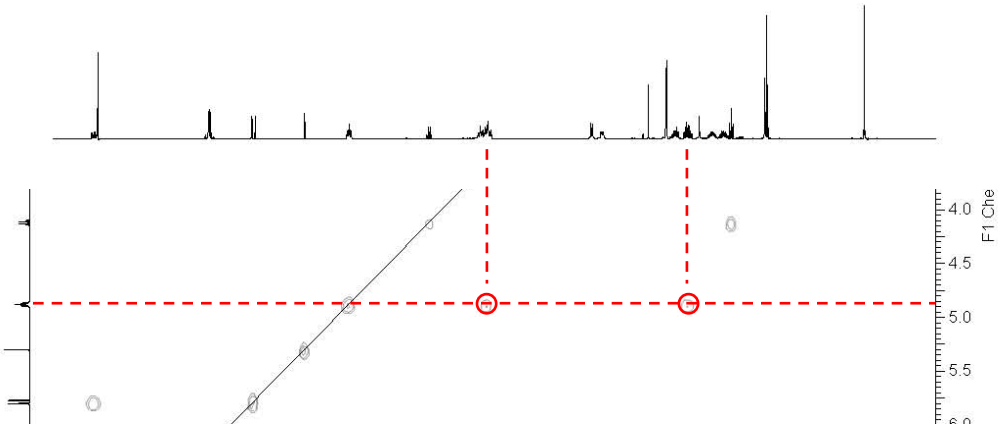
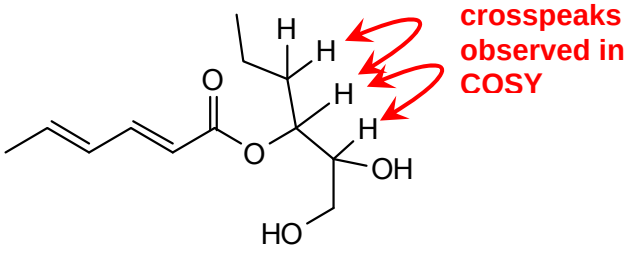
Chemistry 4361/8361 Fall 2012

Problem Set 4 Solutions
2D Correlated NMR Spectroscopy

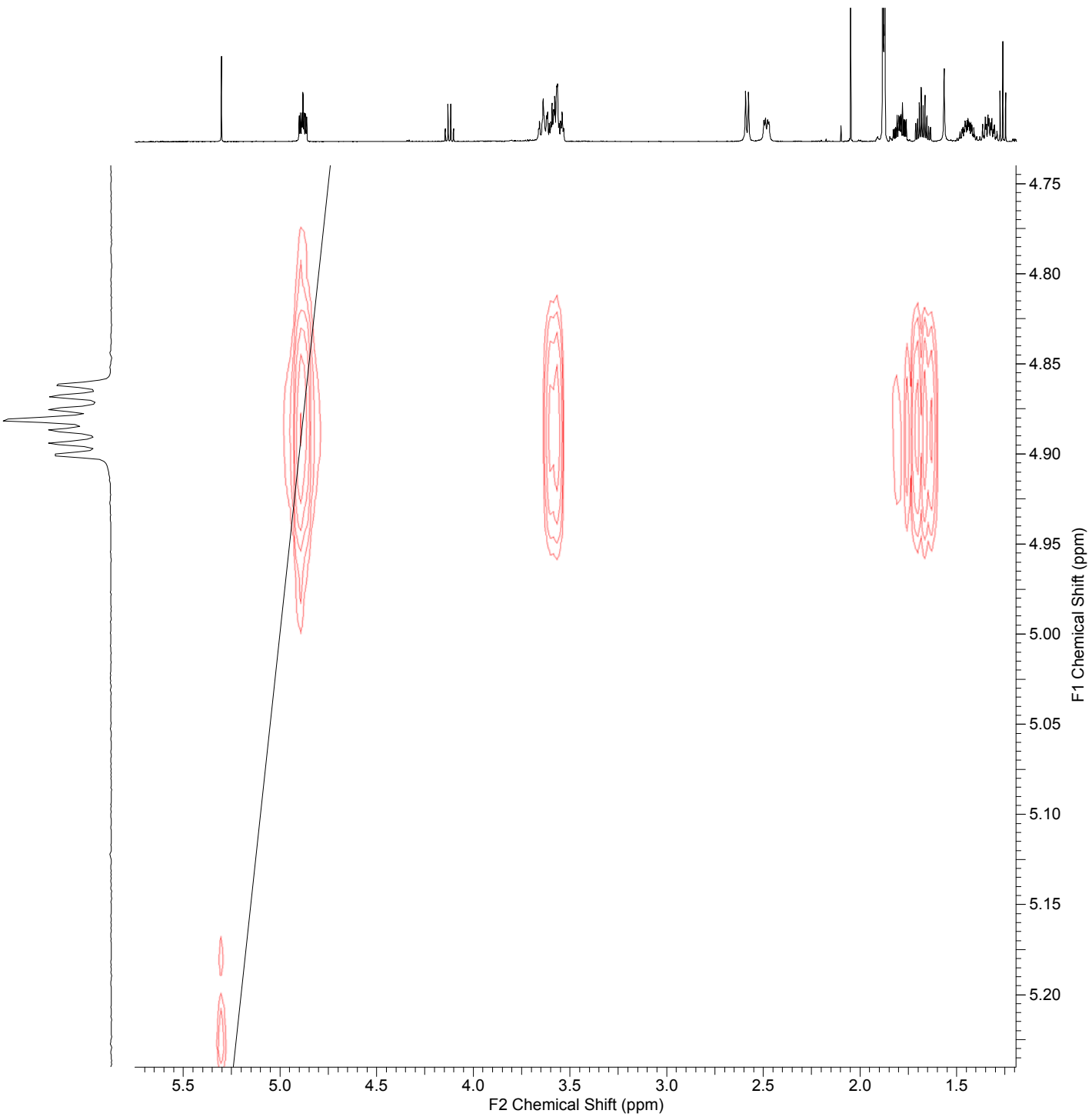
1. One of the nice things about COSY spectroscopy is that it makes it possible to focus only on the coupling relationships you are interested in, and not the ones you aren't. In this case, we are asking only one question: Is the proton that is α to the ester oxygen adjacent to 3 -CHOH- protons, or is it adjacent to 1 -CHOH- proton and two alkyl (-CH_2-) protons? To answer this question all we need to do is

   - Locate the proton α to the ester oxygen. The ester will be more electron-withdrawing than a typical alcohol or ether oxygen, so I would expect this proton to be downfield of 4 ppm. Sure enough, there is a multiplet at δ = 4.88 that fits the bill.
   - See what crosspeaks are observed in the COSY NMR to that signal. If we draw a horizontal line at δ = 4.88 in the COSY, we see two off-diagonal peaks: one pointing to the right-hand side of the overlapping (-CHOH-) multiplets at δ = 3.6, and one pointing to the (alkyl -CH_2-) multiplet at δ = 1.67.

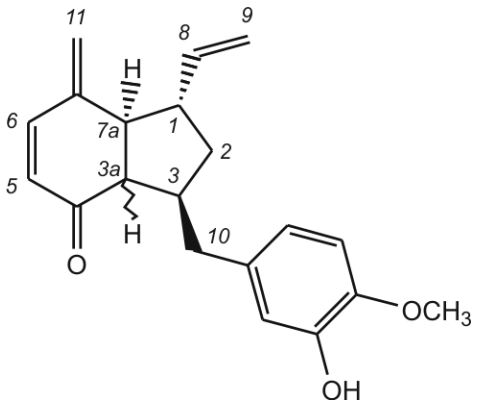




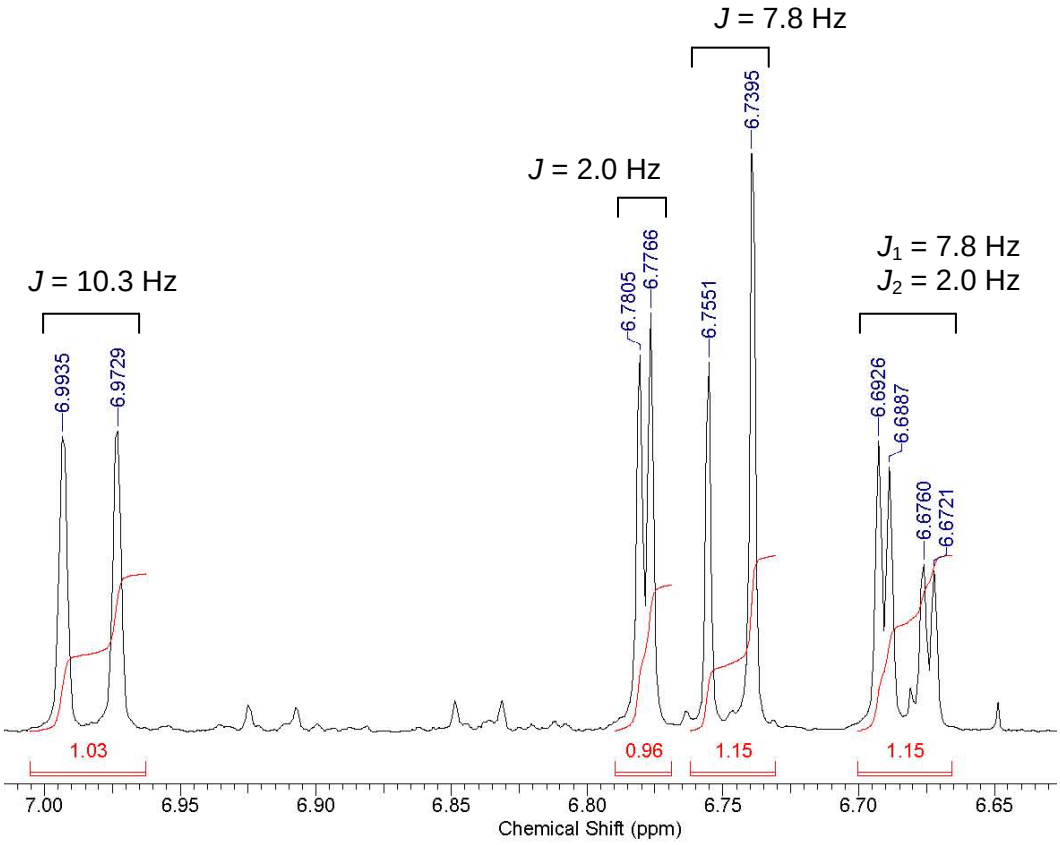
This means that the product must be the first one. Hearing this, though, you might very well ask, "Wait a minute. There's one more vicinal coupling relationship in the structure on the right—to another -CH2- proton—that you didn't draw. Why isn't that observed in the COSY spectrum?" Well, actually it is, just not at the vertical slice level that I chose for your problem set. If you lower the topological cutoff, and close in on that section of the COSY, you get the spectrum on the next page. This clearly shows another crosspeak, to the multiplet at δ = 1.80 ppm.


4.75
4.80
4.85
4.90
4.95
5.00
5.05
5.10
5.15
5.20
F1 Chemical Shift (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
F2 Chemical Shift (ppm)

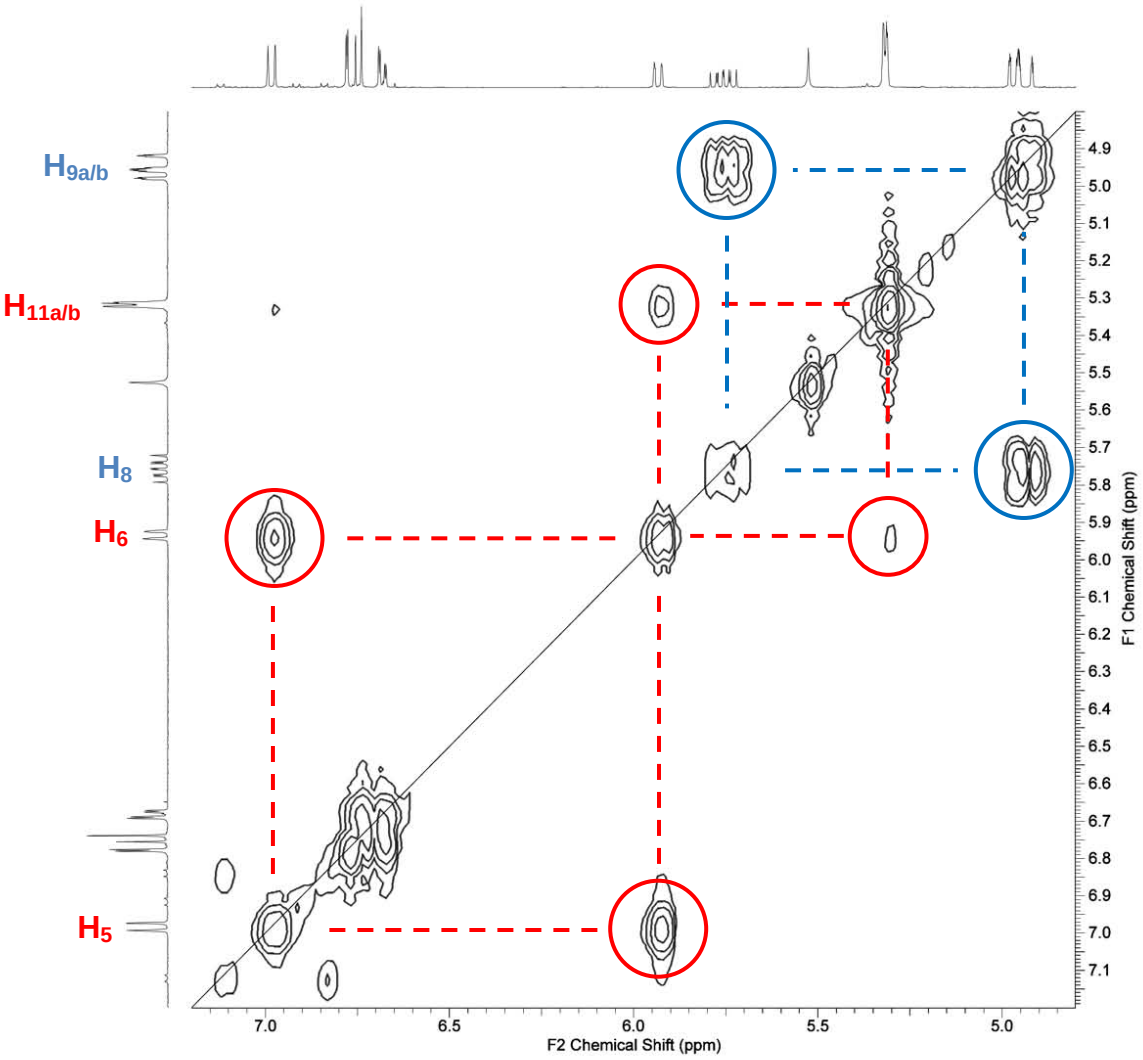
2. In ottelione A, there are a number of different proton types that should show up in distinct areas of the ^{1}H NMR spectrum. There are 3 aryl protons that should couple amongst themselves and appear far downfield; there are two sets of alkene protons (4 and 3 protons each); there is an OCH_3 group; and there are 8 alkyl protons.



The aryl region of the spectrum (6.5 ppm and up) already starts out a bit confusing, for a couple of reasons. In the COSY spectrum, it looks like there are a number of crosspeaks that belong to tiny impurity peaks rather than the main molecule. We'll ignore these. Then, in the aryl closeup, it looks like there are four resonances for just three aryl protons. One of these must belong to an alkenyl proton, and fortunately, coupling constants tell us that it must be the δ = 6.98 ppm peak that doesn't belong:



In the COSY, that δ = 6.98 ppm peak is coupled to other resonances, so it belongs to one of the alkene systems, probably the one conjugated to the electron-withdrawing carbonyl. This is confirmed by the COSY closeup:



The red lines above indicate the four-proton, ketone-conjugated system; and the blue lines indicate the exocyclic vinyl group. Even though the two protons at C_{11} are technically inequivalent, it looks as though the one 2H-intensity peak represents them both.

When I'm trying to analyze COSY spectra, one thing I look for is correlations that are far off the diagonal, in the hope that I can identify obvious pairs of dissimilar protons. Two such crosspeaks that are visible in the full COSY are $^{3}J(H_8,H_1)$ and $^{4}J(H_{11},H_{7a})$. Knowing $\delta(H_1)$ and $\delta(H_{7a})$ then allows you to walk around the molecule.

a.

proton	δ (ppm)
H_1	2.62
$H_{2\alpha}$	1.73
$H_{2\beta}$	1.56
H_3	2.50
H_{3a}	2.86
H_5	6.98
H_6	5.93
H_{7a}	2.78
H_8	5.76
$H_{9\alpha}$	4.97
$H_{9\beta}$	4.94
$H_{10\alpha}$	3.05
$H_{10\beta}$	2.50
$H_{11\alpha/\beta}$	5.32

b. The only coupling constant that the H_{3a} dd and the H_{7a} triplet have in common is 8.5 Hz.

c. If you build a model, you'll find that the left-hand side of the molecule is awfully flat. That means that the H_{3a}-H_{7a} dihedral angle will either be ~0° or ~120°. J = 8.5 Hz is larger than the average value of 7 Hz for ^{3}J(H,H), so I'm guessing that H_{3a} is down.