nucleophile

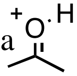


protonation after rate-determining step

General Catalysis

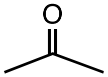
For General Acid Catalysis to occur, protonation must occur in the rate-determining step: Protonation of the transition state must be more favorable thermodynamically than protonation of the starting material

This will be favorable when pKa HA is between that of the protonated carbonyl and that of product

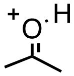
When pKa (HA) > pKa 

(HA is a weaker acid than protonated carbonyl)

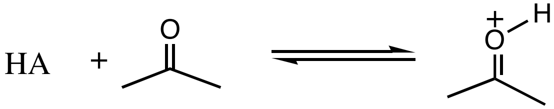
protonation thermodynamically unfavorable

A^- a stronger base than 

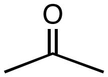
For Specific Catalysis, protonation of the starting material is thermodynamically favorable and occurs prior to nucleophilic attack:

when pKa(HA) < pKa 

(HA is a stronger acid than protonated carbonyl)

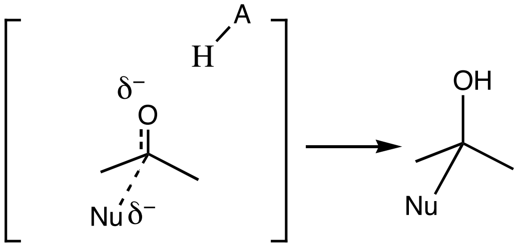


thermodynamically favorable



is a stronger base than A^-

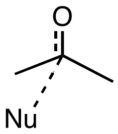
However, when pKa (HA)< pKa (product) carbonyl is becoming more basic as transition state is approached => general base catalysis can occur



pKa(product)> pKa(HA)

pKa of transition state resembles that of product

product is a weaker acid than HA



a stronger base than A^-

General acid or general base catalysis will occur when a thermodynaically unfavorable proton transfer in the ground state is converted to a thermodynamically favorable transfer in the transition state.

Bronsted Catalysis Law: investigate the effect of a series of acid or base catalysts on reaction rate

$\log k = - \alpha \, pK_a + C$ **for general acid catalysis**

$\log k = \beta \, pK_a + C$ **for general base catalysis**

The α, β values are the sensitivity or reaction constants for a reaction under general acid / base catalysis.

Sensitivity is to the pKa of the acid catalyst used or to the pka of the conjugate acid of the base catalyst used.
Sensitivity of the reaction rate to the structure of HA or B

α - extent of proton transfer in the transition state

$\alpha = 1$ acid has completely transferred a proton to reactant @ T.S. - for one pK unit increase in acid strength, there is a 10-fold difference in rate

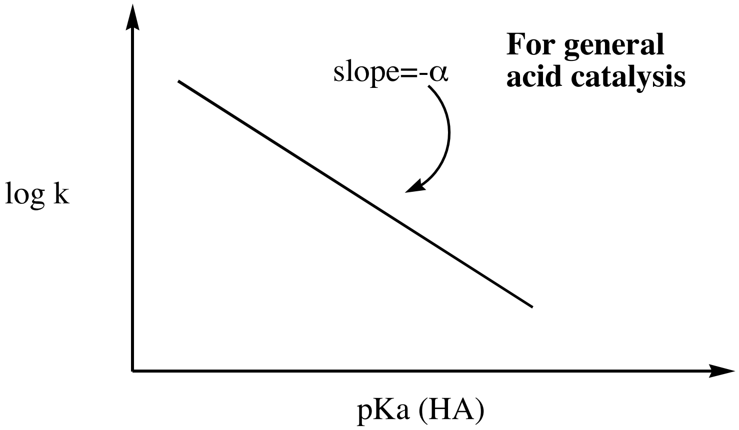
$\alpha = 0$ no sensitivity of the reaction rate to acid strength - the acid is not donating its proton in the rate-determining step this may indicate specific acid catalysis.

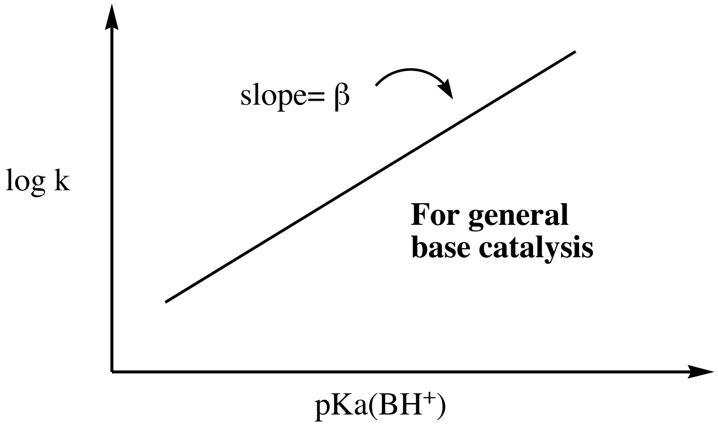
$0<\alpha<1$ intermediate extents of proton transfer in rate-determining transition state

$\beta = 1$ base has completely deprotonated substrate in rate-dtermining transition state

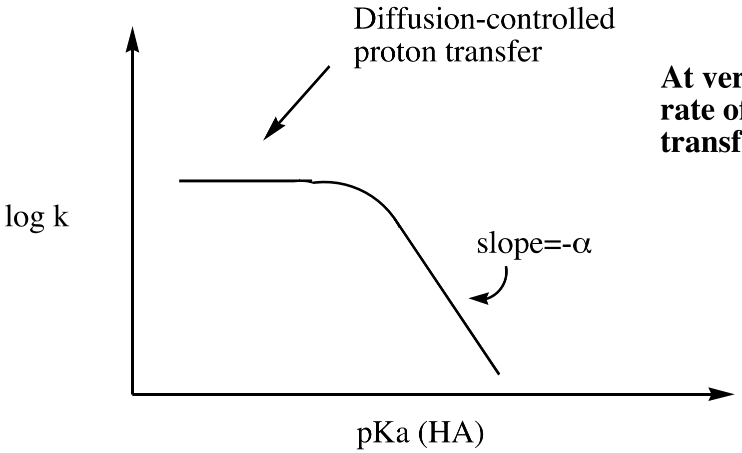
$\beta = 0$ No deprotonation of reactant in rate-determining T.S. Perhaps a specific base process

$0<\beta<1$ intermediate extents of deprotonation in rate-determining transition state





Bronsted Catalysis Law:Limits



At very high acid strengths only the rate of diffusion limits the rate of proton transfer

As long as the pKa of the conjugate acid of the acceptor B is greater than that of the donor HA by two or more units, the rate of proton transfer is found to be diffusion controlled, and thus the rate is independent of acid strength.

Standard rate constants for diffusion of a solute through a solvent are on the order of 10^8-10^9 s^{-1}

When α values are >1 (rare), this means that logk increases faster than $\log K_a$ within a reaction series, implying a reaction that is more sensitive to proton donor ability of the acid than is the protonation of water.

Dynamics of proton transfer:

$$\mathbf{A{-}H + B^-} \longrightarrow \mathbf{A{-}H \cdots B^-}$$

Diffusion together

$$\mathbf{A{-}H \cdots B^-} \longrightarrow \left[\overset{\delta^-}{\mathbf{A}} \mathbf{\cdots H \cdots} \overset{\delta^-}{\mathbf{B}}\right]^{\ddagger} \longrightarrow \mathbf{A^- \cdots H{-}B}$$

Proton transfer

$$\mathbf{A^- \cdots H{-}B} \longrightarrow \mathbf{A^- + H{-}B}$$

Diffusion apart