- What key signals can we look for to differentiate these 3 structures in our product mixture?
- MS.
  - $[M]^+$ and $[M+2]^+$ peaks of equal height is characteristic of bromine, and hence unreacted SM.
  - The most stable fragment for the SM is the tertiary carbocation formed by cleaving the C–Br bond.
  - The most stable fragments for both E_1 and S_N1 have the same mass as the parent peak.
    - ➢ We form an allylic carbocation from E_1 by cleaving the ring β to the alkene.
    - ➢ We form an oxygen-stabilized carbocation from S_N1 by performing α-cleavage adjacent to the ether and then stabiliing the primary carbocation with one of the oxygen's lone pairs.
  - Thus, the bromine-containing SM is the only compound that can truly be distinguished from the other four using MS alone.
- IR.
  - E_1's C=C bond is unique among the four compounds.
  - The hydration product's O–H stretch will likewise be unique.
- ^{13}C NMR.
  - S_N1's ether methyl peak is unique among the four compounds.
  - We can also pick up on E_1's C=C bond here.
- ^{1}H NMR.
  - E_1's proton off the vinyl group is unique.
  - We can also pick up on S_N1's ether methyl peak here.
  - We can also pick up on the hydration product's O–H stretch here.

1.8 Review for Exam 1

9/23:

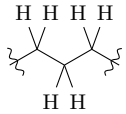
- Lecture 7 recap: Determining the products in Figure 1.37.
  - When you run a reaction (as in Figure 1.37), how do you know what your products are?
    - To answer such questions, chemists use a suite of structure determination techniques!
    - Examples include EA, MS, IR, ^{13}C NMR, and ^{1}H NMR.
  - EA: Can give us the empirical formulae of the compounds.
    - EA takes a while to run, so it might not be our first tool, but it can be useful.
  - MS: Can identify the ^{79}Br and ^{81}Br peaks in the SM.
  - IR: Can identify the O–H and C=C peaks where present.
  - ^{13}C NMR: Can identify the C=C bonds, and some symmetry differences (by number of peaks).
  - ^{1}H NMR: Can identify the C=C and O–Me fragments where present.
    - Recall that this is sometimes our most powerful method.
- Today: Review for Exam 1.
- Lecture outline.
  - Exam logistics and tips.
  - Review (EA → MS → IR → ^{1}H NMR → ^{13}C NMR).
  - Practice problems.

- Exam logistics.
  - Wednesday, 12-1pm in 50-340 (the third floor of the Walker Memorial).
  - Exam starts a 12:05pm on the dot!!
- Study techniques.
  - Study by practicing.
    - This unit is not about reciting information, but about applying techniques.
    - Try timing yourself on the practice exams to get a feel for what it's like to do structure determination problems under a time crunch.
  - Familiarize yourself with the reference material.
    - Know how to look stuff up!
    - Don't waste seconds or minutes searching for information because the first time you're seeing the reference sheets is when you take the exam.
  - Prof. Elkin's test-taking strategy: Go through the exam quickly first, answering what you can right away. Then go back a second time to ensure your answers are consistent with *all* the data.
- Will ^{1}H NMR peaks be labeled, e.g., with their splitting, coupling constant, and integration?
  - There will be some problems where more data is given, and some where less data is given.
- EA review.
  - Combust organic compounds into CO_2 and H_2O.
  - This provides the empirical formula.
- MS review.
  - Identify key atoms (use the parent peak): Cl, Br, and N.
  - Identify key fragments: Stable-ish cations.
  - Watch for common mass differences ($-$Me, $-H_2O$, etc.)
    - Don't do too much math on your calculator! Just look for *common* differences.
- IR review.
  - Key regions: X$-$H, *sp*, and X$=$Y.
  - Stronger bonds have a higher ν (cm^{-1}).
- ^{1}H NMR review.
  - Key regions of chemical shift.
    - A general rule is that more EWGs yields a more downfield/deshielded/to the left peak.
  - Consider integration and symmetry.
  - Coupling (shape and J value) tell us about connectivity.
- ^{13}C NMR review.
  - Key regions of chemical shift.
  - The number of peaks tells us about symmetry.
- Are we responsible for book information or just what was presented in class?
  - Yes and no.
  - You do need to read the textbook, because it explains class concepts in greater depth (specifically, the depth we're expecting you to know).
  - However, we're not going to try to ask "gotcha" questions on specific things in the textbook.

- Example structure determination: 1,1-dichlorocyclobutane.

Figure 1.38: 1,1-dichlorocyclobutane.

  - Given data.
    - EA: C_2H_3Cl.
    - ^{13}C NMR: 84.1, 46.6, 15.4.
    - ^{1}H NMR: 2.94 (t, $J = 7.6\,\text{Hz}$, 4H), 2.15 (pentet, $J = 7.6\,\text{Hz}$, 2H).[14]
  - Let's start by deducing the molecular formula.
    - How can we do this if we don't have MS data?
    - Instead, sum the ^{1}H NMR integrations to learn that the molecule has 6H total. Thus, since the empirical formula has only 3H, we must double the empirical formula to get $C_4H_6Cl_2$.
  - Let's now look for the presence of symmetry in the molecule.
    - Even though the molecule has 4 carbons, there are only 2 proton peaks — and their matching J values indicate that the protons in the peaks couple to each other.
    - Additionally, since the 2.94 triplet integrates to *four* protons, this peak probably corresponds to 2 sets containing 2 chemically equivalent protons each. Indeed, the only time when four protons are located on the same carbon is in methane!
  - This analysis of the ^{1}H NMR data can be used to draw the following molecular fragment.



    - The bottom two protons correspond to the pentet, since they are split by the other four (chemically equivalent) protons.
    - The other four protons are, in turn, split into a triplet by the two pentet protons.
  - Having constructed the above fragment, we only have one carbon left in our molecular formula.
    - We must maintain symmetry, so we can't just add it to one side or the other of the above fragment.
    - If we can't add it to one side or the other, we must add it to both! That is, let's close this fragment into a cyclobutane ring.
    - Then the last two atoms we have are the two chlorines, and we can bond these to the new carbon to fill its octet, include them in the molecule, and eliminate the possibility of any hydrogens on this last carbon interfering with the splitting of the other two sets of hydrogens.
  - Sanity check: Does this molecule match the ^{13}C NMR peaks?
    - It is a symmetric molecule with only three chemically unique carbon positions, so we expect three peaks (which we see).
    - We expect one of these peaks to be in the R–X region ($50 - 100\,\text{ppm}$), which we see.
    - We expect the other two peaks to be in the alkyl region ($0 - 50\,\text{ppm}$), with one significantly more downfield than the other due to the nearby chlorine EWGs. We see this, too.
  - Therefore, since 1,1-dichlorocyclobutane was deduced from our data and matches it all, we can be fairly confident that it is the right structure.

[14] Pentets are also sometimes referred to as quintets.

- Example structure determination: Dimethoxyethane.

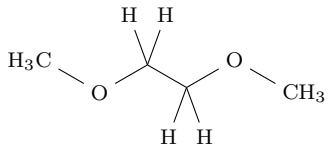
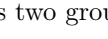
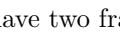


Figure 1.39: Dimethoxyethane.

  - Given data.
    - EA: C_2H_5O.
    - MS: 90, 45.
    - ^{13}C NMR: 71.3, 59.3.
    - ^{1}H NMR: 3.55 (s, 4H), 3.40 (s, 6H).
  - As before, let's start by deducing the molecular formula.
    - Via ^{1}H NMR: 10H total, so double the empirical to $C_4H_{10}O_2$.
    - Via MS: C_2H_5O has a mass of 45, so double the empirical to $C_4H_{10}O_2$ (mass 90).
  - Key signals.
    - The ^{1}H NMR peak at 3.40 ppm has an integration of 6H, so it likely corresponds to two chemically equivalent methyl groups. Additionally, the relatively downfield chemical shift (and lack of splitting) indicates that the methyl groups are coordinated to a heteroatom.
      - ➢ From the molecular formula, the heteroatom would have to be oxygen!
      - ➢ This means that our molecule contains two methoxy () groups.
    - The ^{1}H NMR peak at 3.55 ppm has an integration of 4H, so it likely corresponds to two chemically equivalent CH_2 groups. As before, its relatively downfield chemical shift (and lack of splitting) also indicates coordination to oxygen.
      - ➢ This means that our molecule also contains two groups that look like this: 
  - Now how do we couple the fragments?
    - The methoxy groups must go at either end of the molecule, and this forces coordination to an additional CH_2 past the oxygen. Now we have two fragments that look like this: 
    - Since this consists of all atoms, the only thing left to do is combine these two fragments to make the molecule in Figure 1.39 — in spite of the fact that this appears to bring protons that we *know* don't couple right next to each other.
    - However, looking at the full molecule, we can observe that it has rotational symmetry! (In other words, if you rotate the molecule 180° in the plane of the page, you get the same molecule.) This explains the lack of coupling: All four protons in the center of the molecule are actually chemically equivalent, and adjacent but chemically equivalent protons don't couple each other!
  - Sanity check: Could this molecule fragment to give the right MS peaks?
    - Yes!
    - The molecular ion would give rise to the parent peak at 90.
    - Cleavage of the central C–C bond would break the molecule in half, yielding a resonance-stabilized fragment half the weight of the molecule (i.e., $m/z = 45$).

- When do we need to take long-range coupling into account?
  - It is oftentimes very small, and we can't really see it on low-resolution NMR machines.
  - Mainly, you should know that it exists, but you should not expect too many examples of it on the exam.

- Example structure determination: Isobutyl acetate.

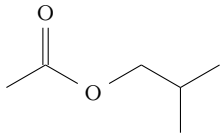


Figure 1.40: Isobutyl acetate.

  - Given data.
    - Molecular formula: $C_6H_{12}O_2$.
    - IR: 1746.
    - ^{13}C NMR: 170.2, 70.4, 27.6, 20.7, 19.4.
    - ^{1}H NMR: 3.76 (d, $J = 7.0\,\text{Hz}$, 2H), 2.04 (s, 3H), 1.97 (triplet of septets, $J = 7.0, 6.8\,\text{Hz}$, 1H), 0.95 (d, $J = 6.8\,\text{Hz}$, 6H).
  - Key signals.
    - The sole IR stretch and most downfield ^{13}C NMR peak both suggest a carbonyl: 
    - The second most downfield ^{13}C NMR peak and 3.76 ppm ^{1}H NMR peak combine to suggest a carbon adjacent to a heteroatom and bearing 2 hydrogens: 
      - ➢ Again, the molecular formula implies that the heteroatom would have to be oxygen: 
    - The two most upfield ^{1}H NMR peaks combine to suggest an isopropyl group: 
      - ➢ Indeed, in this isopropyl group, the drawn proton will split all 6 methyl protons into a doublet, and the six chemically equivalent methyl protons will split the drawn proton into a septet (the triplet part must then come from additional protons vicinal to the fragment).
    - The last remaining ^{1}H NMR peak (2.04 ppm) suggests a methyl group: 
  - We can now hijack the J values to find out exactly how to assemble these fragments.
    - The two methyl groups in the isopropyl group have $J = 6.8\,\text{Hz}$.
    - Thus, they are coupled to the other proton(s) with $J = 6.8\,\text{Hz}$. We can see that this is the sole proton in the triplet of septets, which corresponds to the hydrogen in the isopropyl group, as we would expect. This hydrogen also couples to some other group with $J = 7.0\,\text{Hz}$.
    - The other group with $J = 7.0\,\text{Hz}$ is the peak at 3.76 ppm, and which corresponds to the fragment. Therefore, we can join these two fragments to create: 
    - At this point, we've used everything except the methyl group and the carbonyl. But the only way to include both of these is to bond the carbonyl to the above fragment and then the methyl to the carbonyl. This bonding will yield the final structure in Figure 1.40.
  - Sanity check: Do the protons and carbons in isobutyl acetate have the chemical shifts we'd expect based on their position in the molecule?

^{1}H NMR	Region
3.76	α-heteroatom
2.04	alkyl
1.97	alkyl
0.95	alkyl

(a) ^{1}H NMR.

^{13}C NMR	Region
170.2	carbonyl
70.4	α-heteroatom
27.6	alkyl
20.7	alkyl
19.4	alkyl

(b) ^{13}C NMR.

Table 1.6: Correlating isobutyl acetate's NMR peaks and functional groups.

    - Per Table 1.6, yes!
    - Note: The 2.04 ppm peak corresponds to the methyl group α to the carbonyl.
    - Note: The 1.97 ppm peak corresponds to the substituted proton β to the oxygen.
        - ➢ Recall from Lecture 4 that this hydrogen is relatively downfield because it's surrounded by "electronegative" carbon atoms!

- When does a peak display complex splitting, versus a "simple" doublet, triplet, quartet, etc.?
    - You're a "something of somethings" if you couple chemically distinct protons, and you're just a "something" if you only couple one type of chemically equivalent protons.