Chemistry 4361/8361 Wednesday, November 14, 2012

Exam 3
Answer Key

Exam 3 Mean: 70
Exam 3 Median: 73
Exam 3 St. Dev.: 17

1. Our EI-MS experiment has induced too much fragmentation in the molecule. If we insist on still running an EI-MS experiment, the simplest way to reduce fragmentation is to reduce the electron-beam acceleration voltage. In class, we looked at examples in which reducing beam voltage from 70 kV to 15 kV increased the relative parent mass intensity, at the expense of the overall signal intensity (because fewer molecules were ionized).

   Rubric: 6 points for "reduce electron beam acceleration voltage", or something similar that indicates the same thing.
   Grader has leeway to give partial credit, but what we're looking for is pretty specific; don't know what other answers would receive partial credit.

2. Is your molecule

   [✓ **atenolol**] ④ , **"blocker acid"** , *or* **"tertiary amine"** ? *(Circle one.)*

   (I'll explain this as we go along.)

3. Electrospray ionization typically yields **protonated** ions; unlike EI, ESI does not rip an electron off of the parent molecule. So, if a parent ion is present in the ESI-MS, we would expect it to be $[\mathbf{M} + \mathrm{H}]^+$, and we would expect it to have a mass 1 amu greater than the neutral parent. Our ESI-MS has a pretty strong peak at m/z = 267, which I think could only come from protonated atenolol (266 + 1). There is no similar peak at m/z = 268 or 474, which we would expect for the other two molecules.

   ESI-MS works well for atenolol because it has Lewis-basic electrons ready to pick up a proton. So where will the proton be? At the most basic site: the secondary amine.

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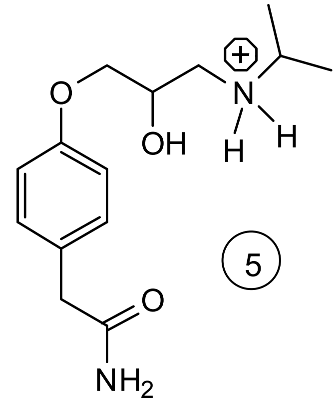
Rubric:
5 points for correct ion structure.
3 points partial for protonating atenolol at a different location.
No partial credit for structures related to blocker acid or tertiary amine. They don't make sense for m/z = 267.

structure of m/z = 267 ion



4. The peaks at m/z = 289, 305 and 533 are clearly minority peaks, with higher-than-expected masses. In class, I mentioned two things that sometimes occurs with mild ionization techniques:

   - Alkali metals in place of protons. Molecules will occasionally coordinate sodium, potassium, or other metals that they pick up from their environment (glassware surfaces, buffers, etc.). That happened here:

     m/z = 289 ③

     $[\mathbf{M}\bullet\mathrm{Na}]^{+}$

     m/z = 305 ③

     $[\mathbf{M}\bullet\mathrm{K}]^{+}$

   - The protonated species coordinates other molecules—solvent, proton donors, or another copy of the parent—via hydrogen bonding. That happened here:

     m/z = 533 ③

     $[\mathbf{M}\bullet\mathrm{H}\bullet\mathbf{M}]^{+}$

Rubric: *(9 points total this problem.)*
3 points for each box.
We didn't grade on the format of your answer (whether you used brackets or not, used a dot or a plus, etc.), only on the concept, and the charge. (All are +1.)

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5. Acetonitrile is a great solvent for ESI-MS because, along with being polar enough to dissolve ions at the electrospray source, it is also volatile enough to evaporate after droplets leave the electrospray nozzle. DMSO, on the other hand, is a high-boiling, low-volatility solvent that can't evaporate away from ions.

   Rubric: *(16 points total this problem.16 points was really too many for this problem, so:)*
   Automatic 8 points. (!)
   4 points for stating that DMSO has low volatility (or a higher boiling point, or doesn't evaporate, or something analogous).
   4 points for putting this in the context of *droplet* evaporation after the electrospray *needle/nozzle*. (We were really just looking for those two terms.)

6. If you wanted to achieve high mass resolution,

   Ion source: If you wanted to keep the molecule in acetonitrile, you could do electrospray into a **quadropole ion trap** instead of a linear quadropole. An ion trap is sort of both an ion source and a mass selection technique, but the mass selection is rough, and most ion traps are combined with a subsequent (pulsed), higher-resolution detection technique. Not as direct would be to combine the sample with matrix and use **MALDI** to ionize.

   Mass selection: The highest mass-resolution selection technique in routine use is probably **time-of-flight** (TOF) resolution. FT-ICR is also high-resolution, but pretty obscure—you'd have to search to find such an instrument available.

   Rubric: *(10 points total this problem.)*
   5 points for describing an alternate ion source. Can't do EI/CI/APCI/APPI though.
   5 points for describing an alternate mass selection method. Ion trap by itself isn't enough.

7.

ν (cm^{-1})	functional group	ν (cm^{-1})	functional group
3350	O-H ③	2964	C_{sp3}-H ③
3164	N-H ③	1634	amide C=O ③

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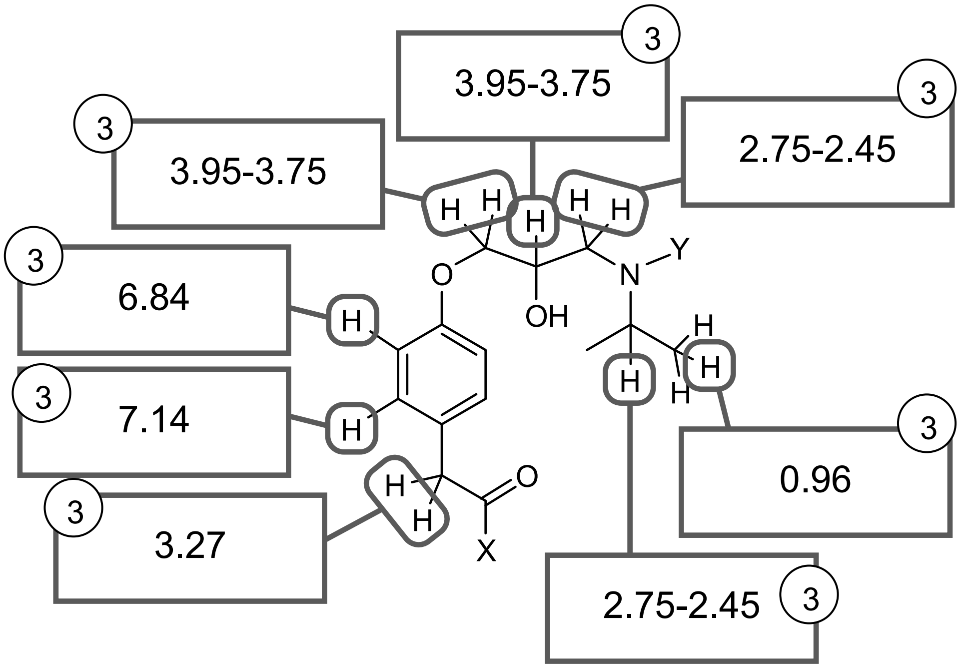
In the last box, you could just write “C=O” or “carbonyl” for full credit. But importantly, the fact that this absorption is at such a low wavenumber value pretty much guarantees that the unknown molecule has an amide group in it, and not a carboxylic acid (which you’d expect to see in the low 1700’s).

One thing that was kind of weird—I expected there to be one or more peaks to the left of the 3000 cm^{-1} line, corresponding to C_{sp2}-H stretches. Other IR spectra I found for atenolol after I wrote the test did have peaks in the > 3000 cm^{-1} region, but not this one.

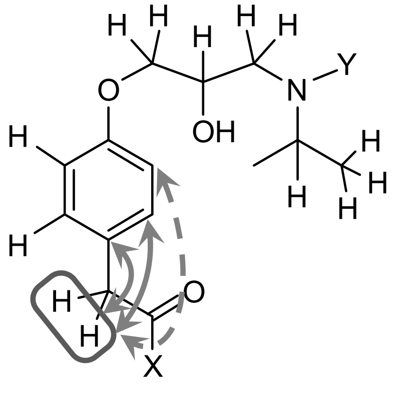
8.

δ values observed in ^{1}H NMR (in ppm):

7.37
7.14
6.84
6.82
4.95
3.95-3.75
3.27
2.75-2.45
1.48
0.96



9. Keep in mind, HMBC is a heteronuclear correlation technique—it looks at correlations between ^{1}H and ^{13}C nuclei. So, we’re looking for correlations between the circled protons and <u>carbon</u> atoms. The unique ones that would show proximity to the benzene ring are shown at right; I think the ^2J and ^3J shown with solid-line arrows would be clear, but ^4J correlations are sometimes strong enough to be observed in HMBC, and we accepted the one shown with a dashed arrow as well. One thing we didn’t accept was two arrows to equivalent carbons (say, to both ortho carbons)—that’s not two different correlations.



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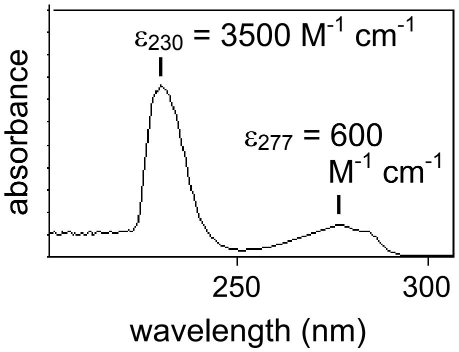
Rubric: 3 points for each arrow. *(6 points total this problem.)*

If two arrows were redundant (show the same correlation twice), we gave credit for just one of the two arrows.

10.

λ = 230 nm π ② $\longrightarrow$ π^* ②

λ = 277 nm *n* or π ② $\longrightarrow$ π^* ②



Our UV-vis spectrum has two peaks, a taller one (with a large extinction coefficient) at higher energy, and a shorter one at low energy. The taller one probably corresponds to an allowed transition of an intensely absorbing chromophore. The benzene ring is the strongest chromophore in the molecule, and this peak could be due to a symmetry-allowed, $\pi \rightarrow \pi^*$ transition in that ring. Looking at the detailed UV-vis section in Pretsch, aromatics typically have an intense (ε = 2000-10000 M^{-1} cm^{-1}) absorbance in the low 200's, and the tall peak is probably that transition.

The smaller, higher-wavelength peak is probably a symmetry-forbidden transition of some type. There are two possible origins of that transition in the molecule: an excitation of the adjacent oxygen *sp*^{2} lone pair into the ring π^* orbital, which would be an n $\rightarrow$ π^* transition; or a forbidden $\pi \rightarrow \pi^*$ transition in the ring. We accepted either of these answers.