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5.111 Principles of Chemical Science  
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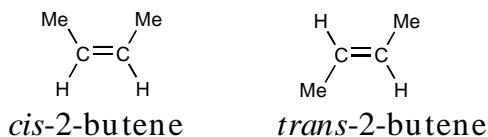
## Restriction of Rotation around Double Bonds

See pages 5 and 6 of lecture 15 notes for a description of double bonds using valence bond theory and hybridization.

Atoms attached by single bonds can rotate freely around the bond axis.

In contrast double bonds prevent rotation around the bond axis, since rotation would break the pi bond (see lecture 15 notes for a discussion of sigma and pi bonds).

This means that molecules are made rigid by double bonds, locking a molecule into a specific conformation. For example, *cis*-butene and *trans*-butene shown below are two distinct molecules. There is NO rotation around the double bond. *Cis* and *trans*-butene are examples of geometric or “*cis-trans*” isomers.



### Example from lecture 15

In drugs containing double bonds, one geometric isomer may be significantly more potent than the other isomer, since the lack of rotation around the bond prevents rotational inter-conversion between the two forms. This means that one isomer may be able to achieve the necessary conformation to bind a target molecule (such as an enzyme or receptor), while the other isomer may not be able to bind at all or may be an inferior binding partner.

For example, chlorprothixine is a first generation antipsychotic drug that was first used to treat schizophrenia and other disorders in the 1950's. The drug functions by blocking certain receptors in neurons, which requires binding of the drug to the receptor. Research has shown that *cis*-chlorprothixene is biologically active, while the *trans* form is almost completely inactive. In fact, the *trans* isomer is considered a contaminant in the drug formulation.

