1. Acetanilide is more reactive than N-methylbenzamide in an electrophilic aromatic substitution reaction with chlorosulfonic acid even though both compounds have amide functional groups bonded to the aromatic ring. Why is there a difference in the reactivity of these two compounds? Use structures to help explain your answer. (10 points)

2. Sulfanilamide is an effective antibiotic because it interferes with the synthesis of folic acid in certain types of bacteria. Folic acid is essential for the in vivo synthesis of DNA. Why doesn't sulfanilamide interfere with the synthesis of DNA in humans? (5 points)

3. Draw the ionization schemes for each of the two ionizable functional groups in sulfanilamide. Calculate a pH range at which sulfanilamide is completely unionized. (10 points)
Organic Chemistry Laboratory II
Worksheet: Synthesis of Sulfanilamide

Name: ________________________________                           Lab Section: _______________

4. Sulfanilamide is not used today as an antibiotic largely because it tends to crystallize (referred to as “crystalluria”) in the urine (pH ~ 6) and cause severe kidney damage. Sulfanilamide is only soluble in aqueous urine when its sulfonamide functional group (pKa ~ 10.4) is in its ionized form. However, numerous second generation sulfonamides are used today clinically. One of these sulfa drugs is sulfisoxazole. Look up the structure and pKa of sulfisoxazole (in a medicinal chemistry textbook found in the library) and draw the ionization scheme for this drug. Explain why this compound can be used clinically without worrying about crystalluria. (15 points)

5. Why must the nitrogen atom be acetylated prior to reaction with chlorosulfonic acid? (10 points)

6. p-Aminobenzoic acid (PABA) is a compound which is endogenous to bacteria. In bacteria, sulfanilamide competes with PABA for an enzyme which is essential for the synthesis of folic acid. (The folic acid is used to synthesize DNA.) Compare the structures of PABA and sulfanilamide and explain why sulfanilamide is a good competitive substrate for the enzyme which reacts with PABA. (15 points)

7. Report what organisms were used to evaluate the biological activity of your synthesized sulfanilamide. Report the concentration of drug used and the zones of inhibition that were found for each concentration. Use the table provided below for your answers. (10 points)