Module 2.4 Kinetics and stereochemical outcome of a S_Ni reaction

Objectives:

At the end of this module, learners will be able to

- Distinguish a S_Ni reaction from S_N1 and S_N2.
- Compare the kinetics of a S_Ni reaction with S_N1 & S_N2
- Predict the stereochemical outcome of a given S_Ni reaction

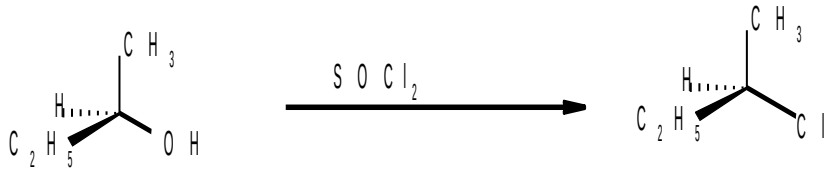
Content:

2.4.1 Introduction

In the previous modules we have discussed S_N1 and S_N2 mechanisms. While the former is unimolecular, proceeding through formation of a carbocation intermediate and resulting in partial racemisation of the product; the latter is bimolecular, proceeding through a T.S and resulting in 100% inversion of the product. There are still other reactions, whose stereochemical outcome as well as kinetics cannot be explained on the basis of S_N1 and S_N2 mechanism. This module will discuss these reactions, which are said to follow the S_Ni or Substitution Nucleophilic Internal mechanism.

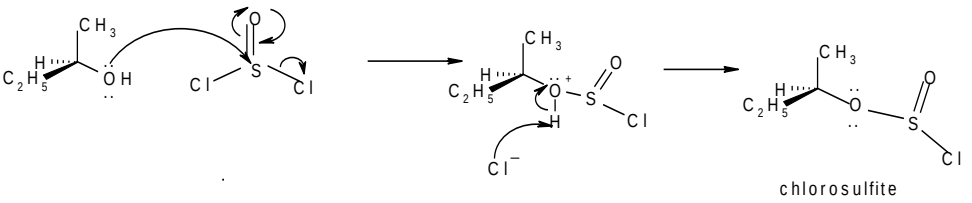
2.4.2 Substitution Nucleophilic Internal (S_Ni)

An example is reaction of a chiral alcohol like (R) -2-methyl butanol with $SOCl_2$ to give the corresponding halide.



(R) (R)

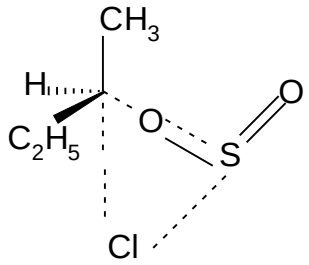
If the reaction were proceeding by a S_N2 mechanism, the product obtained should have had the (S) configuration. If it were an S_N1 mechanism, it should have resulted in partial racemisation. However, what is observed is that the reaction proceeds though 100 % retention of configuration. This implies that the incoming nucleophile attacks the carbon from the same side as that of the leaving group. These observations were explained by the S_Ni mechanism, involving initial formation of a chlorosulfite (which has been isolated) by nucleophilic attack of the -OH on the sulfur of the thionyl chloride as shown below. The chlorosulfite is formed with retention of configuration, as the bond to the chiral carbon is not broken.



chlorosulfite

Here Cl^- acts as a base and facilitates the deprotonation to give the chlorosulfite. Once the chlorosulfite is formed, the Cl which is now present within the molecule, acts as a nucleophile and attacks the carbon from the front side, resulting in the formation of the product.

The T.S can be represented as a 4-centre type.

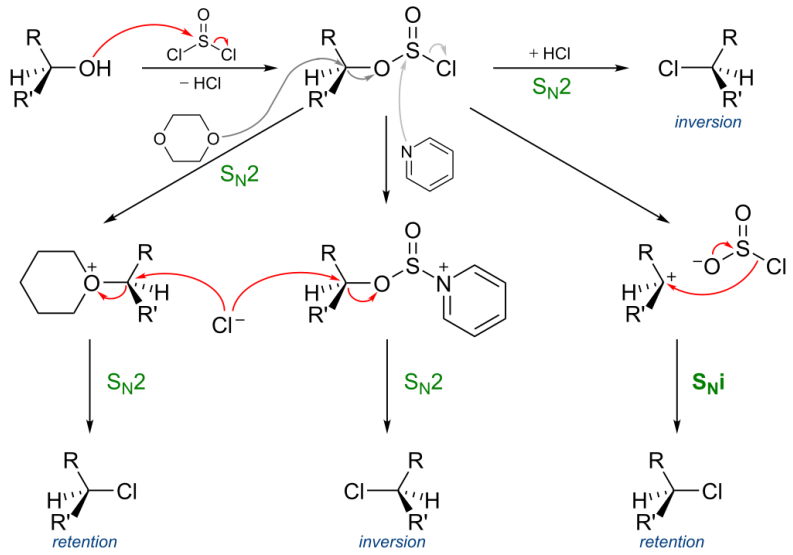


2.4.3 Kinetics and stereochemical outcome of the reaction

The r.d.s step is the formation of the chlorosulfite and hence the reaction is bimolecular w.r.t the alcohol and $SOCl_2$. Rate of further dissociation of the chlorosulfite to the product is found to increase with increase in the polarity of the solvent, and also with increasing stability of the carbocation. This suggests that there is formation of a close intimate ion pair of the type $R^{+}\,^{-}OSOCl$ within the solvent cage. In an intimate ion pair, both the counterions are in very close association without any solvent molecules between them. Collapse of the intimate ion pair to form the products occurs rapidly, suggesting that attack of Cl^- occurs from the same side as that of the leaving group resulting in retention of configuration.

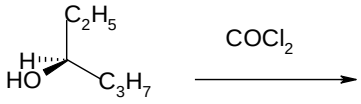
2.4.4 Effect of varying solvent

Carrying out the reaction in the presence of dioxane as the solvent also yields a product with retention of configuration. However, here retention arises due to two consecutive S_N2 reactions, In the case of pyridine, the HCl gas released as a by product reacts with pyridine to form a salt $C_6H_5NH^+Cl^-$. Cl^- being a good nucleophile attacks from the back side in a S_N2 fashion resulting in inversion of configuration.



https://en.wikipedia.org/wiki/SNi#/media/File:SNi_reaction_mechanism.svg

Problem 3.1: A similar mechanism is also found to operate when an alcohol is reacted with phosgene ($COCl_2$), to give the corresponding halide. Outline the steps in the mechanism involved in the following reaction. What would be the by product formed in this case?



So far we have discussed how by varying the substrates, nucleophiles and solvents , the mechanism of the nucleophilic substitution can be altered. Which mechanism is operating can be predicted based on the kinetics and stereochemical reactions. While modules 1 and 2 discussed nucleophilic substitution reactions involving aliphatic or alicyclic halides, the next module will discuss the mechanisms operating in aromatic halides.