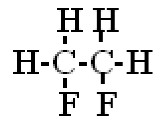
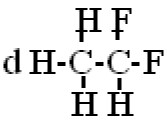
1.5 Isomers

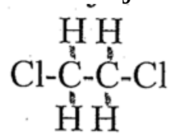
Let's look at the following 2 molecules:

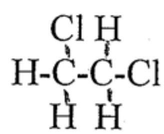
 and 

Note that although these 2 structures have the same atomic composition ($C_2H_4F_2$), in the first molecule there is one F on each of the C atoms whereas on the second molecule both F atoms are on the same C atom. No matter how we rotate the molecule or turn it over or around, these 2 structures are fundamentally different molecules. We call these molecules **structural or constitutional isomers.**

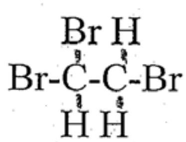
Definition: Molecules which have the same formula, but which have a difference in structure (in what atoms are bonded to each other) are called **structural or constitutional isomers.**

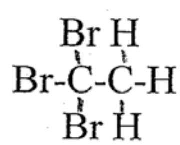
For each of the pairs of molecular structures shown below, are the pairs of molecules isomers or just different representations of the same molecule?



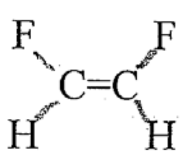


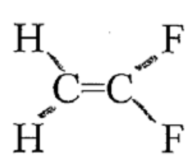
(Answer: These are different representations of the same structure because of free rotation around the C-Cl bonds. We can rotate the C-Cl bonds in any direction we want without creating a new structure.)



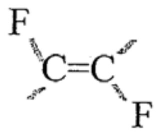


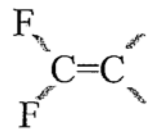
(Answer: These are structural isomers because the structure on the left has 2 Br atoms on one C atom and 1 Br atom on the other. The second structure has all 3 Br atoms on one C atom. We can't rotate or flip our way out of this one. These two structures have the same formula but different bonding and are hence structural isomers.)



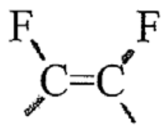


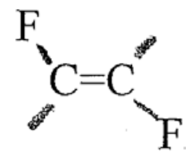
(Answer: Each C atom has one F atom in the structure on the left, while the structure on the right has both F atoms on the same C atom. These are structural isomers.)





(Answer: Each C atom has one F atom in the structure on the left, while the structure on the right has both F atoms on the same C atom. These are structural isomers.)





This last pair of molecules is an example of a different type of isomer. All the atoms are bonded to the same atoms in both structures, but the F atoms are pointed the same direction (**cis or Z)** in the first structure and in opposite direction (**trans or E**) in the second structure. (In Latin cis means on the same side and trans means across. In German, Z stands for **zusammen** (same) and E stands for **entgegen**(opposite).

If there were a single bond between the 2 C atoms we could simply rotate around the C -C bond and make the F atoms point whichever direction we wanted, but remember there is NO free rotation in C=C bonds! If the 2 F atoms in a structure are pointing the same direction on a C=C they must stay that way and if the 2 F atoms are pointing opposite directions on a C=C double bond they will stay that way. Hence they are different molecules. Since they have the same formula we call these molecules isomers, but we do not call them structural isomers because both molecules have exactly the same atoms bonded to each other; they differ only in the direction in which atoms point. Since they differ only in geometry, we call them **geometric isomers**. We call the isomer in which both F atoms are pointing in the same direction the cis or Z isomer and the isomer in which the two F atoms are pointing in opposite directions the trans or E isomer.

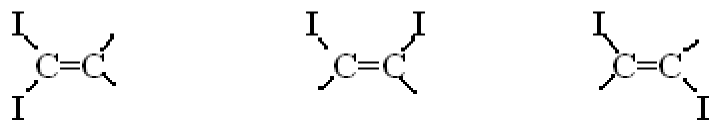
Geometric isomers

Definition: Molecules which have the same formula and the same atoms bonded to each other, and differ only in geometry, are called geometric isomers. Geometric isomers can only occur when there is no free rotation around bonds, either on a C=C double bond or on a ring.

Note that we cannot look at a single structure and say that it is a structural isomer or geometric isomer. We have to look and compare 2 different molecules.

Consider the following 3 molecules:

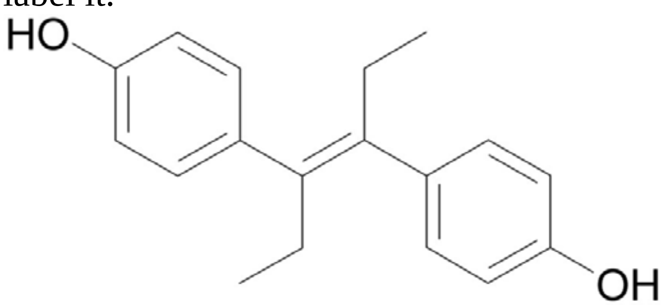
A B C



All three molecules have the same formula. Molecules B and C differ only in which direction the I atoms are pointing. Hence they are geometric isomers. Both B and C differ from A in the terms of which atoms are bonded to each other. Hence B and C are both structural isomers of isomer A. Thus molecule B(cis) is a geometric isomer of molecule C(trans) and a structural isomer of molecule A. A molecule can be both a geometric and structural isomer. Likewise molecule A is a structural isomer of both molecule B and C.

DES (Diethylstilbestrol)

An example of medically important cis-trans isomer is DES, diethylstilbestrol. Its structure is shown below. It can exist in both the cis and trans form. Which form is shown below? Draw the other form and label it.



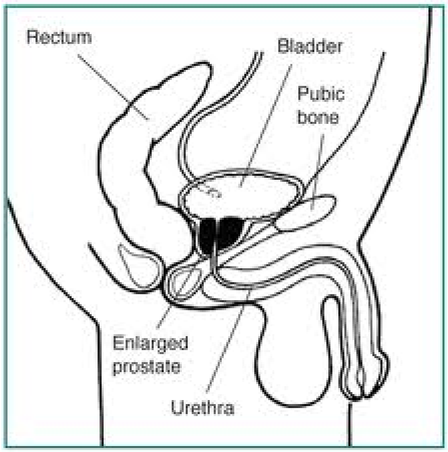
The other geometric isomer has only about 7% of the biological activity of the first form. This is because the DES binds to a receptor in the cell membranes which has a shape complementary to the one geometric isomer. The other geometric isomer does not fit nearly as well and has very little activity as a result.

The use of DES as a drug was first approved in the early 1940s to prevent miscarriages. Other approved uses included stopping milk flow in mothers who were not nursing, slowing down the spread of prostate cancer in men, as a “morning-after” pill, and several other uses. It is estimated that approximately 5-10 million people have taken DES.

Figure 2
Medical journal advertisement for prenatal tablets with vitamins and diethylstilbestrol

In 1953 a **double blind study** showed that DES was not actually any more effective than placebo for reducing the incidence of miscarriages , but this conclusion did not get adequate publicity among doctors and its use continued into the 1960’s and an outright ban on prescribing it for this purpose did not occur until 1971.

No immediate adverse effects were noted with the babies born by mothers taking DES. However as the **DES daughters** reached puberty a variety of vaginal and cervical tissue abnormalities were noted. DES daughters are at increased risk of vaginal, cervical, and breast cancer. These women generally need to have Pap smears done on a regular basis to monitor whether these abnormal cells have become full blown cancer cells. They are also at increased risk for having difficulties in pregnancy and auto-immune disorders. In **DES sons** there appears to be an increased risk of epididymal cysts (in the testicles) and autoimmune diseases.



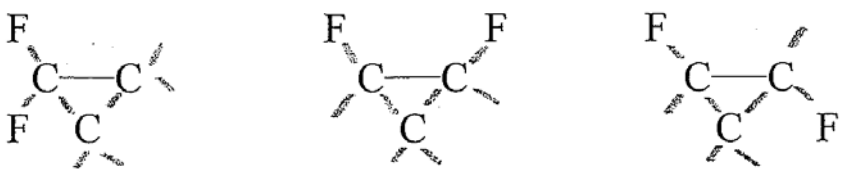
DES continued to be used to treat prostate cancer into the mid 1990's. Prostate cancer cells are dependent on male hormone for their continued growth and removal of male hormones will stop or at least greatly slow down the growth of prostate cancer cells. The original method for stopping testosterone production was a surgical orchiectomy(also spelled orchidectomy).

DES is an analog of female hormone which non-surgically reduces levels of male hormones, decreasing the rate of prostate cancer growth. Unfortunately, the prostate cancer cells eventually lose their requirement for male hormones and the cancer then progresses, frequently metastasizing to the bone. DES has been replaced with other **antiandrogens** and is rarely used on humans anymore, although veterinarians may still use it to treat female canine incontinence. (What is an antiandrogen?)

Geometric isomers in rings

As already indicated in the definition one can have geometric isomers only when one has restricted free rotation. This can occur on a double bond as in the previous example that we just looked at. It can also occur in ring structures. Consider the three molecules shown below.

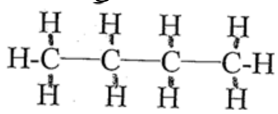
A B C

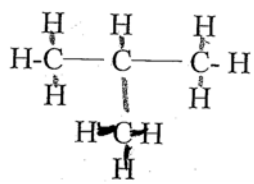


What is the relationship between molecules A and B?

What is the relationship between molecules B and C?
What is the relationship between molecule A and C?

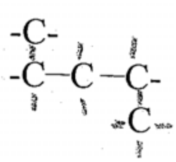
Structural Isomers with Branching
We can also have isomers by branching of a C chain. Consider the following two structures:

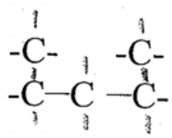




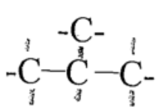
Observe that both structures have the same formula, C_4H_{10}, but that they do not have the same structure. The second structure has a C **branch** off the second C atom while the first molecule is an unbranched "straight" chain.

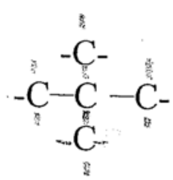
One has to be careful in determining whether a chain is branched or not. If one can put ones pencil down on one end of a carbon chain and trace all the C atoms in the structure without "backtracking" or lifting one's pencil, then the structure is not branched, even if one did several zig-zags. Thus the molecular structures shown below are **not** branched.





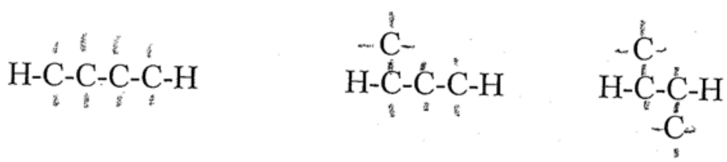
(These are different representations of the same structure, pentane.)
On the other hand, if one cannot trace all the C atoms in a single trace without backtracking, then there is a fundamental branch in the chain, as in the examples below.

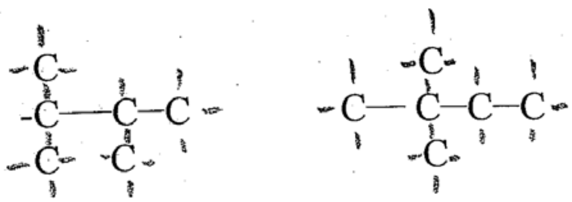




There is one branch in the first structure and two branches in the second structure.

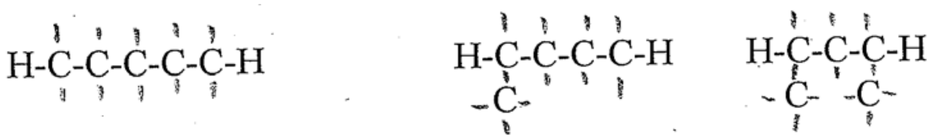
Study the structures shown below and decide whether they are structural isomers, geometric isomers, or the same molecule drawn differently.

1) 

2) 

Decide whether the following structures are structural isomers, geometric isomers, or the same molecule drawn differently

A B C

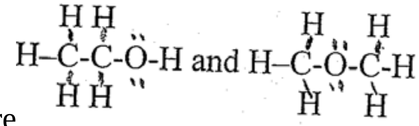
1) 

Using branches, find three isomers with the formula C_5H_{12}. (The first isomer is the straight chain that was mentioned earlier)

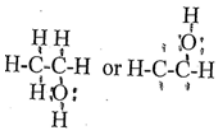
Using branches, find five isomers with the formula C_6H_{14}.

Isomers with O in the formula

Let's look at some isomers that contain O in the formula. Remember that O is in Group VI and has 6 electrons. Since it wants 8 total electrons it will tend to form 2 bonds, either 2 single bonds as in water (H_2O) or a double bond as in O_2.
Draw 2 isomers with the formula C_2H_6O.

Answer: The two isomers are 

If you drew



note that free rotation of the OH off the C atoms makes all these the same molecule!

Draw the structure of 2 isomers with the formula C_2H_4O. This formula has 2 less hydrogen atoms than the C_2H_6O formula we just drew. In order to meet the bonding rules, all of the structures you draw will need to contain either a double bond or a ring.

Draw the structure of 3 isomers with the formula C_3H_8O.(No double bonds or rings needed.)