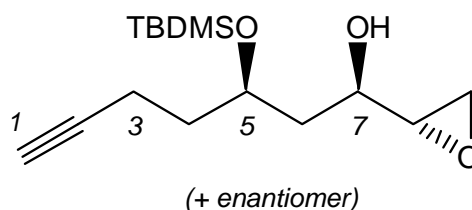


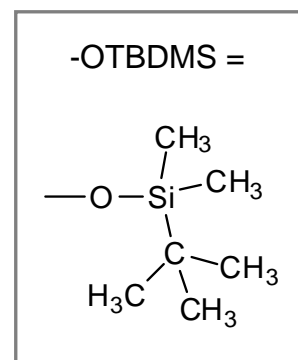
Exam 2 Answer Key

Exam 2 Mean: 82
Exam 2 Median: 89
Exam 2 St. Dev.: 22

Mandy's synthetic intermediate has a couple of features that stand out in the 1D and 2D ^1H NMR spectra. First, the molecule has 15 protons in its -OTBDMS group. (Synthetic chemists will often abbreviate this "-OTBS", but I find that abbreviation less informative for non-synthetic chemists.) Apart from that, the molecule has 12 C-H protons, but the NMR shows 13H intensity aside from the upfield silyl group—so that 13th proton must come from somewhere else, probably the -OH proton. (This doesn't happen often—H-bonding usually smears -OH protons out—but Mandy took this NMR at low concentration, and must have kept her solvent very dry. So that helped.)



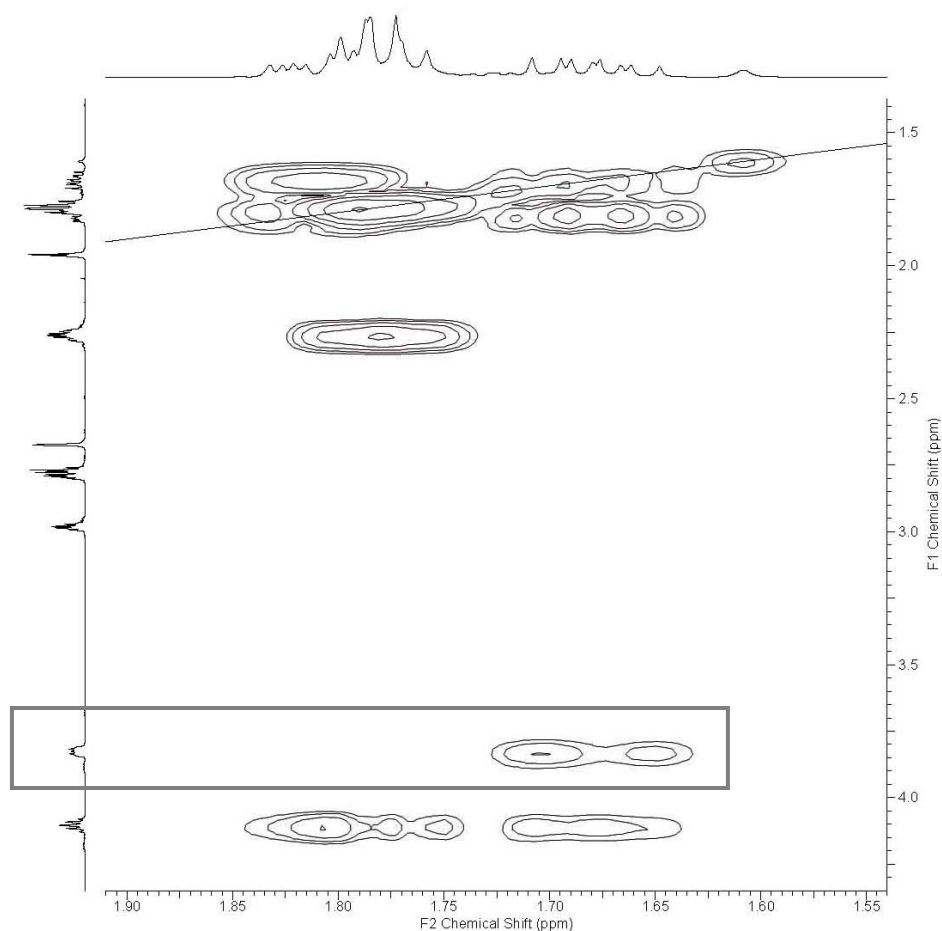
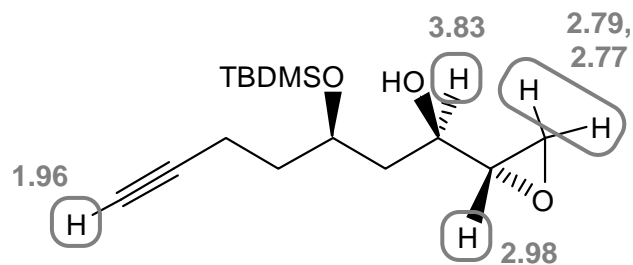
We've seen terminal alkyne protons before—they tend to show 4J coupling with CH_2 protons on the other side of the alkyne. That means if we can find a triplet in the ^1H NMR with a small coupling constant, that's probably our terminal alkyne proton. Sure enough, there's one at $\delta = 1.96$ ppm with $J = 2.5$ Hz, which must be H(1).



The molecule has 5 protons that are α to oxygen atoms, but Pretsch says that we would expect the three epoxide C-H's to appear upfield of the other two. Sure enough, our ^1H NMR has two protons downfield at $\delta = 4.1$ and 3.8 ppm, and then four more in the $\delta = 2.5 - 3$ ppm region. Out of those four, the three that split one another into multiplets of multiplets are probably the three epoxide C-H's. But I don't think we can assign any of these explicitly, or any of their neighbors, without the 2D NMR data.

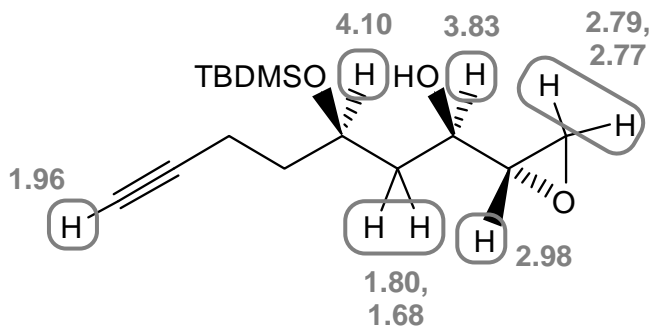
In the COSY spectrum, there are a number of crosspeaks that tell us about neighboring relationships. Starting with the epoxide protons, it's pretty clear that the three ^1H resonances we identified above—the 1H-intensity resonance at $\delta = 2.98$ ppm, and the 2H-intensity set at $\delta = 2.78$ —are coupled to one another, and must be the three epoxide H's. Out of these three, only one is coupled to another proton outside the set; the 1H multiplet at $\delta = 2.98$ ppm is correlated with the broad multiplet at $\delta = 3.83$ ppm. This means we can assign the right-hand side of the molecule:

The COSY spectrum shows that the 3.83 ppm resonance is correlated with a few other resonances. It is coupled to one partner that has no other partners: the doublet at 2.67 ppm, which must be the -OH proton. It then also couples to one or more protons in the crowded set of overlapping 1.7 ppm peaks. I think the closeup COSY tells us a little more about the OH's neighbors. It appears to be coupled to the multiplet at 1.68 ppm, but not anything else:



So it seems likely that the 1H 1.68 ppm multiplet is H(6a), but it's not immediately clear where H(6b) is. Fortunately, finding inequivalent geminal protons is a strength of HMQC. Looking at the HMQC, it appears that the ^{13}C resonance at $\delta = 40$ ppm is associated not only with that 1.68 ppm multiplet, but also with the left-hand side of the broad mess at 1.80 ppm. (Actually, you could imagine that left-hand side being a ddd, where we can only see four of the eight constituent peaks.) These two also

show crosspeaks with one another in the closeup. I don't know why there's no crosspeak for this resonance with H(7) in the COSY—maybe the coupling constant is too low. In any case, the HMQC allows us to assign H(6b).



Now all we have left are the H(3)'s and H(4)'s. The H(3)'s are coupled to the terminal alkyne proton, and this shows up in the COSY as a crosspeak with the resonance at 2.26 ppm. Both the COSY and HMQC show this resonance as not being correlated with geminal protons at any other chemical shift, so both C(3) protons must be at 2.26 ppm. In the COSY, these C(3a/b) protons are correlated with the unassigned remainder of the 1.7 ppm set, which must be both C(4) peaks.

I thought it was easiest to assign ^1H resonances, and then use the HMQC to associate those known ^1H nuclei with their attached ^{13}C nuclei. So that means the charts look like:

1.

carbon	δ (ppm)
C(3)	15
C(4)	36
C(5)	71
C(6)	41

carbon	δ (ppm)
C(7)	69
C(8)	55
C(9)	45

3 for each box.

proton	δ (ppm)
H(1)	1.96
H(3a)	2.27
H(3b)	2.25
H(4a)	1.78
H(4b)	1.77

proton	δ (ppm)
H(5)	4.10
H(6a)	1.80
H(6b)	1.68
H(7)	3.83
H(8)	2.98

proton	δ (ppm)
H(9a)	2.79
H(9b)	2.77
-OH	2.67
-Si(CH ₃) ₂	0.12
[x2]	0.11
-SiC(CH ₃) ₃	0.90

3 for each box.

Rubric: 3 points for each box. (23 boxes, so that's 69 points total for problem 1.)

¹H resonances must be within 0.05 ppm for credit.

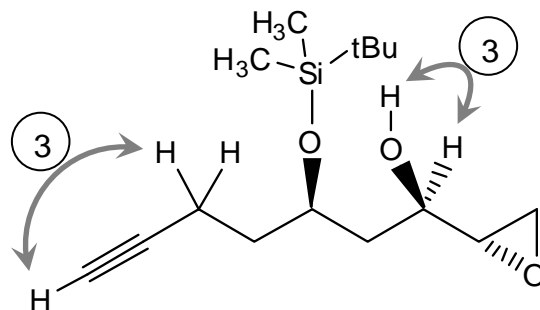
¹³C resonances must be within 5 ppm for credit.

2. The two circled crosspeaks in the COSY spectrum correlate

1.96 with **2.26**

and

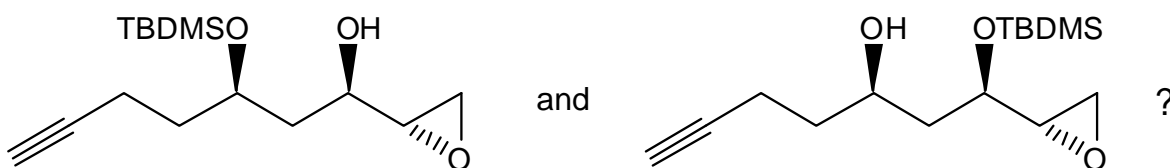
2.67 with **3.83**



We accepted any double-headed arrow that matched up with the entries in your table; you did not have to have the correct answer to receive full credit.

Rubric: 3 points for each arrow. (6 points total this part.)

3. (Mandy wasn't actually concerned about silyl transfer. I made that part up.) So this problem is basically asking, how do you tell the difference between



There are a couple of ways to do this, but I think an NOE experiment would be the best way to go. With NOE, it's extremely important that the protons/chemical shift you irradiate are distinct, that there is no overlap with other protons, so you couldn't just choose any proton here. The alcohol proton and the protons in the TBDMS group are in very distinct locations in the NMR spectrum, so it would be pretty easy to selectively irradiate either of them and look for enhancements in other nearby distinct protons—say, the epoxide multiplets on one side, or H(3a/b) on the other. Other protons are not so distinct. For example, H(4a/b) and H(6a/b) overlap, so we can't irradiate those. Also, some of you suggested irradiating H(5) or H(7), but I think the point of the problem is that Mandy might not know which was H(5) or H(7)—that if the -OH group was on the other side, H(5) would look like H(7) and vice-versa.

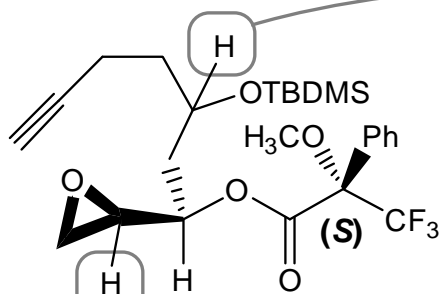
You could also do an HMBC experiment, and see what long-range correlations you could see between the alcohol proton and nearby carbons, and especially the epoxide carbons. (I think the TBDMS protons are too far from the backbone to see correlations there.) I don't think this would work as well as NOE, but we accepted this answer.

Rubric: (10 points this part)

5 points for either "NOE" or "HMBC" in the answer.

5 points for explaining what experiment would say. If NOE, answer should propose an excitation target. If HMBC, answer should propose what long-range correlations you're looking for. Grader has discretion on partial credit with these points.

4. When thinking about MTPA esters, I always think in terms of the (S)-ester. Here I've drawn this ester to highlight the spatial relationships between Mandy's alcohol and the MTPA substituents.



This proton is on the same side as the OCH₃ substituent in the (S)-ester, which moves its δ downfield, to higher values.

$\Delta\delta > 0$ or $\Delta\delta < 0$?

3

This proton is on the same side as the Ph substituent in the (S)-ester, which moves its δ upfield, to lower values.

$\Delta\delta > 0$ or $\Delta\delta < 0$?

3

5. Mandy didn't perform DEPT experiments on her molecule. If she had, would she have observed 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
C(1)	$\boxed{+}$ - or $\mathbf{0}$?	$\boxed{+}$ - or $\mathbf{0}$?
C(2)	+ - or $\boxed{0}$?	+ - or $\boxed{0}$?
C(3)	+ $\boxed{-}$ or $\mathbf{0}$?	+ - or $\boxed{0}$?

3

3

3

Rubric: (9 points total this part)

For each row,

2 points for 1 correct answer, 3 points for both correct.