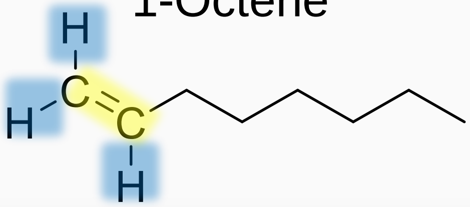
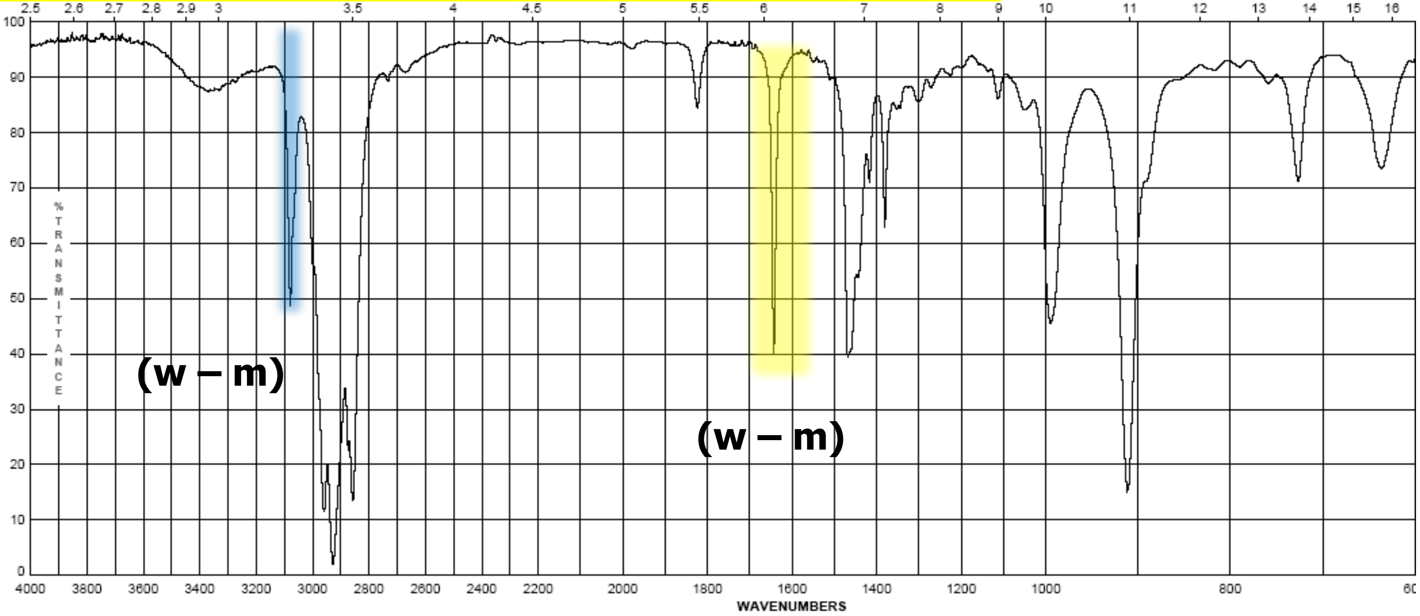
Infrared Spectroscopy

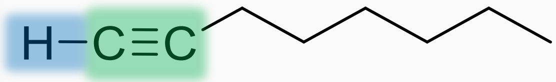
2. **Alkenes** – addition of the C=C and vinyl C-H bonds
   - C=C stretch at 1620-1680 cm^{-1} weaker as substitution increases
   - vinyl C-H stretch occurs at 3000-3100 cm^{-1}
   - The difference between alkane, alkene or alkyne C-H is important:
   - If the band is slightly above 3000 it is alkene or alkyne C-H.
   - If it is below 3000 cm^{-1} it is alkane C-H.

1-Octene





Infrared Spectroscopy

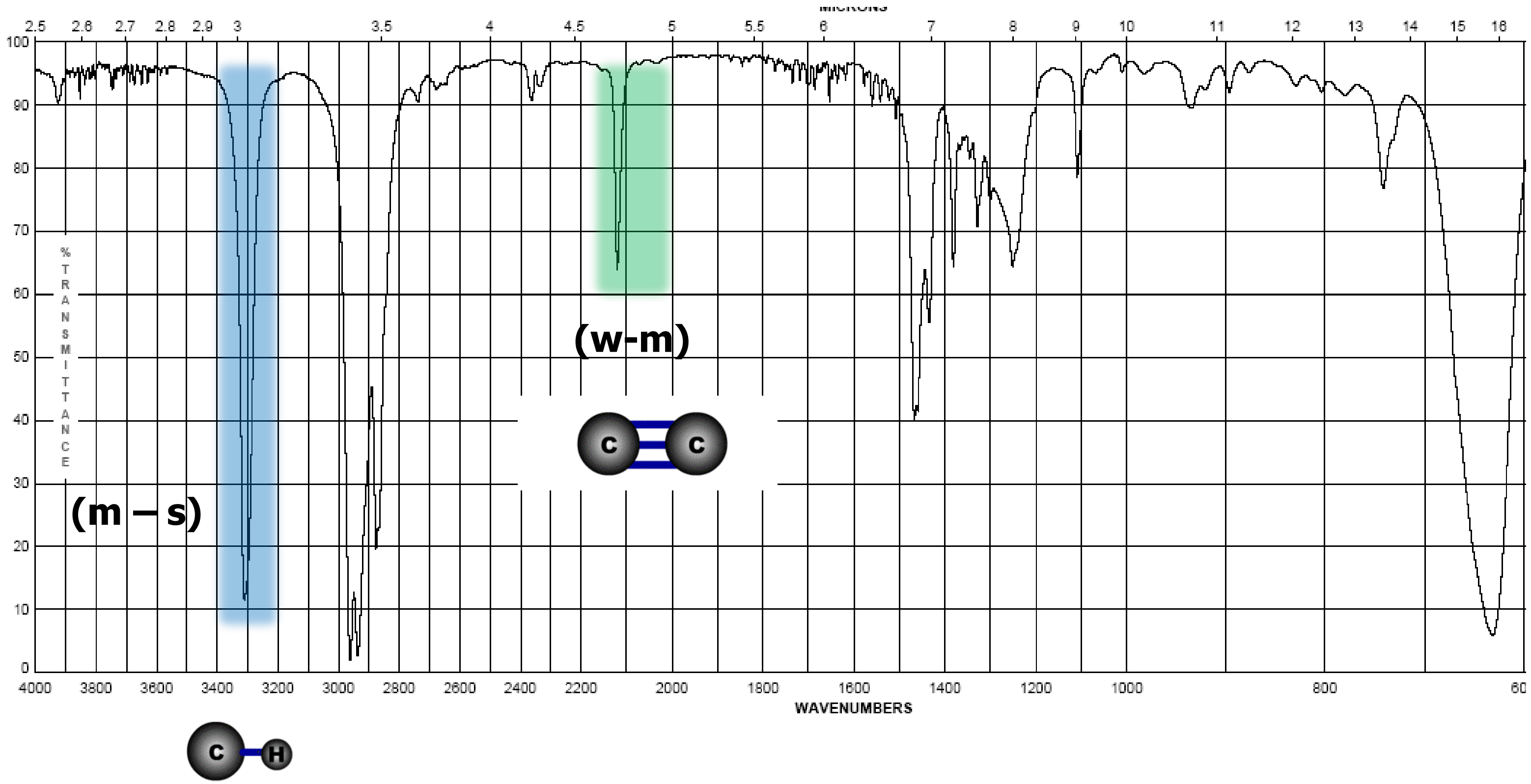


1-Octyne

3. **Alkynes** – addition of the C≡C and alkyne terminal C-H bonds:
   - C≡C stretch 2100-2260 cm^{-1}; strength depends on asymmetry of bond, strongest for terminal alkynes, weakest for symmetrical internal alkynes.

   - C-H for ***terminal*** alkynes occurs at 3200-3300cm^{-1}

   - Internal alkynes (R-C≡C-R) would not have this band!



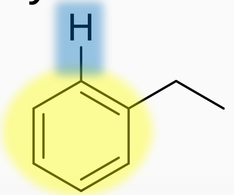
Infrared Spectroscopy

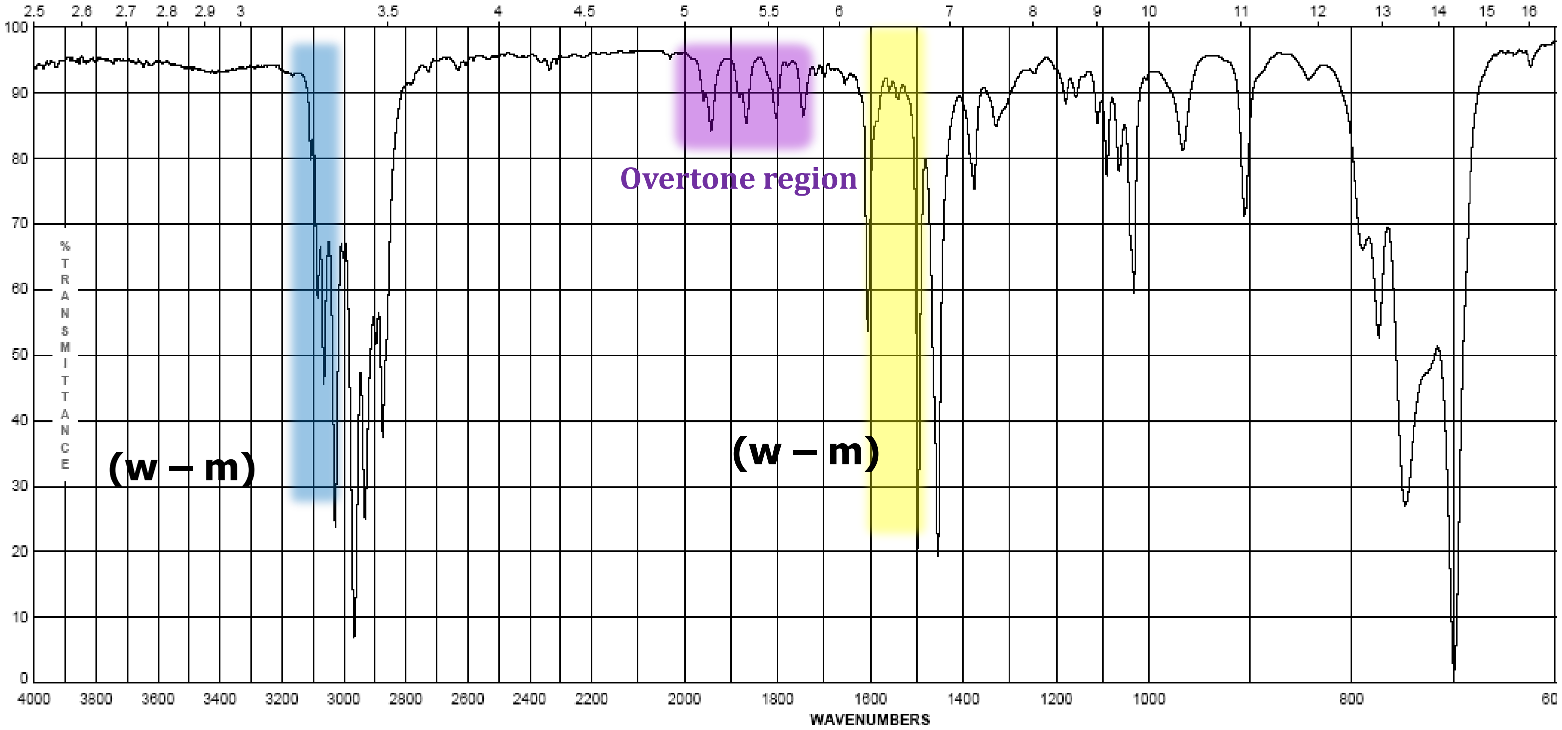
4. Aromatics

- Due to the delocalization of e$^-$ in the ring, the stretching frequency for these bonds is slightly lower in energy than normal C=C.
- These show up as a ***pair*** of sharp bands, 1500 & 1600 cm^{-1}.

- C-H bonds off the ring show up similar to vinyl C-H at 3000-3100 cm^{-1}

Ethyl benzene

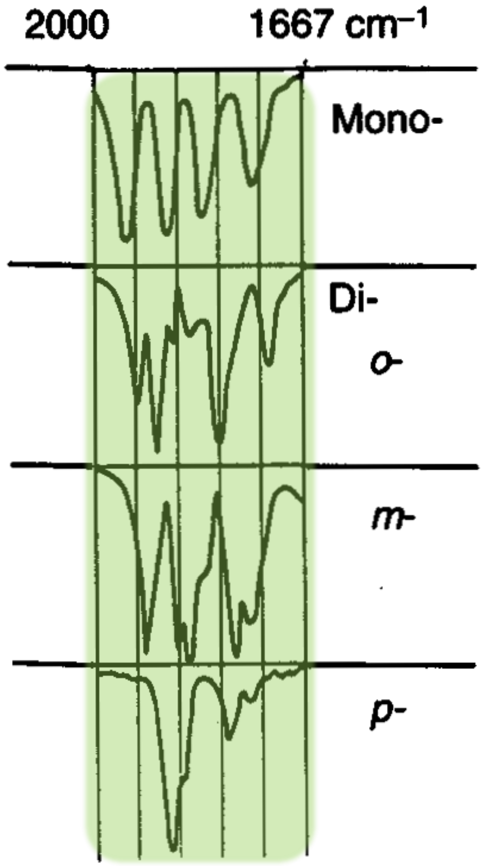


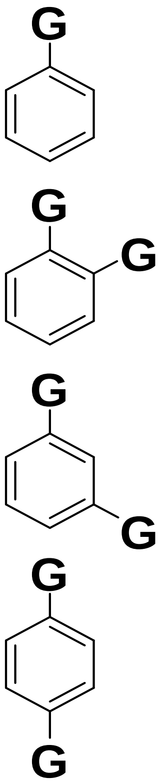


Infrared Spectroscopy

4. Aromatics

- If the region between 1667-2000 cm^{-1} (w) is free of interference (C=O stretching frequency is in this region) a weak grouping of peaks is observed for aromatic systems
- Analysis of this region, called the *overtone of bending* region, can lead to a determination of the substitution pattern on the aromatic ring.





Monosubstituted

1,2 disubstituted (*ortho* or *o*-)

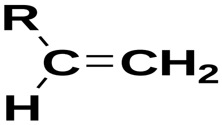
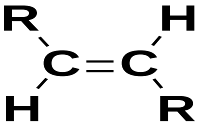
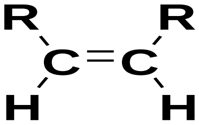
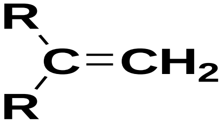
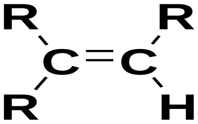
1,2 disubstituted (*meta* or *m*-)

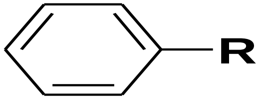
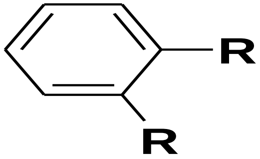
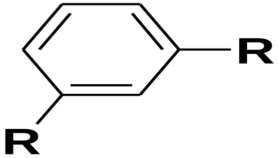
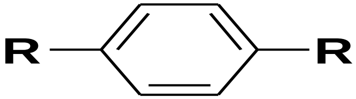
1,4 disubstituted (*para* or *p*-)

Infrared Spectroscopy

5. **Unsaturated Systems** – substitution patterns

- The substitution of aromatics and alkenes can also be discerned through the out-of-plane bending vibration region
- However, other peaks often are apparent in this region. *These peaks should only be used for reinforcement of what is known or for hypothesizing as to the functional pattern.*

	cm^{-1}
	985-997 905-915
	960-980
	665-730
	885-895
	790-840

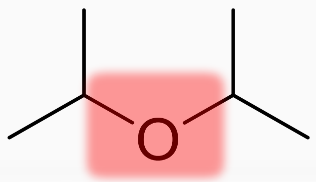
	cm^{-1}
	730-770 690-710
	735-770
	860-900 750-810 680-725
	800-860

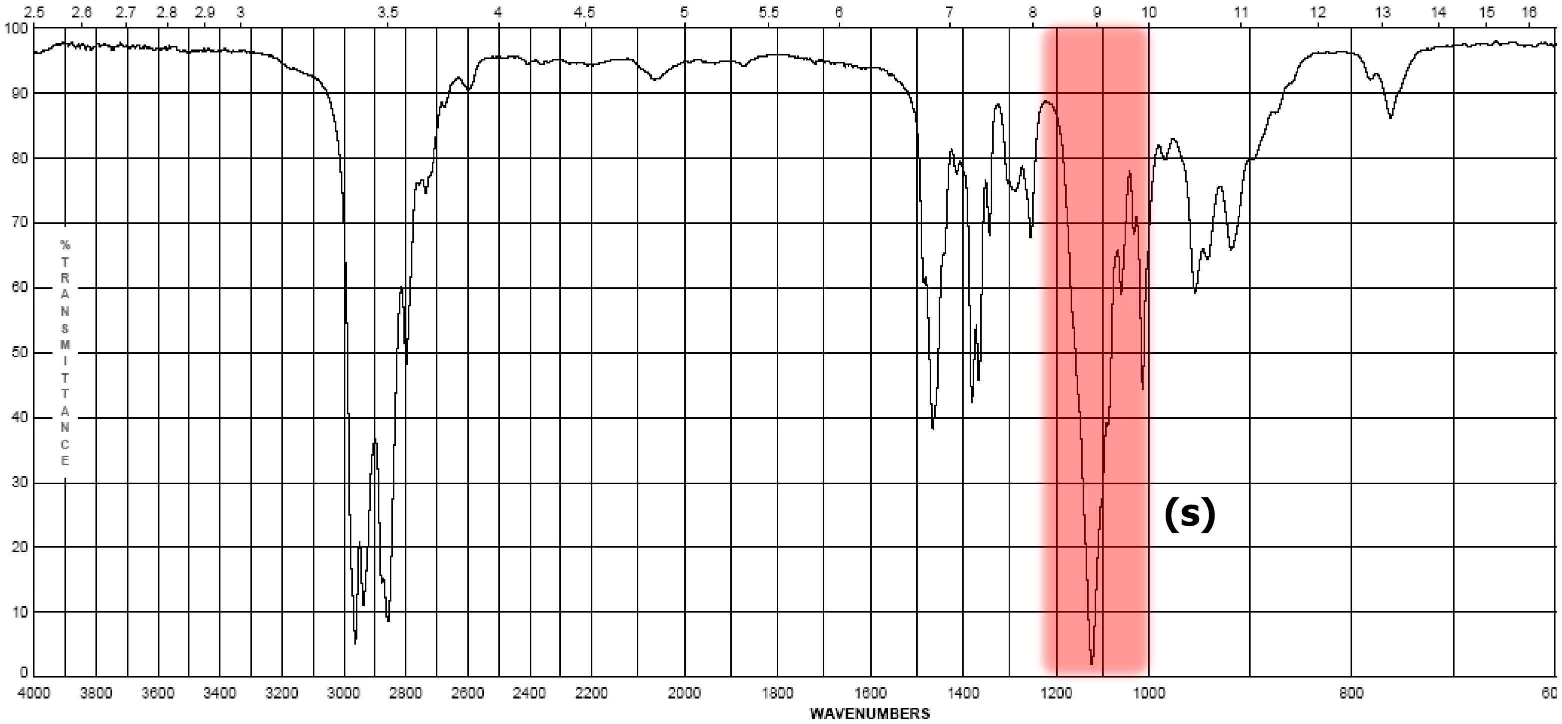
Infrared Spectroscopy

6. Ethers –

- Show a strong band for the symmetric C-O-C stretch at 1050-1150 cm^{-1}

Diisopropyl ether

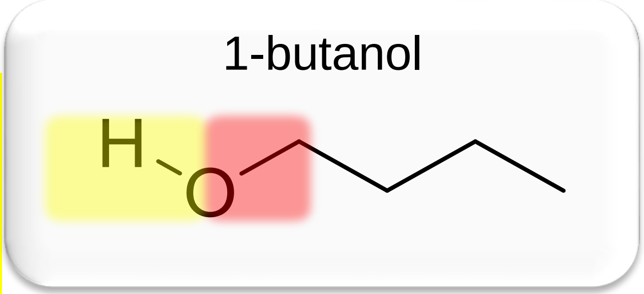


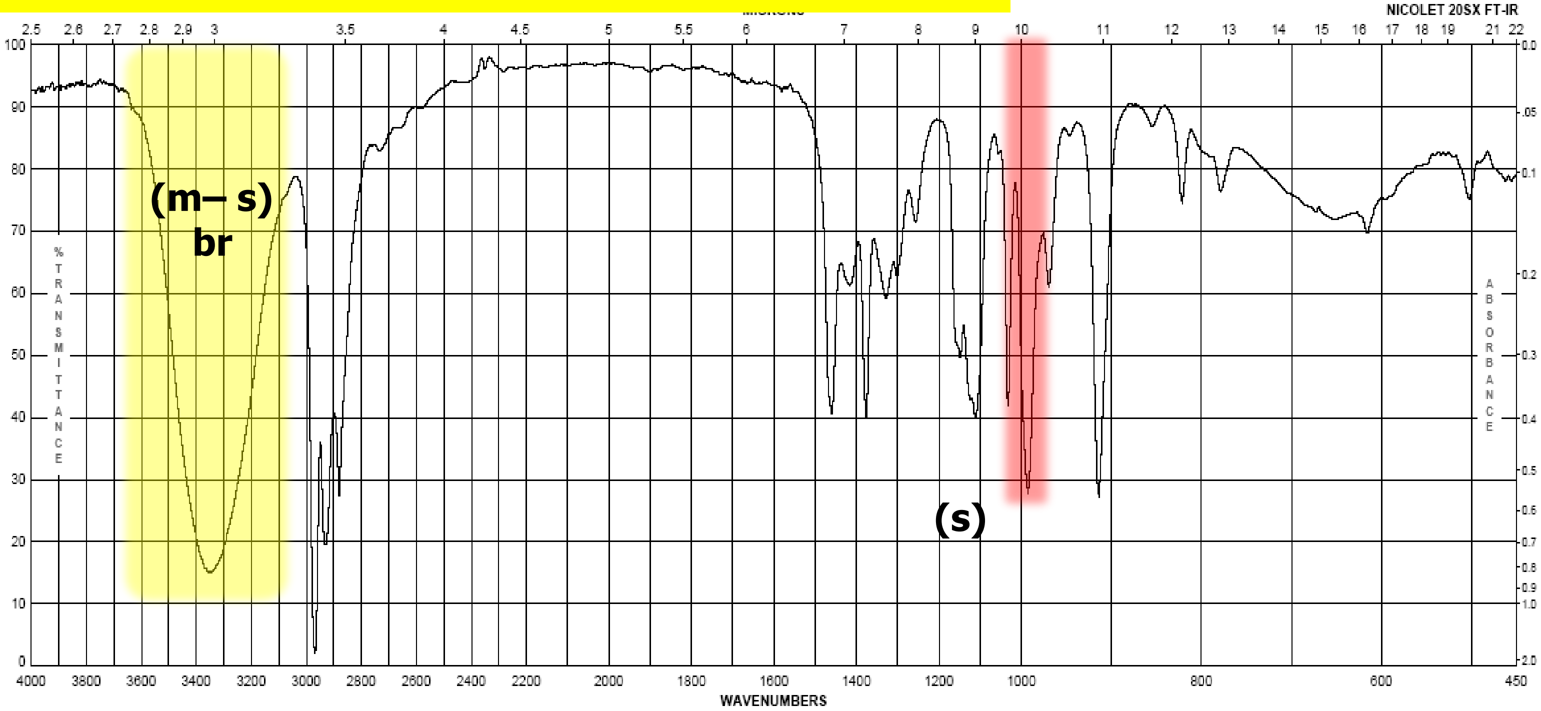


Infrared Spectroscopy

7. Alcohols

- Strong, broad O-H stretch from 3200-3400 cm^{-1}
- Like ethers, C-O stretch from 1050-1260 cm^{-1}
- Band position changes depending on the alcohols substitution: 1° 1000-1075; 2° 1075-1150; 3° 1100-1200; phenol 1180-1260
- The shape is due to the presence of hydrogen bonding


1-butanol

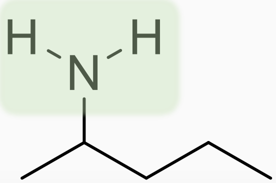


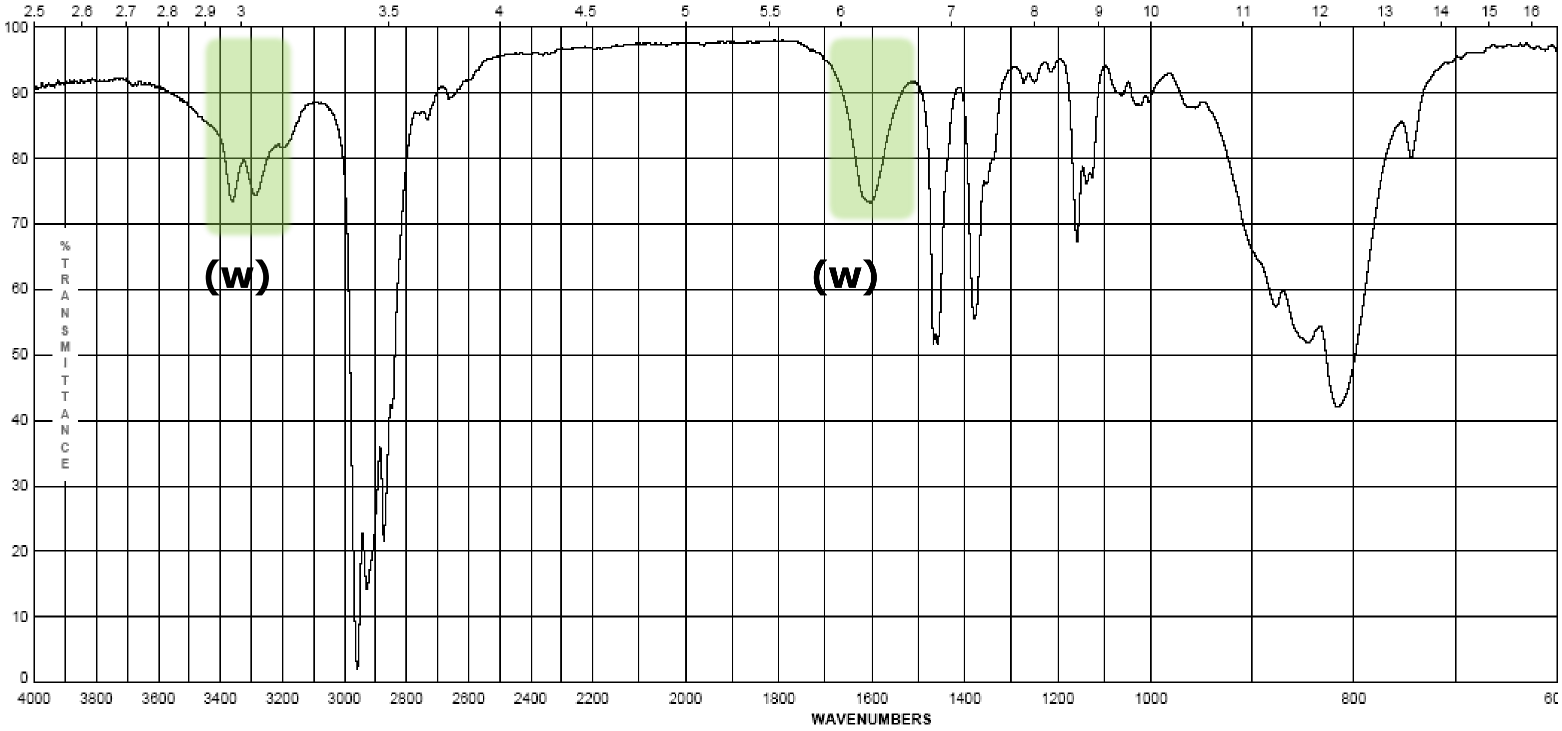
Infrared Spectroscopy

8. Amines - Primary

- Shows the –N-H stretch for NH_2 as a ***doublet*** between 3200-3500 cm^{-1} (symmetric and asymmetric (anti-symmetric) modes)
- -NH_2 has deformation band from 1590-1650 cm^{-1}
- Additionally there is a “wag” band at 780-820 cm^{-1} that is not diagnostic

2-aminopentane





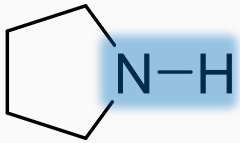
Infrared Spectroscopy

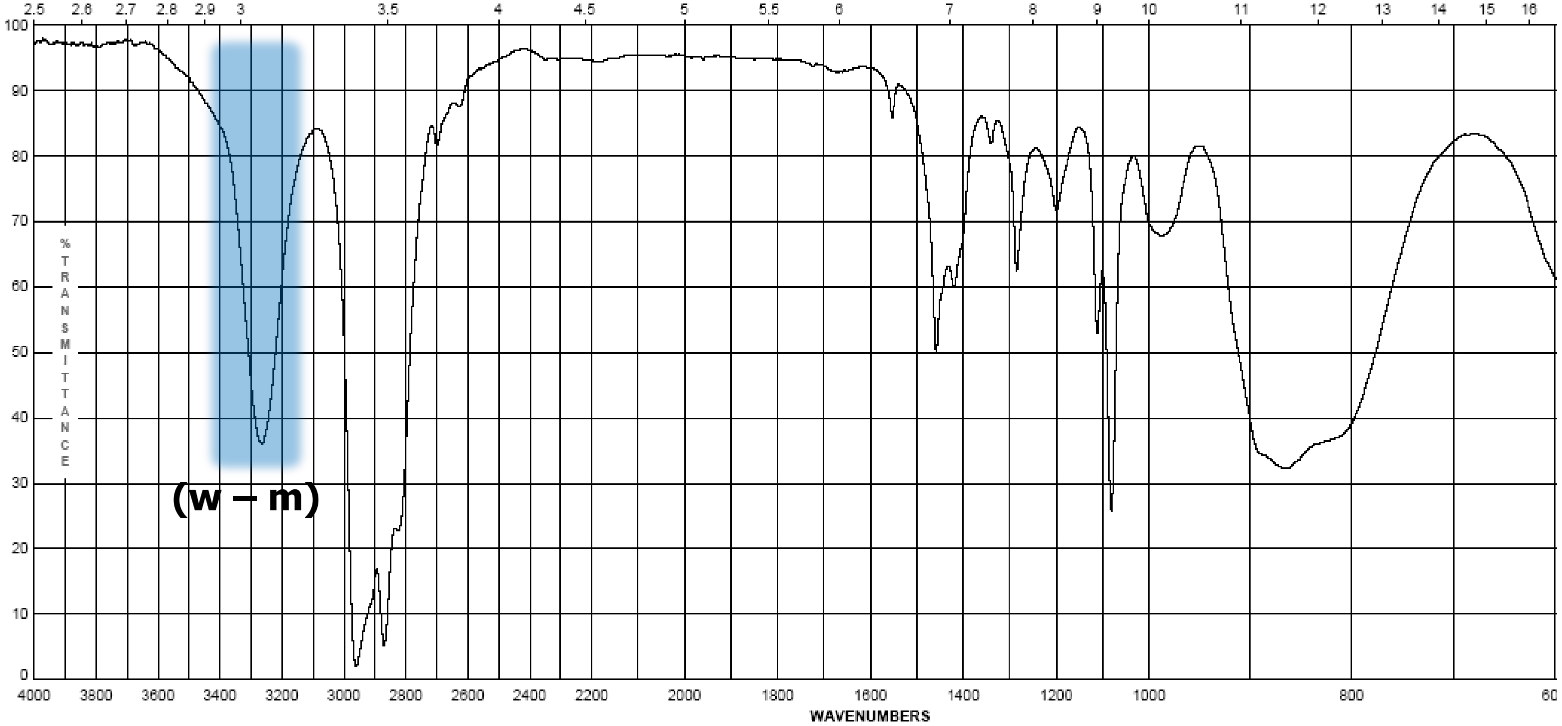
9. Amines – Secondary

- N-H band for R_2N-H occurs at 3200-3500 cm^{-1} as a single sharp peak weaker than –O-H

- Tertiary amines (R_3N) have no N-H bond and *will not* have a band in this region

pyrrolidine

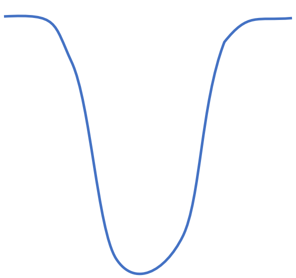




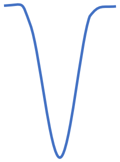
Infrared Spectroscopy

Pause and Review

- Inspect the bonds to H region (2700 – 4000 cm^{-1})
- Peaks from 2850-3000 are simply sp^3 C-H in most organic molecules

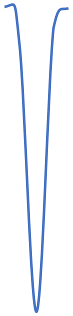


Broad U-shape peak
-**O—H** bond



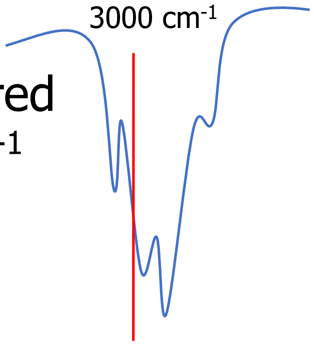
V-shape peak
-N—H bond for 2°
amine (R$_2$**N—H**)

W-shape peak
-N—H bond for 1°
amine (R**NH**$_2$)



Sharp spike
-C≡**C—H** bond

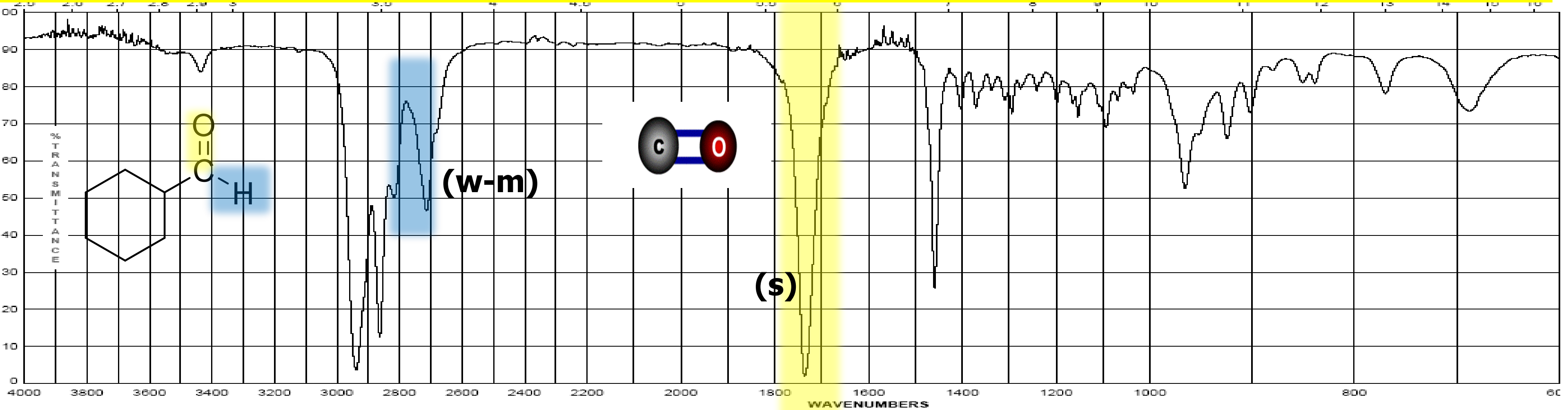
Small peak shouldered
just above 3000 cm^{-1}
C=**C—H** or Ph**—H**

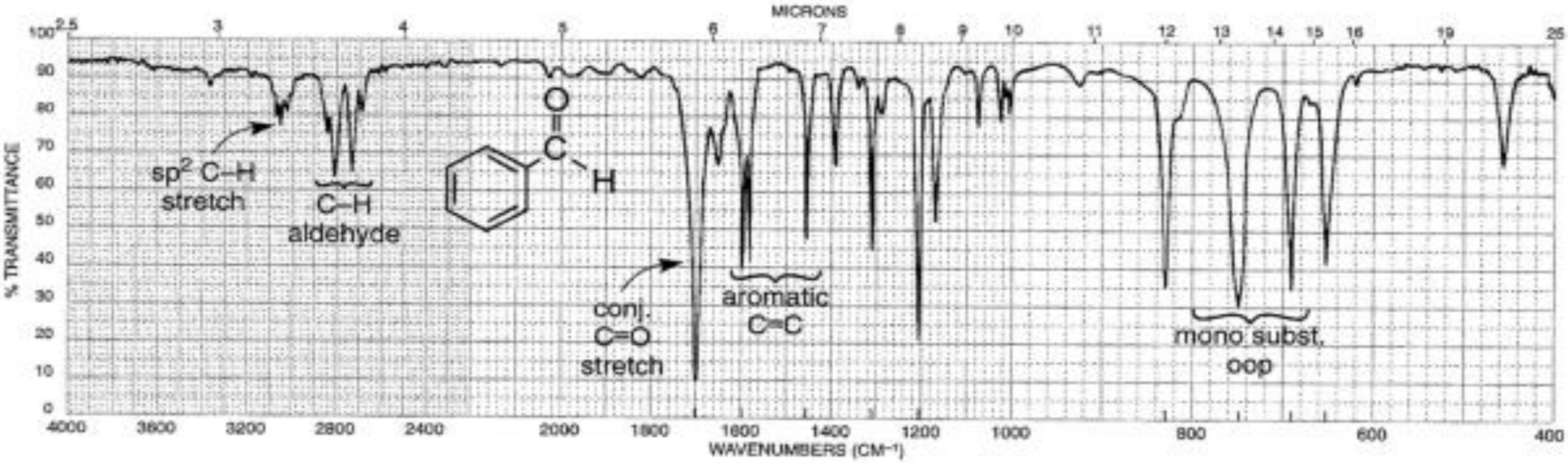


Infrared Spectroscopy

10. Aldehydes

- C=O (carbonyl) stretch from 1720-1740 cm^{-1}
- Band is sensitive to conjugation, as are all carbonyls (upcoming slide)
- A highly unique sp^2 C-H stretch appears as a doublet, 2720 & 2820 cm^{-1} called a "*Fermi doublet*"





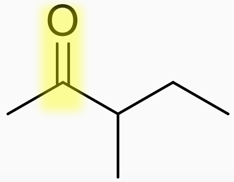
Infrared Spectroscopy

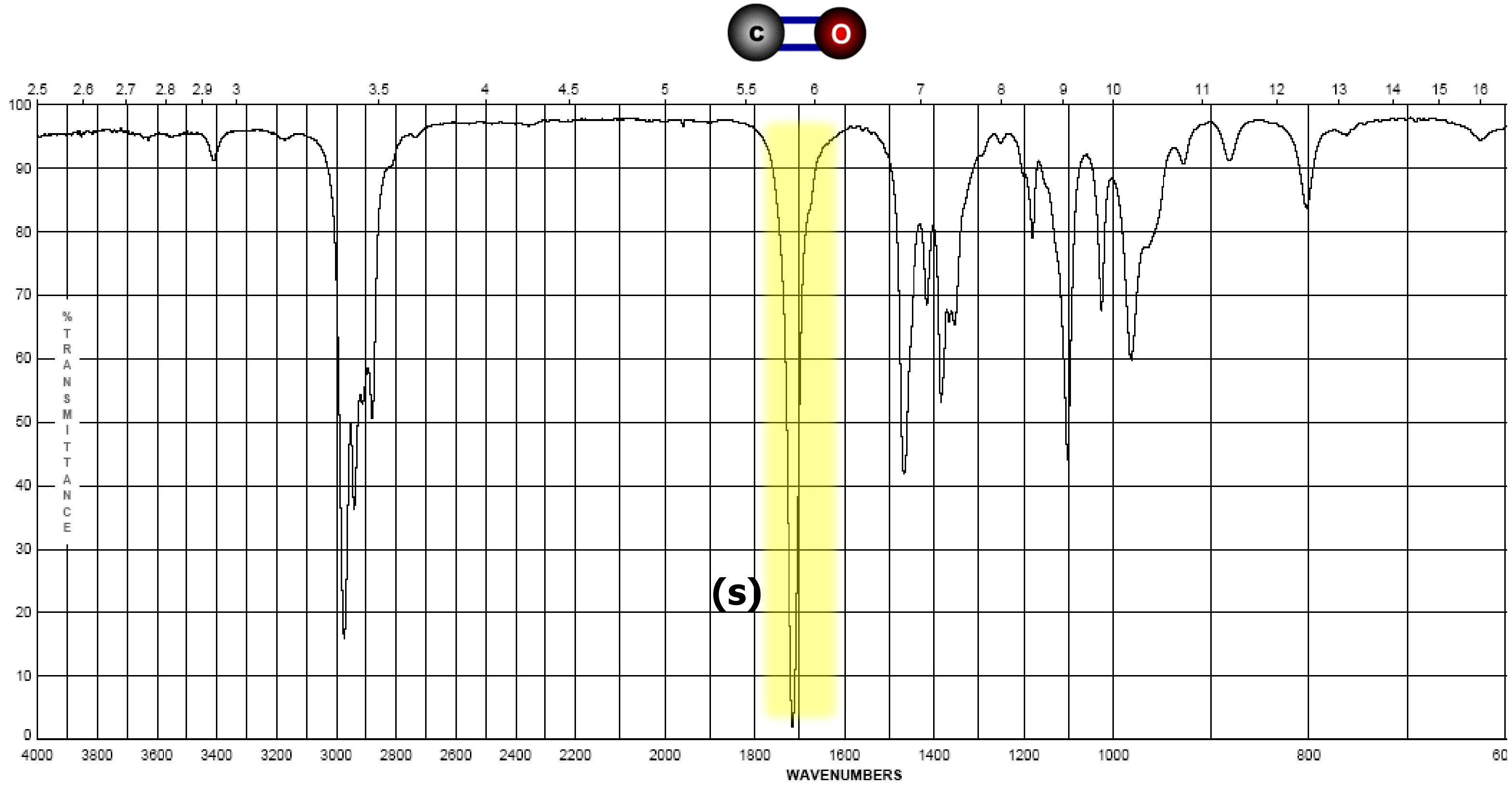
11. Ketones

- Simplest of the carbonyl compounds as far as IR spectrum – carbonyl only

- C=O stretch occurs at 1705-1725 cm^{-1}

3-methyl-2-pentanone



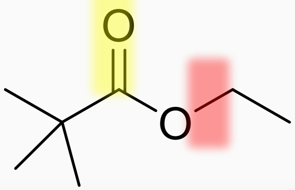


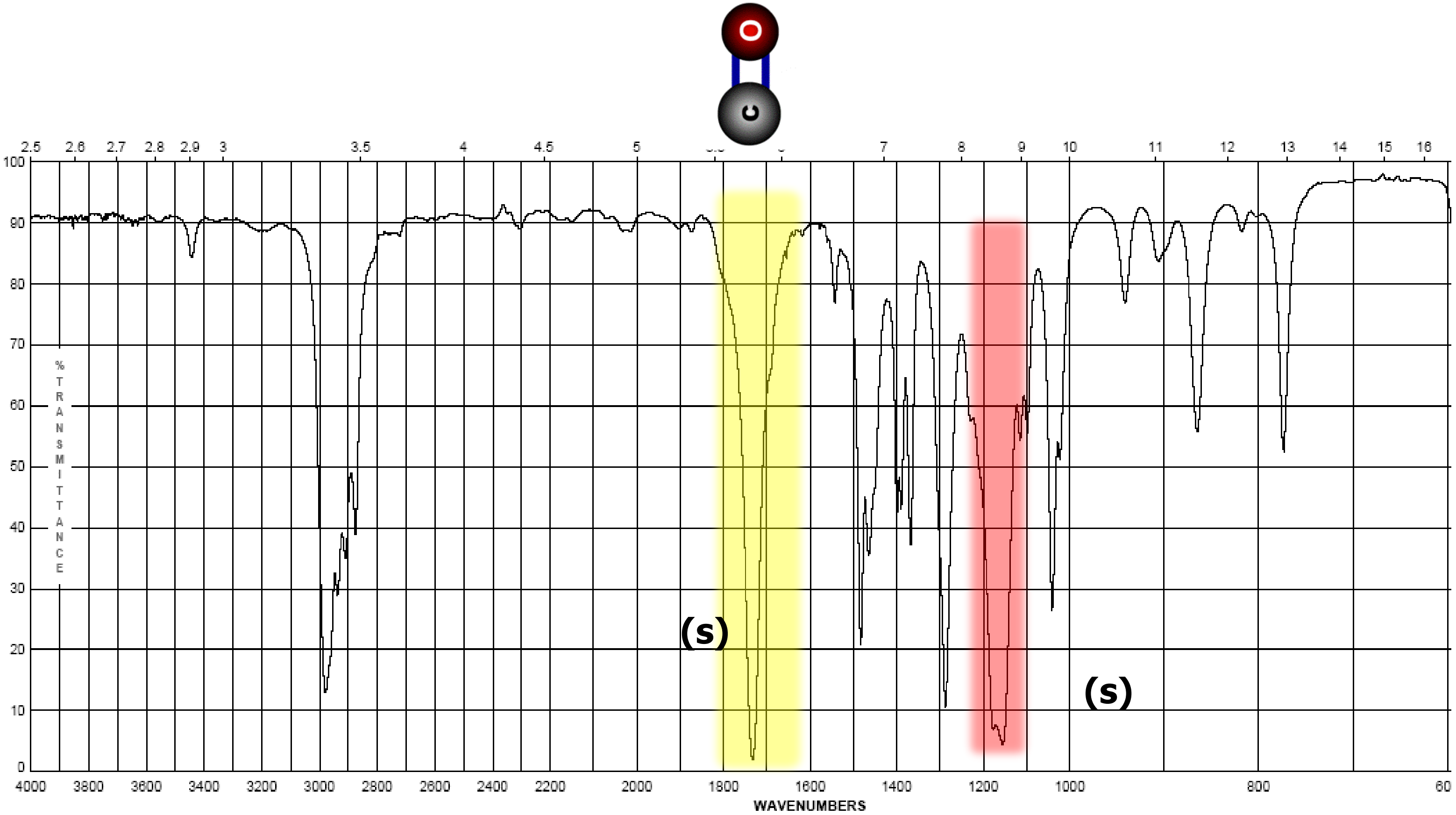
Infrared Spectroscopy

12. Esters

- C=O stretch at 1735-1750 cm^{-1}
- Strong band for C-O at a higher frequency than ethers or alcohols at 1150-1250 cm^{-1}

Ethyl pivalate



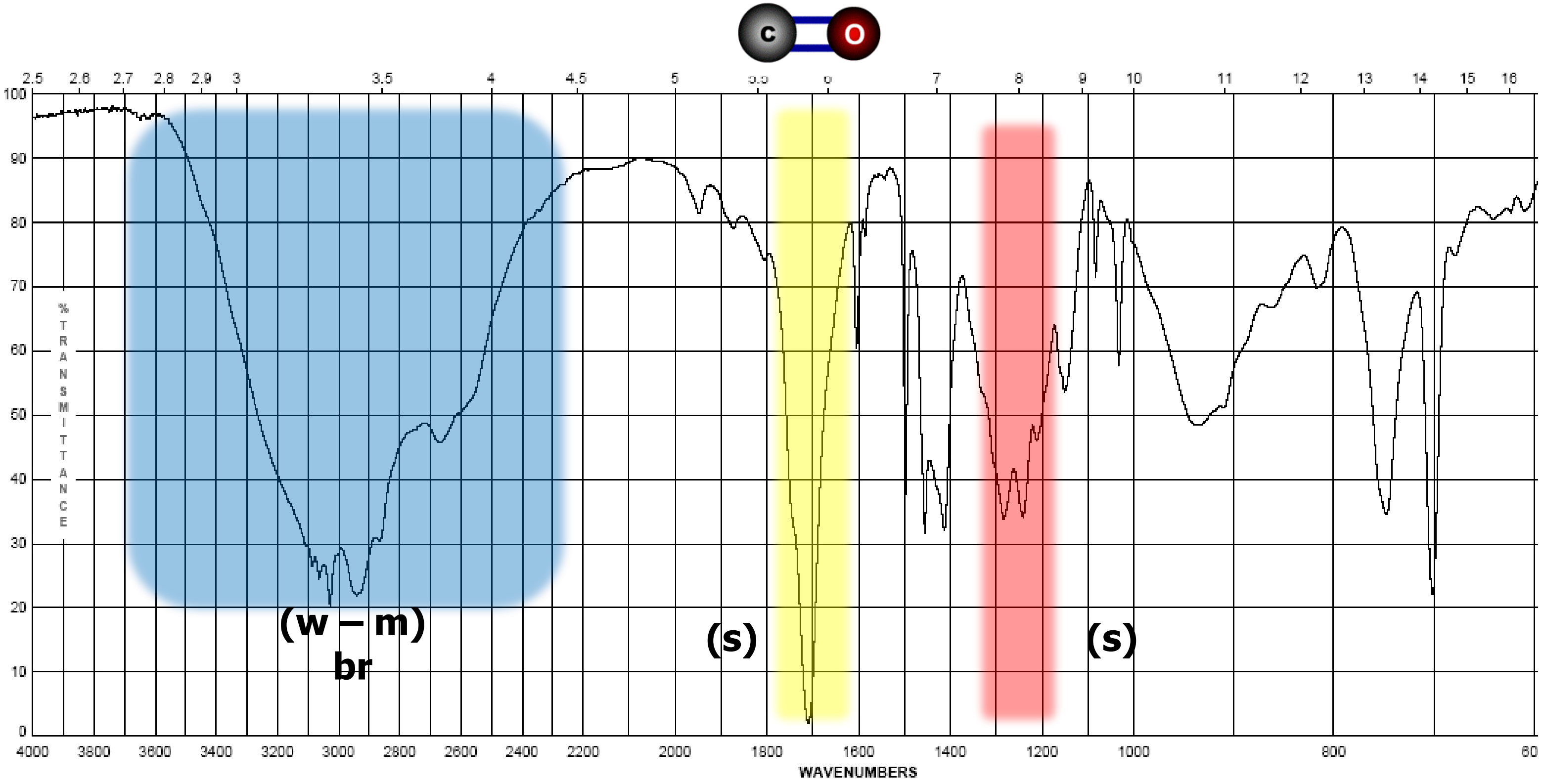


Infrared Spectroscopy

4-phenylbutyric acid

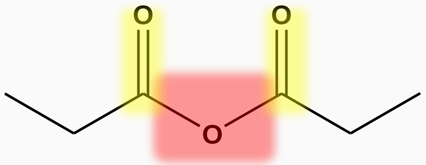
13. Carboxylic Acids:

- Gives the messiest of IR spectra
- C=O band occurs between 1700-1725 cm^{-1}
- The highly dissociated O-H bond has a broad band from 2400-3500 cm^{-1} covering up to half the IR spectrum in some cases



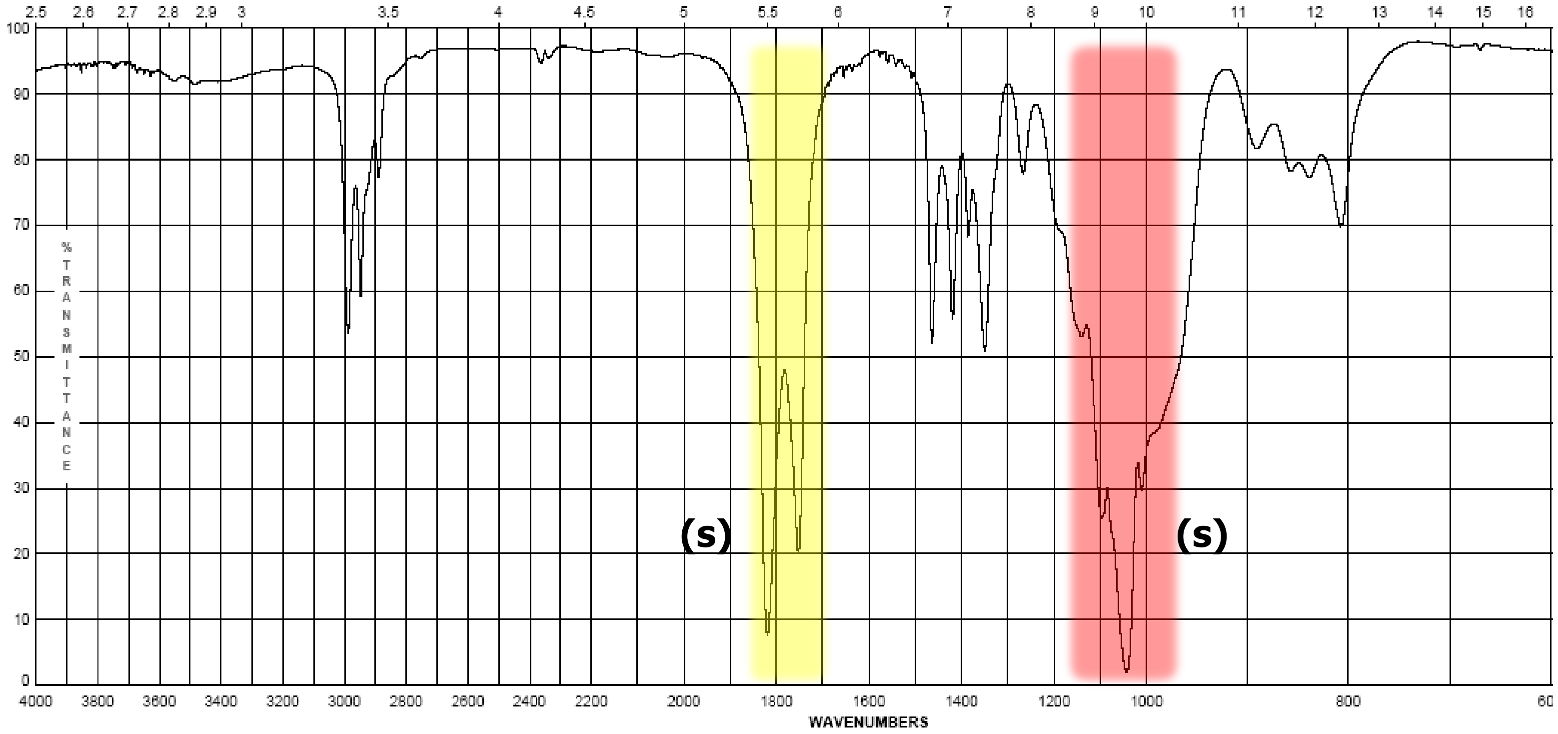
Infrared Spectroscopy

Propionic anhydride



14. Acid anhydrides

- Coupling of the anhydride though the ether oxygen splits the carbonyl band into two with a separation of 70 cm^{-1}
- Bands are at 1740-1770 cm^{-1} and 1810-1840 cm^{-1}
- Mixed mode C-O stretch at 1000-1100 cm^{-1}



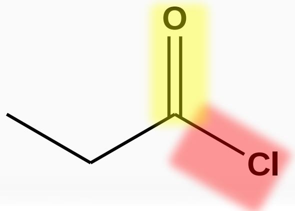
Infrared Spectroscopy

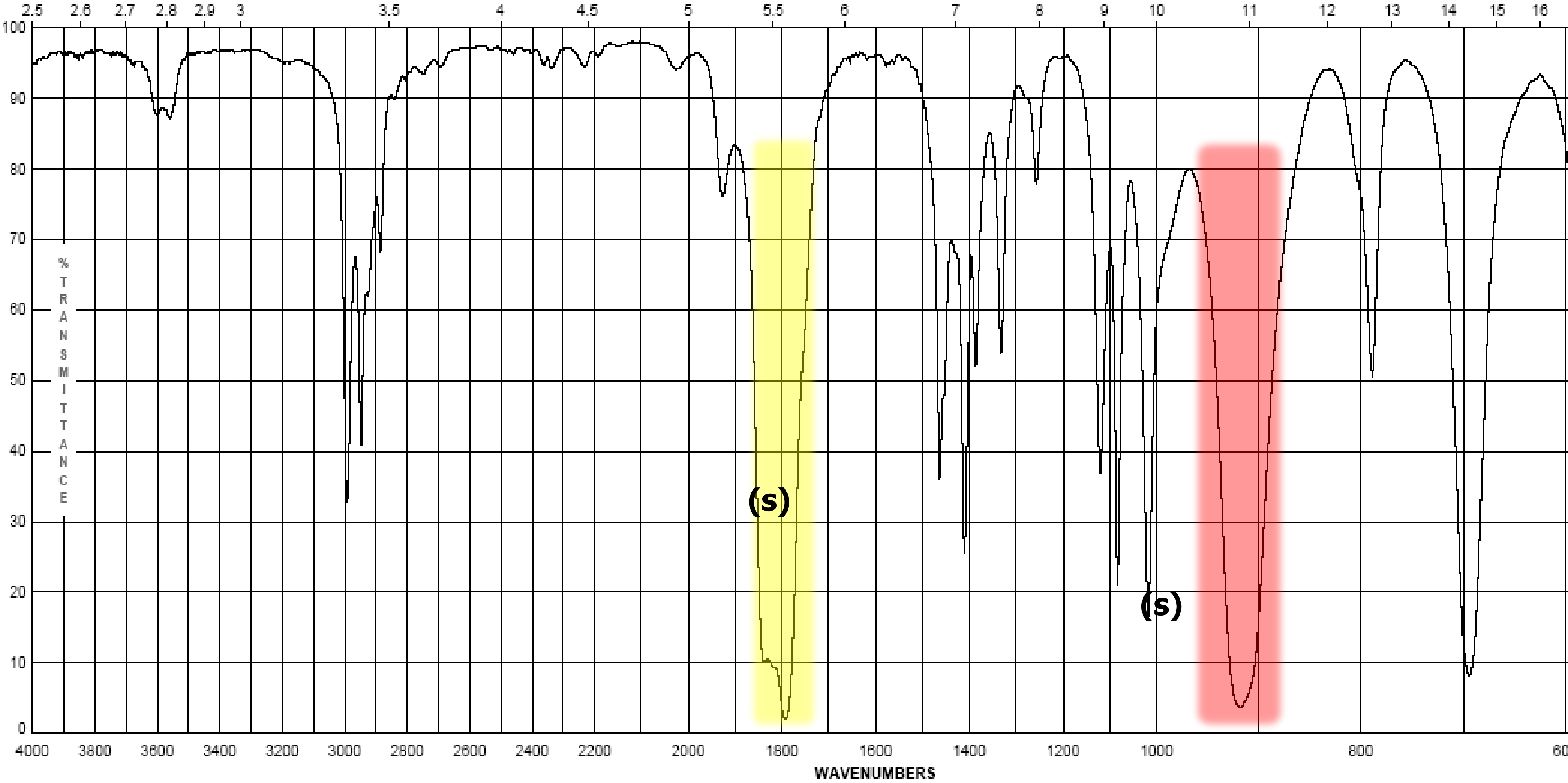
15. Acid halides

- Clefted band at 1770-1820 cm^{-1} for C=O

- Bonds to halogens, due to their size occur at low frequencies, only Cl is light enough to have a band on IR, C-Cl is at 600-800 cm^{-1}

Propionyl chloride

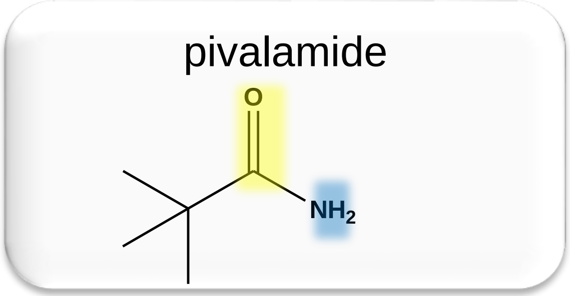


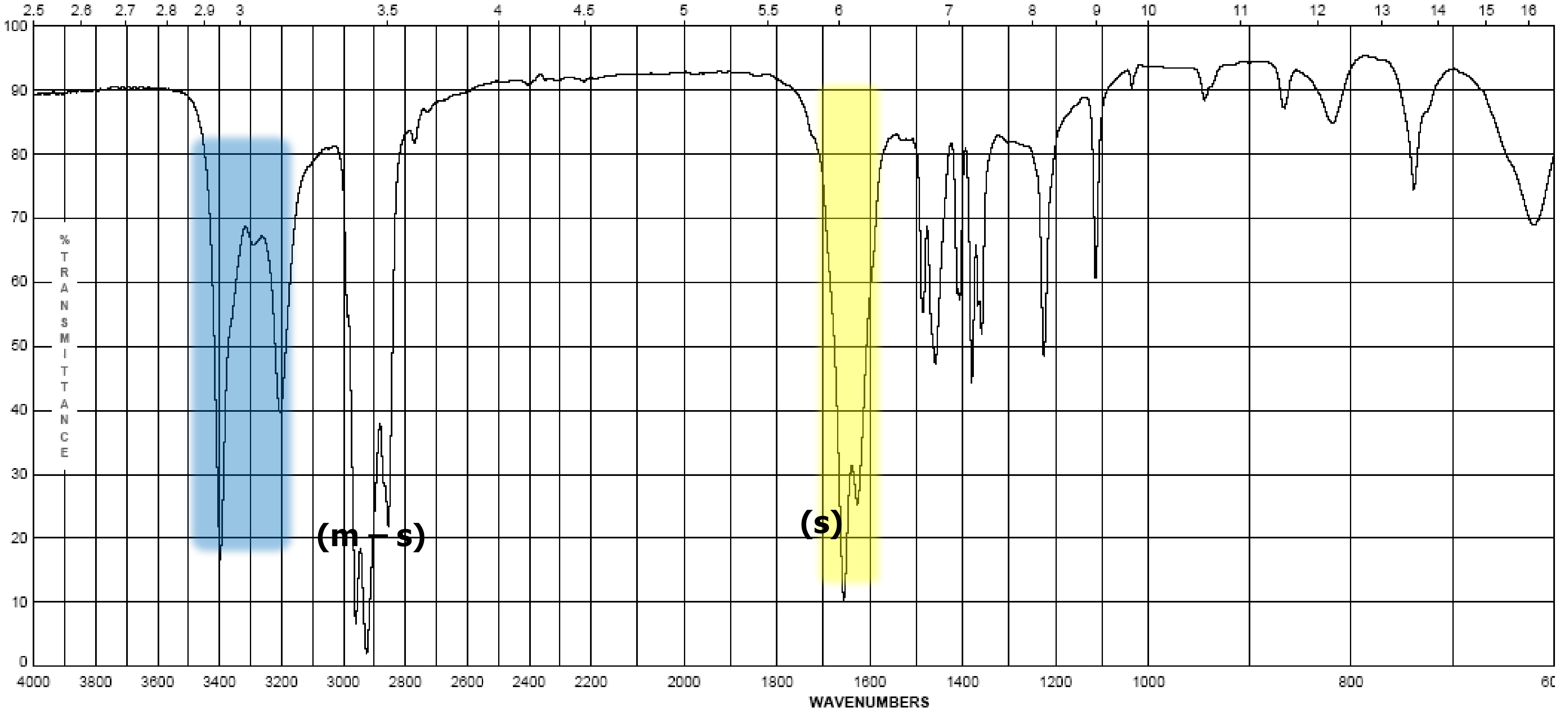


Infrared Spectroscopy

16. Amides

- Display features of amines and carbonyl compounds
- C=O stretch at 1640-1680 cm^{-1}
- If the amide is primary (-NH$_2$) the N-H stretch occurs from 3200-3500 cm^{-1} as a doublet
- If the amide is secondary (-NHR) the N-H stretch occurs at 3200-3500 cm^{-1} as a sharp singlet



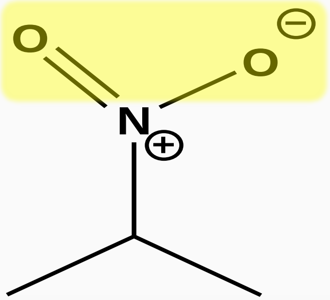


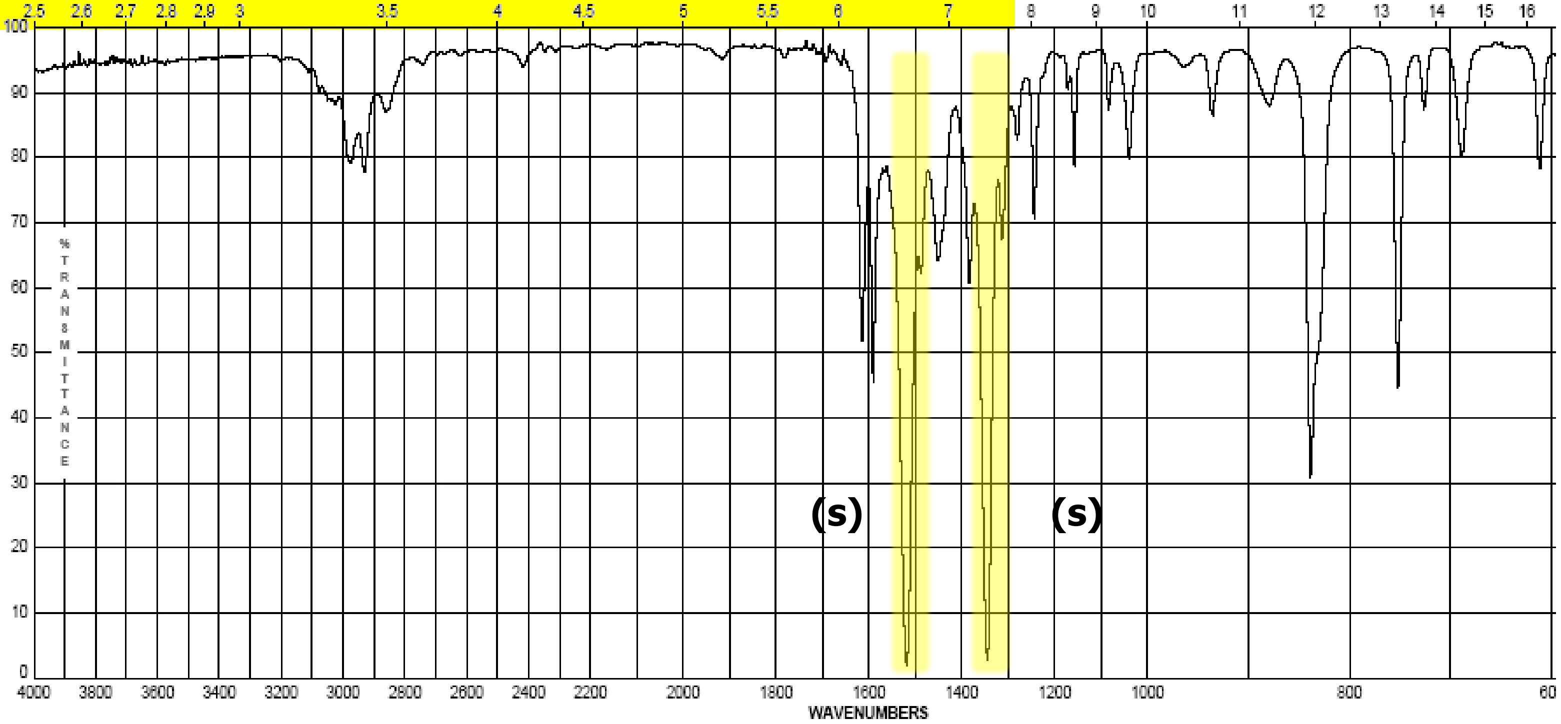
Infrared Spectroscopy

17. Nitro group (-NO_2)

- Proper Lewis structure gives a bond order of 1.5 from nitrogen to each oxygen
- Two bands are seen (symmetric and asymmetric) at 1300-1380 cm^{-1} and 1500-1570 cm^{-1}
- This group is a strong resonance withdrawing group and is itself vulnerable (susceptible) to resonance effects

2-nitropropane



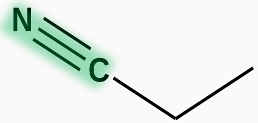


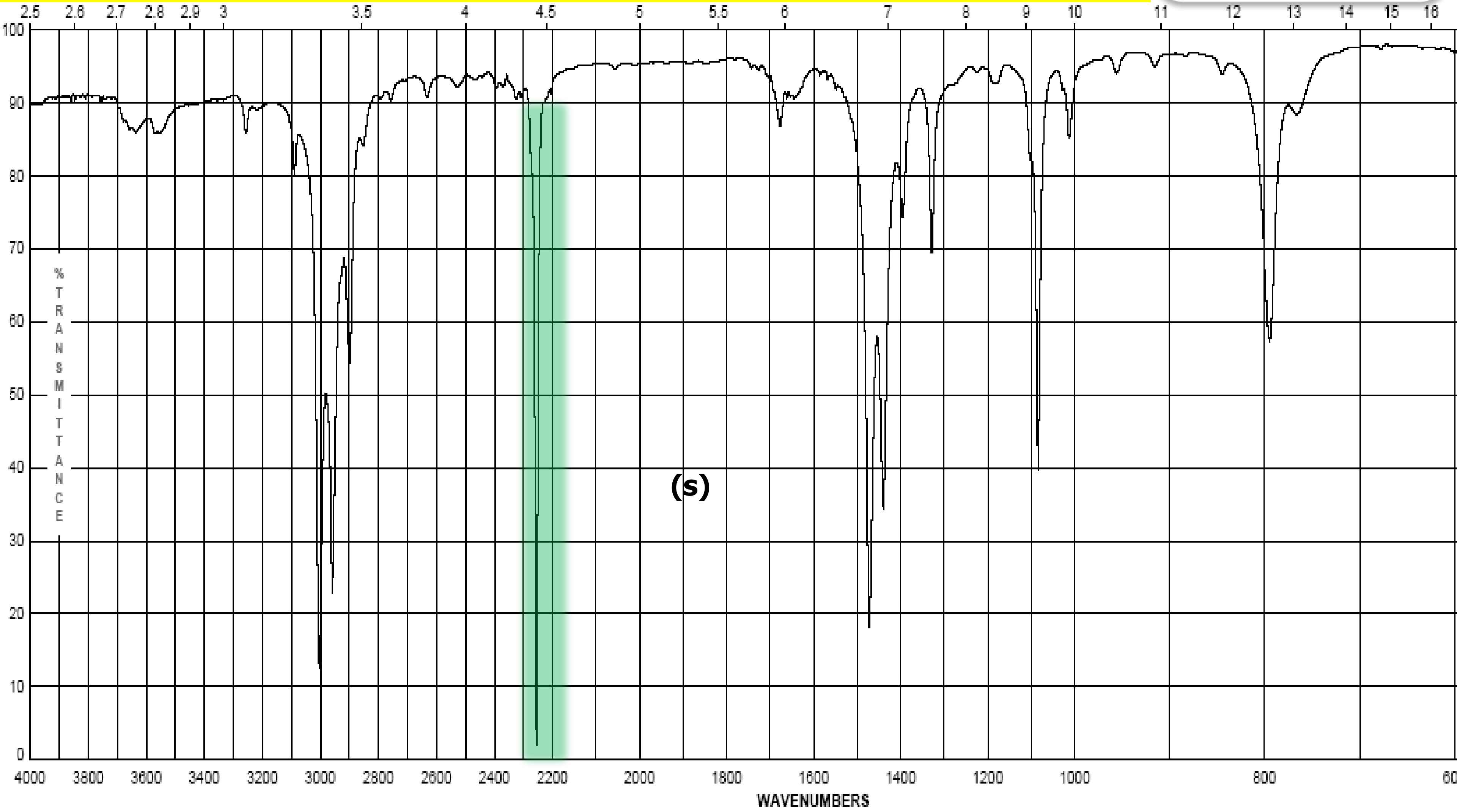
Infrared Spectroscopy

18. Nitriles (the cyano- or –C≡N group)

- Principle group is the carbon nitrogen triple bond at 2100-2280 cm^{-1}
- This peak is usually much more intense than that of the alkyne due to the electronegativity difference between carbon and nitrogen

propionitrile





Fingerprint region

In the region from ≈ 1300 to 400 cm^{-1}, vibrational frequencies are affected by the entire molecule, as the broader ranges for group absorptions in the figure below – **fingerprint region**.

Absorption in this fingerprint region is characteristic of the molecule as a whole. This region finds widespread use for identification purpose by comparison with library spectra.

H.W: does the fingerprint region useful in characterization of drug molecules?

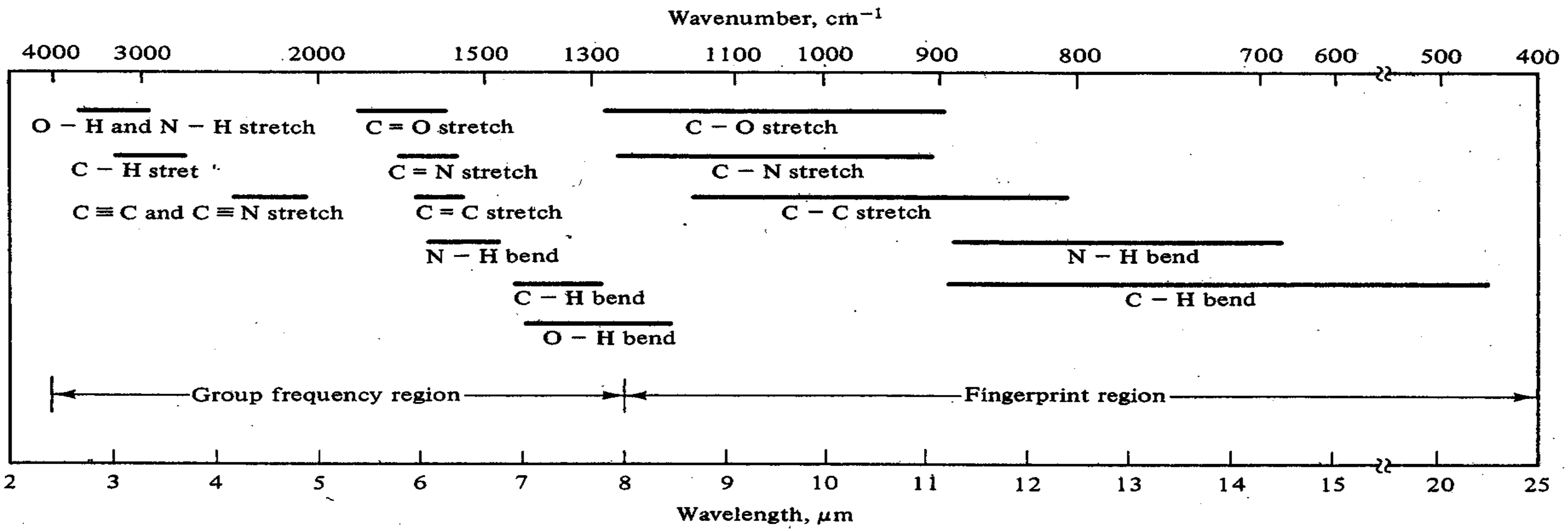
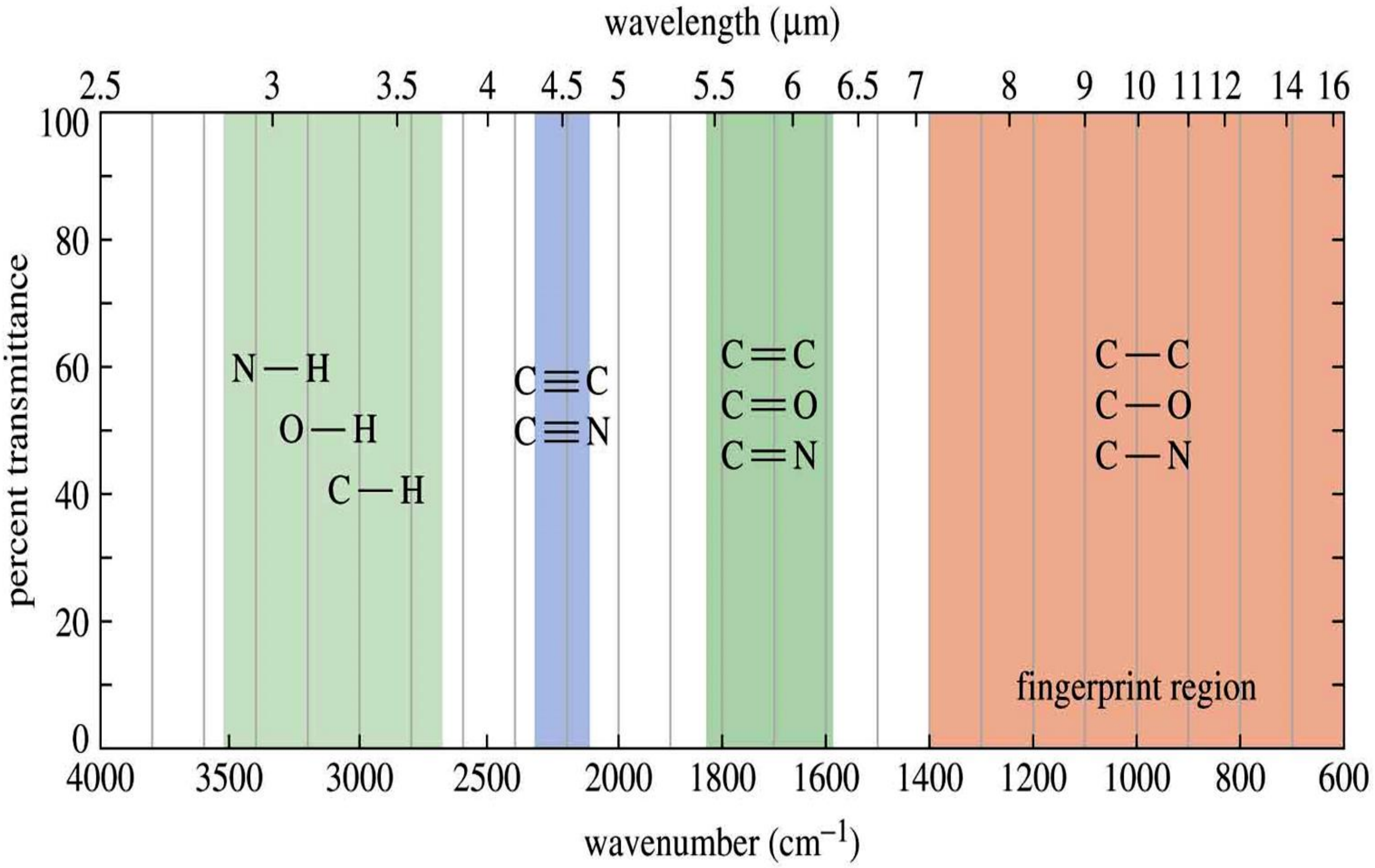
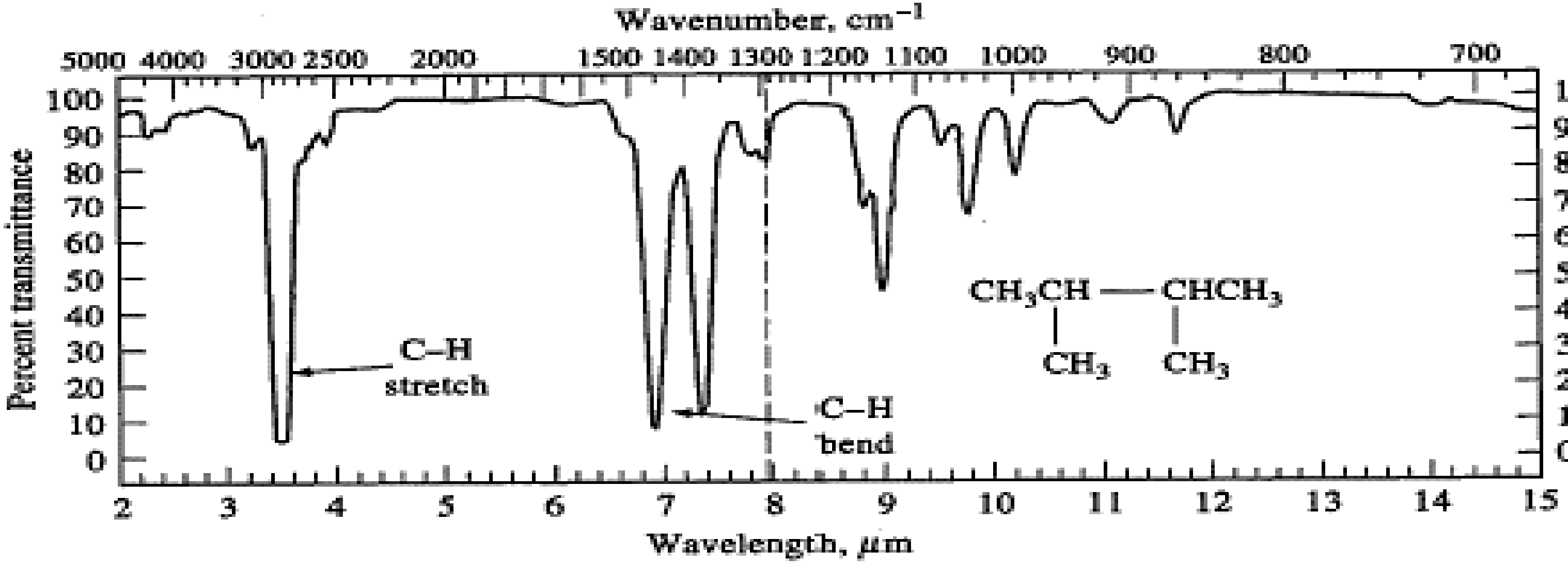


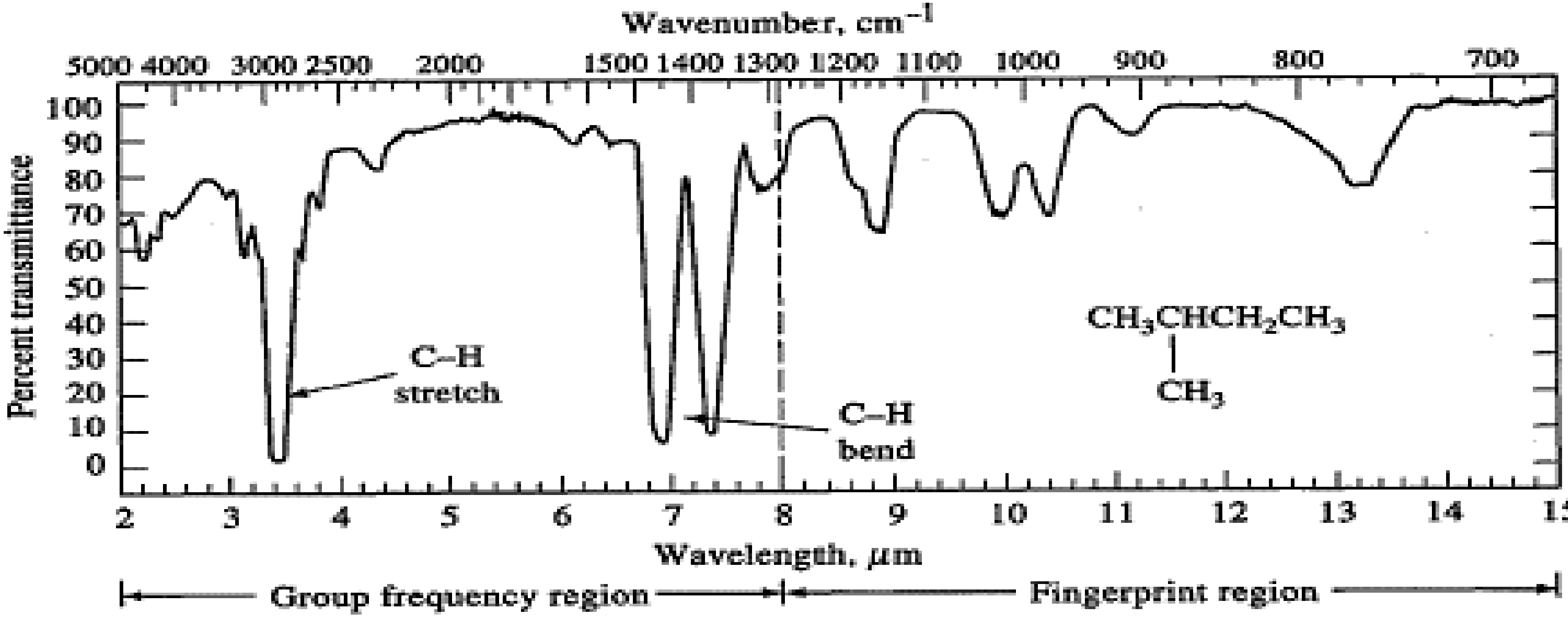
FIGURE 14-3 Frequencies of various group vibrations in the group frequency region and in the fingerprint region.

Summary of IR Absorptions




Wavenumber, cm^{-1}
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900 800 700
Percent transmittance
100 90 80 70 60 50 40 30 20 10 0
C–H stretch
C–H bend
$CH_3CH—CHCH_3$
CH_3 CH_3
2 3 4 5 6 7 8 9 10 11 12 13 14 15
Wavelength, μm

(a)

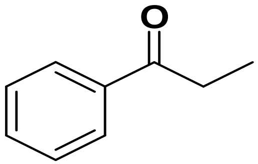

Wavenumber, cm^{-1}
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900 800 700
Percent transmittance
100 90 80 70 60 50 40 30 20 10 0
C–H stretch
C–H bend
$CH_3CHCH_2CH_3$
CH_3
2 3 4 5 6 7 8 9 10 11 12 13 14 15
Wavelength, μm
Group frequency region
Fingerprint region

(b)

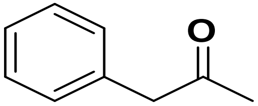
Infrared Spectroscopy

Effects on IR bands

1. **Conjugation** – by resonance, conjugation lowers the energy of a double or triple bond. The effect of this is readily observed in the IR spectrum:

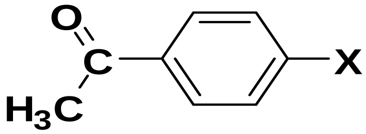


1684 cm^{-1}
C=O

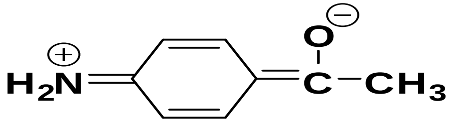


1715 cm^{-1}
C=O

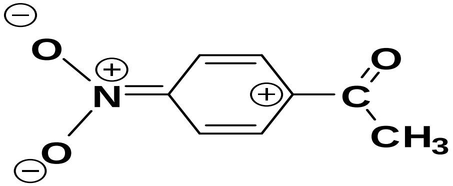
- Conjugation will lower the observed IR band for a carbonyl from 20-40 cm^{-1} provided conjugation gives a strong resonance contributor



X =	**NH_2**	**CH_3**	**Cl**	**NO_2**	
	1677	**1687**	**1692**	**1700**	**cm^{-1}**



vs.



Strong resonance contributor

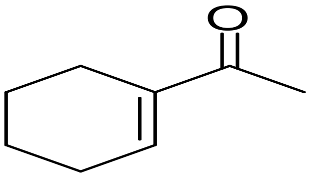
Poor resonance contributor
(cannot resonate with C=O)

- Inductive effects are usually small, unless coupled with a resonance contributor (note $–CH_3$ and –Cl above)

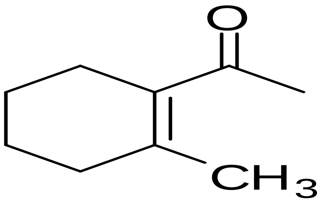
Infrared Spectroscopy

Effects on IR bands

2. **Steric effects** – usually not important in IR spectroscopy, unless they reduce the strength of a bond (usually π) by interfering with proper orbital overlap:



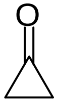
C=O: 1686 cm^{-1}



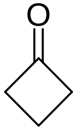
C=O: 1693 cm^{-1}

- Here the methyl group in the structure at the right causes the carbonyl group to be slightly out of plane, interfering with resonance

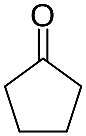
3. **Strain effects** – changes in bond angle forced by the constraints of a ring will cause a slight change in hybridization, and therefore, bond strength



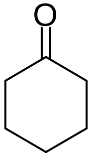
1815 cm^{-1}



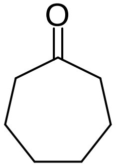
1775 cm^{-1}



1750 cm^{-1}



1715 cm^{-1}



1705 cm^{-1}

- As bond angle decreases, carbon becomes more electronegative, as well as less sp^2 hybridized (bond angle < 120°)

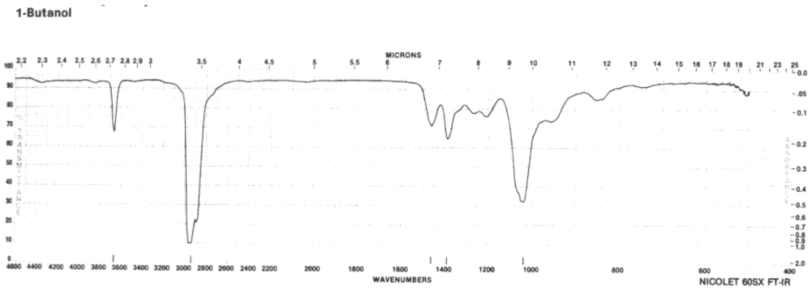
Infrared Spectroscopy

Effects on IR bands

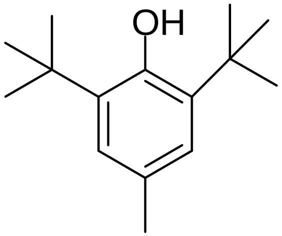
4. Hydrogen bonding

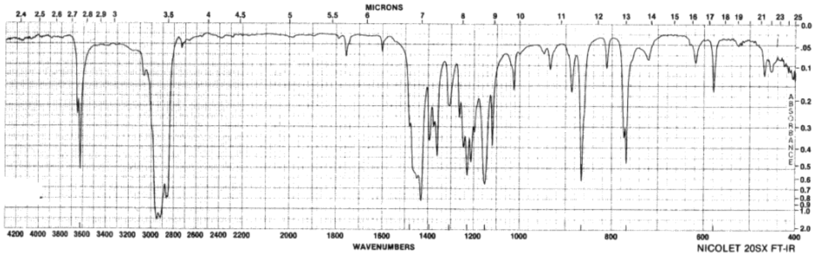
- Hydrogen bonding causes a broadening in the band due to the creation of a continuum of bond energies associated with it
- In the solution phase these effects are readily apparent; in the gas phase where these effects disappear or in lieu of steric effects, the band appears as sharp as all other IR bands:

Gas phase spectrum of 1-butanol

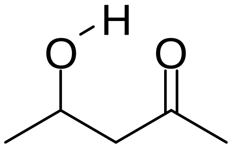


Steric hindrance to H-bonding in a di-*tert*-butylphenol





- H-bonding can ***interact*** with other functional groups to lower frequencies



C=O; 1701 cm^{-1}

Main uses of IR spectroscopy:

1. **Fundamental chemistry:**
    a. *Determination of molecular structure.*
    b. *Determination of molecular geometry.*
        e.g. Determination of bond lengths, bond angles of gaseous molecules.
1. **Qualitative analysis:** – simple, fast, nondestructive
    i. *Monitoring trace gases: NDIR.*
    ii. *Rapid, simultaneous analysis of GC, moisture, N in soil.*
    iii. *Analysis of fragments left at the scene (place) of a crime.*
2. **Quantitative analysis:**
    A. *determination of hydrocarbons on filters.*
    B. *determination of hydrocarbons in air.*
    C. *determination of hydrocarbons in water*

Near-infrared and Far-infrared absorption

The techniques and applications of near-infrared (NIR) and far-infrared (FIR) spectrometry are quite different from those discussed above for conventional, mid-IR spectrometry.

Near-infrared: 0.8 -2.5 μm, 12500 - 4000 cm^{-1}

Mid-infrared: 2.5 - 50 μm, 4000 - 200 cm^{-1}

Far-infrared: 50 - 1000 μm, 200 - 10 cm^{-1}

Divisions arise because of different optical materials and instrumentation.

Strengths and Limitations

- IR alone cannot determine a structure.
- Some signals may be ambiguous.
- The functional group is usually indicated.
- The *absence* of a signal is definite proof that the functional group is absent.
- Correspondence with a known sample's IR spectrum confirms the identity of the compound.

Applications of IR :

- Applications of IR Fourier Transformed Infrared (IR) is important tool for

1. the solid state characterization of pharmaceutical solids and for the identification of their chemical structures. Generally this method is applied in combination with other methods for solid state characterization of pharmaceutical solids (e.g. X- ray powder diffraction, DSC, TG).
2. characterization of polymorphism and detection in drug product. this method is also suitable for the identification/ detection of the polymorphic form in the tablet.

Advantages of FTIR :

1. Very high resolution required- Gaseous Mixtures
2. Study of samples having very high absorption
3. Study of samples with weak absorption bands
4. Used in protein structure determination
5. Very small sample size: Obtaining Reflection spectra IR emission study.

Applications of Near IR :

1. good penetration properties
2. Minimal sample penetration required
3. Thick layers can be analyzed
4. Not much useful for identification
5. Quantitative analysis of compounds containing functional groups made of H bonded to O, C, N
6. Determination of 10, 20, 30 amines.

Applications of ATR-FTIR :

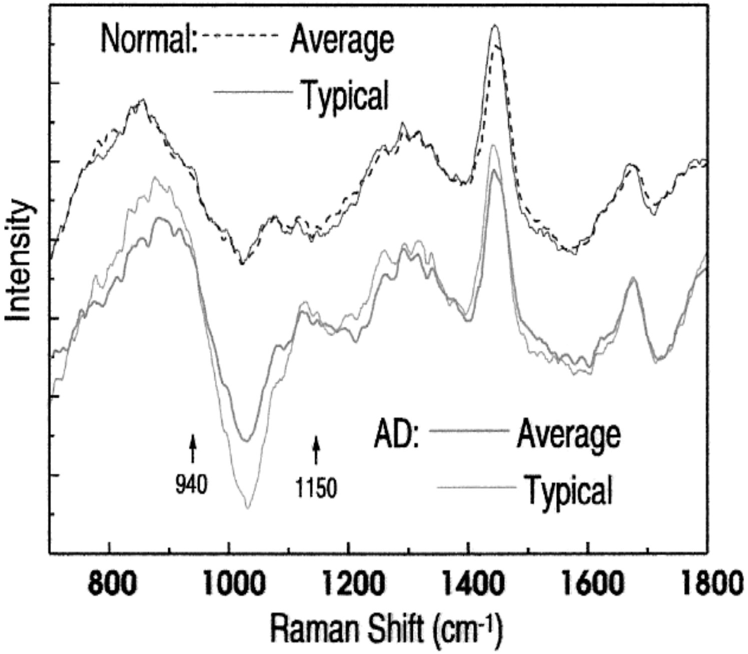
1. Surface analysis of biological structures
2. Monitoring reaction processes
3. Evaluation of fermented foods.

Pharmaceutical applications of Mid-IR

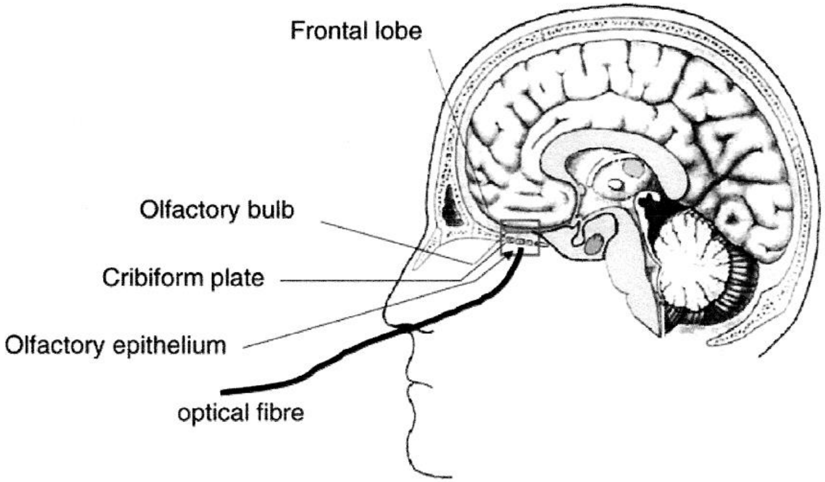
- ✓Mid-IR and Raman spectroscopy are versatile tools in pharmaceutics and biopharmaceutics, with a wide field of applications ranging from characterization of drug formulations to elucidation of kinetic processes in drug delivery.
- ✓New developments in applications of these methods for studying drug delivery systems.
- ✓FTIR-ATR is a well-established standard method used to study drug release in semisolid formulations, drug penetration, and influence of penetration modifiers; it is also capable of in vivo studies.

Alzheimer's Disease (AD)

- NIR FT-Raman spectra of control and tumour brain tissue (white and grey matter of normal brain tissue identifiable).



- Raman spectra of AD brain tissue show distinct differences from normal tissue spectra



- Mizuno A, Kitajima H, Kawauchi K, Muraishi S and Ozaki Y (1994) Near infrared Fourier transform Raman spectroscopic study of human brain tissues and tumours *J. Raman Spectrosc.* **25** 265–9

Pathology:

Breast implant

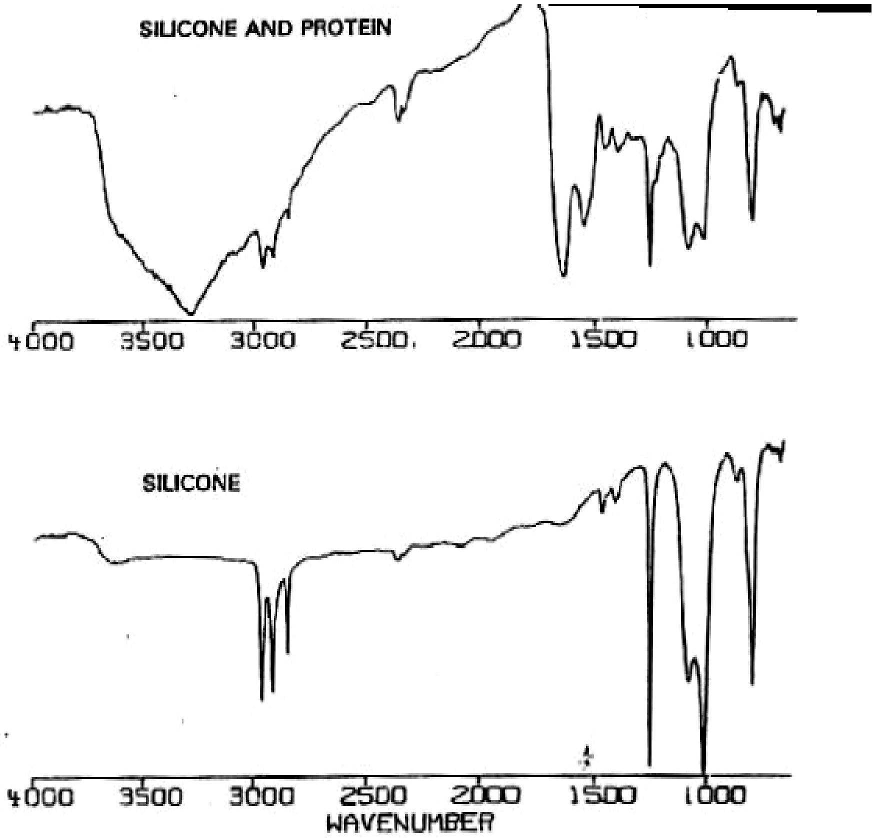


Figure 28. FT-IR spectra of breast biopsy tissue showing regions containing silicone and protein (upper trace) and isolated silicone (lower trace).

Breast tumor

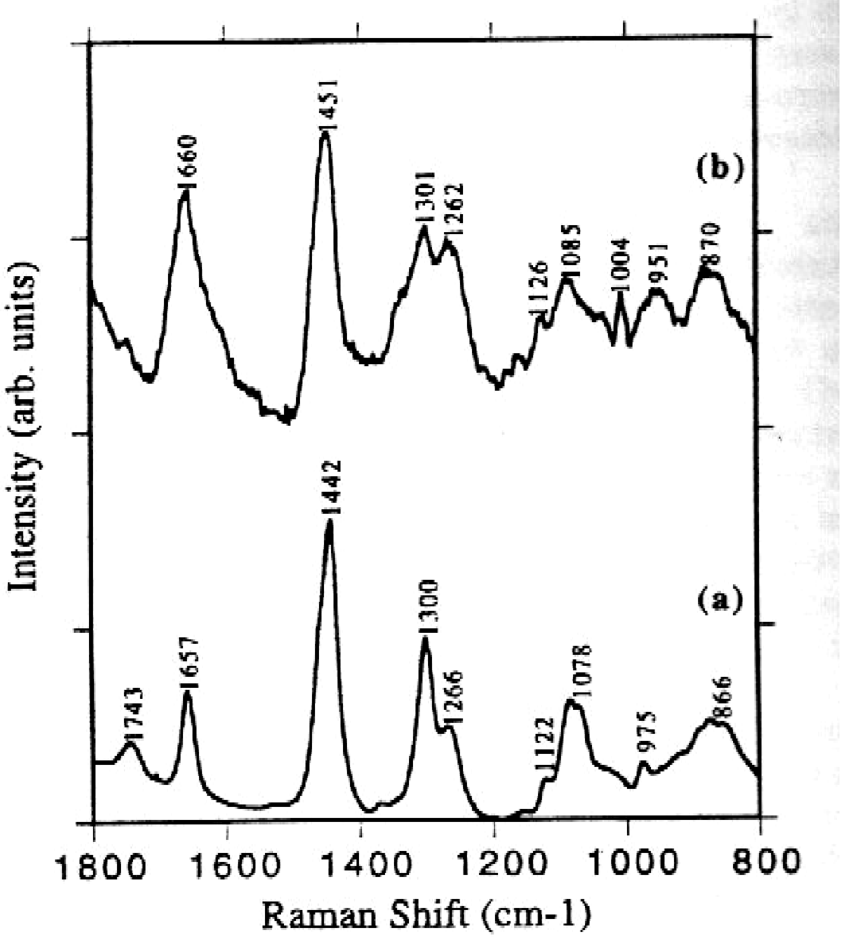


Fig. 15. Near-IR Raman spectra of (a) normal breast tissue and (b) breast tumor. 830 nm excitation.

References:

1. Spectrometric Identification of Organic Compounds by Silverstein, Bassler and Morrill;
2. Applications of absorption spectroscopy of organic compounds by Dyer JR.
3. Organic Chemistry by McMurry; 5thed; Thomason learning CA, USA 2000.
4. J. Workman, A.W. Springsteen, "Applied Spectroscopy", Academic Press, 1998.
5. J.M. Hollas, "Modern Spectroscopy", John Wiley&Sons, 1996.
6. B. Stuart, W.O. George, D.J. Ando, "Modern Infrared Spectroscopy", John Wiley&Sons, 1997.
7. N.N. Colthup, L.H. Daly, S.E. Wiberly, S.E. Wiberly, "Introduction to Infrared and Raman Spectroscopy", Academic Press, 1997.
8. B. Schrader, D. Bougeard, "Infrared and Raman Spectroscopy: Methods and Applications", John Wiley&Sons, 1995.