

Chem4315/6315  
Organic Medicinal Chemistry  
Take-home followup to Midterm Examination I

Name: \_\_\_\_\_

This followup to Midterm Examination I is worth  $\frac{1}{2}$  the number of points you failed to earn on Midterm Examination I. This followup may be done outside class. You may use the Merck Index, the chemical literature, the WWW (but not people contacted via the WWW) your textbooks (both for this class, and for previous chemistry courses), and the MOE or CAChe software to complete this followup. You may also refer to Midterm Examination I and your class notes. Do not discuss this with other students or instructors other than Dr. Parrill. This followup is designed to help you figure out the most common mistakes made by the class as a whole. **Turn in the followup AND Midterm I on March 29.**

### **Followup to questions 5:**

The aromatic hydroxyl groups on the third and fourth structures are unlikely to be ionized at pH 7. Look up a pK value for a relevant reference compound – show the reference compound and its pK.

Amines in aromatic rings are unlikely to be charged at pH 7, although amines without adjacent sp<sup>2</sup>-hybridized atoms are. Provide relevant analogue structures (One with a delocalized electron pair, and one without) and their pK values to demonstrate this point.

Identify at least **three** pharmacophore elements in the Kain receptor agonists.

Which structure has the least conformational flexibility in the region connecting the three pharmacophore elements? Explain your selection.

**Followup to questions 6:**

The first reaction in the Bayer reaction generates a nucleophilic species. Show all resonance forms of this nucleophilic species.

The pKa of phenol is approximately 9. Why is it necessary to acidify before allowing the phenolic oxygen to react with acetic anhydride in the last step?

The last step involves nucleophilic attack on acetic anhydride. Draw the intermediate formed in this reaction (it is NOT concerted) and explain why the reaction cannot be concerted. It may be helpful to consider the three-dimensional requirements of a concerted substitution (such as an SN2) and the three-dimensional structure of acetic anhydride.

**Additional followup:**

Provide corrected answers to any problems you missed that are not specifically addressed by the previous followup questions.