Massachusetts Institute of Technology
Organic Chemistry 5.512

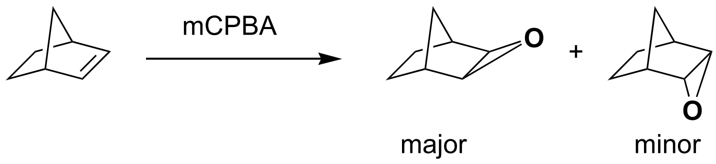
Problem Set 1 Solutions
Review of Stereochemical Principles

1. Define "stereogenic center". What is the difference between a chiral center and a stereogenic center?

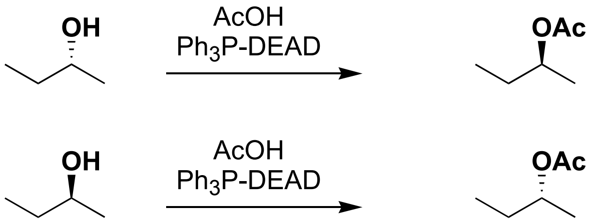
A stereogenic center is an element where the interchange of two substituents will lead to a stereoisomer. A chiral center is a specific type of stereogenic center where reflection of the molecule results in a non-superimposable mirror image of that center.

2. Define the terms "stereoselective reaction" and "stereospecific reaction" and give an example of each.

A "stereoselective reaction" results in the preferential formation of one stereoisomer over the other possible stereoisomers. A reaction is stereospecific if starting materials which are stereoisomeric react (under the same conditions) to give products that are stereoisomeric.



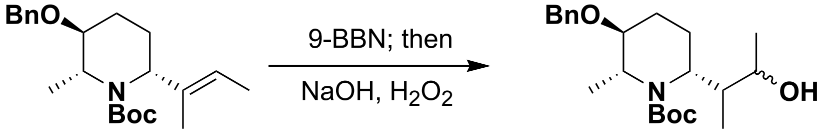
Stereoselective reaction



Stereospecific reaction

3. Define the terms "diastereotopic face" and "enantiotopic face" and give an example of each.

A functional group is considered to have a diastereotopic face if addition to one face results in a product that is a diastereomer of the product formed from addition to the other face. Likewise, an enantiotopic face is characteristic of a substrate that upon addition to one face is transformed into an enantiomer of the product resulting from addition to the other face



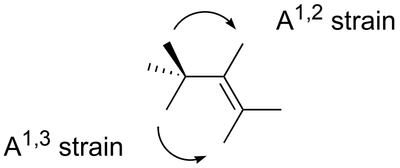
The hydroboration reaction shown provides a mixture of diastereomeric products; therefore, the alkene of the starting piperidine has diastereotopic faces.

4. Why is the following title nonsensical? "A Chiral Total Synthesis of Strychnine"

Chiral is an adjective meaning "not superimposable with its mirror image" and can only be applied to physical objects.

5. Define "allylic strain". Give an example of a molecule with $A^{1,2}$ strain and one with $A^{1,3}$ strain.

Allylic strain is the destabilization of a molecule due to van der Waals repulsion between substituents on a double bond and those in an allylic position.



6. Why will we discuss the products of reactions in terms of "enantiomeric purity" rather than "optical purity" in 5.512?

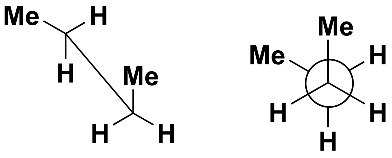
Enantiomeric purity is a measure of the ratio of the enantiomers present in a sample. Optical purity instead refers to the ratio of the optical rotation of a sample containing enantiomers to the optical rotation of a pure sample of a single enantiomer. Optical purity does not always correlate directly to the ratio of the enantiomers present in a sample. In addition, optical rotation can be difficult to measure accurately due to the presence of trace impurities having large rotations.

7. Define "kinetic resolution".

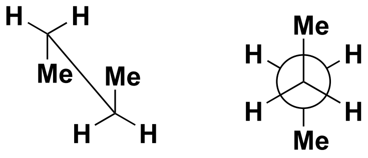
Kinetic resolution is the separation (or partial separation) of an enantiomer from a racemic mixture by reaction of the mixture with a chiral reagent that reacts faster with and consumes the undesired enantiomer (with the reaction not being run to completion).

8. Define "antiperiplanar"and "synclinal" and illustrate each using both Newman projections and sawhorse representations for *n*-butane.

Two groups are synclinal if they are attached to adjacent, bound atoms and the angle formed by the groups, when viewed along the axis of the bound atoms, is approximately 60 degrees (+30 to +90 degrees or -30 to -90 degrees). Two groups are antiperiplanar if they are attached to adjacent, bound atoms and the angle formed is approximately 180 degrees (-150 to +150).



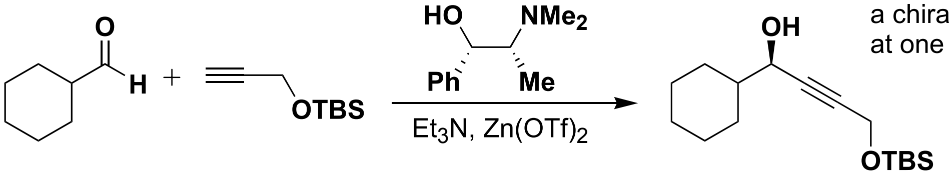
synclinical



antiperiplanar

9. Define "prochiral faces" and illustrate with an example.

If addition of a reagent to one face of a functional group within an achiral molecule leads to a chiral product, then that face is prochiral.

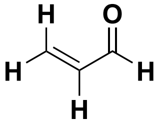


The Carreira alkynylation can produce a chiral product by stereoselective reaction at one prochiral face of the aldehyde.

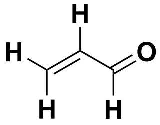
10. What is the barrier to rotation (in kcal/mol) about the carbon-carbon bond in ethane?

2.9 kcal/mol

11. Draw the *s-cis* and *s-trans* conformations of acrolein. Which is lower in energy?



s-cis



s-trans

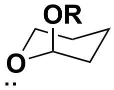
s-trans is more stable by 1.7 kcal/mol

12. Rank the following substituents in term of conformation free energies on cyclohexane rings: CH_3, OH, CN, OMe, ethynyl, *i*-Pr, CHO, Br, CO_2Et, H.

H < CN < ethynyl < OH ~ OMe ~ CHO ~ Br < CO_2Et < Me < *i*-Pr

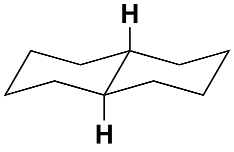
13. Define the "anomeric effect" and provide an example.

The anomeric effect is the preference for synclinal isomers in fragments of type Y-C-X-C where Y and X are heteroatoms with at least one being O, N, or F possessing a lone pair of electrons. It is generally attributed to stabilization resulting from donation of electron density from an adjacent antiperiplanar lone pair into the σ^* orbital of a carbon-heteroatom bond.

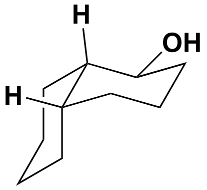


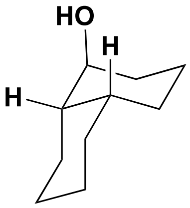
the axial position
is prefered

14. Draw an artistic and accurate representation of *trans*-decalin and the two alternative conformers of *cis*-1-hydroxydecalin.

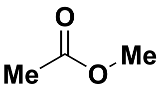


trans-decalin

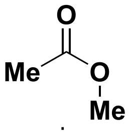




15. Draw the cis and trans conformational isomers of methyl acetate. Which is lower in energy? By how much?



trans



cis

The trans isomer is lower by 8.5 kcal/mol