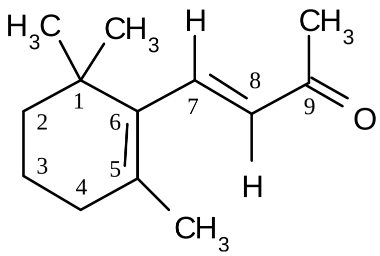
Nuclear Overhauser Effect Spectroscopy

Reading Assignment: T. D. W. Claridge, *High-Resolution NMR Techniques in Organic Chemistry*: Chapt. 5.1-5.4, Chapt. 8.1-8.7 (or A. E. Derome, *Modern NMR Techniques for Chemistry Research*, Pergammon, Oxford, 1987, Chapt. 5 and sections 8.1-8.3.4).

Purpose Use COSEY and NOESY 2-dimensional NMR spectroscopy to find the conformation of the bonds in β-ionone.

Introduction

β-Ionone has the structure shown below. The carbon atoms are numbered arbitrarily.



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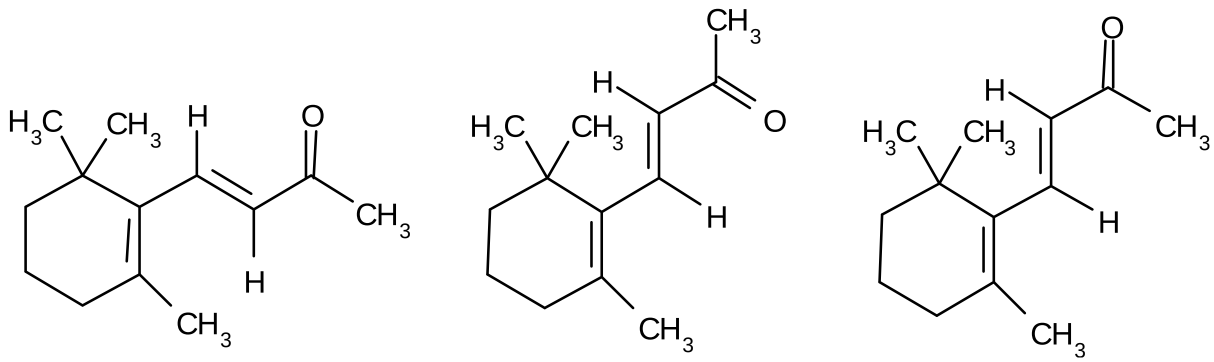
The question to be addressed in this laboratory is: what are the conformations of bonds 6-7 and 8-9. If β-ionone has a completely conjugated structure, there are three additional possibilities for the structure:



2 **3** **4**

In each of these structures, carbon atoms 5, 6, 7, 8, 9, and the oxygen atom all lie in a plane. If either bond 6-7 or 8-9 are not strongly conjugated, then the respective bond will be rotated out of the plane. For example, if bond 8-9 is not conjugated then the oxygen atom and the methyl group will not lie in the plane of the paper, and they will point towards you or away from you. Build the structure of β-ionone using molecular mechanics (MOE or Spartan, for example) and explore the possible conformations of the bonds. Minimize the structure, but then set the conformation to those in structures 1-4 and compare the distances.

Please complete the reading assignment in Claridge before continuing. In the discussion below we will denote the methyl groups attached to carbon 1 as the 1,1'-methyl groups, the methyl group attached to carbon 5 as the 5-methyl group, etc.

Part A: Information about whether a given bond is conjugated can sometimes be obtained from chemical shifts. Use the NMR chemical shift tables that were handed out in class, which was copied from D. H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry*, to decide if bonds 6-7 and 8-9 are conjugated. [Hint: using Table 3.21, you will need to do eight calculations for this comparison.]

Part B: Nuclear Overhauser effect spectroscopy (nOe) is a powerful technique for structural studies. Protons that are less than about 6Å apart can show an nOe; however, 4Å is a good general cut-off distance for observable nOe's. Knowing approximate distances between certain protons in a molecule can help to establish the conformation of a molecule. nOe information is commonly used in biochemical studies on the conformation of large proteins and nucleic acids. We will study the nOe's between either proton 7 or 8 and the methyl groups in β-ionone. The nOe's will allow us to decide which of structures **1-4** is the most stable conformation. In conjunction with the results from Part A we will also be able to decide if bonds 6-7 or 8-9 are rotated out of the plane that would be expected if strong conjugation is present.

The strength of the nOe is a function of the distance between two protons, assuming that the predominant relaxation mechanism is through dipole-dipole coupling and that the two protons are not isolated from other protons in the molecule. We can use the relative strength of the observable nOe's in β-ionone to get a rough idea of the distances between proton 7 and its nearby methyl groups or proton 8 and its nearby methyl groups. For example, if we find that proton 7 is close to the 1,1'-methyl groups, while proton 8 is close to the 5-methyl group and the 9-methyl group, then structure **2** must be the proper structure.

As a way of judging whether proton 7 or proton 8 are closer to a given methyl group, we can use relative enhancement ratios. Let the normal intensity in a 1-D spectrum for protons 7 and 8 be written as $1D_7$ and $1D_8$, respectively. Let the intensity of an nOe cross-peak between methyl group i and proton 7 and 8 be written as NOE_{7i} and NOE_{8i}, respectively. The relative enhancement ratio is then:

$$re_i = \frac{NOE_{7i} / NOE_{8i}}{1D_7 / 1D_8}$$

If proton 7 is closer to methyl group i than proton 8 then $re_i > 1$. If proton 7 is farther away from methyl group i then $re_i < 1$. A caution is in order, however. This reasoning is subject to many approximations, such as the predominant means of relaxation must be dipole-dipole. Therefore, we must be careful to verify our conclusions by other techniques.

Report

Use relative enhancement ratios to decide which methyls are closer to which of protons 7 or 8. Assume first that you have a completely conjugated structure and choose which of structures **1-4** is closest to the proper conformation of β-ionone. Use MOE, MM2 (through the Distance Geometry on-line applet on the course home page), or Spartan with fixed conformations to measure distances to aid in the comparison.

Then, combine your results from Part A on the conjugation of the bonds in β-ionone with your results from Part B on the relative distances and possible conformations of the two bonds. If either bond is not conjugated, refine your prediction from Part B. Do your results from Part A and Part B support each other in predicting the extent of conjugation? Use the completely minimized MOE or Spartan structure to compare distances.

Your report need only have the discussion indicated above.