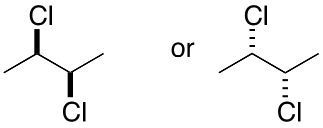
CHEM 203

Topics Discussed on Oct. 5

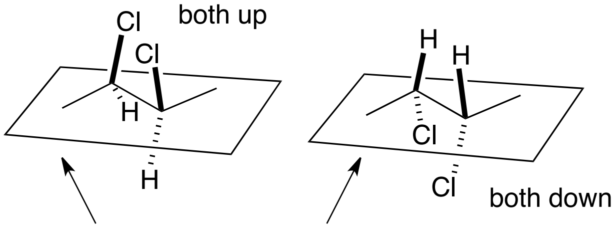
Syn and *anti* diastereomers of the product of chlorination of, e.g., 2-butene:

(a) draw the carbon backbone in an extended (*anti*-butane) conformation and consider the orientation of the halogen atoms relative to the geometric plane containing the main carbon chain

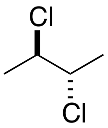
(b) if the halogen atoms are protruding out of the same face of the plane, then the stereoisomer in question is the *syn* diastereomer; if they are pointing in opposite directions, then the stereoisomer in question is the *anti* diastereomer:



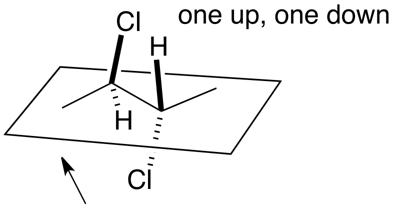
enantiomeric forms of the *syn* diastereomer, because in either molecule the Cl atoms reside on the same face of the plane defined by the main chain of the molecule in an extended conformation



molecular plane defined by the main chain in an extended conformation



anti diastereomer,because the Cl atoms reside on opposite faces of the plane defined by the main chain of the molecule in an extended conformation



molecular plane defined by the main chain in an extended conformation

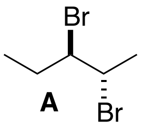
Attention: the stereochemical descriptors *syn* and *anti* as referred to the mode of addition to an alkene, or to a molecular property of diastereomers, mean two different things:

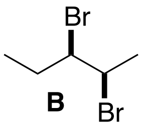
- as applied to the *mode* of addition, they indicate whether a generic X–Y adds to the π bond of an alkene in such a way that X and Y connect to the C atoms of the olefin from the same side (*syn* addition) or from opposite sides (*anti* addition) of the plane of the π bond.

- as applied to a *diastereomer*, they indicate whether groups X and Y end up pointing toward the same face (*syn* diastereomer) or opposite faces (*anti* distereomer) of a geometric plane containing the main carbon chain of the molecule in an *extended (=anti-butane) conformation*.

Consequence of the stereochemical properties of the halogenation reaction:

suppose that we need to prepare the *anti*-diastereomer of 2,3-dibromopentane (compound **A** below) and the *syn*-diastereomer of the same molecule (compound **B**): how could we proceed?



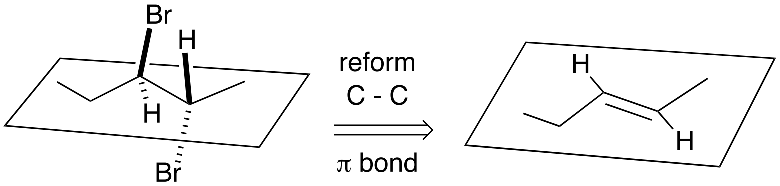


(i) both compounds are 1,2-dibromides, which are available by direct bromination of "2-pentene;"

(ii) the C atoms connected to the halogens must have been part of an olefinic system, which has has subsequently reacted with Br_2; **but** …

(ii) the addition of Br_2 to an alkene is a strictly *anti*-process; meaning that the halogens must have added from opposite faces of the π system. **So**:

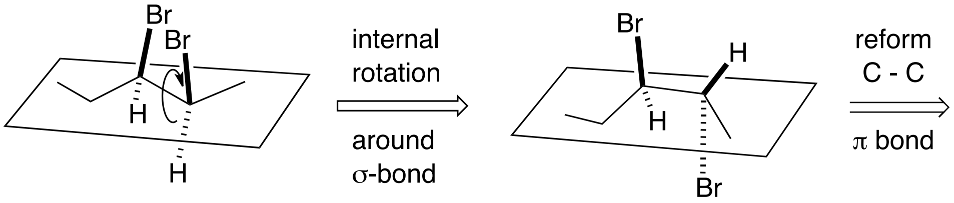
Compound **A** is an *anti*-diastereomer, which must have resulted from the *anti*-addition of Br_2 to *trans*-2-pentene:



Br's on opposite faces
of the molecular plane

compound **A** can be made by
anti-addition of Br_2 to *trans*-2-pentene

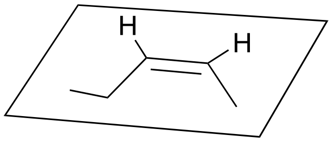
Compound **B** is an *syn*-diastereomer. One cannot produce **B** by the addition of Br_2 to *trans*-2-pentene, because the *anti*-nature of the addition process will furnish the *anti*-diastereomer (**A**). To deduce how we could create **B**, we must imagine a conformer of the molecule in which the halogen atoms are oriented in opposite directions relative to the molecular plane:



Br's on the same face
of the molecular plane

Br's now on opposite
faces of the molecular plane

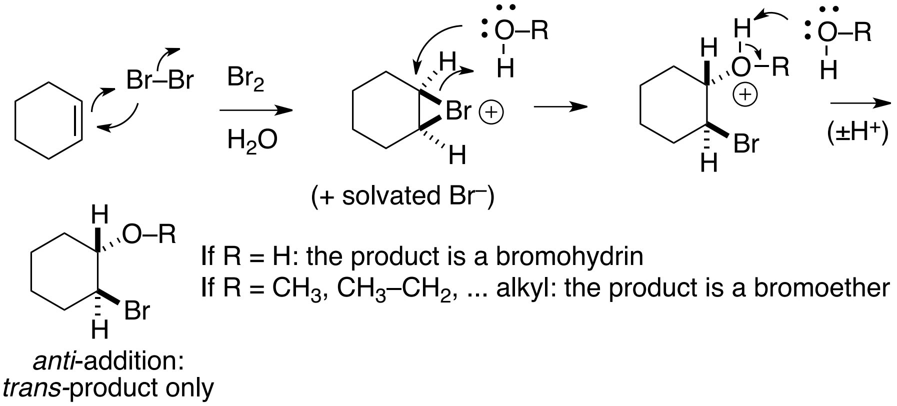
consequently . . .



compound **C** can be
made by *anti*-addition
of Br_2 to *cis*-2-pentene

Driving force in the above reactions: the electronegative halogen atoms, initially in an unfavorable oxidation state of 0, are reduced to the favorable oxidation state of −1

Capture of halonium ions with nucleophiles other than halide ion: reaction of an olefin with Cl_2 (Br_2) and water or simple alcohols: formation of halohydrins (chlorohydrins, bromohydrins, etc.) or haloethers via an overall *anti* addition process:



(+ solvated Br⁻)

If R = H: the product is a bromohydrin
If R = CH_3, CH_3–CH_2, ... alkyl: the product is a bromoether

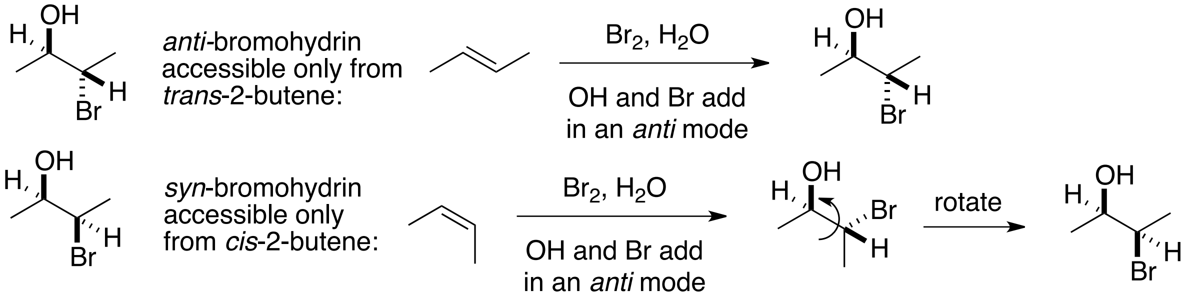
anti-addition:
trans-product only

The halohydrin reaction as a strictly *anti*-addition to the π bond

The halohydrin reaction as a diastereoselective process (*anti*-addition only)

Technological importance of halohydrins

Additional examples: preparation of acyclic (= non-cyclic) halohydrins, e.g. bromohydrins, e.g.:



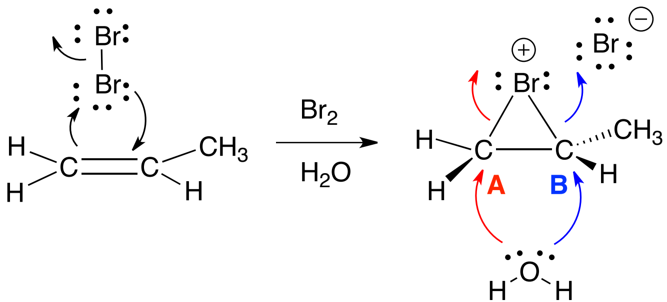
anti-bromohydrin accessible only from *trans*-2-butene:

syn-bromohydrin accessible only from *cis*-2-butene:

Reminder: the halohydrins shown above are chiral molecules that are produced from achiral reactants; consequently, they will be obtained in racemic form. For convenience, we depict them as individual enantiomers, with the understanding that both enantiomers are actually present in equal proportions

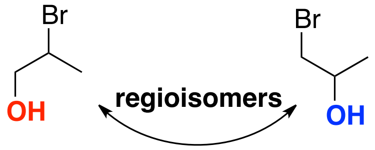
The question of regioselectivity in halohydrin formation from unsymmetrical halonium ions, e.g.:

propene: a simple unsymmetrical alkene



an unsymmetrical bromonium ion: H_2O could react at atom **A** or atom **B**

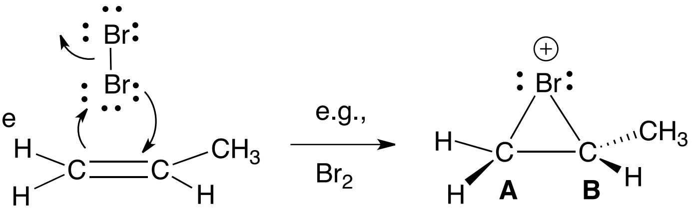
ultimate product of reaction at atom **A:**



ultimate product of reaction at atom **B:**

will the H_2O molecule prefer to attack atom **A** or **B** ?

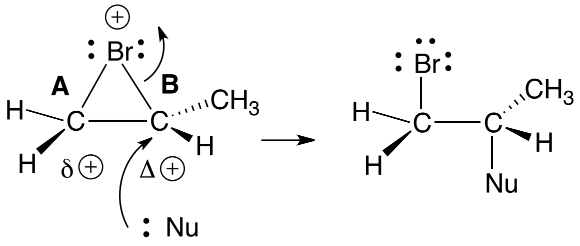
propene: a simple unsymmetrical alkene



an unsymmetrical bromonium ion: a nucleophile could react at atom **A** or at atom **B**

will a nucleophile prefer to attack atom **A** or **B** ?

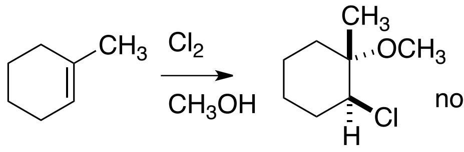
- The Br–C bonds are highly polarized (there is a + charge on Br), so the C atoms of the bromonium ion support a significant fraction of + charge.
- Carbon atom **B** accumulates a greater fraction of + charge than **A**, because it is better suited to sustain cationic character due to a greater number of C–H hyperconjugative interactions



A nucleophile, Nu (=electron-rich species, therefore electrostaticallly negative), will be attracted to the site of greater + character, so one may predict that it will preferentially attack carbon atom **B**

Principle: an external nucleophile will attack an unsymmetrical chloronium (bromonium, … halonium) ion preferentially at the carbon that can sustains the greatest fraction of positive charge (= the more highly polarized C atom)

Additional examples of halohydrin-like reactions:



(racemic)
notice *anti* addition