Experiment 5

Fig. 5-1

SYNTHESIS USING REFLUX: SAPONIFICATION OF AN ESTER

R. B. Woodward (1917 - 1979), Nobel Prize, 1965. One of the most prominent synthetic organic chemists of the 20th century.
http://nobelprize.org/chemistry/laureates/1965/woodward-bio.html

Text Topics, New Techniques and Comments

Organic synthesis, saponification, reflux. ***Experiment 32*** can also be used to provide an experience with the technique of refluxing .

Discussion

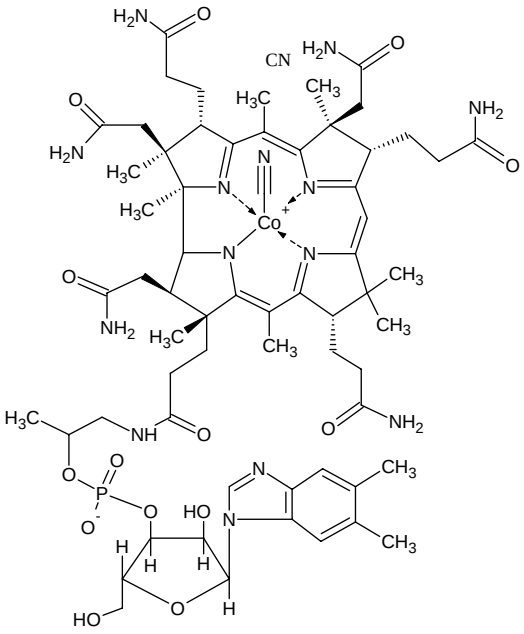


Fig. 5-2

Imagine for a moment that you are standing almost 6 miles above sea level on the top of Mt. Everest. You would certainly feel great joy and a huge sense of accomplishment for having climbed the earth's tallest mountain. When Dr. Robert Burns Woodward's team of graduate students and postdoctoral researchers in collaboration with Dr. A. Eschenmoser's group in the year 1973 reported the first successful total synthesis of Vitamin B_{12}, Dr. Woodward and his team undoubtedly felt the same kind of exhilaration and sense of accomplishment that Mt. Everest climbers attain. For the multitude of his synthetic successes and even more importantly, the invaluable techniques, theories and insight developed along the way, Dr. Woodward was awarded the most prestigious award in science in 1965, the Nobel Prize in chemistry. Because of the imagination and creativity required to accomplish these beautiful and very important syntheses, Dr. Woodward's accomplishments are often recognized not only as great works of science but also great works of art.

This course that you are currently taking called organic chemistry will have organic synthesis as its central theme. Ultimately, the goal of organic chemistry is to synthesize new compounds that can be used to make better fabrics, plastics and medicines to raise the quality of life. To be able to devise synthetic routes to desired compounds, the organic chemist must have a deep understanding of how structural changes and solvents affect chemical behavior. The synthetic chemist must consider safety, availability of starting materials, cost, time and yields. Because of safety, cost and time considerations, you will be given instructions for most of the syntheses that you will run in this course. But do consider how challenging, exciting and rewarding it is when you have designed a feasible synthetic route to a desired product and your laboratory work indicates that you have successfully achieved your goal.

As an example, Penicillin G (the first penicillin discovered and tested) was not very effective when taken orally. It has a tendency to decompose rapidly in the acidic media of the stomach. As syringes are inconvenient and feared by many, organic chemists set out to synthesize a penicillin like structure that would maintain its antibiotic properties but be stable in the stomach. Ampicillin was one of the successful synthetic results (what happens to ampicillin in acidic media?).

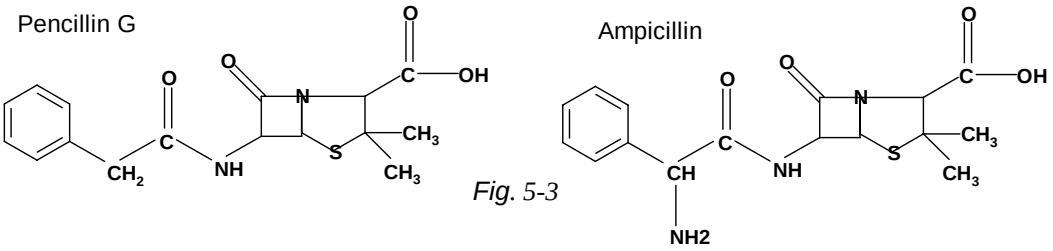
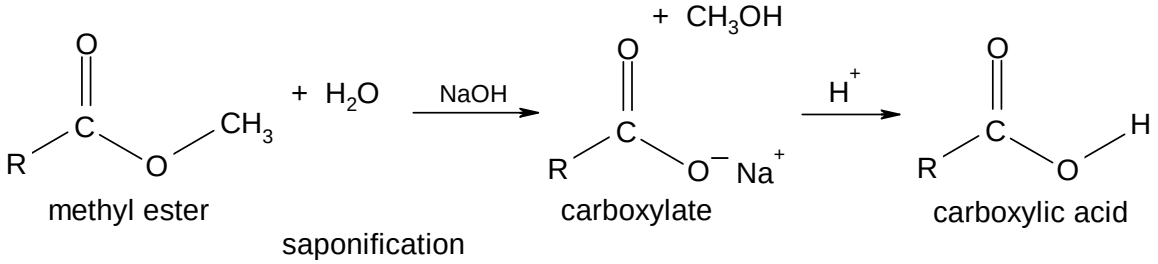
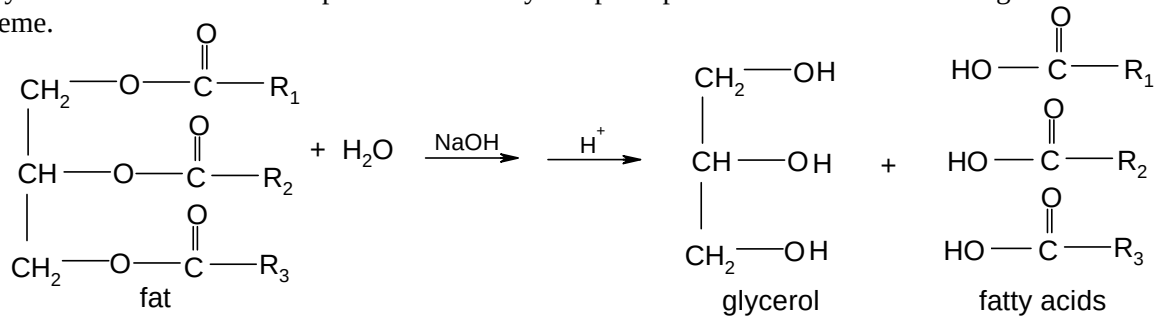


Fig. 5-3

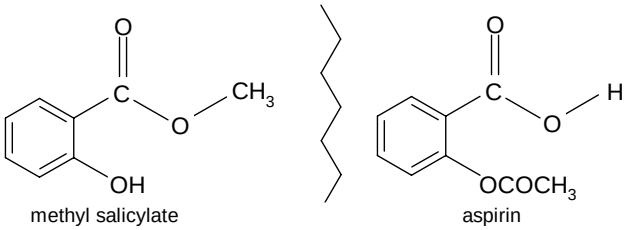
The laboratory experiment today involves a common reaction of esters and is included to give you experience with the technique called refluxing. When heated in the presence of base, esters react to form carboxylates (the conjugate base of the corresponding carboxylic acid) in a reaction called saponification. Subsequent addition of acid results in formation of the carboxylic acid.



Fatty acids that are used in soaps are obtained by a triple saponification of fats according to the following scheme.



In today's experiment, you will attempt to saponify methyl salicylate (also called oil of wintergreen). Methyl salicylate can be obtained by extraction from the wintergreen plant or the bark of sweet birch trees but is usually obtained for commercial use by esterification of salicylic acid. Wintergreen oil finds considerable use as a flavoring agent.



The heating process for the reaction will employ the technique called refluxing. The product will be purified using recrystallization. The identity and purity of the product will be determined from melting range measurements.

Techniques

The saponification reaction will be carried out using a technique called refluxing. Many reactions are endothermic and need to be heated to move the reaction toward products. One of the main concerns when heating is the control of temperature. It is very difficult to control the temperature simply by heating the reaction mixture on a hot plate. One of the most common ways to limit the temperature is to heat the mixture at the boiling point of the solvent. As long as solvent is present, the temperature cannot go above the boiling point of the solvent. However, this technique would result in loss of solvent and could be dangerous if all of the solvent boiled off. To avoid loss of solvent, a water jacketed column is inserted in the boiling flask. The vapor from the boiling solvent is condensed in the column and returns to the boiling flask with very little loss. **Be sure the top end of the column is open to the air either directly or via a drying tube** (if only dried air is desired in the system). If the top end is stoppered, pressure will build up and an explosion could result. For the water jacketed column, distillation columns work fine. The water enters in the bottom and leaves out the top *(why not the reverse?)*.

Fig. 5-4

After the saponification reaction has been run and the reaction mixture acidified, a precipitate should result. The precipitate will be collected by vacuum filtration and will be purified by recrystallization.

Procedure

Assemble an apparatus as shown above with a 50 or 100 mL round bottom flask containing 2.0 grams of methyl salicylate, 20 mL of 6 M sodium hydroxide, 2 boiling chips (or a magnetic stirring bar) and a condenser all mounted in a heating mantle. If lab jacks are available, it will be convenient later if the heating mantle is on a lab jack so that it can be lowered easily without any touching of the hot equipment required. Turn on the condenser water (the flow should be continuous but slow) and heat until the solution boils. Continue to heat for 30 minutes at a rate that keeps the condensation ring (if you look carefully at the condenser, you will see a ring which is the highest place that condensation is occurring) somewhere between the bottom and the middle of the condenser. After the reaction time is up, lower the heating mantle and allow the reaction mixture to cool.

Transfer the mixture to a 250 mL beaker. While keeping the beaker and its contents cold in an ice bath, add 21 mL of 3 M sulfuric acid slowly with stirring. Test the pH of the solution with 0-13 pH paper. If the pH > 2, add more sulfuric acid dropwise until the pH is 2 or lower. Continue to cool until the temperature of the mixture dips below 5^{o}C. Collect the product using vacuum filtration. Normally, it would be best to allow the sample to dry before weighing and determination of the melting point. However, because of time restrictions, you will proceed on. Divide the sample as closely as possible into halves making sure you know the mass of each portion. Put aside one portion for a future lab period for weighing and a melting point measurement. Recrystallize the second portion from water.

After the samples are dry, determine the mass and melting range of each portion and the percent recovery from the recrystallization. To determine the percent yield from the synthesis step, use the mass of the portion of product that was not purified times an appropriate mass ratio (approximately 2) to determine the experimental yield of dried product.

References

Nicolaou, K. C.; Vourloumis, D.; Winssinger, W.; Baran, P. S. *Angew. Chem Int. Ed.*, **2000**, *39*, 44-122.

Prelaboratory Preparation - *Experiment 5*

First, be sure to list all the goals of the experiment. Based on the general reaction for saponification, write the reaction for the saponification of methyl salicylate and include the product structure and name. Prepare a table for insertion of useful and observed data such as molecular mass, mass, moles, melting points, percent yields and recoveries. Find saponificaton of an ester to a carboxylic acid in the *Reaction-Map of Organic Chemistry* in ***Appendix C*** and include the number of the reaction in your report.

Observations

Report all relevant observations including, masses and melting ranges.

Conclusions

This section should include the following:

1. Were the goals of the experiment achieved? Explain your answer.
2. What was the identity of your product and did it agree with your prediction? Explain your answer.
3. How could the percent yield and recoveries have been improved?
4. Was the reflux method a good technique for heating the reaction? Explain your answer.