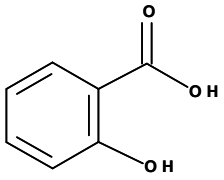
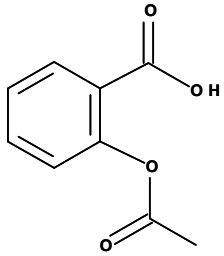
CHEM 4000A: SciFinder Assignment
6 + 17 + 18 + 5 = 46 marks total
Due at 5:00pm on Thursday, February 1st, 2024

The structures of salicylic acid and N-acetylsalicylic acid (aka aspirin) are shown below.



salicylic acid



***N*-acetylsalicylic acid**

Use SciFinder[n] to answer the following questions about these two compounds. Please explicitly draw the H of all OH groups when performing searches. Failing to do so will dramatically increase the number of hits you get.

1. Use the "Substances" tab for this question and use the drawing tool to draw aspirin.

(a) How many hits does the Structure Match show for aspirin "As Drawn"? **[1]**

(b) How many hits does the Structure Match show for aspirin as a "Substructure"? **[1]**

(c) Refine your search by filtering. Choose "Number of Components = 1" and "Substance Class = Organic/Inorganic Small Molecule". Now, how many hits do you have "As Drawn"? **[1]**

(d) Why is the answer to part (c) not 1? Make sure you address at least two key factors. **[2]**

(e) Under what circumstances do you think it would be helpful to do a "substructure search" rather than an "exact search"? **[1]**

2. Use substance 50-78-2 (the first hit generated in question 1(c)) for this question.
Every chemical referenced in any chemistry publication has a unique CAS Registry Number that serves as a language-independent identifier. (CAS = Chemical Abstracts Service)

(a) Give the CAS name for this compound. *Most publications name organic compounds either by their CAS name or IUPAC name. For simple structures, these two names are the same.* **[1]**

(b) Look at the Experimental Properties link for substance 50-78-2.
Under Biological Properties:

(i) What is the median lethal dose (LD50) for aspirin administered orally to rabbits? Click on the link provided for the reference for this information. In what language was the original article providing this information? Since you are not able to read the original article, it is appropriate to cite the information as provided by SciFinder. **[2]**
e.g. *SciFinder Scholar*, version 2018; Chemical Abstracts Service: Columbus, OH, 2018; RN 50-78-2 (accessed Jan 1, 2019).

(ii) What is the LD50 for aspirin administered orally to rats? **[1]**

(iii) What is the range of reported LD50 values for aspirin administered orally to mice? **[1]**

(iv) In plain language, explain what an LD50 value means. **[1]**

(v) A small adult human weighs 50 kg. Calculate the median lethal dose (in mg) predicted for a population of 50 kg individuals based on each animal model. **[3]**

(vi) Which of the three animal models would you feel most comfortable using as a model for human intake of this particular medication? Why? **[2]**
Note that no animal model is a perfect predictor of human reaction and that different animal models are best for different classes of medication. There is no universal "best model".

(c) Look at the Experimental Properties link for substance 50-78-2.

(i) Under Density Properties: Rounding to 1 decimal place, what is the density of aspirin? **[1]**

(ii) Under Thermal Properties: What are the reported boiling points for aspirin? Why do they differ? Is it reasonable to have two different reported values? Why or why not? **[3]**

(iii) Under Experimental Spectral, view the proton NMR spectra provided for aspirin. Reference 5 (BIORAD) provides two spectra; how do they differ from each other? **[2]**

3. Return "Home". Switch to the "Reactions" tab, and use the drawing tool.

(a) Search for reactions in which salicylic acid is made from phenol. (This means drawing both molecules and using an arrow to identify phenol as reactant and salicylic acid as product.)

(i) How many hits does the Structure Match show for the reaction "as drawn"? **[1]**

(ii) How many hits does the Structure Match show for the reaction "as a substructure"? **[1]**

(iii) Write a balanced equation for the first option presented under Scheme 1 "as drawn". Reagents for each step should be listed over the arrow with each step numbered. **[1]**

(iv) Suggest a reasonable mechanism by which this reaction could proceed. Clearly indicate when experimental conditions change (i.e. when a new step starts). **[5]**

(b) Switch from looking at Structure Match "as drawn" to "substructure".

(i) How does Scheme 2 of this search differ from the top hits for the "as drawn" search? Include a reaction equation for this hit in your answer. It does not have to be balanced, but it should still have the reagents listed over the arrow. **[1]**

(ii) How does Scheme 3 of this search differ from the top hits for the "as drawn" search? Include a reaction equation for this hit in your answer, and suggest a reasonable mechanism for this reaction. **[4]**

(c) "Edit" your drawing, and explicitly draw in the hydrogens ortho to the alcohol group in both phenol and salicylic acid. Repeat your search.

(i) How many hits does the Structure Match show for the reaction "as drawn"? **[1]**

(ii) How many hits does the Structure Match show for the reaction "as a substructure"? **[1]**

(iii) The early hits for the Structure Match "as a substructure" look very much like the "as drawn" hits from part (a) of this question; however, now we do not miss reactions that would probably work but were just tested on a different system – e.g. 4-methylphenol. Go to the last page of hits to see some very large molecules in which the desired reaction is not going on at all. Why have these reactions turned up in this search? **[1]**

(d) "Edit" your drawing, and use the "map atoms in a reaction" feature to map the carbon attached to the oxygen in phenol to the same carbon in the product. Repeat the search. Now, how many hits does the Structure Match show for the reaction "as a substructure"? **[1]**

(e) "Edit" your drawing again, and use the "mark bonds to be formed or broken tool". Select the C-H bond that is broken in phenol and the C-C bond that is formed in salicylic acid. Repeat the search. Now, how many hits does the Structure Match show for the reaction "as a substructure"? **[1]**

The goal in all these searches is to find reactions that could plausibly perform the desired transformation. We don't usually care if there is an extra methyl group (or similar) in a part of the molecule that is not reacting. On the other hand, we don't want to do a search so general that it turns up irrelevant reactions.

4. Use the "References" tab for this question.

(a) Search for "Sharpless epoxidation". How many hits do you get? **[1]**

(b) That's more papers than you want to skim through, and most of them just use the Sharpless epoxidation as one step in a synthesis. If you want to learn about the reaction in general, a review article would probably be most useful. Filter by "Document Type = Review". Now, how many hits do you get? **[1]**

(c) One of the hits (the fourth one when I did the search) is called "Applications of Sharpless Asymmetric Epoxidation in Total Synthesis". Choose that hit then click on "View Source". If you are logged into your University of Lethbridge account, this will take you to the article itself because our university library subscribes to the journal in which it was published.

What is a Sharpless epoxidation? Include a sample reaction equation in your answer and clearly describe what properties of the reaction make it "Sharpless". **[3]**

(K. Barry Sharpless is an organic chemist at Scripps who shared the 2001 Nobel prize for his work developing specific types of reactions.)

I use the reported hit counts to confirm that you performed a search correctly. Because articles are added to SciFinder on a daily basis, I perform all searches before distributing the assignment <u>and</u> after they are submitted so that I know the range within which each answer should fall.