Exam 2
**Answer Key**

Exam 2 Mean: 64
Exam 2 Median: 70
Exam 2 St. Dev.: 19

1. Looking at the ^{1}H NMR spectrum, there are a
    few assignments we can make right off the bat.
    Our molecule has two alkenyl protons (H5 and
    H6), and there are two 1H-intensity resonances
    in the alkene region of the spectrum (at δ = 6.70
    and 6.25 ppm). I think the Pretsch charts don't
    make it obvious which of these is which, so I'll
    leave it an open question for now. The ^{1}H
    spectrum shows three 3H-intensity resonances
    for the three methyl groups in the molecule. We
    would expect just one of them to be split into a
    doublet (H13, split by H12), but it looks like *all* of them are split, one by a larger *J*
    than the other two. We can guess that the larger-*J* doublet (at δ = 1.28 ppm) is
    probably H13, and the smaller-*J* doublets must be due to long-range coupling.
    Based on chemical shift, I'd assign H15 to be δ = 2.13 ppm, and H14 to 1.33 ppm.
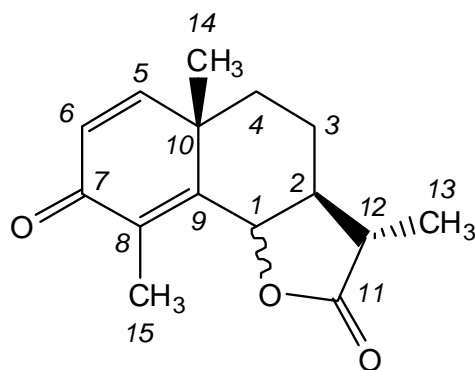
    The ^{1}H NMR also shows one doublet of quartets pretty far downfield at δ = 4.80
    ppm. The chemical shift matches H1, the only proton in the molecule adjacent to an
    oxygen atom. But the splitting pattern is a bit confusing; what could H1 be coupled to
    other than neighboring H2? Probably more long-range coupling for us to worry
    about. So, we can already fill in some of our table:

| proton	δ (ppm)	proton	δ (ppm)	proton	δ (ppm)
H1	4.80	H4ax		H12	
H2		H4eq		H13	1.28
H3ax		H5	6.70 *or* 6.25	H14	1.33
H3eq		H6	6.70 *or* 6.25	H15	2.13

The remaining protons are all part of a coupled chain, which we should be able to see in the COSY spectrum. In the COSY, we can "walk" from H13 to H12, and then from H12 to H2. H2 is then coupled to the two H3 protons (shown in green arrows on the left, sorry it's hard to see). That H2-H3 coupling is easier to see in th ehorizontal direction than in the vertical direction; if you only looked on the vertical, you might ask yourself, which of these peaks might be the other H3 proton?
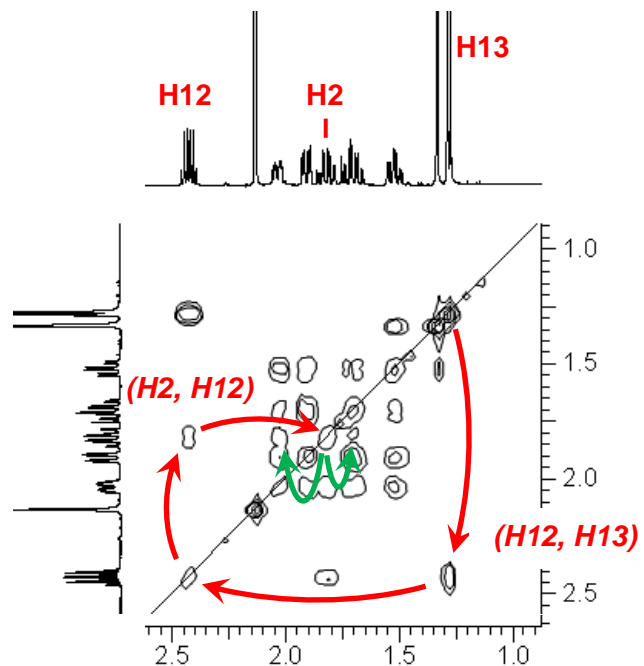

I think that the HSQC showed which protons were the H3's and which were the H4's. looking at that spectrum, only two carbons in the whole molecule have two inequivalent protons attached. One carbon has the exact same protons we drew coupled to H2 above; these must be the H3 protons. Even if we only assigned one of these two above, the HSQC gives us the other one. The other two circled protons must be the H4 protons.
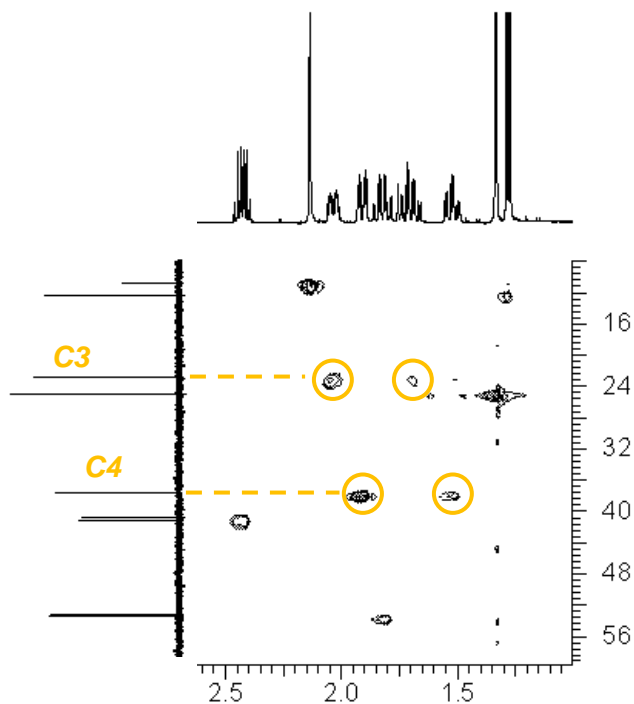
But which H3/H4 is equatorial, and which is axial? There are a couple of ways we could have figured this out. The easiest way was probably based on chemical shift. Pretsch says that equatorial H's on 6-membered rings are usually downfield of axial H's, which would mean the 1.9 and 2.1 ppm resonances would be equatorial. But another way of looking at the question would be to match dihedral angles to splitting. Looking at the two C3 protons, they are both doublets of quartets. However, the downfield resonance has one large J and three small Js, while the upfield resonance has one small J and three large Js. Looking at the molecule, H3eq has 60° dihedral angles with all three vicinal neighbors, which we would

expect to give small J's. On the other hand, H3ax has 180° dihedral angles with two vicinal neighbors, which should yield large J's. This confirms the assignments we made above; H3eq must be downfield of H3ax. The same analysis can be done for H4eq and H4ax.
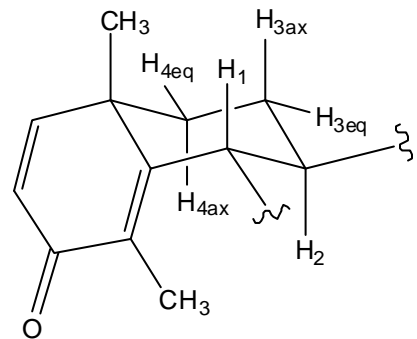
At this point, really our only question is, which alkene H is H5, and which is H6? In the COSY, there is a single crosspeak between one of the alkene H's and the H15 methyl protons. That's a long way! I think the only feasible coupling there would be between H6 and H15, which would be a ^5J; H5-H15 coupling would be a ^6J, and I've never seen that before.

Using this info we can complete both of our charts:

proton	δ (ppm)
H1	4.80
H2	1.82
H3ax	1.70
H3eq	2.05

proton	δ (ppm)
H4ax	1.52
H4eq	1.91
H5	6.70
H6	6.25

proton	δ (ppm)
H12	2.43
H13	1.28
H14	1.33
H15	2.13

carbon	δ (ppm)
C1	81.3
C2	53.5
C3	23.0
C4	37.8

carbon	δ (ppm)
C5	154.8
C6	125.8
C12	41

| carbon	δ (ppm)
C13	12.5
C14	25.1
C15	10.9

2.
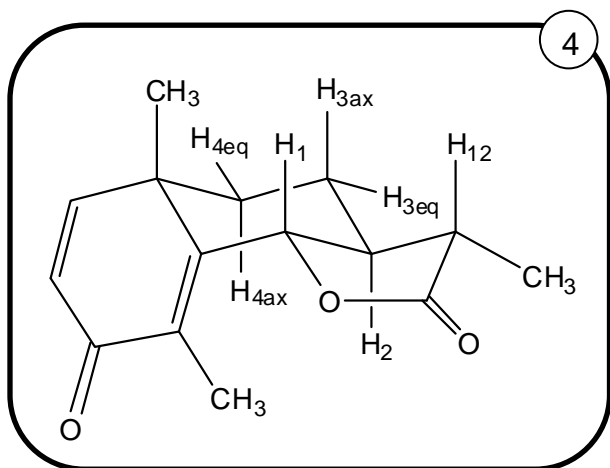
or   ?
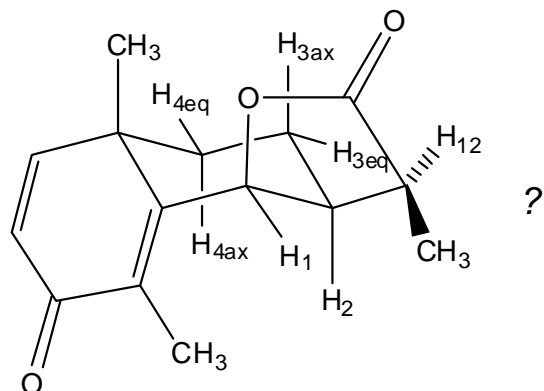
I think you know this from coupling constants. H1 shows up as a doublet of quartets (dq) in the 1D NMR, which the COSY says is due to splitting by both H2 and by the three H14 protons. (Again, a long way!) The "doublet" part of the H1 dq shows J(H1,H2) = 12.3 Hz, which is really large. That can only come from the *anti*-orientation of the two protons in the left-hand structure, and certainly not the 60° angle in the right-hand structure.

3.
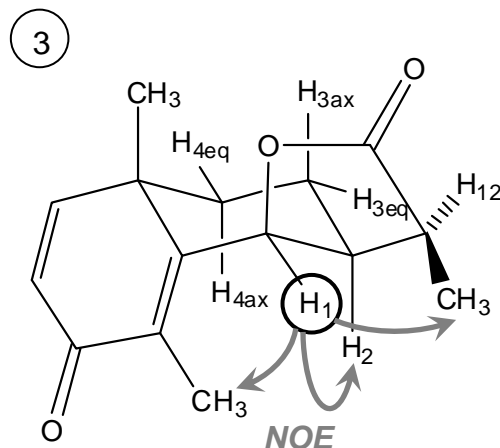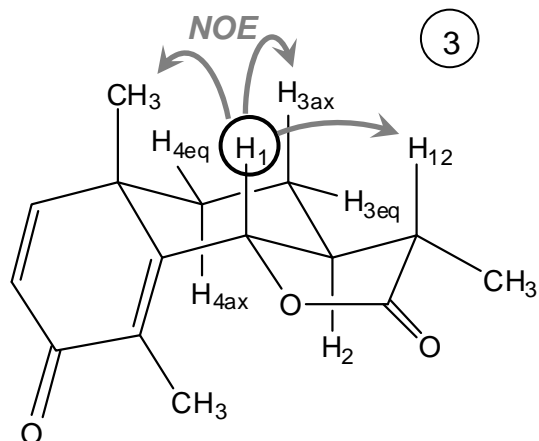
1D NOE experiments require that the proton to be irradiated be distant—practically speaking, at least 0.1-0.2 ppm away—from any other resonance. That's tough for this molecule, because many of the cyclohexane protons are so close to one

another. Luckily, two protons stand apart: H1, which would be my choice for this experiment; and H2, which is a little close to the C15 methyl proton peak, but could probably be selectively irradiated. I've shown lots of potential arrows for irradiation of H1; you only had to draw one arrow per structure.

If you chose to irradiate H2, I don't think there is any unique NOE that would be observed on the left that isn't also present on the right. The design of the experiment would be something like, "If I don't see any NOE, then my structure is the one on the left." The flaw in that design is that there are many reasons why you might not see an NOE (especially experimental reasons), and so I don't think irradiation at H2 was a good choice.

<u>Rubric:</u> *(6 points this part)*
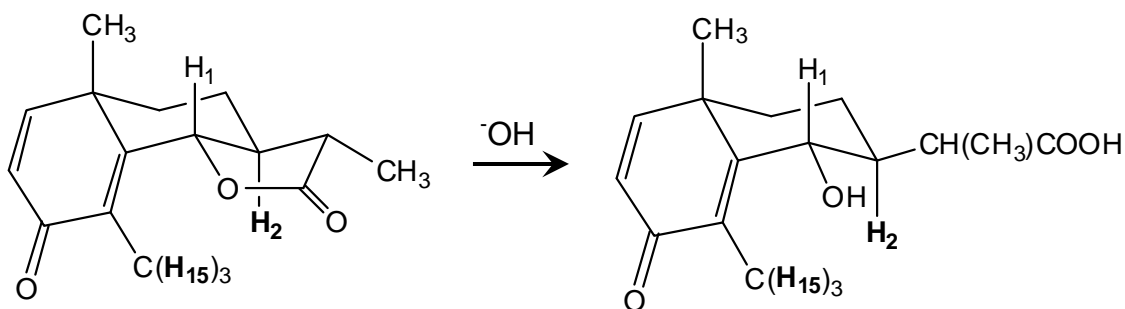   3 points for each unique arrow from H1 (one arrow per side).
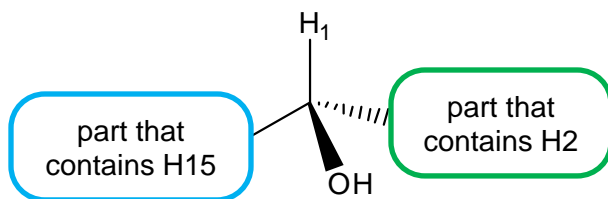   *3 points partial for an arrow on the right from H2. (No points for H2 on the left.)*

4.

or
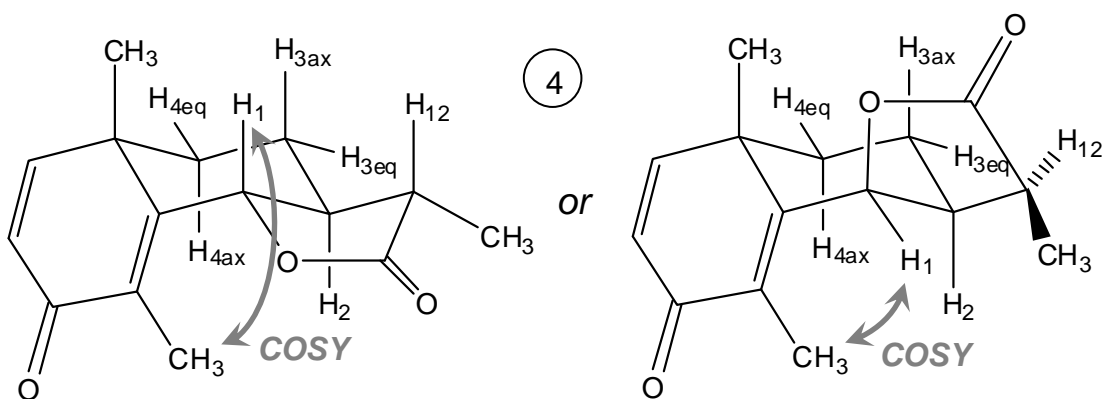
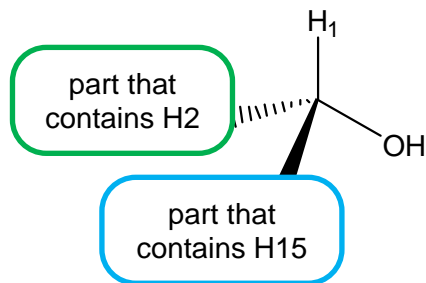An unusual, long-range (^5J) coupling, but not unheard of. (Pretsch describes it as *homoallylic*.)

5. This answer depended on what you circled in problem #2. If you circled the structure on the left:
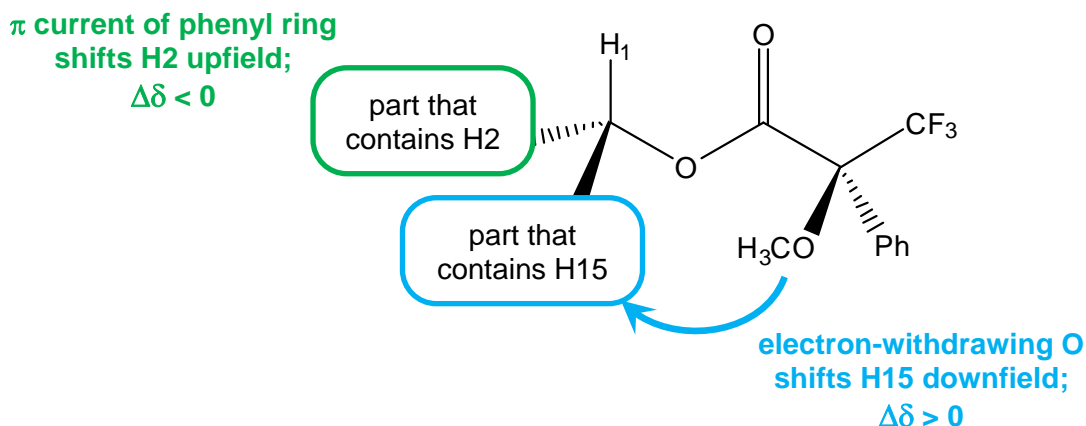
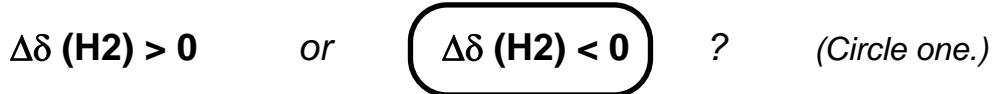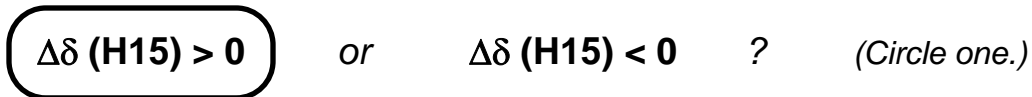I'll abbreviate the structure on the right as:

or, rotating this a little,

When I'm thinking about Mosher esters, I like to use the (*S*)-ester as the starting point, because it contributes positively to $\Delta\delta$. That ester looks like:

π current of phenyl ring shifts H2 upfield; $\Delta\delta < 0$

electron-withdrawing O shifts H15 downfield; $\Delta\delta > 0$

So, if you circled the molecule on the <u>left</u> in problem #2,

$\Delta\delta$ **(H15) > 0**   *or* $\Delta\delta$ **(H15) < 0**   *?*   *(Circle one.)*

$\Delta\delta$ **(H2) > 0**   *or* $\Delta\delta$ **(H2) < 0**   *?*   *(Circle one.)*

(4)

On the other hand, if you circled the structure on the <u>right</u> in problem #2, you would come up with the opposite answers:

CH$_3$

OH

CH(CH$_3$)COOH

H$_2$

C(H$_{15}$)$_3$

O

equals

OH

part that
contains H15

part that
contains H2

H$_1$

equals

H$_1$

part that
contains H15

OH

part that
contains H2
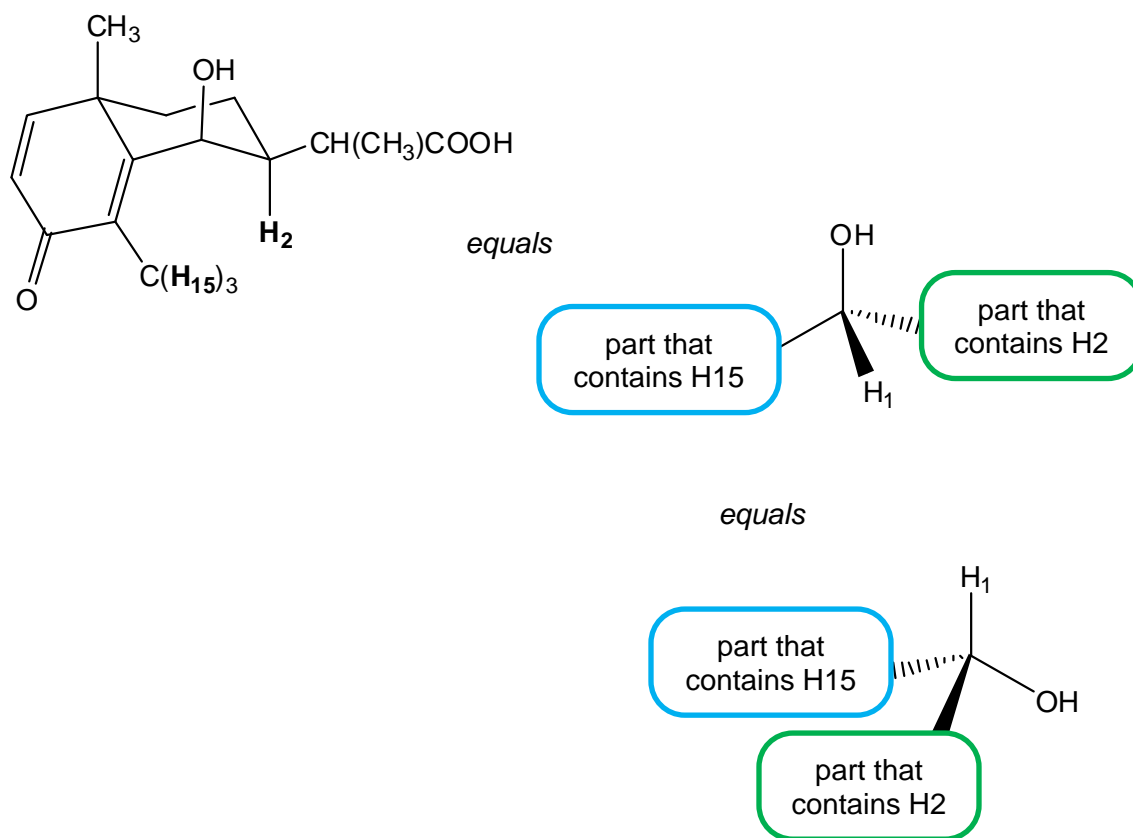
And this abbreviated structure is the mirror image of the one on the previous page, and gives the opposite answers.

Rubric: 4 points for perfect answer that matches your answer to problem 2.
  2 points partial for circling one answer correct and leaving the other one blank.
  No partial credit for hedging your bets and circling the same answer (both > 0, or both < 0) for both protons.

6. Unfortunately, I listed the irradiated resonance as one of the possible protons, which means I screwed up writing this problem.

Automatic 4 points.

7. The exam also doesn't include a DEPT spectrum. But if there was one, would it show a positive-intensity peak (**+**), a negative-intensity peak (**–**), or no peak (**0**) for each of the following carbon atoms? (Circle one answer in each box.)

carbon	DEPT-135	DEPT-90
C11	**+** **–** *or* (**0**)① ?	**+** **–** *or* (**0**)① ?
C12	(**+**)① **–** *or* **0** ?	(**+**)① **–** *or* **0** ?
C13	(**+**)① **–** *or* **0** ?	**+** **–** *or* (**0**)① ?

<u>Rubric:</u> 1 point for each circle. (*6 points total this problem.*)

8. The ^{1}H-^{13}C H**S**QC spectrum shown in this exam provides the same information as an ^{1}H-^{13}C H**M**QC spectrum. Name one advantage and one disadvantage of the HSQC method relative to HMQC.

> *advantage of HSQC:* ③
>
> The quantum filter in HSQC makes crosspeaks sharper, easier to see, relative to noise. (It doesn't really affect noise, but I guess in a relative sense it does.)
>
> <u>Rubric:</u> 3 points for any answer saying any one of these things. *Grader has leeway on judging whether your answer matches this description.*

> *disadvantage of HSQC:* ③
>
> HSQC is more complicated than HMQC—there are more pulses in the pulse train—and as a result, it is more sensitive to things like field quality, shimming, and sample quality. (Put another way, it's easier to screw it up.)
>
> <u>Rubric:</u> 3 points for any answer saying any one of these things. *Again, grader has leeway on judging whether your answer matches this description.*