# Extension 14: Reaction Mechanisms, Enzymes and the Graphical Determination of Arrhenius Activation Energy

This extension builds on the material covered in Unit 14, the Speed of Chemical Reactions. It is organised into three sections:

A. More about reaction mechanisms
B. Enzymes
C. The graphical determination of Arrhenius Activation Energy

## Part A: More about reaction mechanisms

### 1. Reaction mechanism

In Unit 14 we introduced the idea of a **reaction mechanism,** outlining how the kinetics of a reaction can be useful in proposing or supporting a particular mechanism. A reaction mechanism is the precise sequence of molecular events (elementary reactions) that is involved in an overall chemical change.

For example, the production of chloromethane ($CH_3Cl(g)$) follows the overall equation:

$$CH_4(g) + Cl_2(g) \rightarrow CH_3Cl(g) + HCl(g) \qquad (1)$$

We might suggest that chloromethane is formed as a result of a collision between methane and chlorine molecules in accordance with equation (1), but it is believed that this does not happen and that the reaction proceeds in several steps, starting with the production of chlorine free radicals (chlorine atoms):

$$Cl_2(g) \rightarrow 2Cl\cdot(g) \qquad (2)$$

The energy for the breaking of the Cl-Cl bond comes from the absorption of UV light or from the energy of a Bunsen flame. The chlorine radicals then take part in a sequence of reactions including:

$$Cl\cdot(g) + CH_4(g) \rightarrow CH_3Cl(g)$$

Details of this mechanism are given in the book (p.363 and p. 257), but the fact that interests us most here is that the production of chloromethane does not occur in one step, as suggested by equation (1).

Mechanisms involving more than one stage (i.e. more than one elementary reaction) are known as 'complex'. The reason that multi-staged mechanisms are so common is that they are generally more feasible overall than single-staged reactions with large activation energies. **Since low activation energies usually mean faster reactions, several sequential reactions with relatively small activation energies will produce the desired product much faster than a single reaction with a large activation energy.**

In the next three sections we examine three reaction mechanisms in greater detail.

## 2. Example of reaction mechanism: the decomposition of nitryl chloride, $NO_2Cl$

The decomposition of nitryl chloride:

$$2NO_2Cl(g) \rightarrow 2NO_2(g) + Cl_2(g) \qquad (3)$$

Is believed to occur in two stages:

$$NO_2Cl(g) \rightarrow NO_2(g) + Cl(g) \qquad (3a)$$

$$NO_2Cl(g) + Cl \rightarrow NO_2(g) + Cl_2(g) \qquad (3b)$$

Note that the addition of (3a) to (3b) gives equation (3).

Experimentally, the rate of decomposition of $NO_2Cl$ follows the rate expression:

$$\text{Rate} = k\,[NO_2Cl] \qquad (3c)$$

Reaction (3b) involves a free radical and is likely to be much faster than reaction (3a). This makes reaction (3a) the **rate determining step** in the mechanism i.e. the slowest reaction and the one which controls the rate of the overall reaction. Any chlorine atoms produced in reaction (3a) are rapidly consumed in reaction (3b). We can therefore re-write equation (3c) as:

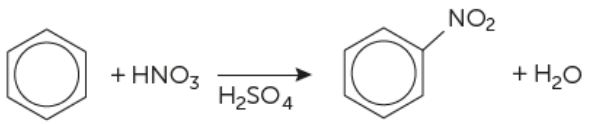
$$\text{Rate} = k_{3a}\,[NO_2Cl] \qquad (3d)$$

where we have identified the rate constant in equation (3c) as that which applies to reaction (3a). While the rate expression is consistent with the above mechanism it does not prove it: this is often the case with reaction mechanisms. Even the detection of chlorine atoms would not prove the mechanism, but it would confirm their participation in the reaction.

A narrow bridge over a river is sometimes used as an analogy for a date determining step. No matter how fast the roads are leading to the bridge – how fast the cars are able to travel to that point - cars can only proceed further in single-file. Queues quickly form at the bridge, which acts as a bottleneck.

## 3. Example of reaction mechanism: the nitration of benzene

The nitration of benzene using a mixture of nitric and sulfuric acids is discussed in the book (p. 366):




We might suggest that the reaction involves the nitrate ion ($NO_3^-$) colliding directly with the benzene ring, but when a mixture of fuming (highly concentrated) nitric and sulfuric acids is placed in an infrared spectrometer, a new infrared spectrum is observed which does not appear in the infrared spectrum of pure nitric or pure sulfuric acids. To experts in infrared spectroscopy, the appearance of the spectrum suggests a molecule similar to $CO_2$ and the new species is identified as $NO_2^+$, the nitronium ion:

$O{=}N^+{=}O$

This may be compared with carbon dioxide:

O=C=O

$NO_2^+$ is linear with a charged N atom at its centre (see Fig. 14.1).

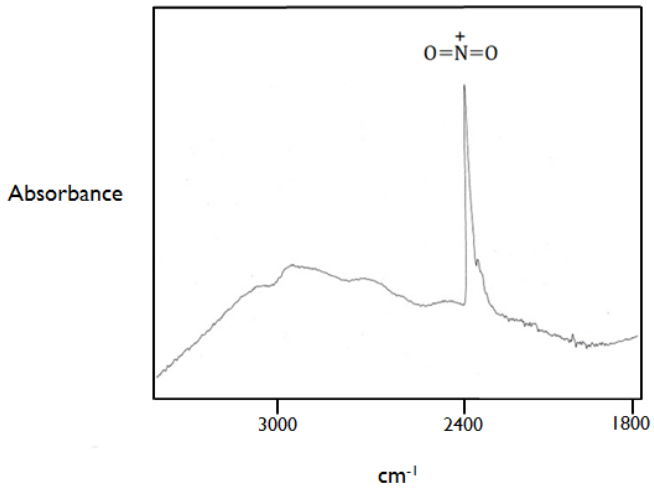
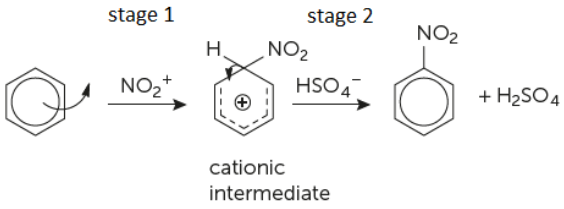



**Fig. 14.1** Infrared spectrum of mixture of fuming nitric and sulfuric acids. The absorption peak at 2360 $cm^{-1}$ is assigned to the vibration of $NO_2^+$ in which one N=O bond stretches as the other N=O bond compresses.

The nitronium ion is generated by the acid mixture:

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^-$$

It is believed that nitronium ion that attacks the benzene ring, and the nitration is believed to take place in two stages:




(4)

There are two intermediates involved in this mechanism: the nitronium ion and a positively charged intermediate called the cationic intermediate. We cannot detect the cationic intermediate, since its infrared spectrum would be obscured by the other species so we are some way from proving the mechanism overall. Kinetic experiments suggest that stage two is much faster than stage one: stage one is the **rate determining step**: in other words, any cationic intermediate that is formed rapidly converts to nitrobenzene.

## 4. Reaction mechanism: the synthesis of ammonia from hydrogen and nitrogen gases

The reaction between hydrogen and nitrogen gases to produce ammonia:

$$N_2(g) + 3H_2(g) \rightarrow 2NH_3(g) \qquad (5)$$

is achieved commercially in the Haber-Bosch process (see book, p. 277). The reaction proceeds at a viable rate using an iron catalyst.

Reaction (5) cannot occur in one step. Chemists have found that even reactions that involve the collision of three molecules are slow, but it is extremely unlikely that four molecules will collide at a perceptible rate. If direct reaction is precluded, what is the mechanism for ammonia formation? The mechanism is believed to be similar to that described for the hydrogenation of ethane (book, p259). In the first stage, nitrogen is adsorbed on the surface of iron catalyst:

1. $N_2$ (g) → $N_2$ (adsorbed on Fe)

Next, the bonds between the nitrogen atoms in the nitrogen molecule are broken and the individual nitrogen atoms bonded to the iron catalyst:

2. $N_2$ (adsorbed on Fe) → 2 N (adsorbed on Fe)

A similar process is undergone by the hydrogen atoms in the hydrogen molecule:

3. $H_2$ (g) → $H_2$ (adsorbed on Fe)
4. $H_2$ (adsorbed on Fe) → 2 H (adsorbed on Fe)

The nitrogen and hydrogen atoms are locked in place on the catalyst and they react on its surface in several stages with the overall reaction being:

5. N (adsorbed on Fe) + 3H(adsorbed on Fe)→ $NH_3$ (adsorbed on Fe)

Finally, the ammonia molecules move into the gaseous phase.

6. $NH_3$ (adsorbed on Fe) → $NH_3$ (g)

The slowest, and therefore the rate determining step in this mechanism is step (2). This is because the nitrogen molecule[1] contains a triple bond and in the gaseous state it takes a massive 945 kJ to break one mol of N≡N:

$$N{\equiv}N(g) \rightarrow N(g) + N(g) \qquad \Delta H^{\ominus} = 945 \text{ kJ mol}^{-1}$$

Once nitrogen atoms form on the iron surface, they react relatively rapidly. The presence of nitrogen atoms on the iron catalyst surface was confirmed by Gerhard Ertl and co-workers using a technique called photoelectron spectroscopy. For his work on chemical processes on solid surfaces, Gerhard Ertl was awarded the 2007 Nobel Prize for chemistry.

[1] See table of bond enthalpies (bond energies) in the book, p. 236

# Part B: Enzymes

## 5. Prerequisites

| Topic | Book page |
|---|---|
| Amino acids | 356 |
| Protein | 357 |
| Peptide bond | 357 |
| Rate of reaction and concentration | 243 |
| Activation energy | 244 |
| pH | 152, 298 |
| Buffer | 308 |
| Le Chatelier's Principle | 274 |

## 6. Introduction

The name 'enzyme' comes from the Greek words meaning 'in yeast' (Fig. 14.2). Enzymes are biological catalysts that are widely used in the food, beer and spirits industries.

**Fig. 14.2** Most of the bakery foods eaten throughout the world are made from yeast-leavened doughs. Yeast cells themselves add an assortment of vitamins and protein. Photograph © iStockphoto/lleerogers.

All enzymes are proteins and consist of amino acid units linked together by strong peptide bonds (Fig. 14.3). A protein may contain several hundred or several thousand amino acids linked in a long chain, but always with the $–NH_2$ group at the start of the chain and the $–CO_2H$ group at the end. The chains twist and bend like a long piece of plastic ribbon, but weaker bonds between the chains add rigidity to the structure and so help the protein keeps its shape.

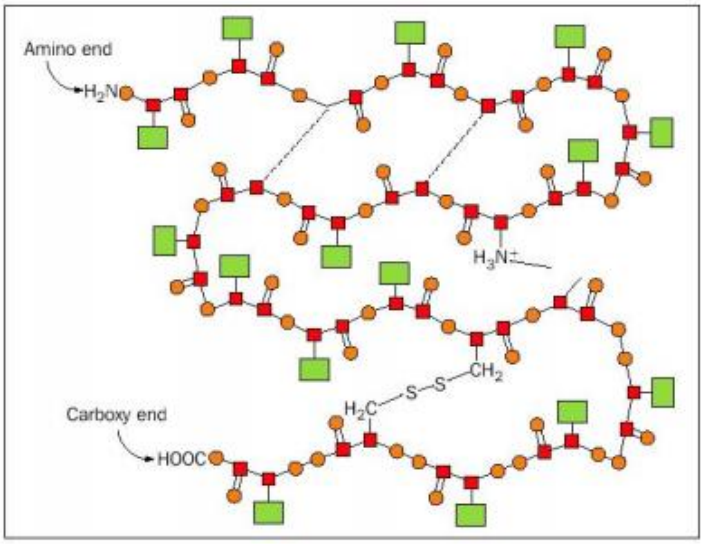



**Fig. 14.3** The structure of a protein may be likened to an extremely long necklace consisting of hundreds or thousands of amino acid molecules (of several types) held together by peptide bonds. A variety of weaker bonds and interactions help give the protein its shape.

## 7. Enzymes as supercatalysts

Enzymes are remarkably effective catalysts. For example, the enzyme called invertase hydrolyses sucrose (common sugar) into the simpler sugars, glucose and fructose. In the laboratory, the hydrolysis of sucrose can be accomplished using hot acid, but such extreme conditions cannot be tolerated in the body. Not only does the use of invertase avoid the use of hot acid, but the enzyme-catalysed reaction is billions of times faster than the acid-initiated hydrolysis.

## 8. How enzymes work

Like all catalysts, enzymes provide an alternative mechanism for a reaction, one that involves a lower activation energy. The lower activation energy means that the products are produced faster. The reactant that is converted to products by the enzyme is given a special name in biochemistry and is called the **substrate**. The part of the enzyme molecule where catalytic activity takes place is called the **active site**.

The active site consists of amino acids that are capable of forming temporary bonds with the substrate, so catalysing the reaction. The amino acid groups in the active site are positioned in the protein chain in exactly the right place to accept the substrate: this is why it is important that the protein chain keeps its shape.

Enzymes operate in two stages. In the first stage, enzymes react with the substrate forming a molecule with the grand title of **enzyme–substrate complex** (ES for short). In the second step, the ES breaks down to free the product and the enzyme. The whole mechanism is represented by the scheme:

$$\text{enzyme} + \text{substrate} \xrightarrow{①} \text{ES} \xrightarrow{②} \text{products} + \text{enzyme}$$

Like all catalysts, the enzyme is not used up. After the breakup of the ES, the enzyme is free to attach itself to another substrate.

Deriving a rate expression for the rate at which the products form in step ② is fairly complicated because ES is involved in both reactions. However, if the substrate concentration is much greater than the enzyme concentration it is found that, after an initial period, the following rate expression applies:

$$\text{Rate of product formation} = k\,[\text{E}] \qquad (1)$$

where $k$ is a constant (but one that depends upon temperature) and [E] is the total concentration of enzyme. The total concentration of enzyme in an experiment is usually constant because the enzyme is regenerated. That means that the rate of formation of a product is also a constant. This behaviour is very different from that usually observed for many reactions in the laboratory, where the rate of a reaction usually falls as soon as the reactants are mixed.

The explanation for the constant reaction rate is simply that in the presence of excess substrate, all the active sites on the enzyme are occupied. The overall rate of product formation is now dependent upon the rate of step ①, which has become slower than step ②.

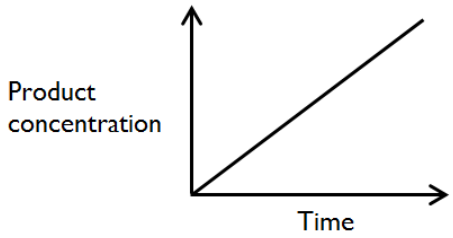
### EXERCISE 14A

The enzyme catalase decomposes hydrogen peroxide into oxygen and water. When some catalase is added to a test tube of hydrogen peroxide, the rate at which oxygen is produced is found to remain constant as long as the peroxide is in excess. Explain this behaviour and sketch a graph showing the way that the concentration of product varies with time during the constant rate period.

***Answer***

The reaction follows equation (1). During this period, the addition of more peroxide will not affect the reaction rate because all the catalase molecules already have peroxide molecules docked in their active sites. The peroxide molecules must wait their turn to enter the active sites, just as any passenger must do to get into a crowded bus.

A graph showing the variation of product concentration with time would have a constant gradient, like this:




## 9. The lock and key theory of enzyme action

Enzymes, such as pepsin and trypsin catalyse many different reactions because they must be able to digest the different types of protein found in foods, but other enzymes are much more specific and a few enzymes are believed to speed up only one reaction. An example of a highly specific enzyme is thrombin, which plays a vital role in the blood clotting process. Thrombin reacts only with the protein fibrinogen, converting fibrinogen into fibrin which then polymerizes to form a blood clot:

$$\text{fibrinogen} \xrightarrow{\text{thrombin}} \text{fibrin} \longrightarrow \text{blood clot}$$

Without this clotting process, even minor cuts could be fatal. It is the complexity of the protein chains making up the enzyme (their shape and relative orientation and the precise location of the amino acids in the chain) that explains why some enzymes are so specific. In order to bump into the amino acid groups in the active site which carry out the catalysis, the substrate molecule must be exactly the right shape. This is often illustrated as an enzymatic lock engaging with a substrate key (Fig. 14.4).

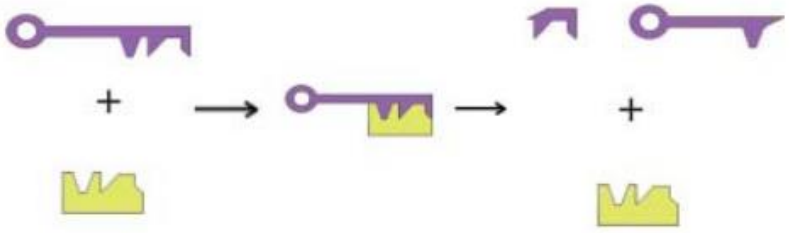


**Fig. 14.4** The lock and key analogy. Many enzymes are highly specific and will only catalyse substrates that have the right molecular shape. The substrate docks at the active site of the enzyme, reaction takes place and the substrate molecule (the 'key') breaks up forming the product molecules.

The amino acids in the active site of the enzyme can only form temporary bonds with the substrate if the pH is right. Most enzymes operate in a narrow pH range. This is commonly pH 6–8, but the enzyme that helps break down proteins in the stomach, pepsin, is unusual in that it operates in a dilute solution of hydrochloric acid at pH 2.

Enzyme action can be speeded up by modest increases in temperature but, if the temperature exceeds about 60 °C, the molecules making up the protein chains have enough energy to break away from each other. Once the protein chains are disentangled, they cannot reform again and the enzyme is said to be denatured. As the relative orientation of the amino acids has changed, the molecule is no longer capable of enzymatic action.

### 10. Enzymes and health

Blood consists of cells in a liquid called plasma. When blood is exposed to air (e.g. when stored in a test-tube), it starts to clot and becomes sticky and jellylike. Eventually, the jelly is seen to be floating on a straw-coloured liquid known as blood serum. An analysis of the blood serum for enzymes can give doctors important clues as to the illnesses of their patients.

Enzymes normally live in the cells and tissues that contain the reactions they catalyse, but in some diseases the enzymes leak out from the cell and are present in the blood serum. For example, if the starch-digesting enzyme amylase is detected in the blood serum of a patient this is strong evidence that the patient is suffering from a mumps or a disease or obstruction of the pancreas. If acid phosphatase is found in serum, this indicates that the patient may be suffering from cancer of the prostrate gland.

## Part C: Graphical Determination of Arrhenius Activation Energy

### 11. Prerequisites

| Topic | Book page |
|---|---|
| Temperature | 156B |
| Rate of reaction | 243 |
| Rate constant | 247 |
| Activation energy | 244 |
| Arrhenius equation | 249B |

**B indicates that the topic is treated in a boxed feature on that page.*

### 12. Calculating the Arrhenius activation energy

In this section, we look at a graphical way of calculating the Arrhenius activation energy. The Arrhenius equation was introduced in Box 14.2 on page 249 in the book, and the following equation was derived:

$$\ln k = \ln A - \frac{E}{RT} \qquad (1)$$

where:

- $k$ is the rate constant of a reaction at temperature $T$ kelvin. The units of k will depend upon the order of the reaction;
- $A$ is a constant for a particular reaction with the same units as $k$;
- $E$ is the Arrhenius activation energy (in J $mol^{-1}$) of the reaction. This is a constant and does not vary with temperature.
- $R$ is the gas constant (8.3145 J $mol^{-1}$ $K^{-1}$).
- ln means log to the base e.

A plot of ln $k$ against $1/T$ follows the form '$y = mx$' and should be a straight line. The slope (gradient) of the line is equal to $-E/R$ from which $E$ may be calculated.

Since logs are involved in equation (1), the rate constant $k$ is very 'sensitive' to activation energy and temperature. For example, suppose two reactions with activation energies 50 kJ $mol^{-1}$ and 70 kJ $mol^{-1}$ respectively possess the same $A$ factor and that they both take place at 300 K. Calculations of the rate constants using the Arrhenius equation show that the reaction with the lower activation energy has a rate constant which is about 3000 times larger than that of the reaction with $E$ = 70 kJ $mol^{-1}$. Since the rate constant is the speed of reaction with the reactants at unit concentration, high activation energies may make reactions non-viable. Doubling the activation energy may reduce $k$ so much that the reaction virtually stops.

## EXAMPLE 1

The rate constant for the hydrolysis of bromoethane by sodium hydroxide:

$$C_2H_5Br(aq) + OH^-(aq) \rightarrow C_2H_5OH + Br^-(aq)$$

was measured at six temperatures. The results were:

| $T$ / K | $k$ / $mol^{-1}$ $dm^3$ $s^{-1}$ |
|---|---|
| 300 | $1.123 \times 10^{-4}$ |
| 310 | $3.574 \times 10^{-4}$ |
| 320 | $1.058 \times 10^{-3}$ |
| 330 | $2.932 \times 10^{-3}$ |
| 340 | $7.652 \times 10^{-3}$ |
| 350 | $1.891 \times 10^{-2}$ |

Calculate the activation energy of reaction, expressing your answer to three significant figures.

Answer

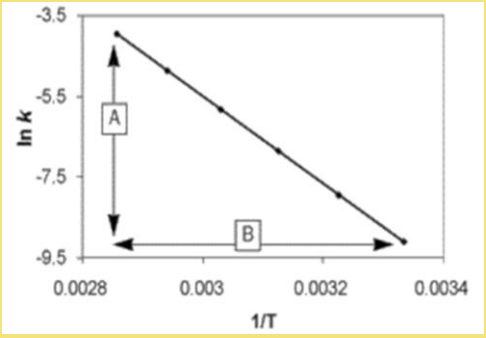
We start by calculating ln $k$ and $(1/T)$ as shown in Table 14.1:

**Table 14.1**

| $T$ / K | $k$ / $mol^{-1}$ $dm^3$ $s^{-1}$ | ln $k$ | $1/T$ |
|---|---|---|---|
| 300 | $1.123 \times 10^{-4}$ | −9.0940 | $3.333 \times 10^{-3}$ |
| 310 | $3.574 \times 10^{-4}$ | −7.9366 | $3.226 \times 10^{-3}$ |
| 320 | $1.058 \times 10^{-3}$ | −6.8515 | $3.125 \times 10^{-3}$ |
| 330 | $2.932 \times 10^{-3}$ | −5.8321 | $3.03 \times 10^{-3}$ |
| 340 | $7.652 \times 10^{-3}$ | −4.8727 | $2.941 \times 10^{-3}$ |
| 350 | $1.891 \times 10^{-2}$ | −3.9682 | $2.857 \times 10^{-3}$ |

We then plot ln $k$ against $1/T$, and fit a 'best line' through the points, preferably using a spreadsheet such as Microsoft Excel.

EXAMPLE 1 *(continued)*




The slope of a graph is the 'perpendicular distance' (shown as arrow A) divided by the 'horizontal distance' (arrow B). From the graph, these distances are −5.13 and $4.76 \times 10^{-4}$ $K^{-1}$ respectively.

Slope = $-5.13/4.76 \times 10^{-4}$ $K^{-1}$ = **−10780** K

The minus sign of the slope is a mathematical convention, meaning that the graph slopes from right to left. The units of the slope are kelvin, *K*.

According to Equation (1), the slope of the graph equals $-E/R$

**−10780** K = $-E/R$.
and
$E$ = (**10780** K) × (**8.3145** J $mol^{-1}$ $K^{-1}$) = **89600** J $mol^{-1}$

*Conclusion*: The Arrhenius activation energy for the hydrolysis of bromoethane is **89.6** kJ

## Revision questions

**1.** To study the dramatic effect of high activation energies upon *k* values, recalculate the rate constants for the hydrolysis of bromoethane (above) at 300 K and 350 K, but based upon a hypothetical activation energy of 200 kJ $mol^{-1}$. [Assume that the 'A' factor is unchanged at $4.30 \times 10^{11}$ $mol^{-1}$ $dm^3$ $s^{-1}$].

**2.** The rate constant for the decomposition of nitrogen (V) oxide:

$$N_2O_5 \rightarrow 4NO_2 + O_2$$

was studied at six temperatures:

| *T* | *k* |
|---|---|
| 300 | $5.76 \times 10^{-5}$ |
| 310 | $2.18 \times 10^{-4}$ |
| 320 | $7.61 \times 10^{-4}$ |
| 330 | $2.46 \times 10^{-3}$ |
| 340 | $7.41 \times 10^{-3}$ |
| 350 | $2.10 \times 10^{-2}$ |

Calculate *E* to three significant figures.

## Answers

**1.** To work out *k* at 300 K with *E* = 200 000 J $mol^{-1}$:

$k = Ae^{-E/RT} = 4.30 \times 10^{11} \times e^{-((200\,000)/(8.3145 \times 300))} = 4.30 \times 10^{11} \times e^{-80.18} = 6.47 \times 10^{-24}$ mol$^{-1}$ dm$^3$ s$^{-1}$.

A similar calculation is made at 350 K. The following table: compares the rate constants for both the true and hypothetical activation energies and shows that increasing the activation energy in this way produces rate constants that are virtually zero.

| | $k$ / mol$^{-1}$ dm$^3$ s$^{-1}$ | |
|---|---|---|
| ***T*/K** | ***E* = 89.6 kJ mol$^{-1}$** | ***E* = 200 kJ mol$^{-1}$** |
| 300 | 0.0001123 | $6.47 \times 10^{-24}$ |
| 350 | 0.01891 | $6.10 \times 10^{-19}$ |

These calculations are artificial in the sense that a named reaction has only one value of *E*. Nevertheless, it is clear that reactions with roughly equal A factors but different activation energies will have enormously different rate constants. Even slight differences in activation energy can produce very different rate constants because the $e^{-E/RT}$ factor *amplifies* any differences.

**2.**

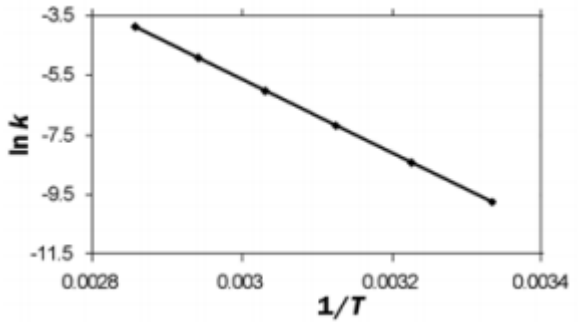
| ***T*/K** | ***k* / s−1** | **ln *k*** | **1/T** |
|---|---|---|---|
| 300 | $5.76 \times 10^{-5}$ | −9.762 | $3.333 \times 10^{-3}$ |
| 310 | $2.18 \times 10^{-4}$ | −8.431 | $3.226 \times 10^{-3}$ |
| 320 | $7.61 \times 10^{-4}$ | −7.181 | $3.125 \times 10^{-3}$ |
| 330 | $2.46 \times 10^{-3}$ | −6.008 | $3.03 \times 10^{-3}$ |
| 340 | $7.41 \times 10^{-3}$ | −4.905 | $2.941 \times 10^{-3}$ |
| 350 | $2.10 \times 10^{-2}$ | −3.863 | $2.857 \times 10^{-3}$ |

Slope = 5.90/4.76 $10^{-3}$ K$^{-1}$ = **12390** K

**−12390** K = *E*/*R*.

and

*E* = (12390 K) (8.3145 J mol$^{-1}$ K$^{-1}$) = **103000** J mol$^{-1}$.




Film Clip: Activation Energy: https://www.youtube.com/watch?v=VblaK6PLrRM