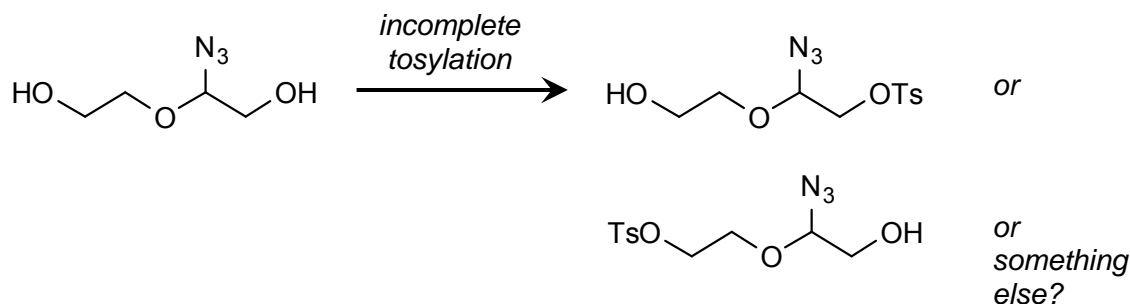
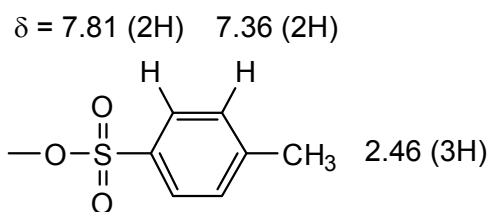


**Problem Set 2 Solutions**  
Advanced 1D NMR Interpretation

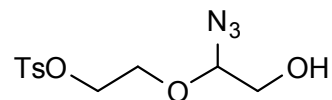
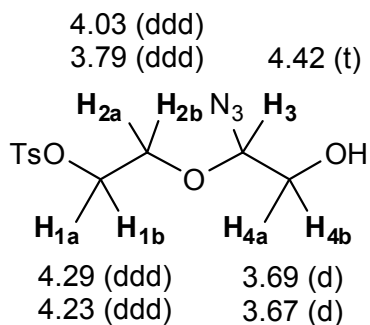
1. a. Right off the bat, our two product NMRs have peaks in them that correspond to tosyl groups. But the relative intensities of these peaks indicate that there is only one tosyl group for every 7 other protons present—one tosyl group per molecule. Because the reaction was an unsuccessful di-tosylation, it makes some sense that failure products might be mono-tosylates. But are they the monotosylates we might think they are? And which is which?



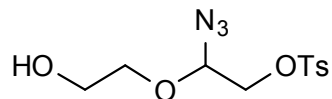
In both the expected product and in the incomplete products, there are seven protons, all adjacent to oxygen. So, the fact that all of the resonances in the two products are in the  $\delta = 3.0 - 4.5$  ppm range is no surprise. Many of the resonances look like doublets of doublets of doublets, with three coupled neighbors, which could correspond to protons in the  $-\text{OCH}_2\text{CH}_2\text{O}-$  part of the molecule, and some look like triplets or doublets of doublets, which could correspond to the  $-\text{OCH}(\text{N}_3)\text{CH}_2\text{O}-$  part. In both cases, the peak that is most deshielded is a triplet. This should be the proton on the azide-modified carbon, deshielded by the electron-poor azide group. (No azides in Pretsch's book, but you can find some tables with azide chemical shifts online. I like Hans Reich's at the University of Wisconsin, <http://www.chem.wisc.edu/areas/reich/handouts/nmr-h/hdata.htm>).

In unknown 1, the other two protons on the azide side—represented by a 2H doublet of doublets—are the farthest upfield, at  $\delta = 3.68$ . Because a tosylate group is pretty electron-withdrawing, this is inconsistent with a tosylate on the azide side. If unknown 1 were either of the molecules, it would have to be the second one. By contrast, in the spectrum for unknown 2, the azide triplet is farther downfield, which is more consistent with the other monotosylate.

In the case of unknown 1, I'm guessing



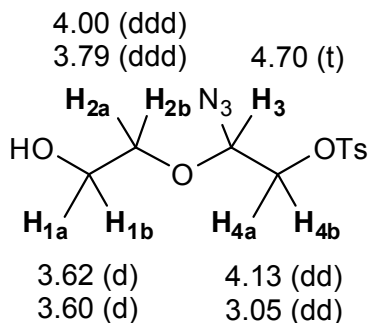
*unknown 1?*



*unknown 2?*

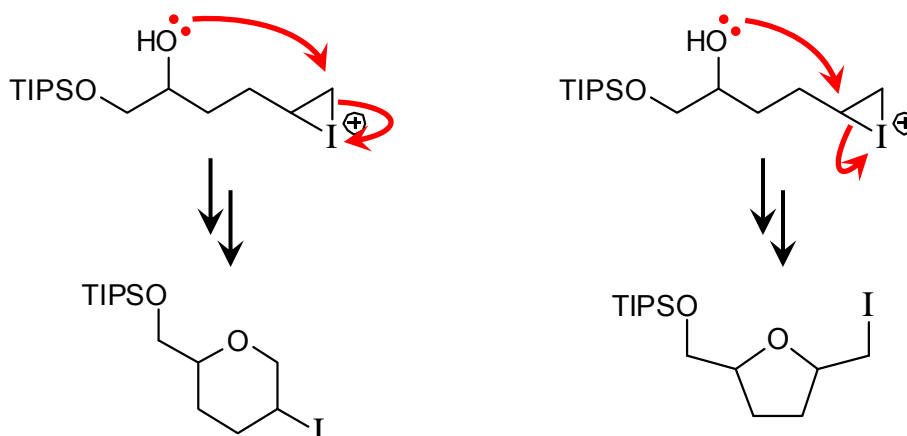
I'm not sure which shift is for which proton (stereochemically speaking), so I haven't illustrated stereochemistry. One thing that is strange about the splitting in this molecule is the two doublets at  $\delta = 3.68$ . This set of peaks has intensity 2H, and initially I thought it was a doublet of doublets, but I'm pretty sure that's impossible. They split with  $H_3$ , but the two  $H_4$  protons can only split each other if they have different chemical shifts, and that would yield two doublets of doublets, not one. The only other explanation is that  $H_{4a}$  and  $H_{4b}$  both couple with  $H_3$ , but not with each other. Or, put another way,  $J(H_{4a}, H_{4b}) \approx 0$ .

For unknown 2,

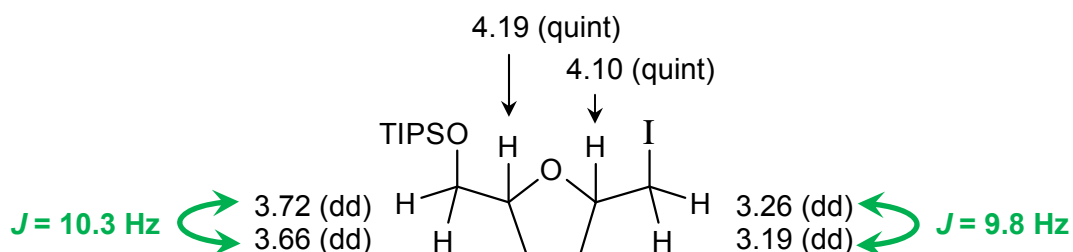


Once again, there's a weird situation with a pair of inequivalent protons that don't couple to one another (this time on the left side).

2. a. There are two possible products that we're considering:



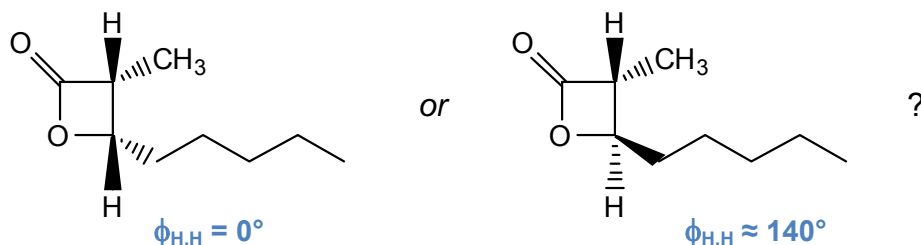
There are three substituents in these compounds that would affect chemical shift:  $-\text{OCR}_3$  groups, which have a pretty large downfield effect ( $-2.0$  ppm) on chemical shift, according to Pretsch; the  $-\text{OTIPS}$  group, which should have less of an effect; and an iodide group, which should have the least effect. The molecule on the left has five protons adjacent to oxygen and one adjacent to iodine, whereas the molecule on the right has four adjacent to oxygen and two adjacent to iodide. I think the NMR is more consistent with the molecule on the right. In the NMR, the protons farthest downfield are quintets, with four neighbors, corresponding to the ring ether protons. (Well, they're not perfect quintets. But I'm still guessing four neighbors.) Then the next four are doublets of doublets, indicating protons with two neighbors (presumably one geminal, one vicinal in this case).



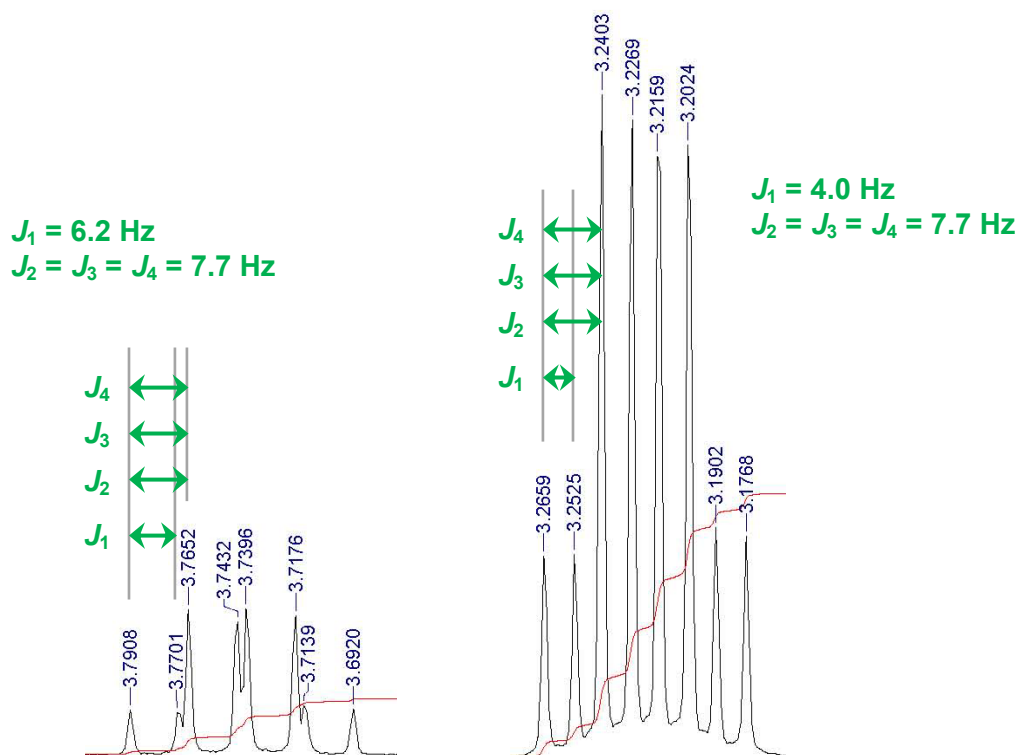
In the doublets of doublets, I was originally worried about the assignment of them in pairs; it might be possible for one dd in one set to actually be coupled to a dd in the other set. However, if you measure the larger  $J$  values for each set, you find that they are actually slightly different, which confirms the pairing.

b. The "quintets" are pretty impossible to get coupling constants from, as are the multiplets corresponding to the  $-\text{CH}_2-$  ring protons. I don't think it's possible to extract stereochemistry from these NMRs.

3. a. To answer this question, you really didn't need to go through the process of assigning the entire spectrum. All you needed to do was focus on the stereochemistry in the ring, and ask, are the two ring protons *cis* or *trans* with respect to each other? (Or, put another way, what is the dihedral angle between them?)



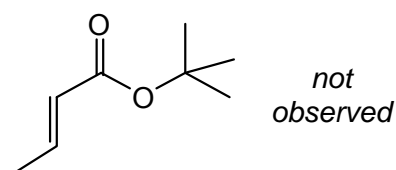
Fortunately for us, these two protons are extremely clear in the NMR spectra; the proton  $\alpha$  to the carbonyl is at  $\delta \approx 3.5$  ppm, and the proton  $\alpha$  to the ester oxygen is at  $\delta \approx 4.3$  ppm. (Both of these values are downfield of where they would normally be; I assume this is due to ring strain. See Pretsch tables for how ring strain affects  $\delta$ .) For this analysis, I choose the proton  $\alpha$  to the carbonyl, because it should be the simplest; it should be a doublet of quartets, with coupling to only the other ring proton (the d part of dq) and to the  $-\text{CH}_3$  group (the q part of dq).



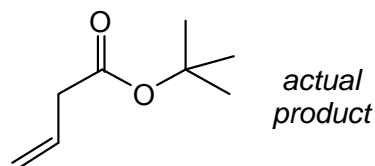
The  $J_1$  value for the multiplet on the left—the one that relates the two ring H's—is larger than the  $J_1$  on the right. The Karplus equation says that a  $0^\circ$  dihedral angle should give the larger  $J$  value. So this means that the less intense multiplets belong to the *cis*-isomer, and the more intense ones to the *trans*-isomer. That makes great sense, because the *trans*-isomer is the more stable product.

- b. Using the integrals, the major isomer is  $(1.00)/(1.00 + 0.21) = 82.6\%$  of the mixture. So  $de = 2(82.6\%) - 100\% = 65.2\%$ .

4. a. There are some important differences and similarities between the observed spectrum and the expected product. The spectrum does have a strong singlet at  $\delta = 1.45$  ppm that has an integrated intensity that matches, roughly, the expected *t*-butyl group (9H). The number of other protons in the spectrum (5 more H) also matches the expected product. But there the similarities end. The spectrum has 3H in the alkene region, not 2, and 2H in the allylic/ $\alpha$ -carbonyl region. Imagining the minimum perturbation of our expected product, the real product is probably:



This structure matches the three alkenyl protons; the internal proton is a doublet of doublets of triplets, and the two terminal H's are complicated by allylic coupling with the  $-\text{CH}_2-$  group. The  $^{13}\text{C}$  spectrum also matches.



- b. Lots of potential experimental solutions to this problem.

- Increase the sample concentration.
- Take more scans.
- Increase the pulse delay time  $\tau$ . Or more explicitly, measure  $T_1$  for that carbon, and then increase  $\tau$  to  $> 5T_1$ .
- Degas the sample. Oxygen and other paramagnetic impurities decrease peak intensities. (Though, to be honest, this rarely helps a lot.)
- Improve signal to noise by applying a window function to the FID.

- c. I meant ppm, not MHz. The 77 ppm 1:1:1 triplet is from  $\text{CDCl}_3$ , and the splitting is due to  $^{13}\text{C}$ - $^2\text{D}$  coupling.