Science Education Collection

# Exploring Relative Rates Of Nucleophilic Substitution Reactions

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## Overview

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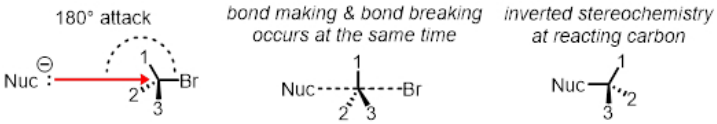
Nucleophilic substitution reactions are among the most fundamental topics covered in organic chemistry. A nucleophilic substitution reaction is one where a nucleophile (electron-rich Lewis base) replaces a leaving group from a carbon atom.

$S_N1$ (S = Substitution, N = Nucleophilic, 1 = first-order kinetics)
$S_N2$ (S = Substitution, N = Nucleophilic, 2 = second-order kinetics)

This video will help to visualize the subtle differences between an $S_N1$ and $S_N2$ reaction and what factors help to speed up each type of nucleophilic substitution reaction. The first section will focus on reactions that will help to better understand and learn about nucleophilic substitution reactions. The second section will focus on a real-world example of a substitution reaction.

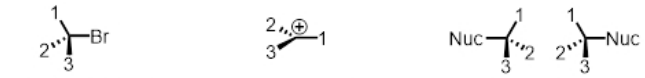
## Principles

In a nucleophilic substitution reaction, a nucleophile replaces a leaving group on a carbon atom. A one-step nucleophilic substitution is an example of the $S_N2$ mechanism. This reaction is a concerted reaction where the bonds breaking and forming are occurring at the same time. One thing to keep in mind is that the molecular orbitals involved in the reaction indicate that the nucleophilic attack must come at 180 ° from the leaving group. Therefore, some nickname the $S_N2$ reaction the "back-side attack". This back-side attack inverts the stereochemistry on the reacting carbon. This is an example of a stereospecific reaction where the stereochemistry at the onset of the reaction dictates the outcome of the stereochemistry after the reaction.




***$S_N2$***: Nucleophile attacks 180° from the leaving group. Inversion of stereochemistry.

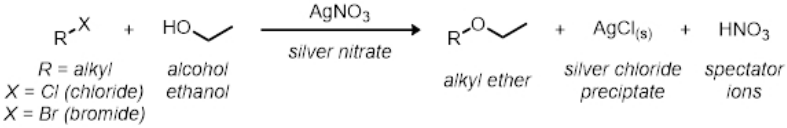
A two-step nucleophilic substitution is an example of the $S_N1$ mechanism. In the first step, the leaving group leaves and forms an intermediate called a carbocation. In the second step, the nucleophile attacks the carbocation. Since the carbocation is achiral (not chiral), any stereochemistry at the beginning of the reaction is lost. The product is still chiral, but now is an even mixture of both enantiomers which is called a racemic mixture. $S_N1$ reactions are not stereospecific.




***$S_N1$***: Loss of stereochemistry from two-step reaction forming achiral carbocation.

In two parts, we will examine the factors that affect the relative rates of the $S_N1$ and $S_N2$ reactions.

In part one, we will study the $S_N1$ reaction using 11 test tube reactions. All reactions have the same general reaction scheme:




All rates of the reactions are relative to each other. The reaction rate will be determined by the visual indicator in the reaction. Since silver chloride precipitates out of solution, the moment the reaction goes from clear to cloudy gives a visual indication of the relative reaction speed.

In three of the test tube reactions, how the alkyl halide structure plays a role in the rate of the reactions will be tested. Three different alkyl chlorides under the same conditions will be tested:

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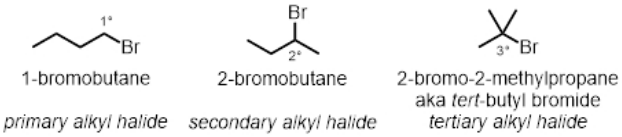
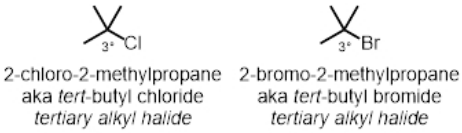



In two of the test tube reactions, the solvent polarity effects on the reaction will be tested. Two different solvents will be tested:

| *Test Tube* | *Solvent* | *Type of Solvent* |
|---|---|---|
| 1 | 100% ethanol | Polar protic |
| 2 | 5% ethanol:95% acetone | Mostly Polar Aprotic |

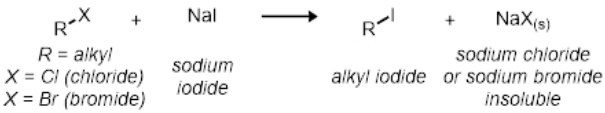
In two of the test tube reactions, the leaving group effects will be tested. Two different alkyl halides will be used:




Finally, four of the test tubes will be used to measure the rate law of the reactions. The rate of the reaction will be measured with varying concentrations of sodium iodide solution and 1-bromobutane solutions.

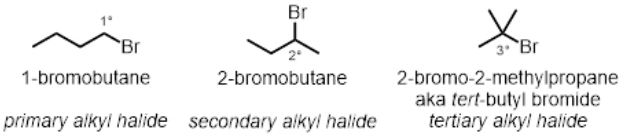
| *Test Tube* | *tert-Butyl chloride concentration* | *Silver nitrate concentration* | *Time until precipitation* |
|---|---|---|---|
| 1 | 0.1 M | 0.1 M | |
| 2 | 0.2 M | 0.1 M | |
| 3 | 0.1 M | 0.1 M | |
| 4 | 0.1 M | 0.05 M | |

In part two, we will study the $S_N2$ reaction using 11 test tube reactions. All reactions have the same general reaction scheme:

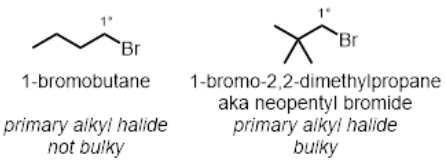



All rates of the reactions are relative to each other. The reaction rate will be determined by the visual indicator of sodium chloride or sodium bromide precipitating out of solution. This will be indicated when the reaction goes from clear to cloudy.

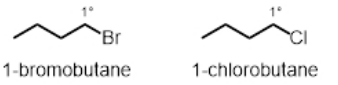
In three of the test tube reactions, how the alkyl halide structure plays a role in the rate of the reactions will be tested. This will compare the steric effects of the carbon that is bound to the bromine. Three different alkyl chlorides under the same conditions will be tested:




In two of the test tube reactions, the secondary steric effects of the alkyl halide will be tested. These are steric effects on the molecule not including the carbon bound to bromide. Two different primary alkyl bromides, under the same conditions, will be tested:




In two of the test tube reactions, the leaving group effects will be tested. Two different alkyl halides will be used:




1-bromobutane 1-chlorobutane

*primary alkyl halide* *primary alkyl halide*

Finally, four test tubes will be used to measure the rate law of the reactions. The rate of the reaction will be measured with varying concentrations of sodium iodide solution and 1-bromobutane solutions.

| *Test Tube* | *Sodium iodide Concentration* | *1-Bromobutane Concentration* | *Time until precipitation* |
|---|---|---|---|
| 1 | 15% | 1.0 M | |
| 2 | 15% | 2.0 M | |
| 3 | 15% | 1.0 M | |
| 4 | 7.5% | 1.0 M | |

## Procedure

### Part 1: Studying $S_N1$ Reactions

### Alkyl Halide Structure:

1. Measure 2 mL of a 0.1 M solution of silver nitrate in absolute ethanol into each of the three test tubes.
2. Add 2 drops of 1-bromobutane into the first test tube. Add 2 drops of 2-bromobutane into the second test tube.
3. Add 2 drops of 2-bromo-2-methylpropane into the final, third test tube.
4. Stopper and shake each test tube.
5. Note the time at which the first signs of cloudiness or precipitate appears.

### Leaving Group Effects:

1. Measure 2 mL of a 0.1 M solution of silver nitrate in absolute ethanol into each of the two test tubes.
2. Add 2 drops of 2-bromo-2-methylpropane into the first test tube and 2 drops of 2-chloro-2-methylpropane into the second test tube.
3. Stopper and shake each test tube.
4. Note the time at which the first signs of cloudiness or precipitate appears.

### Solvent Polarity Effects:

1. Measure 2 mL of a 0.1 M solution of silver nitrate in absolute ethanol into the first test tube and measure 2 mL of a 0.1 M solution of silver nitrate in 5% ethanol/95% acetone into the second test tube.
2. Add 2 drops of 2-bromo-2-methylpropane into both test tubes.
3. Stopper and shake each test tube.
4. Note the time at which the first signs of cloudiness or precipitate appears.

### Determining the $S_N1$ Rate Law:

1. Measure 0.5 mL of a 0.1 M solution of 2-chloro-2-methylpropane in ethanol into the first test tube.
2. Measure 0.5 mL of a 0.2 M solution of 2-chloro-2-methylpropane in ethanol into the second test tube.
3. Add 1.0 mL of a 0.1 M solution of silver nitrate in absolute ethanol into both test tubes.
4. Carefully measure the time it takes to observe cloudiness or precipitation.
5. Measure 1.0 mL of a 0.1 M solution of silver nitrate in ethanol into the third test tube.
6. Into the fourth test tube, measure 0.5 mL of a 0.1 M solution of silver nitrate in ethanol and add an additional 0.5 mL of ethanol.
7. Into both test tubes, add 1.0 mL of 0.1 M 2-chloro-2-methylpropane in ethanol and carefully measure the time it takes to observe cloudiness or precipitation.

### Part 2: Studying $S_N2$ Reactions

### Alkyl Halide Structure:

1. Measure 2 mL of 15% sodium iodide in acetone into each of the three test tubes.
2. Add 2 drops of 1-bromobutane into the first test tube.
3. Add 2 drops of 2-bromobutane into the second test tube.

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4. Finally, add 2 drops of 2-bromo-2-methylpropane into the final, third test tube.
5. Stopper and shake each test tube.
6. Note the time at which the first signs of cloudiness or precipitate appears.

## Steric Effects:

1. Measure 1 mL of 15% sodium iodide in acetone solution into each of the two test tubes.
2. Add 2 drops of 1-bromobutane into the first test tube and add 2 drops of neopentyl bromide into the second test tube.
3. Stopper and shake each test tube.
4. Note the time at which the first signs of cloudiness or precipitate appears.

## Leaving Group Effects:

1. Measure 1 mL of 15% sodium iodide in acetone solution into each of the two test tubes.
2. Add 2 drops of 1-bromobutane into the first test tube and add 2 drops of 1-chlorobutane into the second test tube.
3. Stopper and shake each test tube.
4. Note the time at which the first signs of cloudiness or precipitate appears.

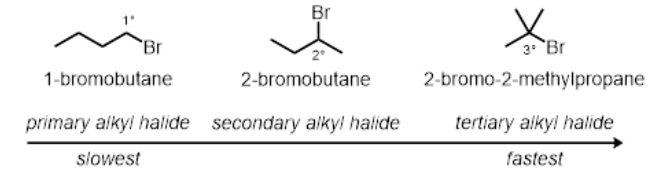
## Determining the $S_N2$ Rate Law:

1. Measure 1.0 mL of 15% sodium iodide in acetone solution into two test tubes.
2. Add 0.1 mL of 1.0 M solution of 1-bromobutane in acetone into the first test tube.
3. Carefully measure the time it takes to observe the first sign of cloudiness.
4. Into the second test tube, add 0.1 mL of a 2.0 M solution of 1-bromobutane in acetone.
5. Carefully measure the time it takes to observe the first sign of cloudiness.
6. Measure 1.0 mL of 1.0 M 1-bromobutane in acetone into the third and fourth test tubes.
7. Add 0.1 mL of a 7.5 % sodium iodide in acetone solution into the third test tube.
8. Carefully measure the time it takes to observe the first sign of cloudiness.
9. Into the fourth test tube, add 0.1 mL of a 15% sodium iodide in acetone solution and carefully measure the time it takes to observe the first sign of cloudiness.

# Results

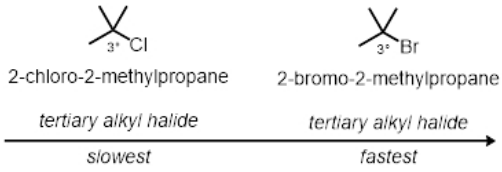
**Part 1: Studying $S_N1$ Reactions**

**Alkyl Halide Structure:**



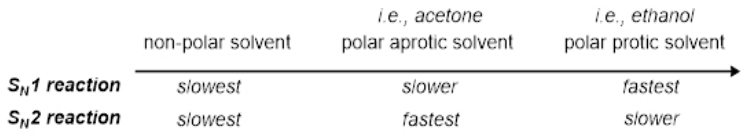

***realtive trend: better stabilizes carbocation intermediate = faster reaction***
***3° > 2° > 1°***

**Leaving Group Effects:**




***realtive trend: better leaving group = faster reaction***
***I > Br > Cl > F***

**Solvent Polarity Effects:**




**Determining the $S_N1$ Rate Law:**

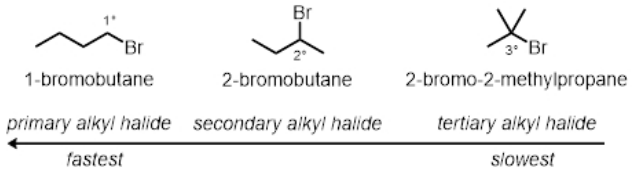
| *Test Tube* | *Silver nitrate Concentration* | *1-Bromobutane Concentration* | *Time until precipitation* |
|---|---|---|---|
| 1 | 0.1 M | 0.1 M | 20 s |
| 2 | 0.1 M | 0.2 M | 10 s |
| 3 | 0.1 M | 0.1 M | 20 s |
| 4 | 0.05 M | 0.1 M | 20 s |

$$rate = k[RX]^n[AgNO_3]^m$$

*since rate doubled when concentration of alkyl halide doubled*
*the reaction is first order with respect to the alkyl halide concentration [RX]*
$n = 1$
*since the rate is unaffected when concentration of $AgNO_3$ is halved*
*the reaction is zeroth order with respect to the $AgNO_3$ concentration $[AgNO_3]$*
$m = 0$
*rate law for $S_N1$ reaction* $rate = k[RX]$
***the reaction overall is first order kinetics***

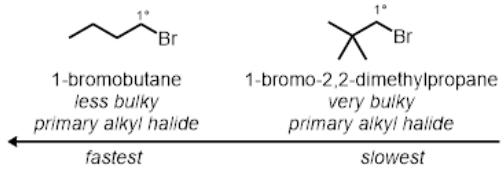
**Part 2: Studying $S_N2$ Reactions**

**Alkyl Halide Structure:**




***realtive trend: less sterically hindered alkyl halide = faster reaction***
***1° > 2° > 3°***

**Steric Effects:**




***realtive trend: less sterically hindered alkyl halide = faster reaction***
***sterically unhindered > sterically bulky***

**Leaving Group Effects:**


***realtive trend: better leaving group = faster reaction***
***I > Br > Cl > F***

**Determining the $S_N2$ Rate Law:**

| Test Tube | Sodium iodide Concentration | 1-Bromobutane Concentration | Time until precipitation |
|---|---|---|---|
| 1 | 15% | 1.0 M | 20 s |
| 2 | 15% | 2.0 M | 10 s |
| 3 | 15% | 1.0 M | 20 s |
| 4 | 7.5% | 1.0 M | 40 s |

$$\textbf{rate} = k[RX]^n[NaI]^m$$

*since rate doubled when concentration of alkyl halide doubled*
*the reaction is first order with respect to the alkyl halide concentration [RX]*

$$n = 1$$

*since the rate is halved when concentration of NaI is halved*
*the reaction is first order with respect to the NaI concentration [NaI]*

$$m = 1$$

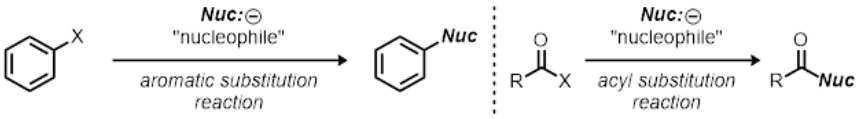
*rate law for $S_N2$ reaction* $\textbf{rate} = k[RX]^1[NaI]^1$

***the reaction overall is second order kinetics***

## Applications and Summary

These experiments are designed to quickly show trends in nucleophilic substitution reactions. Experimentally testing these trends helps to better understand the subtle differences between an $S_N1$ and $S_N2$ reaction. Chemists have learned to develop and optimize reaction conditions. It all stems from first understanding the reaction: what speeds up or slows down a reaction and how can we take advantage of it? Choosing the best solvent, temperature, or concentration of reagents can greatly affect how fast a reaction will finish. Over time, chemists have been not only concerned with speed, but with selectivity and yields as well. Nucleophilic substitution reactions are an important reaction to learn as it can be found throughout synthetic literature.

This demonstration can be used as a resource for nucleophilic substitution reactions; however, it is a rough outline on how to study any organic reaction. How to change reaction conditions (changing one variable at a time) and observing their affects is the basis of using the scientific method. This can be applied to other types of reactions besides substitution reactions, for example, other substitution reactions such as aromatic substitution reactions and acyl substitution reactions.




Reactions are optimized for their yields, selectivity, and speed (efficiency). How the chemist changes the reaction parameters-such as catalyst, temperature, solvent, and leaving-group ability-can largely impact the reaction. Knowing the kinetics of a reaction can lend valuable information about the reaction, and usually this is the beginning to understanding the mechanism of a reaction.

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