

PHYSICAL ORGANIC CHEMISTRY

1. Introduction

In this section we will look primarily at how quantitative measurements on rates and equilibria can be used to determine mechanisms of reactions. First a definition.

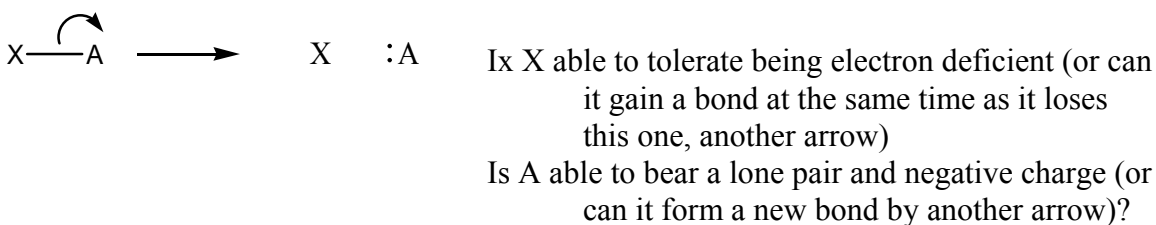
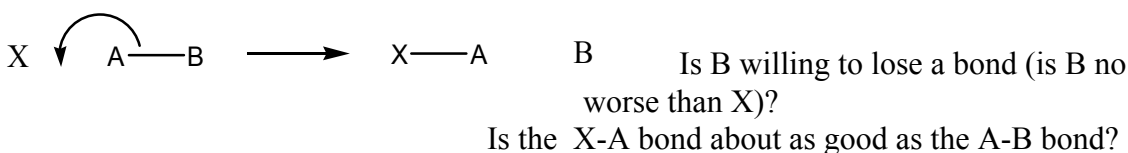
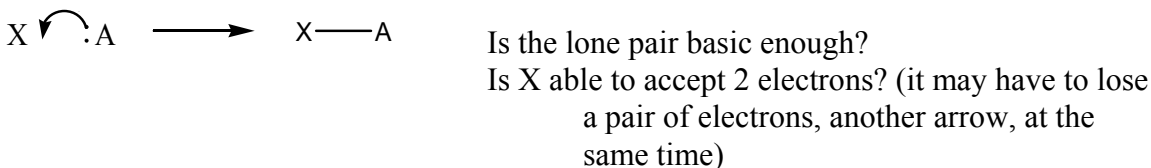
Reaction *mechanism*:

a detailed description of a reacting system as it progresses from reactants to products; it includes identification of all intermediates, the characteristics of the transition state(s), and the factors that affect reactivity.

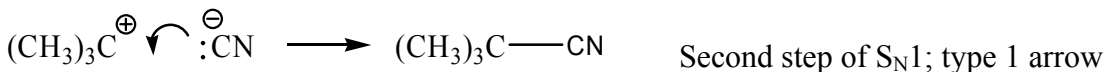
A mechanism is a theory of a reaction and as such gives predictability. A more detailed mechanism allows more detailed predictions. In this course we will be thinking in more detail about mechanisms, and how they are established. This requires being more precise in how we talk about them and draw them. Curly arrows provide a convenient language for talking about mechanisms, and we will use this language extensively in this course. I will now review it briefly.

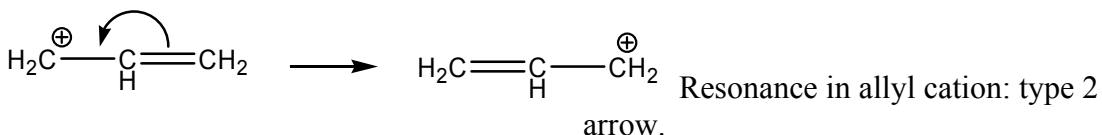
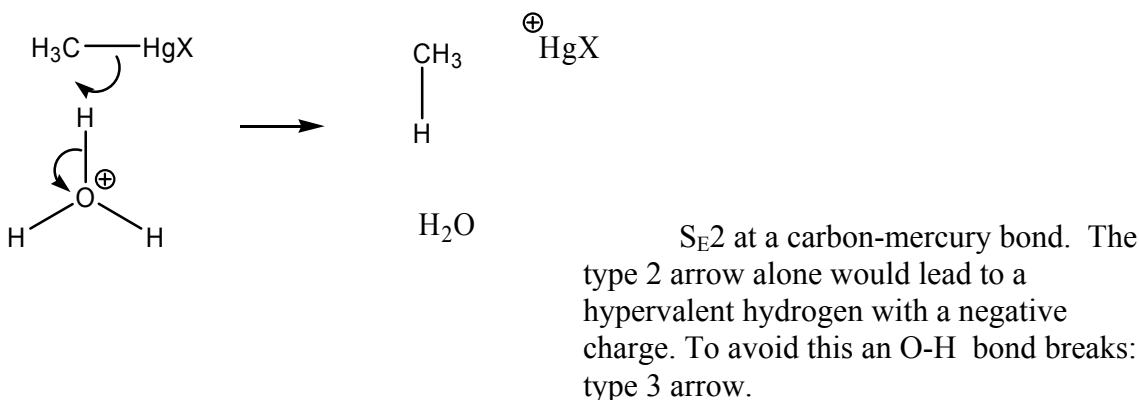
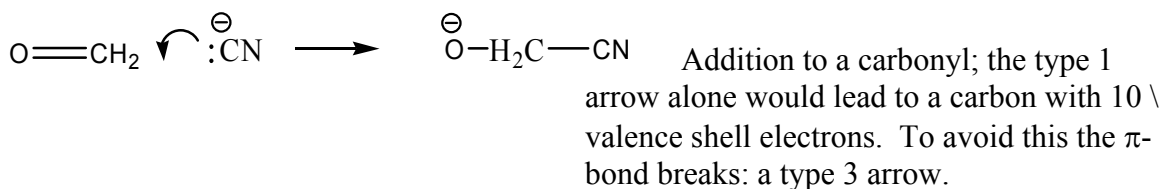
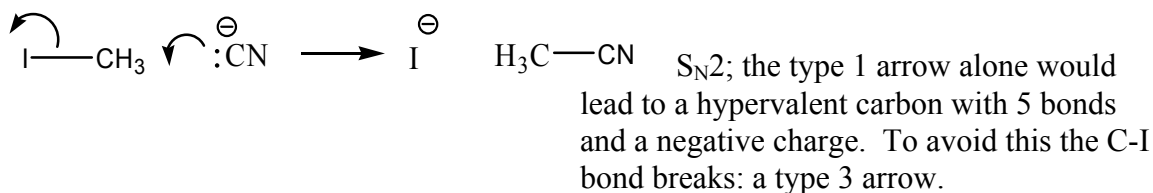
In this course we will use curly arrows in a more detailed fashion than you are used to because we are trying to define the nature of the rate determining transition state. Detailed mechanisms are needed to have control of a reaction and predict how the rate can be changed by changing conditions.

There are three different curly arrows which can be combined to write any mechanism:



These can be illustrated by some familiar reactions





On the course web page are reviews of reaction mechanisms and pKa values for common functional groups.

Now we turn to the detailed study of mechanisms.

2. Kinetics - mostly review

Why do we study kinetics? Anticipating a bit, the answer for mechanistic investigations is that kinetics gives us the composition of the transition state for the rate determining step of a reaction. It remains for us as chemists to work out the structure of the transition state, but knowing the composition strongly constrains the mechanisms we write. The first problem set will use the rate law for a reaction to decide which of two viable mechanisms is being followed.

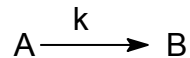
(a) First order, irreversible reaction.

First order chemical reactions and radioactive decay are governed by the same mathematics. In each case there is a definite probability that a molecule or atom will react in any given period of time. Thus the number of molecules reacting, or atoms

decaying, in a given time interval is a constant times the number of molecules or atoms present

$$\text{rate} = k[A]$$

$$\frac{d[A]}{dt} = -k[A]$$



$$\frac{d[A]}{dt} = -k[A]$$

the differential rate equation

First collect terms, [A] on the lhs, t on rhs

$$\frac{d[A]}{[A]} = -kt$$

integration gives

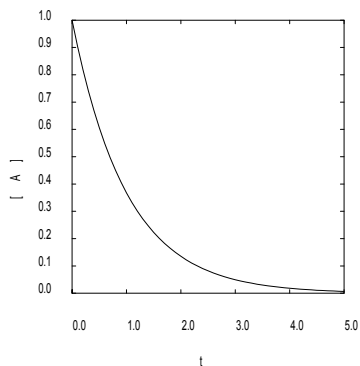
$$\ln \frac{[A]}{[A]_0} = -kt \quad \text{or} \quad \ln[A] = \ln[A]_0 - kt \quad \text{or} \quad [A] = [A]_0 e^{-kt} \quad \text{the integrated rate equation}$$

$$[A]_0 = [A] + [B]; \quad [A] = [A]_0 - [B]; \quad [A]_0 - [B] = [A]_0 e^{-kt}; \quad [B] = [A]_0 (1 - e^{-kt})$$

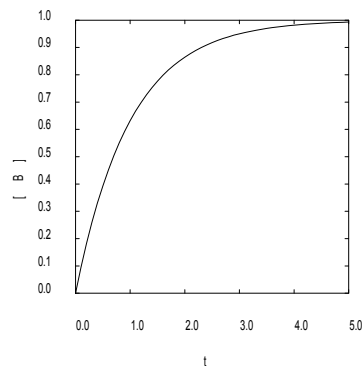
If it is easier to analyze for B than for A the last equation can be rearranged (using $[B]_\infty = [A]_0$) to

$$[B]_\infty - [B] = [B]_\infty e^{-kt} \quad \text{and plot } \ln([B]_\infty - [B]) \text{ vs } t. \quad \text{Since A goes irreversibly to B, } [A]_\infty = 0, \text{ and } [B]_\infty = [A]_0$$

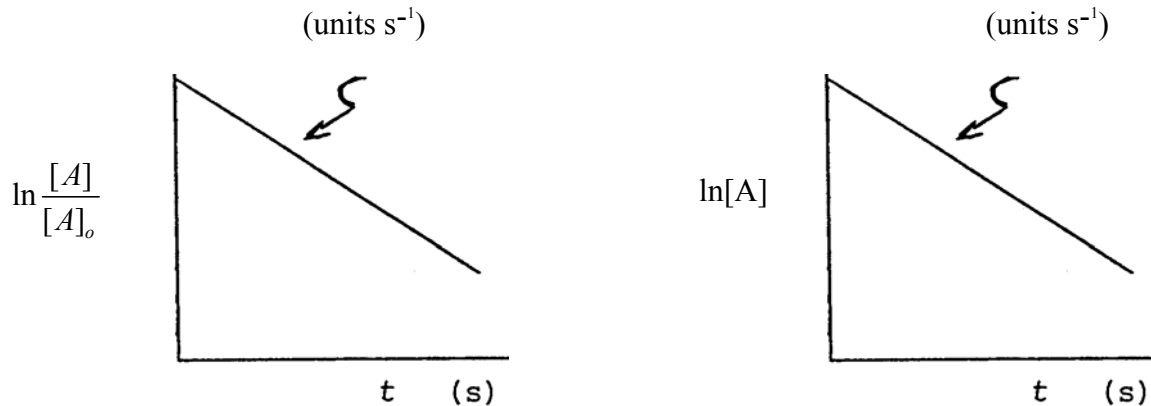
Plotting:



slope = -k,



slope = -k,



Note that in a first-order reaction one only needs to know the fraction of unreacted starting material at a particular time; the actual concentrations are not required. Furthermore one need not know the concentration at $t = 0$. In practice, any measure of the change in concentration will serve, e.g.

(i) The (integral of a peak due to A)/(standard integral), for an nmr experiment.

or

(ii) V , where V refers to the volume of titrant consumed by A, or, alternatively, $\Delta V = V_{\infty} - V$, where the titrant is consumed by B (or a product formed with B).

Various measures of how long a reaction takes

Half life: The time required for the concentration of A to fall to half its initial value

$$\frac{[A]_0}{2} = [A]_0 e^{-kt_{1/2}}; \quad t_{1/2} = \frac{\ln 2}{k} = \frac{.693}{k}$$

for $k = 2 \times 10^{-3} \text{ s}^{-1}$, $t_{1/2} = 347 \text{ s} = 5.8 \text{ min}$.

“Shelf life” The time required for the concentration of A to fall to 90% of its initial value

$$0.9[A]_0 = [A]_0 e^{-kt_{0.9}}; \quad t_{0.9} = \frac{\ln \frac{1}{0.9}}{k} = \frac{0.105}{k}$$

for $k = 2 \times 10^{-3} \text{ s}^{-1}$, $t_{0.9} = 53 \text{ s}$

“Lifetime” The time it would take for $[A]$ to fall to 0.0 if the rate remained $= k[A]_0$ throughout the reaction (i.e. stayed at the initial value).

$$\text{If } [A] = [A]_0 - k[A]_0 t$$

Then, solving for $t = \tau$ when $[A] = 0.0$

$$0 = [A]_0 - k[A]_0\tau \quad k\tau = 1 \quad \tau = 1/k$$

Another interpretation; τ is the time when $[A]$ has fallen from $[A]_0$ to $[A]_0/e$

$$[A] = [A]_0 e^{-k\tau}; \quad [A] = [A]_0 e^{-k/k} = \frac{[A]_0}{e}$$

To get a sense of how to interpret rate constants, look at the corresponding half lives

Rate constant (first order, s ⁻¹)	half life
10 ¹⁰	69.3 psec
10 ⁵	6.93 μsec
10 ⁰	0.693 sec
10 ⁻⁵	19.5 hours
10 ⁻¹⁰	219 years
10 ⁻¹⁵	2.19 x 10 ⁷ years
10 ⁻²⁰	2.19 x 10 ¹² years (life of the earth is 5 x 10 ⁹ years)

(b) Second order, irreversible reaction (one reagent - or two at the same concentration)

For a second order reaction the chemical transformation requires two molecules, either two the same (present case) or two different. Now the rate of the reaction depends on two things: how many collisions per unit time and the probability that a collision leads to reaction. The number of collisions depends on the product of two concentrations or on the square of the concentration of a reactant which reacts with itself. This means that the rate is given by

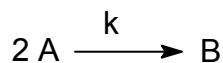
$$\text{rate} = k_r k_c [A]^2$$

where k_c is the collision probability

and k_r is the reaction probability

or $= k[A]^2$ $k = \text{the usual rate constant.}$

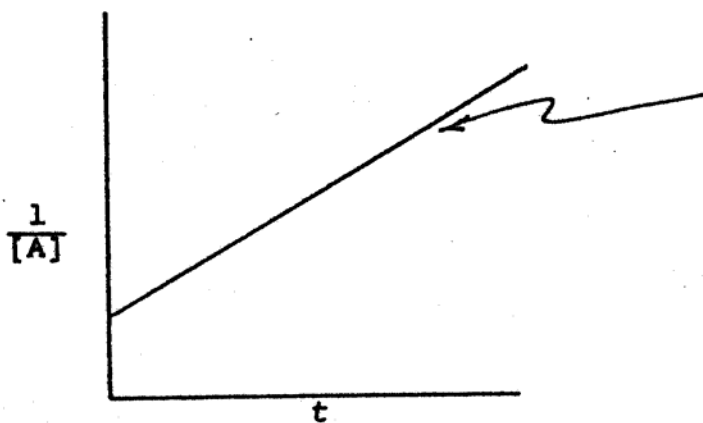
(i)



$$-\frac{d[A]}{dt} = k[A]^2$$

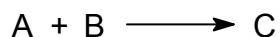
Integration leads to

$$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$$



slope = k
 units of k :
 $(\text{concentration})^{-1}$
 $\times (\text{time units})^{-1}$
 e.g. $\text{M}^{-1}\text{s}^{-1}$
 (or $\text{L mol}^{-1} \text{s}^{-1}$)

The same result is obtained for

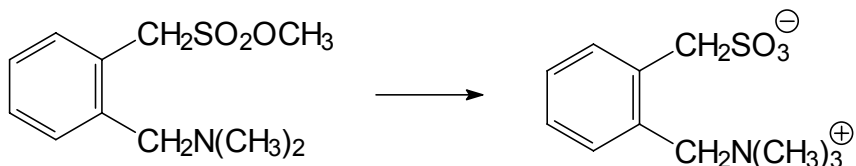


If $[A]_0 = [B]_0$

$$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$$

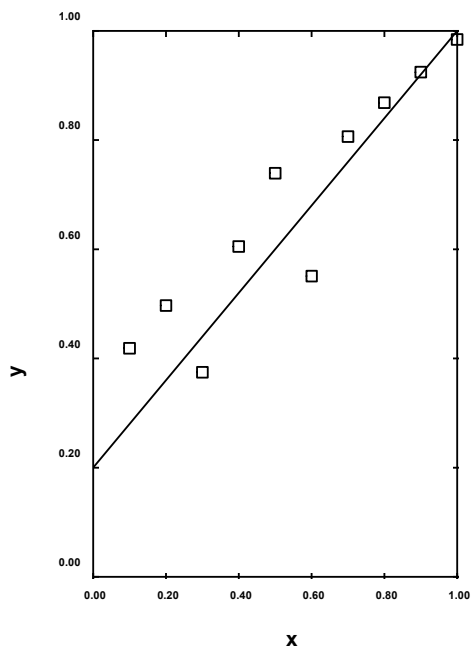
At this point you have the tools to handle the first problem.

The problem is concerned with the following reaction, for which you should be able to write two mechanisms, which differ in the rate law which is implied. This means that a kinetics experiment will allow you to decide which mechanism is actually followed in the reaction. The reaction was carried out in benzene- d_6 .

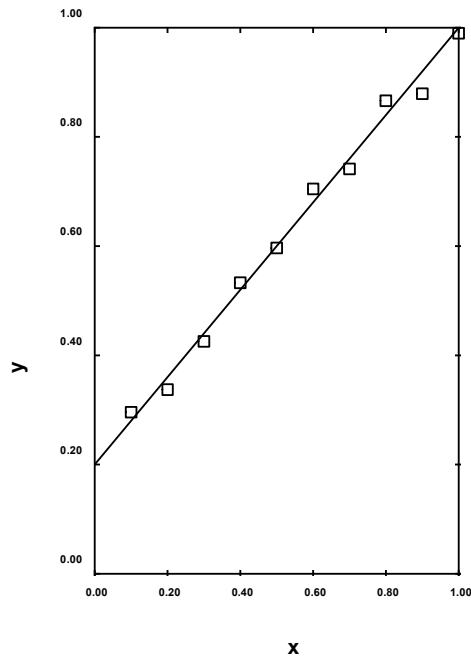


A few words about the use of graphs to analyze data. The human eye is very good at seeing linear relationships, i.e. points which define a straight line. It is not nearly as good at seeing whether points fit a curve. For qualitative analysis it is a good idea to massage the data into a form giving a linear plot, so that one can tell by looking at the data if they fit the expected pattern. For quantitative analysis it is better to use the original non-linear form (provided you have access to a non-linear least squares program).

Some examples:
a passable fit

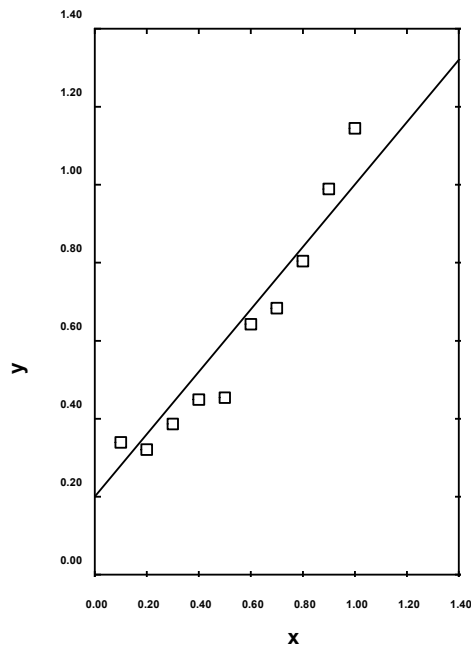
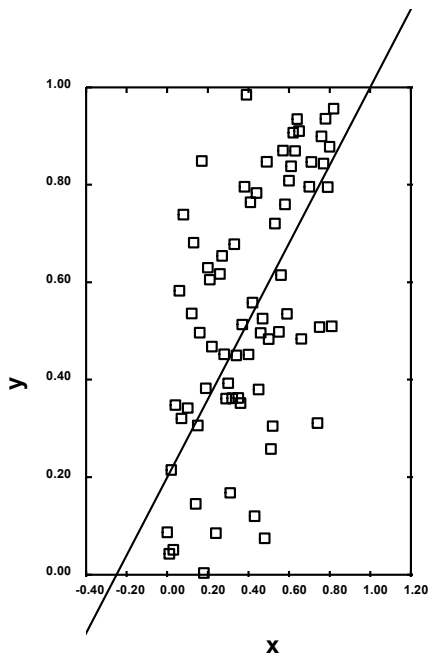


a good fit



a really poor fit

case where the data require
a different equation



One of the great things about first order kinetics is that the half life is independent of the initial concentration, and thus is the same at any stage of the reaction.

First order: $t_{1/2} = 0.693/k$

The time for two half lives, i.e. for $[A]$ to fall from $[A]_0$ to $[A]_0/4$ is $t_{1/4}$ and is given by

$$\begin{aligned}\frac{[A]_0}{4} &= [A]_0 e^{-kt_{1/4}} \\ -\ln(4) &= -kt_{1/4} \\ t_{1/4} &= \frac{\ln(4)}{k} = \frac{2\ln(2)}{k} = 2t_{1/2}\end{aligned}$$

The time for three half lives, i.e. for $[A]$ to fall from $[A]_0$ to $[A]_0/8$ is $t_{1/8}$ and is given by

$$\begin{aligned}\frac{[A]_0}{8} &= [A]_0 e^{-kt_{1/8}} \\ -\ln(8) &= -kt_{1/8} \\ t_{1/8} &= \frac{\ln(8)}{k} = \frac{3\ln(2)}{k} = 3t_{1/2}\end{aligned}$$

For second order kinetics the half life depends on the initial concentration: for the “identical initial concentrations” case,

$$\frac{1}{[A]} - \frac{1}{[A]_0} = kt$$

the time for $[A]$ to fall to $\frac{[A]_0}{2}$ is $t_{1/2}$

$$\frac{1}{([A]_0/2)} - \frac{1}{[A]_0} = kt_{1/2}$$

$$\frac{2}{[A]_0} - \frac{1}{[A]_0} = \frac{1}{[A]_0} = kt_{1/2}$$

$$t_{1/2} = \frac{1}{k[A]_0}$$

similarly the time to fall to $[A]_0/4$, $t_{1/4}$ is

$$\frac{1}{([A]_0/4)} - \frac{1}{[A]_0} = kt_{1/4}$$

$$\frac{4}{[A]_0} - \frac{1}{[A]_0} = \frac{3}{[A]_0} = kt_{1/4}$$

$$t_{1/4} = \frac{3}{k[A]_0}$$

and the second half life (the time for $[A]$ to fall from $[A]_0/2$ to $[A]_0/4$ is $2/k[A]_0$.

By similar means the third half life (time for $[A]$ to fall from $[A]_0/4$ to $[A]_0/8$ can be shown to be $4/k[A]_0$.

How long does it take till a reaction is “over”; it depends on your criterion, and on the nature of the kinetics.

Number of half lives Percent of starting material left

1	50
2	25
3	12.5
4	6.25
5	3.125
6	1.5625
7	0.781
8	0.391
9	0.195
10	0.098

Thus to have less than 1% of the starting material left needs more than 6 half lives; to have less than 0.1% left requires 10 half lives.

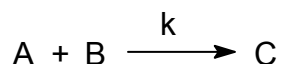
After 10 half lives the concentration of starting material has fallen to $[A]_0/2^{10} = [A]_0/1024$.

For first order kinetics the time for this to happen is given by $t_{10} = \ln(2^{10})/k = 6.93/k$

For second order kinetics this time is given by

$$t_{10} = \left(\frac{1}{k}\right) \left(\frac{2^{10}}{[A]_0} - \frac{1}{[A]_0}\right) = \frac{1023}{k[A]_0}$$

(ii) Second order, irreversible reaction (two reagents, different concentrations)



Mass balance leads to:

$$[A]_0 - [A] = [B]_0 - [B] = [C] \quad (\text{assuming, as is generally the case, that } [C]_0 = 0)$$

$$\text{Then } -[B] = [A]_0 - [A] - [B]_0$$

$$-\frac{d[A]}{dt} = -\frac{d[B]}{dt} = \frac{d[C]}{dt} = k[A][B]$$

Which leads to the integrated rate equation:

$$\frac{1}{([B]_0 - [A]_0)} \left\{ \ln \frac{[B]}{[A]} - \ln \frac{[B]_0}{[A]_0} \right\} = kt$$

(c) Pseudo-first order kinetics When $[B] \approx \text{const}$, e.g.
When $[B]_0 \gg [A]_0$ (and hence also $\gg [A]$)

$$[B]_0 - [A]_0 \approx [B]_0$$

$$[B] \approx [B]_0$$

The above equation for the second order reaction becomes

$$\frac{1}{([B]_0 - [A]_0)} \left\{ \ln \frac{[B]}{[A]} - \ln \frac{[B]_0}{[A]_0} \right\} = kt$$

$$\frac{1}{[B]_0} \left\{ \ln \frac{[B]_0}{[A]} - \ln \frac{[B]_0}{[A]_0} \right\} = kt$$

$$\frac{1}{[B]_0} \left\{ \ln \frac{[B]_0}{[A]} + \ln \frac{[A]_0}{[B]_0} \right\} = kt$$

$$\frac{1}{[B]_0} \left\{ \ln \frac{[A]_0}{[A]} \right\} = kt$$

$$\ln \frac{[A]}{[A]_0} = -[B]_0 kt = -k_{\psi} t = -k_{obs} t = -k_{exp} t$$

which is identical to the expression for the first order reaction except for the factor $[B]_0$. Commonly the most convenient way of determine the second order rate constant, k , is to use $[B]_0 \gg [A]$, so-called pseudo-first order conditions. In practice $[B]_0$ should be at least $5x[A]_0$ and preferably $10x[A]_0$. One does experiments at several values of $[B]_0$ and then plots k_{ψ} vs $[B]_0$. The slope is the second order rate constant. What does it mean if the intercept is not zero?

$$k = \frac{k_{\psi}}{[B]_0} = \frac{k_{obs}}{[B]_0}$$

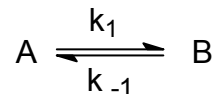
Pseudo-first order and true first order kinetics can easily be distinguished. How?

Note: Pseudofirst order conditions are not restricted to $[B]_0 \gg [A]_0$

The general requirement is that $[B] \approx \text{constant}$

e.g. pH stat or buffers can hold $[H^+]$ constant even though it is small compared to the other reactant. see problem set #7, Q#2

d) Reversible 1st order reactions



If $[A] = [A]_0$ and $[B] = [B]_0$ at $t = 0$ $[A]_e$ is the concentration of A at equilibrium, and $[B]_e$ is the concentration of B at equilibrium, one finds at any time t ,

$$[A]_0 - [A] = [B] - [B]_0$$

$$\ln \frac{[A] - [A]_e}{[A]_0 - [A]_e} = -(k_1 + k_{-1})t$$

i.e. approach to equilibrium is a first order process with the observed rate constant the sum of the forward and reverse k 's; i.e.

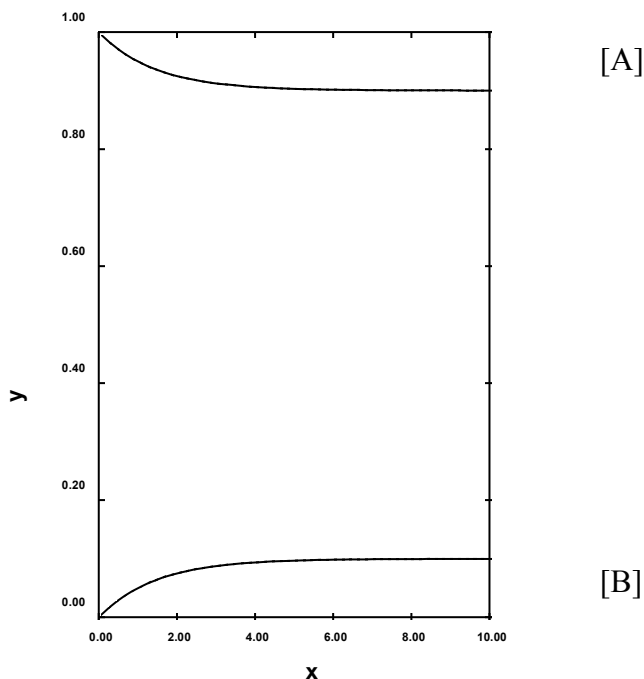
$$k_{\text{obs}} = k_1 + k_{-1}$$

$$\text{Since } K = \frac{[B]_e}{[A]_e} = \frac{[A]_o + [B]_o - [A]_e}{[A]_e} = \frac{k_1}{k_{-1}}$$

we may readily find k_1 and k_{-1} from k_{obs} and K , but note: If you don't know K , measuring k_{obs} will not lead to K but only to $k_1 + k_{-1}$

If one of k_1 or k_{-1} is pseudofirst order (i.e. really second order) then a plot of k_{obs} vs the concentration of the reagent in excess will lead to a separation of the rate constants. This trick requires that you know the rate law, (and know that the reagent in excess is not a catalyst as well as a reagent).

For many people it takes a while to be convinced that the rate of approach to equilibrium is governed by the sum of the forward and reverse rate constants. As a way of considering it first take a system where $K = [B]_e/[A]_e = (1/9)$, so that $[B]_e/([A]_e + [B]_e) = 0.1$. This means $K = k_1/k_{-1} = 1/9$, $k_{-1} = 9 \times k_1$, and $k_1 + k_{-1} = 10 \times k_1$. To make things simple $[A]_o = 1.0$, $[B]_o = 0.0$. $k_1 = 0.1$. This is illustrated in:



We can deduce that at equilibrium $[B]_e = (k_1/k_{-1})[A]_e = (k_1/k_{-1})([A]_o - [B]_e)$. Then solving for $[B]_e$ we get

$$[B]_e(1 + k_1/k_{-1}) = (k_1/k_{-1})[A]_o$$

from which after simplification we get

$$[B]_e = k_1[A]_o/(k_1 + k_{-1})$$

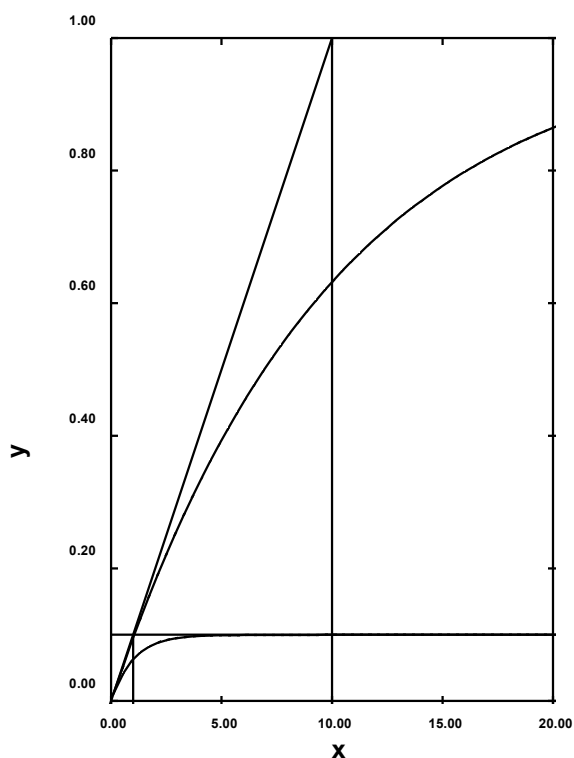
The time for [B] to rise from zero to [B]_e if the initial rate applied throughout (i.e. the lifetime assumption) is given by:

$$[B]_{t=\tau} - [B]_{t=0} = k_1[A]_0(\tau - 0) \text{ or}$$

$$[B]_e = k_1[A]_0\tau$$

$$k_1[A]_0/(k_1 + k_{-1}) = k_1[A]_0\tau, \text{ and } \tau = 1/(k_1 + k_{-1})$$

Now we look at the lifetime graph:



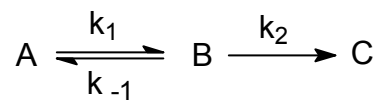
If the reaction were irreversible $A \rightarrow B$ then the lifetime would be $\tau = 1/k_1 = 10$.
If the reaction is reversible, then $\tau = 1/(k_1 + k_{-1}) = 1$.

e) Steady-state approximation

The analytical expressions giving exact solutions to the kinetics of complex systems may be very complex, intractable, or simply unknown. If one (or more) of the species in the scheme is a short-lived intermediate the analysis can be much simplified by setting

$$\frac{d[I]}{dt} = 0$$

To illustrate, consider the following scheme



If B is short lived then either k_{-1} or $k_2 \gg k_1$ and $[B]$ is always small wrt $[A]$ or $[C]$

Since

$$\begin{aligned} \frac{d[C]}{dt} &= k_2[B] \quad \text{and} \\ -\frac{d[A]}{dt} &= k_1[A] - k_{-1}[B] \\ \frac{d[B]}{dt} &= k_1[A] - k_{-1}[B] - k_2[B] = 0 \end{aligned}$$

$$[B] = \frac{k_1[A]}{k_{-1} + k_2}$$

$$\text{and so } \frac{d[C]}{dt} = \frac{k_1 k_2 [A]}{k_{-1} + k_2} = -\frac{d[A]}{dt}$$

because

$$\begin{aligned} -\frac{d[A]}{dt} &= k_1[A] - k_{-1}[B] \\ &= k_1[A] - k_{-1} \frac{k_1[A]}{k_{-1} + k_2} \\ &= \frac{k_1 k_{-1}[A] + k_1 k_2[A] - k_{-1} k_1[A]}{k_{-1} + k_2} \\ &= \frac{k_1 k_2 [A]}{k_{-1} + k_2} \end{aligned}$$

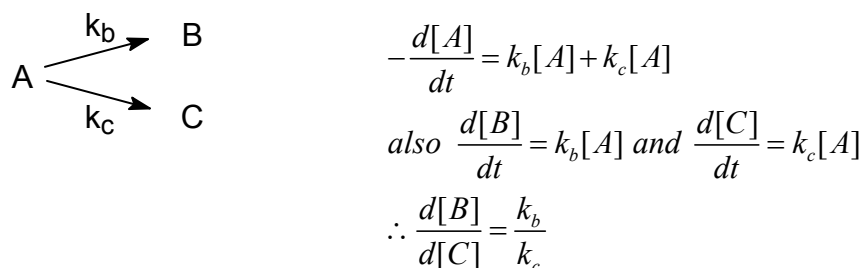
or the observable pseudo 1st-order rate constant for formation of C (or, disappearance of A) is given by

$$k_{obs} = \frac{k_1 k_2}{k_{-1} + k_2}$$

How long does it take to establish the steady state? We can ask the related question: how long would it take to establish equilibrium if k_2 were zero? The rate constant for approach to equilibrium would be $(k_1 + k_{-1})$ and the half life for this process would be $= \ln 2 / (k_1 + k_{-1})$. If $k_{-1} \gg k_1$, then this half life is much less than the half life for the overall reaction, which is $\ln 2 / k_1$. If k_2 is not zero, then the steady state value of $[B]$ will be lower and the approach to equilibrium will be faster.

(Note that for second order schemes under pseudo-first order conditions we may readily write the analogous expression by substituting the rate constants above by a new rate constant multiplied by the appropriate concentration term, e.g. k_1 by $k_1[X]$, etc.)

(f) Parallel reactions

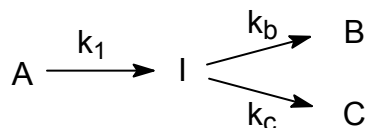


If $[B]_0 = [C]_0 = 0$, integrating gives

$$\frac{[B]}{[C]} = \frac{k_b}{k_c}$$

The ratio $[B]/[C]$ may be determined at any stage of the reaction. The measurements of $[B]$ and $[C]$ must be simultaneous if the reaction is not completed, and one must have confidence that neither formation of B or of C is reversible, and that there is no leakage either converting B and C or changing one or both into something else.

Extending



When $k_1 \ll k_b$ or k_c

$$-\frac{d[A]}{dt} = k_1[A]$$

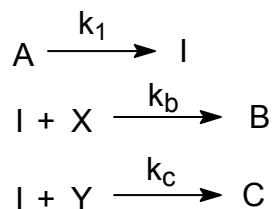
and no information can be obtained about k_b or k_c by measuring the rate.
but, since

$$\frac{[B]}{[C]} = \frac{k_b}{k_c}$$

rate constant ratios can be found from product ratios

This may be readily generalized:

Eg.

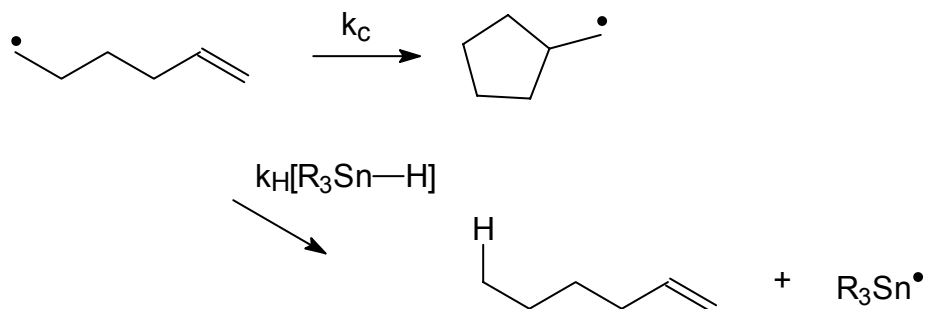


under pseudo-first order conditions ($[X]_0, [Y]_0 \gg [A]_0$)

if $k_1 \ll k_b[X], k_c[Y]$ then

$$\frac{[B]}{[C]} = \frac{k_b[X]}{k_c[Y]}$$

I.e. rate *constant ratios* may readily be obtained from product ratios, provided one has a sound basis for assigning the above (or similar) kinetic scheme (i.e. that one knows the kinetic order of the product-forming steps and that neither product forming reaction is reversible, etc.) This can be used as a “Clock reaction”. For example, the rate constant for cyclization of 5-hexenyl radical to form a cyclopentylmethyl radical is known; this can be used as a clock reaction to measure rates of hydrogen abstraction from a series of tin reagents to see if there is a useful variation which could be used to give selective reaction.



In this case one of the parallel reactions is true first order, the k_c cyclization process, and one is pseudo first order, with a high concentration of tin reagent. Since k_c is known for the reaction conditions (t-butylbenzene as solvent, 80°C) to be $1.12 \times 10^6 \text{ s}^{-1}$ then from product ratios and the concentration of R_3SnH , one can determine the rate constant k_H for this tin reagent.

(g) Other situations - a comment

As noted earlier, many conceivable mechanistic schemes give kinetic expressions which appear difficult or impossible to convert into useful integrated forms. For some of these solutions have been devised and are described in chemical kinetics texts. Any reaction scheme which can be described in differential form can, however, be treated by "numerical", i.e. computer simulation, methods;