Problem Set 1

Following are the group assignments for group homework #1. The goals of this activity are to challenge you to work problems that are more complex and to practice working effectively in a group setting with people that you do not necessarily know well. The person with an 'O' after their name will be the organizer of the group and will be required to arrange meeting times and places to complete the assignment. The person with a 'W' after their name will be the person who prepares the final written assignment to be turned in for a grade. Groups will be re-assigned and roles will be changed for each set of homework, so that you have the opportunity to work with a variety of different people and in different roles throughout the semester.

On the next page is the 'grading' scale for each member of your group. After you have completed the homework assignment, please 'grade' the performance of each group member, including yourself, and turn in separately from the group homework for confidentiality purposes. A person who does not show up for the group meetings or does not participate in the problem solving process should receive an 'F' for the group grade. A person who contributes, asks questions, and helps the other group members to understand the problem and answer deserves an 'A'. A person who requires a little extra help and needs another group member to explain a topic **does not** deserve an 'F'. Their lack of understanding will help you as well because you will have to clearly explain the topic to him/her. If you choose to not turn in grades for your group members, I will assume 'average' participation for the entire group.

Submit only one set of answers per group. Please work with your assigned partners to prepare your final draft of answers. You may find it useful to xerox copies of the answer set, so that each group member may have it for reference. Please do not consult with anyone other than people in your group; you may consult me for question clarification only. You may use your textbooks and any other written references from the library. Do not copy anyone else's work. The honor code pledge is printed on the top of the "grading" scale page. By turning this page in, you are acknowledging that you have read and understand the privileges and responsibilities that this code bestows.

This is due Friday, September 16, at the beginning of class.

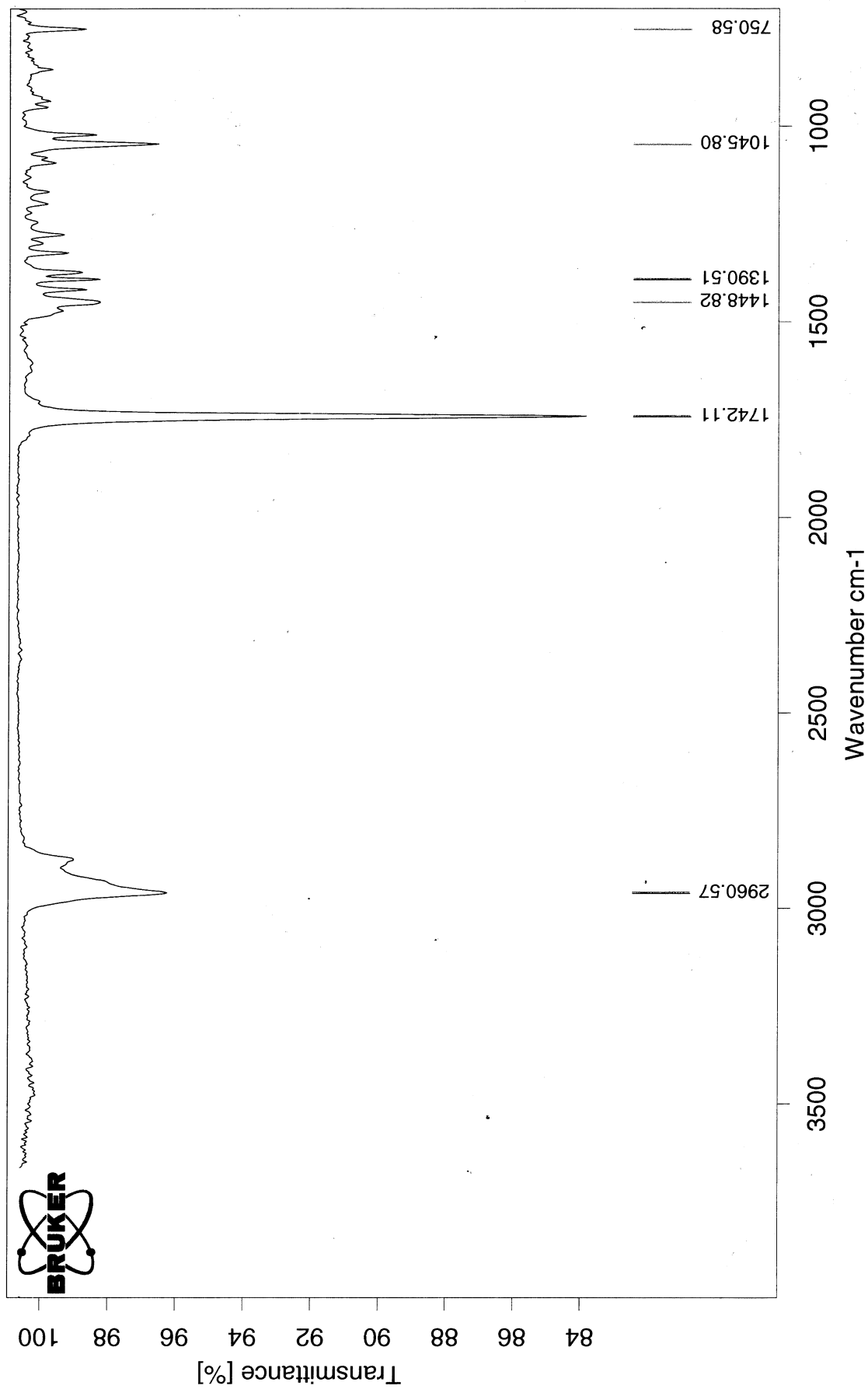|			
Alex Burum Danielle Forstner (O) Jeffrey Rock Ellen Sauter Ben Treichel (W)	Andrew Bryan (O) Erin Ge Doug Schroeder Sunny Sonnabend (W) Luis Valle	Kristen Burson (W) Bryce Gode Bonginkosi Sibiya (O) Michael Stangler Krista Cruse	Kyle Carlson Nissa Hannemann Jill Verchota Zach Alwine (W) Bridget Hoesley (O)
Holly Cooper Steve Howard (O) Zach Walgenbach (W) Michael Butterworth Lauren Hom	Dan Freeman (O) Scott Kyser (W) Alex Burleigh Nate Erickson Fue Vang	Maari Hanson Krystal Long (W) Chris Ditlevson Jennifer Krantz (O) Alyssa Brooks	Ben Levy Brittany Murphy (O) Eric Kraska Raychal Zupancich (W) Brian Castle
Steph Lewis (O) Kathryn Pesch Nick Malm (W) Rachael Chaska Matthew Hoke	Chris Lund Matthew Royer (O) Eric Nelson (O) Micah Deitz Timothy Lamanna	Emily Pelton Stephanie Soiseth Rachel Roberg (W) Douglas Durand (O) Jenna Paulsen	Amy Waldner Kelly Rozenboom Danielle Burras (O) Sarah Erickson (W) Rachel Poppy
Leah Swanson David Wold (O) Ryan Casper Aaron Insley (W) Marcus Perry	Brianna Vaa (O) Conner Ziegler Mackenzie Consoer Brent McConahey (W) Aaron Roessler	Morgan Wells Nate Bower (O) Rachel Elvebak (W) Kristen Oldenburg	Trevor Wittwer Arie DeGrio Jenna Kesty (O) Eric Anderson (W)
David Wray (W) Sarah Duncan (O) Chris Leonard Kari Maffit	Emily Barnard (O) Justin Hahn Matija Novakovic (W) Chad Olson		

Peer Evaluation Grading Sheet

On my honor, I pledge that I have not given, received, nor tolerated others' use of unauthorized aid in completing this work.

_____	A	B	C	D	F
Group member #1					

_____	A	B	C	D	F
Group member #2					

_____	A	B	C	D	F
Group member #3					

_____	A	B	C	D	F
Group member #4					

_____	A	B	C	D	F
Group member #5					

Comments:

1) (20 pts) A molecule with a molecular formula of $C_{10}H_{16}O$ was isolated from the essential oil of *Artemisia vulgaris*. The waxy solid was found to have an optical rotation of $[\alpha]^{25}_{D} = +44.1°$ (*c*=10, EtOH). It gave a positive qualitative functional group test for DNP, but negative for the ignition, iodoform and chromic acid tests. It does not discolor bromine solutions. On the following pages are several spectra of the compound (IR, ^1H NMR, ^{13}C NMR, DEPT, Hetcor).

Propose a structure and assign the resonances in the IR, ^1H NMR, and ^{13}C NMR. (Do the best you can and be sure to provide some reasoning behind the assignment.)
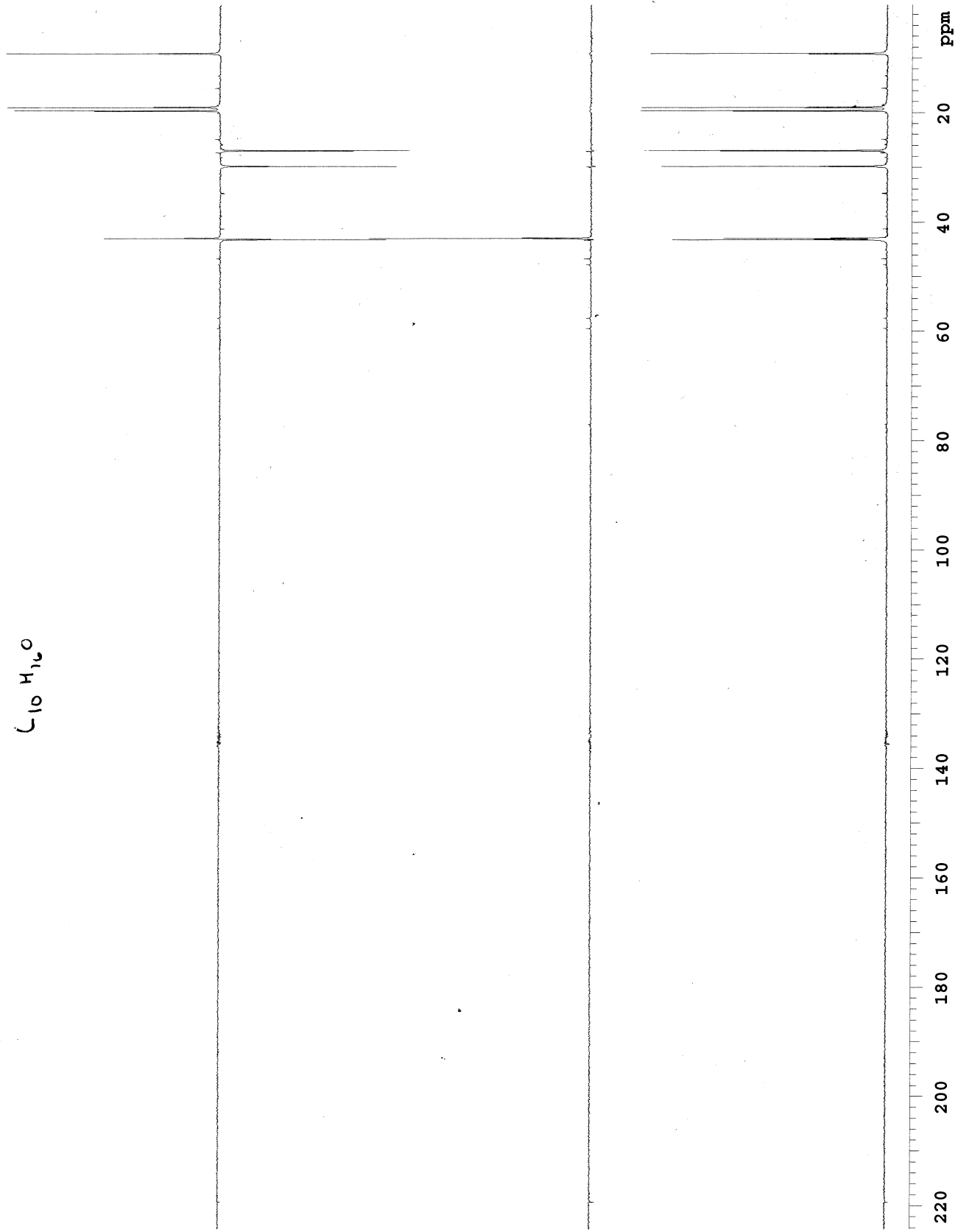
$C_{10}H_{16}O$

Transmittance [%]

Wavenumber cm-1

750.58
1045.80
1390.51
1448.82
1742.11
2960.57

BRUKER

C₁₀H₁₆O

ppm

2.4   2.2   2.0   1.8   1.6   1.4   1.2   1.0   0.8

$C_{10}H_{16}O$
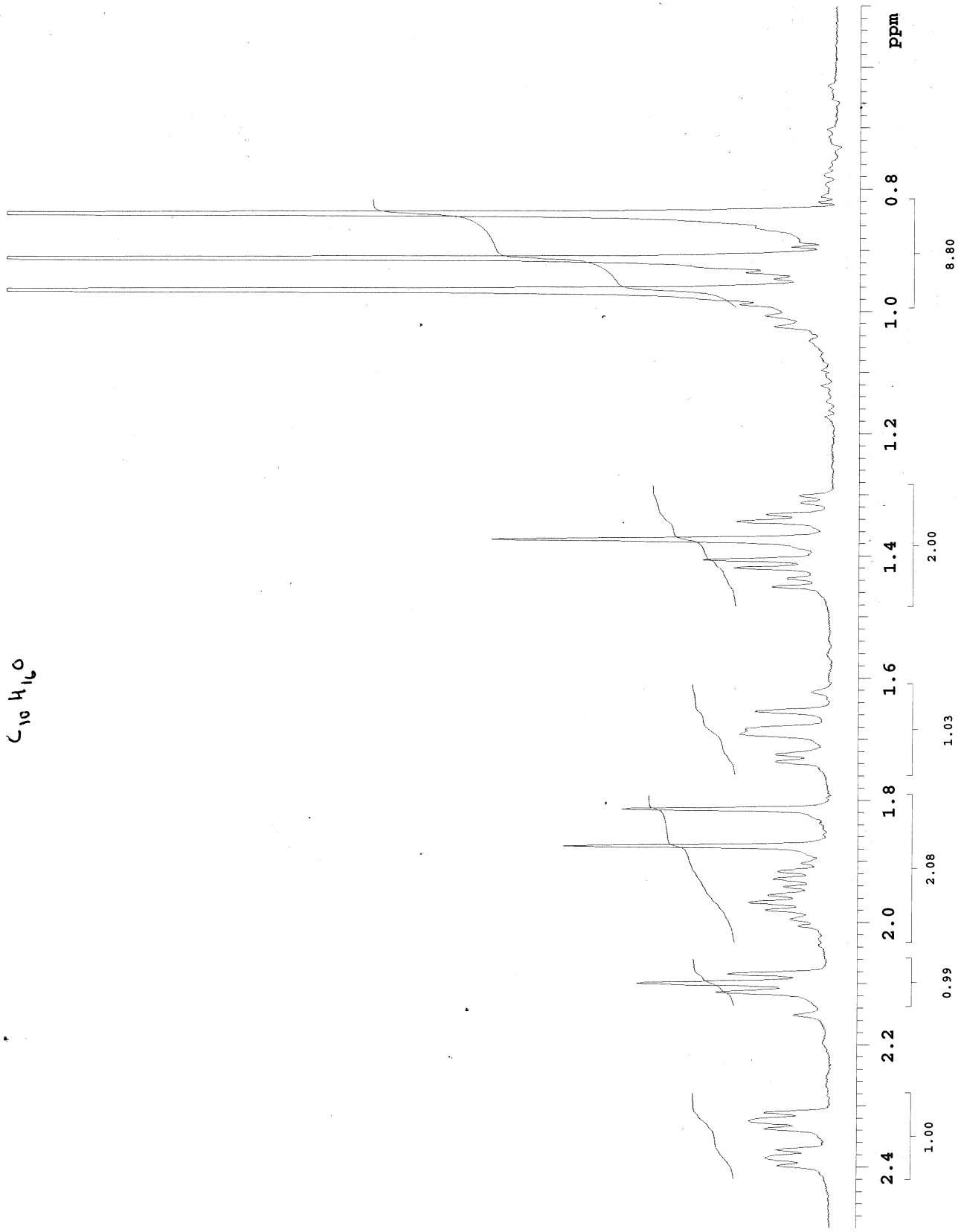
INDEX	FREQUENCY	PPM	HEIGHT
1	16532.325	219.108	17.8
2	5841.932	77.425	51.4
3	5809.867	77.000	53.0
4	5777.801	76.575	50.1
5	4337.146	57.482	36.3
6	3514.896	46.584	38.4
7	3253.792	43.124	148.3
8	3241.195	42.957	128.3
9	2248.311	29.798	155.6
10	2030.724	26.914	162.0
11	1478.740	19.598	156.4
12	1431.787	18.976	146.5
13	683.975	9.065	135.4

ppm
220 200 180 160 140 120 100 80 60 40 20

$C_{10}H_{16}O$

ppm
20
40
60
80
100
120
140
160
180
200
220
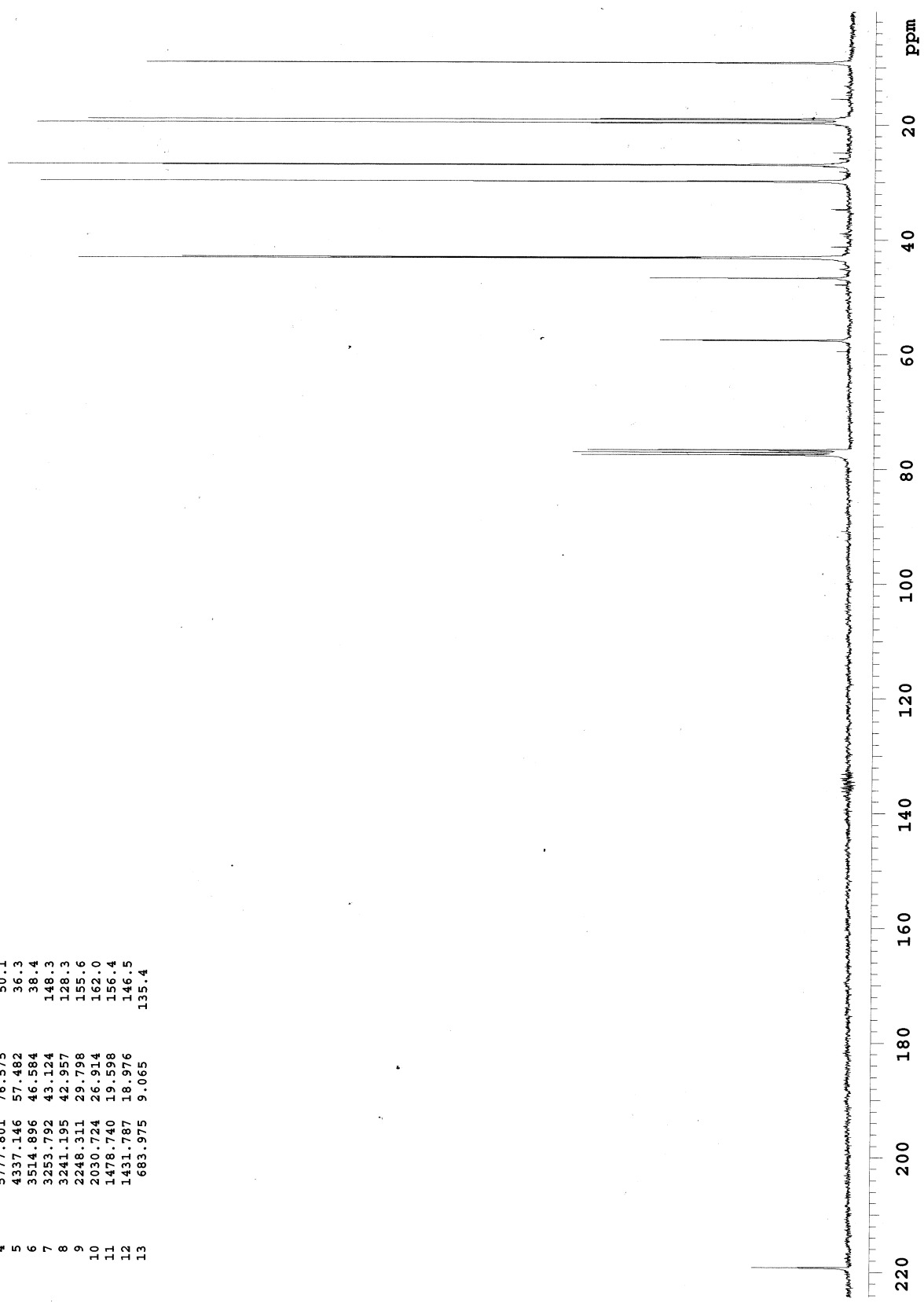
C₁₀H₁₆O

13C OBSERVE

Pulse Sequence: hetcor

Solvent: cdcl3
Ambient temperature
GEMINI-300BB "unknown"

Relax. delay 2.000 sec
Acq. time 0.085 sec
Width   6035.2 Hz
2D Width 900.2 Hz
64 repetitions
64 increments
OBSERVE C13, 75.4528156 MHz
DECOUPLE H1, 300.0710345 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
F1 DATA PROCESSING
  Line broadening 0.3 Hz
FT size 1024 x 256
Total time 2 hr, 29 min, 23 sec

F2
(ppm)

10

20

30

40

50

60

70

F1 (ppm)

2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2
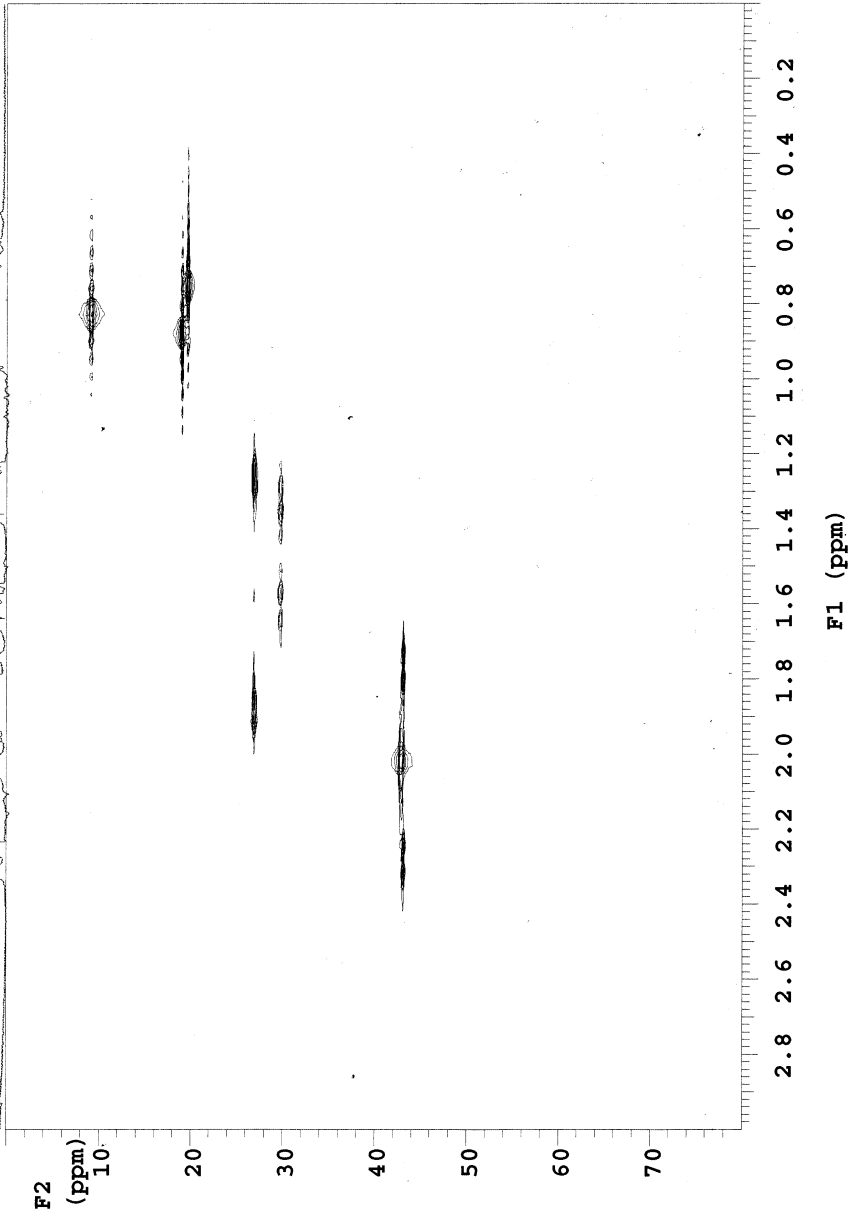
2) (15 pts) Moclobemide (**1**, marketed as Manerix by Roche) is an inhibitor of the enzyme monoamine oxidase (MAO). Clinically, this means that is can be used to treat depression. Neurotransmitters that contain a primary amine functional group, such as seratonin (**2**), norepinepherine (**3**), and dopamine (**4**), appear to play a major role in mood and emotion. Neurotransmitters are released from one neuron (nerve cell) into the synaptic cleft (the area between an axon and dendrite from an adjacent neuron). These molecules then find specific places (called receptors) on the surface of the dendrite and cause the neuron associated with that dendrite to "fire." This causes the transmission of information from one neuron to another. Once the neuron fires, the need for the neurotransmitter diminishes, so the synaptic cleft must be cleared of the signaling molecules. This can happen either by "reuptake" (absorption of the molecule back into the axon from which it came) or it can be destroyed in the synaptic cleft. The molecules **2**, **3**, and **4** are cleared through a degradation process mediated by MAO. Depression often results from a lack or imbalance of these neurotransmitters. By inhibiting the mechanism that destroys them, the concentration of these molecules can be increased, and the clinical signs of depression are alleviated.
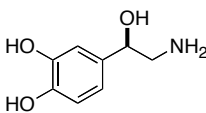
The synthesis of moclobemide starts with mopholine (**5**) and ends with the acylation of **6**. **Propose a synthetic route for the conversion of 5 to 6. You may use any inorganic reagents, but organic reagents must contain 2 or fewer carbons.**
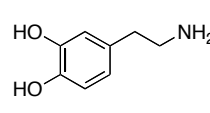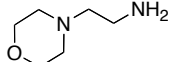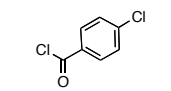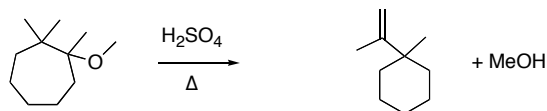

1

2

3

4

5

6
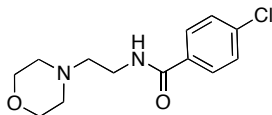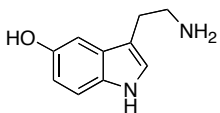
3) (15 pts) Provide a mechanism, using curved arrow notation, that explains the following reaction:


4) (15 pts) Morphine (**7**) and codeine (**8**) are isolated from opium poppies. Morphine is a potent analgesic (pain reliever). Codeine is not nearly as good an analgesic, but is a good antitussive (cough suppressant). It is thought that codeine is not an analgesic at all, but rather is converted to morphine by the action of an enzyme. Without knowing what the enzyme is, what is the mechanism through which this enzyme acts (*i.e.* use curved arrow notation)? It might help if you use H-A, B⁻, and Nu⁻ as general "reagents."
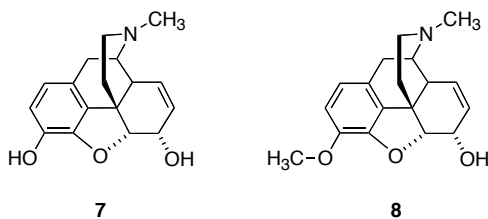

5) (15 pts) Sugars that contain 6-membered rings are important biological molecules. Although glucose (**9**) is the most common example used, there are many sugars that play important roles. In many biochemical reactions that involve sugars, the carbon bearing two single bonds to oxygen (*i.e.* the carbon labeled ***a***) is the reactive center. To interrupt the enzymes that carry out these various transformations, chemists can make molecules that look like the substrate for the enzyme, but which cannot actually do the chemistry of the native sugar substrate, by removing the oxygen found in the ring of the sugars. In essence, the enzyme is tricked into thinking it is bound to the right molecule but gets stuck when it cannot carry out the right chemical transformation. This ties the enzyme up and "removes" it from the chemical equilibria in the cell.

   Starting from cyclohexylbromide (**10**), show how one might make the sugar mimic *trans*-1,2-dihydroxycyclohexane (**11**).
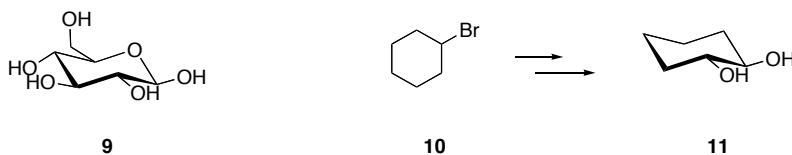
6) (20 pts) Given what you have learned about the reaction of ethers with Brønsted acids, propose a what product(s) will be formed and provide a mechanism, using curved arrow notation, for the following reaction:

HCl
————→   ????
H_2O
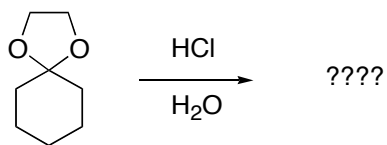
Extra Credit: (10 pts)

Meperidine (**12**) was discovered in Germany in 1937. It is only $1/8^{th}$ as potent as morphine in pain relief, but is much shorter acting and is more quickly metabolized. Consequently, it was thought that this drug might be a good substitute for morphine without having the liability or tolerance or addition. Unfortunately, this is not the case. It is, however, still used as an obstetric and anesthetic premedication. As an obstetric analgesic, it appears to depress the respiration of the fetus less than morphine and does not cause constipation like morphine (much to the relief of the patient). The following is a "road map" for the synthesis of meperidine. Fill in the missing reagents/products for the scheme. You may need to consult chapters in your book that have not yet been covered, but you actually know everything you need to figure it out.