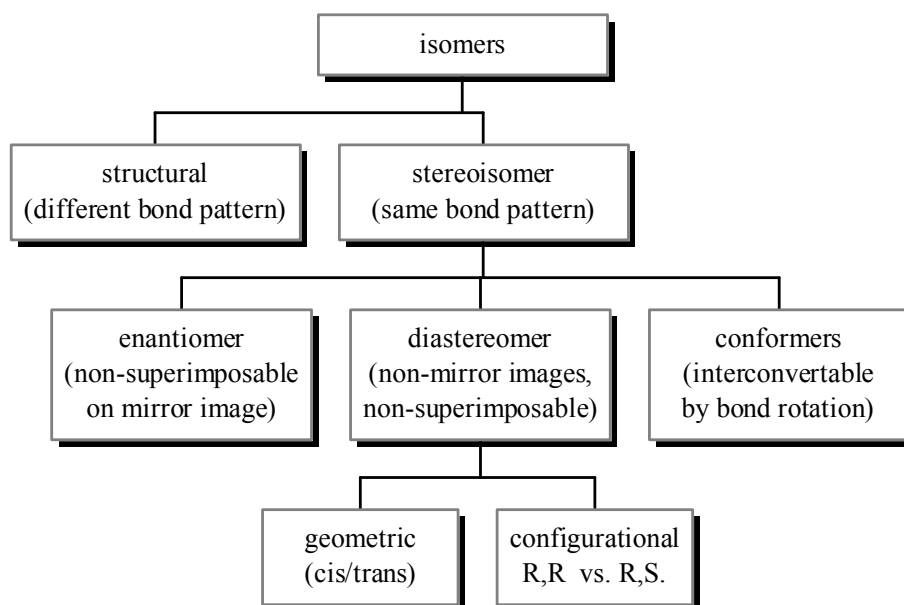


ISOMERS: Same song, different dance.

Isomer = “one of two or more compounds, radicals, or ions that contain the same number of atoms of the same elements but differ in structural arrangement and properties.”

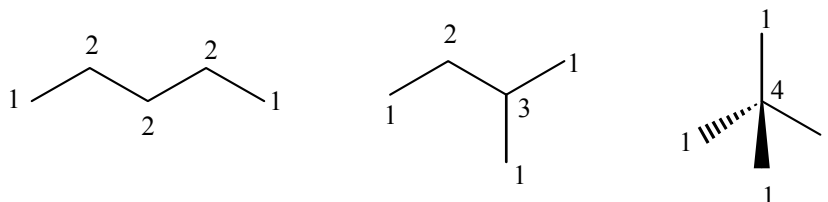
-Websters.

You began learning about isomers in GenChem, now they are going to be integral to your understanding of organic chemistry. Below is a schematic showing the relationships between the different kinds of isomers that we are going to study...



Various forms of this isomer tree appear in different books, but this is a good place to start. In this short section, we'll look at the easy difference between structural isomers and all others.

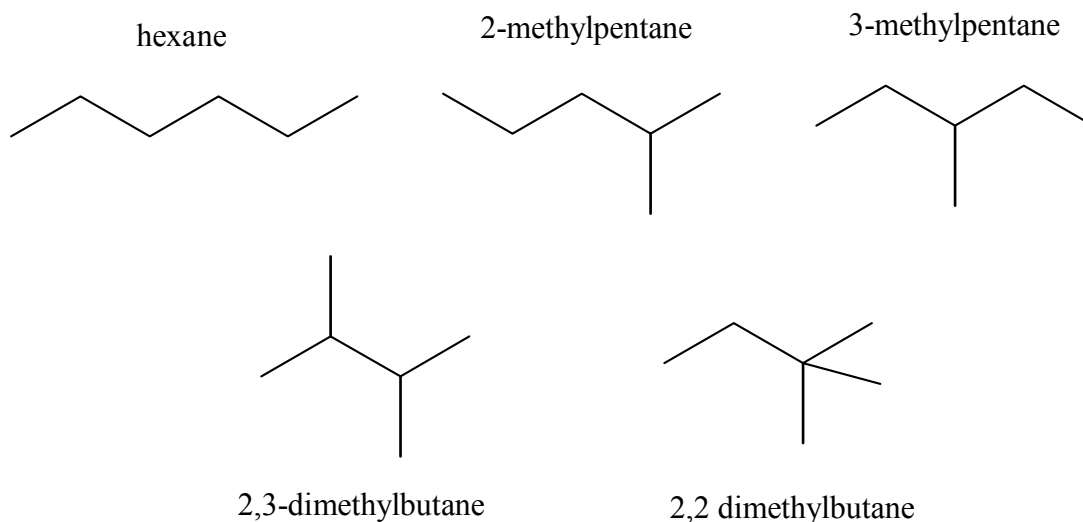
Consider pentane (n-, bp = 36.1 °C; mp = -129.8 °C). It has a molecular formula of C₅H₁₂...with 3 structural isomers: n-pentane, isopentane...neopentane



The numbers designate the primary (1°), secondary (2°), tertiary (3°), quaternary (4°) carbon...(dependent on how many other carbons are attached). There are 8 pentyl derivatives...3 n-pentyl, 4 isopentyl and 1 neopentyl, (if 1 substitution allowed)

There are 5 structural isomers of hexane, 9 heptane isomers, but 18 octane isomers...yikes. C_{10} – 75 isomers; C_{15} – 4,347 isomers; C_{20} - 366,319 isomers...double yikes. How do you draw them?...Just be systematic about it.

Draw the 5 hexane isomers (each with a molecular formula of C_6H_{14})...

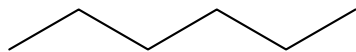


Again, the compounds above all have the same molecular formula (C_6H_{14}). What varies is the connectivity, or the different bond patterns (literally, what is attached to what) of the different compounds. These compounds all have unique chemistry (bp, mp, NMR spectra, etc.). They are all structural isomers of one another.

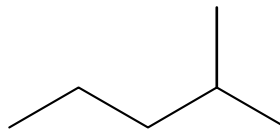
isomer	bp ($^\circ\text{C}$)	mp ($^\circ\text{C}$)	density
n-hexane	69	-95	.6603
2-methylpentane	60.3	-153	.6532
3-methylpentane	63.3		.6645
2,3-dimethylbutane	58	-128.5	.6616
2,2-dimethylbutane	49.7	-99.9	.6485

“iso, sec and tert”

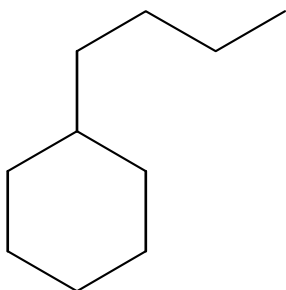
Now is a good place to introduce some more nomenclature. The best way to explain the prefixes iso, sec and tert, is by example...



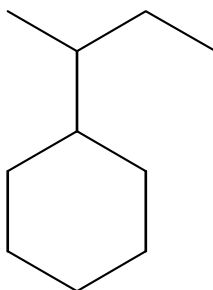
hexane



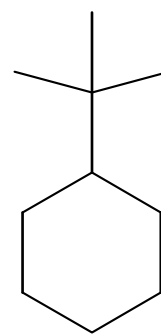
isohexane



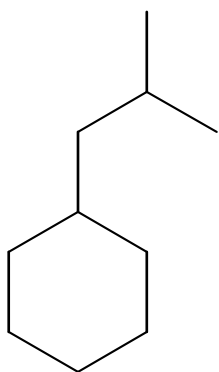
butylcyclohexane



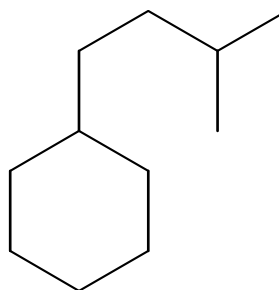
sec-butylcyclohexane



tert-butylcyclohexane



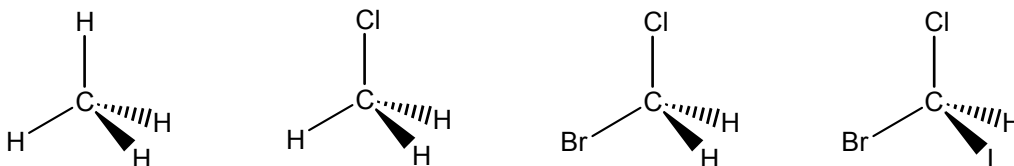
isobutylcyclohexane



isopentylcyclohexane

4. STEREOCHEMISTRY: Molecules through the looking glass.

Consider methane. The simplest hydrocarbon. A gas at RT; bp = $-162\text{ }^{\circ}\text{C}$; mp = $-182.5\text{ }^{\circ}\text{C}$. CH_4 . Tetrahedral. Very boring. It's only real reaction of practical value is combustion (reaction with O_2) to give carbon dioxide and water. Oh, and it is a very important green house gas with a major source being bovine ruminations (cow farts). Boring. Now let me ask you a question. If you start to take off the hydrogens one at a time and replace them with different things, how many can you replace and still have the same compound? Lets replace hydrogens one at a time with Cl, Br and I.



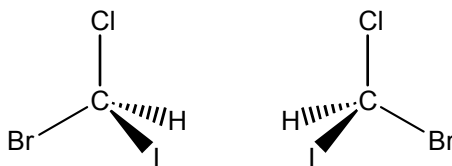
Now, for the first compound...methane...if I shuffle the H's around, will I still end up with the same compound, no matter how I shuffle the H's? Yes. How about for chloromethane? Yes. How about bromochloromethane? Yes. How about the last one, bromochloroiodomethane? NO. There are two different possibilities. The game of identifying different spatial arrangements of atoms in organic molecules is called *stereochemistry*.

4.1 Chirality...

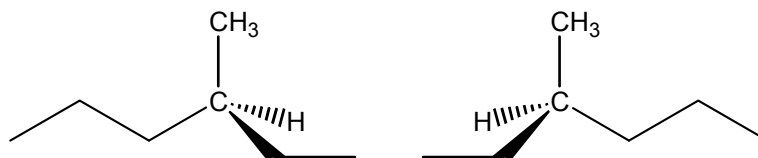
Chirality = handedness. It is usually determined/defined by having a mirror image that is non-superimposable...usually a carbon center with 4 different substituents

Examples...

bromochloroiodomethane



3-methylhexane



The above example, no matter which way I try to rotate or otherwise orient the molecules, I cannot get them to superimpose on one another. They are different isomers of the same

compound. They are *enantiomers*...isomeric compounds that are non-superimposable mirror images of one another.

So, how do we distinguish one enantiomer from another?

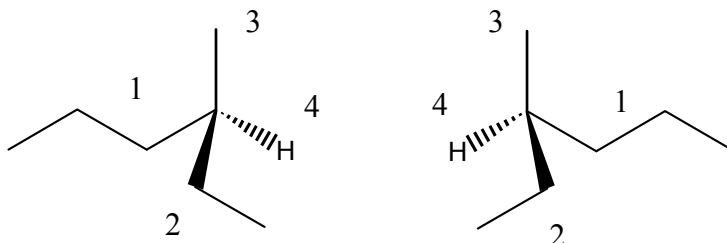
...assign priority to groups.

...highest (1) to lowest (4), based on molecular weight.

...look down the carbon – (4) bond

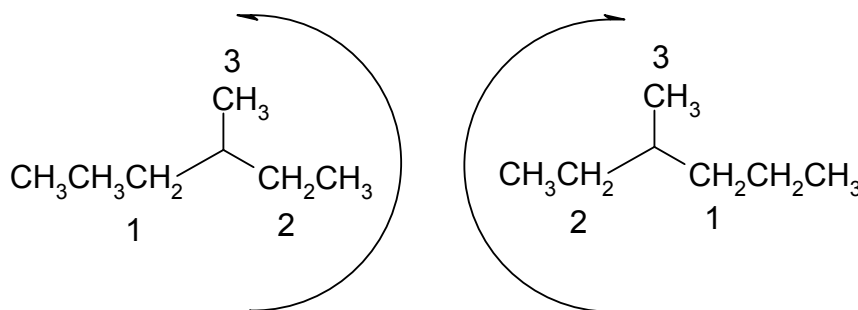
...1 - 2 - 3 goes clockwise, then R.

...1 - 2 - 3 goes counterclockwise, then S.



(S)-3-methylhexane

(R)-3-methylhexane



Do more examples (cyclo) in class...

Or...L and D notation.

Based on the rotation of light. Chiral molecules can rotate plane polarized light.

L = levorotary (-) = counterclockwise rotation of light.

D = dextrorotary (+) = clockwise rotation of light.

Best examples of light rotation are likely shown in your book...

$[\alpha]$ = specific rotation, rotation induced by 1mg/mL over 10 dm (1 m).

= $\alpha / (c * l)$

where c = concentration in mg/mL

l = optical path length in dm

α = observed rotation.

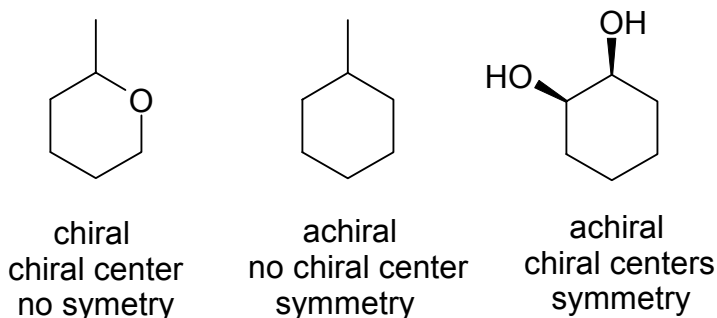
Notation $[\alpha]_D^{20}$ = angle measured at 20°C, using sodium D line (589 nm)

Compounds that have no chiral (stereogenic) centers do not rotate light.
 50:50 mixtures of R/S or L/D do not rotate light...RACEMIC MIXTURES
 R/S/ notation does NOT relate to L/D (+/-)

Chirality affects the reactivity and the outcome of final products due to reaction. For example, life is "handed"...we (biology) are based on L amino acids that bind to D sugars. One way we know that amino acids found in/on meteorites is extraterrestrial is to look for an enantiomeric excess of D amino acids.

4.2 Stereogenic Centers vs. Chiral Molecules

"Molecules are chiral...atoms are not" (...or so says Maitland Jones)

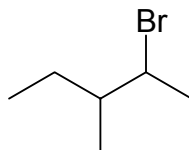


DIASTEREOMERS

- ...two or more chiral centers
- ...stereoisomers that are not mirror images (not enantiomeric).
- ...different compounds.

For every N stereogenic (chiral) centers, there are potentially 2^N stereoisomers.

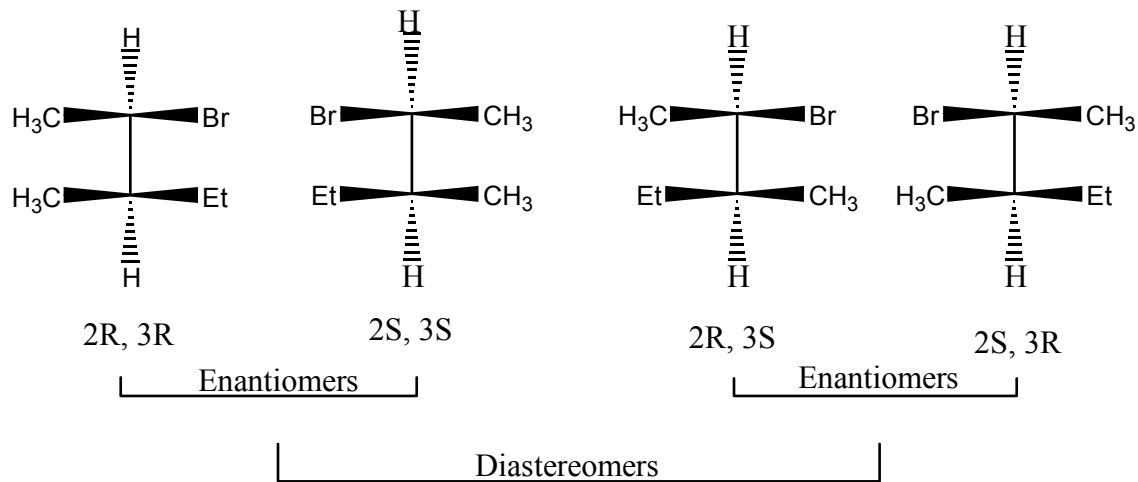
For example...



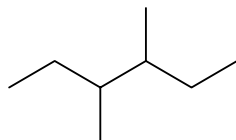
2-bromo-3-methylpentane

How many stereogenic centers? **2** (C2 and C3). # of stereoisomers? **4**

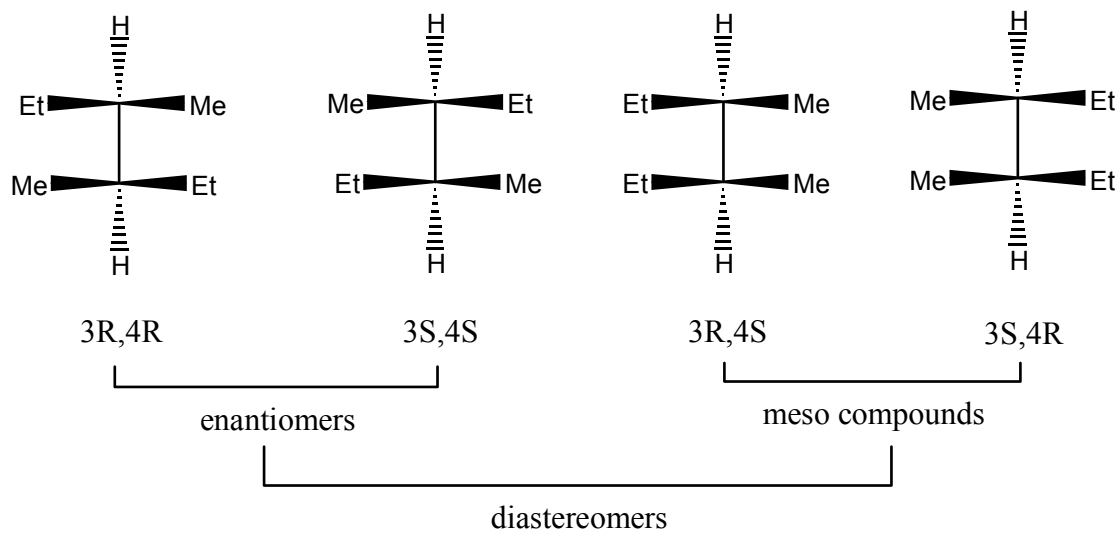
Draw the 4 isomers (as Fisher projections...)



MESO Compounds...compounds with chiral centers, but due to a plane of symmetry, apparent enantiomers are actually identical compounds.



3,4-dimethylhexane

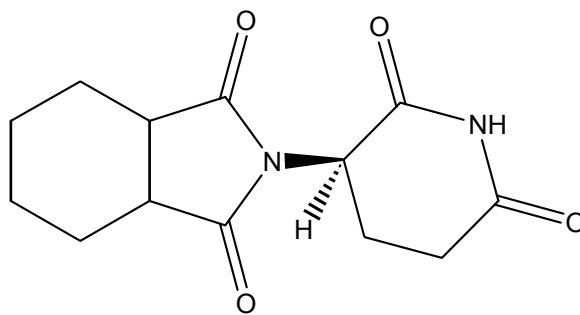


EPIMERS...two compounds that differ in configuration around only one specific carbon atom. e.g., (3R,4R) and (3R,4S)- 3,4-dimethyl hexane or (3S,4S) and (3S,4R)-3,4-dimethyl hexane.

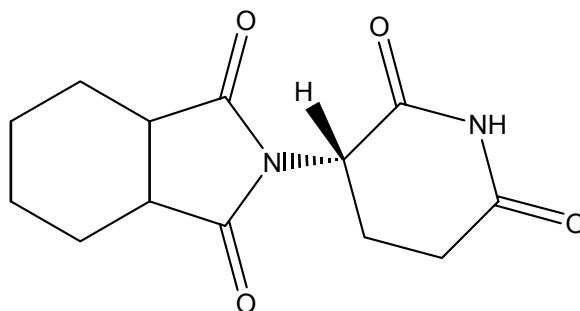
STRUCTURAL ISOMERS...Same molecular formula, different bond arrangements. I.e., 2-chloropentane vs. 3-chloropentane. (as opposed to conformational isomers R-2-chloropentane vs. S-2-chloropentane.

REACTIVITY DIFFERENCES DUE TO R/S (L/D)

Life...D sugars and L amino acids.
D amino acid enantiomeric excess in meteorites
R and S thalidomide



(R)-thalidomide



(S)-thalidomide

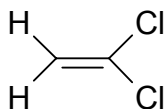
R – antiabortive agent, used to help prevent miscarriages (late fifties, early sixties?)

S - very potent teratogen (any environmental agent, be it a drug, chemical, infection or pollutant which harms a developing embryo or fetus).

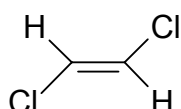
Drug was marketed in South America in racemic form...with disastrous results. Never licensed in the US, but not without a major power struggle.

4.3 Alkene Stereochemistry

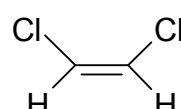
Consider ethene. How many hydrogens can we replace before we have to worry about isomers? The answer is 2. Once we have the formula $C_2H_2X_2$, we have to worry about which “side” of the double bond the substituents are located...for example,



1,1-dichloroethene



E-1,2-dichloroethene



Z-1,2-dichloroethene

E = entgegen...german for opposite = trans

Z = zusammen...german for together = cis

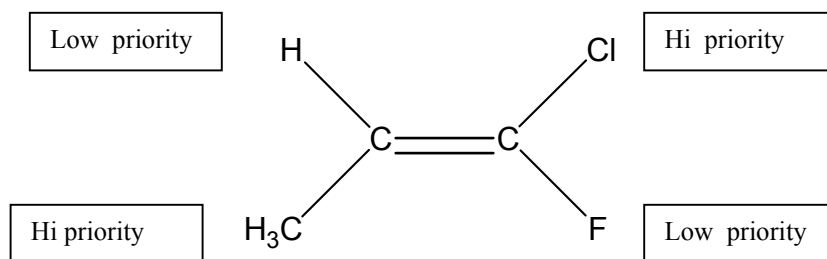
So, how do we more properly name compounds that contain double bonds? First, all previous rules apply...find longest chain/ring with double bond.

Begin numbering at the first double bond with lowest possible numbering scheme.
(OH is the exception and generally takes precedence...)

E or Z (trans or cis)...

- 1) set priorities based on molecular weight...(**Cahn-Ingold-Prelog**)
- 2) determine the two highest priority, not on the same carbon
- 3) assign Z or E (cis or trans)

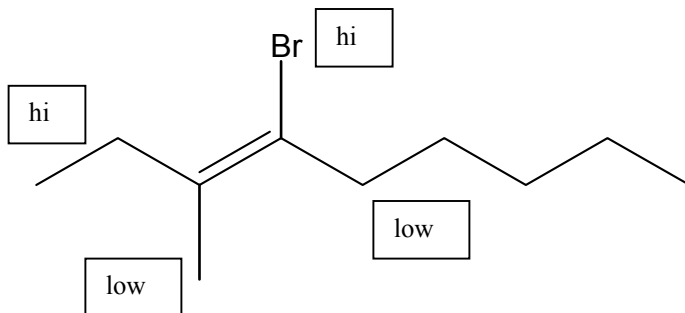
an example...



by the rules... (E)-1-chloro-1-fluoropropene

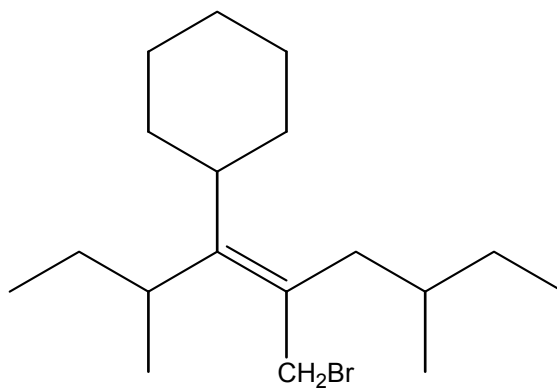
More rules...

...when there is more than one carbon, i.e. an ethyl group or higher, you look at the atomic number of what is attached to the carbons to decide...for example,



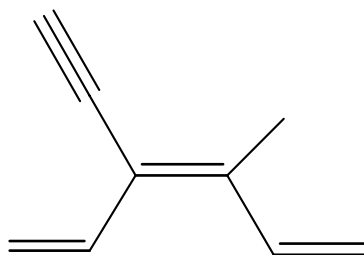
(Z)-4-bromo-3-methyl-3-nonene

or...



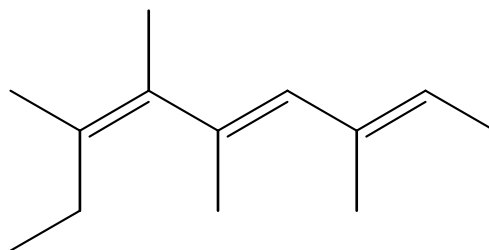
trans-4-cyclohexyl-5-methylbromo-3,7-dimethyl-4-nonene

Double and triple bonds as substituents are treated as if they are bound to 2 and 3 carbons respectively...for example,



(E)-3-ethenyl-4-methyl-3,5-hexadieneyne (?) ...but at least it is **E** (trans)!

What about naming multiple double-bonded systems?



Go back to the rules...

Longest carbon chain...lowest numbering system...Cahn-Ingold-Prelog priority to all groups attached to a double bond...assemble the name...

...(2E,4E,6Z)-3,5,6,7-tetramethyl-2,4,6-nonatriene