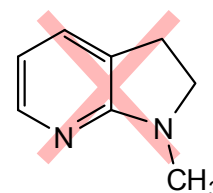


### Workshop 1 Solutions

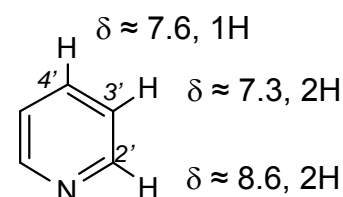
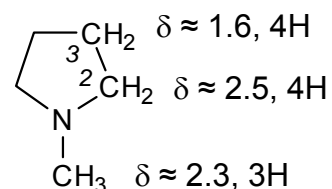
#### Analyzing 1D NMR Spectra

1. Pyridine normally has five H's, and *N*-methylpyrrolidine normally has 11. Our  $^1\text{H}$  NMR spectrum of the joined molecule has a total of 14 H's—4 in the aromatic region, corresponding to the pyridine ring, and 10 farther upfield, corresponding to the aliphatic *N*-methylpyrrolidine ring. So each ring is missing 1 H relative to its parent, and thus our two rings are probably joined at just one position; they are probably not fused at two positions.

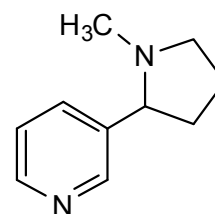


In principle, there are three attachment points on *N*-methylpyrrolidine—C2, C3, or the methyl group—and three attachment points on pyridine—C2', C3', or C4'. We can use chemical shift tables to imagine where the protons will be, and see if any of those resonances are missing from the NMR spectrum—whatever H is missing must be a connection point. I've used the Pretsch book tables for  $\text{CDCl}_3$ ; substitution and the difference between  $\text{D}_2\text{O}$  and  $\text{CDCl}_3$  will perturb these values, but we'll try to use trends in our analysis. The aromatic region of the  $^1\text{H}$  NMR spectrum shows 2H downfield, 1H in the middle, and 1H upfield; it looks like one C3' proton is missing from pyridine, so that's where it connects.

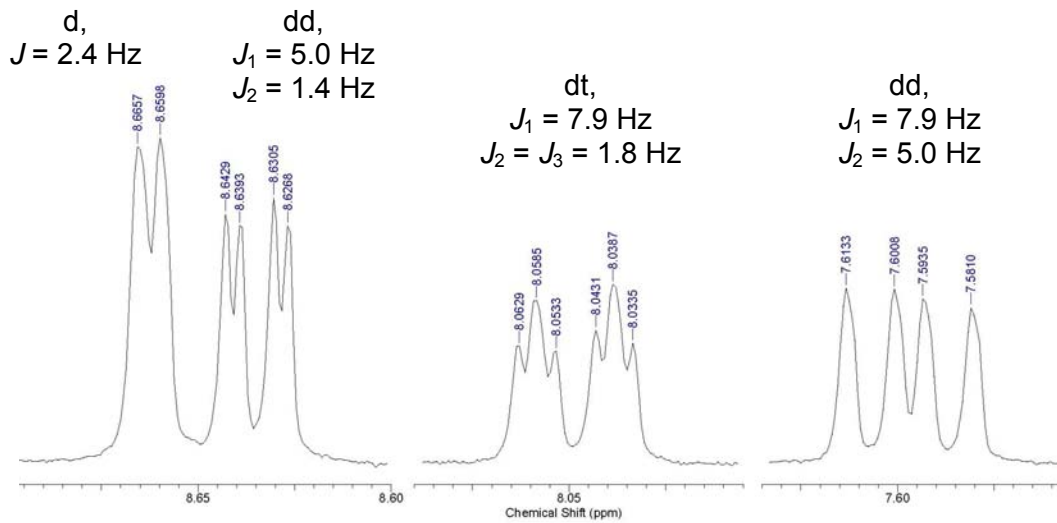
Pretsch predictions:



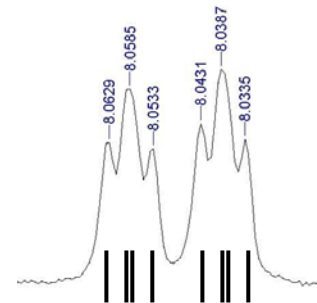
On the pyrrolidine ring, the spectrum contains a 3H methyl group at  $\delta = 2.7$ , and there are 4H worth of protons upfield of that. But there are only 3H worth of protons downfield of the methyl group, and that leads me to believe that the connection point for pyrrolidine is C2. That would give us the structure on the right for nicotine, which is correct!



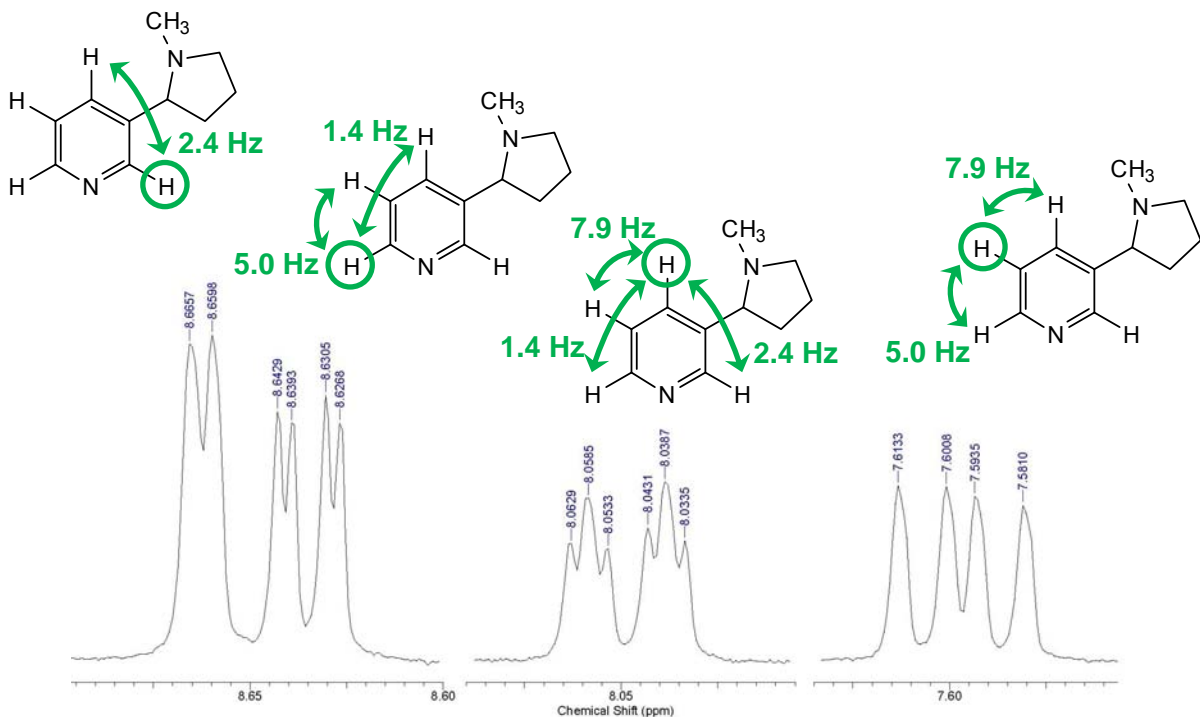
Now let's assign resonances just to be sure. In the aromatic region, the protons exhibit both large and small coupling constants. My bet is that the large coupling constants are  $^3J$ s (vicinal), while the small coupling constants are long-range  $^4J$ s or  $^5J$ s. There is a simple doublet, two doublets of doublets, and one doublet of triplets. (See next page.)



It looks as though the small  $J$ 's on the leftmost peaks (2.4 and 1.4 Hz) don't match very well with the small  $J$ 's in the doublet of triplets. But keep in mind that resolution in the NMR spectrum isn't perfect. The doublet of triplets might very well be a doublet of doublet of doublets, with the central peaks being so close together that they combine.



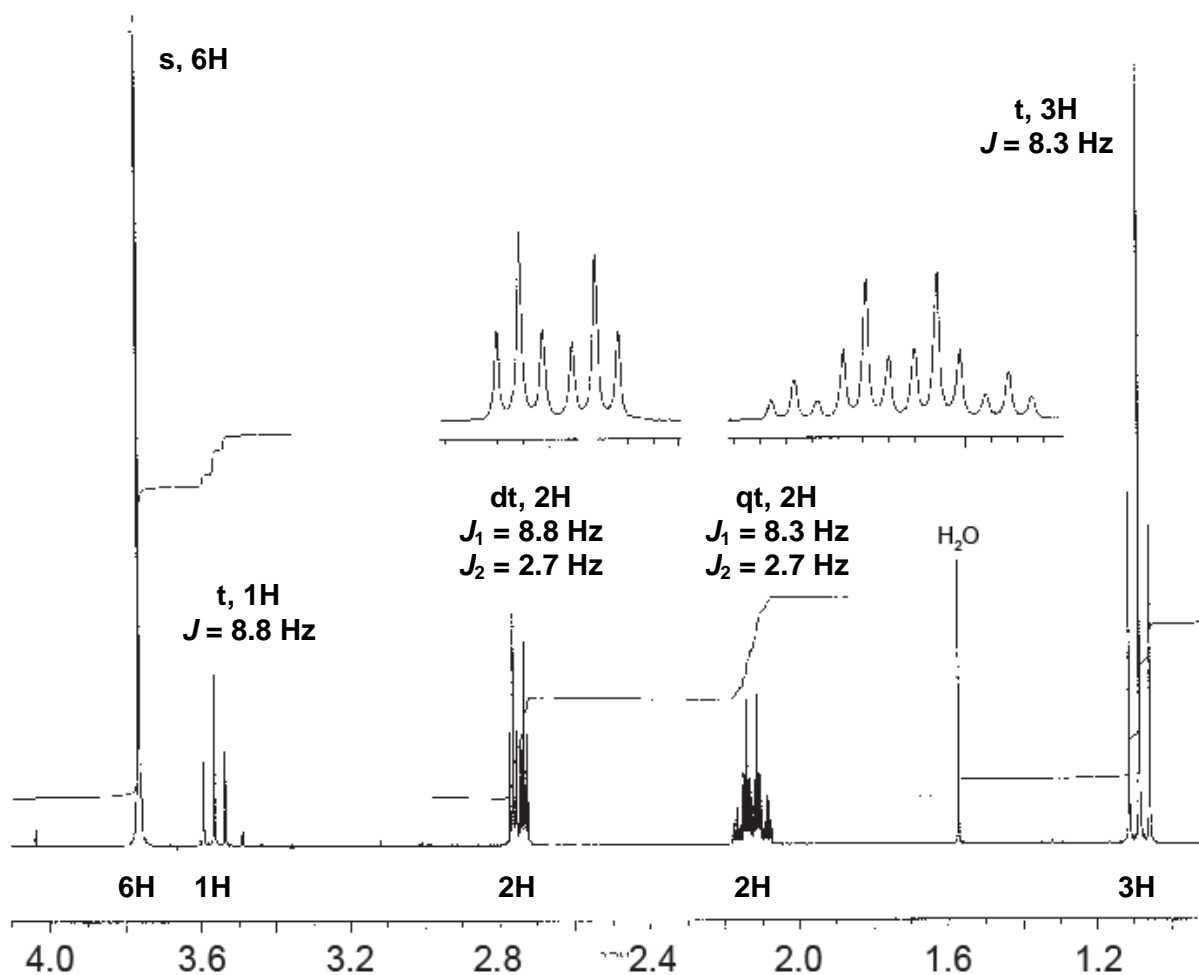
Using both the chemical shift guesses we made and the coupling constants we just measured, I think that means:



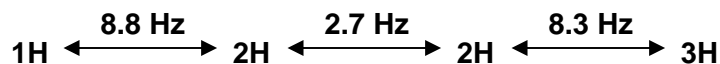
The pyrrolidine is a little more complicated; the multiplets at  $\delta = 2.3-2.6$  ppm are too messy for us to assign, but they surely correspond, collectively, to the protons at C3 and C4. The doublet of doublets at  $\delta = 4.42$  ppm has only two coupling partners, whereas the doublet of triplets at  $\delta = 3.31$  ppm and the complex multiplet at  $\delta = 3.80$  ppm have more than two. (The “complex multiplet” at  $\delta = 3.80$  ppm looks to me like a doublet of doublet of doublets, where the second, third and fourth peaks are double peaks like on the previous page.) This must mean that the dd at  $\delta = 4.42$  ppm must correspond to H2, and the others must be for H5 $\alpha$  and H5 $\beta$ .

2. The NMR spectrum doesn't show any resonances in the  $\delta = 4.5 - 6.5$  ppm region, so our side product probably doesn't have any vinyl protons in it (as the expected product does). The spectrum does, however, have a 6H intensity singlet, suggesting that the malonate fragment (with its two equivalent  $-\text{OCH}_3$  groups) is probably a part of the side product.

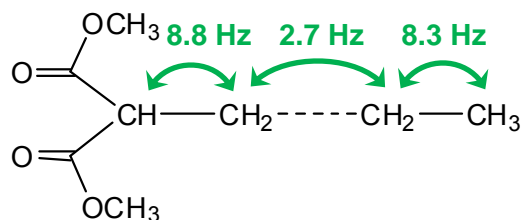
We can assign intensities and coupling constants to the  $^1\text{H}$  NMR spectrum:



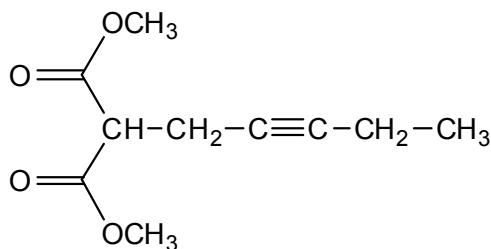
The multiplet coupling constants match nicely, and allow us to create a "map" of the molecule:



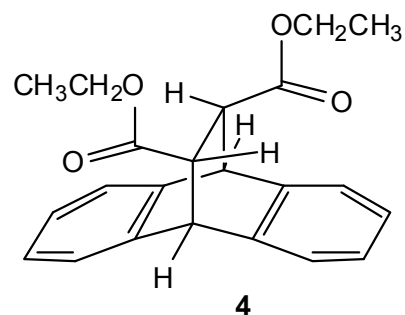
According to chemical shift tables, if any of these protons comes from a malonyl group, it must be the 1H at  $\delta = 3.6$  ppm. If that were true, the side product might actually look a lot like the intended product:



The only question here would be, what is between the two carbons in the middle? In the intended product there are two more carbons, but the NMR spectrum has no more protons. One way to include two carbons but no protons would be as an alkyne:



3. a. Even though the four protons in the center of the molecule are vicinal to one another, they have dihedral angles of around  $90^\circ$ . Karplus' equation says that coupling will be minimal in this geometry.



b. This part was pretty tricky. At first glance, the set of peaks at  $\delta = 4.0$  ppm looks like a quartet of quartets, but that would require a proton with two sets of three neighbors, and there aren't any such protons on this molecule. The protons that have the most neighbors are the ethyl  $-\text{CH}_2-$  protons, who have just three neighbors.

The key to answering this question was recognizing that those  $-\text{CH}_2-$  protons are diastereotopic, and thus inequivalent. If they split one another (geminally), then each one will give rise to a doublet of quartets. That is in fact what is observed at  $\delta = 4.0$  ppm—two overlapping doublets of quartets. The intensities of the multiplets are distorted (like the linalool spectrum we looked at in class) because the difference in chemical shift between the two resonances is comparable to the value between them.

