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# 6

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## KINETICS, CATALYSIS, AND REACTION ENGINEERING

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### 6.1 BASIC CONCEPT OF RATE

#### 6.1.1 Definition of Reaction Rate

Molecules are in constant molecular motion. The molecules may collide at either a high or low speed depending on the concentration of species present and the temperature of the medium. The electrons from one molecule interact with those of another molecule, leading to the formation of a new chemical species. The amount of time it takes for that change to occur is called the *rate of the reaction*, and the study of reaction rate is termed *kinetics*. In other words, kinetics is just a fancy way of describing how fast reactions happen.

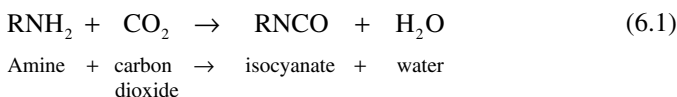
To quantify the speed at which a reaction occurs, it is necessary to determine the *reaction rate* defined as the change in the concentration of reactants or products over a period of time.

For example, the following non-phosgene isocyanate synthesis leading ultimately to the production of polyurethanes used in solvent-based adhesive systems can be represented as follows:

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*Green Chemistry and Engineering: A Pathway to Sustainability*,  
Anne E. Marteel-Parrish and Martin A. Abraham.

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This synthesis was developed by a group at Monsanto Company.

The rate can be measured as the change in the concentration of the amine per unit of time:

$$\text{Rate} = -\Delta[\text{RNH}_2] / \Delta t = -\{[\text{RNH}_2]_f - [\text{RNH}_2]_i\} / \{t_f - t_i\} \quad (6.2)$$

with *i* and *f* standing for initial and final, respectively.

The rate can also be expressed as the change in the concentration of the isocyanate per unit of time:

$$\text{Rate} = +\Delta[\text{RNCO}] / \Delta t = +\{[\text{RNCO}]_f - [\text{RNCO}]_i\} / \{t_f - t_i\} \quad (6.3)$$

In this case, the change in the concentration of a product is positive whereas the change in the concentration of a reactant is negative. Since products are formed during a chemical reaction, their concentration will increase over time. Reactants are consumed during a chemical reaction; therefore, the concentrations of the reactants decrease over time. Since rates of reactions are expressed as positive quantities, it is necessary to add a negative sign in front of the change of concentrations of reactants.

In many cases, it will be easier to refer to the *conversion* of a particular reactant, rather than looking at molar amounts or flow rates. We define the conversion of a reactant as the fraction of material that is used up in the reaction. This provides

$$X = \frac{N_{j,0} - N_j}{N_{j,0}} = 1 - \frac{N_j}{N_{j,0}} \quad (6.4)$$

where *X* is the conversion and *N* is the number of moles of the species. Here, the subscript *j* is used to indicate any species in the reaction, with the subscript 0 (zero) indicating the initial amount. If one were to divide the number of moles by the volume of the system, then Equation 6.4 would represent the change in concentration of the species, similar to that described by Equation 6.2.

Equation 6.4 is always correct but most easily applied to a static system. In some cases, reactions are carried out in flowing systems, in which case we substitute the molar flow rate in place of the amount, to provide

$$X = \frac{F_{j,0} - F_j}{F_{j,0}} = 1 - \frac{F_j}{F_{j,0}} \quad (6.5)$$

The only difference between Equation 6.5 and Equation 6.4 is the use of the molar flow rate (*F*) in place of the number of moles of the species.

We also like to normalize the composition of the species that are produced in the reaction, and define the *yield* of a material as

$$Y_i = \frac{N_i}{N_{j,0}} = \frac{F_i}{F_{j,0}} \quad (6.6)$$

where component  $i$  is the species of interest and component  $j$  is the *limiting* reactant. The limiting reactant is the one that will be used up first if the reaction is allowed to proceed for a long enough time.

When a chemical reaction involves stoichiometric coefficients that are different from one (1), it is necessary to take the stoichiometry into account in the expression of the reaction rate.

For example, ozone decomposes naturally to form oxygen as follows:



In this case, the reaction rate can be expressed as

$$\text{Rate} = -\frac{1}{2}\Delta[\text{O}_3] / \Delta t \quad (\text{with respect to the reactant}) \quad (6.8)$$

or

$$\text{Rate} = +\frac{1}{3}\Delta[\text{O}_2] / \Delta t \quad (\text{with respect to the product}) \quad (6.9)$$

The rate will be the same regardless of whether the product concentrations or the reactant concentrations are used in the calculations.

For a general reaction involving A and B as reactants and C and D as products,



the rate is defined as

$$\begin{aligned} \text{Rate} &= -(1/a)\Delta[\text{A}] / \Delta t = -(1/b)\Delta[\text{B}] / \Delta t \\ &= +(1/c)\Delta[\text{C}] / \Delta t = (1/d)\Delta[\text{D}] / \Delta t \end{aligned} \quad (6.11)$$

Engineers use an algebraic method to keep track of the interdependence between the amounts of the various materials participating in the chemical reaction. Since the number of moles of the product is related to the conversion of the reactant, a single stoichiometric variable is used. The bookkeeping system is called the *stoichiometric table*. We will use the conversion as a basis for calculation.

Let's start by defining the stoichiometric coefficient,  $\nu_i$ , which is the number of moles of species  $i$  that reacts (or is formed) according to the chemical equation. By

convention, we define  $v_i$  as being *positive* for material produced by the reaction. We start by defining the extent of the reaction,

$$\xi = \frac{N_i - N_{i,0}}{v_i} = \frac{F_i - F_{i,0}}{v_i} \quad (6.12)$$

In developing this definition, we have used the stoichiometric coefficient,  $v_i$ , which is the number of moles of species  $i$  that reacts or is formed according to the chemical equation. For a constant volume system, we can easily convert this expression from moles to concentration simply by dividing the molar terms in the numerator by the volume,

$$\xi = \frac{N_i / V - N_{i,0} / V}{v_i} = \frac{C_i - C_{i,0}}{v_i} \quad (6.13)$$

The extent of reaction is related to the conversion according to

$$\xi = \frac{-N_{i,0} X}{v_i} \quad (6.14)$$

You can see that this method provides the same relationship provided in Equation 6.12.

This method is a very powerful tool, enabling one to keep track of many components at the same time. It can be extended easily to account for inert species, multiple reactions, and other more complicated systems. See Highlight 6.1.

### 6.1.2 Parallel Reactions

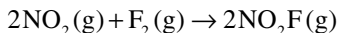
In the real world, several reactions usually occur at the same time. In this case, we must write the various reactions as separate, independent reactions. So, for example, in the case of combustion, carbon monoxide can be produced through incomplete combustion of a fuel. In order to describe the production of both CO and CO<sub>2</sub>, we write each reaction separately:



By controlling the rate of formation of the desired product relative to the rate of formation of the undesired product, we control the selectivity of the reaction and the amount of waste produced.

### Highlight 6.1 Expressing and Determining the Reaction Rate

Consider the following reaction between nitrogen dioxide and fluorine:



In the first 10.0 seconds of the reaction, the concentration of fluorine dropped from 0.10 M to 0.082 M.

- Calculate the average rate of this reaction in the first 10.0 seconds.
- Calculate the amount of nitrogen dioxide consumed in this time interval.

**Solution:**

- Using Equation 6.11 the average rate of this reaction is expressed as

$$\begin{aligned} \text{Rate} &= -\Delta[\text{F}_2] / \Delta t = -(0.082 \text{ M} - 0.10 \text{ M}) / (10.0 \text{ s}) = 0.0018 \text{ M/s} \\ &= 1.8 \times 10^{-3} \text{ M/s} \end{aligned}$$

- The extent of reaction can be calculated from the consumption of  $\text{F}_2$ . According to Equation 6.13

$$\xi = \frac{C_i - C_{i,0}}{\nu_i} = \frac{0.082 \text{ M} - 0.10 \text{ M}}{-1} = 0.018 \text{ M}$$

The amount of  $\text{NO}_2$  can now be obtained by a second application of this equation, except now where the extent of reaction is known and the change in  $\text{NO}_2$  concentration is the unknown:

$$\begin{aligned} \xi &= \frac{C_i - C_{i,0}}{\nu_i} \\ 0.018 \text{ M} &= \frac{\Delta C}{-2} \\ \Delta C &= -0.036 \text{ M} \end{aligned}$$

This algebraic relationship allows easy conversion between the concentrations of each species in the reaction that is either consumed or produced.

In the following discussion, we generalize this situation to that of reactant A, which is converted to two products, the desired product D and the undesired product U. We can write these reactions as

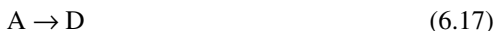


TABLE 6.1. Example Stoichiometric Table for Parallel Reactions

Species	Inlet	Stoichiometric Coefficient Reaction 1	Stoichiometric Coefficient Reaction 2	Outlet
A	$A_i \text{ mol}$	-1	-1	$A_i - \xi_1 - \xi_2$
D	0 mol	+1		$\xi_1$
U	0		+1	$\xi_2$

In order to solve problems of this type, we need to define two different extents of reaction—the extent of reaction 1 describes the amount of A that is converted to product D while the extent of reaction 2 describes the amount of A that is converted to product U. If we want to know the total amount of A converted, it can be obtained as the extent of reactions 1 and 2, combined. In terms of the stoichiometric table (Table 6.1) we include these elements within our table as separate columns, and then proceed with our calculations as we would for a single reaction.

If we knew two pieces of information (e.g., the conversion and the amount of D produced), then we could solve this problem to find, for example, the amount of U produced, or the composition of the product.

In practical applications, the important question to ask is not only how much D can be produced, but also how much U is formed (and how much we will need to throw away). We can characterize this parameter as the *selectivity* ( $S$ ), or the ratio of the yield (as defined in Equation 6.6) of one product relative to another. In a general sense, this can be written as

$$S = \frac{Y_{\text{desired product}}}{Y_{\text{undesired product}}} \quad (6.19)$$

An alternate definition provides selectivity as the ratio of the amount of the desired product relative to the total conversion ( $X$ , defined in Equation 6.5)

$$S = \frac{Y_{\text{desired product}}}{X} \quad (6.20)$$

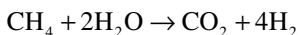
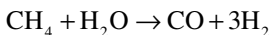
These two definitions provide alternative measures of the same concept and can be used interchangeably. Note that the latter method requires that selectivity be between 0 and 1, whereas in the former method the selectivity may approach infinity. See Highlight 6.2.

**Highlight 6.2 Parallel Reactions**

Steam reforming of natural gas (90% methane and the remainder CO<sub>2</sub>) is being considered for the production of hydrogen. The conversion of methane can produce either CO or CO<sub>2</sub>, depending on the amount of steam included in the process. In one particular case, a steam to carbon ratio of 5 is used, resulting in a selectivity to CO<sub>2</sub> (relative to CO) of 3. What is the percentage of hydrogen in the product gas at complete methane conversion?

**Solution:**

Let's begin by writing the two parallel reactions:



and then put the information into the stoichiometric table (Table 6.2).

TABLE 6.2. Stoichiometric Table for Parallel Reactions in Steam Reforming

Species	Inlet	Stoichiometric Coefficient Reaction 1	Stoichiometric Coefficient Reaction 2	Outlet
CH <sub>4</sub>	9 mol	-1	-1	9 - ξ <sub>1</sub> - ξ <sub>2</sub>
H <sub>2</sub> O	45 mol	- 1	- 2	45 - ξ <sub>1</sub> - 2 ξ <sub>2</sub>
CO	0	+1		ξ <sub>1</sub>
CO <sub>2</sub>	1 mol	0	+1	1 + ξ <sub>2</sub>
H <sub>2</sub>	0	+3	+4	3 ξ <sub>1</sub> + 4 ξ <sub>2</sub>

We have two unknowns, and two pieces of information that we can use to solve the problem. First, complete conversion of methane provides

$$9 - \xi_1 - \xi_2 = 0$$

The selectivity describes the amount of CO<sub>2</sub> produced relative to the amount of CO and is given as 3. This can be expressed mathematically as

$$3 = \frac{\xi_2}{\xi_1}$$

and then substitution into the conversion equation provides the unknown extents of reaction.

$$0 = 9 - \xi_1 - 3\xi_1$$

$$\xi_1 = 2.25$$

From which we can directly evaluate  $\xi_2 = 6.75$ . Finally, substituting numbers into Table 6.2 provides the number of moles for each product species:

$$F_{\text{H}_2\text{O}} = 45 \text{ mol} - (2.25 \text{ mol}) - (2)(6.75 \text{ mol}) = 29.25 \text{ mol}$$

$$F_{\text{CO}} = 2.25 \text{ mol}$$

$$F_{\text{CO}_2} = 1 + (6.75 \text{ mol}) = 7.75 \text{ mol}$$

$$F_{\text{H}_2} = 3(2.25 \text{ mol}) + (4)(6.75 \text{ mol}) = 33.75 \text{ mol}$$

So the percentage of hydrogen in the product gas is simply the amount of hydrogen relative to the total amount of gas produced.

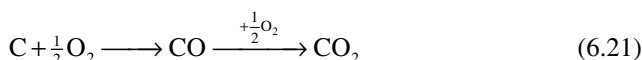
$$\% \text{H}_2 = \frac{33.75 \text{ mol}}{29.25 \text{ mol} + 2.25 \text{ mol} + 7.75 \text{ mol} + 33.75 \text{ mol}} = 46.2\%$$

It is also useful to calculate the percent hydrogen on a “dry basis” (a dry basis is defined as the amount of gas excluding water—since water can easily be condensed and removed from the gas stream). In this case, the result is

$$\% \text{H}_2 = \frac{33.75 \text{ mol}}{2.25 \text{ mol} + 7.75 \text{ mol} + 33.75 \text{ mol}} = 77.1\%$$

### 6.1.3 Consecutive Reactions

In addition to the situation of parallel reactions, it is also possible for the product of the reaction to react further to additional (usually undesired) products. This is termed *reactions in series* or *consecutive reactions*. Continuing with the combustion reaction as an example, we note that complete oxidation of a fuel may actually occur by partial oxidation of C to CO, followed by oxidation of CO to CO<sub>2</sub>. In this case, the overall reaction must be written as



Although this is described as fundamentally different from the situation with parallel reactions, both types of problems can be solved by defining two extents of reaction and



TABLE 6.3. Example Stoichiometric Table for General Reactions in Series

Species	Inlet	Stoichiometric Coefficient Reaction 1	Stoichiometric Coefficient Reaction 2	Outlet
A	$A_i$ mol	-1	0	$A_i - \xi_1$
D	0 mol	+1	-1	$\xi_1 - \xi_2$
U	0 mol		+1	$\xi_2$

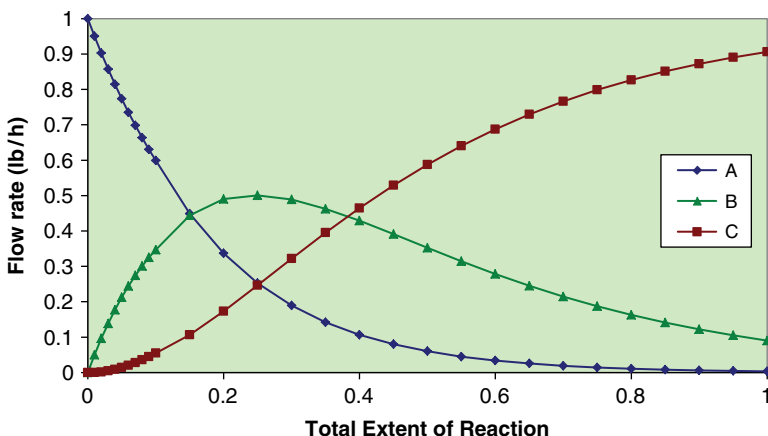


Figure 6.1. Example concentration profile for reactions in series.

combining the reactions mathematically. In order to keep things simple, let us rewrite the combustion reaction above in terms of arbitrary species A, D, and U. Thus, we have



Assuming that A is the only component in the feed to the reactor, we obtain a stoichiometric table very similar to the one developed for the case of parallel reactions (Table 6.3).

As before, if we know two pieces of information about this system (e.g., conversion and the amount of D produced), we can calculate the composition of the product stream.

It is instructive to consider the composition within a tubular reactor, or the composition change along the reaction coordinate, for a consecutive reaction. Recall that our consecutive reactions are described as



If we plot the concentration profile as a function of the extent of reaction, we find that the concentration of species B reaches a maximum at some intermediate extent of reaction (Figure 6.1).

Now, if species B is the desired product, then to maximize the production of B we should only run the reaction to about 15% extent, which is equivalent to about 40% conversion of reactant A. Since we also want to maximize the consumption of species A, we clearly need to recover the unreacted reactant from the exit stream and recycle it back.

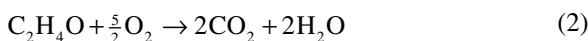
Highlight 6.3 better illustrates this concept.

### Highlight 6.3 Consecutive Reactions

The reaction of ethylene to produce ethylene oxide is carried out in the vapor phase over a silver catalyst. Unfortunately, the ethylene oxide can be converted into  $\text{CO}_2$  in the same reactor. In order to minimize the amount of  $\text{CO}_2$  produced, the feed to the process contains 2 mol/h of oxygen and 10 mol/h ethylene. At an ethylene conversion of 25%, the oxygen is completely consumed. What is the composition of the product gas?

#### Solution:

We will write the series reaction as two separate reaction processes:



and relate the amount of each species to the extent of each reaction. For example, ethylene oxide is produced in reaction 1 but consumed in reaction 2. Thus, the amount of ethylene oxide in the reactor at any point can be evaluated as

$$N_{\text{C}_2\text{H}_4\text{O}} = \xi_1 - \xi_2$$

We summarize this, and similar equations for each species, in the stoichiometric table.

We know both the inlet and outlet flow rates for ethylene and oxygen, so we can write the stoichiometric table (Table 6.4).

TABLE 6.4. Stoichiometric Table for Vapor Phase Oxidation of Ethylene

Species	Inlet	Stoichiometric Coefficient Reaction 1	Stoichiometric Coefficient Reaction 2	Outlet
$\text{C}_2\text{H}_4$	10 mol/h	-1	0	$10 - \xi_1$
$\text{O}_2$	2 mol/h	$-\frac{1}{2}$	$-\frac{5}{2}$	$2 - \frac{1}{2}\xi_1 = \frac{5}{2}\xi_2$
$\text{C}_2\text{H}_4\text{O}$	0	+1	-1	$\xi_1 - \xi_2$
$\text{CO}_2$	0	0	+2	$2\xi_2$
$\text{H}_2\text{O}$	0	0	+2	$2\xi_2$

Now, we need to use the conversion of ethylene (25%) and the exit flow rate of oxygen (zero, since it is completely consumed) to determine the extents of reaction. First, we know that the total conversion of ethylene is 25%, which provides

$$\begin{aligned} X = 0.25 &= \frac{10 - (10 - \xi_1)}{10} \\ &= \frac{\xi_1}{10} \\ 2.5 &= \xi_1 \end{aligned}$$

Second, we know that oxygen is completely used up in the reaction, so

$$\begin{aligned} F_{\text{O}_2, \text{out}} &= 2 - \frac{1}{2}\xi_1 - \frac{5}{2}\xi_2 = 0 \\ \xi_2 &= \frac{2}{5}\left(2 - \frac{1}{2}(2.5)\right) \\ &= 0.30 \end{aligned}$$

With these two values, it is now a relatively simple task to substitute these numbers into the equations in the last column of the stoichiometric table to determine the flow rate for each of the exiting species:

$$\begin{aligned} F_{\text{ethylene}} &= 10 \text{ mol/h} - 2.5 \text{ mol/h} = 7.5 \text{ mol/h} \\ F_{\text{oxygen}} &= 2 \text{ mol/h} - \left(\frac{1}{2}\right)(2.5 \text{ mol/h}) - (2.5)(0.3 \text{ mol/h}) = 0 \text{ mol/h} \\ F_{\text{ethylene oxide}} &= 2.5 \text{ mol/h} - 0.3 \text{ mol/h} = 2.2 \text{ mol/h} \\ F_{\text{CO}_2} &= F_{\text{water}} = 2(0.3 \text{ mol/h}) = 0.6 \text{ mol/h} \end{aligned}$$

Finally, if we wanted to put these results in terms of mole fractions, we need to add up the flow rates for all of the exiting species to find  $F_{\text{total}} = 10.9 \text{ mol/h}$ , from which we can determine the mole fractions as

$$y_{\text{ethylene}} = \frac{7.5 \text{ mol/h}}{10.9 \text{ mol/h}} = 0.688$$

for example.

### 6.1.4 Chemical Equilibrium

No reaction proceeds to 100% conversion. The conversion of all reactions is controlled by equilibrium. Just as equilibrium controls the ratio of vapor and liquid and the composition of each phase, equilibrium also controls the relative amounts of products that can be converted or reactants that can be formed in the chemical reaction.

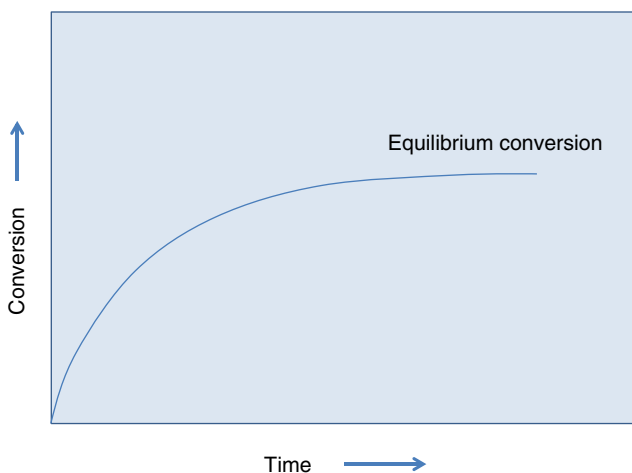
One may think of an equilibrium reaction as two reactions occurring in parallel:



The amount of A that exists at equilibrium is controlled by how much B is present, and vice versa. In some cases, the equilibrium condition gives extremely high conversion, which approaches 100%. In these cases, we say that the reaction goes to completion and we assume that complete conversion can actually be achieved. However, other cases exist in which less than 100% conversion may be obtained as a result of the thermodynamic limitations. It is these cases with which we are concerned in this section.

In most cases in which reversible reactions are present, we characterize the final product based on the maximum amount of conversion that we can achieve (i.e., the amount that would be present if we let the reaction run for a really long time). This can be illustrated better by looking at Figure 6.2.

If we allow the reaction to go long enough (to the right of Figure 6.2), then the conversion no longer increases and the reaction is said to be at equilibrium.



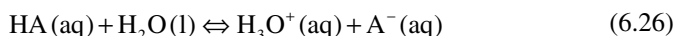
**Figure 6.2.** Example of conversion at equilibrium.

In terms of kinetics, a chemical equilibrium is reached when the rate of the forward reaction is equal to the rate of the reverse reaction. This is often described as a dynamic equilibrium and a double arrow ( $\rightleftharpoons$ ) is usually drawn between reactants and products.

#### 6.1.4.1 Example of Acid–Base Reactions at Equilibrium

In Chapter 4 (Section 4.6), we introduced the concept of acids and bases. We can now look at the concept of equilibrium associated with the dissociation of weak acids and weak bases in water. Remember that strong acids and strong bases dissociate in water, they completely dissociate and a forward reaction does not exist.

When a weak acid HA dissolves in water, it gives an  $\text{H}^+$  to water (which becomes  $\text{H}_3\text{O}^+$ ) and produces a conjugate base  $\text{A}^-$ . The ionization reaction can be summarized as follows:



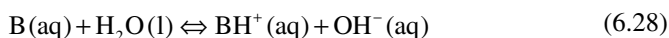
We can also write an equilibrium constant expression for this reaction, where the equilibrium concentrations of the products appear in the numerator and the equilibrium concentrations of the reactants appear in the denominator. The equilibrium constant expression does not involve pure solids or pure liquids (including water).

For equilibrium associated with the dissociation of weak acids, the equilibrium constant expression is called the *acid ionization constant expression*  $K_a$ :

$$K_a = [\text{H}_3\text{O}^+][\text{A}^-]/[\text{HA}] \quad (6.27)$$

All weak acids have very small values of  $K_a$  (much smaller than 1), which means that the reaction is reactant-favored. On the opposite side, large values of  $K_a$  (more than 1) indicate a product-favored reaction.

When a weak base B dissolves in water, it accepts an  $\text{H}^+$  from water (and becomes  $\text{BH}^+$ ). In this case  $\text{BH}^+$  is called the conjugate acid. Water loses an  $\text{H}^+$  and produces  $\text{OH}^-$ . The ionization reaction can be summarized as follows:



For equilibrium associated with the dissociation of weak bases, the equilibrium constant expression is called the *base ionization constant expression*  $K_b$ :

$$K_b = [\text{BH}^+][\text{OH}^-]/[\text{B}] \quad (6.29)$$

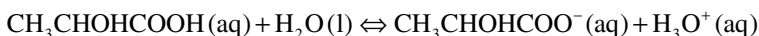
Knowing the value of  $K_a$  or  $K_b$ , we can calculate the equilibrium concentrations of all species present, or vice versa (knowing the equilibrium concentrations of all species present, we can deduce the value of  $K_a$  or  $K_b$ ). When the value for the equilibrium concentration of  $\text{H}_3\text{O}^+$  is determined, we can then deduce what the value of the pH of the solution is since  $\text{pH} = -\log [\text{H}_3\text{O}^+]$ . Highlight 6.4 shows an example of calculation of pH knowing the acid ionization constant value  $K_a$ .

### Highlight 6.4 Calculation of pH for Lactic Acid

Lactic acid, or  $\text{CH}_3\text{CHOHCOOH}$ , dissociates partially in water to produce the lactate anion,  $\text{CH}_3\text{CHOHCOO}^-$ , with a value of  $K_a$  of  $1.4 \times 10^{-4}$ . Calculate the pH of a 0.020 M solution of lactic acid at 25 °C.

**Solution:**

The first step is to write down the dissociation of lactic acid in water:



The second step is to express the acid ionization constant  $K_a$ :

$$K_a = \frac{[\text{CH}_3\text{CHOHCOO}^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{CHOHCOOH}]} = 1.4 \times 10^{-4}$$

The goal is to calculate the pH of this solution, in other words to determine the concentration of  $\text{H}_3\text{O}^+$ . (Remember:  $\text{pH} = -\log [\text{H}_3\text{O}^+]$ .) To do so we need to build a table that summarizes information about initial concentrations, changes in the concentrations as the reaction proceeds, and resulting equilibrium concentrations. Chemists will sometimes call this table the ICE table (I—Initial; C—change; E—equilibrium), but we described it previously as a stoichiometric table (Table 6.5).

TABLE 6.5. Example of an ICE Table

Species	Initial Concentration (mol/L)	Stoichiometric Coefficient	Final Concentration (mol/L)
Lactic acid, $\text{CH}_3\text{CHOHCOOH}$	0.020	-1	$0.020 - \xi$
$\text{H}_3\text{O}^+$		+1	$\xi$
Lactate anion		+1	$\xi$

Remember since  $\text{H}_2\text{O}$  is a liquid, its concentration does not have an effect on the equilibrium.

We can substitute the concentrations by their values in the expression of  $K_a$ :

$$K_a = \frac{[\text{CH}_3\text{CHOHCOO}^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{CHOHCOOH}]} = \frac{\xi \times \xi}{(0.020 - \xi)} = 1.4 \times 10^{-4}$$

Because  $K_a$  is very small, this implies that the reaction is reactant-favored and not much of the products will form. In other words,  $\xi$  will be very small and much smaller than 0.020 M. We can approximate that  $0.020 - \xi$  will be almost equivalent to 0.020 to get

$$K_a = \frac{[\text{CH}_3\text{CHOHCOO}^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{CHOHCOOH}]} = \frac{\xi^2}{(0.020)} = 1.4 \times 10^{-4}$$

We can solve for  $\xi$ :

$$\xi = \sqrt{(1.4 \times 10^{-4})(0.020)} = 1.7 \times 10^{-3} \text{ M} = [\text{H}_3\text{O}^+]$$

Knowing the value of  $[\text{H}_3\text{O}^+]$ , we deduce that the pH of this lactic acid solution is

$$\text{pH} = -\log (1.7 \times 10^{-3}) = 2.77$$

This solution is acidic ( $\text{pH} < 7.0$ ). We can also measure the percent (%) ionization by comparing the  $\text{H}_3\text{O}^+$  concentration at equilibrium with the initial concentration of the acid:

$$\% \text{ ionization} = \frac{[\text{H}_3\text{O}^+]_{\text{equilibrium}}}{[\text{lactic acid}]_{\text{initial}}} \times 100\% = \frac{1.7 \times 10^{-3} \text{ M}}{0.020 \text{ M}} \times 100\% = 8.5\%$$

This makes sense since lactic acid is a weak acid; its  $K_a$  value is very small and it is only 8.5% ionized.

### 6.1.5 Effect of Concentration on Reaction Rate

The concentration of one or more reactants influences the rate of a reaction. The relationship between the reaction rate and the concentration of a reactant is called the *rate law* and for a simple reaction such as  $\text{A} \rightarrow \text{products}$ , the rate may be defined according to what is known as power law kinetics:

$$\text{Rate} = k[\text{A}]^n \quad (6.30)$$

where  $k$  is the proportionality constant between the rate and the concentration, also known as the *rate constant*, and  $n$  is an integer called the reaction order.

If  $n=0$ , the reaction is zero order; in this case, the rate is independent of the concentration and is equal to the proportionality constant.

$$\text{Rate} = k[\text{A}]^n = k[\text{A}]^0 = k \quad (6.31)$$

If  $n=1$ , the reaction is first order; the rate is directly proportional to the concentration of reactant:

$$\text{Rate} = k[A]^n = k[A]^1 = k[A] \quad (6.32)$$

If  $n=2$ , the reaction is second order; the rate is proportional to the square of the concentration of reactant:

$$\text{Rate} = k[A]^n = k[A]^2 \quad (6.33)$$

Increasing the reaction order increases the sensitivity of the rate to the concentration. For a second order reaction, a change in the concentration will affect the rate more greatly than it would for a first order reaction.

For multiple reactants, the reaction rate is affected accordingly. For the general reaction



the rate law is expressed as follows:

$$\text{Rate} = k[A]^m[B]^n \quad (6.35)$$

with  $m$  and  $n$  being the reaction orders with respect to A and B, respectively.

One of the major challenges is to determine an appropriate kinetic model that describes the rate of the reaction. There are two common methods in use to determine kinetics, both of which can be used equally. The choice of method usually comes down to an experimental question—what reactor is available for the tests. We will look at both techniques.

### 6.1.5.1 Integral Method

In this process, we begin by assuming a specific form for the rate expression and then compare this form against the experimental data.

The integral method is based on data that provides concentration as a function of time. This is most easily obtained in a batch system, where the reactor can be loaded with the reactants at time zero, the reaction initiated, and samples taken on a periodic basis to determine the concentration of the various species, or the conversion of the reactant.

For a batch reactor, the change in conversion with respect to time can be related through the mass balance

$$C_{A,0} \frac{dX}{dt} = -r_A \quad (6.36)$$

Recall that  $C_{A,0}$  is the initial concentration of species A in the reactor,  $X$  is the conversion (which will be measured as a function of time,  $t$ ), and  $r_A$  is the rate of depletion of species A.

We can integrate this equation through separation of variables, which gives the general formula



$$C_{A,0} \int \frac{dX}{-r_A} = t \quad (6.37)$$

In some specific cases, such as the power law expression given previously, the term within the integral may be obtained analytically, providing a mathematical relationship between conversion, initial concentration, and reaction time.

In the case where  $n=1$ , the reaction is said to be *first order*. In this case,

$$-r_A = kC_A = kC_{A,0}(1-X) \quad (6.38)$$

which when substituted into the combined expression provides

$$\int \frac{dX}{1-X} = kt \quad (6.39)$$

This is integrated from  $X=0$  to  $X=X_t$  to get

$$-\ln(1-X) = kt \quad (6.40)$$

There are many chemical reactions that can be approximated through first order kinetics.

Now let's consider the case of *second order* kinetics. In this case,

$$-r_A = kC_A^2 = kC_{A,0}^2(1-X)^2 \quad (6.41)$$

which provides, after substitution into the general power law expression or integration of the combined material balance and rate expression,

$$\frac{X}{1-X} = C_{A,0} kt \quad (6.42)$$

In order to make use of the rate expression, we need to put it into a form which is amenable to linear regression, so that the data can be compared with the proposed rate model. Let's consider the second order rate expression, given above. Recall that we have data in the form of  $X$  versus  $t$ . However, if the reaction can be modeled with second order kinetics, then a plot of  $X/(1-X)$  versus  $t$  should yield a straight line. Comparison of this result with the general second order rate expression reveals that the line should pass through the origin and have a slope of  $C_{A,0}k$ .

Highlight 6.5 will help to illustrate this method.

### Highlight 6.5 Evaluating the Reaction Rate

The hydrogenation of latex polymer was accomplished using nanoparticle polymers in aqueous solution, without added solvent, and using Wilkinson's catalyst. The use of extremely small latex particles allows high reaction rates with lower catalyst concentrations, two green chemistry benefits. At 120°C, 1 wt % catalyst, and 35.3 nm particles, the data in Table 6.6 is reported.

TABLE 6.6. Reaction Conversion Data [1]

Time (min)	Conversion
1	0.10
4	0.26
5	0.34
7	0.44
9	0.55
12	0.65
15	0.73
18	0.80
28	0.91

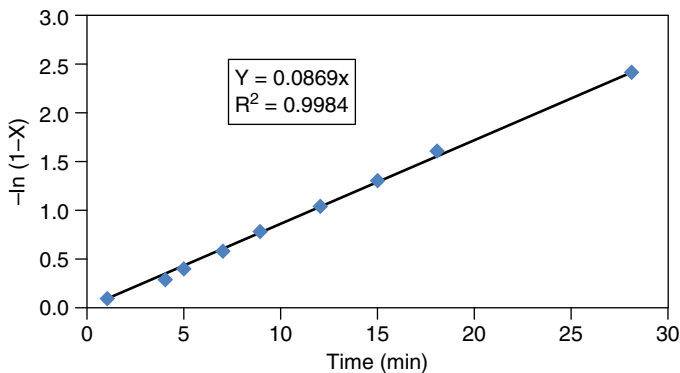
#### Solution:

Let's assume that first order kinetics apply (although this may not be correct, it is the simplest place to begin). Recall that for first order kinetics

$$-\ln(1 - X) = kt$$

so that a plot of  $-\ln(1 - X)$  versus  $t$  should yield a straight line that passes through the origin with a slope equal to  $k$ . To test this hypothesis, we use a spreadsheet to convert the data to the proper form and then complete the regression analysis.

Time (min)	Conversion	$-\ln(1 - X)$
1	0.1	0.1054
4	0.26	0.3011
5	0.34	0.4155
7	0.44	0.5798
9	0.55	0.7985
12	0.65	1.0498
15	0.73	1.3093
18	0.8	1.6094
28	0.91	2.4079



The graph, shown above is a plot of  $-\ln(1-X)$  versus time, as required to satisfy first order kinetics. The trendline indicated on the graph reveals that this data is very well approximated through first order kinetics, and the slope of 0.0869 corresponds to a first order rate constant of  $0.0869 \text{ min}^{-1}$ .

### 6.1.5.2 Differential Method

Another type of reactor is the plug flow reactor, in which we often can find conversion data for a fixed residence time, but at different inlet concentrations. In this case, we can show that the rate is a function of conversion, initial concentration, and time, according to the simplified mass balance,

$$C_{A,0} \frac{dX}{d\tau} = -r_A \quad (6.43)$$

In Equation 6.43, the variable  $\tau$  represents the residence time, which is the amount of time that an element of the fluid remains within the reactor ( $\tau$  is the Greek version of  $t$ , which is the symbol we use for time). The differential method is based on this form of the mass balance equation. Although it is impossible to directly measure the reaction rate, the left-hand side (LHS) (including the derivative) may be approximated by a difference equation, if the conversion is kept low (usually, the conversion is assumed to be low enough if it is less than 20%). In writing the difference equation, we substitute for the derivative

$$C_{A,0} \frac{X-0}{\tau-0} = -r_A \quad (6.44)$$

where  $X$  is the conversion at residence time  $\tau$  and there is zero conversion at the entrance to the reactor ( $\tau=0$ ). Removing the zeros provides

$$C_{A,0} \frac{X}{\tau} = -r_A \quad (6.45)$$

Now, if we substitute the general form of the rate expression, we find

$$C_{A,0} \frac{X}{\tau} = -kC_{A,0}^n (1-X)^n \quad (6.46)$$

Our goal is to find the values of the constants,  $k$  and  $n$ . Our data, however, is usually obtained in the form of  $X$  as a function of  $C_{A,0}$  (it is often the case that these experiments are only performed at a single residence time). We would like to transform our equation into a linear form, where the slope and intercept can be used to obtain the constants. Taking logarithms of both sides provides the desired linear form.

$$-\ln\left(C_{A,0} \frac{X}{\tau}\right) = \ln k + n \ln(C_{A,0}(1-X)) \quad (6.47)$$

Now, a straight line should pass through the data when plotted as

$$\ln\left(C_{A,0} \frac{X}{\tau}\right) \text{ versus } \ln(C_{A,0}(1-X)) \quad (6.48)$$

with the slope equal to the reaction order,  $n$ , and the intercept providing the value of the rate constant,  $k$ . Notice that in this case, we do not need to make any initial assumptions about the reaction order and that it falls out as a natural consequence of the data analysis. See Highlight 6.6.

### Highlight 6.6 Kinetics by the Differential Method

The catalytic performance of montmorillonite clay ion-exchanged with ionic liquids in the cycloaddition of carbon dioxide to allyl glycidyl ether (AGE) was evaluated under a range of  $\text{CO}_2$  feed pressures [2]. Under a specific set of conditions (AGE=40 mmol, catalyst (TDAC-MMT)=0.2 g, temperature=100 °C, reaction time=2 h), the conversion of AGE was measured to determine the effect of  $\text{CO}_2$ . Estimate the reaction order in  $\text{CO}_2$  and the rate constant.

#### Solution:

The data is shown in the Excel spreadsheet below. We note that there are four initial concentrations of  $\text{CO}_2$ , and the conversion increases with increasing  $\text{CO}_2$  pressure. In order to use the differential method, we need to compare the rate of the reaction with the initial concentration of  $\text{CO}_2$ . The reaction rate is estimated from the data as

$$C_{\text{CO}_2,0} X/t$$

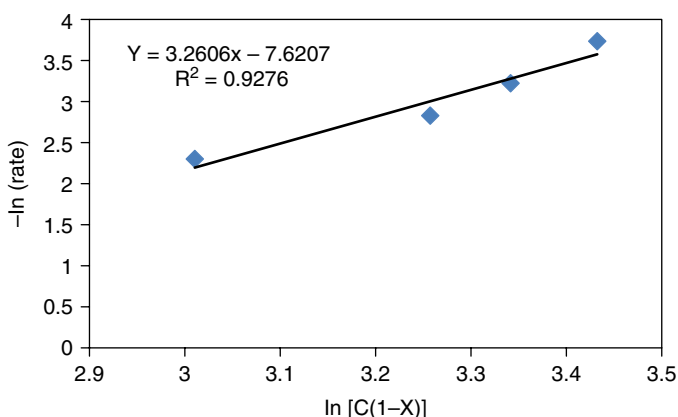
and the conversion of AGE provides the data for the right-hand side, as

$$C_{\text{AGE},0}(1-X)$$

We then take the log of both sides and plot. The result is a straight line, as shown in the graph.

CO <sub>2</sub> pressure	Conc (mol/L)	Conversion	LHS	RHS
0.65	0.209601557	0.227	3.738499	3.431403
0.86	0.277318983	0.293	3.203317	3.342155
1.07	0.345036409	0.351	2.804222	3.256557
1.27	0.409529196	0.492	2.295171	3.011606

Age=40mmol, catalyst (TDAC-MMT)=0.2g, temperature=100 °C, reaction time=2h.



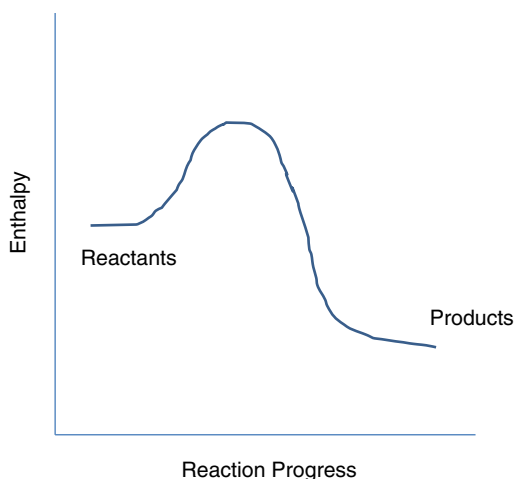
The slope on this graph should correspond to the reaction order, which in this case is found to be 3.26. That reaction order is very high and indicates that the effect of CO<sub>2</sub> concentration goes beyond kinetics and probably involves equilibrium and transport issues. The value of the rate constant is found by taking the exponential of the intercept:

$$k = \exp(-7.6207) = 4.90 \times 10^{-4} \text{ mol/L}\cdot\text{h}$$

While these results are somewhat unusual for a typical chemical reaction, this reaction involves dissolution of CO<sub>2</sub> into an ionic liquid, a rather unique situation. This is an excellent green chemistry example, however. We are using a benign solvent for the utilization of CO<sub>2</sub>, addressing two very important green chemistry principles.

### 6.1.6 Effect of Temperature on Reaction Rate

Molecules move faster when the temperature is increased. We often read in experimental procedures that increasing the temperature hastens the reaction. Therefore, rates of reactions are sensitive to temperature. The effect of the temperature on the reaction rate is actually contained in the rate constant (which is only a constant at a specific temperature; in other words, rate constants vary with the temperature at which the



**Figure 6.3.** Representation of the activation energy with R=reactants and P=products.

reaction is performed). When the temperature is increased, the rate constant,  $k$ , and the reaction rate are also increased.

The relationship between rate constant  $k$  and temperature  $T$  originally defined by the Swedish chemist Swante Arrhenius is an exponential relationship:

$$k = Ae^{-E_a/RT} \quad (\text{Arrhenius equation}) \quad (6.49)$$

where  $A$  is a constant called the *frequency factor* (or the preexponential factor),  $E_a$  is the *activation energy* (or activation barrier),  $R$  is the *gas constant* (8.314 J/mol.K), and  $T$  is the temperature expressed in kelvin units.

For a reaction to take place, it is often necessary to add energy to the system. The energy of the products is lower than that of the reactants but the reactants must go over an energy barrier before they are transformed into products. When reactants reach this higher energy state level they are in a transition state (also called activated complex). As temperature increases, the number of molecules on the reactants side having enough energy to overcome the activation barrier increases.

The activation barrier is often represented in term of enthalpy versus reaction progress: see Figure 6.3.

In its modern form, the Arrhenius equation is mostly used by taking the natural log of both sides of the equation:

$$\begin{aligned} \ln k &= \ln \left\{ Ae^{-E_a/RT} \right\} \\ \ln k &= \ln A + \ln e^{-E_a/RT} = \ln A - E_a/RT \\ \ln k &= -E_a/R \times 1/T + \ln A \end{aligned} \quad (6.50)$$

The plot of  $\ln k$  versus  $1/T$  generates a straight line with a slope of  $-E_a/R$  and a y-intercept of  $\ln A$ .

Knowing the slope allows for the determination of the activation energy and knowing the y-intercept is useful to determine the frequency factor  $A$ . See Highlight 6.7.

### Highlight 6.7 Evaluating the Activation Energy for a Component Decomposition

In a series of experiments, we evaluated the decomposition of dipotassium orthophthalate, a synthetic lubricant [3]. Experimental data was fit to a first order kinetic scheme, and the rate constants given in Table 6.7 were obtained as a function of temperature.

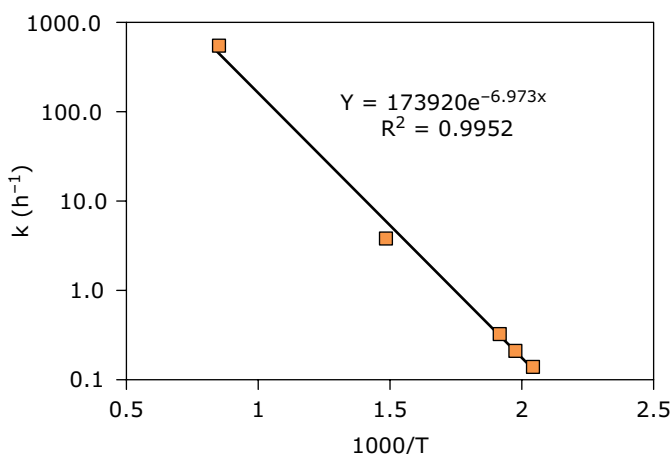
TABLE 6.7. Rate Constants for Deactivation as a Function of Temperature

$T$ ( $^{\circ}\text{C}$ )	$k$ ( $\text{h}^{-1}$ )
218	0.1357
235	0.1937
250	0.3042
400	3.633
900	548

Determine the activation energy and the preexponential factor.

#### Solution:

We carry out the data reduction as described in the previous discussion. The data is plotted in the prescribed form in the graph below, and the regression line is that of an exponential fit (as required according to the Arrhenius law).



The exponential value of  $-6.9727$  corresponds to an activation energy of

$$E_a = (6.9727)(8.314 \text{ kJ/mol}) \\ = 57.97 \text{ kJ/mol}$$

The preexponential factor is simply the value indicated in the graph,  $1.74 \times 10^5 \text{ h}^{-1}$ , or  $48.3 \text{ s}^{-1}$ .

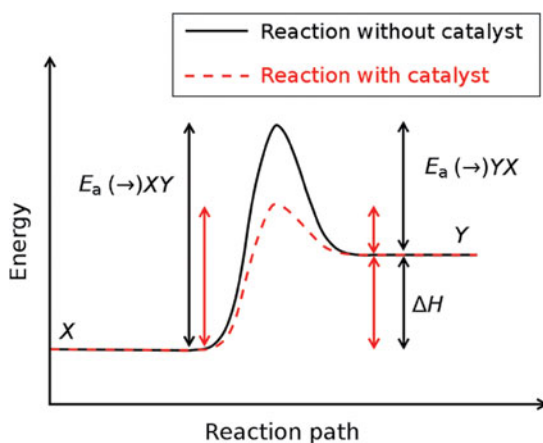
## 6.2 ROLE OF INDUSTRIAL AND BIOLOGICAL CATALYSTS

### 6.2.1 Definition of Catalysts

While it is always possible to increase the rate of a chemical reaction by increasing the concentration of the reactants or by increasing the temperature, it is not always practical to do so. It is not always possible to make highly concentrated mixtures of reactants, maybe because the reactant would promote a phase separation, it would be hazardous in the concentration required, producing the required concentration would be too costly, or many other possible reasons. Increasing the temperature requires a source of heat, which can also be costly and almost certainly leads to undesirable emissions, but may also lead to the decomposition of a reactant. So chemists and engineers require another tool that can be employed to change the reaction path in order to design an energy-efficient process leading to the desired product, with high yield and selectivity. Fortunately, many such species exist, and when employed to accelerate the rate of a chemical reaction, they are termed *catalysts*.

A catalyst increases the rate of a chemical reaction without being consumed by the reaction. The role of a catalyst is to lower the activation barrier, which leads to a faster reaction rate, a higher selectivity (a greater proportion of the desired product is formed), and a higher atom economy. A catalyst does not change the chemical equilibrium of a reaction; it only favors a chemical pathway that will normally not be possible at lower temperatures and atmospheric pressure. Figure 6.4 represents the decrease in the activation energy using a catalyst.

Choosing the most effective catalyst, especially for a commercial process, depends on a number of criteria such as the concentration of the catalyst used, the catalytic turnover, the selectivity of the catalyst to the desired product, and the ability to recover the catalyst after reaction.



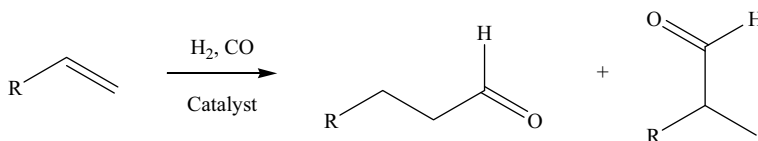
**Figure 6.4.** Representation of the activation energy of a reaction with and without a catalyst [4].



The catalytic turnover number (TON) is the number of moles of product per mole of catalyst; in other words, it is also the number of catalytic cycles for a given process.

The catalytic turnover frequency (TOF) is the catalytic turnover per unit time; that is, the number of moles of product per mole of catalyst per unit time.

The selectivity of a catalyst can be measured in terms of regioselectivity and chemoselectivity. Let's look at the typical transformation of alkenes into aldehydes in the presence of CO and H<sub>2</sub>. This reaction is called hydroformylation and is presented in Scheme 6.1.



**Scheme 6.1** Hydroformylation reaction.

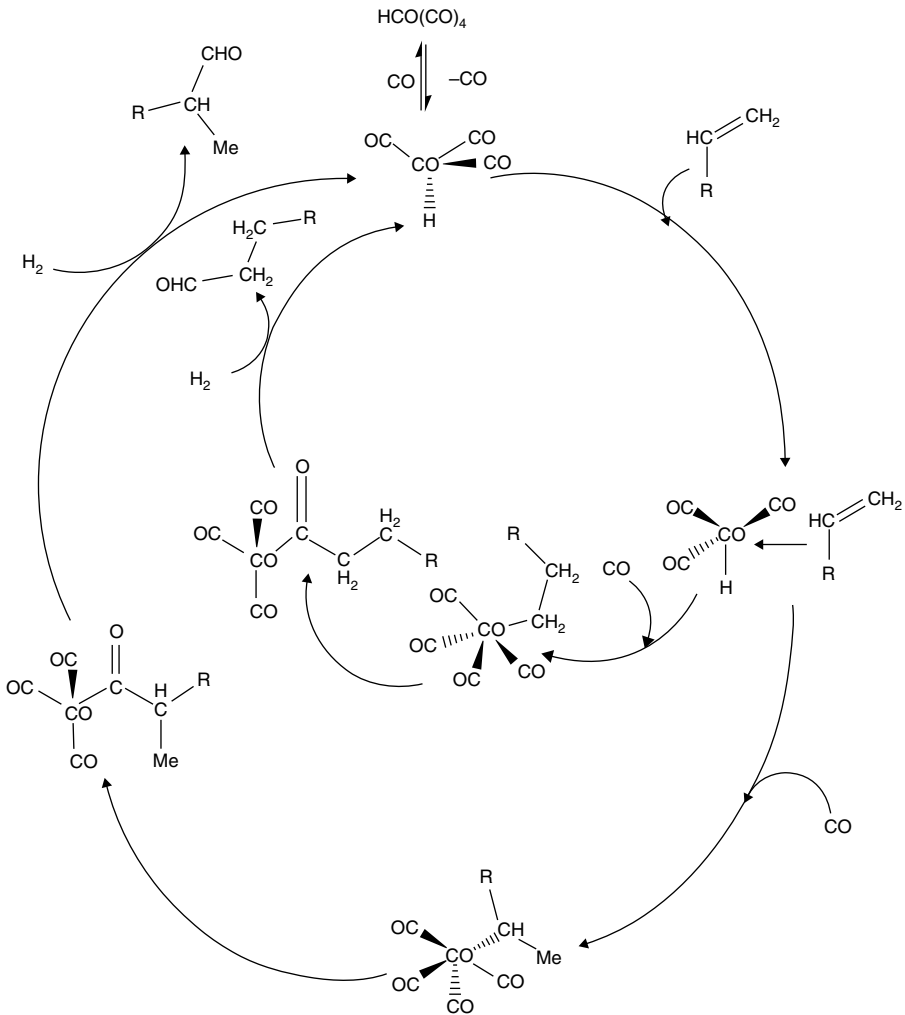
The regioselectivity of the reaction is defined as the ratio of normal-to-branched (or linear-to-branched) aldehydes (*n:i* ratio). The chemoselectivity of the reaction is measured in terms of the ratio of different chemical species produced by the reaction. For example, side reactions can also occur at the same time as the hydroformylation reaction. The hydrogenation of aldehydes to alcohols as well as the alkene isomerization are two major competing reactions to the hydroformylation process. In this case, the chemoselectivity is defined as the aldehyde-to-alcohol ratio for a given chain.

Figure 6.5 shows the typical catalytic cycle for the hydroformylation process.

The hydroformylation or oxo process was discovered in 1938 by Otto Roelen of Ruhrchemie AG in Germany. “Oxo” means carbonyl in German and the hydroformylation (or oxonation) initially produces carbonyl compounds. Commercially both cobalt and rhodium carbonyl catalysts have been exploited since World War II. The same catalyst can be regenerated and reused through many cycles but the catalyst will eventually degrade and lose its activity or it can also be poisoned by impurities that are likely present in the feedstock.

There are different types of catalysts depending on whether the catalyst ends up in the same phase as the product or in a different phase. If the catalyst is part of the same phase as the products, it is termed a homogeneous catalyst. Such materials are often used in relatively large quantities and cannot easily be recovered and reused. A good example of homogeneous catalysts are the Lewis acids, which were discussed in Chapter 5.

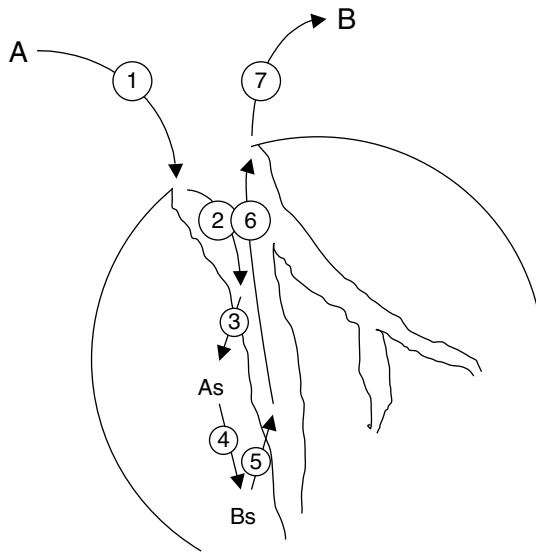
When one chooses to use a catalyst in a phase that is different from the phase in which the reaction occurs, this is termed a heterogeneous catalyst. In many cases, it is possible to replace the homogeneous catalyst with a heterogeneous one. The major advantage of a heterogeneous catalyst is that separation of solid catalysts from the reaction mixture can easily be accomplished. This eliminates the need for a separate



**Figure 6.5.** Typical hydroformylation reaction cycle

catalyst recovery step, greatly simplifying the process. And because the catalyst is often expensive, the ability to completely recover the catalyst has significant economic advantages, and thus many industrial processes use heterogeneous catalysts. Of course, there are many reasons why a homogeneous catalyst may be preferred; most homogeneously catalyzed reactions operate at milder conditions and provide higher selectivity than a comparable heterogeneously catalyzed process. In addition, mass transfer can play an important role in limiting the effectiveness of a heterogeneous catalyst.

A heterogeneously catalyzed reaction can be written as proceeding through seven consecutive rate processes, described below and shown schematically in Figure 6.6.



**Figure 6.6.** Mechanism of a heterogeneous reaction.

1. *External Mass Transfer.* Movement of the reactant from the bulk gas phase flow to the mouth of the catalyst pore.
2. *Internal Mass Transfer.* Movement of the reactant through the catalyst pores to the *active site* of the catalyst. The active site is the location that contains the catalytic material and is where the reaction actually occurs.
3. *Adsorption.* In order for the reaction to take place, a chemical bond must occur between the surface of the catalyst and the reactant. In this sense, adsorption is really a chemical reaction, and this process is frequently termed chemisorption. Chemisorption refers to the binding of the reactant to the surface in a state of minimum energy. Adsorption is an equilibrium process.
4. *Surface Reaction.* The actual chemical reaction occurs while the reactant is bound to the surface. The transformation is from one (or more) adsorbed species to another.
5. *Desorption.* The products are chemically bound to the surface following the reaction. In order for the product to leave the reactor, it must unbind from the surface, in a chemical reaction. The process of breaking the surface–product bond is termed desorption. This step is the opposite of adsorption and is also controlled by equilibrium.
6. *Internal Mass Transfer.* After leaving the surface, the product must make its way through the pores of the catalyst to the external surface of the catalyst particle.
7. *External Mass Transfer.* Once at the pore mouth, the gas phase product returns to the bulk flow of the gas in the reactor.

In order for the entire process to occur at steady state (i.e., no accumulation of species in any particular location), the rate for all of the various steps must be the same. Frequently, one of the steps will occur more slowly than the others. In order to remain at steady state, all of the other steps must slow down to the rate of the slowest step. This slowest step is termed the *rate-limiting step*.

## 6.2.2 Catalytic Kinetics

The presence of several rate processes occurring in series leads to the development of complex rate expressions, often described as Langmuir–Hinshelwood kinetics. Before going on, we need to separate the chemical steps from the mass transfer steps (a mass transfer step is one in which the species moves into position to react but does not undergo a chemical change). In this section, we consider only the chemical steps that lead to the development of a Langmuir–Hinshelwood rate expression; we reserve the mass transfer issues for the following section.

Because we have three consecutive reactions occurring in series (steps 3, 4, and 5 from above), the development of the overall rate expression can be fairly complex. However, the procedure provides a general expression that is well known and fairly common. Once the more detailed expression can be obtained, simplification can provide a more manageable form for use in engineering calculations.

Let's start by considering a catalytic reaction that is carried out in the gas phase over a solid catalyst. We write the overall reaction as



According to our description above, this reaction must occur through three separate steps (adsorption, surface reaction, desorption), so we can write a chemical equation for each step,



where the symbol  $S$  is used to denote an active site on the surface of the catalyst and the symbol  $As$  is used to indicate an  $A$  molecule adsorbed on the active site. Now, the rate of the reaction is given by the rate of the slowest step. Assuming that the surface reaction is the rate limiting step, we obtain

$$-r_A = kC_{As} \quad (6.54)$$

In order to use this rate expression, we require the concentration of component  $A$  adsorbed on the catalyst surface. This is obtained by assuming that the adsorption reaction is in pseudo-steady state. This means that the rate of the forward reaction



is equal to the rate of the reverse reaction



or

$$-r_{As} = k_f C_{As} - k_r C_A C_S = 0 \tag{6.57}$$

and then solving for  $C_{As}$  provides

$$C_{As} = \frac{k_r p_A C_S}{k_f} = k_A p_A C_S \tag{6.58}$$

After substitution, we obtain

$$-r_A = k K_A p_A C_S \tag{6.59}$$

Now, we need an expression for the concentration of vacant sites. A site balance reveals that all sites are occupied either by a species A molecule, a species B molecule, or that the site is vacant. Mathematically, this provides

$$C_t = C_S + C_{As} + C_{Bs} \tag{6.60}$$

We already have a suitable expression for  $C_{As}$  and can obtain an equivalent expression for component B:

$$C_{Bs} = K_B p_B C_S \tag{6.61}$$

Substitution provides

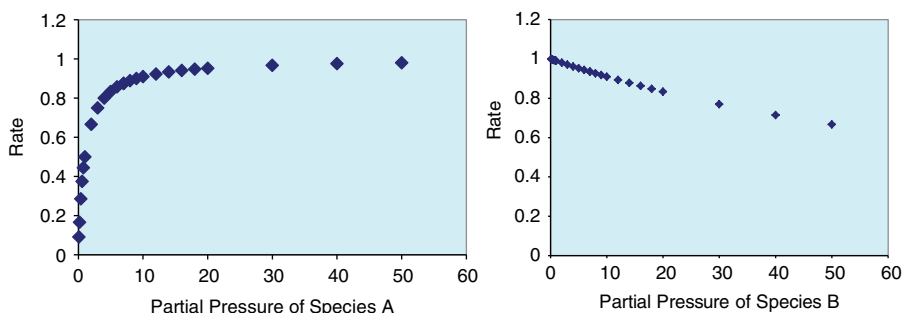
$$C_t = C_S (1 + K_A p_A + K_B p_B) \tag{6.62}$$

Solving Equation 6.62 for  $C_S$  and substitution into Equation 6.59 provides the Langmuir–Hinshelwood rate expression:

$$-r_A = \frac{k K_A C_t p_A}{(1 + K_A p_A + K_B p_B)} \tag{6.63}$$

This fairly complex rate expression is typical of those obtained for catalytic reactions and is valuable for further discussion of the kinetics of heterogeneously catalyzed reactions.

Heterogeneously catalyzed reactions are often accomplished in a packed bed reactor, which is essentially a tube packed with catalyst particles. In a packed bed reactor, the weight of catalyst takes the place of the residence time, and so we can show that the rate of the reaction is dependent on the flow rate of the reactant and the weight of catalyst:



**Figure 6.7.** Illustration of the effect of species concentration on rate of reaction for complex Langmuir–Hinshelwood kinetics.

$$-r_A = -\frac{dF_A}{dW} \approx \frac{F_{A,0} - F_A}{W} \quad (6.64)$$

where the last equality is approximately true for low conversions.

What can we do with this? Let's suppose that we have only a small amount of catalyst in the bed, so that the conversion of the reactant is small. Also, for a gas phase catalytic reaction we can use the partial pressure of the species in the gas phase in place of the concentration. In this case, we can assume  $p_A \approx p_{A,0}$  and  $p_B \approx p_{B,0}$ . Also, we can replace the derivative with a differential, to provide

$$-r_A \approx \frac{F_{A,0} - F_A}{W} = \frac{kC_t K_A p_{A,0}}{(1 + K_A p_{A,0} + K_B p_{B,0})} \quad (6.65)$$

This is a big improvement, because now we can measure the exit concentration of the reactant, convert to a molar flow rate (mol/s), and evaluate the effect of inlet concentration on the reaction rate. For the example provided, we would obtain two graphs (Figure 6.7).

In the first case, increasing the initial partial pressure of reactant A increases the rate of the reaction at low partial pressures, but appears to have essentially no effect at higher partial pressures. At high pressure,  $K_A p_A \gg 1$  and the effect of the term  $K_A p_A$  in the numerator cancels with the term in the denominator, making a net zero impact.

In the graph on the right, increasing partial pressure of B always decreases the rate. Here, species B is an *inhibitor*. It occupies catalytic sites, which become unavailable for the reaction because they are already in use. Unfortunately, the occupying species cannot be converted to product, so no reaction can take place on that site.

Another category of catalyst is the type present in the human body or any other biological system. Biological catalysts found in living organisms are usually large protein molecules called enzymes. Biochemical reactions operate within a relatively

tight range of temperatures, pressures, and pH; efforts to operate outside the stable range of the enzyme will denature the protein and destroy its catalytic effect. Therefore, enzymes provide the means for reactions to occur in an organism at body temperature.

In enzymatic systems, the reaction often follows Michaelis–Menton kinetics. In this case, the rate of reaction is written as

$$-r_A = \frac{k[E][A]}{K + [A]} \tag{6.66}$$

where [E] is the concentration of an enzyme that catalyzes the reaction, [A] is the concentration of the reactant, and  $k$  and  $K$  are two different characteristic constants. This is more conventionally written as

$$-r_A = \frac{V_{\max} [A]}{K_m + [A]} \tag{6.67}$$

where  $V_{\max}$  is the maximum rate of reaction for a specific enzyme concentration. Operating under differential conditions, we substitute the rate expression into the material balance:

$$[A] \frac{X}{\tau} = \frac{V_{\max} [A]}{K_m + [A]} \tag{6.68}$$

Now, simplifying this expression provides

$$\frac{X}{\tau} = \frac{V_{\max}}{K_m + [A]} \tag{6.69}$$

We can linearize this equation by taking the inverse of both sides, and then split the RHS into two parts:

$$\begin{aligned} \frac{\tau}{X} &= \frac{K_m + [A]}{V_{\max}} \\ &= \frac{K_m}{V_{\max}} + \frac{1}{V_{\max}} [A] \end{aligned} \tag{6.70}$$

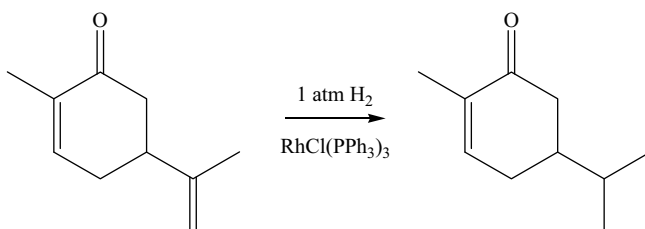
So we see that a plot of  $\tau/X$  versus [A] should yield a straight line with a slope equal to  $K_m/V_{\max}$  and an intercept equal to  $1/V_{\max}$ . This analysis for enzyme kinetics has the special name of Lineweaver–Burke plot. The reality is that the results for enzyme kinetics are entirely consistent with those of other catalyzed reactions and can be developed in a parallel way.

### 6.2.3 Types of Catalysts and Impact on Green Chemistry

Because of the opportunities to control selectivity and improve reaction conditions, many commercially important reactions are conducted with a catalyst. Some examples follow.

#### 6.2.3.1 Homogeneous Catalysts

One common form of catalyst is a metal complex composed of a central metal ion surrounded by one or more groups of atoms coordinated to the central metal ion, called ligands. Homogeneous catalysts are in the same state (i.e., solid, liquid, and gas) as the reactants. One of the most well-known homogeneous catalysis reactions is the alkene hydrogenation using a catalyst called rhodium-tris(triphenylphosphine) chloride(I)  $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$  created by Wilkinson in 1965. The Wilkinson catalyst is used for the oxidative addition reaction of dihydrogen to an alkene to provide an alkane (Scheme 6.2).



**Scheme 6.2.** Hydrogenation reaction

The addition of  $\text{H}_2$  to a double bond is thermodynamically favored but the kinetic barrier is high and for the reaction to be performed at 298 K and 1 bar  $\text{H}_2$ , a catalyst is needed.

Wilkinson's catalyst can be used to produce important biological products including antibiotics, steroids, and prostaglandins. In these cases, it is particularly important that the molecule have at least one asymmetric center (all four ligands are different around the metal center) in order to produce proper biological activity. The concept of asymmetric catalysis will be covered in the Section 6.2.4 on biocatalysis.

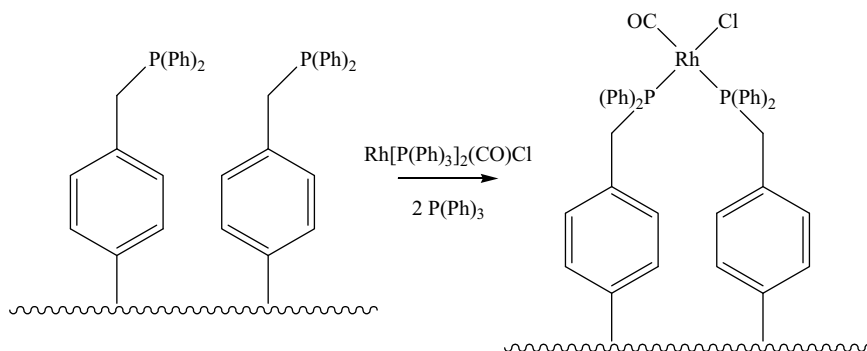
#### 6.2.3.2 Development of Immobilized Homogeneous Catalysts

The development of new homogeneous catalysts retaining the advantages of mild operating conditions and selectivity while overcoming the difficulty in catalyst separation has attracted considerable interest. Different strategies have been proposed to address the problem of catalyst separation.



**IMMOBILIZATION ON SOLID SUPPORTS.** Solid supports mainly include polymeric organic, inorganic, and dendrimeric supports. In order to attach the catalyst to a support, it is necessary to functionalize the support with a ligand that can be used to bind to the catalytic metal center. Usually the polymeric supports have a high degree of cross-linking or large surface areas or can be microporous with a low degree of cross-linking.

Polymer-supported catalysts have been used since the early 1960s but are still the subject of improvement. A common polymer is cross-linked polystyrene, which can bind the catalyst directly [5]. The other common example is the use of phosphine-functionalized surface to attach a Rh(I) catalyst (Scheme 6.3).



**Scheme 6.3.** Phosphine-functionalized surface

Even if polymers are easily functionalized, they exhibit poor heat transfer ability and poor mechanical properties and are often temperature sensitive. The choice of a reaction solvent is also important since some solvents cause the polymers to swell. Another issue is the leaching of metal from the polymer, resulting in the deactivation of the catalyst. These drawbacks can be partially eliminated if the catalyst precursors are covalently anchored on inorganic supports.

Silica, alumina, carbon nanotubes, and zeolites are common inorganic supports for catalyst precursors. For example, silica can be found in the amorphous form of a high-surface-area silica gel (200–800 m<sup>2</sup>/g) with an average pore diameter of 2.2–2.6 nm or as low-density gel with a surface area of 300–400 m<sup>2</sup>/g and an average pore diameter of 10–15 nm. Silica supports are usually more mechanically stable and resistant against aging, solvents, and high temperatures than the organic polymeric supports. Many metals grafted on silica and silica-supported complexes are used in hydroformylation of olefins.

Different active-carbon supports also have been tested. For example, Zhang and co-workers performed the hydroformylation of propene using carbon nanotube-supported rhodium–phosphine catalysts [6]. They found that using carbon nanotubes as supports did not improve the conversion of propene to propanal; however, the regioselectivity increased with carbon nanotubes as supports. The activity and regioselectivity were higher when using carbon nanotubes as supports versus active carbons. However, the rhodium catalyst deactivated over 30 hours due to the degradation of the ligand and/or its oxidation of PPh<sub>3</sub> to OPPh<sub>3</sub>.

A considerable amount of research has been devoted to the study of zeolite-encapsulated metal complexes. Zeolites are crystalline aluminosilicates with typical pore diameters varying between 0.4 and 1.4 nm. Due to the confined space of the zeolite cavity the selectivity is improved by diffusion. It has been found that the regioselectivities improve over those obtained with typical homogeneous catalysts but the activities are lower than in homogeneous systems.

In 1992, a new family of silicate/aluminosilicate mesoporous molecular sieves M 41S with pore diameters varying between 2 and 50 nm was discovered by Beck and co-workers at Mobil Corporation [7]. The synthesis of molecular sieves is based on surfactant/silicate solution chemistry. The template is a surfactant with alkyl chain lengths varying from 8 to 16 carbon atoms. The dimensions of the carbon chain length determine the pore size of the MCM-41 (Mobil Corporation Materials).

Contrary to zeolites, MCM structures do not exhibit any acidic character and have been used in a variety of reactions ranging from olefin polymerization to esterification and hydrogenation reactions.

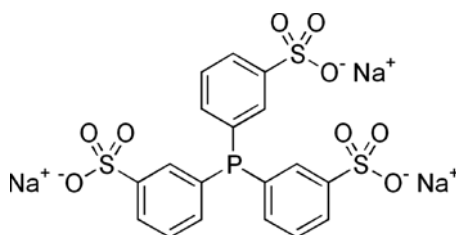
Dendrimeric supports are high molecular weight phosphine supports allowing precise distribution of catalytic sites and easily separated from the reaction products by precipitation and microporous membrane filtration.

**BIPHASIC CATALYSTS.** One means of recovering the catalyst is to perform the reaction in a two-phase system in which the catalyst naturally distributes into the nonproduct phase after reaction. These approaches have been used to achieve high activity and selectivity with water-soluble catalyst systems. Water is the only processing solvent that is naturally abundant and nontoxic. The immiscibility of water with nonpolar organic compounds creates unique opportunities for catalyst recycling. The catalyst is located in the aqueous phase and the feedstock and organic products are recovered in the organic phase. The reaction usually takes place at the organic–aqueous interface.

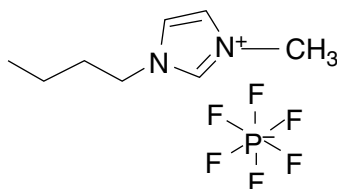
The more common, water-soluble, phosphine-based ligands are arylphosphines with polar functional groups ( $-\text{SO}_3^-$ ,  $-\text{CO}_2^-$ ,  $-\text{NR}_3^+$ ) attached to the aryl rings [8].

Much research has been devoted to water-soluble sulfonated phosphines and, in particular, the well-known TPPTS (triphenylphosphine tris-sulfonated sodium salt) ligand used in propene hydroformylation on an industrial scale by Ruhrchemie/Rhône-Poulenc since 1982 (Figure 6.8) [9, 10].

Prior to the development of aqueous biphasic catalysis, fluorous biphasic catalysis was proposed as another alternative to overcome the low solubility of substrates. The fluorous and organic phases form a homogeneous phase at high temperatures and are immiscible at room temperature. In 1994, Horvath and Rabai modified some phosphine ligands with long-chain “fluoroponytails” to enable catalysts to be recovered in the fluorous phase of the solvent while the products would be recovered in the organic phase upon cooling at room temperature [11]. Many reactions have been performed in fluorous biphasic systems including hydroformylation of 1-alkenes, hydrogenation, hydride reduction, hydroboration, and alkene epoxidation. However, it should be noted that fluorinated compounds are persistent in the environment, and while the catalyst recovery makes the process more green, the use of the fluorous



**Figure 6.8.** Structure of TPPTS.



**Figure 6.9.** Example of ionic liquid 1-butyl-3-methylimidazolium-hexafluorophosphate (BMIM- $\text{PF}_6$ ).

solvent makes an overall unsustainable process. The presence of multiple fluoroponytails on catalysts to increase solubility of organometallic complexes is often undesirable.

**IONIC LIQUIDS.** In earlier catalytic processes the use of organic solvents was predominant due to the low water solubility of olefins. An alternative to this problem is the use of ionic liquids introduced in Chapter 5. Ionic liquids are salts that melt at a temperature below 100 °C. Nonvolatile ionic liquids, such as those based on the 1-butyl-3-methyl-imidazolium (BMIM) cation, are used extensively to prevent the lack of thermal stability of homogeneous catalysts during the distillation recovery step and allow the catalyst to be used several times without being deactivated (Figure 6.9).

The nature of cations and anions of the ionic liquid can be adjusted to be compatible with the nature of the ligands used. The other advantage of ionic liquids is their nonvolatility and nonflammability as well as their lower energy use during processes compared to organic solvents.

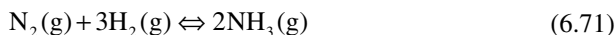
### 6.2.3.3 Heterogeneous Catalysts

Most industrial processes use either heterogeneous catalysts or immobilized homogeneous complexes. Most catalysts can be heterogenized by covalently anchoring ligands to a support or to a polymer. This implies that ligands be modified extensively to suit the solubility of the substrate. This approach allows the reaction to be performed homogeneously while easy recovery is also practical. Recyclable solid

acid catalysts have gained notoriety in the oil refining and petrochemical industries and in the manufacture of pharmaceuticals, agrochemicals, flavors, and fragrances. They constitute the ultimate replacement for the traditional Lewis acids leading to the generation of inorganic salts in aqueous waste streams. They also eliminate the need for separation at the end of the reaction as well the cost associated with the neutralization and disposal steps.

The process of heterogeneous catalysis involves the adsorption of molecules of reactants onto the catalyst surface and after the reaction is performed, the products undergo desorption. The process of adsorption can involve either weak van der Waals interactions between the surface of the catalyst and the adsorbed species (physisorption) or covalent bonds between surface atoms and the adsorbate (chemisorption). These reaction steps were explored previously when discussing the kinetics of catalytic processes.

In commercial applications diverse catalyst types can be used. For example, the production of ammonia,  $\text{NH}_3$ , from nitrogen and hydrogen through the Haber process, uses a heterogeneous catalyst based on Fe on  $\text{SiO}_2$  or  $\text{Al}_2\text{O}_3$  support as shown in Equation 6.71.

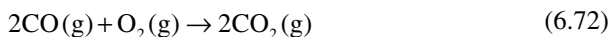


Without a catalyst this reaction would proceed very slowly because the activation barrier for the dissociation of  $\text{N}_2$  and  $\text{H}_2$  into adsorbed atoms in the gas phase is very high. The adsorbates of N and H then combine to form the product  $\text{NH}_3$ , which is then desorbed.

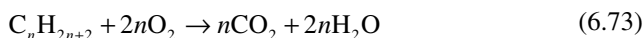
Another example of heterogeneous catalysts is found in the polymer industry. In 1953, Ziegler discovered that the polymerization of ethene to high molecular weight polyethene can be performed at low pressures in the presence of Ti-based heterogeneous catalysts. The latest generation of catalysts in use since the 1980s involves  $\text{TiCl}_4$  supported on anhydrous  $\text{MgCl}_2$  with  $\text{Et}_3\text{Al}$  as cocatalyst. Karl Ziegler and Giulio Natta were awarded the 1963 Nobel Prize in Chemistry for their discovery.

We previously described zeolites as catalytic supports, but they represent another important type of catalyst used in catalytic cracking of heavy petroleum distillates. Zeolites function as Lewis acids and provide higher selectivities and reaction rates compared to those obtained with alumina/silica catalytic equivalents. The most well-known zeolites used for their robustness to withstand the conditions of the cracking process are ultrastable Y (USY) zeolites. Ultrastable Y zeolites are often coupled to ZSM-5 used as a cocatalyst due to its shape selectivity. The other advantage of using USY zeolites in catalytic cracking is the increase in gasoline octane number. The catalyst ZSM-5 is also used in the conversion of methanol-to-gasoline process (called MTG), developed by Mobil in the 1970s. ZSM-5 is able to convert methanol to a mixture of  $>\text{C}_5$  alkanes, cycloalkanes, and aromatics. Zeolites have largely replaced acid catalysts in many manufacturing processes because of their ease in recovery and reduced environmental footprint.

The last example using heterogeneous catalysts is the one used in automobile catalytic converters. Catalytic converters are used to reduce the toxicity of emissions from an internal combustion engine. Chemical species found in engine exhaust are carbon monoxide (CO), unburned hydrocarbons ( $C_nH_{2n+2}$ ), and nitrogen oxides ( $NO_x$ ). As mentioned in Chapter 3, these products contribute to air pollution. The three-way catalytic converter simultaneously converts CO and unburned hydrocarbons to  $CO_2$  and oxidizes  $NO_x$  to  $N_2$ , thereby reducing or eliminating most of the harmful emissions from the combustion engine: for example, the oxidation of carbon monoxide to carbon dioxide,



the oxidation or combustion of typical unburned hydrocarbons to carbon dioxide and water,



and the reduction of NO to diatomic nitrogen,



Catalytic converters built after 1981 can simultaneously promote both oxidation and reduction and are commonly referred to as “three-way” catalytic converters.

The converter requires high temperatures to operate and is heated by the exhaust from the engine. As a result, the greatest majority of emissions from the automobile are released immediately after starting the vehicle. In the 1920s lead additives were introduced in gasoline to raise octane levels and unfortunately lead poisoned the catalyst and deactivated it. It was not until the 1970s that lead additives were eliminated from gasoline. A catalytic converter is made of three components:

1. A core or substrate, often a ceramic honeycomb structure typically made from a low porosity alumina.
2. An alumina washcoat applied to the ceramic substrate to increase the surface area available for reaction. The washcoat often contains other materials added to stabilize the alumina.
3. Fine particles of precious metals, Pt, Pd, and Rh (catalytic active species), are added to the washcoat in suspension to promote the specific reactions. New developments have reduced the amount of metal species required for successful operation of the catalytic converter.

#### 6.2.4 Biocatalysis

Biocatalysts are enzymes used from naturally occurring organisms such as yeasts, bacteria, and plants. Biocatalysts can be applied to nearly any field involving chemical reactions. Many chemical companies are interested in this new market such as Dow Chemical, BASF, DuPont, and Cargill, just to name a few. Biocatalysis uses

cleaner processes with no hazardous waste from unnecessary solvents, has high and efficient yields, has high atom economy, and achieves high chemo-, regio-, and stereoselectivity. Enzymes have a long lifespan and allow for higher yields of pure enantiomeric reactions and 50:50 racemic mixtures while operating under mild conditions. However, biocatalysts are also extremely expensive, and their selectivity limits their applicability to specific reagents, reducing the ability to apply biocatalysts across classes of compounds. We illustrate biocatalysis by looking at pharmaceutical and food industries.

#### **6.2.4.1 Pharmaceutical Industries and Chirality**

Chirality plays a major role in the development of drugs. A chiral molecule is defined as nonsuperimposable on its mirror image. Two chiral molecules commonly called enantiomers are often compared to the right and left hands. The same type and number of atoms are in the two enantiomers but the spatial arrangement of atoms is different. Usually one enantiomer is preferred over the other. In the pharmaceutical industry chiral molecules constitute a large portion of pharmaceutical sales. More than half the drugs approved worldwide are chiral. Examples include Lipitor<sup>®</sup> and Zocor<sup>®</sup>, as well as ibuprofen sold under the common brand names Motrin<sup>®</sup> and Advil<sup>®</sup>.

Lonza, a Swiss company, developed an enzyme-based process for the production of the world's best selling drug that lowers cholesterol, Lipitor. Codexis, the designer of the key chiral building block in the synthesis of the active pharmaceutical ingredient in Lipitor, received the 2006 Presidential Green Chemistry Challenge Award from the U.S. Environmental Protection Agency [12].

The key chiral building block is hydroxynitrile (HN) or ethyl (*R*)-4-cyano-3-hydroxybutyrate whose demand is estimated to be about 200 metric tons annually. Traditional commercial processes are based on:

- The use of chiral precursors.
- The use of hydrogen bromide to generate a bromohydrin for cyanation.
- The substitution of cyanide for halide under heated alkaline conditions, resulting in the formation of by-products.
- A high-vacuum fractional distillation to obtain a purified final product leading to a further decrease of the yield.

The three-step green process designed by Codexis is centered around the activity, selectivity, and stability of three enzymes created using cutting-edge genetic methods. This new process involves:

- Mild, neutral conditions with fewer steps.
- A high-quality product due to the activity and stability of the enzymes.
- An increase in the volumetric productivity of the first step reaction by approximately 100-fold and that of the second step by approximately 4000-fold.

- An increase in the yield, and a decrease in the formation of by-products and generation of waste.
- A reduction of solvents and purification equipment, increasing worker safety.

Merck and Co., Inc. is a global pharmaceutical company established in 1891. Merck is devoted to addressing urgent medical needs through far-reaching programs “that can make a difference in people’s lives and create a healthier future” [13]. Merck puts the well-being of its patients first while committed to environmental best practices. Their “green by design” initiative through chemo- and biocatalysis generates benefits summarized by the “triple bottom line” of economics, society, and environment.

A standout example of using catalysis to reduce the number of process steps and waste, and thereby decreasing the cost of manufacturing, is Merck’s Januvia™ treatment for type 2 diabetes. This case study will guide you through the understanding of how catalysis can be applied to green chemistry.

### *Part I: Introduction and Traditional Way to Produce Type 2 Diabetes Drugs*

Insulin is a hormone secreted by the pancreas to allow the blood sugar or glucose to enter the body’s cells to be used for energy. When insulin is not performing normally, too much glucose accumulates in the blood and over time can do substantial damage to eyes, heart, blood vessels, and kidneys. Type 2 diabetes is the most common form of diabetes and is a lifelong disease. One-third of all people who have diabetes are not aware of their condition [14]. Type 2 diabetes symptoms may include feeling more thirsty and hungry than usual, as well as having to urinate more frequently, losing weight without trying to, and feeling more tired.

Normally, a controlled diet and exercise should help maintain normal blood glucose levels. When these are not sufficient, medication may need to be prescribed. Medications available today either increase the insulin supply (such as sulfonylureas, secretagogues), decrease the insulin resistance, or improve its effectiveness (biguanides and thiazolidinediones) [15]. Another group of medications is called alpha-glucosidase inhibitors, which reduce the rate of glucose absorption.

Traditional oral medications such as Diabinese and Tolinase cost between \$26 and \$27 per month. Other medications such as Starlix and Prandin cost from \$77 to \$84 per month because no generic brand is available. Side effects of these medications include hypoglycemia and sometimes weight gain. Most of these medications should not be taken if a condition of heart disease is known. The other type of medication would be insulin, which is injected under the skin.

The traditional pathway to synthesize the active ingredient for type 2 diabetes drugs requires the production of aminoacid derivatives. Sitagliptin, a chiral  $\beta$ -amino acid derivative, is the active ingredient in Januvia, which is a recent treatment for type 2 diabetes. The process required eight steps as well as high-molecular-weight reagents that were not present in the final molecule and contributed to waste.

### *Part II: Environmentally Benign Pathway—Another Shot at Januvia*

Merck, in collaboration with Solvias, a company specializing in catalytic hydrogenation, came up with a new method for generating  $\beta$ -amino acids. Merck researchers discovered that amino acid derivatives can be produced via the asymmetric catalytic hydrogenation of unprotected enamines. The catalyst is a rhodium salt of a ferrocenyl-based ligand. The hydrogenation step reduces waste by 80% and the cost of manufacture by 70%.

Merck was also able to recover and recycle over 95% of the rhodium after hydrogenation. This new synthesis has only three steps and the overall yield is increased by almost 50%. The amounts of raw materials, processing time, energy, and waste were reduced, leading to a reduction of 220 pounds of waste for each pound of sitagliptin manufactured. Because the reactive amino group of sitagliptin is created in the last step of the synthesis, there is no need for protecting groups.

Biocatalysis is a rising market within the pharmaceutical and fine chemical industry. Many companies are joining the market to help with the creation of new biocatalysts, which ultimately allow for greater specificity and activity, and therefore lower the cost of products for consumers.

#### **6.2.4.2 Food Industry and Flavors**

Heterogeneous catalysts can also be used in the food industry. University of California–Riverside researchers led by Francisco Zaera designed a platinum-based heterogeneous catalyst which favors the production of partially hydrogenated oils without making *trans* fats. The process of hydrogenation, which is the addition of hydrogen to natural oils to increase the shelf life of foods, results in the production of *trans* fats found in vegetable shortenings, fried foods, doughnuts, pastries, cookies, crackers, and snacks. *Trans* fats are known to raise the “bad” cholesterol levels (LDL) and lower the “good” ones (HDL) and are commonly associated with the development of heart disease, stroke, and type 2 diabetes.

Researchers in Zaera’s lab found that by controlling the shape of the platinum particles used in the catalyst, the catalyst increased selectivity toward hydrogenated oils while minimizing the production of *trans* fats.

Another controversial food group is the low calorie sweeteners (also referred to as nonnutritive sweeteners, artificial sweeteners, or sugar substitutes). Artificial sweeteners provide sweetness without the addition of excessive calories. They can be found in diet soft drinks, sugar-free puddings, light yogurts, candies, and as table-top packets.

Some of the most common low-calorie sweeteners approved for use in the United States are:

- Acesulfame potassium (Ace-K; brand names: Sunett, Sweet One), which does not cause any human health problems but it is not broken down by the body. Therefore, it is eliminated in its original form by the kidneys.
- Sucralose (brand name: Splenda) is about 600 times sweeter than regular sugar. It was approved in 1998 by the FDA to be used in diabetic diet and for blood glucose control.

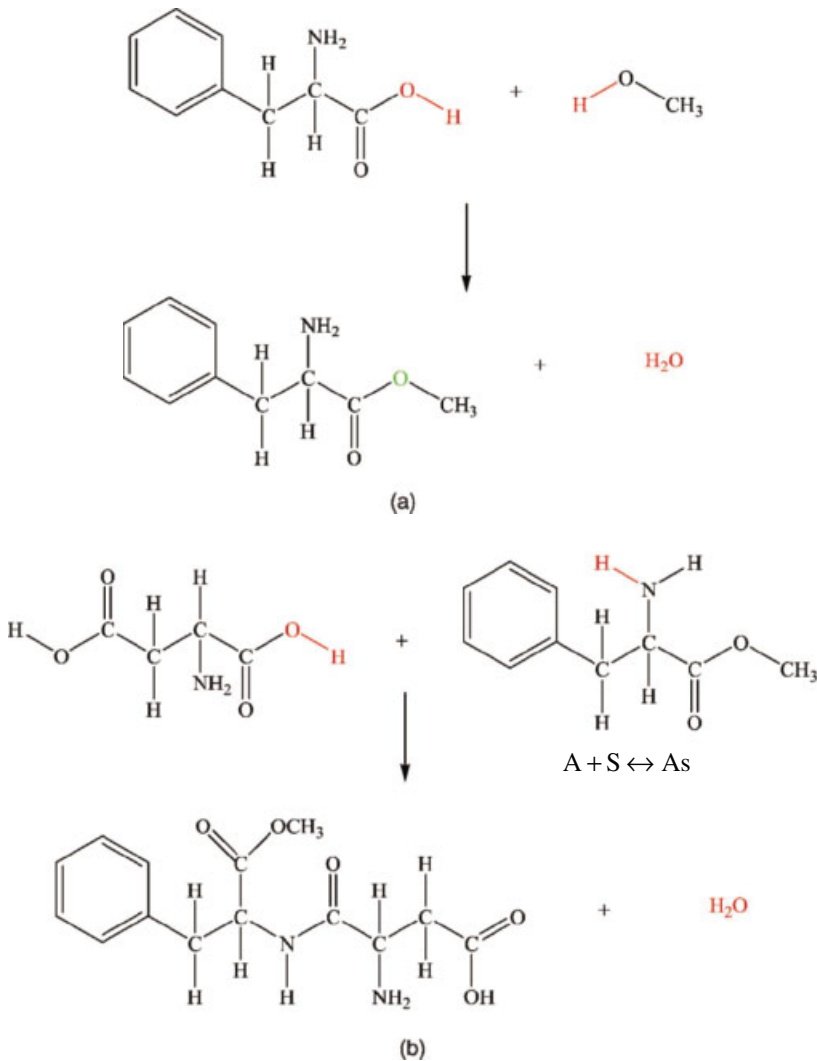


- Neotame (brand name: n/a) was approved in 2002 by the FDA as a general purpose sweetener, which is approximately 7000 times sweeter than sugar.
- Stevia Sweeteners (brand names: PureVia, Sun Crystals, Truvia) are highly purified steviol glycosides, found naturally in the stevia plant. They contain zero calories and are about 200–300 times sweeter than sugar.
- Saccharin (brand names: Sweet’N Low, Sweet Twin, Sugar Twin), one of the oldest discovered artificial sweeteners, was discovered in 1878. It raised a lot of concerns about thirty years ago when a study found that saccharin consumption was linked to stomach cancer. Saccharin was then banned by the FDA. However, in 2001, the National Institutes of Health (NIH) removed saccharin from the list of potential carcinogens. Saccharin is still widely used today.
- Aspartame (brand names: NutraSweet, Equal) was approved as a general purpose sweetener by the FDA in 1996. The safety of aspartame was challenged due to some concerns over its long-term possible carcinogenicity [16]. The only unsafe use would be for individuals with phenylketonuria (PKU), which is a genetic disorder causing a baby to have very low levels of the enzyme phenylalanine hydroxylase (PAH). This enzyme is necessary to convert the amino acid phenylalanine into tyrosine, another amino acid. Aspartame is not recommended for baking because it often breaks down at high temperature and loses its sweetness. Because of this issue, aspartame has lost a good share of the artificial sweeteners market to sucralose, which does not lose its sweetness when heated.

Aspartame was discovered by accident by Jim Schlatter, a chemist at G.D. Searle in 1965. Jim Schlatter was working on drugs for the treatment of gastric ulcers when he spilled some aspartyl-phenylalanine on his hand. He later licked his finger and noticed the sweet taste of the compound, which later became aspartame. Aspartame is the methyl ester of the dipeptide of the natural amino acids L-aspartic acid and L-phenylalanine. There are four possible diastereoisomers for aspartame but aspartame is the only one having sweetening properties. The taste of aspartame would not have been predictable based on its amino acid constituents.

Aspartame is made of two amino acids that are chiral. The chemical synthesis starts with a racemic mixture, which contains equal quantities of both isomers of the two amino acids. The L isomers of both phenylalanine and aspartic acid are the only desired ones. The other isomers must be removed, therefore becoming waste.

The first step in the synthesis of aspartame is the ester synthesis where L-phenylalanine reacts with methanol in the presence of hydrochloric acid. The product is the methyl ester of phenylalanine (Scheme 6.4a). The second step is the amide synthesis, which is the reaction of the methyl ester of phenylalanine with aspartic acid (Scheme 6.4b).



**Scheme 6.4.** (a) First step in the synthesis of aspartame and (b) second step in the synthesis of aspartame.

Due to the necessity to resolve a racemic mixture, the traditional chemical synthesis of L-aspartic acid is very costly. An alternative would be to use a chiral catalyst that would selectively synthesize the L-enantiomer or one that would eliminate the D-enantiomer. Some of the most useful chiral catalysts provided by nature are enzymes.

There is a one-step enzymatic conversion to produce aspartic acid that consists of reacting fumaric acid with the aspartase from a bacteria, *Bacillus subtilis*, strain ASP-4, NRRL B-15536. The loss of enzyme activity can be inhibited by adding a source of ammonium ions and fumaric acid in the fermentation process [17].

### 6.3 REACTION ENGINEERING

Reactions are conducted in reactors, vessels designed to allow the reactants to come into contact under specific conditions. In order to determine the size of a reactor needed to carry out a specific reaction, we use a material balance equation, written in maximum generality as follows:

$$\begin{aligned} &\text{Flow rate entering the system} + \text{Generation or depletion due to chemical reaction} \\ &+ \text{Accumulation or depletion} = \text{Flow rate leaving the system} \end{aligned}$$

The engineer who wants to determine the size of the vessel needs to use symbols in order to solve specific examples of this general mass balance. Written symbolically, we get the following very general equation:

$$F_{i,0} + \int r_j dV + \frac{dN_i}{dt} = F_i \quad (6.75)$$

where

$$\begin{aligned} F_{i,0} &= \text{Flow rate of component } i \text{ entering the reactor (mol/time)} \\ F_i &= \text{Flow rate of component } i \text{ leaving the reactor (mol/time)} \\ \int r_j dV &= \text{Rate of formation of component } i \text{ due to reaction } j \text{ (mol/ time), and } r_j \text{ is the} \\ &\quad \text{reaction rate (mol/vol-time)} \\ V &= \text{Volume of the reactor (vol)} \end{aligned}$$

This is a very complicated expression that contains both a derivative and an integral. The integral term is included to account for the possibility that the reactor is not well mixed, and the rate of reaction will then be an “average” based on the concentration everywhere within the reactor. The differential term accounts for the reality that certain components may be accumulated within the reactor, depending on the design of the system.

While it is true that this is a very difficult mathematical expression, the good news is that we very rarely need to work with the full equation to complete our basic reactor design. Through the next few sections, we consider several ideal reactors, where simplification of the general material balance equation is possible.

#### 6.3.1 Batch Reactor

The batch reactor, shown schematically in Figure 6.10, is comparable to a batch process in that there is no flow of material into or out of the system. The components are placed in the reactor at the beginning of the process and are removed from the reactor at the end. Thus,

$$F_{j,0} = F_j = 0$$



**Figure 6.10.** Picture of a batch reactor [18].

Recall that  $F_i$  corresponds to the flow rate of the reactant or product. We also assume that the contents of the reactor are well mixed. This simplifies the calculation of the rate:

$$\int r_j dV = r_j V \quad (6.76)$$

Substituting these assumptions into the material balance provides

$$\frac{dN_j}{dt} = r_j V \quad (6.77)$$

We can rearrange this equation, and rewrite the number of moles in terms of the concentration and reactor volume,  $N_j = C_j V$ . Then, for a constant volume reactor, we find

$$r_j = \frac{1}{V} \frac{d}{dt} (C_j V) = \frac{dC_j}{dt} \quad (6.78)$$

We can put this equation in terms of the conversion by noting that

$$N_j = N_{j,0} - N_{j,0} X_j$$

Thus,

$$\frac{dN_j}{dt} = -N_{j,0} \frac{dX_j}{dt} \quad (6.79)$$

which provides, upon substitution,

$$N_{j,0} \frac{dX_j}{dt} = -r_j V \quad (6.80)$$

and for a constant volume process

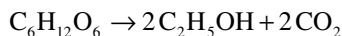
$$C_{j,0} \frac{dX_j}{dt} = -r_j \quad (6.81)$$

In most cases, we are interested in either the time needed to achieve a particular conversion, or the conversion that will be obtained after a specific reaction time. Highlight 6.8 provides an application example related to the production of ethanol.

### Highlight 6.8 Production of Ethanol from Waste Corn Cobs

Ethanol can be produced from waste corn cobs through the conversion of the cellulose in the cob under fermentation with yeast. At an initial concentration of 100 g/L, the rate expression is shown to be first order, with a rate constant of 0.0131 h<sup>-1</sup>. The reaction is to be performed in a batch reactor with a reaction time of 24 h. If 1000 g of cellulose is used in the initial batch, what is the final concentration of ethanol in solution?

Assume the reaction stoichiometry as



#### Solution:

We start by calculating the conversion of cellulose that can be achieved in one day. This can be obtained by solving the material balance equation for the batch reactor

$$C_{A,0} \frac{dX_A}{dt} = -r_A$$

The rate is a function of conversion, so we need to separate variables and integrate. Rewriting the rate expression in terms of conversion provides

$$-r_A = kC_{A,0}(1 - X)$$

Substituting into the mass balance expression and rearranging provides

$$C_{A,0} \frac{dX_A}{dt} = -r_A = kC_{A,0}(1-X)$$

or

$$\frac{dX}{1-X} = k dt$$

Now we can integrate both sides, noting that  $X=0$  at  $t=0$ :

$$\int_0^{X_f} \frac{dX}{1-X} = k \int_0^{t_f} dt$$

$$-\ln(1-X_f) = kt_f$$

Since we know  $t=24$ h, we rearrange to solve for  $X$ , and then substitute known values and solve:

$$X = 1 - e^{-kt}$$

$$= 1 - e^{-(0.0133\text{h}^{-1})(24\text{h})}$$

$$= 0.27$$

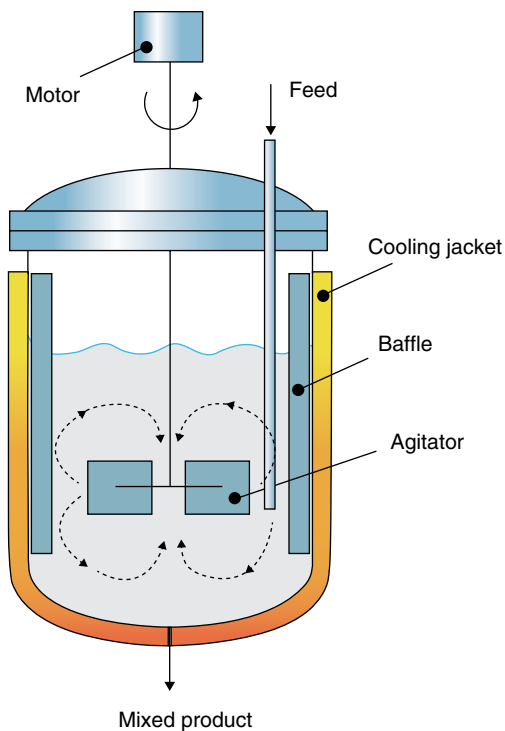
We start with 1000 g of cellulose, so we convert 270 g in the allotted time. Based on the assumed molecular formula of cellulose, the molecular weight is 180 g/mol, so 270 g corresponds to

$$N_{\text{converted}} = \frac{(270 \text{ g})}{(180 \text{ g/mol})} = 1.5 \text{ mol}$$

From the stoichiometry of the reaction, 1.5 mol of converted cellulose produces 3 mol of ethanol. The initial concentration was 100 g/L, so 1000 g of cellulose corresponds to 10 L of solution. As a result, the final concentration of ethanol is 0.3 mol/L.

### 6.3.2 Continuous Stirred Tank Reactor

A continuous stirred tank reactor (CSTR) looks like a batch reactor, in that material enters the reactor, resides in the reactor for some time, and then leaves the reactor (Figure 6.11). The difference is that, in this case, the reactor is operating continuously, with new feed continually entering the reactor and products continually being removed. We assume that the contents of the reactor are well mixed, which means that the concentration everywhere within the reactor is the same. Thus, the



**Figure 6.11.** A CSTR used in a fermentation reaction [19].

material entering the reactor is immediately converted to the concentration within the reactor and the concentration of material leaving the reactor is the same as that inside.

Now, we can develop the material balance equation starting from the general balance equation given earlier, noting that there is no accumulation within the reactor (this system operates at steady state).

$$F_j - F_{j,0} = \int r_j dV \tag{6.82}$$

Since the composition of the fluid inside the reactor is identical everywhere, the reaction rate must be the same everywhere. We replace the integral with a simple multiplication, which provides

$$F_j - F_{j,0} = r_j V \tag{6.83}$$

Now, solving for the reactor volume provides

$$V = \frac{F_{j,0} - F_j}{-r_j} \tag{6.84}$$

We frequently prefer to define reaction rates in terms of concentration. In order to make this transformation, we need to define the *mean residence time*, which is the average length of time that an element of fluid remains within the reactor. The residence time can be calculated from the volumetric flow rate and the volume of the reactor.

$$\tau = \frac{V}{V} \quad (6.85)$$

Now, we write the molar flow rate as  $F_j = C_j V_0$  and the volume as  $V = \tau V_0$ , which provides the required residence time as a function of concentration

$$\tau = \frac{(C_{j,0} - C_j)}{-r_j} \quad (6.86)$$

Finally, we can rewrite the equation in terms of the reactant conversion

$$\tau = \frac{(C_{j,0} X_j)}{-r_{j,\text{exit}}} \quad (6.87)$$

or

$$V = \frac{F_{j,0} X_j}{-r_{j,\text{exit}}} \quad (6.88)$$

in which the use of the term  $-r_{j,\text{exit}}$  reminds us that the reaction rate is constant everywhere within the reactor and equal to the rate at the reactor exit. Highlight 6.9 gives an example of how to calculate residence time.

Highlight 6.9 demonstrates that the conversion for two CSTRs in series is always greater than that of one CSTR of equal size. This is because of the way a CSTR operates. Remember, the concentration inside the tank is the same everywhere, and the same as the exit concentration. So if we break the tank into two, then the concentration within the first CSTR is higher, and the reaction rate is higher because it is proportional to the concentration. We could get even better conversion if we used three CSTRs connected in series, and likewise continue to improve as we add more (and smaller) reactors. We can generalize the result to any number of equal-sized CSTRs connected in series and obtain a single equation relating the residence time to the conversion. We find

$$X = 1 - \frac{1}{(1 + k\tau)^n} \quad (6.89)$$

if the reaction can be described by first order kinetics. While we could improve the performance using many consecutive reactors, this is not practical because of the need for many multiple vessels for the reactions and pumps needed to move the fluid from one reactor to the next.



### Highlight 6.9 Oxidation of Pentane

The oxidation of pentane is occurring in a continuous stirred tank reactor. Under these conditions, the rate of the reaction is given by  $-r_p(\text{mol/L}\cdot\text{min})=0.1 C_p$  ; independent of oxygen. What is the reactor residence time required to achieve 60% conversion?

**Solution:**

We start from the material balance equation, written in terms of residence time and conversion:

$$\tau = \frac{C_{p,0} X_p}{-r_{p,\text{exit}}}$$

and now substitute in the rate expression, also written in terms of conversion,

$$\tau = \frac{C_{p,0} X_p}{C_{p,0} (0.1 \text{ min}^{-1})(1 - X_p)} = \frac{X_p}{(0.1 \text{ min}^{-1})(1 - X_p)}$$

The conversion that must be obtained is 60%, so substitution in this equation provides

$$\begin{aligned} \tau &= \frac{0.6}{(0.1 \text{ min}^{-1})(1 - 0.6)} \\ &= 15 \text{ min} \end{aligned}$$

Suppose we wanted to run the same reaction in two identical CSTRs connected in series. What residence time in each CSTR would be required? Would it be 7.5 min in each? In order to determine the answer, let's assume that we have two 30L reactors connected in series, so the volumetric flow rate needs to be 4L/min to achieve a residence time of 7.5 min in each reactor. Given this condition, let's calculate the conversion.

Previously, we showed that the conversion and the residence time in a CSTR could be related according to

$$\tau = \frac{X}{k(1 - X)}$$

We can now rearrange this equation and solve for  $X$  to find

$$X = \frac{k\tau}{1 + k\tau}$$

Substituting the given values of the rate constant and residence time, we find the conversion from each reactor can be obtained as

$$X = \frac{k\tau}{1+k\tau}$$

$$= \frac{(0.1 \text{ min}^{-1})(7.5 \text{ min})}{1+(0.1 \text{ min}^{-1})(7.5 \text{ min})} = 0.429$$

So how much material is remaining in the stream leaving reactor 1? If we started with 1 mol/L of the reactant, then 0.571 mol/L remains at the end. This is also the amount entering reactor 2. So 42.9% conversion from this reactor then provides an exit composition of

$$C_A = C_{A,0}(1-X)$$

$$= (0.571 \text{ mol/L})(1-0.429)$$

$$= 0.326 \text{ mol/L}$$

which corresponds to an overall conversion of 0.674. This is higher than the conversion obtained from a single CSTR with twice the residence time.

### 6.3.3 Plug Flow Reactor (PFR)

A reaction can also occur as a fluid moves along a length of heated pipe. We assume that the fluid moves in a plug and that the plug of fluid moves without mixing with any other fluid elements. As the plug moves along the tube, reaction occurs. Fresh feed continuously enters at one end of the tube, and product is continuously removed from the other end of the tube (Figure 6.12).

Now we apply the general mole balance, assuming that the reactor operates at steady state,

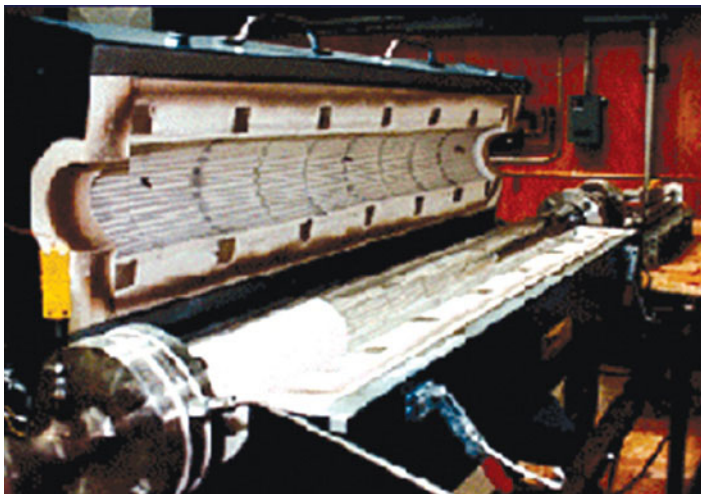
$$F_j = F_{j,0} + \int_V r_j dV \quad (6.90)$$

or, in terms of a differential reactor element,

$$-r_j dV = F_j - (F_j + dF_j) \quad (6.91)$$

which simplifies to give

$$\frac{dF_j}{dV} = r_j \quad (6.92)$$



**Figure 6.12.** A tubular (plug flow) reactor inside a tube furnace [20]. (Courtesy of Robert Hesketh, Rowan University, Glassboro, NJ.)

Now, we write the molar flow rate as  $F_j = C_j V$  and the volume as  $V = \tau V$ , which is substituted into the equation to give

$$\frac{d(C_j V)}{d(\tau V)} = \frac{dC_j}{d\tau} = r_j \quad (6.93)$$

where the last expression requires that the volumetric flowrate  $V$  be constant along the length of the reactor. Note that this last result is identical to the result obtained for the batch reactor, except that the time is now expressed as a residence time, rather than process time.

Because of the similarity between the PFR and the batch reactor, we can by analogy develop an expression of the material balance, which is based on conversion:

$$C_{j,0} \frac{dX_j}{d\tau} = -r_j \quad (6.94)$$

or in integral form, and in terms of the reactor volume,

$$F_{j,0} \int_0^x \frac{dX}{-r_j} = V \quad (6.95)$$

Highlight 6.10 provides another example about residence time required for conversion of pentane.

If we compare Highlights 6.9 and 6.10, we see that we have an identical reaction with an identical reaction rate. However, the residence time required in the

### Highlight 6.10 Oxidation of Pentane

The oxidation of pentane is occurring in a plug flow reactor. Under these conditions, the rate of the reaction is related to the composition according to  $-r_p = 0.1 C_p$  (mol/L·min)—independent of oxygen. Calculate the residence time required to achieve 60% conversion (the half-life on the reactant).

#### Solution:

We start from the material balance equation and substitute the rate expression given by the problem statement:

$$\tau = C_{p,0} \int_0^{X=0.6} \frac{dX_p}{0.1 C_p}$$

and recognize that  $C_p = C_{p,0} (1 - X_p)$ , which gives, after substitution,

$$\tau = \int_0^{X=0.6} \frac{dX_p}{0.1(1 - X_p)}$$

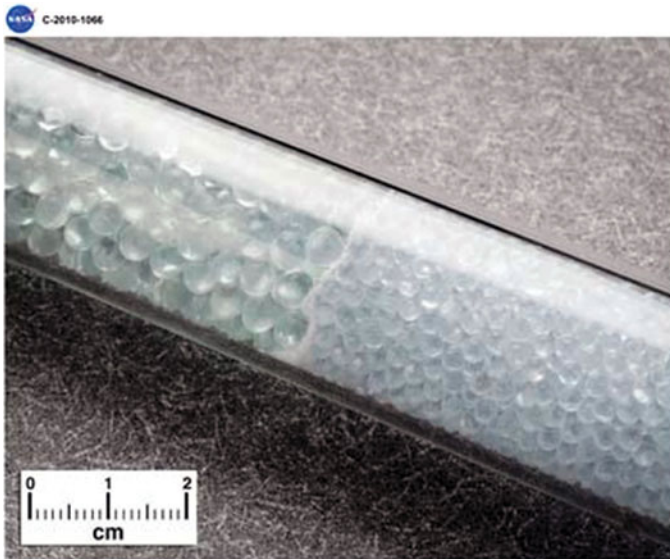
Integration provides

$$\tau = \frac{-\ln(1 - X_p)}{0.1 \text{ min}^{-1}}$$

and after substitution of  $X_p = 0.6$  provides the answer,  $\tau = 9.16$  min.

plug flow reactor is less than that required in the CSTR, or even in two identical CSTRs connected in series. The reason is again the decreasing concentration as the reaction proceeds, leading to a continually decreasing reaction rate. At all points in the reactor, the concentration is the highest, and thus the reaction rate is maximized.

Although we looked at only a few specific types of reactor systems, the green chemist and green engineer have many different variations on these ideal systems that can be used to maximize the performance of the reactor. For example, it is possible to use microwave energy to add heat to a reactor, and because of the penetration of the microwaves, this delivers energy directly to the reactants rather than the vessel. High shear systems can add large amounts of energy and provide good mixing in viscous systems. There are many vessel types that allow for contacting between species in a gas phase with those in a liquid phase. In all cases, the purpose is to maximize the concentration of the reacting species in the phase in which the reaction will occur, and to deliver heat energy to the location of the reaction in an efficient manner. Analysis of the reactor system often follows as illustrated in the three ideal situations considered above.



**Figure 6.13.** Photograph of a packed bed reactor, in which fluid enters at the top and flows down through the catalyst bed [21].

### 6.3.4 Multiphase Reactor Design

There are numerous other types of reactors that can be used to carry out a chemical reaction. The choice of reactor depends on the physical situation, and the economics of the process. In most cases, design of the reactor can be completed through a variation of that used for one of the “basic” reactor profiles.

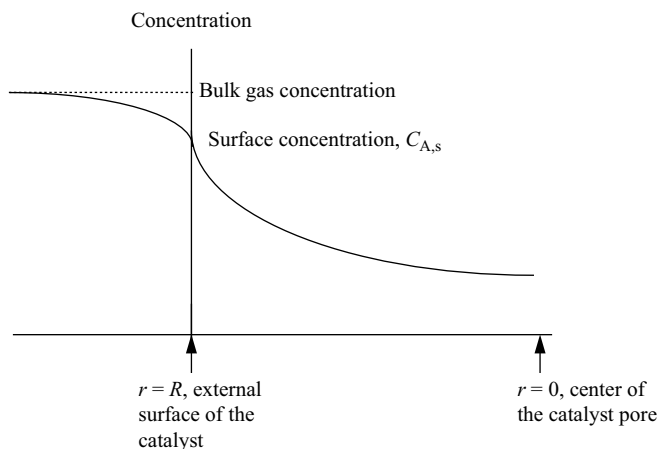
First, let’s briefly describe the packed bed reactor—the analog of the PFR for heterogeneously catalyzed reactions. The packed bed is essentially a tube in which catalyst particles are packed (Figure 6.13).

As gas flows across the catalyst particles, reactant is converted into product. In the plug flow reactor, the concentration of the reactant varied along the length of the reactor—here, the length (or volume) is replaced with the weight of the catalyst. As a result, the material balance for a packed bed reactor provides

$$\frac{dF_j}{dW} = r_j \quad (6.96)$$

or in integral form,

$$F_{j,0} \int_0^X \frac{dX}{-r_j} = W \quad (6.97)$$



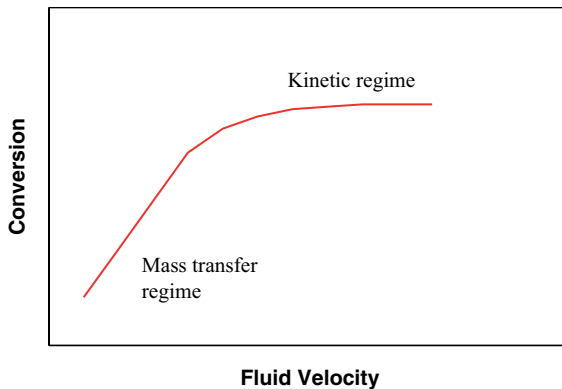
**Figure 6.14.** Schematic diagram of the concentration profile in a catalytic system.

This equation is essentially identical to that for the plug flow reactor, except the volume of the reactor is now replaced with the catalyst weight. If the reaction rate is defined in terms of catalyst weight (as would be common for a heterogeneously catalyzed reaction), then all of the units cancel and the design of the packed bed reactor is completely analogous to that of the PFR.

Slurry reactors are three-phase reactors used for contacting a gas, a liquid, and a solid. They are often used during hydrocarbon processing, such as in hydrogenation. The gaseous reactant (hydrogen) must diffuse through the liquid layer (usually the hydrocarbon) to the surface of the solid catalyst, where the reaction can occur. The reactor can be arranged so that the liquid and gas pass in a continuous flow arrangement, maintaining the catalyst particles within the reactor through the use of a screen or filter. In this case, the reactor is designed using the basic equations of a CSTR. These reactors provide good temperature control and are useful for cases in which the catalyst cannot be palletized. However, the need to separate the catalyst from the liquid phase can cause problems of plugging, sometimes making these types of systems less desirable.

Whenever we consider a reaction between species in different phases, we must confront the issue of mass transfer. Because of the presence of the phase boundary, the concentration of the species at the point where the reaction occurs is different from the concentration of the species in the bulk fluid. The concentration profile is shown schematically in Figure 6.14. Since the rate of reaction is dependent on the concentration of the reacting species, we see that the effect of mass transfer is to decrease the rate below that which would be expected based on the bulk fluid concentration.

The concentration profile outside the catalyst particle is controlled by the principles of convective mass transfer (or in a packed bed, interparticle mass transfer). Although the details of convective transport are beyond the scope of this course, it is



**Figure 6.15.** Schematic description of the effect of external mass transfer on conversion.

sufficient to know that increasing the fluid velocity around the outside of the particle will increase the rate of mass transfer.

Usually, we choose to run the reaction in such a way that the external mass transfer rate is sufficiently high and the effect of external mass transfer may be neglected. The standard test for determining if external mass transfer is important is to vary the flow rate through the reactor, at a constant residence time (it is necessary to keep the residence time constant so that the kinetically controlled conversion will remain fixed). This is achieved by varying the flow rate and the weight of catalyst simultaneously. If the change in flow rate does not affect the measured conversion, then external mass transfer can be neglected. A typical graph of the experimental result is shown in Figure 6.15.

Internal mass transfer is more difficult to work with, since the concentration of the reactant decreases as you move further within the catalyst pore. Although it is possible to calculate the concentration at every point within the pore, the mathematics quickly becomes very difficult. What is normally done is to define a term that accounts for the inhibition of the rate due to internal mass transfer. This is termed the effectiveness factor, which is defined as

$$\eta = \frac{\text{actual rate of the reaction}}{\text{rate of the reaction that would result if the entire pellet were exposed to the reactant at the surface concentration}} \quad (6.98)$$

Based on this definition, we write, for a first order reaction,

$$-r_{\text{app}} = \eta k_1 C_A \quad (6.99)$$

which provides the apparent rate of reaction within the particular catalyst pellet.

To determine if internal mass transfer is important, one performs the reaction using several different sized catalyst pellets, all with the same surface area per unit volume. As the catalyst particle size increases, the importance of internal mass transfer also increases. If the particles are small enough, internal mass transfer will become unimportant. As shown in Figure 6.14, a graph is obtained which is similar to that obtained for external mass transfer, except the kinetic regime is now found to occur at small catalyst particles.

## 6.4 SUMMARY

The green chemist has many tools available to decrease the environmental footprint of a selected reaction. By adjusting the reaction conditions, it is possible to reduce the amount of undesired product. Adding a catalyst can reduce the temperature of the reaction or improve its selectivity. There is a choice of homogeneous or heterogeneous catalyst, and there are many types of reactors that can be used. The successful green chemist will put all of these tools together to create a reaction system that can be scaled for production while keeping attention on the waste produced.

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