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CH 15: Benzene and Aromaticity

Topics:

Benzene and Benzene Derivatives

Naming

Unusual Stability of Aromatics

Determining Aromaticity

Other Aromatic Species

Aromaticity and Biomolecules

Aromatic ^{1}H and ^{13}C NMR and IR.

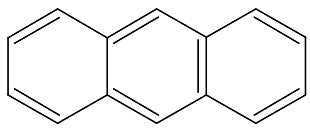
Summaries

1. Name aromatics and draw aromatics from names.
2. Draw resonance structures of aromatics. What is the structure of benzene?
3. What is aromaticity?
4. How is aromatic stability calculated?
5. Write a molecular orbital diagram of benzene. Write an orbital diagram of any aromatic polygon.
6. Determine which organic cyclic cations and anions are aromatic, anti-aromatic or not aromatic.
7. Determine the aromaticity of heterocylics.
8. Determine if aromatic N compounds are basic (nucleophilic) or not.
9. Understand ^{1}H NMR of aromatics. Predict structure and assign NMR's.
10. Understand ^{13}C NMR of aromatics. Predict structure and assign NMR's.
11. Retain a little bit about IR of aromatics.

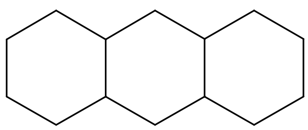
Benzene and Derivatives: Unusually Stable Molecules

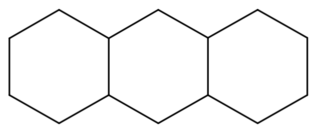
We have a whole two chapters on Aromatic molecules. Aromatic molecules are so interesting because they are unusually _______________
Structure of Benzene: It's fun to draw resonance structures of Benzene:
Draw two:

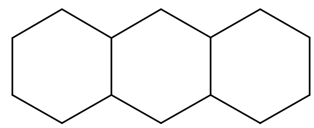
How about anthracene:



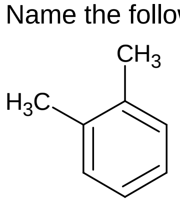
Draw 3 more resonance structures!

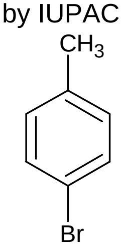


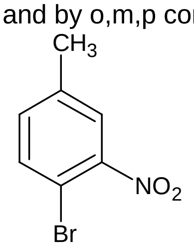


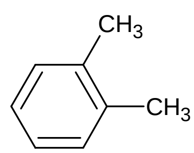


Naming:
Name the following by IUPAC names and by o,m,p convention:



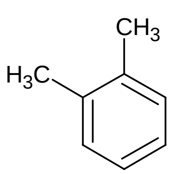


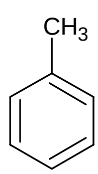


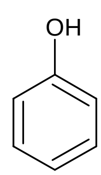


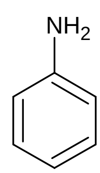
IUPAC
o,m,p:

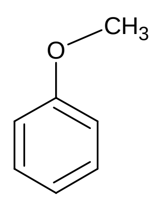
Common names. You can't avoid these names so don't even try!

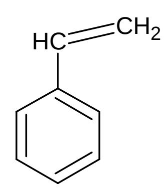












o-xylene toluene phenol aniline anisole styrene

IUPAC
Names

Sometimes benzene is a substituent: Draw
(S) 2-Phenyl pentane Benzyl chloride Diphenyl acetylene trans-1,2-diphenyl ethylene

Stability of Benzene

What is aromaticity?

What is the difference between benzene and cyclohexatriene?

(a) How about structure? Normal C=C bond length=134pm normal C-C bond length=154pm.

What is the meaning of this?

What bond lengths would we expect for cyclohexatriene?

C-C

C=C

You can refer to butadiene, (C-C)=148pm; (C=C)=135pm.

What bond lengths would we expect for benzene?

C-C

C=C

Can you justify the actual C-C and C=C bond lengths being the same and equal to <u>140pm.</u>

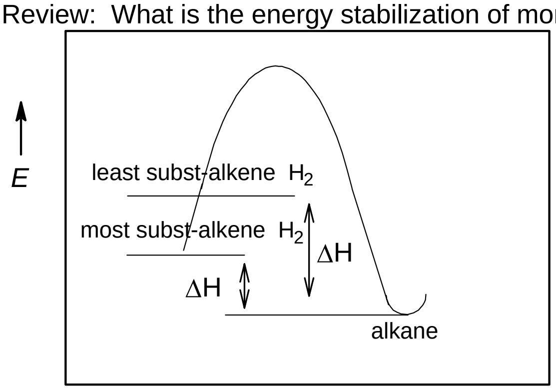
(b) What about heats of hydrogenation?

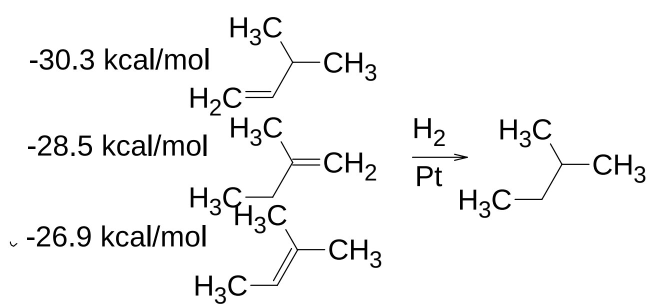
ΔH(Hydrogenation) = Heat released when a pi bonds reacts with H_2.

$R_2C{=}CR_2 + H_2 \rightarrow HR_2C\text{-}CR_2H$ ΔH(RXN) =ΔH(Hydrogenation)

Typically, ~30Kcal/mole for the above reaction.*

Review: What is the energy stabilization of more substituted alkenes vs less substituted alkenes.

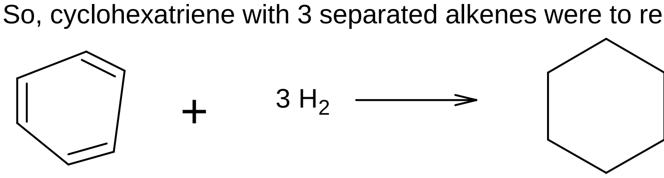




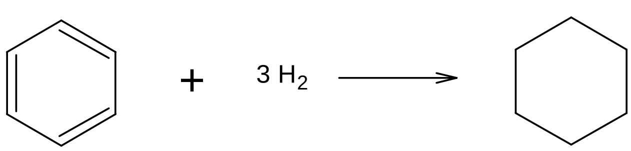
The alkene with lowest or highest ΔH(Hydrogenation) is the most or least stable?

For ease of calculation assume 30 kcal/mol for each double bond.

So, cyclohexatriene with 3 separated alkenes were to react with 3 moles of H_2,



What is the ΔH(Hyd) =?______________________



<u>Measured ΔH(Hyd) for benzene = 50Kcal/mol.</u>

Benzene has a much smaller ΔH(Hyd) than 3 separated double bonds.This means that less energy is released in the reaction. We can say that ____________ Kcal/mole is hidden or tied up in Benzene and cannot come out in this reaction.

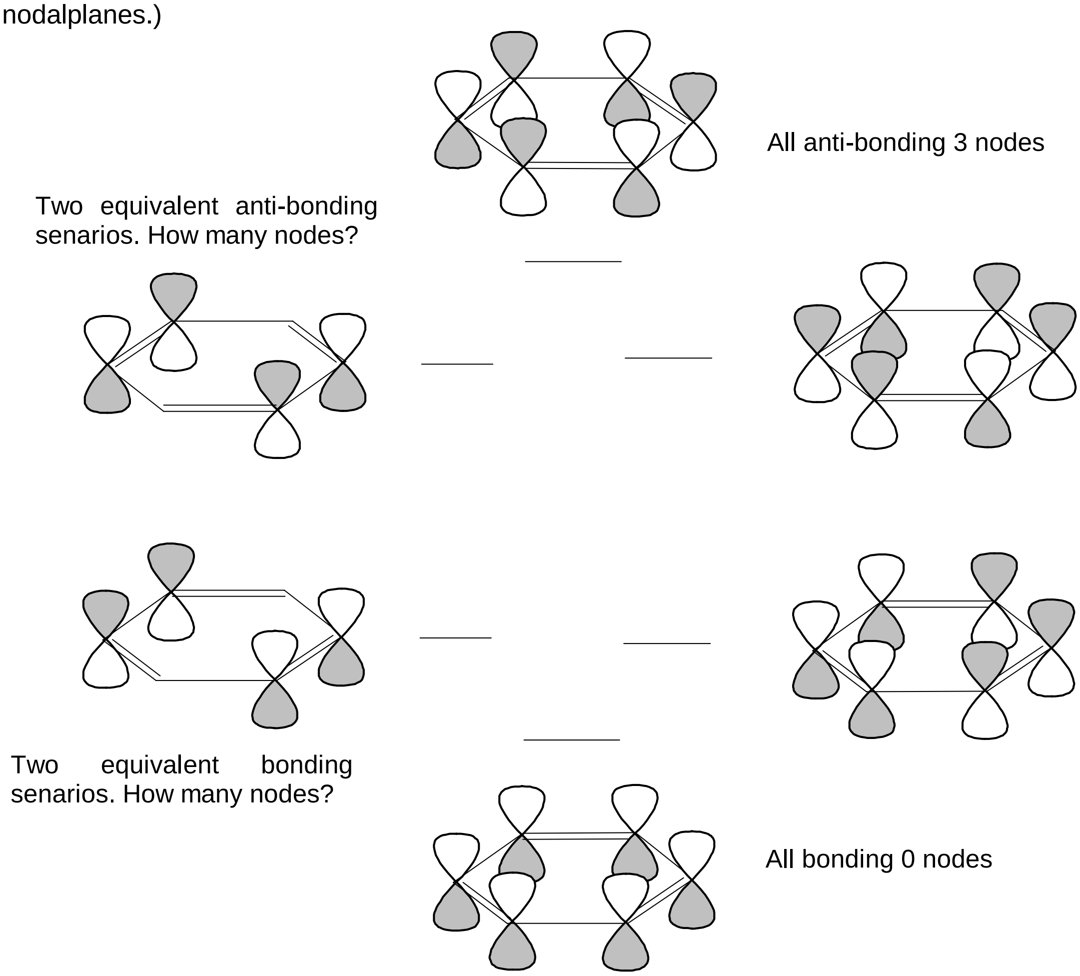
This difference is called the resonance energy of benzene. That is, less energy is released when benzene is hydrogenated. The double bonds must be separated from each other (or the conjugation* must be broken) in order to react.

*One problem with this type of calculation is that the actual first hydrogenation energy is not 30 Kcal/mole, but 28 Kcal/mole. The second double bond releases 30 Kcal/mole. Why is 2 Kcal/mole less released for the first double bond?

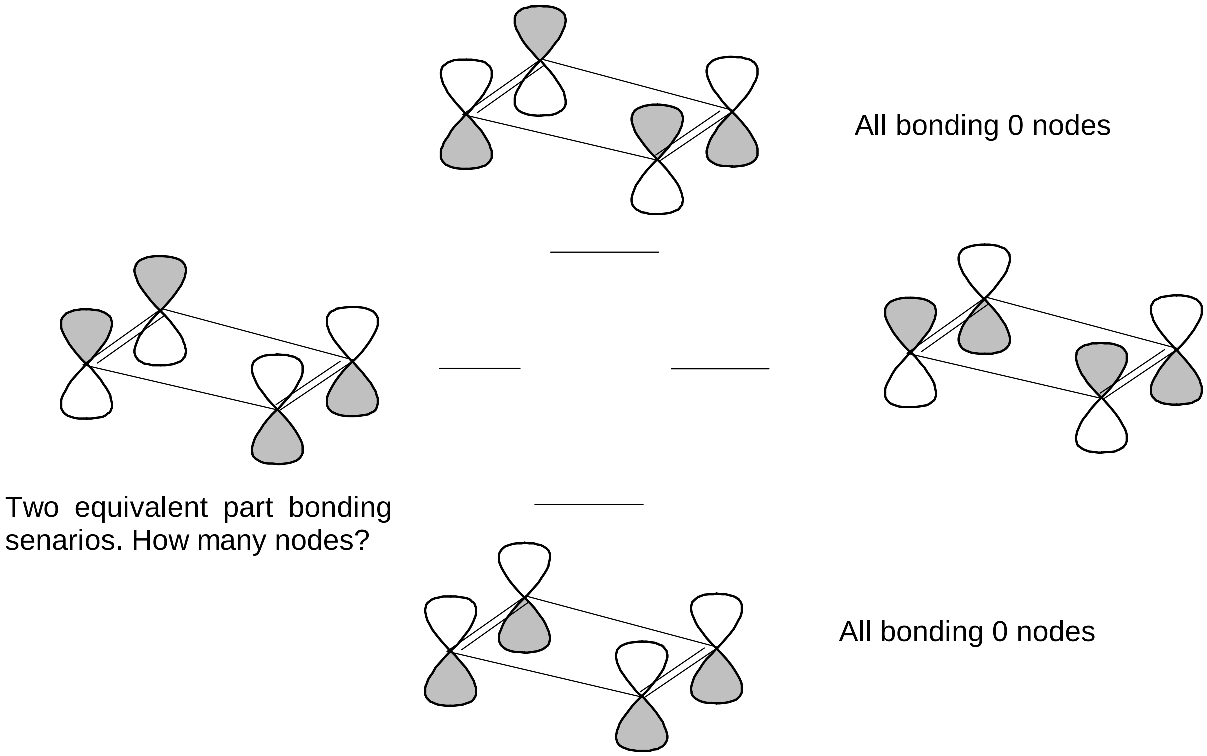
Huckel Rule: Since Benzene is so stable, people have tried to find the property that makes benzene so special.
We have come up with the following rules so far.
(1) A cyclic compound that is planar.
(2) All sp^2 atoms or ________________.
(3) The number of pi electrons must fit an equation based on 4n+2, where n is a natural #: from the set (0,1,2,3,4,…). Giving solutions = 2, 6, 10, 14, 18, ….
Molecules with these properties are called __________________ and are unusually ___________

Molecules with the alternate even number electrons (4, 8, …) are called anti-___________ and are un-________________.
<u>Only simple cyclic compounds can possibly be anti-aromatic, since most molecules will distort from planarity to avoid being destabilized electronically!</u>
These are numbers are derived by the molecular orbitals of the molecules involved.

Justification for the Huckel Rule
Examine the orbitals of benzene. (Only the three of the orbitals are filled. Don't memorize – just count nodalplanes.)

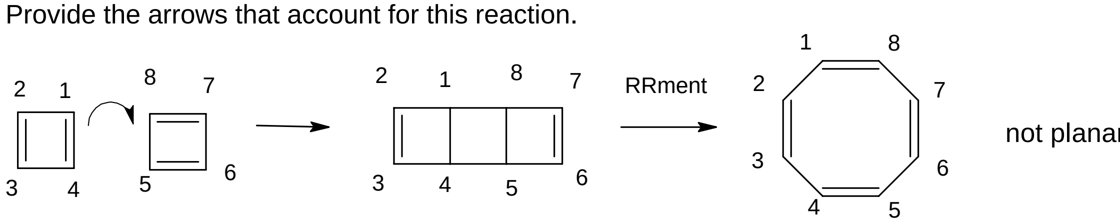


These orbitals are made from 6 p orbitals. How many e⁻s are in the benzene system? __________Put these electrons in the benzene system above. Use Hund's rule. Are all the electrons paired?
Now examine the bonding orbitals for cyclobutadiene: (The highest orbital is not shown).



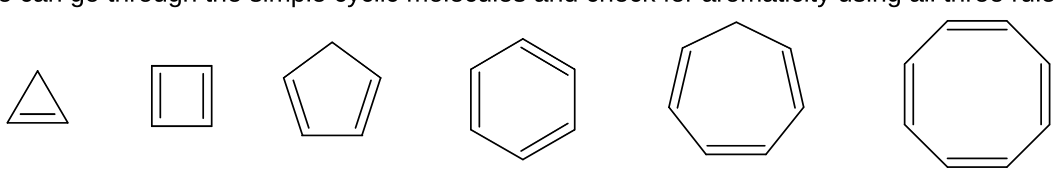
These orbitals are made from 4 p orbitals. How many e^{-}s in the butadiene system? __________
Populate the orbitals according to Hund's rule. What is the result? Is this a stable molecule?
We call this situation **antiaromatic** and these molecules do not hang around.

Fate of cyclobutadiene
Provide the arrows that account for this reaction.



If planar would cyclooctatetraene be aromatic? How does cyclooctatetraene avoid being antiaromatic?

Applying the Huckel Rule: Check the following structures and ions for aromaticity.
We can go through the simple cyclic molecules and check for aromaticity using all three rules.



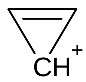
ring= 3 4 5 6 7 8
To orient the orbitals use the shape of the polygon.
1. Put an apex down. 2. Put an orbital at every vertex. 3. Fill the orbitals with the proper # of e^{-}s.
If all of the orbitals have paired electrons the molecule is aromatic. If there are unpaired electrons, the planar structure would be anti-aromatic.

Ring=3 First draw cyclopropene. Is it aromatic? Use all rules.

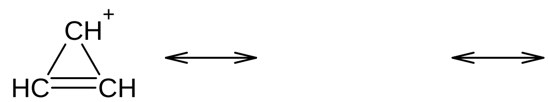
Draw the reaction that removes $H:^{-}$ (hydride) to make cyclopropene cation or cycloprenium cation

Is cypr$^+$ aromatic? How many pi electrons? Draw all 3 resonance structures.

______ ______

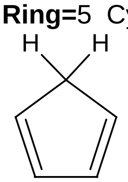


______



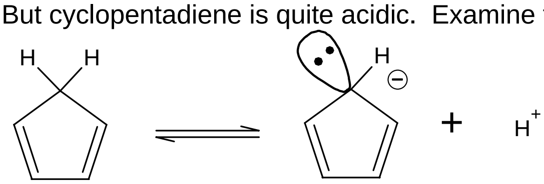
Ring=4 Butadiene (previously discussed) is unstable because it is ________________________.
Draw the square form of butadiene and fill the orbtials:

Ring=5 Cyclpentadiene is not aromatic. Why?



Are there any resonance structures?

But cyclopentadiene is quite acidic. Examine the acid dissociation reaction below.

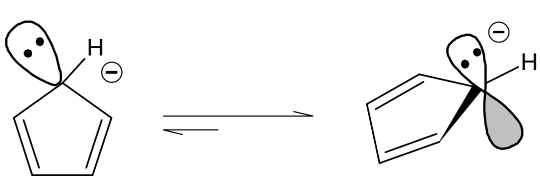


pKa = 15

Draw a pentagon and fill the orbitals for $C_5H_5^+$ and $C_5H_5^{--}$.

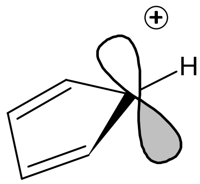
Proof of aromaticity of cylcopentadienyl anion lies in the pKa of C-H in cyclopentadiene (15) vs C-H of an aliphatic R_3C-H (45). How many times more acidic is cyclopentadiene? ________ Why is cyclopentadiene so much more acidic? It has to do with the stability of the anion. How would this work?

How is cyclopentadienyl anion aromatic? You might think that the hybrization of C with the anion is sp^3. But the C can rehybridize. When the 2 pi electrons populate a p orbital, how many electrons are in the pi system? ____________. The reaction below goes far to the right. Why? How many resonance structures are there for cyclopentadienyl anion? Draw some.

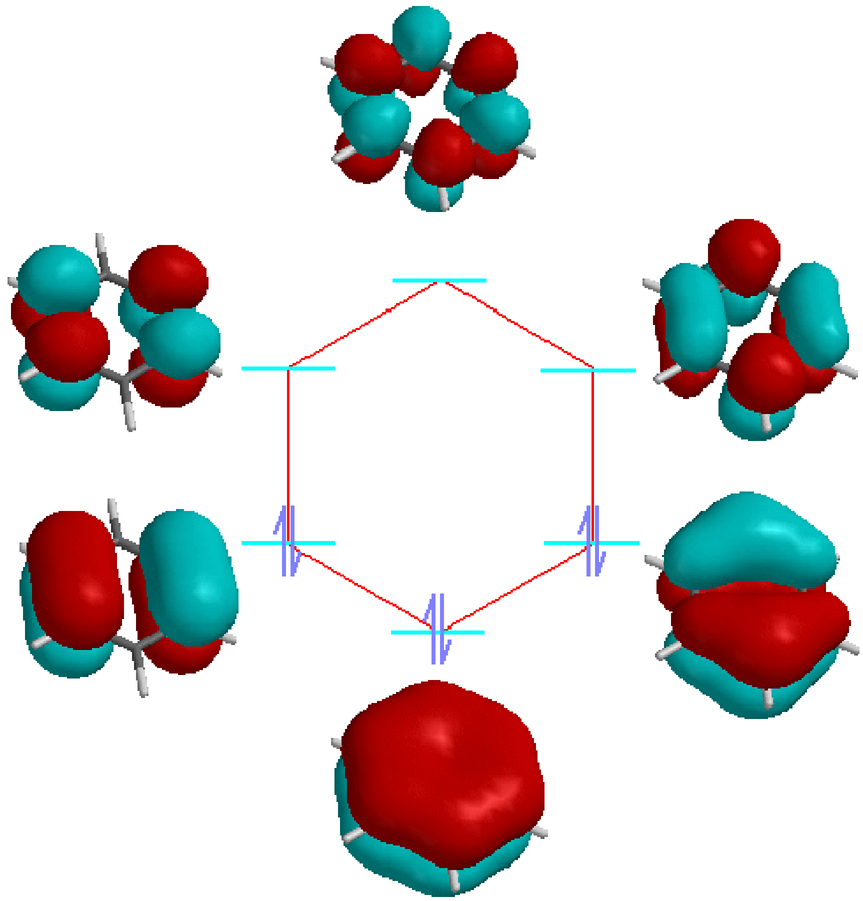


The molecule exists in the most stable form!!!!!! That's how nature works.

Practice
Removing hydride gives cyclopentadienyl cation? What about this molecule? Is it aromatic? Are there resonance structures? Draw some. This is an example where resonance does not lead to stability.

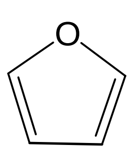


Orbitals of Benzene



http://user.mc.net/~buckeroo/ARSY.html

Benzene and Derivatives Step by Step
The Story of Furan:

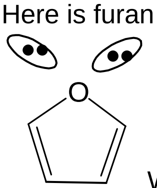


How many pi electrons from C=C? ___________

How many LP electrons on O? ___________

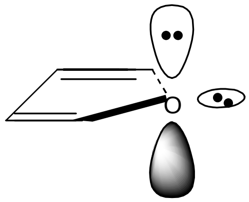
Is furan aromatic just be pi electrons from C=C? ___________

Here is furan with LP's shown:



What is the hybridization of the O? ______________

Now, what would be the advantage of one of the LP changing to a p-orbital yielding:



How many pi electrons now? _________

What is the hybridization of the O now? _______

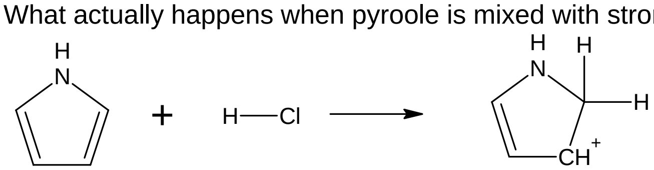
Make sure you understand why the O rehybridizes!!!!! Ask questions until you understand!

Now, consider pyrrole. Pyrrole has the formula C_4H_5N. Draw pyrrole wth its LP:

Which atom rehybridizes? ___________.
Why does pyrrole rehybridize?

Redraw pyrrole.

One way we know that pyrrole is aromatic is that the lone pair on the N: has almost no basicity. What actually happens when pyroole is mixed with strong acid is this reaction. Explain.



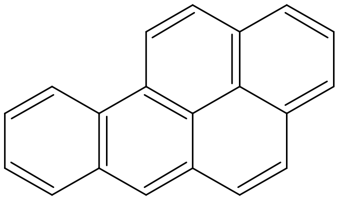
Notice the N: does not react at all. What type of reaction occurs.

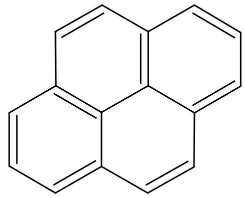
Pyridine has the formula C_5H_5N. Draw pyridine with LP.

Can the LP on pyridine be basic without breaking the aromaticity of the ring?
Draw the acid reaction of pyridine with H^+.

The pyridinium ion, $C_5H_6N^+$, has a pKa of 5. More on this in chapter 24.

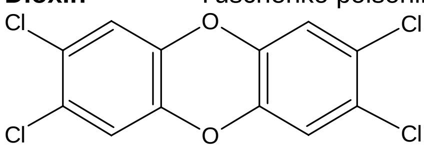
Aromatic Molecules and Cancer:
PAHs do not break down very rapidly.

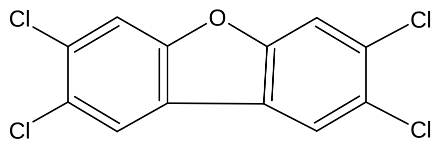




Benzo[a]pyrene Pyrene

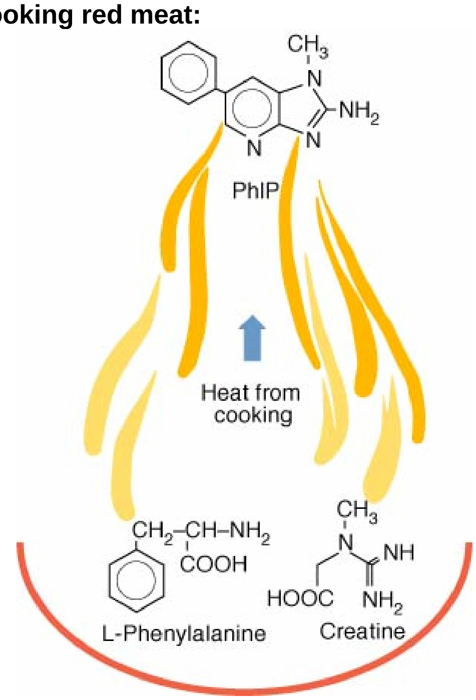
Dioxin Yuschenko poisoning agent





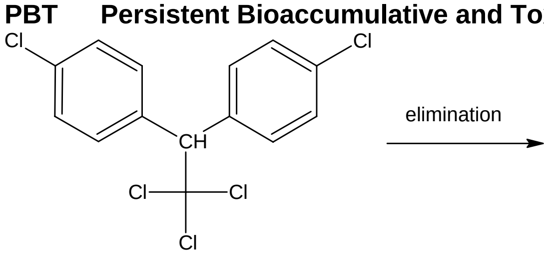
2,3,6,7-tetrachlorodibenzodioxin 2,3,6,7-tetrachlorodibenzofuran
stays in the environment for up to 7 years.
http://www.websorcerer.com/Dioxin/index.html

HCAs from cooking red meat:



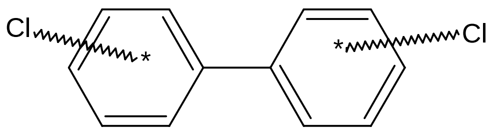
http://www.envimed.com/emb14.shtml http://neoplasia.nci.nih.gov/ccs/results.html

PBT Persistent Bioaccumulative and Toxic Chemicals --- mostly pesticides



DDT DDE
para-**D**ichloro**d**iphenyl**t**richloroethane
http://www.epa.gov/opptintr/pbt/fact.htm http://pops.gpa.unep.org/01what.htm
http://www.ecoinfo.ec.gc.ca/env_ind/region/toxin_descript/toxin_description_e.cfm

PCB's



poly-chlorobiphenyls

More on aromaticity and basicity

Let's go over the basicity of N: Ammonia is a weak base. Draw the reaction of NH_3 with water:

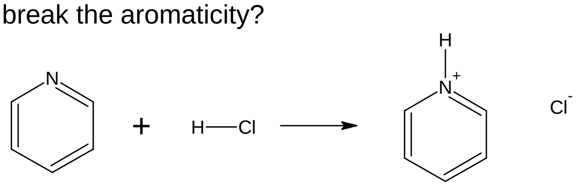
<u>For practice: Given that pKa(H_2O)=16, pKa(NH_3)=33, pKa(NH_4^+)=9, predict the direction and extent.</u>

Can pyrrole be an effective base?

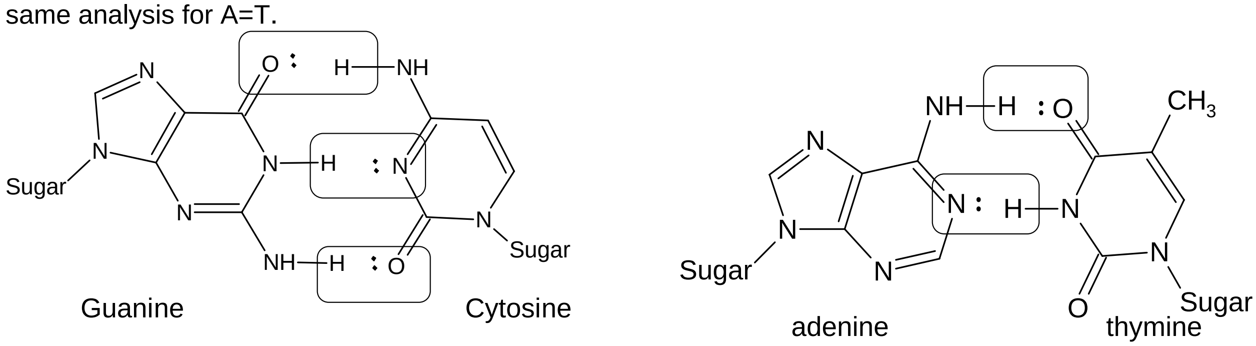
What is the problem with the protonated pryrrole mentioned above?

Can pyridine be an effective base?

Does the cation break the aromaticity?



We can relate this property to H-bonding: Consider these bases. Are the bases aromatic? Explain the middle H bond. Circle the pyridine type N's and put a box around the pyrrole type N's. You can do the same analysis for A=T.



a purine a pyrimidine a purine a pyrimidine

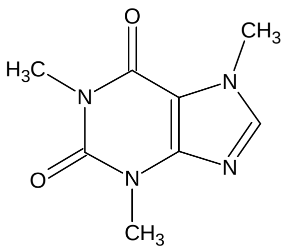
http://www.imb-jena.de/IMAGE_BPDIR.html

The H-bonding must occur like this. What would happen if the cytosine slipped down. Could the N-H on the cytosine be H-boned by the N: from the guanine. Why or why not?

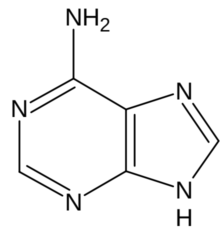
Other examples of aromatic molecules you might know. Consider the NSAIDS: These molecules depend on the stable scaffold of the aromatic system.

Salicylic Acid Aspirin Acetaminophen Ibuprofen Naproxen

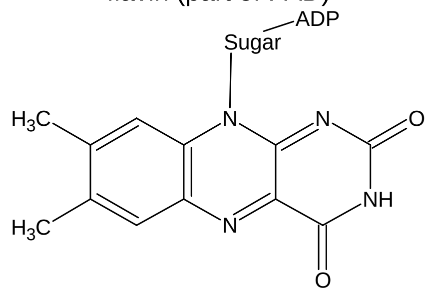
Caffeine



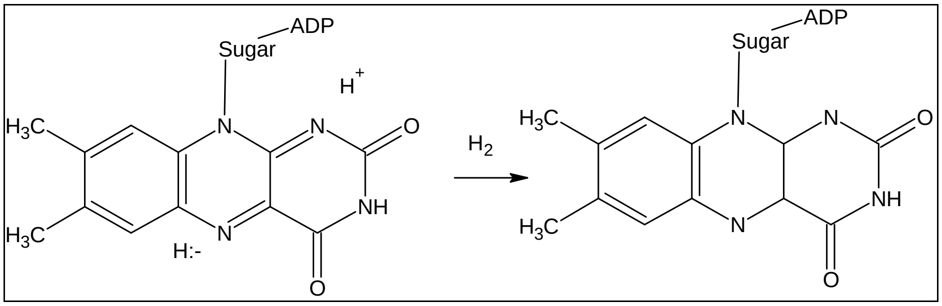
Adenine (part of ATP)



flavin (part of FAD)

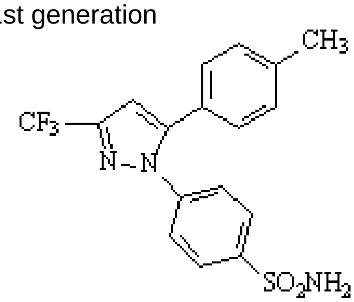
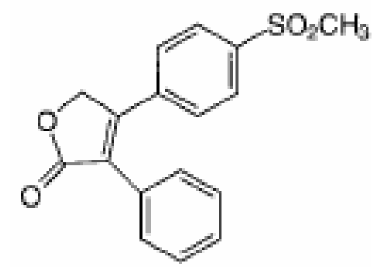
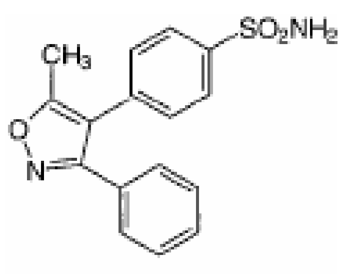
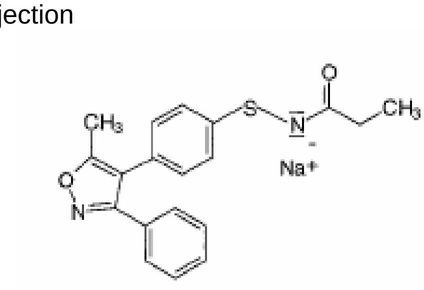
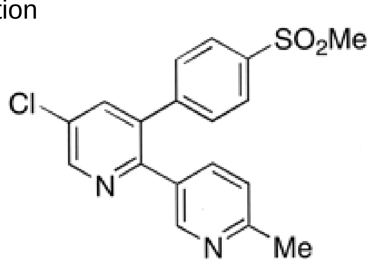
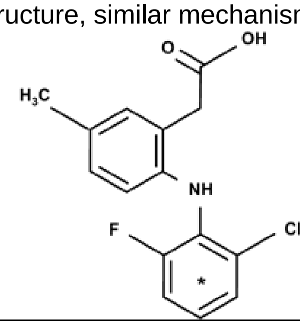


FAD



$FADH_2$

More advanced NSAIDS – Cox-2 Inhibitors

Celecoxib (Celebrex™) Pfizer, 1st generation 	Rofecoxib (Vioxx™) Merck, 1st generation 
Valdecoxib (Bextra™) Pfizer, 2nd generation 	Parecoxib (Dynastat™) Pfizer, 2nd generation Prodrug of Bextra IV injection 
Etoricoxib (Arcoxia™) Merck, 2nd generation NDA under review IV injection 	Lumiracoxib (Prexige™) Novartis, 2nd generation Phase III trials Distinct structure, similar mechanism. 

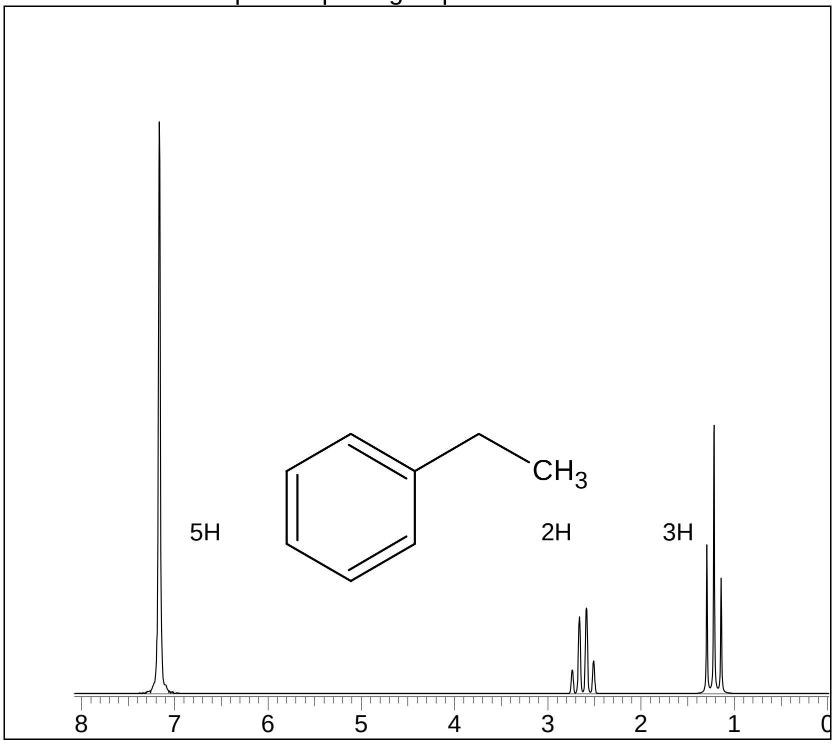
http://www.rci.rutgers.edu/~sji/GROUPFINAL111.ppt

Sex link to aromaticity? http://www.ceri.com/q_v7n2q3.htm

Aromatic NMR

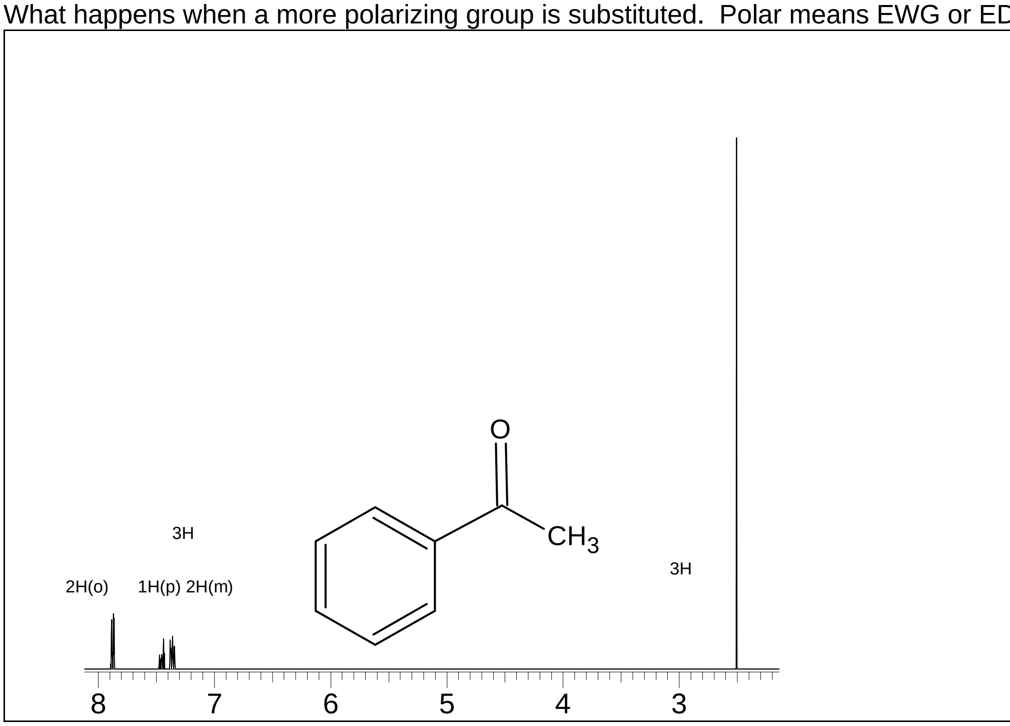
Single substitution

First consider a simple nonpolar group on benzene.



Notice that there is a peak between 6-8 (aromatic) that integrates to 5H. Notice the lack of splitting.

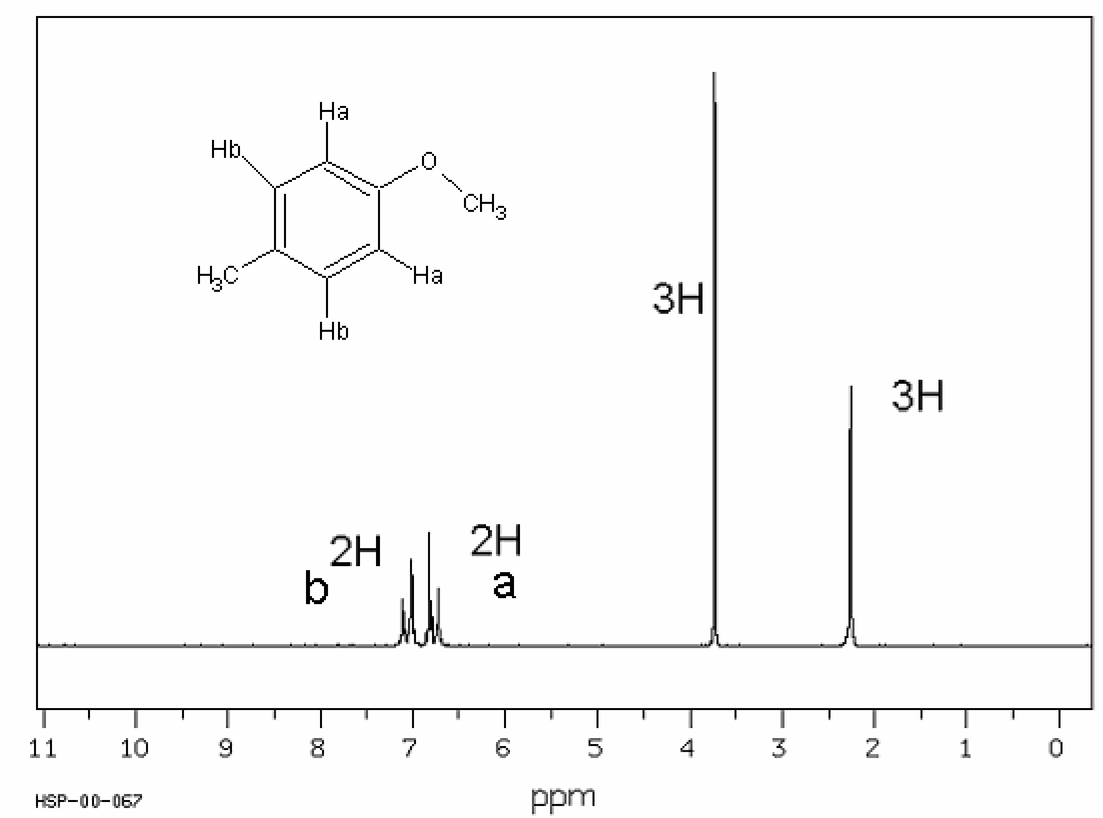
What happens when a more polarizing group is substituted. Polar means EWG or EDG.



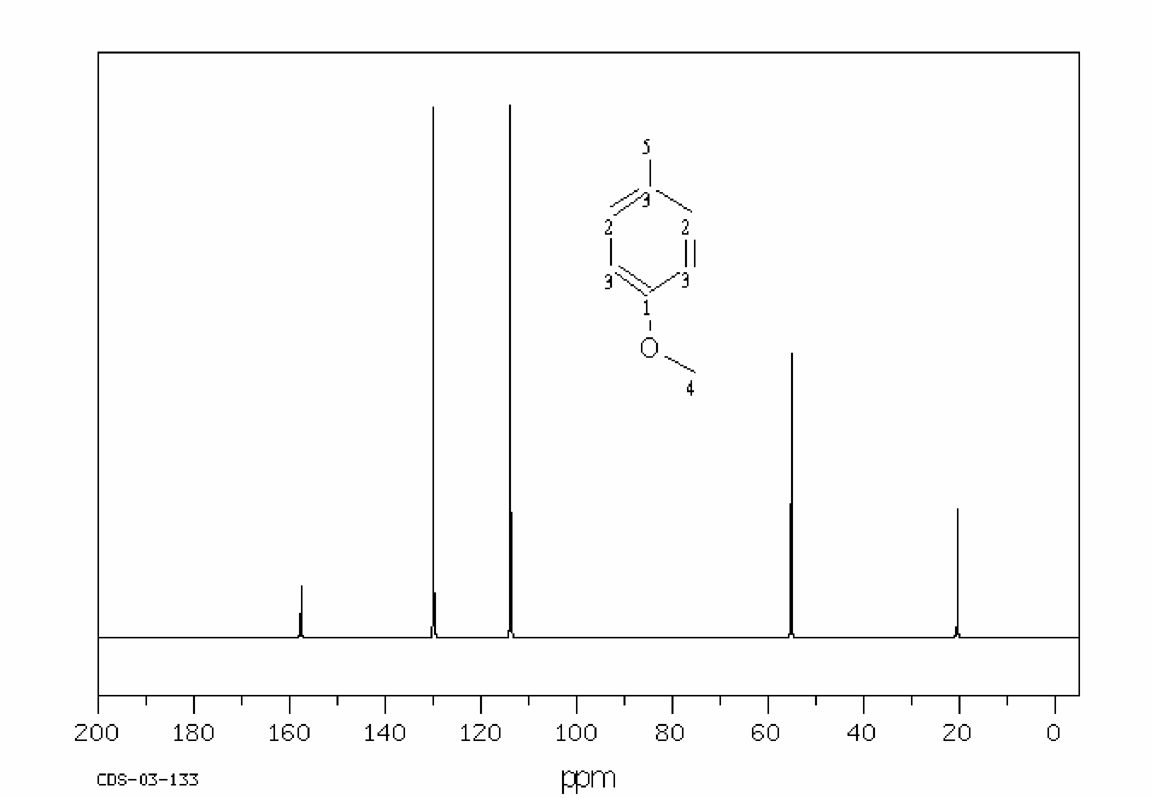
Notice that the aromatic region is split into at least two parts, 2:3. The 2 are usually ortho because the polar groups influence is greatest in that postion. The 3 is usually meta and para, because they are the farthest away from the substitution site.

Now consider ortho, meta para. Para is the easy one. Ortho and meta are messy.

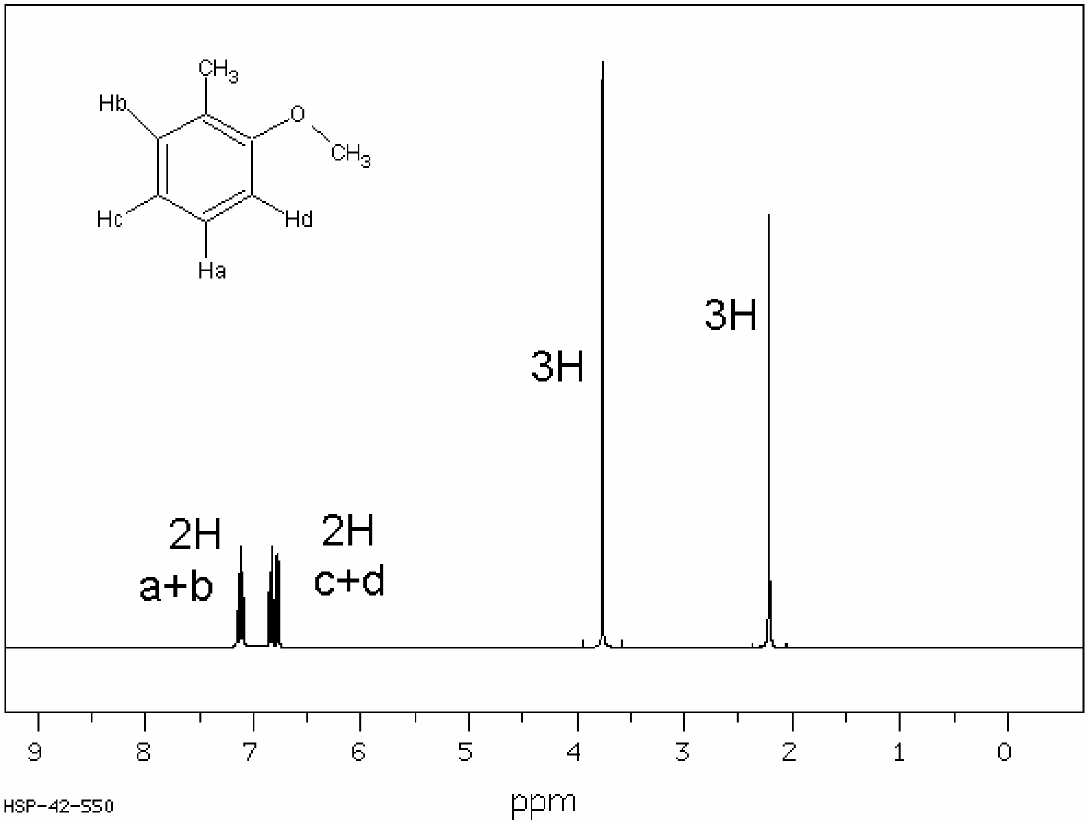
p-methoxytoluene: (top ^{1}H NMR bottom ^{13}C NMR)



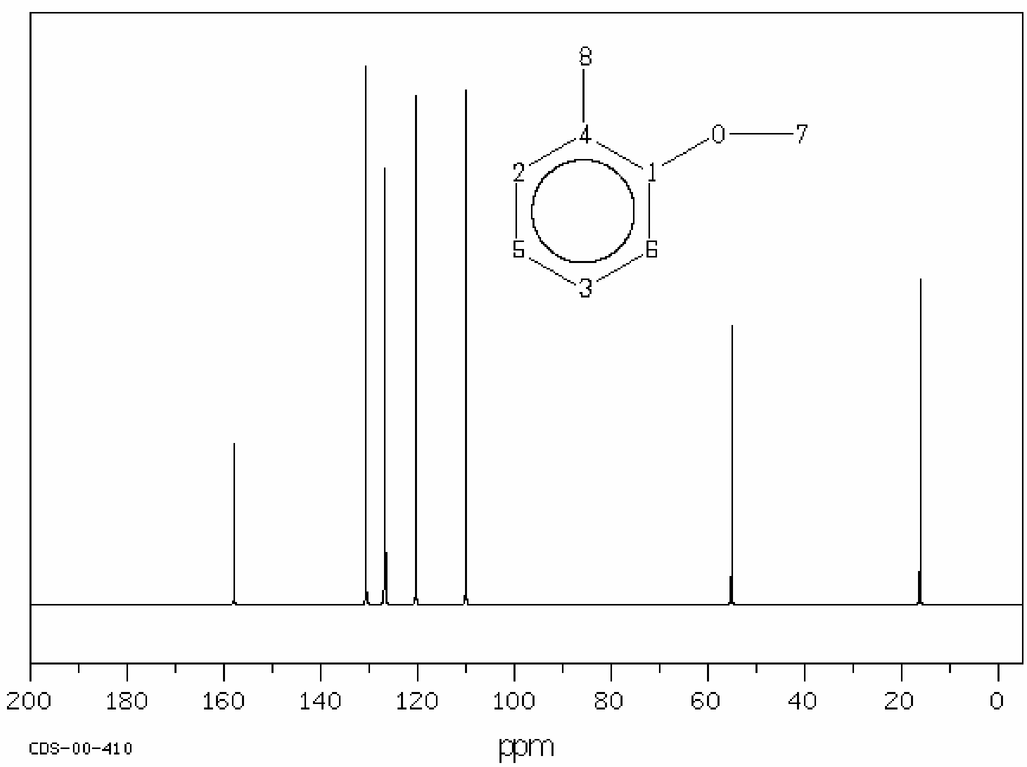
Depending on polarity of the substituents, para has two sets of doublets. What would you expect from substitution with almost no polarity difference?



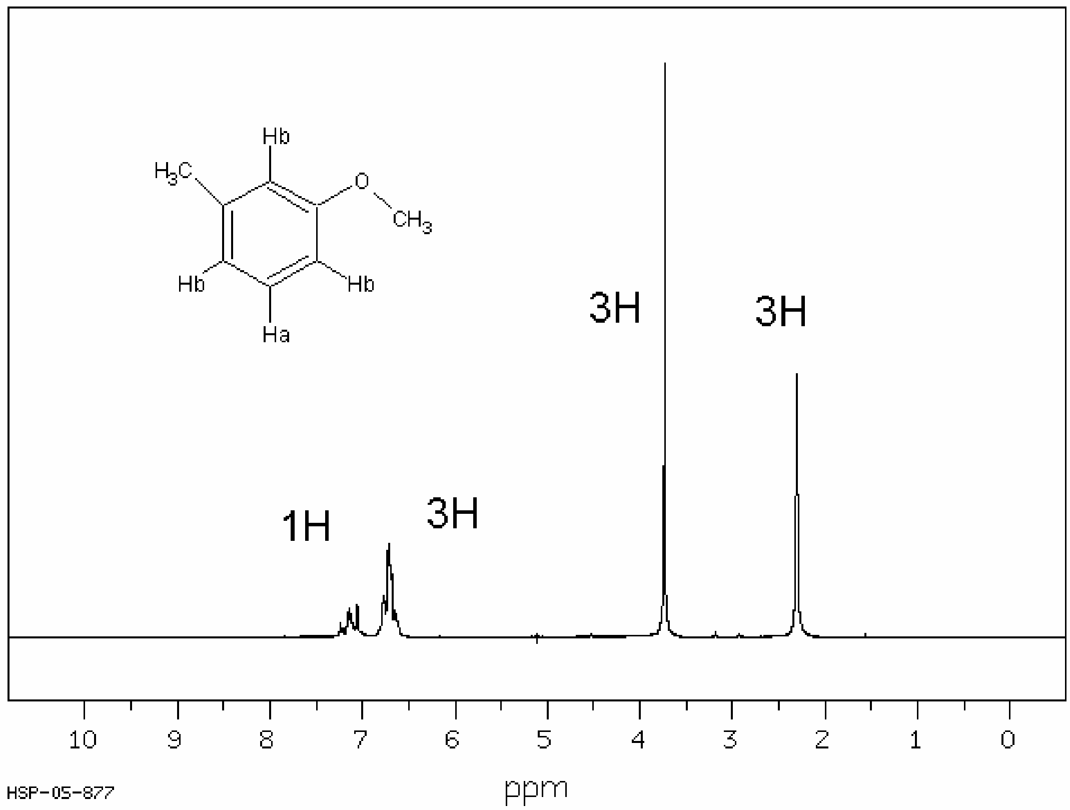
Assignments (ppm => ^{13}C): 157.65 => 1, 129.94 => 2, 113.81 => 3*, 55.15 => 4, 20.41 => 5.
* accidental equivalence



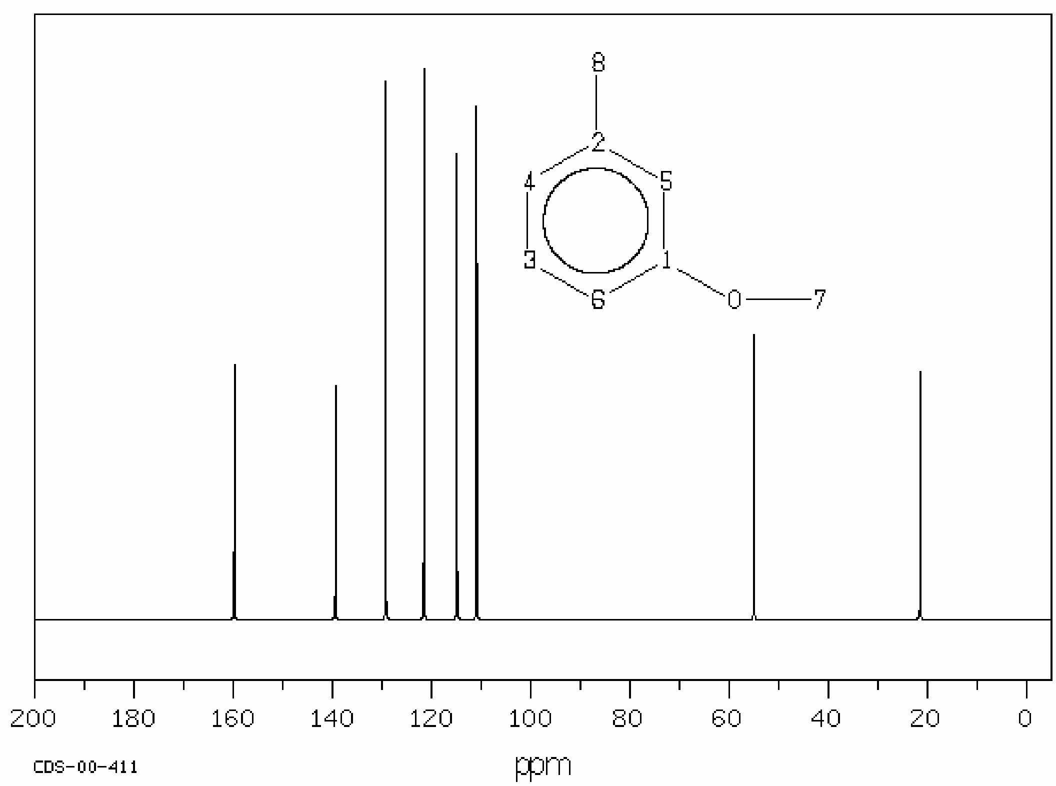
You know there are two substituents because of the integration = 4H in aromatic region, but what nasty splittiings and assignments???!!!



Assignments (ppm => ^{13}C): 157.90 => 1, 130.68 => 2, 126.88 => 3, 126.65 => 4, 120.38 => 5, 110.02 => 6, 55.12 => 7, 16.17 => 8



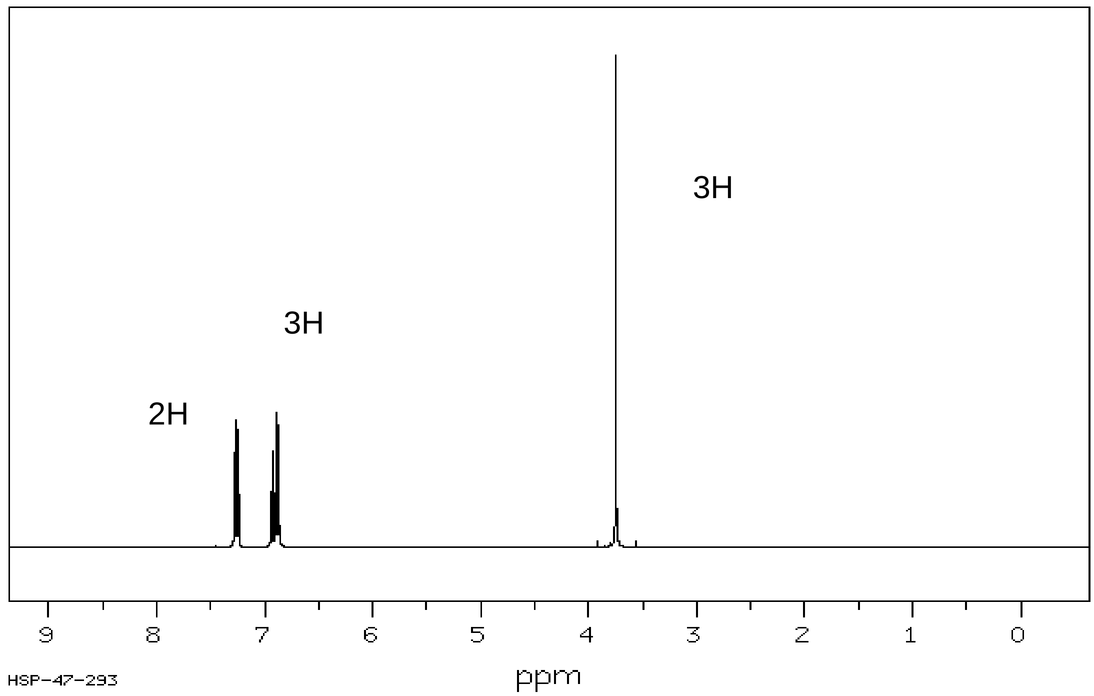
Note the strange stuff in the aromatic region.



Assignments (ppm => ^{13}C): 159.81 => 1, 139.42 => 2, 129.23 => 3, 121.55 => 4, 114.87 => 5, 110.89 => 6, 54.98 => 7, 21.47 => 8.

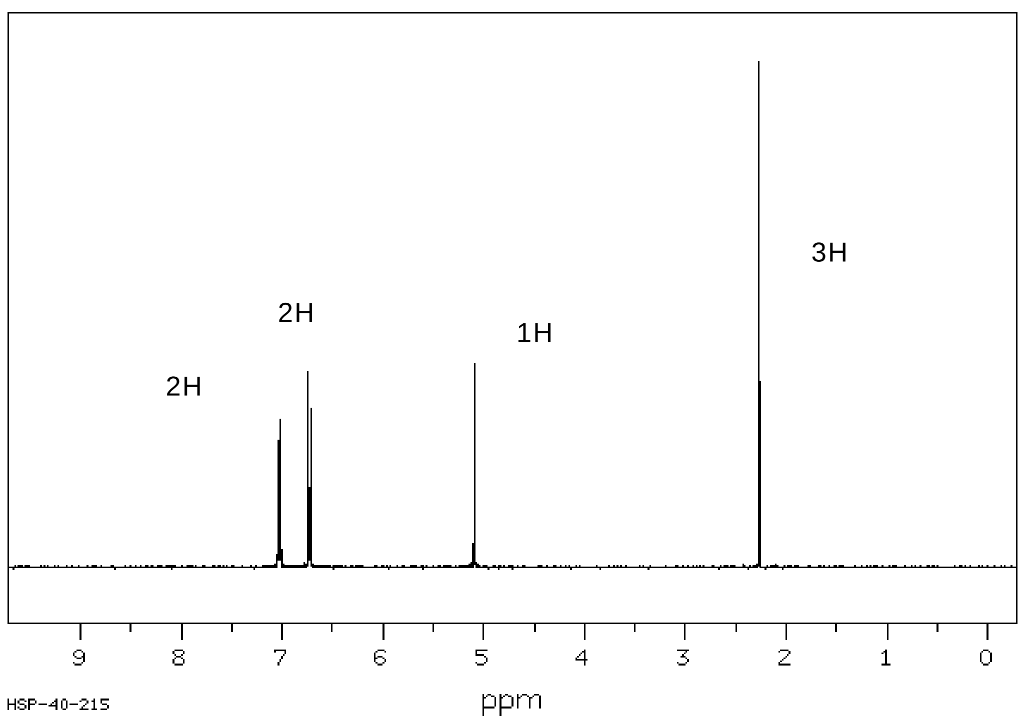
Practice:

Predict the structures of the formula C_7H_8O. Assign all peaks.

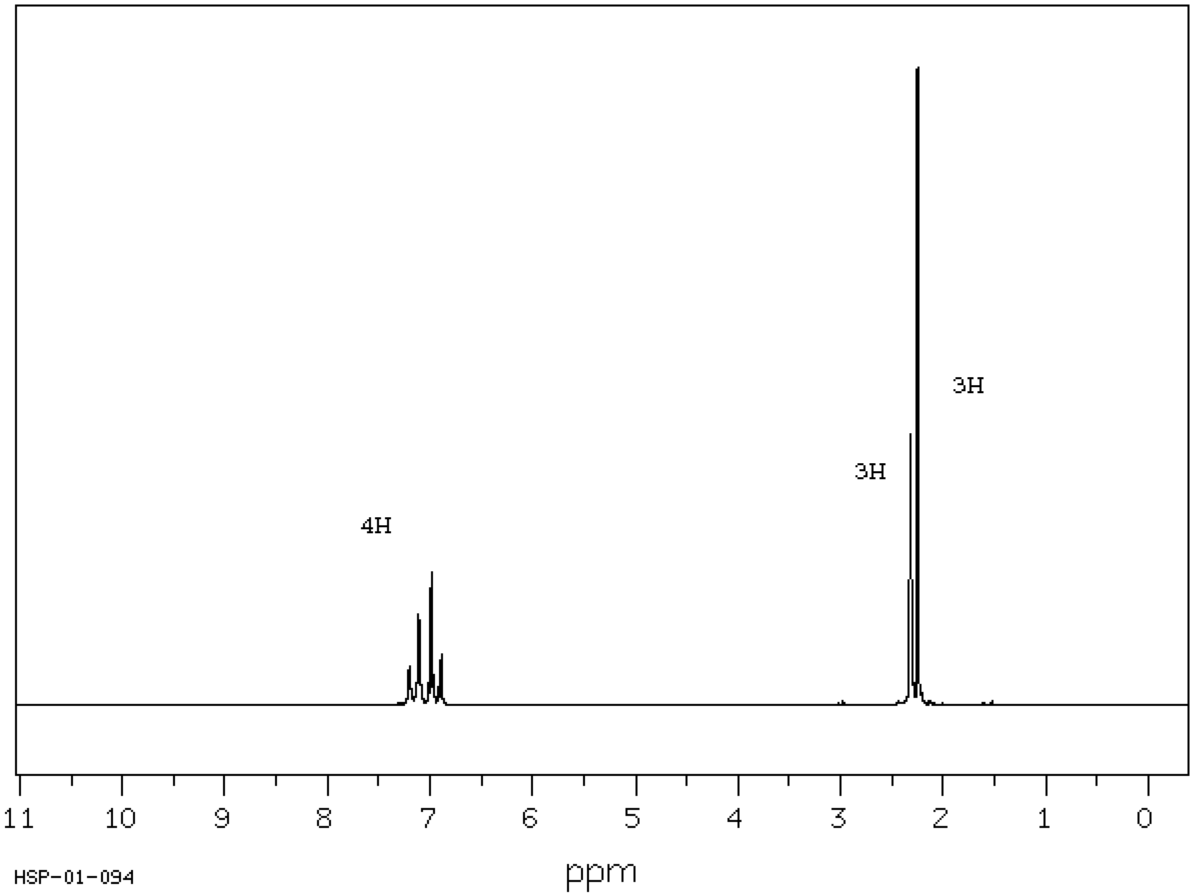


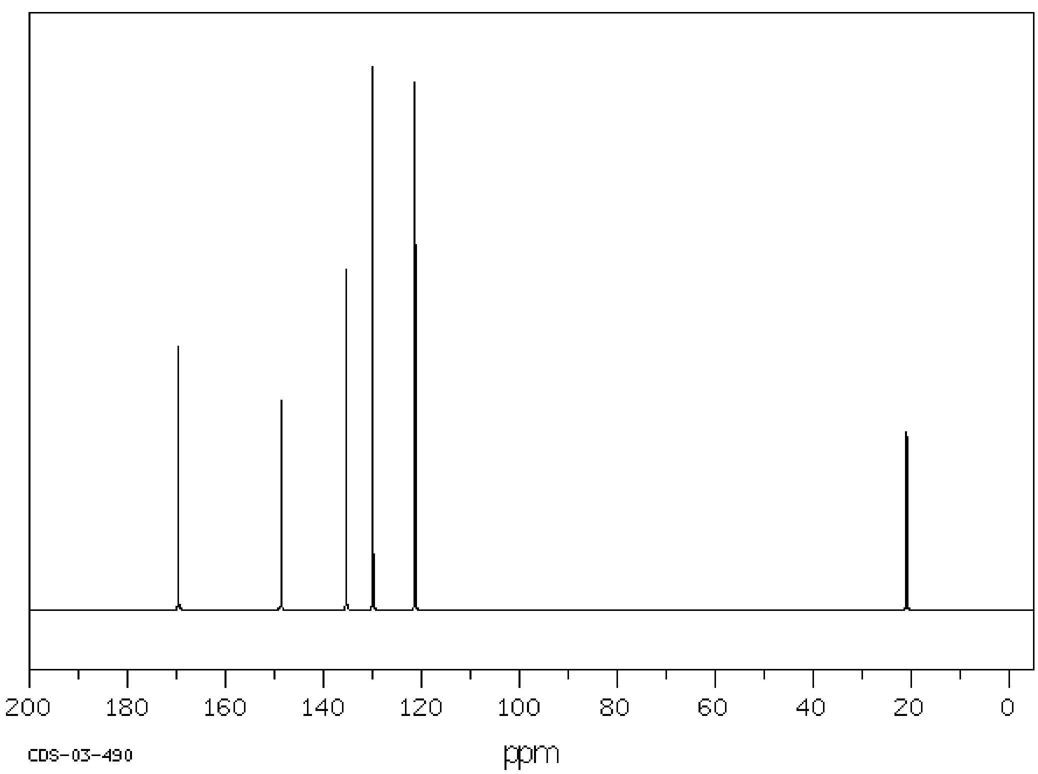
Notice 5 H in the aromatic region: monosubstituted by polarizing group. Must be O. No alcohol, so which functional group?

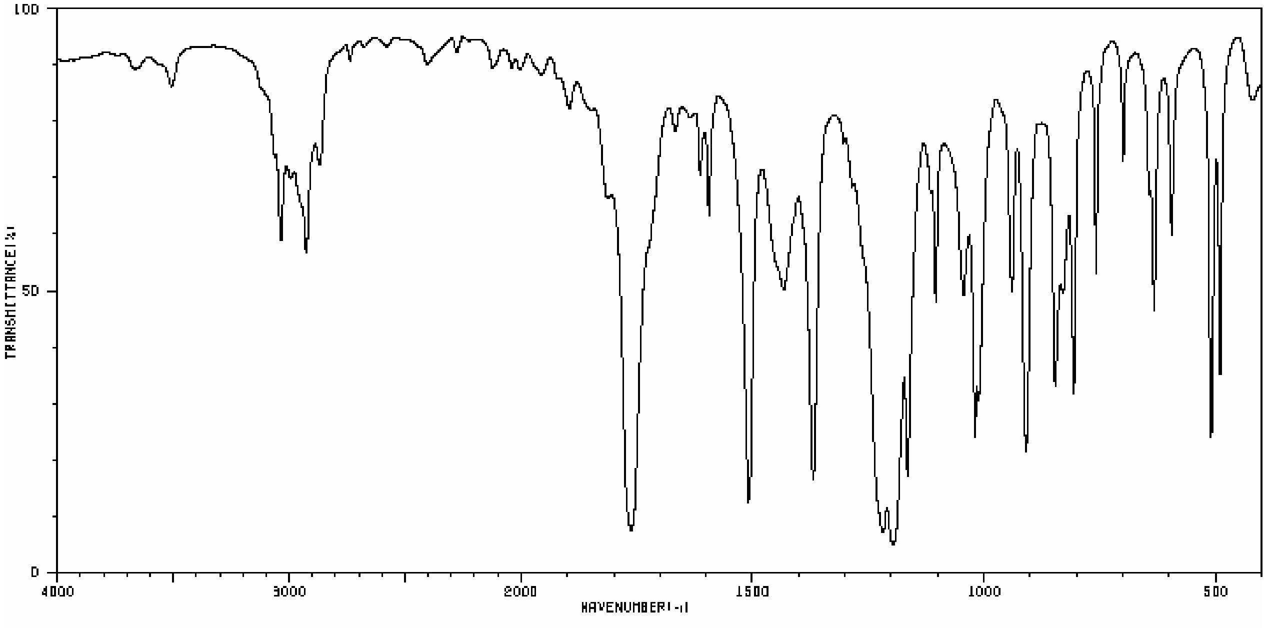
The next compound is an isomer of the above compound: C_7H_8O and shows alcohol in the IR:



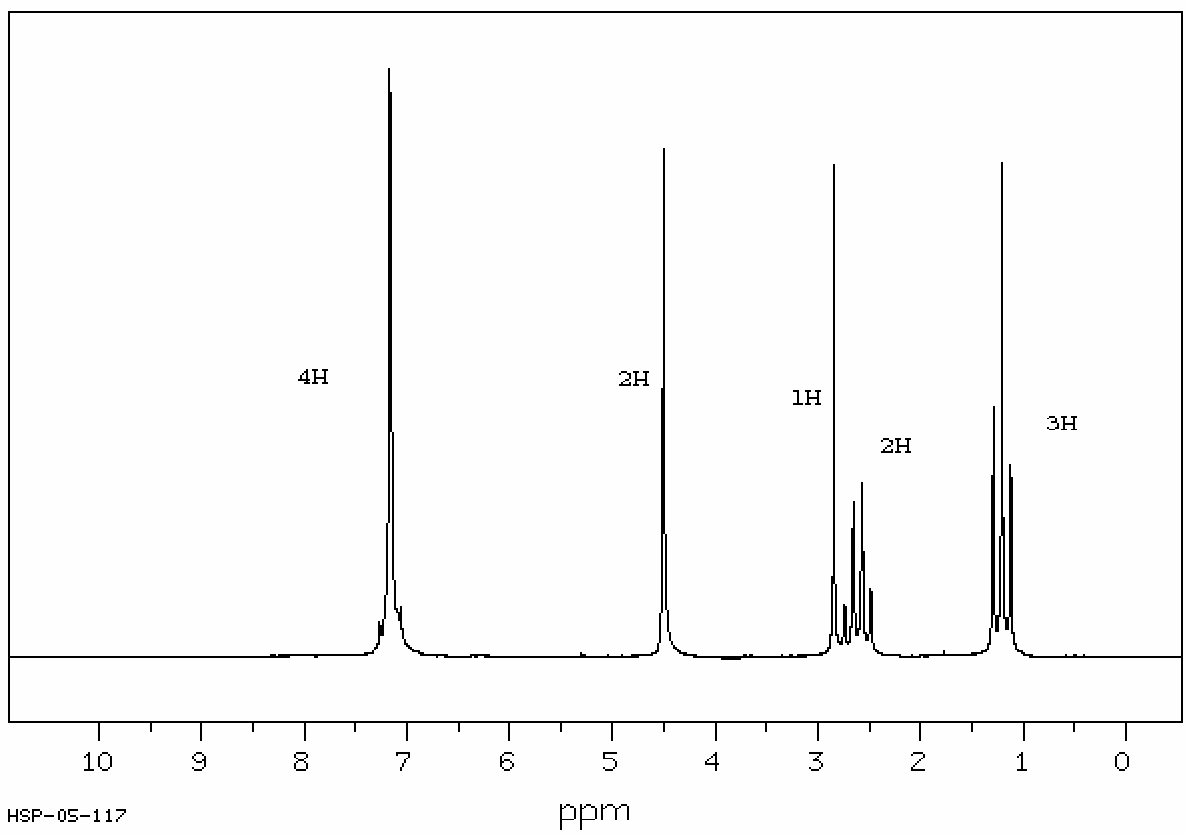
The following compound has the formula $C_9H_{10}O_2$. IR shows a strong peak near 1700 cm^{-1}.

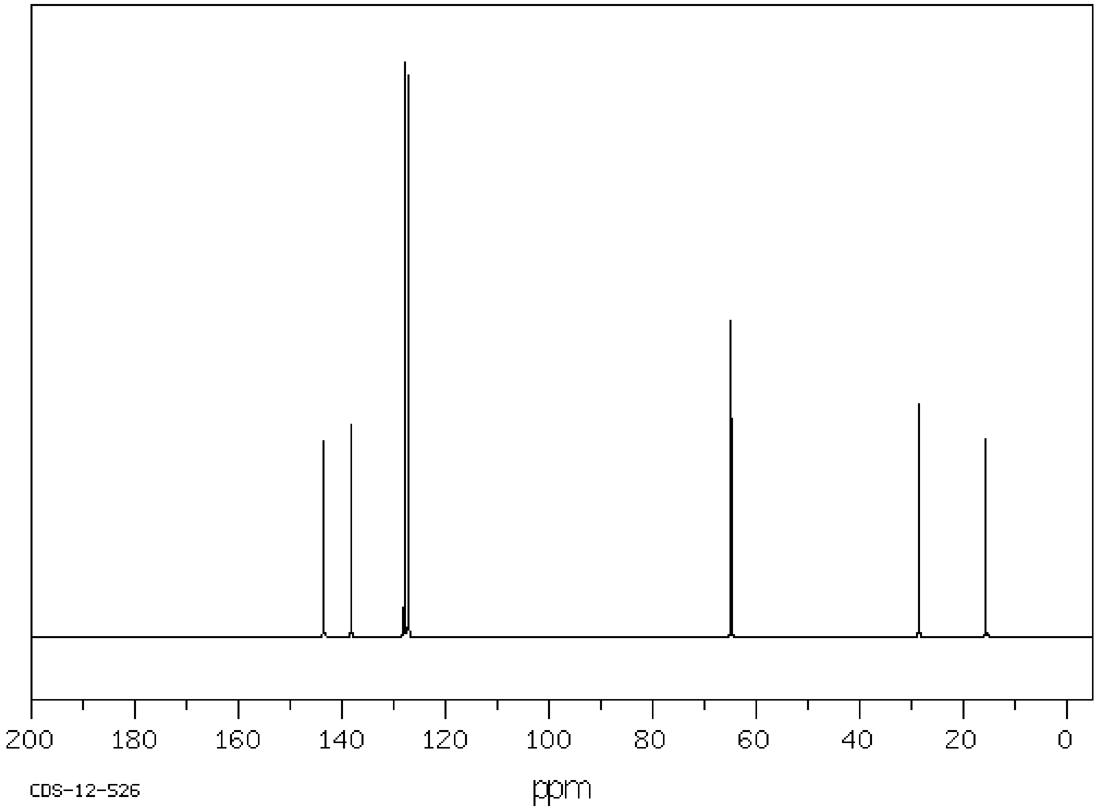






The following compound has the formula $C_9H_{12}O$. IR shows a broad peak between 3300-3600 cm^{-1}.

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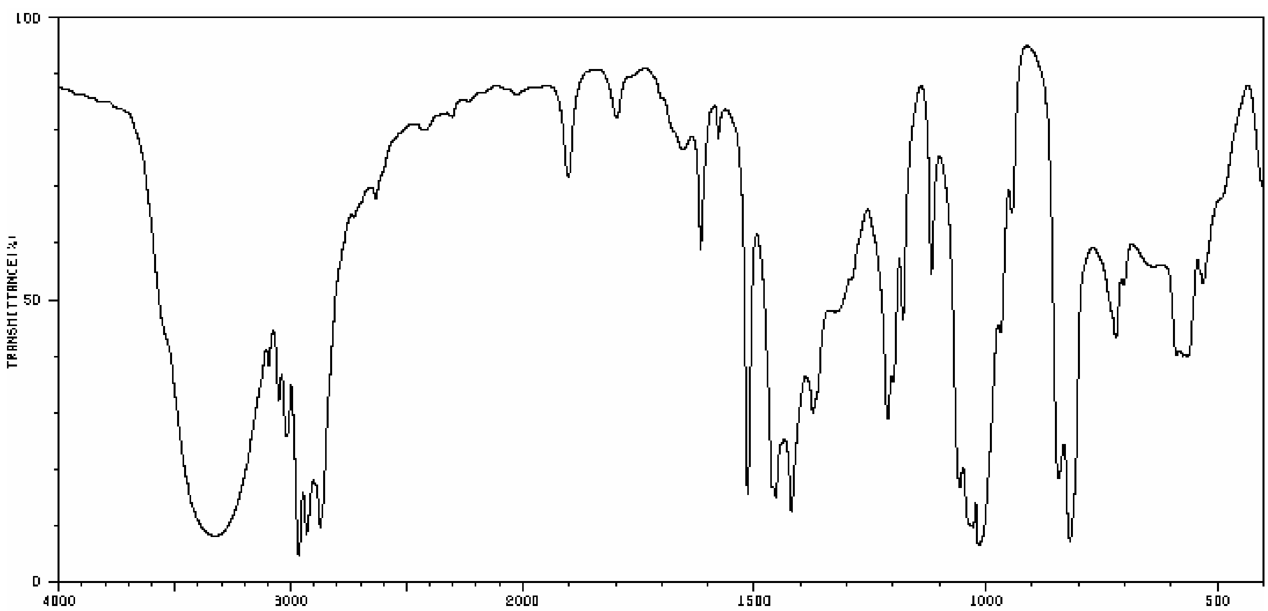
140
120
100
80
60
40
20
0
CDS-12-526
ppm


100
50
0
TRANSMITTANCE[%]
4000
3000
2000
1500
1000
500
WAVENUMBER[-1]