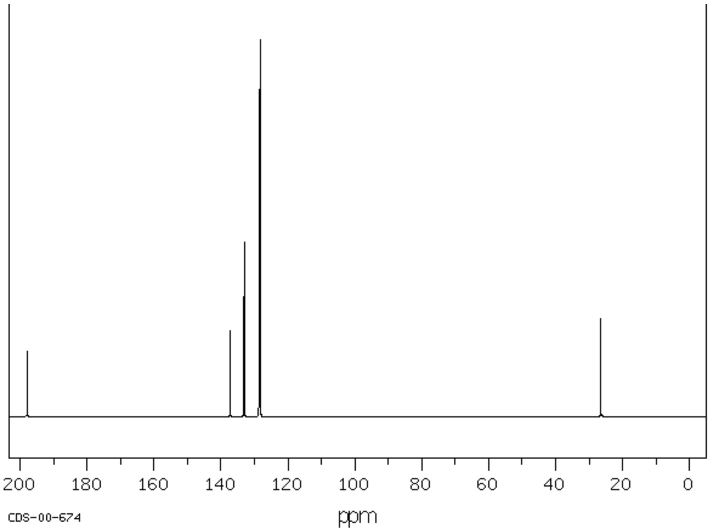
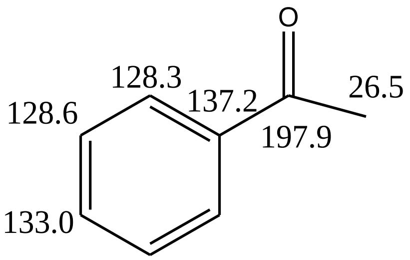
1. 2Carbon NMR
    1.1. appearance of spectra
        1.1.1. ^{12}C has no spin, ^{13}C has 1.1% abundance and spin of ½
        1.1.2. Chemical shift range is 200 ppm, over 10 times greater than proton
        1.1.3. C-C coupling minor!!
            1.1.3.1. probability of adjacent ^{13}C = 0.011%, doublet = 0.0055%
        1.1.4. C-H coupling
            1.1.4.1. reduces intensity and overlap is bad for large compounds
            1.1.4.2. cholesterol –Figure 4.1 (e223) CHO and CH3 peaks -
        1.1.5. broad-band proton decoupling converts to singlets – taller than multiplet
        1.1.6. NOE further increases intensity except for quaternary carbon
        1.1.7. number of peaks corresponds to number of unique carbons – aromatics?
        1.1.8. quaternary carbons have low intensity/poor relaxation without attached proton
        1.1.9. coupled spectra – rich information – Figure 4.6 (e230)
    1.2. peak areas and heights of routine(decoupled) carbon spectra are not proportional
        1.2.1. spectra optimized for fast acquisition – frequent pulsing for signal averaging
            1.2.1.1. long T_1 causes incomplete relaxation between pulses
        1.2.2. NOE caused by decoupling not same for every carbon
        1.2.3. inadequate digital resolution
        1.2.4. quaternary carbons – Figure 4.8 (e232)
    1.3. Chemical shift depends on shielding, similar to proton (see Tables, e242, 13C_NMR_graph.pdf)

1.3.1. acetophenone



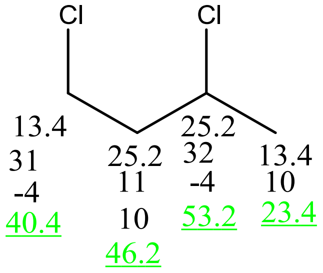


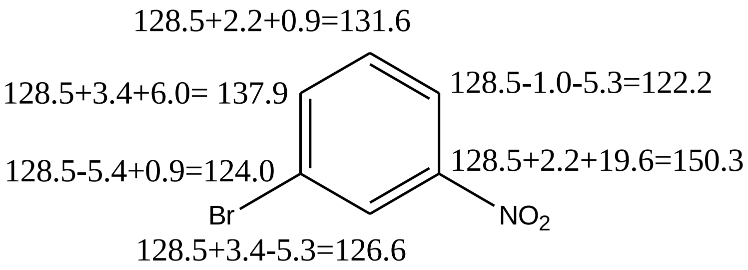
1.4. Calculation of carbon chemical shifts: Tables 4.5, 4.6 (e237), 4.12 (e241)

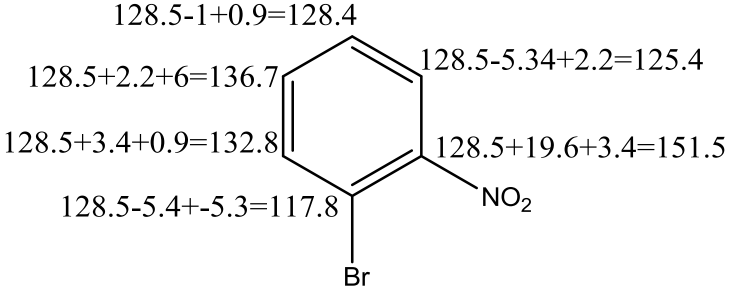
1.4.1. Alkane chains: 1,3-dichlorobutane (25.17, 41.82, 42.67,55.02)

1.4.2. Aromatics: 1,3-bromonitrobenzene

(122.14,122.88,126.71,130.67,137.62,148.85) 128.5

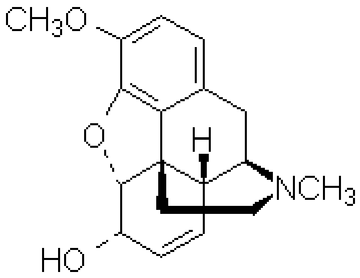






1.4.3. DEPT: Distortionless Enhanced Polarization Transfer (APT)

1.4.4. indicates number of <u>attached</u> proton



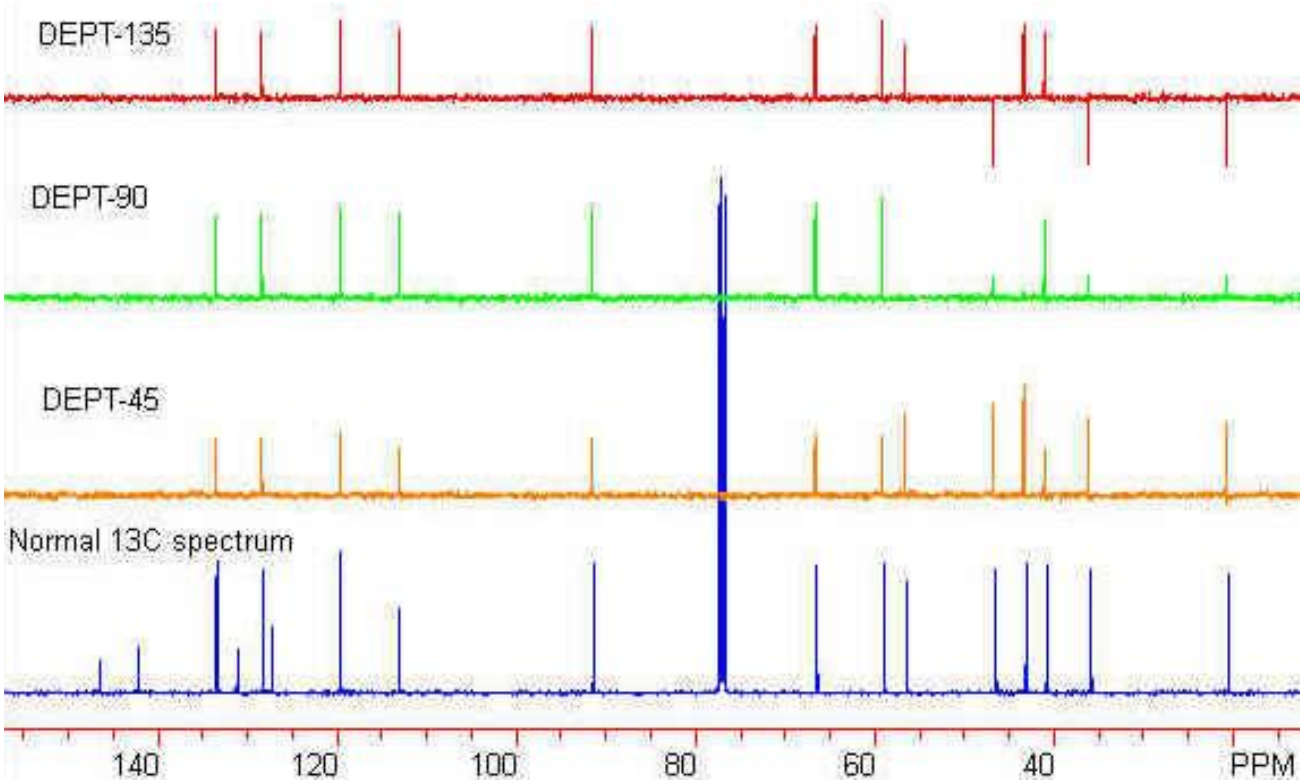
1.4.5. subspectra for CH, CH_2 and CH_3

1.4.6. old method has A (CH) and B subspectra (CH and CH_3 up, CH_2 down)

1.4.7. SWK saves space and places 1, 2 or 3 near peaks of decoupled spectrum

1.4.8. DEPT-135 (CH and CH_3 peaks up, CH_2 peaks inverted) DEPT-90 (CH peaks only) DEPT-45 (all protonated carbons normal ^{13}C spectrum)

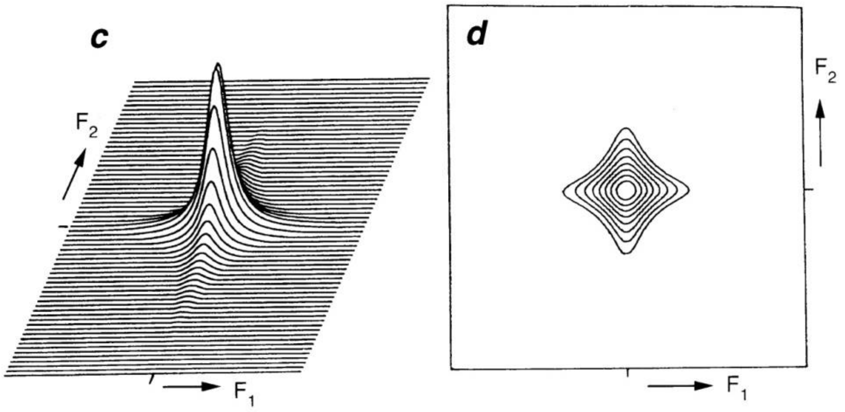
1.4.9. how are quaternary determined?



http://www.acornnmr.com/codeine/dept.htm

2. 2D NMR – Correlation Spectroscopy: 1D NMR amplitude versus frequency (really 2D)

   2.1. 2 D spectrum: frequency versus frequency, amplitude in third direction



2.2. Contour plot on right is more common for spectra with several peaks

2.3. peaks in two spectra are correlated, nuclei are related (coupling, distance)

2.4. Ipsenol – proton-proton correlate spectra, COSY: correlated spectroscopy

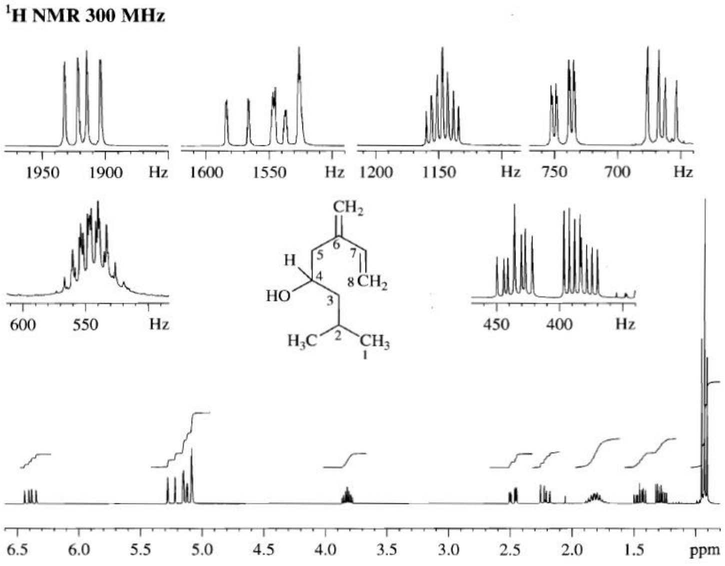
  2.4.1. travel vertically (or horizontally) from an axis to a cross peak

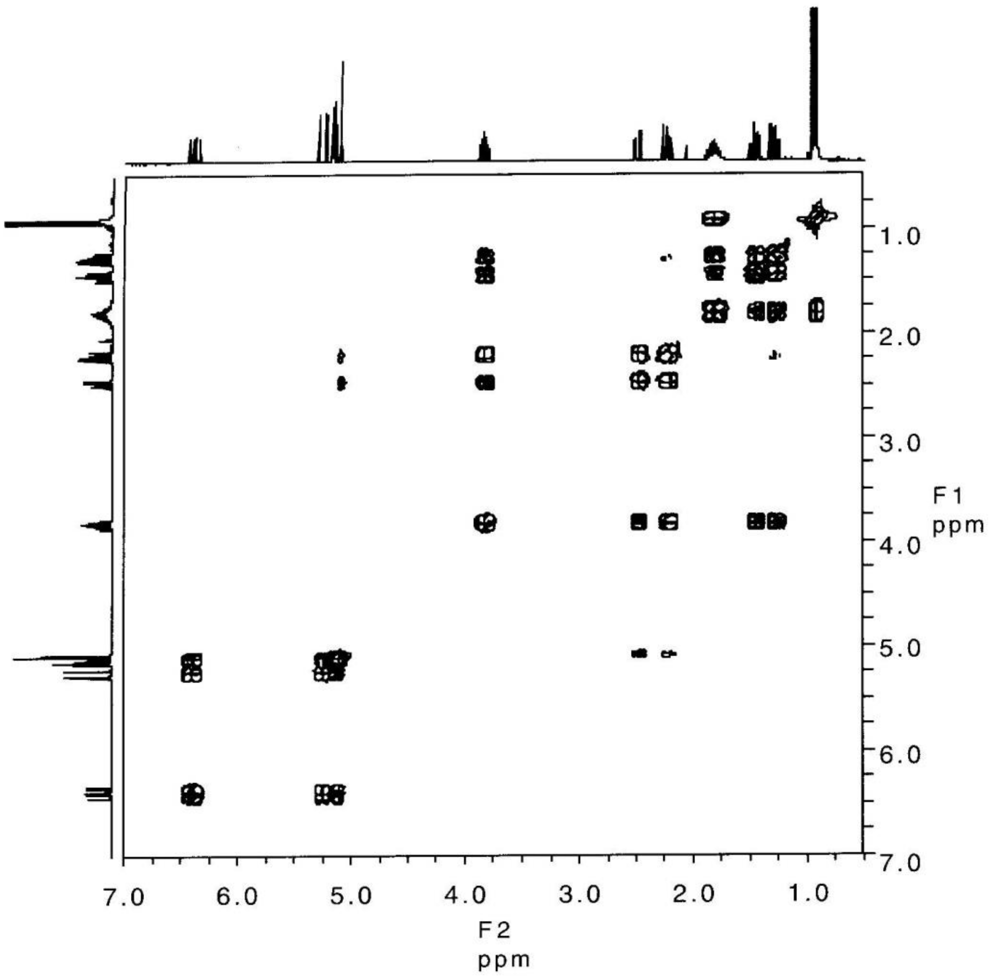
  2.4.2. travel horizontal (or vertically) to the correlated peak(s)

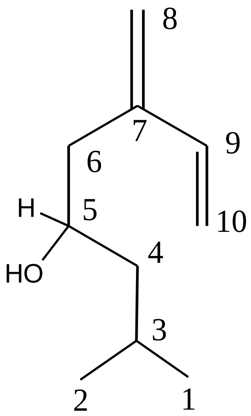
  2.4.3. COSY indicates coupled peaks ???

  2.4.4. easier than determining coupling constants, especially in 2nd order spin systems

  2.4.5. DQF methods (double quantum filter) minimizes large diagonal (self correlated) peaks (seen below)







2.4.6. start with easily identified peaks, **5** at 3.82 ppm, **1,2** at 0.9 ppm (2 doublets, area 3 each) only connect to **3** at 1.80 ppm.

2.4.7. **3** is also connected to **4** (CH_2: 1.28, 1.42 ppm).

2.4.8. Two protons at **4** are connected to each other and to **5** (CH, 3.82 ppm).

2.4.9. **5** is connected to **6** (CH_2 at 2.21, 2.48 ppm).

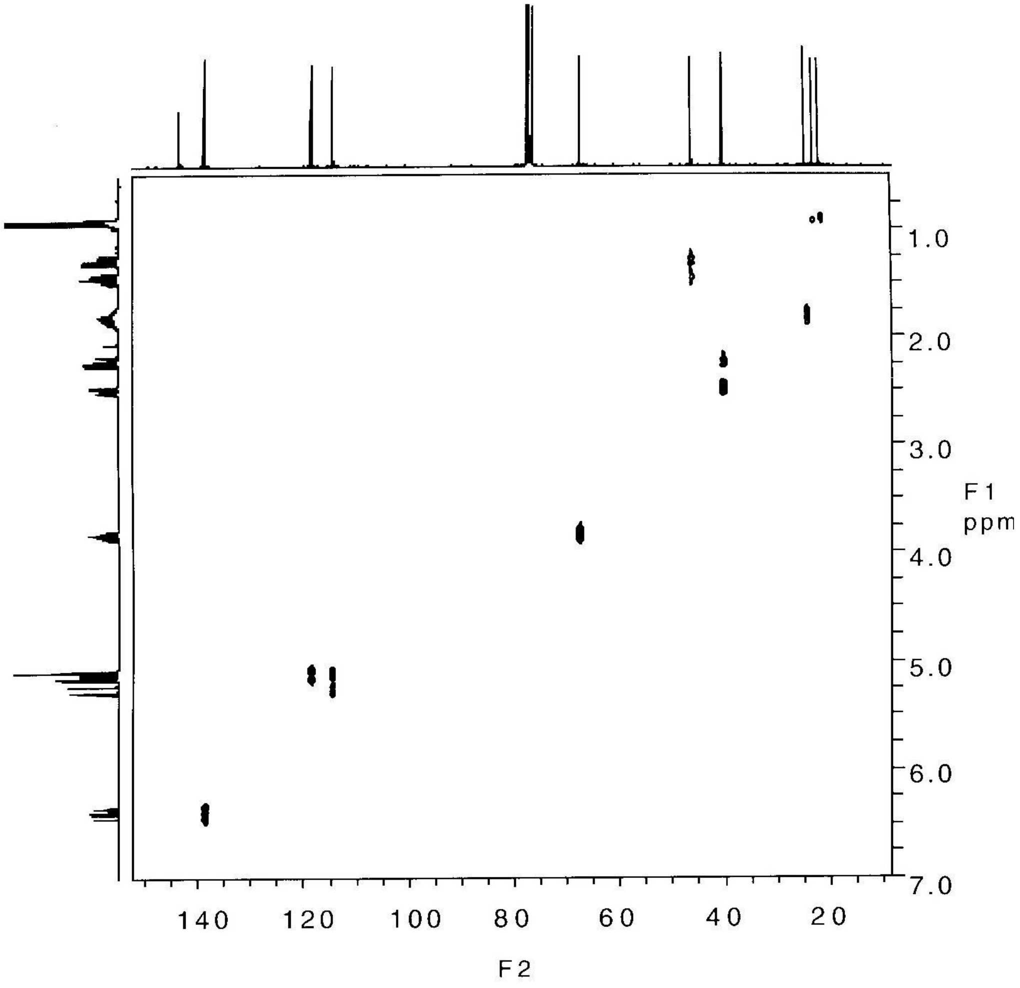
2.4.10. Two hydrogens at **6** are connected to each other and one **6** proton at 2.21 ppm is connected weakly to one **4** proton at 1.28 ppm.

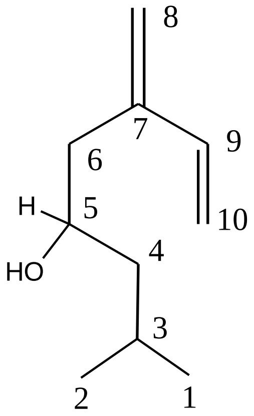
2.4.11. Both hydrogens at **6** are weakly connected to one cis at **8** (CH_2, 5.08/5.14 ppm)

2.4.12. Proton at 6.40 ppm (1H) is **9** can't be **8** or **10** because proton at 6.4 ppm is connected to **10** (5.14, 5.25 ppm) and **8** (5.08 ppm) .

2.5. proton-carbon COSY: heteronuclear correlation, HETCOR/HMQC

2.5.1. correlation of proton and carbon signals





2.5.2. 0.9 (**1**/**2**) 1.28/1.42 (**4**) 1.8 (**3**) 2.21/2.48 (**6**) 3.82 (**5**) 5.08/5.14 (**8**) 5.14/5.25 (**10**) 6.40 (**9**)

2.5.3. olefin carbons are 143-108 ppm

2.5.4. **7** is quaternary not correlated a 143 ppm.

2.5.5. carbon 138 ppm is correlated to proton 6.4 ppm must be **9** (see DEPT, Figure 4.12)

2.5.6. carbon 118 ppm is correlated to proton 5.08 and 5.14 ppm: **8** (near **6** must be not **10**.

2.5.7. carbon 114 ppm is correlated to proton 5.14 and 5.25 ppm must be **10.**

2.5.8. carbon 68 ppm is alcohol and correlated to proton 3.82 ppm must be **5**.

2.5.9. carbon 47 ppm is correlated to proton 1.28/1.42 ppm must be **4**.

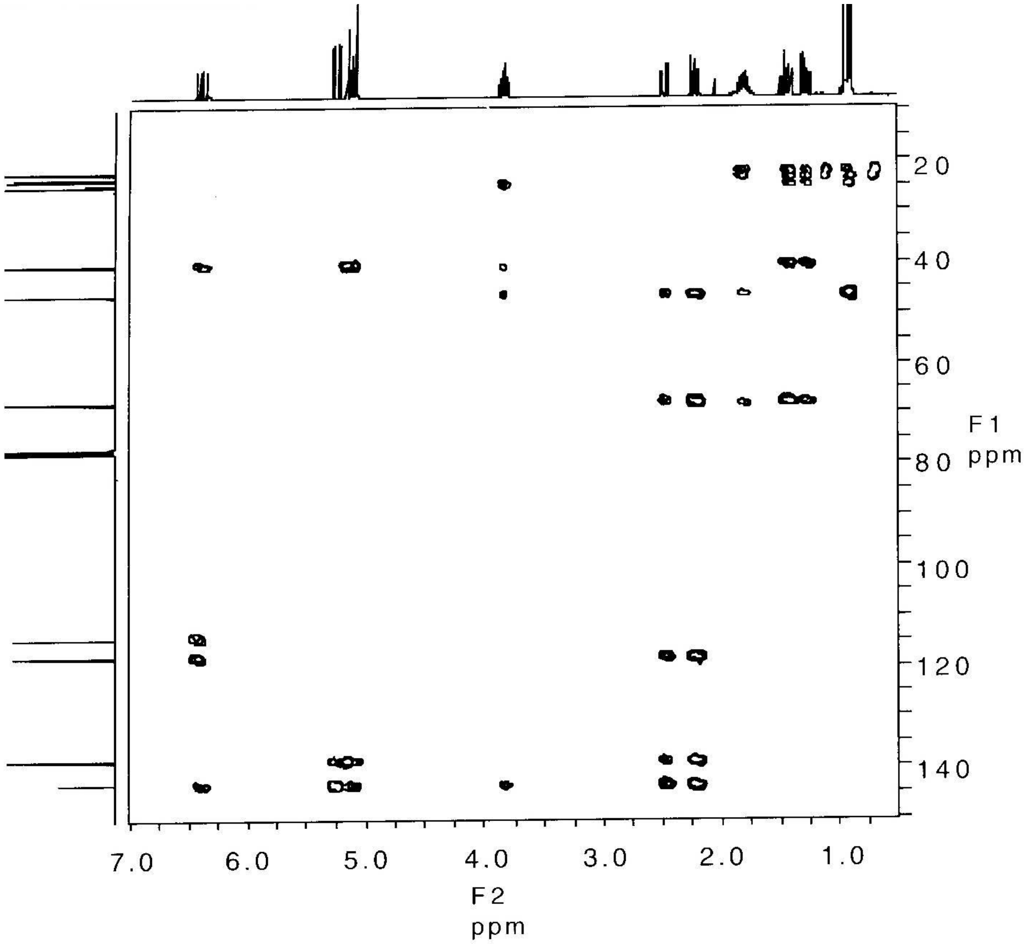
2.5.10. carbon 41 ppm is correlated to proton 2.21/2.48 ppm must be **6**

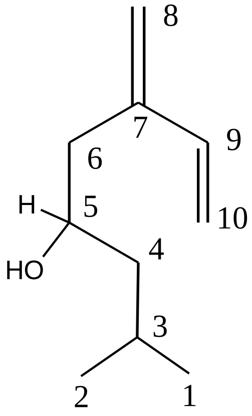
2.5.11. carbon 25 ppm is correlated to proton 1.8 ppm must be **3**

2.5.12. carbon 22/23 ppm are correlated to proton 0.9 ppm must be **1** and **2**

2.6. HMBC – heteronuclear multiple bond correlation

2.6.1. like HETCOR with two and three bond but no one bond coupling (no attached proton)





  - 2.6.2. consider carbon at 41, it is coupled to protons 6.4 (**9**), 5.08 (**8**), 3.82 (**5**), 1.42 (**4**), and1.28 (**4**) ppm. Which carbon is 2/3 bond coupled to protons on C4,5,8,9? From carbon spectrum, 41 ppm is **6** and shows no correlation to attached proton (2.21/2.48 ppm) in HMBC spectrum

3. **Analysis** where to start?
  - 3.1. solvent peaks
  - 3.2. water
  - 3.3. Figure out plausible <u>molecular weights</u> based on the mass spectra
    - 3.3.1. # of carbons (M+1) nitrogen rule (odd M+), halogens, hetero atoms (M+2)
      - 3.3.1.1. Be wary that the M+1/M+ ratio is sometimes off by 1%.
    - 3.3.2. Start with CH formulas with maximum carbons that fit
    - 3.3.3. see if N, O, halogen or other atoms fit
  - 3.4. Is the number of carbon peaks consistent with the molecular formulas?
  - 3.5. Check the area of the NMR peaks
    - 3.5.1. minimum number of hydrogens in your compound
    - 3.5.2. the smallest NMR peak can be no less than one hydrogen and could be whole number multiple
  - 3.6. aromatic, or other unsaturated groups?
  - 3.7. go back and see which molecular formulas can be eliminated
  - 3.8. Calculate <u>degrees of unsaturation</u>
  - 3.9. Check for function groups –IR (4000-1500 cm^{-1}), PMR (aromatic, alkene, heteroatom, methyl, ethyls, OH, aldeyhyde) CNMR (carbonyl, aromatic, olefin, alkyne, aliphatic), DEPT (attached protons)

3.10. Determine adjacent CH groups from multiplicities (coupling and COSY)

3.11. Draw partial structures

3.12. piece them together for possible structures

3.13. Assign all proton and carbon NMR peaks

3.14. check to see if structure is consistent with all spectral data