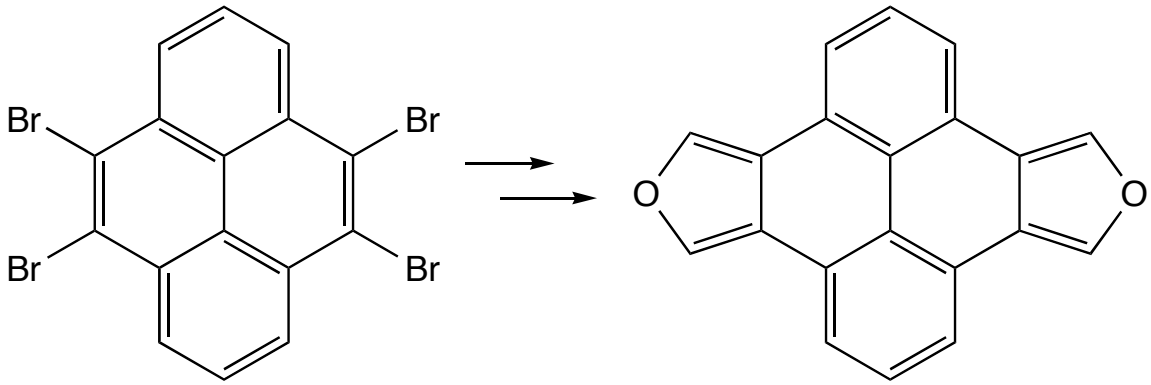
Chemistry 3250 Spring 2012
Assignment 1

Due: Tuesday, Jan. 24, 12:15 p.m.

The following questions were contributed by Dr Peter Dibble and are written in his voice. Note that these are real questions that came up in the course of doing real research, so the answers are not always what you would expect for a typical assignment problem.

There are several reasons why a synthetic chemist might do structure searches. I'll give a few examples involving different search types.

Most commonly, we are looking for preparations of compounds that we would like to use. For example, I was looking for a preparation of the following tetrabromopyrene in order that I might use it to prepare the pyrenodifuran shown:



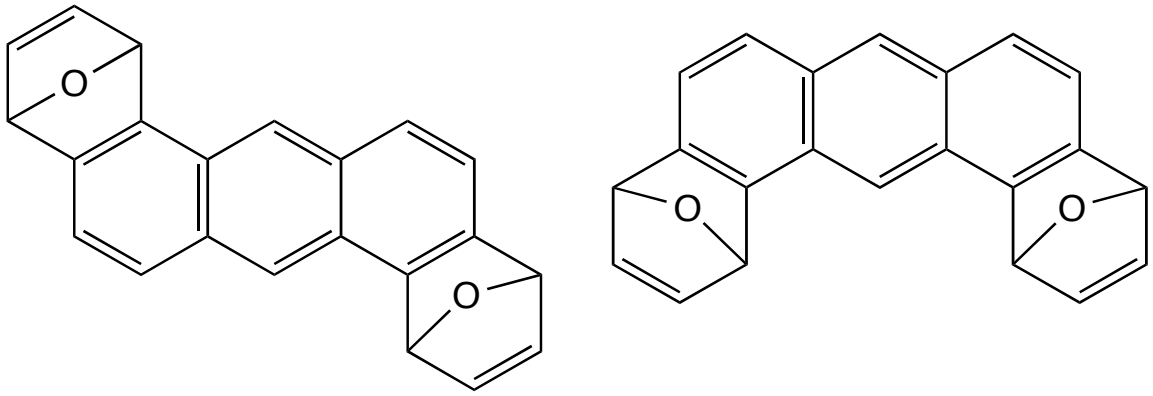
An exact search for the tetrabromide might not be successful, but a substructure search will yield at least one substituted example that is just as useful. The authors of the paper that described its synthesis came as a surprise to me.

Question 1: Perform a substructure search to identify a paper that gives a possible synthetic route for a substituted version of the tetrabromide illustrated above. Give the literature reference to the relevant paper. [2 marks]

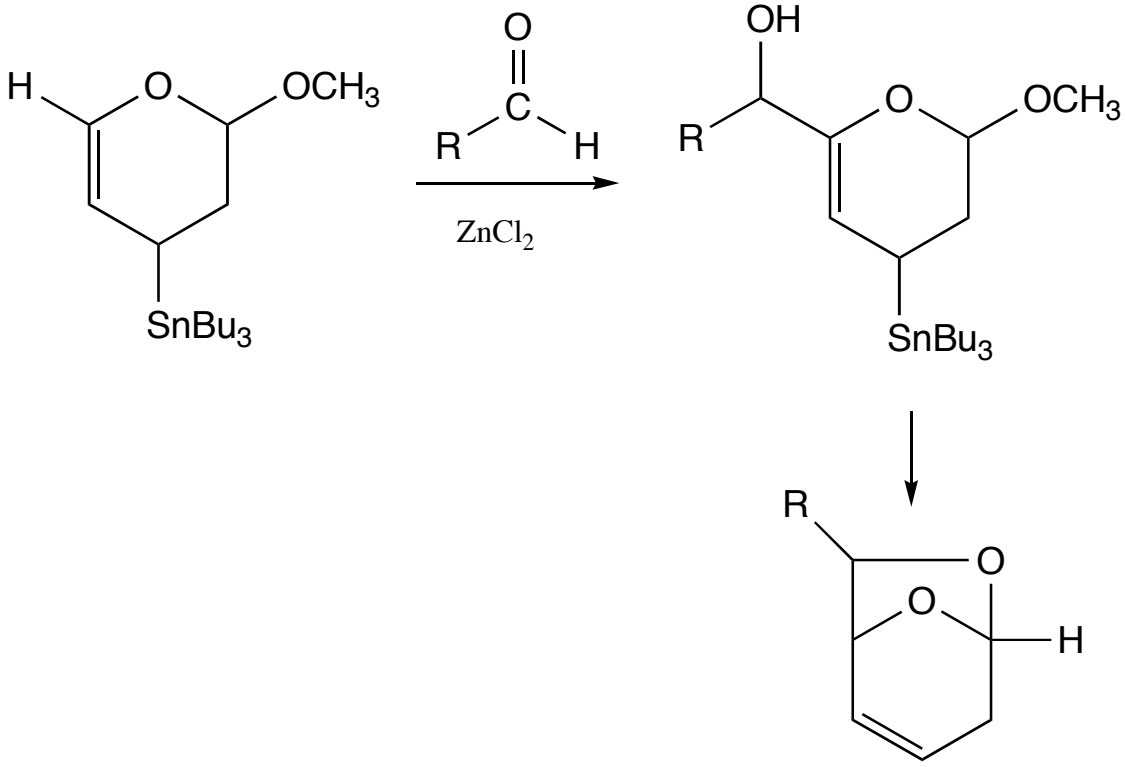
Bonus: Can you identify the paper providing a synthesis of a derivative of the tetrabromide whose authors were a surprise to Dr Dibble?

Whenever a synthetic chemist makes a molecule that is unprecedented, it must be characterized completely. To check that a given molecule has never been reported before, we do an exact structure search.

Question 2: The following are molecules recently made in the Dibble lab. Has anyone else made them before? If so, give the reference(s). [2 marks]

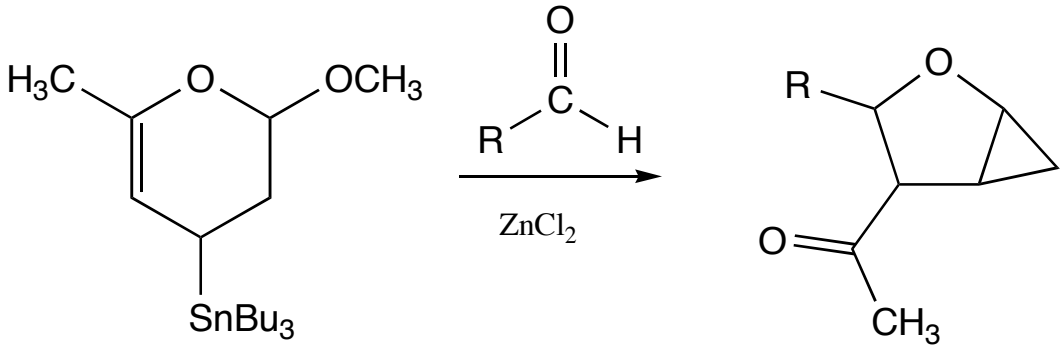


Sometimes (or often) one encounters an unusual and unexpected reaction. My most spectacular example of this is the following. I was looking at tin allylation reactions of the following reactant and obtained the expected product, which cyclized under the reaction conditions. The final product is a substructure of many different animal pheromones. I did this reaction for R = CH_2CH_3. This might be a naturally occurring molecule. If so, it is my only total synthesis of a natural product.



Question 3: Is the final product with R = CH_2CH_3 known to be a naturally occurring compound? If so, where does it occur? What, if anything, is known about its biological activity? [2 marks]

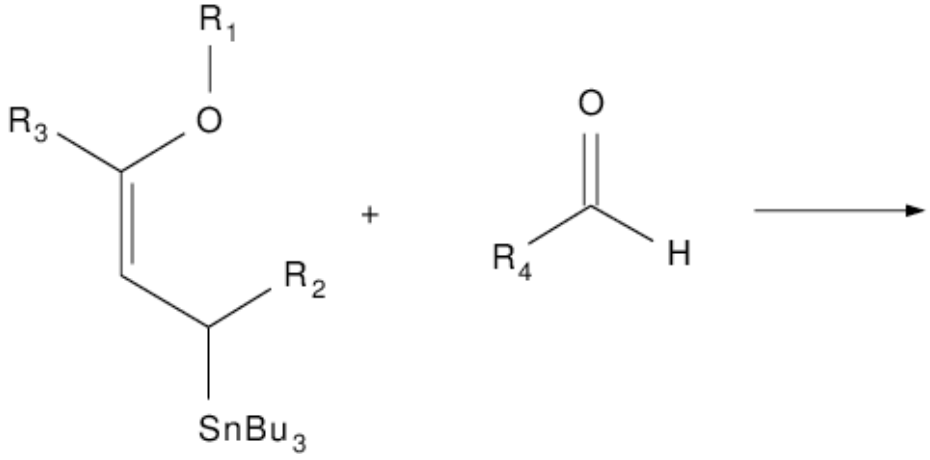
When one proton on the reactant is replaced by a methyl group, an entirely different reaction takes place giving a very unusual ring system:



Coming up with a synthesis of such a molecule would be quite a challenge, but I managed it completely by accident. All I needed to do was find an example of some known compound that had this basic structure and that was a natural product, or had been used to prepare a natural product, and I was in business. Here, a substructure search for the structure shown (minus the R, which can be varied) told me everything I needed to know about how useful this synthesis was.

Question 4: Perform the substructure search suggested. Explain Dr Dibble's cryptic comment that this search told him everything he "needed to know about how useful this synthesis was". [2 marks]

The reactions in questions 3 and 4 are both special cases of the following general reaction scheme:



Question 5: Find another example of a reaction of this type. Show the reaction, including all reactants, products, catalysts and reaction conditions (solvent, temperature, etc.), and give the reference to the paper where you found it. [4 marks]

Bonus: Can you find another example where there are dramatic differences in reactivity for R_3 = H vs R_3 = CH_3? If so, show the chemistry and give the full reference.