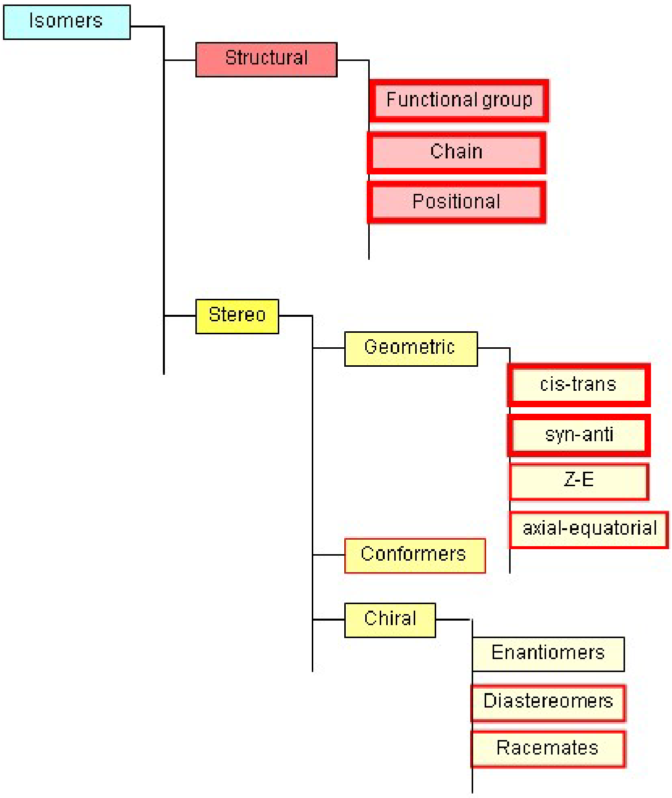
APPLICATION NOTE 025

IR Applied to Isomer Analysis

Infrared spectra provide valuable information about local configurations of atoms in molecules. As such, they are one of the best tools for differentiating isomeric organic compounds. In this note, we present a summary of the primary types of organic isomers, and the value that IR brings to bear on each.

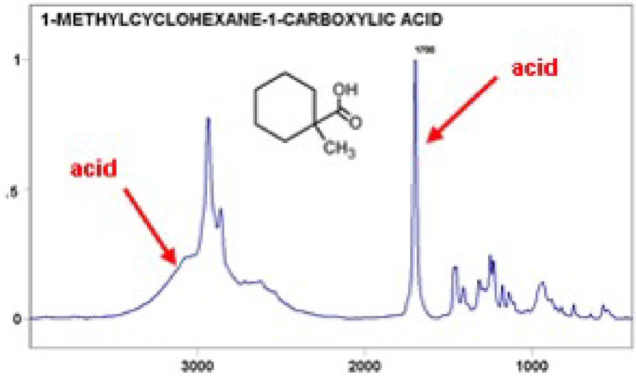
Isomer: *One of two or more compounds having identical molecular formula and weight, but differing in the arrangement or configuration of the atoms.*

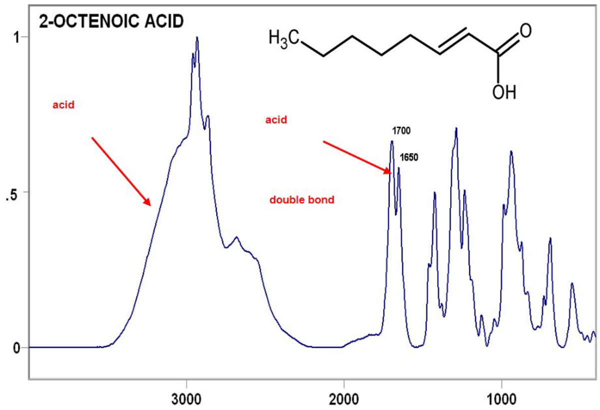
Various classes and subcategories of isomers are shown below, with those where IR provides especially useful information outlined in red. On the following pages we discuss these categories, and the application of IR spectra to each.

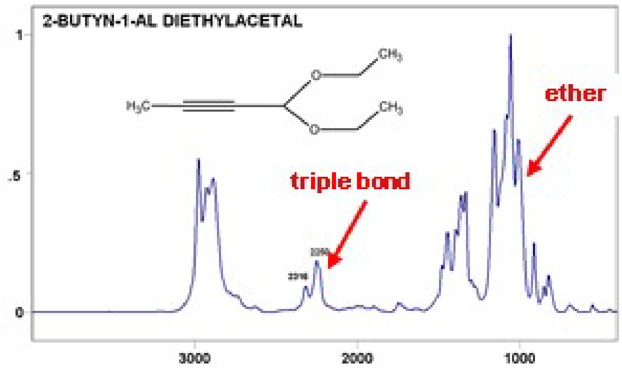


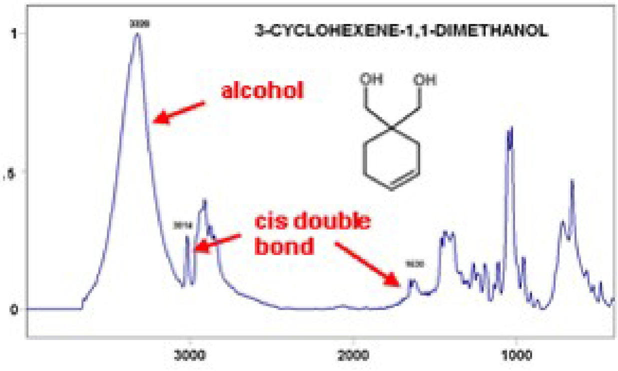
Isomers with different functional groups

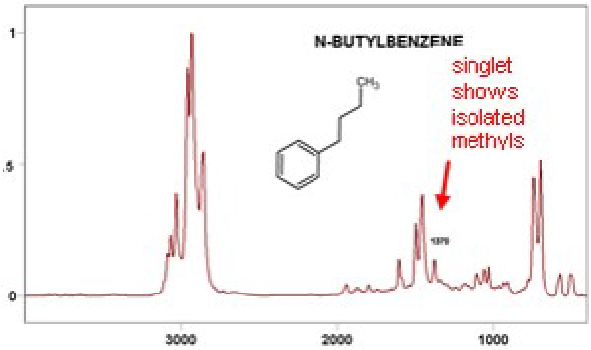
The IR spectrum is especially strong differentiating isomers of diverse functional groups, being the spectroscopy of choice for instant classification of molecules. By way of illustration, the eight compounds whose spectra follow are all isomers with molecular formula C8H14O2. They all have two degrees of unsaturation (rings plus double bonds), plus a variety of functionalities that the oxygen atoms may take. Spectral features immediately point out which groups are in each, to the eye of a spectroscopist or to a library searching program. See the red notations on the spectra for which groups the spectral features suggest.

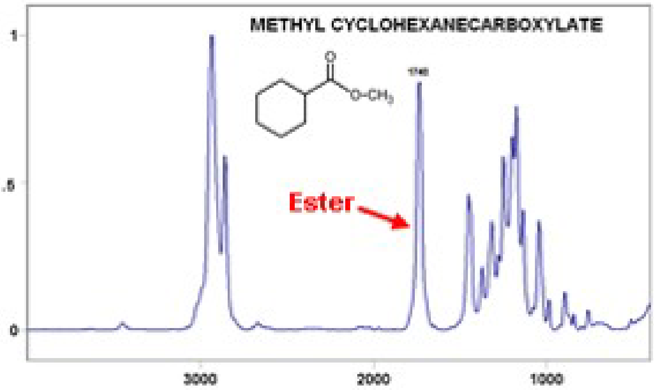


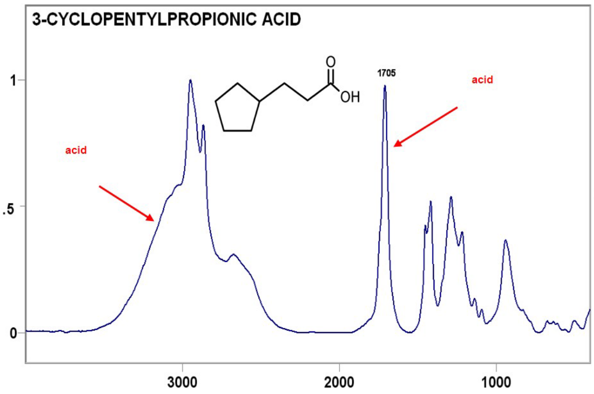


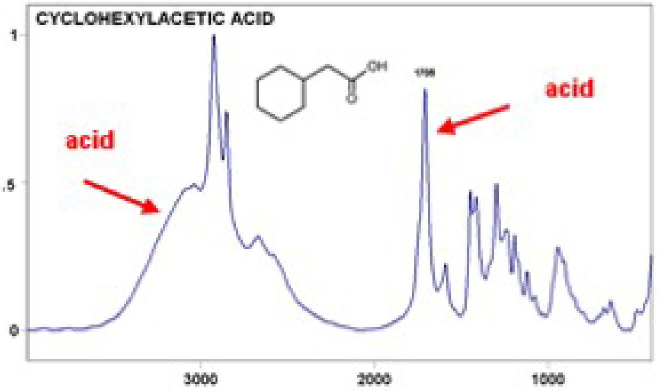






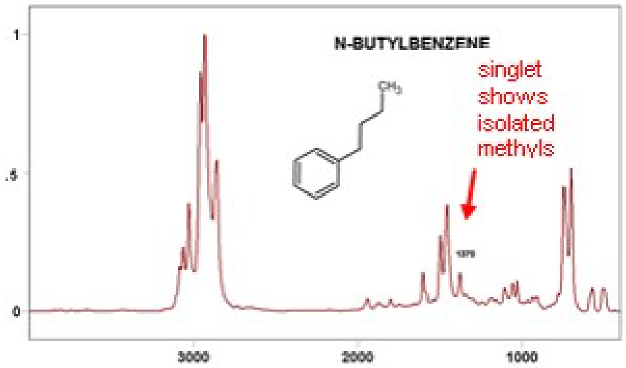






Isomers with different hydrocarbon backbones / chains

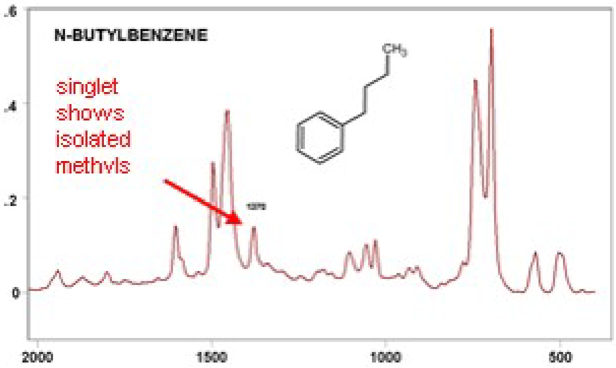
The IR spectrum exposes differences in the hydrocarbon backbone. Especially useful, for example, are the unique bands which show the number of methyl groups attached to a central carbon. Thus isopropyl groups (two identical methyls attached to the same carbon) and t-butyl groups (three identical methyls on the same carbon atom) stand out, and differentiate easily from their normal counterparts, as shown in the spectra on the following page. The methyl vibrational band near 1370 cm-1 tells the story.



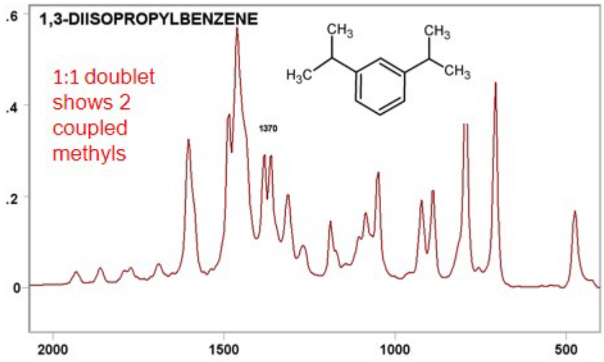
singlet shows isolated methyls

Full spectrum (at left) and fingerprint region (below) of n-butylbenzene. Most methyl groups, as in this case, show a singlet band at 1370 cm-1.

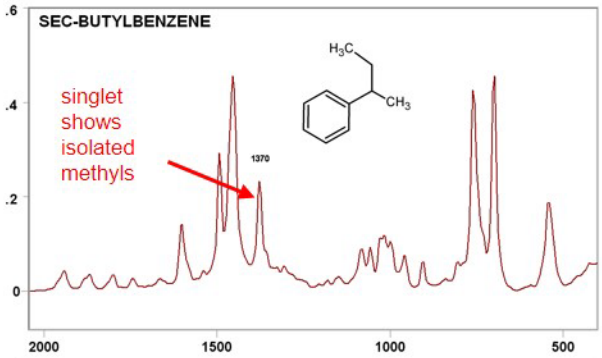
Note, however, that when two equivalent methyl groups are attached to the same carbon atom, this band splits into two of equal intensity. With three equivalent methyls on the same carbon, it splits into two, with the higher-wave-number band 1/3 the intensity of the main band. Makes it easy to spot isomers with isopropyl or t-butyl groups.



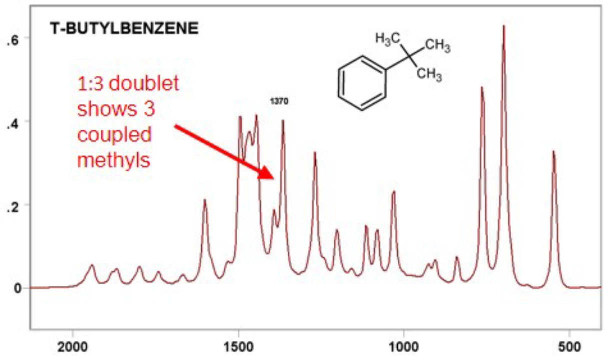
singlet shows isolated methyls



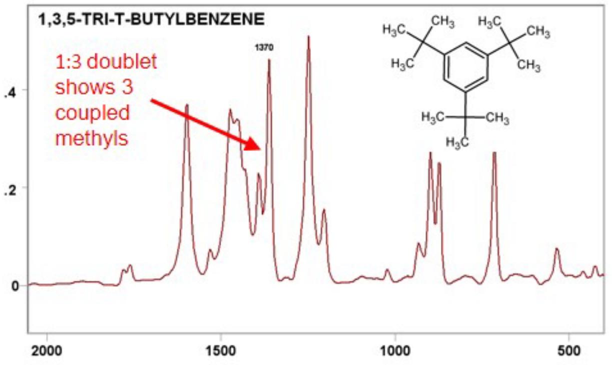
1:1 doublet shows 2 coupled methyls



singlet shows isolated methyls



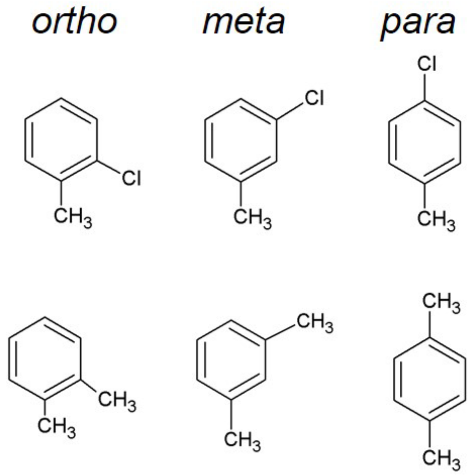
1:3 doublet shows 3 coupled methyls

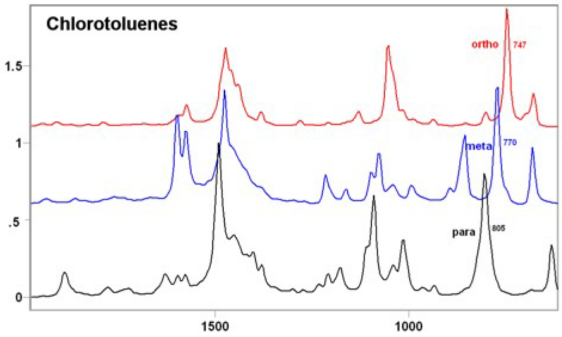


1:3 doublet shows 3 coupled methyls

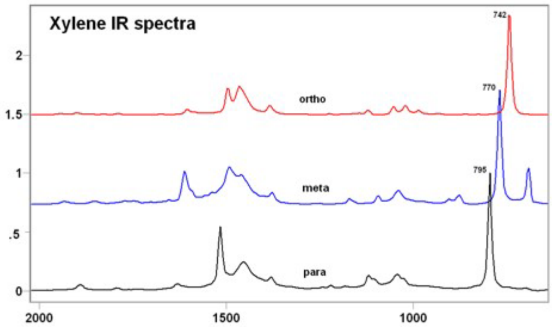
Aromatic positional isomers

Several well-characterized IR bands show the substitution pattern on aromatic rings. As an example, the C-H wag band near 800 cm-1 differentiates between o (~750), m (~770), and p (~805) isomers, as shown in the spectra below. Even in more complex structures (next page), this band can be used to pinpoint the configuration of a substructure.

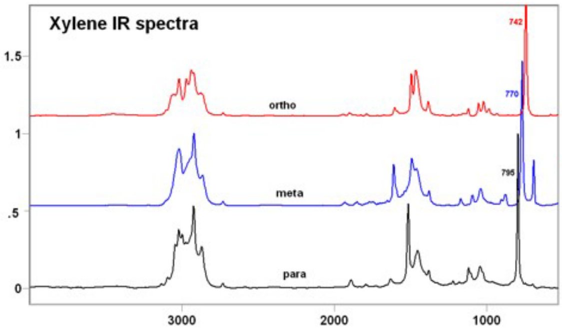




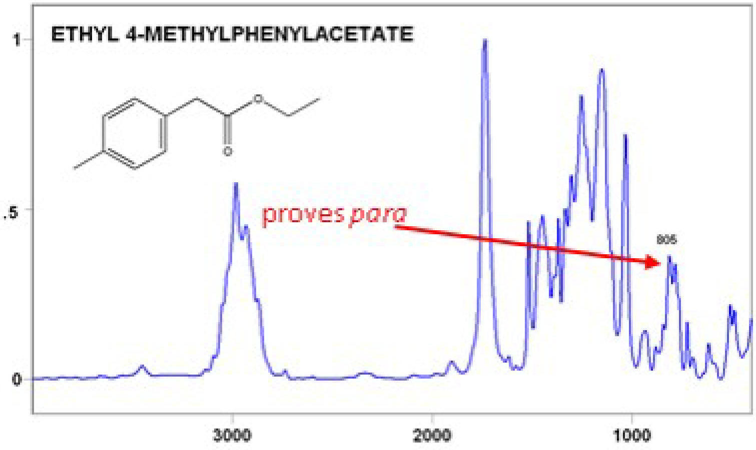
740 – 820 band showing o, m, p configuration

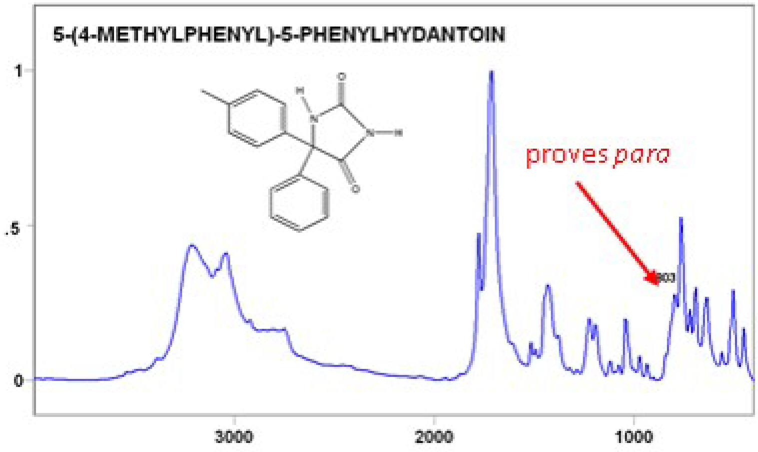


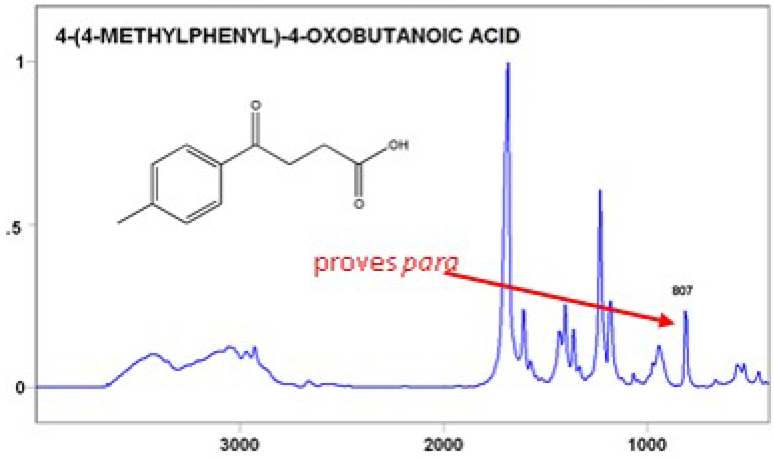
740 – 820 band showing o, m, p configuration



The IR band near 800 indicates that it is the para-disubstituted isomer in each case, even in spectra such as these with additional complexities in the molecules.



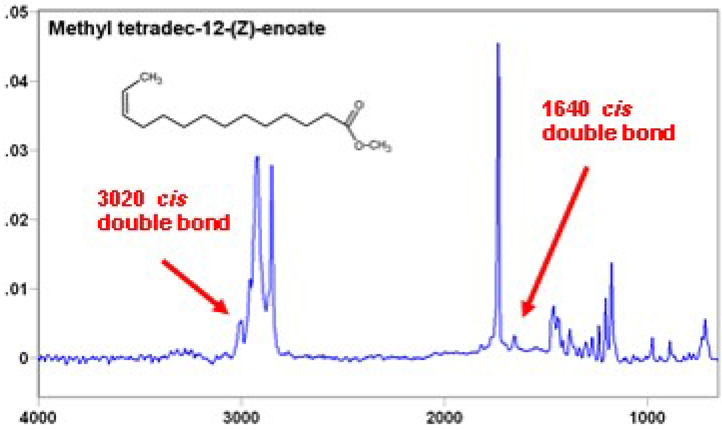


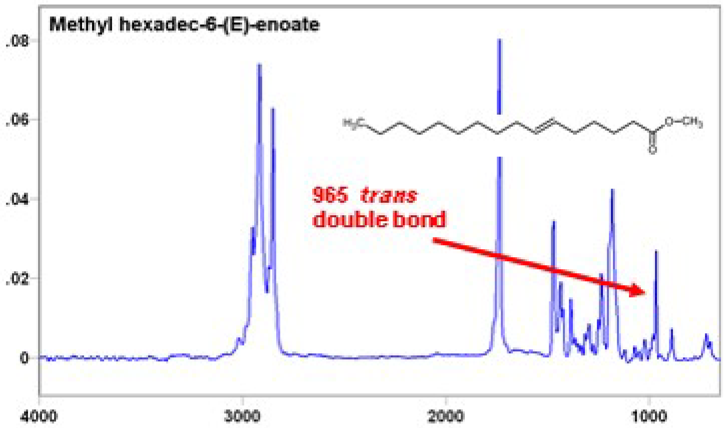


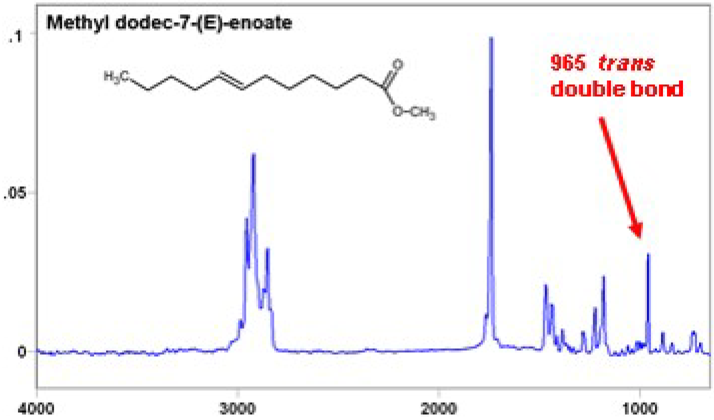
cis – trans Isomers

Generally, the configuration around a di-substituted double bond is easy to determine from the IR spectra.

The trans configuration gives a characteristic band at 965 cm-1, while the cis configuration gives a weak band at 1640 cm-1 and a medium band at 3020 cm-1.







Diastereomers (Diastereoisomers)

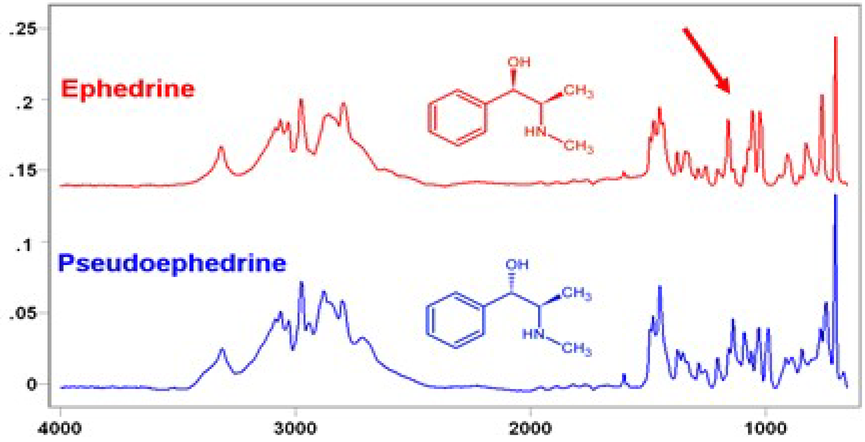
IR spectral bands may be categorized as either “well-behaved” group frequencies (useful for determining the presence of a functional group) or “shifty”. In general, the group frequencies come from stretching or bending vibrational modes in which one, two, or three specific atoms do the lion’s share of the moving. An example is the C=O carbonyl double bond stretch mode, where the carbon and oxygen atoms move away from each other, then back towards each other in unison. The energy / force constants of these vibrations is determined by the local group, and being pretty much independent of the rest of the molecule, these bands occur at the same wavenumber in the spectrum of any compound that contains that specific group.

The other type, the shifty bands, derives from more complex motions of parts of the molecules, with many atoms moving various directions in a floppy, but periodic motion. As long as the atoms move in unison, each going through a coupled motion cycle in the exact same measure of time, the combined energy of their motions can show up as an IR band. But the exact motion is almost impossible to model or determine from a theoretical calculation. These IR bands occur mostly between 1600 – 600 cm-1, which is termed the “fingerprint” region of the spectrum.

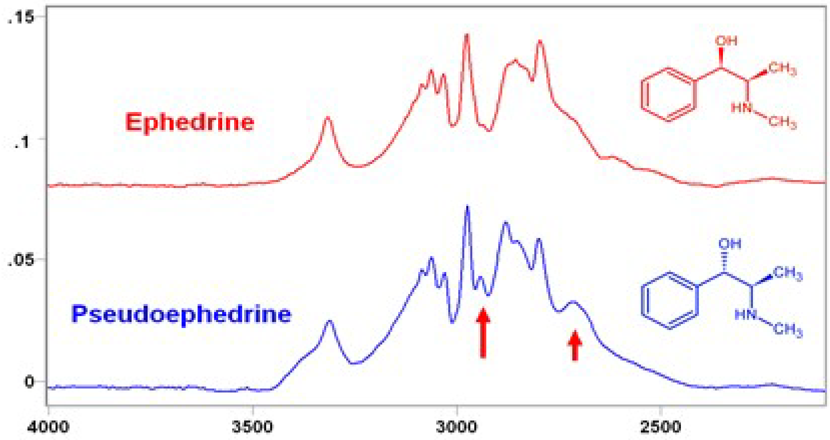
Most of the IR bands above 1600 cm-1 are well behaved. The fingerprint region below 1600 cm-1 is a mix of well behaved and shifty bands.

And about diastereomers? Diastereomers are isomers with two or more chiral centers, differing only in the configuration of one, but not all, chiral centers. Thus they have the exact same functional groups and group frequencies. But spectral differences show up in some of the “shifty” bands, and these differences provide different spectral fingerprints, which are useful as library standards to differentiate the isomers. An unknown material may be proven to be one diastereomer, and not the other, by simple spectral comparison.

As an example, Ephedrine and Pseudoephedrine are diastereomers, differing only in the R/S configuration at the carbon holding the OH group shown below. We will look in detail on the next page at the set of three bands noted by the arrow below:

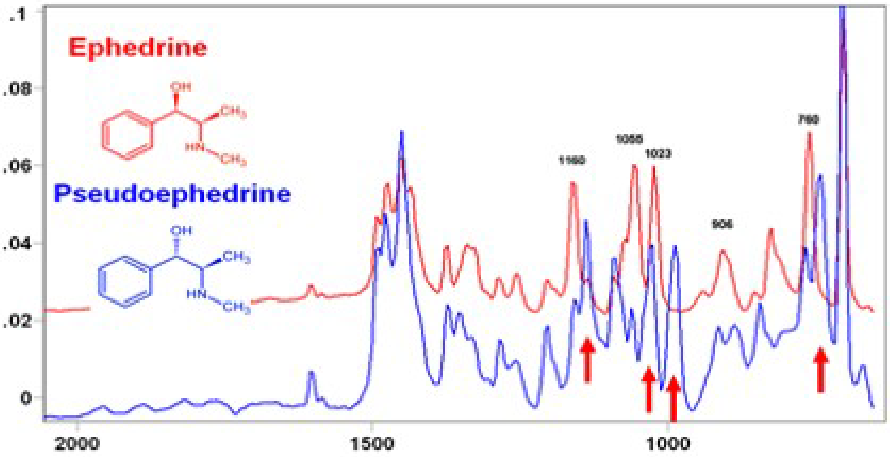


In the O-H, N-H, and C-H stretch region of the spectrum centered on 3000 cm-1, we see some subtle differences.



In the fingerprint region, we see that the set of three bands centered on 1100 is shifted slightly from one spectrum to the other.

Other bands, those reliable group frequencies as marked by the blue arrows, are the same in both spectra.



Thus each of these spectra becomes a standard which can prove the exact diastereomer, through examination of the unknown’s spectrum.

Other Isomer types

Epimers and racemates

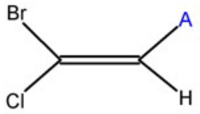
Optical isomers, or epimers, have identical IR spectra, since IR energy has no chirality. However, frequently a pure epimer will form one crystal structure, while a one-to-one racemic mix will form a different one. In these cases, an epimer may be differentiated from the racemate in a manner analogous to differentiation of diastereomers.

Z-E isomers, syn-anti oximes, and cis-trans ring structures

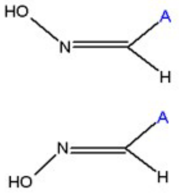
The Z (from the German Zusammen, meaning together) and E (Entgegen, opposite) system for defining the configuration around a double bond is an extension of the cis-trans system. It applies to any double bond with two, three, or four substituents.

The terms syn and anti define conformational isomers. Oximes and as shown below, are an example of stable conformers, which do not normally interconvert

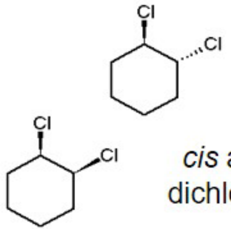
As with diastereoisomers, IR spectra provide distinct spectra for each different isomeric configuration of these compounds, which serve as a paper or electronic standard with which to compare the spectrum of an unknown.



double bond Z configuration (Br relative to A)



syn and *anti* oxime configuration



cis and *trans* dichlorocyclohexane

Concluding remarks

The IR spectrum provides a wealth of information about the isomeric configuration of molecules. In many cases it may show exactly the chemical functionality of an isomer, such as flagging ketones, aldehydes, alcohols, etc. In other cases it can show the relative positions of substituents, such as cis-trans or ortho-meta-para sets. In cases where it cannot show the exact configuration from first principles, such as diastereoisomers, it still provides different fingerprints of each isomer, which provide excellent electronic standards with to compare unknown materials for proof of identity. These are but a few examples of the power that IR brings to the characterization of isomeric materials.