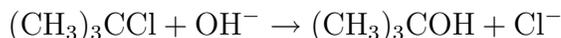
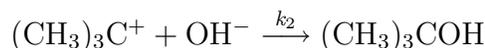
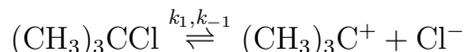


5.2 Exercise

Consider a nucleophilic substitution reaction:



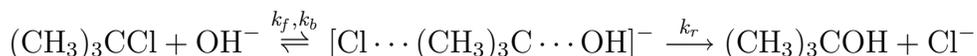
Let us first assume the following mechanism



Q1. Apply the steady-state approximation for the intermediate $(\text{CH}_3)_3\text{C}^+$ and derive the rate law.

Q2. Show that the rate law is 1st-order when $[\text{OH}^-]$ is in excess or when $k_{-1} \ll k_2$

Let us next consider an alternative mechanism



Q3. Apply the steady-state approximation for the intermediate complex and show that this mechanism gives a 2nd-order rate law.

Answers:

1.

$$\text{Rate} = \frac{k_1 k_2 [(\text{CH}_3)_3\text{CCl}] [\text{OH}^-]}{k_{-1} [\text{Cl}^-] + k_2 [\text{OH}^-]}$$

2.

$$\text{Rate} \simeq k_1 [(\text{CH}_3)_3\text{CCl}] \text{ when } k_{-1} [\text{Cl}^-] \ll k_2 [\text{OH}^-]$$

3.

$$\text{Rate} = \frac{k_f k_r}{k_b + k_r} [(\text{CH}_3)_3\text{CCl}] [\text{OH}^-]$$

5.3 Michaelis-Menten equation

Let us consider an enzyme catalysis reaction in which the enzyme E and a substrate S form an intermediate complex ES and then the reaction occurs to release the product P:



This looks similar to the scheme in Eq (49), and hence the steady-state approximation will give

$$\text{Rate} = \frac{k_1 k_2}{k_2 + k_{-1}} [\text{E}][\text{S}]$$

(It will be a good exercise to derive and confirm this.) However, this looks very different from the famous Michaelis-Menten equation:

$$\text{Rate} = \frac{V_{\max}[\text{S}]}{[\text{S}] + K_M}$$

We notice that one of the major difference is that the enzyme concentration $[\text{E}]$ is not involved in the latter. We therefore try to eliminate $[\text{E}]$ in the course of the application of the steady-state approximation. To this end, it is essential to recognize that the enzyme is a catalyst. Therefore, it is not destroyed by the reaction and the total number of enzyme molecules is kept constant. This is described by

$$[\text{E}] + [\text{ES}] = \text{constant} = [\text{E}]_0 \quad (52)$$

in which $[\text{E}]_0$ is the initially prepared concentration of the enzyme. Now we apply the recipe of the steady-state approximation. First we identify that the ES complex is the intermediate. Its change in the scheme (51) is written as

$$\frac{d[\text{ES}]}{dt} = k_1[\text{E}][\text{S}] - k_{-1}[\text{ES}] - k_2[\text{ES}]$$

The steady-state approximation sets the right hand side to be equal to zero. But before doing it, we will eliminate $[\text{E}]$ by using Eq (52):

$$k_1([\text{E}]_0 - [\text{ES}])[\text{S}] - k_{-1}[\text{ES}] - k_2[\text{ES}] \simeq 0$$

$$\Rightarrow [\text{ES}]_{\text{ss}} = \frac{k_1[\text{E}]_0[\text{S}]}{k_1[\text{S}] + k_{-1} + k_2} \quad (53)$$

The overall rate is that of the product formation determined by the final step of the scheme (51):

$$\text{Rate} = \frac{d[\text{P}]}{dt} = k_2[\text{ES}]$$

We replace $[\text{ES}]$ by Eq (53):

$$\text{Rate} = \frac{k_2 k_1 [\text{E}]_0 [\text{S}]}{k_1 [\text{S}] + k_{-1} + k_2} = \frac{k_2 [\text{E}]_0 [\text{S}]}{[\text{S}] + \frac{k_{-1} + k_2}{k_1}} = \frac{V_{\max} [\text{S}]}{[\text{S}] + K_M}$$

in which $V_{\max} = k_2[\text{E}]_0$ is the maximum rate and $K_M = (k_{-1} + k_2)/k_1$ is the Michaelis constant.

Further Readings

Now there would be two ways for you to proceed. One is to review the basics again by reading the recommended textbooks. In particular, it would be a good idea to attempt the worked examples and problems in order to see how the theories work in more practical situations and to confirm your understanding of the theories. It is also useful to read explanations by different authors. This is because no one can explain things perfectly and you will have to build your own way of understanding by repeating reading and thinking.

Another way forward would be to read advanced books and research papers. One of recommendable books is:

- A Fersht, Structure and Mechanism in Protein Science, Freeman.
(There are 8 long loan and 2 week loan copies in Barnes Library, Medical School, Shelfmark QP 551/F.)

I trust that this lecture course has provided sufficient background to get ready for this and other books and papers.