PS #6 Practice Questions – Mechanisms (Mannich Reaction; Electrophilic Aromatic Substitution), Chemoselective Reduction of Carbonyl Groups

Part I. In the Mannich reaction a secondary amine (R_2NH) is condensed with formaldehyde to form a reactive imine salt. The imine salt is reacted with any enolizable aldehyde or ketone to form an amino-ketone product (Mannich base). Show the detailed mechanism for the formation of the Mannich base (**Step 1**), then alkylate and eliminate to form the enone (**Step 2**). Refer to pages 712 – 715 in Clayden and Greeves.

 $\textbf{Part II.} \ \ \text{Show the detailed mechanism for the electrophilic aromatic substitution of 2,6-dimethylanisole with Br_2.}$

Part III. The following reduction reactions will not work as written. State why and propose an alternate set of conditions that will carry out the desired transformation.

1.
$$O \longrightarrow O$$
 LiAlH₄ $O \longrightarrow O$

LAH will reduce the ester all the way to the alcohol. To stop the reduction at the aldehyde use DIBAL, -78 °C.

 $NaBH_4$ will reduce the ketone and not the acid. Instead use BH_3 to reduce the carboxylic acid; this will not reduce the ketone.

LiBH₄ will reduce the ketone to an alcohol and won't touch the amide. To reduce an amide to an amine in the presence of a ketone, use BH_3 .

4.
$$C_5H_7$$
 LiAlH₄ C_5H_7

Although LAH will reduce the ketone, it is too strong and will also reduce the ester, cleaving the molecule into two alcohol fragments. To reduce the alcohol and leave the ester intact reduce with NaBH₄.