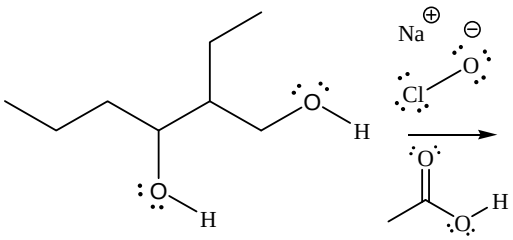
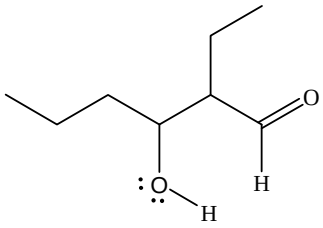
Oxidation is an important process in chemistry. Of course, with any oxidation there must also be reduction, so that's important too. Alcohols are central groups in organic synthesis and can be oxidized to aldehydes, ketones, carboxylic acids or even carbon dioxide. In today's experiment we will start with a diol having a primary and a secondary alcohol. We will use sodium hypochlorite (bleach) as our oxidizing reagent. There are several possible products that might be obtained and part of your job will be to decide what product(s) is (are) obtained. You will have access to your own product IR and real H and C NMR data of the starting material and your reaction product. Additionally, simulated proton and carbon-13 NMR data for all six compounds. The possibilities are presented below.

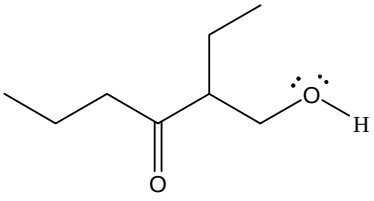


diol
compound 1

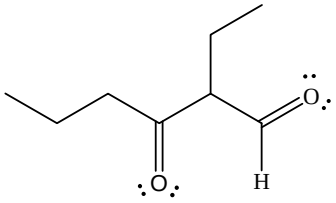
(solvent)
?



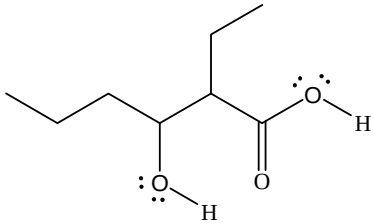
aldehyde-alcohol
compound 2



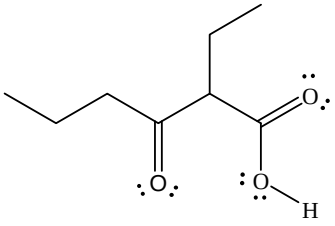
ketone-alcohol
compound 3



aldehyde-ketone
compound 4

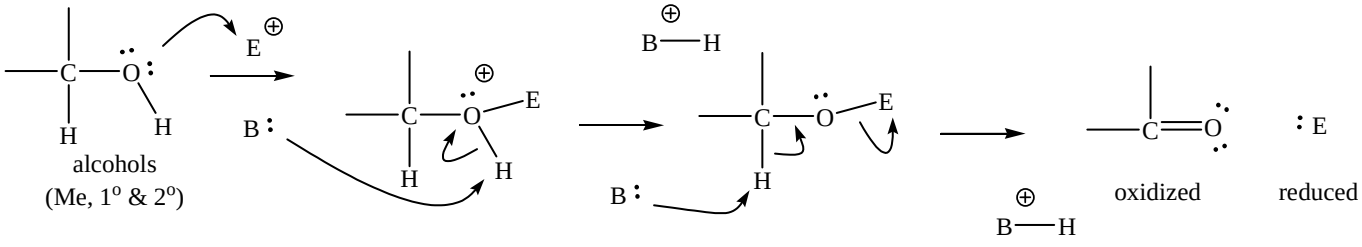


carboxylic acid-alcohol
compound 5



carboxylic acid-aldehyde
compound 6

There are many other reagents that are commonly used to oxidize alcohols. Some examples you might have seen in lecture include: the Swern oxidation (DMSO, oxalyl chloride, triethylamine), Moffatt oxidation (DMSO, DCC), Dess-Martin oxidation (periodane, DMP), PCC (CrO_3, pyridinium hydrochloride), PDC (pyridinium dichromate), Jones (CrO_3, H_2SO_4, acetone) and more. Most of these reagents attach an electron poor atom to the alcohol oxygen which allows an E2-like reaction between a carbon and the alcohol oxygen.



alcohols
(Me, 1° & 2°)

It is possible to distinguish the starting material and all five possible products from one another by IR. Fill in the following table of IR data to show how this can be done.

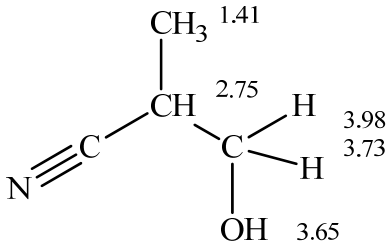
Distinguishing IR peaks for each compound

	alcohols	aldehydes	ketones	carboxylic acids
compound 1				
compound 2				
compound 3				
compound 4				
compound 5				
compound 6				

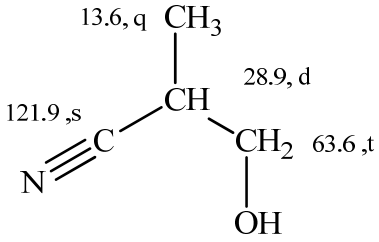
Additionally, the proton and carbon-13 NMRs can easily distinguish each compound from the others. Simulated H and C NMR spectra for each compound are attached. On the proton spectra each chemical shift is listed along with the number of protons, multiplicity and approximate coupling constants (J values). The peaks of each decoupled carbon are listed followed by a letter indicating the number of peaks when the protons are allowed to couple to the carbon atoms (N+1 rule, q = quartet, t = triplet, d = doublet and s = singlet). In the simulated spectra this data is given even when there is overlap and the multiplicity is hard or impossible to see. As you figure out which spectra go with what structure interpret the data as fully as possible. Real NMR data of the starting material and the product are also provided for interpretation. Interpret these spectra too.

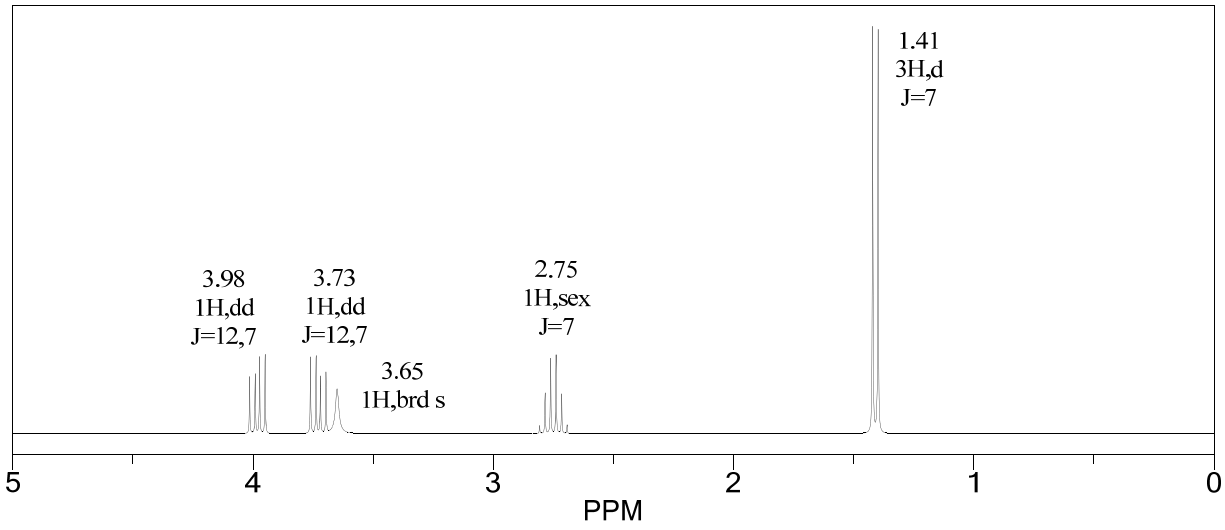
Notice that the starting material has two chiral centers. It turns out that the commercial starting material is a combination of two racemic mixtures of diastereomers (2 sets of enantiomers). One pair of enantiomers is RR/SS and the other is RS/SR. This complicates both the H and C NMR data. Two different 8 carbon diols should show 16 carbon peaks. There are actually 15 carbons showing, though there is one carbon peak about twice as tall as the other carbon peaks. If you examine the alcohol carbon peaks it is clear that they are present in differing amounts. One of the pairs of peaks was integrated to provide an estimate of the ratio of the diastereomers (shown on the ^{13}C spectrum).

Additionally, chiral centers can further complicate the proton NMR spectra by turning equivalent looking protons on a CH_2 into different protons, having different chemical shifts, which then split one another and may even couple with different coupling constants to the same neighbor (s). The following simulated H NMR of 3-hydroxy-2-methylpropanenitrile shows an intermediate level of complexity. The germinal protons have different chemical shifts because of a nearby chiral center and split one another, $J_{geminal}$ = 12 Hz. They are shown with the same coupling constant to their vicinal neighbor ($J_{vicinal}$ = 7 Hz) but in real spectra that may not be the case.



Typical J values
$J_{vicinal}$ = 7 Hz
$J_{geminal}$ = 12 Hz





All of these details make the real proton NMR spectrum of the starting material very complicated because, not only are there two different compounds present, but many of the CH_2's show different chemical shifts which cause complicated coupling patterns. When the peaks get so complicated that we can't interpret them, we call them multiplets (m).

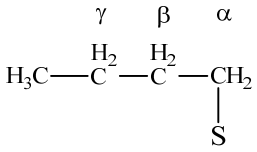
If you examine the possible products at the start, you will see that those possibilities that oxidize the secondary alcohol position destroy one of the chiral centersl. This greatly simplifies the NMR spectra because those products would only have one chiral center (R or S). This would leave only a mixture of enantiomers which provide identical spectra in the absence of a chiral environment. From an NMR point of view there would only be one compound present. You can form your own conclusion by examining the H and C NMRs of the product as to whether this might be the case.

Modified experimental procedure

1. Use your smallest round bottom flask (25 mL). It should be visually clean. If obviously dirty, you can clean it before the reaction. Shake out the water as best you can. A little bit of water won't hurt the reaction because you will be adding an aqueous bleach solution.
2. Use a small beaker (100mL) as a stand to get a tare weight of your round bottom flask.
3. Add approximately 0.5 g of the diol, but weigh it to the maximum accuracy of the balance (Δ = mass of starting material).
4. Add a stir bar and approximately 3 mL of glacial acetic acid and mix. You can do this at the hood to avoid breathing the vapors (vinegar smell).
5. Cap your flask with a septum and stick a 25 guage needle in the top. Pull the lip of the septum over the lip of the flask.
6. Attach the flask to a ring stand over a magnetic stirrer and cool the mixture in an ice bath (use one of the green doggie dishes for your ice bath).
7. At the hood, measure out 5 mL of 8.25% bleach solution in a 50 mL beaker. Use a 5 mL syringe to syringe up 3.2 mL of the bleach solution (use a 19 guage needle). You can parafilm the needle onto the syringe to more securely attach it.
8. Stick the syringe needle through the septum and add about 1mL at a time waiting one minute between each addition of bleach.
9. After all of the bleach has been added remove the ice bath and stir at room temperature for about 40 minutes.
10. Pour the R.B. flask contents into a small beaker (100 mL) containing about 5 g of ice.
11. Add in about 1 mL of sodium sulfite solution to reduce any excess bleach and stir until the ice melts.
12. Add the contents of the beaker to a seporatory funne (total volume about 10-12 mL)l. Make sure the stopcock is secure and closed. Rinse the beaker with about 5 mL of ether (no flames) and add it to the seporatory funnel. Cautiously swirl the sep funnel with the stopper off. Put the stopper on and covering it with one hand turn it over and quickly open the stopcock to relieve any pressure from the ether. Swirl a few times and then close the stopcock and give the sep funnel a brief shake and then open the stopcock. Don't ever point the tip of your sep funnel at any other student (or yourself). Proceed cautiously until you can vigorously shake the sep funnel, always opening the sep funnel to relieve the pressure. This whole process can take less than one minute.
13. Drain the water into a small beaker (you are going to have to add it back in the sep funnel) and drain the ether into a different small beaker. Add the water back in to the sep funnel and repeat this process two more times (extract the aqueous portion with 5 mL of ether each time, 15 mL total ether).
14. On your last extraction drain off the water and discard it in the aqueous waste bottle. Combine all of the ether layers in the sep funnel (leave your last 5 mL ether extraction in the sep funnel).
15. Wash the ether solution with 5 mL of 6M NaOH, 5 mL of water and 5 mL of brine. Discard the aqueous layer each time. On the last rinse with brine make sure to not leave any water in the sep funnel (or you will have to remove it with drying agent; not very effective). Sacrifice a tiny bit of your ether solution here.
16. Dry the ether in a 125 mL erlenmeyer flask over magnesium sulfate or sodium sulfate. Since you are trying to dry a solution over a solid drying agent swirl the flask continuously for about 5 minutes. Slow diffusion-controlled drying overnight would work too, but we don't have that much time. Decant (Na_2SO_4) or gravity filter ($MgSO_4$) into a clean, dry, preweighed 50 mL RB flask. (use a small beaker as a stand) You can use 5 mL of extra ether to rinse the Erlenmeyer flask.
17. Rotovap off the ether. Initially, let the flask cool down out of the water bath until frost just forms on the outside before you lower it into the water bath and there will be less chance of bumping your ether solution up into the rotovap guard (which should always be clean in case it does bump). Ether evaporates pretty quickly once in the water bath. The bath water can be slightly warmed to around 40^oC.
18. When the ether is evaporated, weigh your flask to determine a percent yield. Use a small amount of product to obtain an IR. Your IR should allow you to determine which of the five possible oxidation products you formed. You also have the real proton and carbon NMRs to help you confirm your structure. Completely show how your arrived at your conclusion. In 424 you will have to obtain your own H and C NMRs.
19. Analyze your real NMRs and all of the simulated H and C NMRs to prove which structure goes with each pair of spectral data (proton and carbon-13). As much as possible, match the spectral peaks to the structures.

You can estimate proton shifts using the following equations. The closer a substituent is to the location of a proton or a carbon the larger effect it has on an atom. We only have chemical shift corrections for substituents within 3 carbon atom from the proton or carbon. We will only include the four substituents possible in our experiment, alcohol, aldehyde, ketone and acid. Limited examples are provided below. Other tables exist with most types of organic substituents.

Estimates for sp3 proton chemical shifts having substituents within three carbon away



S = substituent

substituent	α	β	γ
HO- (alcohol)	2.3	0.3	0.1
O=HC- (aldehyde)	1.1	0.4	0.1
O=C (ketone)	1.2	0.3	0.0
HO_2C- (acid)	1.1	0.3	0.1

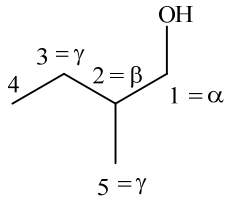
starting δ value for proton on sp3 carbon:

δ_{CH3-} = 0.9 ppm + Σ (all α, β, γ substituent corrections)

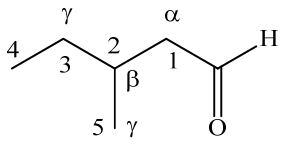
δ_{CH2-} = 1.2 ppm + Σ (all α, β, γ substituent corrections)

δ_{CH-} = 1.5 ppm + Σ (all α, β, γ substituent corrections)

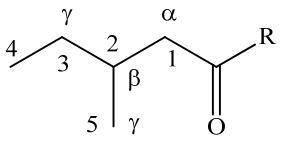
estimated proton shifts (in ppm) for the possible substituents in this lab (ignored diasterotopic possibilities)



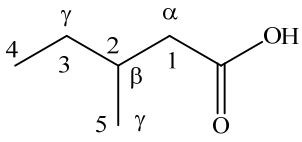
	H_1	H_2	H_3	H_4	H_5
starting value =	1.2	1.5	1.2	0.9	0.9
corrections =	2.3	0.3	0.1	0.0	0.1
δ estimation =	3.3	1.8	1.3	0.9	1.0



	H_1	H_2	H_3	H_4	H_5
starting value =	1.2	1.5	1.2	0.9	0.9
corrections =	1.1	0.4	0.1	0.0	0.1
δ estimation =	2.3	1.9	1.3	0.9	1.0



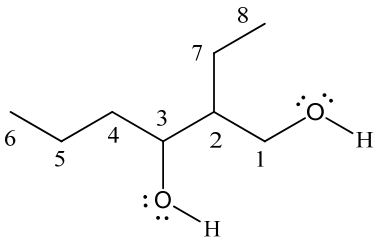
	H_1	H_2	H_3	H_4	H_5
starting value =	1.2	1.5	1.2	0.9	0.9
corrections =	1.2	0.3	0.0	0.0	0.0
δ estimation =	2.4	1.8	1.2	0.9	0.9



	H_1	H_2	H_3	H_4	H_5
starting value =	1.2	1.5	1.2	0.9	0.9
corrections =	1.1	0.3	0.1	0.0	0.1
δ estimation =	2.3	1.8	1.3	0.9	1.0

In a similar way the chemical shifts for the protons below can be calculated. As above limited examples are provided so you can estimate the chemical shifts of the protons in the possible structures presented in this lab. If there are no protons on a particular carbon just enter NA. If there is no special formula to calculate a proton shift, then just estimate its chemical shift from the "generic" table of chemical shifts.

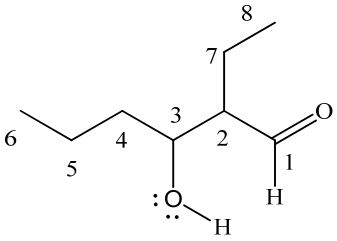
Proton chemical shift calculations (ignore diasterotopic possibilities)



diol

compound 1

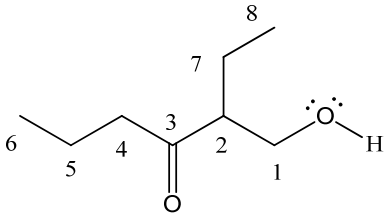
1 2 3 4 5 6 7 8



aldehyde-alcohol

compound 2

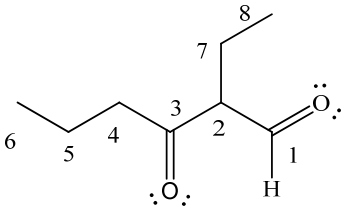
1 2 3 4 5 6 7 8



ketone-alcohol

compound 3

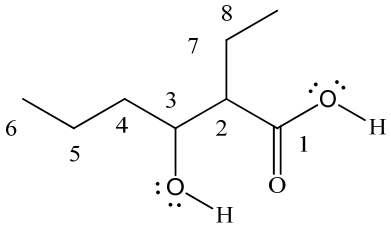
1 2 3 4 5 6 7 8



aldehyde-ketone

compound 4

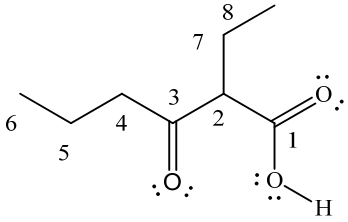
1 2 3 4 5 6 7 8



carboxylic acid-alcohol

compound 5

1 2 3 4 5 6 7 8



carboxylic acid-aldehyde

compound 6

1 2 3 4 5 6 7 8

Estimates for sp3 carbon chemical shifts using an alkane as the starting point (to be modified by substituent and steric corrections)

$$\delta_C = -(2) + 9x(\#\alpha) + 9x(\#\beta) - 2x(\#\gamma) + \text{steric corrections}$$

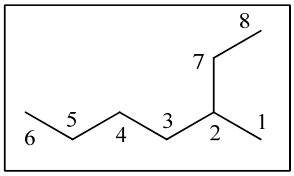
← One possible way to estimate an alkane sp^3 carbon chemical shift, starting from scratch).

Steric Corrections for sp^3 carbon chemical shift calculations

The calculated carbon atom is: ↓ The attached C_α carbons are:

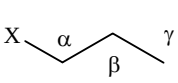
	primary	secondary	tertiary	quaternary
primary	0	0	-1	-3
secondary	0	0	-2	-8
tertiary	0	-4	-9	-15
quaternary	-1	-8	-15	-25

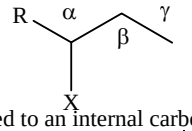
Sample calculations for the alkane skeleton in our starting diol (the experimental values are provided at the bottom)



	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8
starting value =	(-2)	(-2)	(-2)	(-2)	(-2)	(-2)	(-2)	(-2)
(#)x(C_α) =	(1)x(9)	(3)x(9)	(2)x(9)	(2)x(9)	(2)x(9)	(1)x(9)	(2)x(9)	(1)x(9)
(#)x(C_β) =	(2)x(9)	(2)x(9)	(3)x(9)	(2)x(9)	(1)x(9)	(1)x(9)	(2)x(9)	(1)x(9)
(#)x(C_γ) =	(2)x(-2)	(1)x(-2)	(2)x(-2)	(2)x(-2)	(1)x(-2)	(1)x(-2)	(1)x(-2)	(2)x(-2)
steric =	(-1)	(-8)	(-2)	(-0)	(-0)	(-0)	(-2)	(-0)
Total =	20	33	37	30	23	14	30	12
Actual value =	19.3	34.6	36.5	29.7	23.2	14.2	29.6	11.5

Substituent effect modifications found in our structures, used when carbon atom is within three carbons of the substituent). A separate table is used when the substituent is at the end of a chain versus in the middle of a chain.

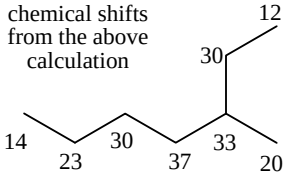




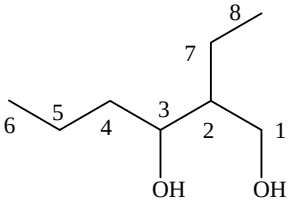
Substituent = X	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
	C_α correction	C_β correction	C_γ correction	C_α correction	C_β correction	C_γ correction
——OH	48	10	-6	44	7	-4
——CH=O	30	0	-3	24	-1	-3
——C=O	31	1	-3	26	0	-3
——CO_2H	22	2	-3	18	1	-3

Use the alkane skeleton chemical shifts as the starting point for the chemical shift estimates in the substituted skeleton.

chemical shifts from the above calculation



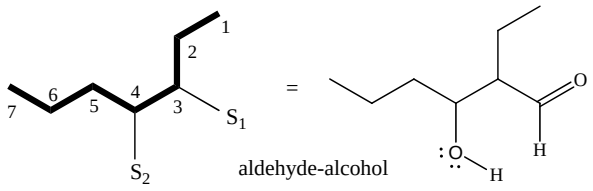
substituted skeleton →



	calculated values	experimental values of diastereomeric mixture
C_1	= 20 + 48 - 4 = 64	64.0 / 63.5
C_2	= 33 + 10 + 7 = 50	46.2 / 45.9
C_3	= 37 + 44 -6 = 75	74.9 / 74.5
C_4	= 30 + 7 = 37	37.8 / 35.3
C_5	= 23 - 4 = 19	21.5 / 19.6
C_6	= 14	14.2 / (same)
C_7	= 30 - 6 - 4 = 20	19.0 / 18.3
C_8	= 12	12.4 / 11.8

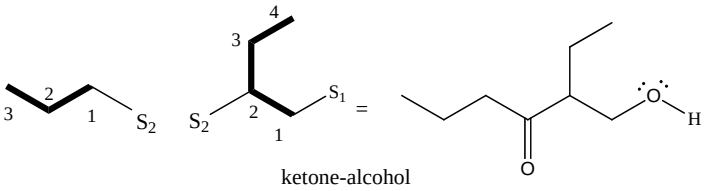
In a similar way to the example above the chemical shifts for carbon atoms below can be calculated. As above limited examples are provided so you can estimate the chemical shifts of the carbon atoms in the possible structures presented in this lab. If there is no special formula to calculate a carbon shift then just estimate its chemical shift from the "generic" table of carbon chemical shifts (e.g. ketones, aldehydes, acids).

Carbon skeletons for the other compounds in this lab would look as follows. You can make your own estimates for those ^{13}C spectra.



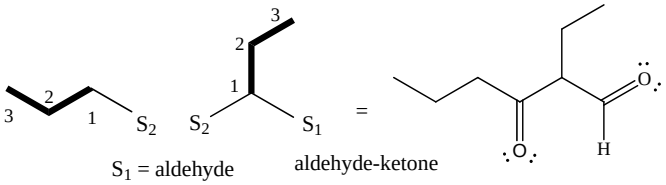
S_1 = aldehyde
S_2 = alcohol

aldehyde-alcohol
compound 2



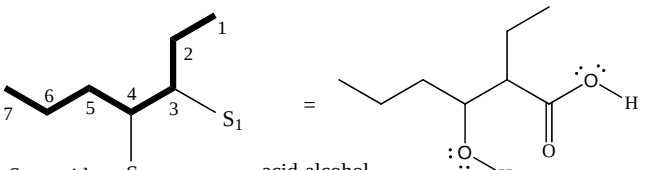
S_1 = alcohol
S_2 = ketone

ketone-alcohol
compound 3



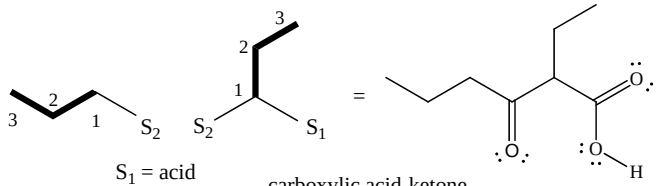
S_1 = aldehyde
S_2 = ketone

aldehyde-ketone
compound 4



S_1 = acid
S_2 = alcohol

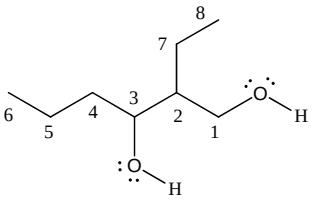
acid-alcohol
compound 5



S_1 = acid
S_2 = ketone

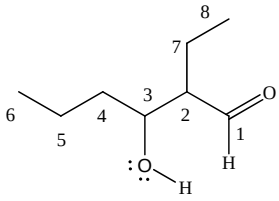
carboxylic acid-ketone
compound 6

Carbon chemical shift calculations



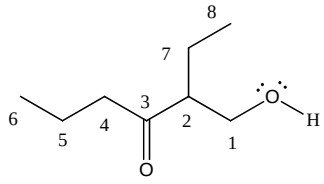
diol
compound 1

1 2 3 4 5 6 7 8



aldehyde-alcohol
compound 2

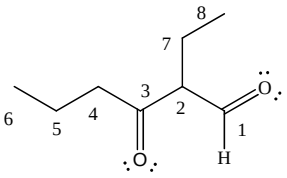
1 2 3 4 5 6 7 8



ketone-alcohol
compound 3

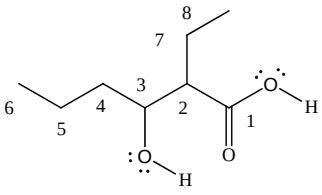
1 2 3 4 5 6 7 8

Example worked
just above



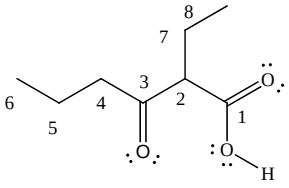
aldehyde-ketone
compound 4

1 2 3 4 5 6 7 8



carboxylic acid-alcohol
compound 5

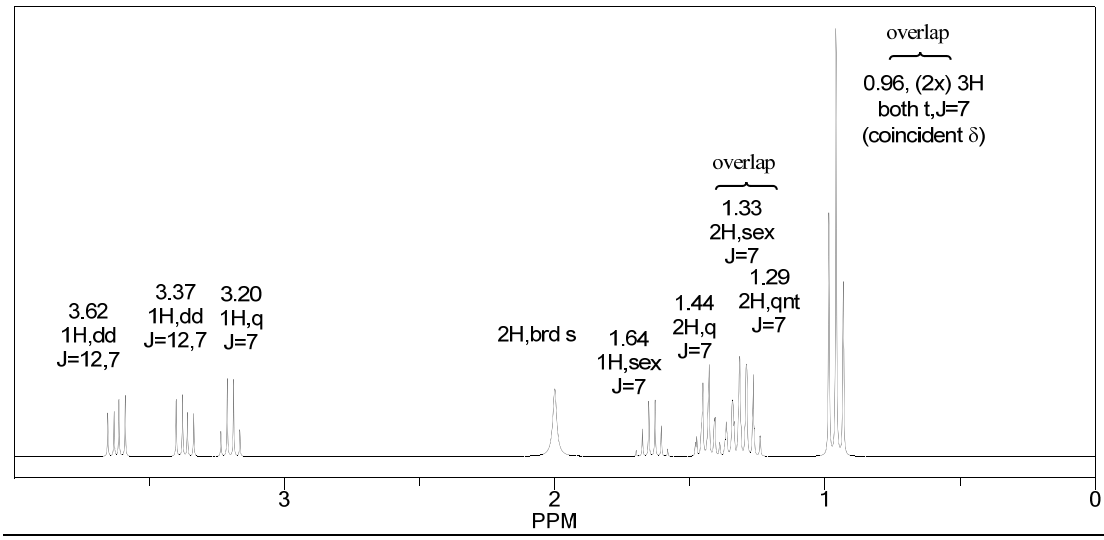
1 2 3 4 5 6 7 8



carboxylic acid-aldehyde
compound 6

1 2 3 4 5 6 7 8

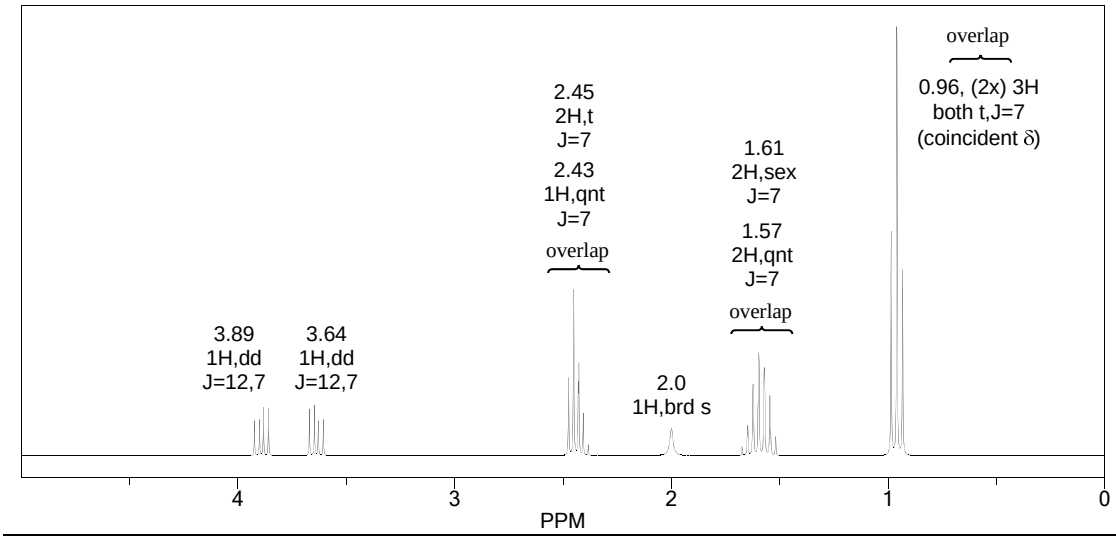
1



^{13}C peaks

68.8,d
61.7t
39.2d
37.9t
18.4t
16.9t
14.4,q
12.2,q

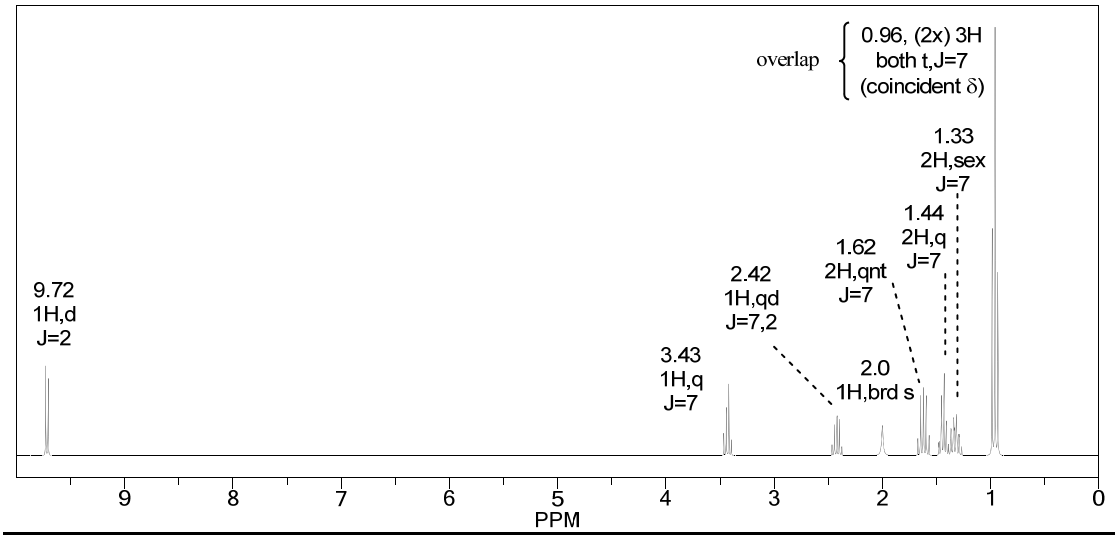
2



^{13}C peaks

213.6,s
61.2,t
55.1,d
42.6,t
18.9,t
17.2,t
13.6,q
11.4,q

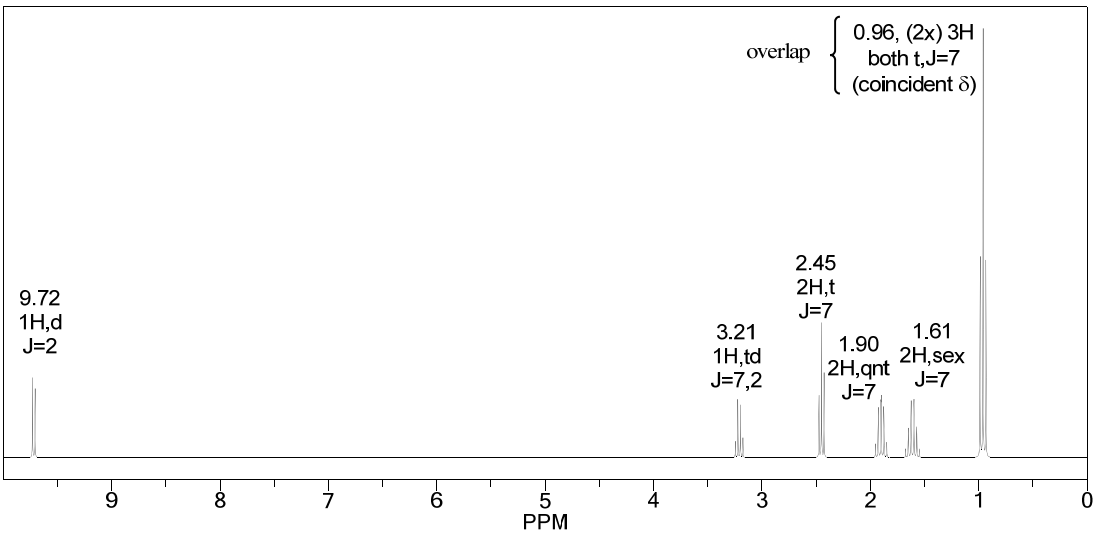
3.



^{13}C peaks

204.1,d
68.4,d
60.3,d
37.4,t
16.6,t
15.3,t
14.4,q
11.7,q

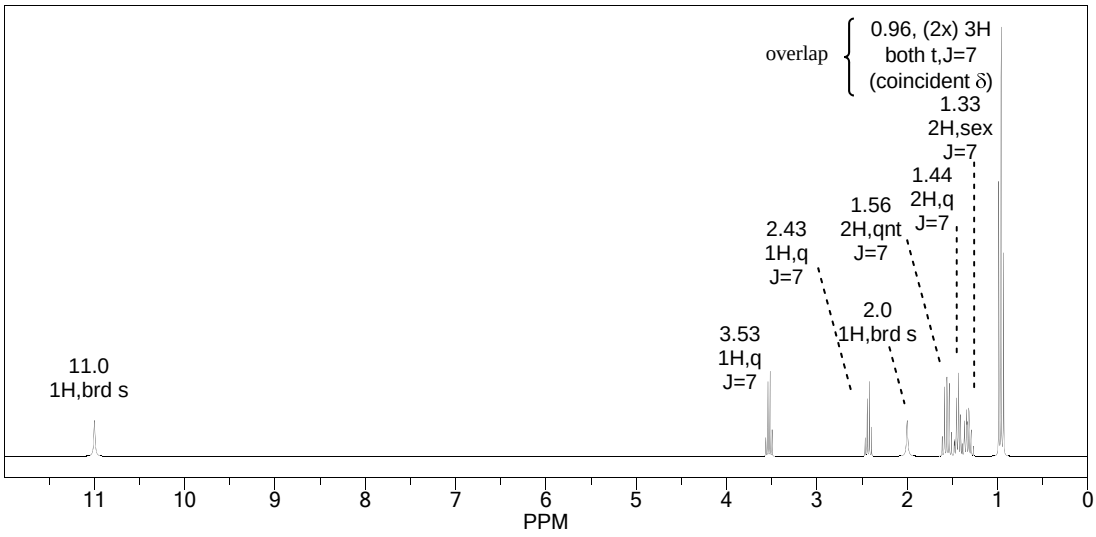
4.



^{13}C peaks

206.6,s
201.5,d
69.5,d
42.1,t
16.9,t
14.3,t
13.6,q
10.9,q

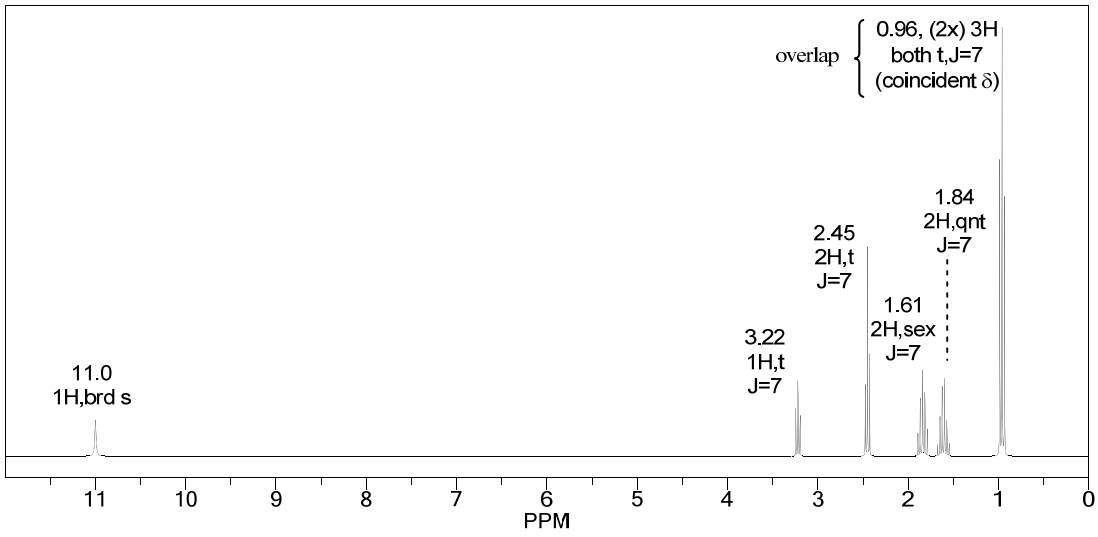
5.



^{13}C peaks

180.0,s
71.0,d
56.1,d
37.3,t
17.9,t
16.6,t
14.4,q
11.6,q

6.



^{13}C peaks

206.6,s
178.1,s
60.6,d
42.0,t
16.9,t
16.7,t
13.6,q
10.8,q