Exam 3
Answer Key

Exam 3 Mean: 59
Exam 3 Median: 57
Exam 3 St. Dev.: 18

1. Electrospray ionization (ESI) is a soft ionization method--different from electron ionization (EI), where an electron is ripped from a molecule under the impact of a high-energy electron beam. In ESI, by contrast, molecules become ionized by being protonated (or, much less often, forming a complex with a heavier or more complex cation). So that means our $m/z = 344$ species corresponds to $[M + H]^+$, and that our molecule's mass is probably 343 amu.

Looking at the exact-mass calculation,

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Elemental Composition Calculator v1.0

Calculations for :   344.2339 +/-  0.002 amu

  C  H  N  O      mass      diff       ppm

 18 28  6  1    344.2324    0.0014      4.1
 20 30  3  2    344.2338    0.0001      0.2
 22 32  0  3    344.2351   -0.0012     -3.6
  6 32  8  8    344.2343   -0.0004     -1.1
  8 34  5  9    344.2356   -0.0017     -5.0
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it looks like the closest guess is $C_{20}H_{30}N_3O_2$. The next closest guesses are a formula with only 6 carbons (can't be--the quinoline alone has 9) and a formula with no nitrogens (again can't be because of the quinoline). SO I think this is a safe guess.

What is the molecular formula of the $m/z = 344$ ion?

$$C_{20}H_{30}N_3O_2{}^+$$
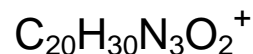
⑦

Given this, what is the molecular formula of the substituted quinoline?
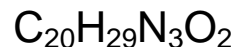
$$C_{20}H_{29}N_3O_2$$

⑤

2. The two most important things to recognize in this problem were (a) that the λ_{max} for the unknown quinoline peak is at longer wavelength, and thus lower energy, than the pyridine peak; and (b) that the difference must be due to the expanded π system of the quinoline. (In other words, the in-plane *n* lone pair of pyridine is essentially the same as that of quinoline.) Drawing this into the orbital energy diagram:
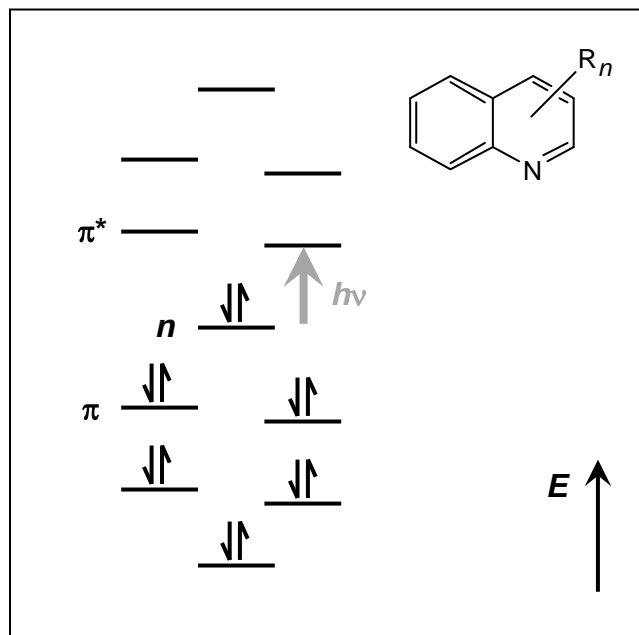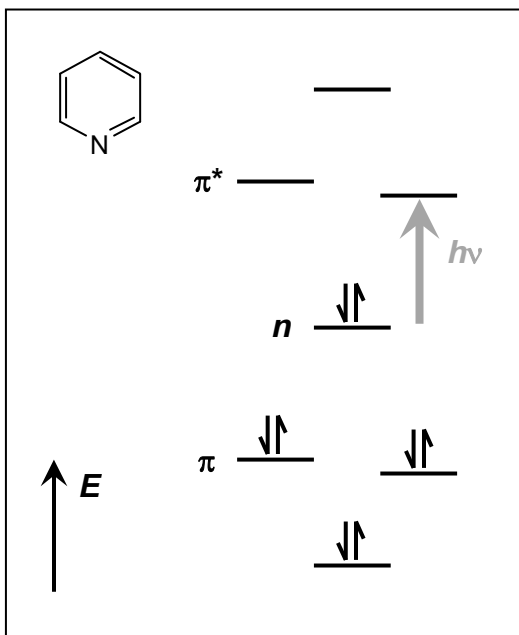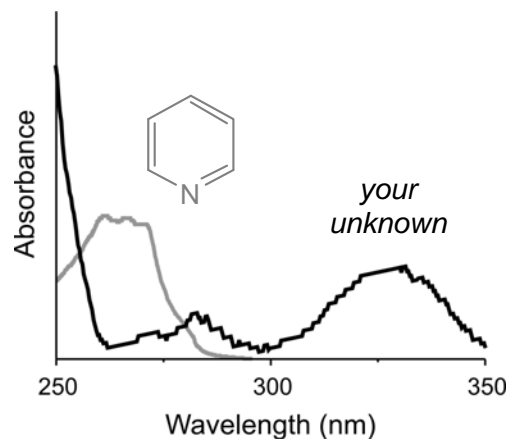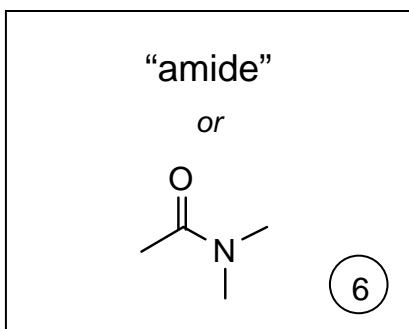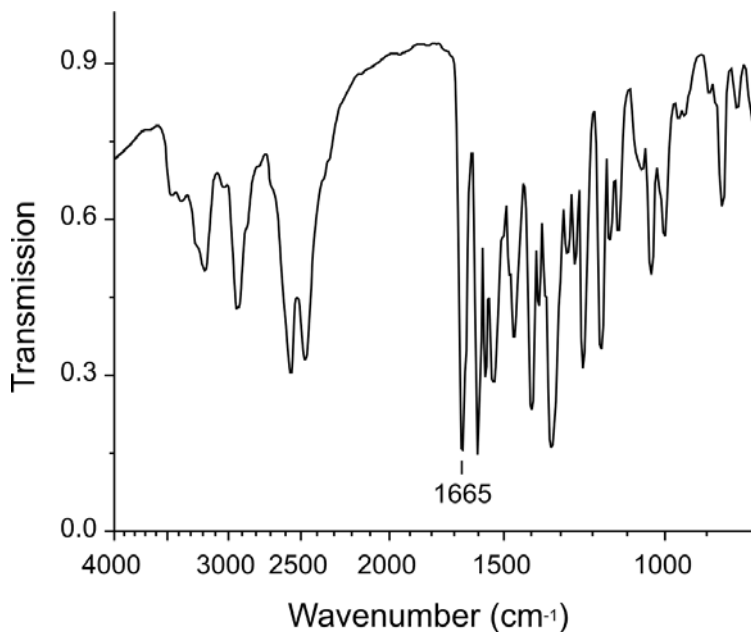
3. $\nu = 1665$ cm^{-1} is at the edge of two IR frequency ranges that correspond to two commonly observed bond types. The peak could be due to C=C double bond stretching, but it's a little high-frequency for that. Also, Pretsch says that aromatic C=C stretching is usually very weak (and this peak is very strong). The peak could also be due to C=O stretching. 1665 cm^{-1} is on

the lower end of the carbonyl stretching range, but there are plenty of C=O types that appear at this frequency (see summary table in Pretsch). In particular, amides appear here (1630-1680 cm^{-1}), and especially aromatic amides (which should be lower in frequency than aliphatic amides).

"amide"

or

⑥

4. Because our unknown has C(sp^2)-H bonds in it (assuming that not every position in the quinoline is substituted), we would expect to see peaks in the IR spectrum just above $\nu = 3000$ cm^{-1}. I have to admit though, 3150 cm^{-1} is not terribly close to 3000 cm^{-1}, which makes me wonder whether C(sp^2)-H stretching could be responsible for this peak. Pretsch also suggests that N-H stretching occurs near this frequency. So we accepted either answer.

C(sp^2)-H

or

N-H

⑥
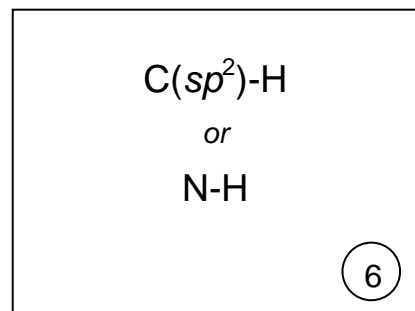
5. Okay, now for the challenging part of the exam. The NMR spectrum of our unknown quinoline certainly has downfield protons that come from the quinoline group, but there are lots of other upfield, aliphatic/heteroatom protons as well. Where do we start?

I think the easiest spectrum to start with in this problem was actually the TOCSY. TOCSY gives you information on coupled sets of protons--tells you which protons are in a row of connected carbons, and which are separated from each other by a coupling "block". Our TOCSY shows four groups of coupled protons:
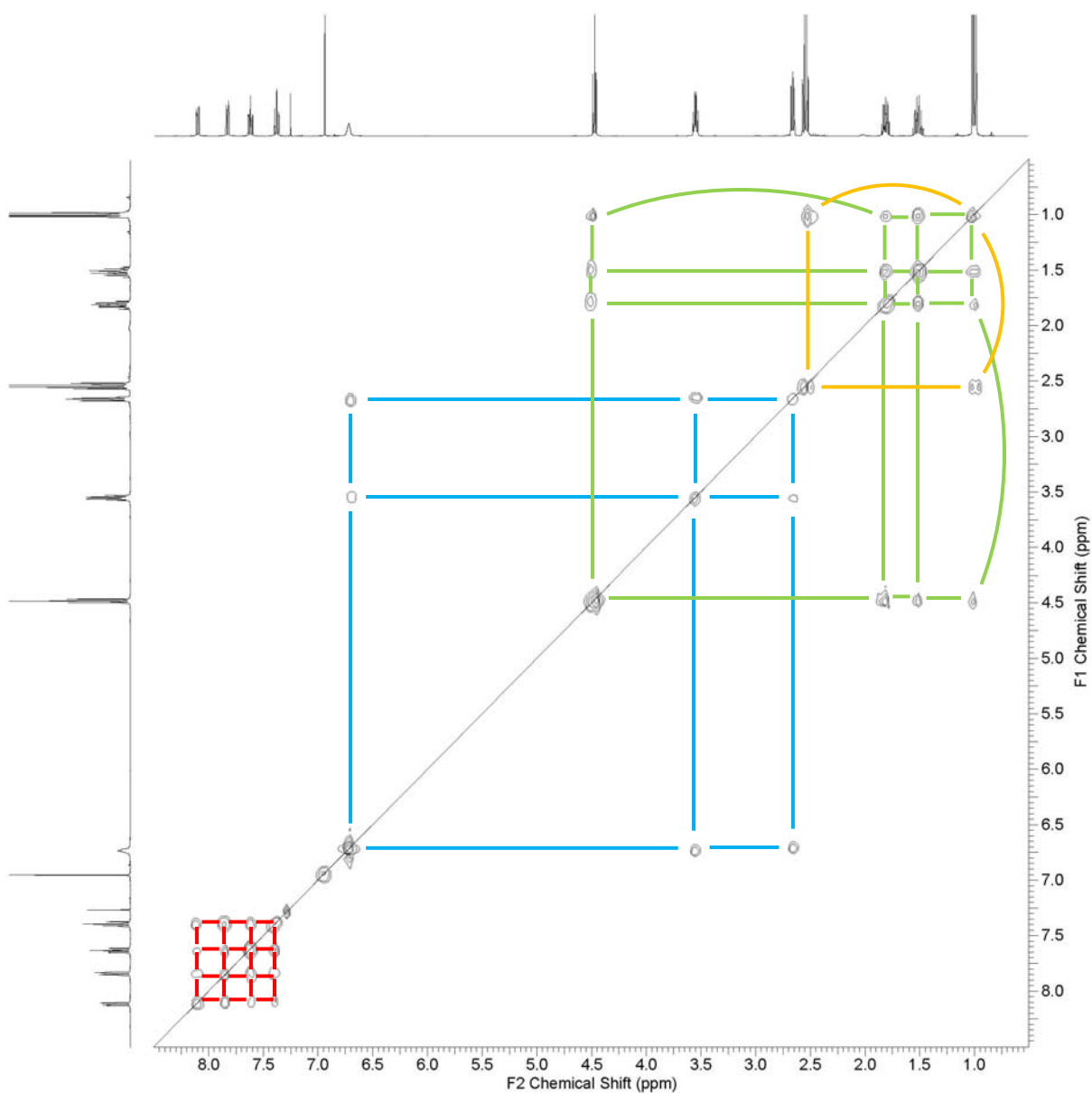
This analysis sets us up with four coupled chains of protons:

i. A set of four, 1H quinoline protons, **a**-**b**-**c**-**d**. There is only one way that four protons on the quinoline ring can be a part of a continuous coupled chain, and that is if the all-carbon ring has no substituents. (So, any substituents we come up with have to be on the pyridine ring.) In the string of four protons, the ones at the ends of the string are going to have only one large (vicinal) J value each, whereas the two in the middle will have two large J values.
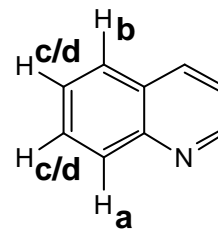
ii. A set of three resonances, **f**-**h**-**i**. Or, with more detail included, **f**(1H)-**h**(2H)-**i**(2H). Peak **f** is pretty far downfield, which initially might make it look like an aromatic H, but it is clearly broader than the other peaks in the spectrum, and there's no easy way that an aromatic H could be coupled to other H's upfield. In any case, **i** is a triplet (two neighbors), and **h** is a quartet (three neighbors), so it seems pretty likely that the three proton sets are in a row.
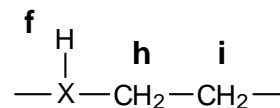
iii. A set of four resonances, **g**(2H)-**k**(2H)-**l**(2H)-**m**(?H). Peak **g** is in the α-heteroatom region of the spectrum, meaning it must be next to an electron-withdrawing atom like O or amide N. The splitting and connectivity of the other peaks make it look like a butyl group.
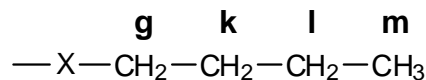
iv. A pair of resonances **j**(4H)-**m**(?H). Now, because there can't be four protons attached to the same carbon that is also attached to other things, peak **j** must belong to protons on multiple carbons. With **j** being a quartet, and **m** a triplet, we can guess that this will be two ethyl groups. In addition, because $\delta(\mathbf{j}) = 2.54$, we know that the ethyl groups aren't bound to an alkyl carbon, but rather something more downfield-shifting--either a multiple bond, or a weakly electron-withdrawing atom. Certainly not an ether oxygen, but maybe a nitrogen?
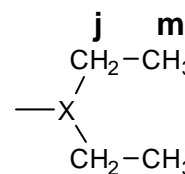
There is also one 1H-intensity peak (**e**) that shows no crosspeaks in the TOCSY. It's sharp, it's in the aromatic region, and it might be associated with the quinoline.

So how do we piece all of these fragments together? Before this section of the class, the best way was probably trial and error. But in this problem, the NOESY spectrum can give us information about what protons are near what other protons. Our NOESY spectrum contains all the same crosspeaks that the TOCSY does, plus a few new ones; I've circled the new ones on the following page.
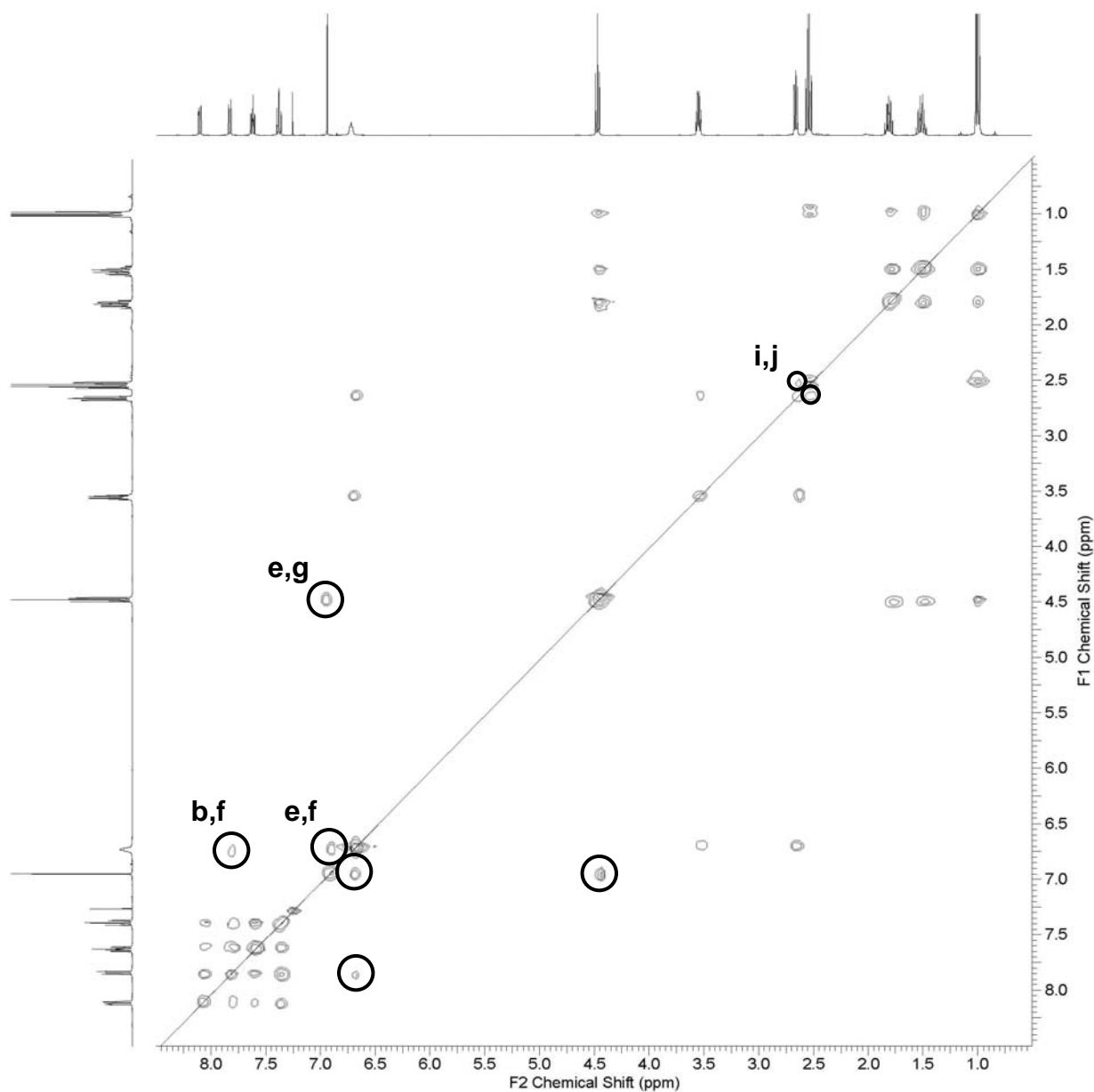
The off-diagonal peaks that don't appear in the TOCSY are through-space correlations. These instruct us to organize our molecular fragments like this:
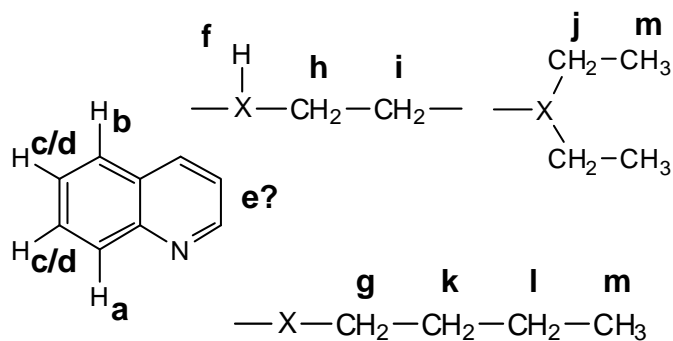
On this fragmented structure, the only things we are missing are two nitrogen atoms, two oxygen atoms, and a carbon. If we take into account the amide stretch from the IR, the only arrangement consistent will all of this data is
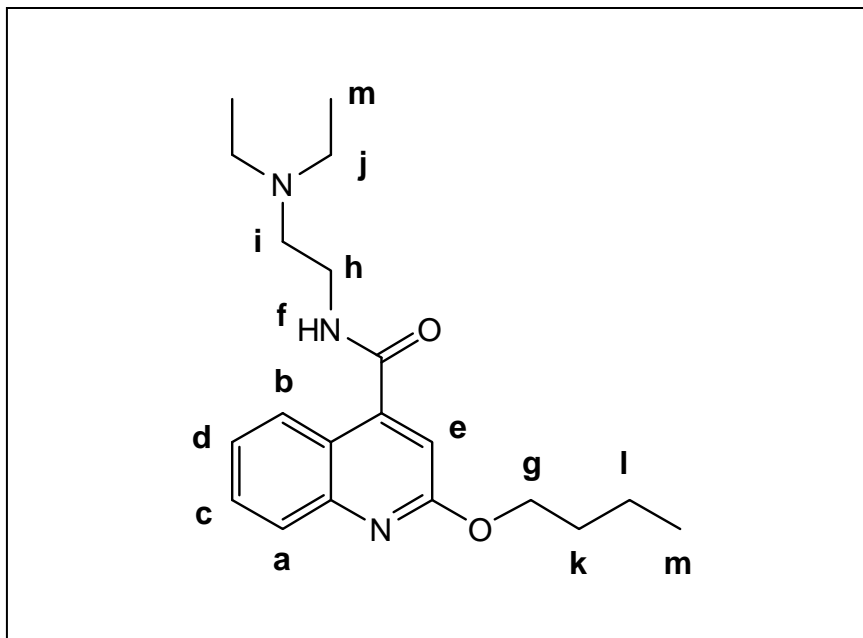
Rubric:

48 of the 66 points in this problem were evaluated based on a scoring chart, shown on the next page. For each letter **a-l**, you received up to 4 points based on the quality of your assignment. For each letter, you received:
   • 1 point for labeling a number of H's consistent with the integral of the resonance;
   • 1 point for labeling H's with the correct number of neighbors;
   • 1 point for labeling H's with the correct chemical shift environment;
   • 1 point for through-space closeness, if indicated in the NOESY.
In the case of letter **m**, you got these points for each of your inequivalent usages of **m**.; if you only label one set **m**, you only get one row of points.

The other 18 points come from:

3 points for drawing any complete structure with two oxygen atoms.
3 points for drawing any complete structure with three nitrogen atoms.
3 points for drawing any complete structure with 20 carbon atoms.
3 points for drawing a disubstituted quinoline with substituents at the 2 and 4 positions of quinoline ring.
6 points for drawing the correct structure.

label	correct number of equivalent protons?	correct number of neighbors?	correct chemical shift environment?	correct through-space neighbors?
a	1	1	must be aside N	
b	1	1	any quinoline proton	near **f**
c	1	2	any quinoline proton	
d	1	2	any quinoline proton	
e	1	0	any quinoline proton	near **f** and **g**
f	1	any number	any -NH or -OH	near **b** and **e**
g	2	2	α to amide N or O	near **e**
h	2	3	α to amide N or O	
i	2	2	α to amine N (not O)	near **j**
j	4	3	α to amine N (not O)	near **i**
k	2	4	alkyl -CH_2-	
l	2	4	alkyl -CH_2-	
m(1)	adds to 9 (2 points)	2	alkyl -CH_3	
m(2)		2	alkyl -CH_3	