CHE 2060: Summary of key concepts
- Module 8, Nucleophilic acyl substitution reactions

- Be able to recognize and draw examples of **carboxylic acid derivative functional groups**:
  - carboxylic acids/carboxylates
  - acyl phosphates (both acyl monophosphate and acyl-AMP)
  - thioesters
  - esters
  - amides
  - acid chlorides
  - carboxylic acid anhydrides
- Know the meaning of the terms: **'acyl', 'acetyl', 'formyl', 'lactone'**, and **'lactam'**.
- You need not memorize the structure of **coenzyme A**, but you should recognize that it contains a key thiol group and often forms thioester linkages, particularly in fatty acid metabolism.
- Understand what happens in a **nucleophilic acyl substitution** (also called acyl transfer reaction) and be able to draw mechanistic arrows for a generalized example.
- Know the **trends in relative reactivity** for the carboxylic acid derivatives:
  - in a **biological context** (acyl phosphates and thioesters as activated acyl groups)
  - in a **laboratory context** (acid chlorides and carboxylic acid anhydrides as activated acyl groups)
- Recognize and understand the **most important types of nucleophilic acyl substitution reactions in biology**:
  - How a carboxylate group, which is unreactive to nucleophilic acyl substitution reactions, is activated in the cell by **ATP-dependent phosphorylation** to either acyl monophosphate or acyl-AMP.
  - Conversion of an acyl phosphate to a thioester, a (carboxylic) ester, or an amide.
  - Transthioesterification, esterification, and transesterification reactions.
  - Conversion of a thioester or ester to an amide
  - Hydrolysis of a thioester, a (carboxylic) ester, or an amide to a carboxylate.
- Understand the **energetics** of the above reactions:
  - Carboxylate to acyl phosphate is **'uphill'** energetically, paid for by coupling to hydrolysis of one ATP
  - Other conversions above are 'downhill': it is unlikely, for example, to see a direct conversion of an amide to an ester.
  - (Notable exception: the lactam (cyclic amide) group in penicillin is very reactive due to **ring strain**, and forms an ester with an active site serine residue in the target protein)
- You need not memorize all of the details of peptide bond formation on the **ribosome**, but you should be able to follow the description in section 7 and recognize the nucleophilic acyl substitution reactions that are occuring.

- Be able to **draw complete mechanisms** for the following lab reactions:
  - acid-catalyzed **esterification** of a carboxylic acid
  - **saponification** (base-catalyzed hydrolysis of an ester), application to soap-making
  - base-catalyzed **transesterification**, application to biodiesel production.
- Understand how **acid chlorides** and **carboxylic acid anhydrides** serve as activated acyl groups in laboratory synthesis. Be able to describe how an amide to ester conversion could be carried out in the laboratory.
- Understand how **polyesters and polyamides** are formed. Given the structure of a polymer be able to identify monomer(s), and vice-versa.
- Be able to recognize, predict products of, and draw mechanisms for the **Gabriel synthesis** of primary amines, using either hydroxide ion or hydrazine to release the amine product.