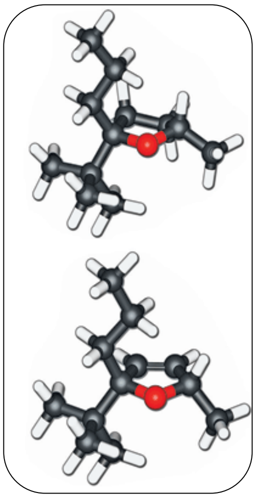
SNIFFING OUT BLACK-CURRANT STRUCTURES



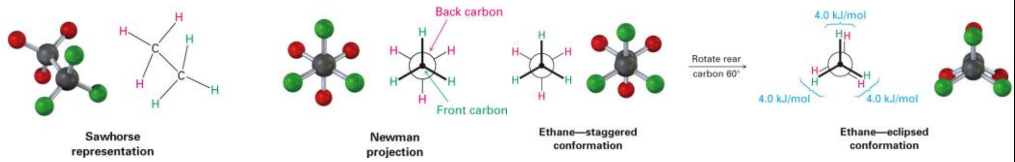
A Cassyrane derivative with a puckered ring (top) has a stronger odor than a compound with a flat ring (bottom).

The secret behind the trendy aroma of black currant may be all about puckering up—five-membered ring puckering, that is. A team at Swiss fragrance firm Givaudan and RWTH Aachen University in Germany has shown that the structure and shape of an ingredient in black-currant scents influence its olfactory properties. Black currant, or cassis in French, is a berry from a plant native to Europe and Asia, and its scent has enjoyed a new surge of popularity with the success of products such as DKNY Be Delicious perfume. The cassis aroma is highly dependent on the stereochemistry of its substituent compounds, and Givaudan chemist Philip Kraft wanted to see whether that held true for Cassyrane, a proprietary black-currant odorant introduced by Givaudan in 2010. With Aachen's Wolfgang Stahl and colleagues, he combined quantum chemistry calculations with microwave spectroscopy to determine gas-phase structures of Cassyrane stereoisomers and derivatives. They found that stereochemistry at Cassyrane's number five carbon determines whether the molecule smells like cassis, and that puckering of the odorant's furan ring enhances its fruity cassis character.

For more information, see *Chemical & Engineering News*, May 30, 2011

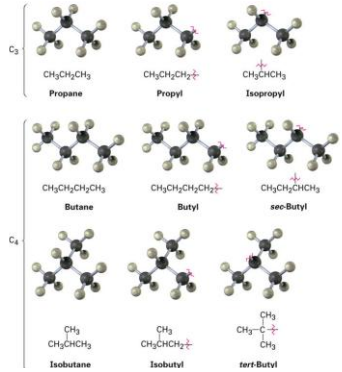
CLASS PLAN – WEDNESDAY, SEPTEMBER 28

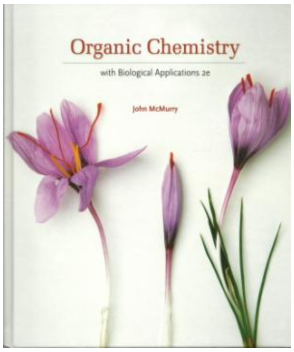
- **OWL Homework – Summary and Feedback**
- **Chapter 3 Mini-Lecture – Newman Projections and Conformational Analysis**
- **Chapter 3 Learning Activities – Conformations of Branched Alkanes**
- **Chapter 4 Mini-Lecture – Cycloalkane Conformations**
- **Chapter 4 Learning Activities – Conformations of Substituted Cyclohexanes**
- **Chapter 4 Mini-Lecture – Disubstituted Cyclohexanes and *Cis/Trans* Isomers**
- **Chapter 4 Learning Activities – Disubstituted Cyclohexanes**
- **Today's Class – Summary**
- **What's Next?**

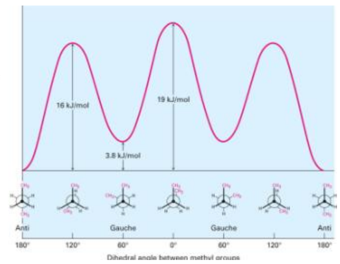


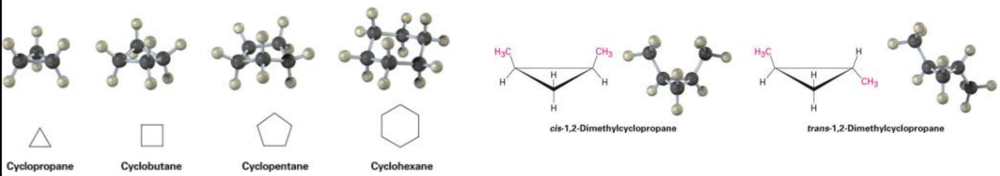
McMurry Chapter 3

ORGANIC COMPOUNDS: ALKANES AND THEIR STEREOCHEMISTRY



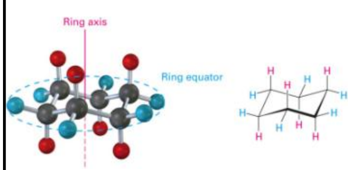


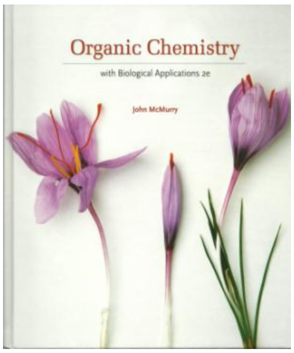


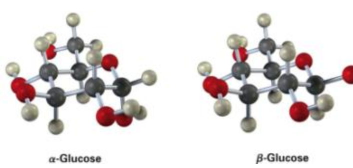


McMurry Chapter 4

ORGANIC COMPOUNDS: CYCLOALKANES AND THEIR STEREOCHEMISTRY







Chapter 3	**Organic Compounds: Alkanes and Their Stereochemistry (excluding 3.5)**
3.1	Functional Groups (+ Degrees of Unsaturation [see 7.1])
3.2-3.4	Alkanes: Structure, Nomenclature and Isomerism
3.6, 3.7	Conformational Analysis of Alkanes

Chapter 4	**Organic Compounds: Cycloalkanes and Their Stereochemistry**
4.1	Naming Cycloalkanes
4.3, 4.4	Stability and Conformations of Cycloalkanes
4.5-4.8	Conformational Analysis of Cyclohexane and Substituted Cyclohexanes
4.2	Cis-Trans Isomerism in Cycloalkanes
4.9	Conformations of Polycyclic Molecules

4

OWL HOMEWORK

5

WEEK 2 POST-CLASS OWL HOMEWORK

3.2 MAS – Drawing Constitutional Isomers

→ **90% participation; mean score: 95%; mastered; 85%; 4 min**

3.3 MAS – C-H Types

→ **90% participation; mean score: 96%; mastered; 84%; 3 min**

3.4b MAS – Alkane Nomenclature - Simple

→ **91% participation; mean score: 96%; mastered: 84%; 5 min**

3.4c MAS – Alkane Nomenclature - Complete

→ **90% participation; mean score: 78%; mastered: 54%; 15 min**

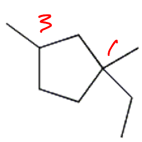
4.1 MAS – Cycloalkane Nomenclature

→ **91% participation; mean score: 57%; mastered; 29%; 16 min**

AVERAGE TIME TO COMPLETE: 43 MIN

6

What is the correct IUPAC name for the following compound?



Number ring so that substituents get lowest numbers possible. (1,1,3 instead of 1,3,3)

ignored when alphabetizing

A. 1-ethyl-1-methyl-3-methylcyclopentane

B. ✓ 1-ethyl-1,3-dimethylcyclopentane

C. 1,3-dimethyl-1-ethylcyclopentane

D. 1,3-dimethyl-3-ethylcyclopentane

E. 1,3-dimethylcyclopropylethane

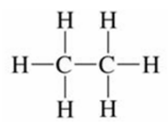
7

ALKANE CONFORMATIONS

8

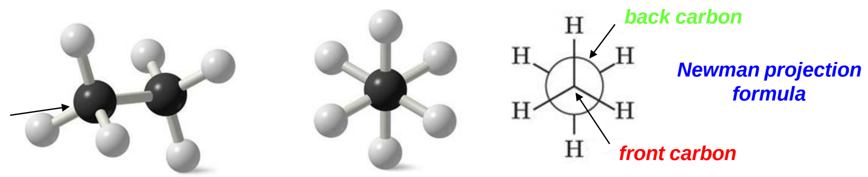
ALKANE CONFORMATIONS

• some representations stress atomic connectivity

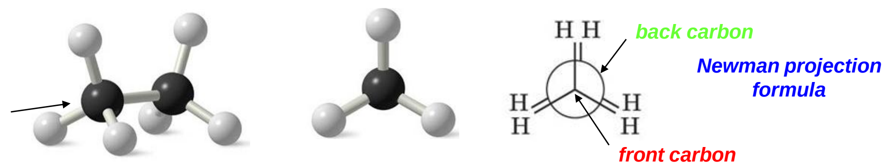


CH_3CH_3

• others stress conformation



• this conformation of ethane is said to be “staggered”

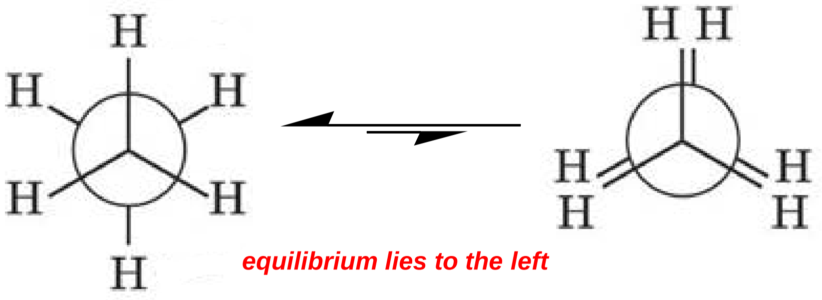


• this conformation of ethane is said to be “eclipsed”

9

CONFORMATIONS OF ETHANE

• conformers of ethane are in equilibrium; interconvert rapidly



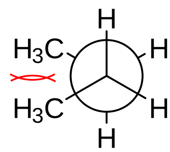
equilibrium lies to the left

• staggered conformation more stable (has less potential energy) than eclipsed conformation

• in eclipsed conformation, electrons in C-H bonds repel each other

• destabilizing effect is called *torsional strain*

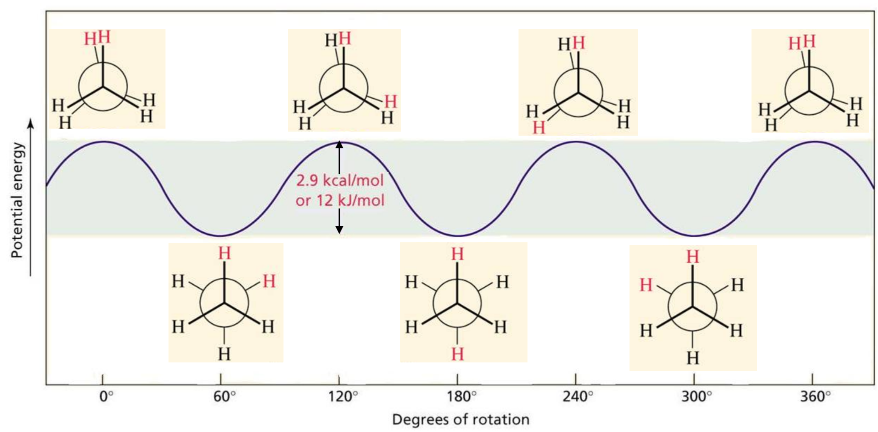
• when larger groups present *steric strain* also an issue



10

CONFORMATIONAL ANALYSIS OF ETHANE

• consider potential energy changes of conformers as one rotates one methyl group of ethane through 360°

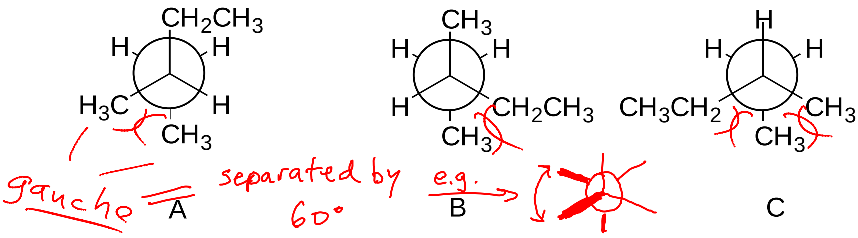


• rotation about C-C bond in ethane is not really "free" → energy barrier

consideration of energy changes associated with rotation about single bonds is called conformational analysis

11

Select the correct order of stability (least stable to most stable) for the conformations shown below.



A. A (least stable), B, C (most stable)

B. A (least stable), C, B (most stable)

C. B (least stable), A, C (most stable)

D. C (least stable), A, B (most stable)

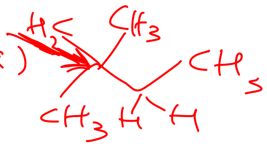
E. C (least stable), B, A (most stable) ✓

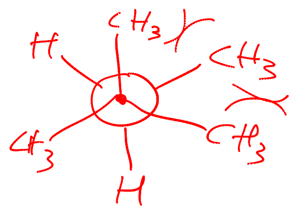
steric destabilization will be encountered whenever large groups are within 60° of each other

CHAPTER 3 LEARNING ACTIVITIES

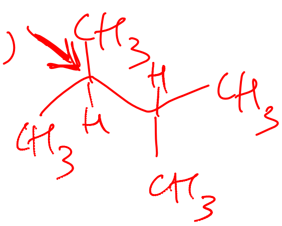
Looking down the C2-C3 bond, draw Newman projection formulas for:
(a) the most stable conformation of 2,2-dimethylbutane.
(b) the two most stable conformations of 2,3-dimethylbutane.

(a)

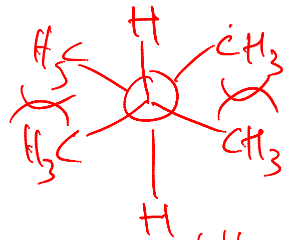




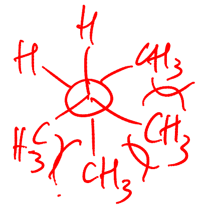
(b)



more gauche interactions = less stable



more stable



less stable

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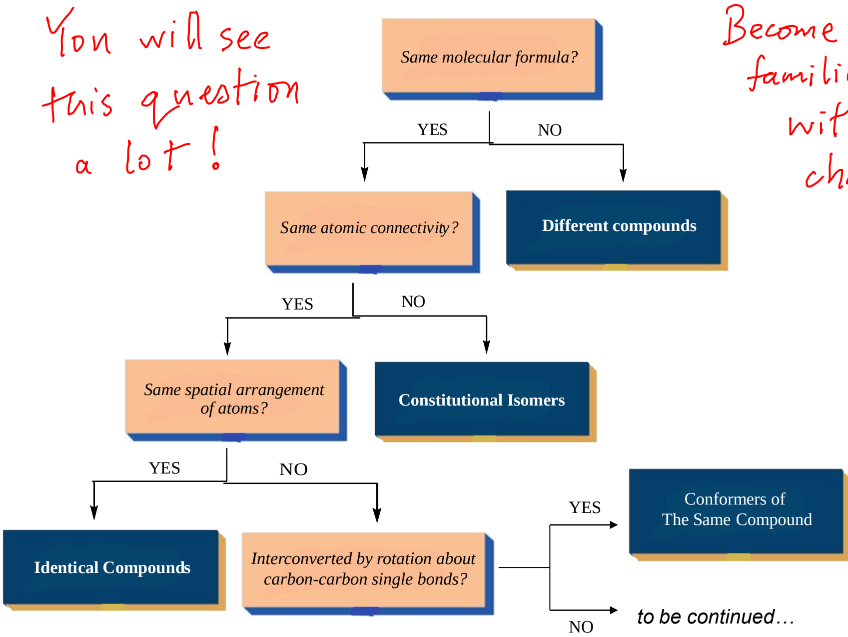
ISOMERISM REVISITED

"What is the relationship between the following compounds?"

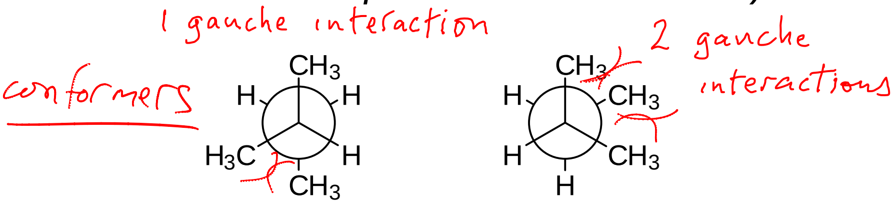
You will see this question a lot!

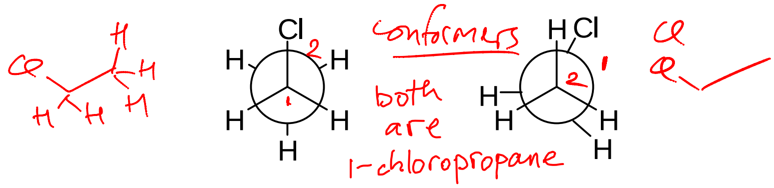
Become familiar with this chart!



15

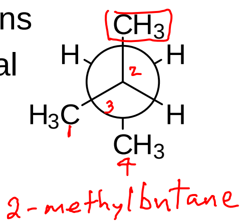
For each of the following pairs of Newman projections, state the relationship (conformations of the same compound or constitutional isomers).

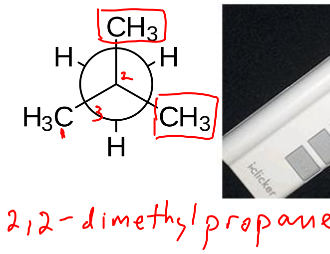




A. Conformations

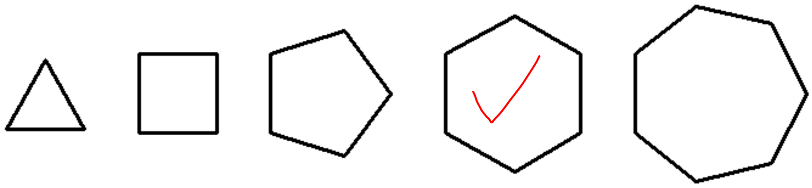
B. Constitutional Isomers ✓





CYCLOALKANE CONFORMATIONS

Which of the following cycloalkanes is the <u>most</u> stable?



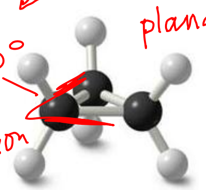
A **B** **C** **D** **E**

See following slides
for explanation

CYCLOALKANE CONFORMATIONS

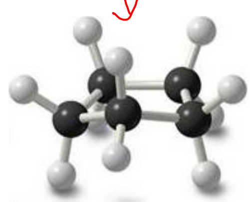
lots of angle strain — planar — nonplanar

60° — deviation from preferred 109.5°



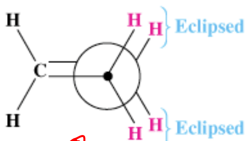
cyclopropane

cyclobutane

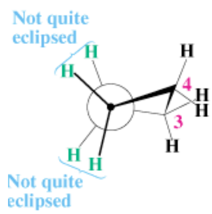


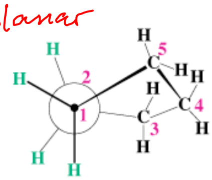
cyclopentane

less torsional strain than if planar



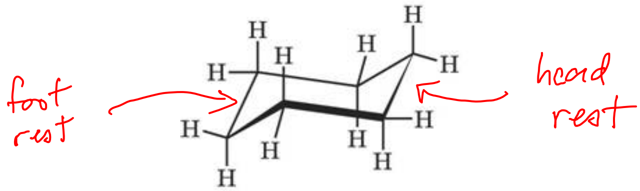
lots of torsional strain



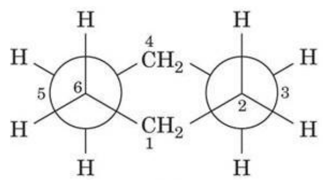


CONFORMATIONS OF CYCLOHEXANE

• most stable conformation of cyclohexane is called the ***chair conformation***



• all carbon-carbon bond angles are 109.5° → no angle strain



• Newman projection shows staggered C-H bonds → no torsional strain

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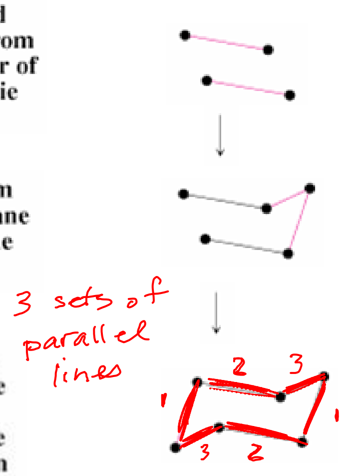
DRAWING CYCLOHEXANE CHAIRS

STEP 1 Draw two parallel lines, slanted downward and slightly offset from each other. This means that four of the cyclohexane carbon atoms lie in a plane.

STEP 2 Locate the topmost carbon atom above and to the right of the plane of the other four and connect the bonds.

STEP 3 Locate the bottommost carbon atom below and to the left of the plane of the middle four and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.



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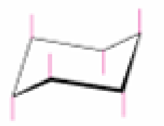
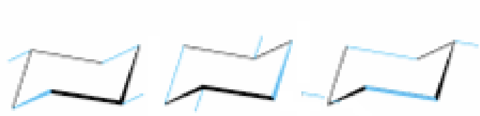
AXIAL AND EQUITORIAL HYDROGENS

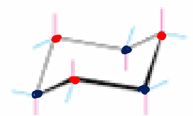
Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.



Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alter- nate between sides around the ring.



Completed cyclohexane



Each carbon has 1 equitorial bond and 1 axial bond

- *3 carbons are pointing "up"; 3 are pointing "down"*
- *axial hydrogens are "up" on "up" carbons*
- *axial hydrogens are "down" on "down" carbons*

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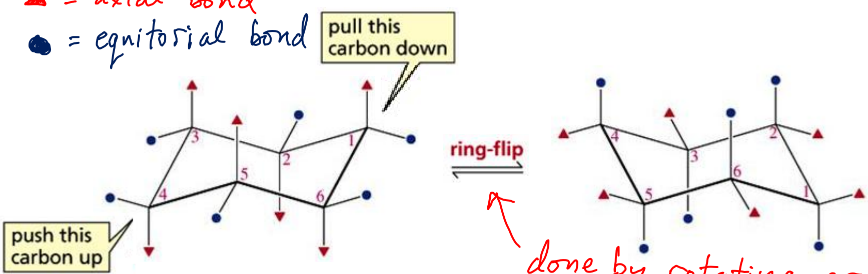
CONFORMATIONAL MOBILITY OF CYCLOHEXANE

- **there is more than one chair conformation of cyclohexane…**

▲ = axial bond
● = equitorial bond



done by rotating around C–C single bonds as opposed to flipping the whole thing

- **chair conformations readily interconvert**
- **one important consequence…**

Ring flip converts all equitorial bonds to axial bonds and all axial bonds to equitorial bonds

- **not important for cyclohexane itself, but for substituted cyclohexanes…**

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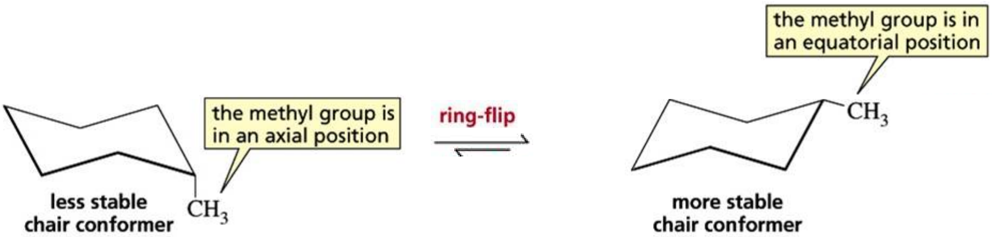
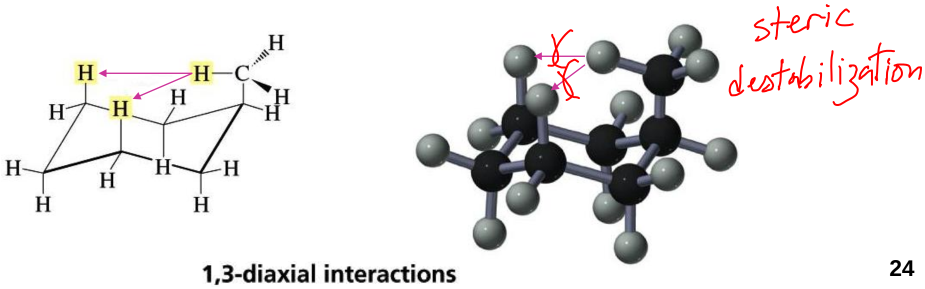
CONFORMATIONS OF MONOSUBSTITUTED CYCLOHEXANES



• **equitorial conformer more stable than axial conformer by 7.6 kJ/mol**



1,3-diaxial interactions

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WHAT HAPPENS WHEN THERE ARE TWO SUBSTITUENTS ON THE CYCLOHEXANE RING?

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CHAPTER 4 LEARNING ACTIVITIES

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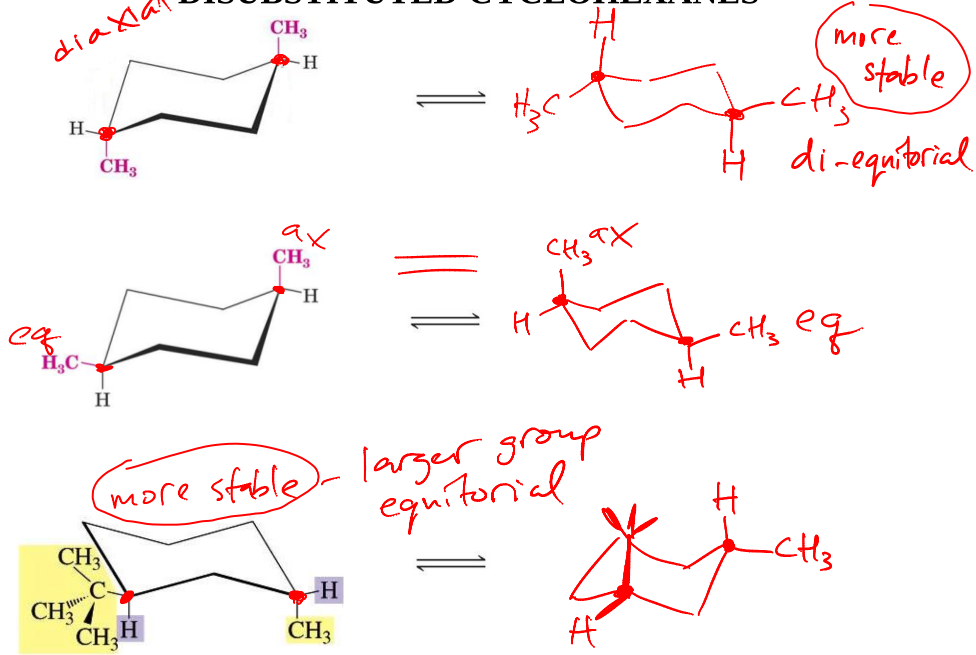
DISUBSTITUTED CYCLOHEXANES



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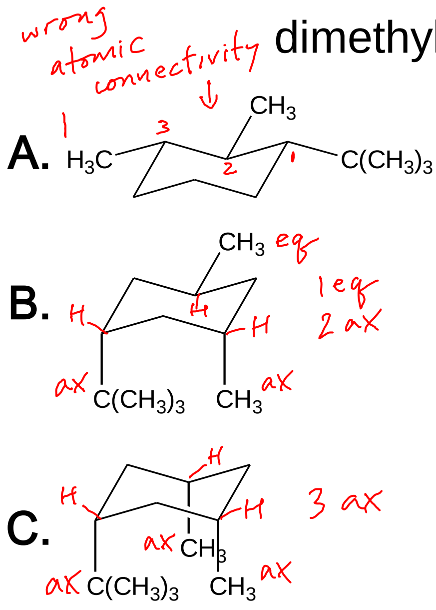
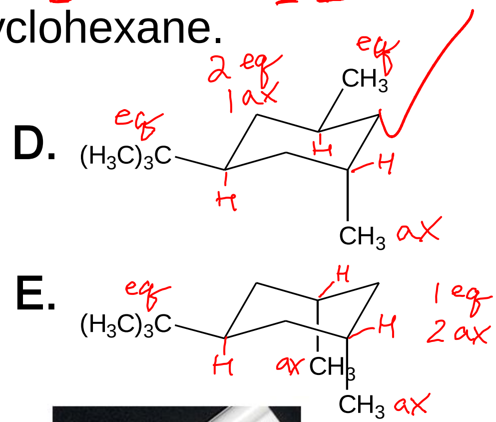
For each, draw the other chair conformation and decide which is more stable.

Of the conformations shown below, select the most stable for 1-*tert*-butyl-3,5-dimethylcyclohexane.





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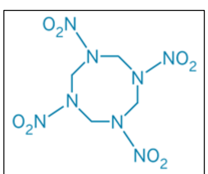
EXAMINING EXPLOSIVES

Countdown LLNL personnel set up flash X-ray equipment at HEAF's 10-kg firing tank.

From outside, the High Explosives Applications Facility at Lawrence Livermore National Laboratory (LLNL) looks like just another office or laboratory building. Inside, however, some of the nation's most dangerous chemistry is performed. HEAF, as the facility is known, is the National Nuclear Security Administration's designated Center of Excellence for High Explosives Research & Development. Scientists use the facility to synthesize, formulate, and characterize explosive materials. Those tasks play a critical role in nuclear stockpile stewardship by providing a means to understand how components of nuclear weapons age and perform over time.



HMX

The high explosive octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (commonly known as HMX, for a variety of phrases including "Her Majesty's eXplosive") has two crystal forms, a "chair" β form and a "boat" δ form. HMX crystallizes in the β form at room temperature and transitions from β to δ at around 165 °C. In an explosion, "the δ phase is often more violent than the β phase," EMC chemist Elizabeth A. Glascoe says. The volume of HMX also expands with the transition, so depending on how explosives makers want the material to behave, they can either physically constrain the material to keep it in β or give it room to expand into δ.

For more information, see *Chemical & Engineering News*, July 18, 2011

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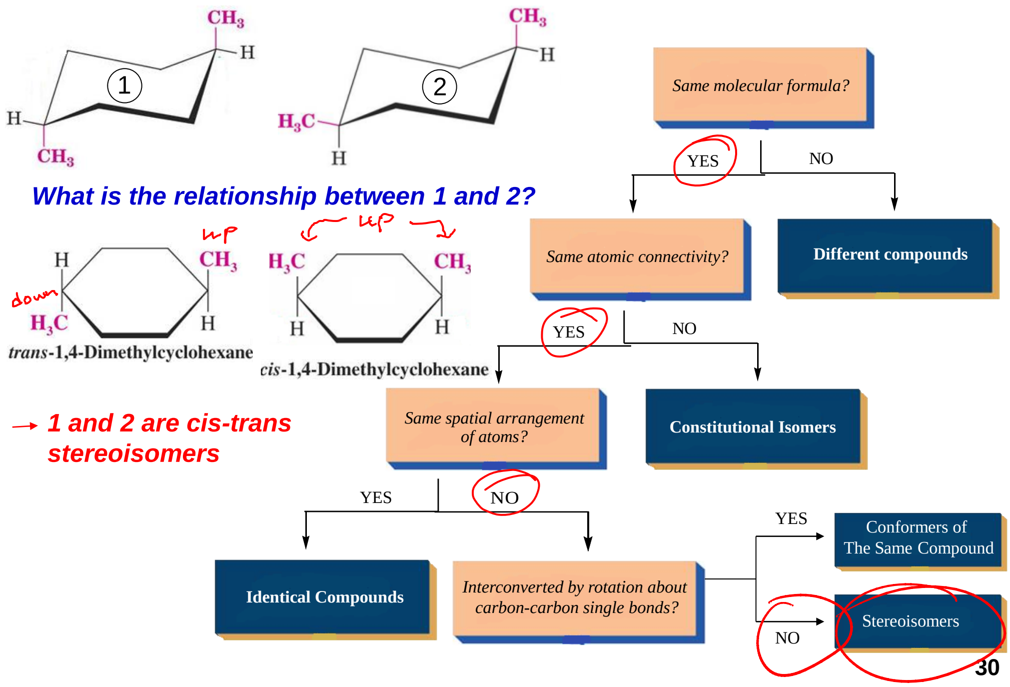
DISUBSTITUTED CYCLOHEXANES



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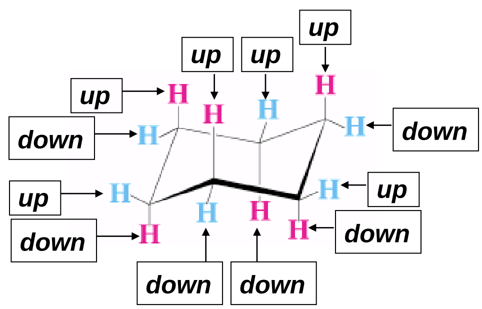
CIS-TRANS ISOMERISM IN CYCLOHEXANES

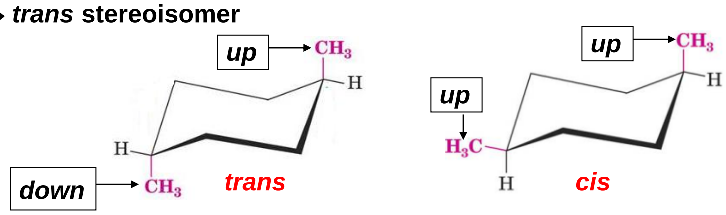
• define substituents on each carbon as "up" or "down"

Most common mistake: both axial ∴ cis ✗ wrong!



• if both substituents are "up" (or both "down") in disubstituted cyclohexane → *cis* stereoisomer

• if one substituent "up" and one "down" in disubstituted cyclohexane → *trans* stereoisomer



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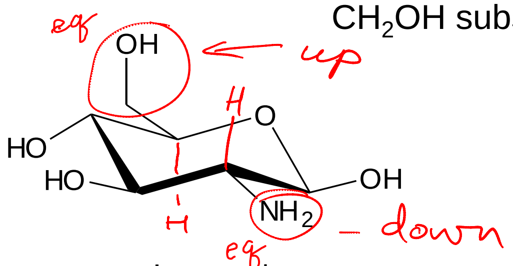
Glucosamine, a naturally occurring substance found in the exoskeleta of marine invertebrates, is believed by some to be helpful in relieving arthritic symptoms in humans. Indicate whether the amino group in glucosamine is cis or trans to the CH_2OH substituent.



glucosamine

Common mistake: both equitorial ∴ cis ✗ wrong!

1. cis
2. trans ✓

one "up" (relative to H bonded to same carbon)
one "down" (relative to ...)
∴ trans

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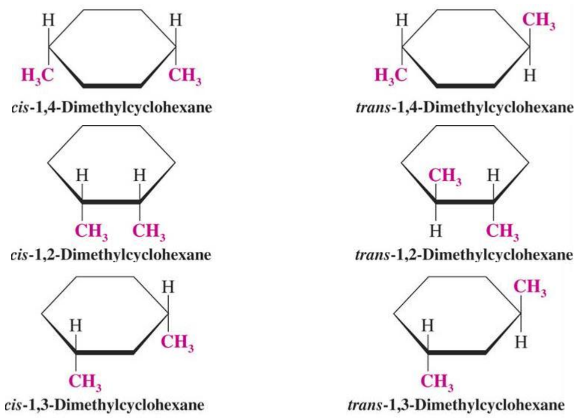
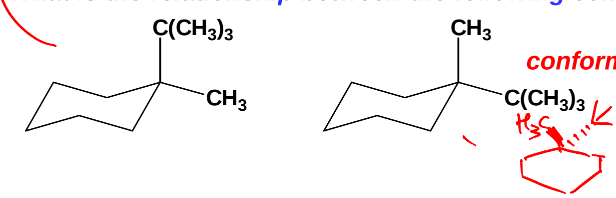
CIS-TRANS ISOMERISM IN CYCLOHEXANES



Cis-trans isomerism exists in 1,2-, 1,3-, and 1,4-disubstituted cyclohexanes.

What is the relationship between the following compounds?



conformers of the same compound

(construct models to find out why)

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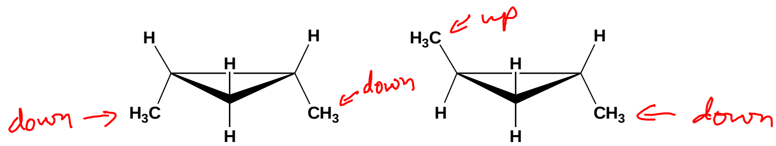
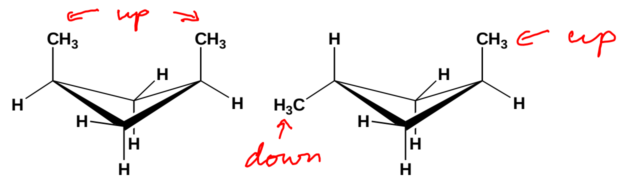
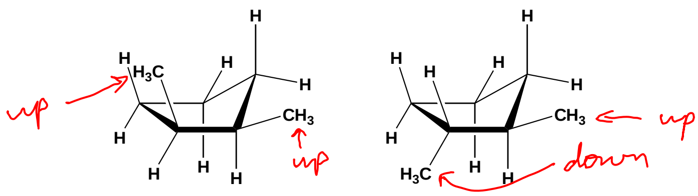
CIS-TRANS ISOMERISM IN OTHER CYCLOALKANES



cis-1,2-dimethylcyclopropane *trans*-1,2-dimethylcyclopropane



cis-1,3-dimethylcyclobutane *trans*-1,3-dimethylcyclobutane



cis-1,2-dimethylcyclopentane *trans*-1,2-dimethylcyclopentane

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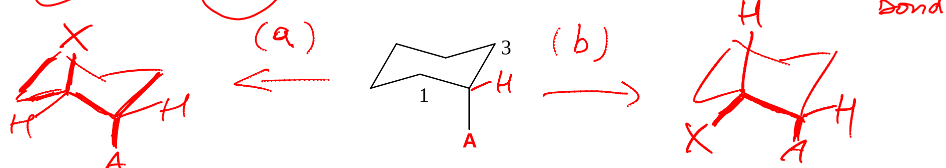
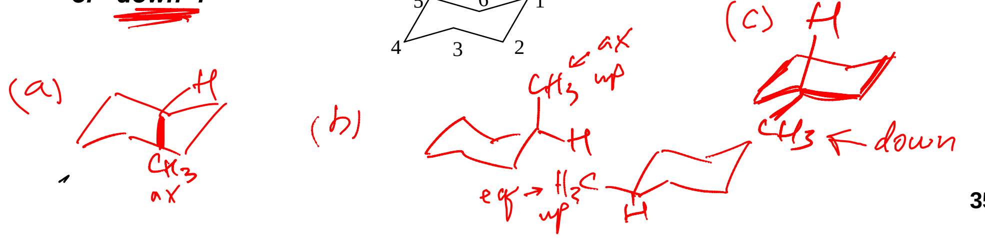
PRACTICE PROBLEMS

Given the following partial structure, add a substituent X to C-1 that is:
(a) Anti to A; (b) Gauche to A.



For the cyclohexane ring depicted:
(a) Is a methyl group at C-6 that is "down" axial or equitorial?
(b) Is a methyl group that is "up" at C-1 more or less stable that a methyl group that is "up" at C-4?
(c) Place a methyl group at C-3 in its more stable orientation. Is it "up" or "down"?



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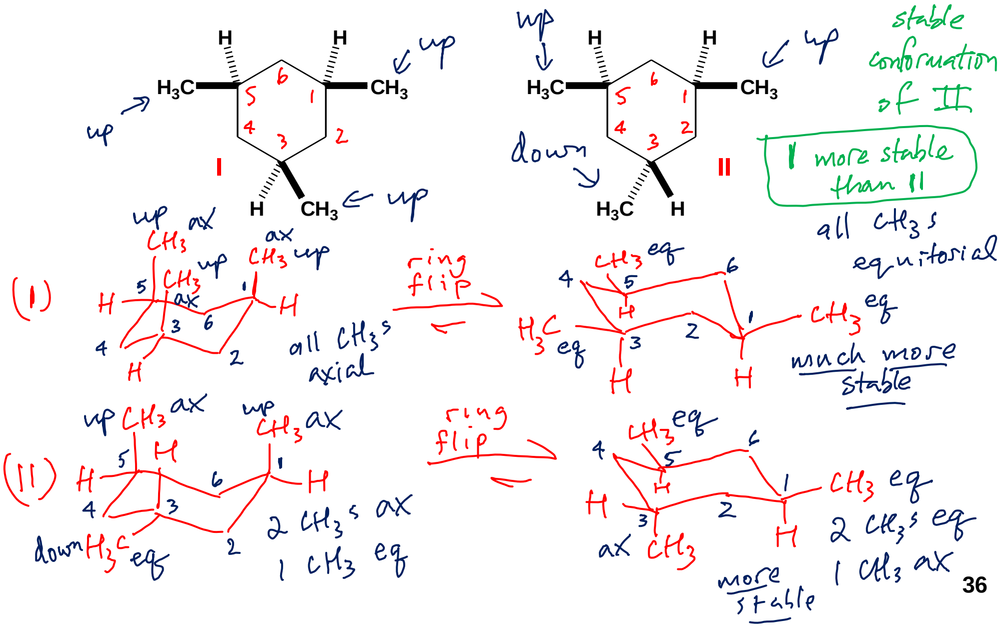
PRACTICE PROBLEM

Compare more stable conformation of I to more stable conformation of II

Which of the following two stereoisomeric 1,3,5-trimethylcyclohexanes would you expect to be more stable?



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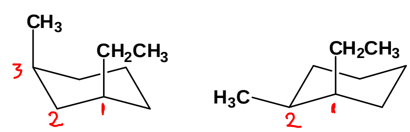
PRACTICE PROBLEMS

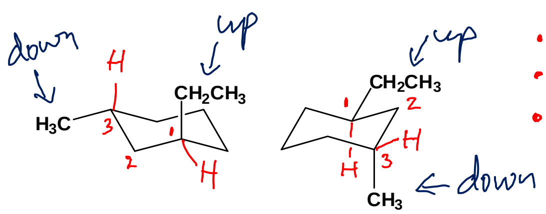
Determine whether the two structures in each of the following pairs represent constitutional isomers, different conformations of the same compound, or stereoisomers that cannot be interconverted by rotation about single bonds.

(a)



- same molecular formula
- different atomic connectivity

∴ constitutional isomers



- same molecular formula
- same atomic connectivity
- different spatial arrangement of atoms (ethyl ax; methyl eq vs ethyl eq; methyl ax)
- but can be interconverted by rotation around C–C bonds (ring flip) ∴ conformers

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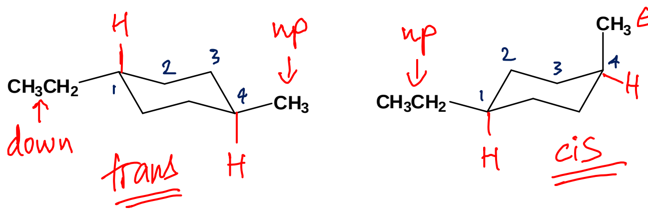
PRACTICE PROBLEMS

Determine whether the two structures in each of the following pairs represent constitutional isomers, different conformations of the same compound, or stereoisomers that cannot be interconverted by rotation about single bonds.

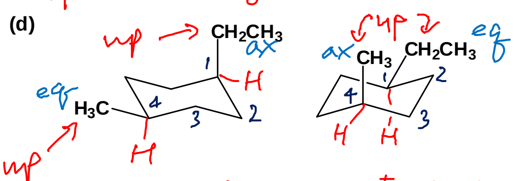
(c)



stereoisomers

• same molecular formula, same atomic connectivity, different spatial arrangement of atoms but cannot be interconverted by rotation around C–C bonds

(d)



same as (c) except can be interconverted by rotation about C–C bonds (ring flip) ∴ conformers

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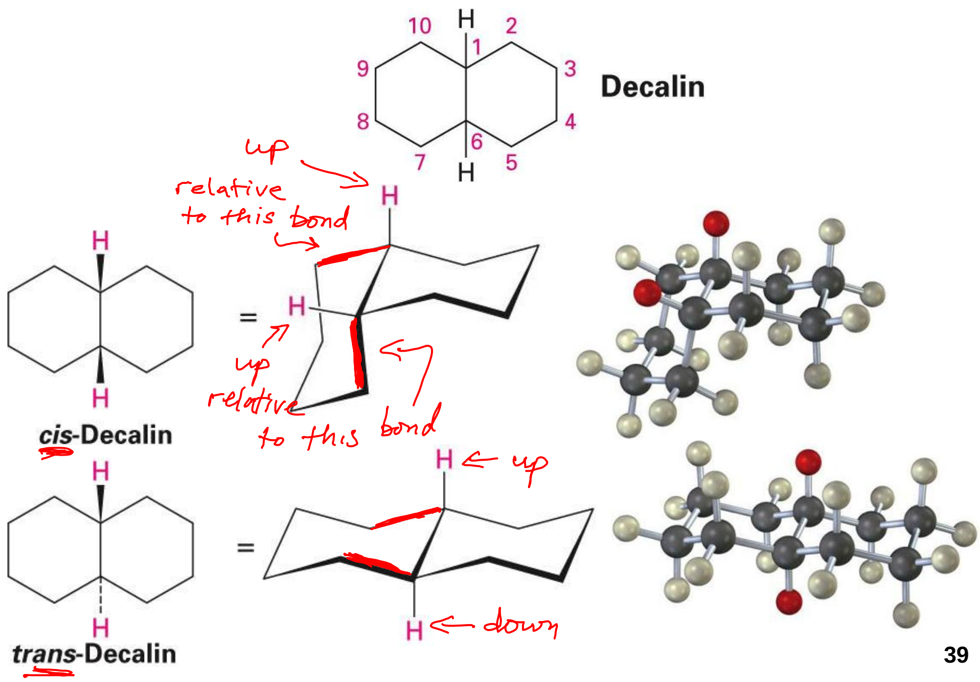
CONFORMATIONS OF POLYCYCLIC MOLECULES



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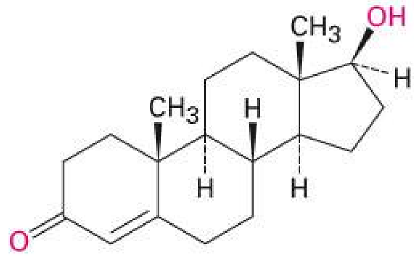
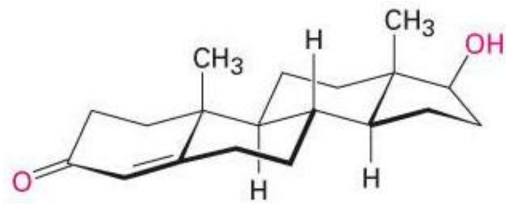
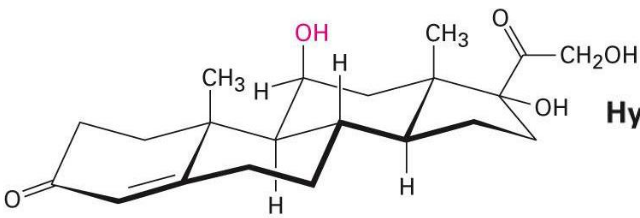
CONFORMATIONS OF POLYCYCLIC MOLECULES



Testosterone





Hydrocortisone

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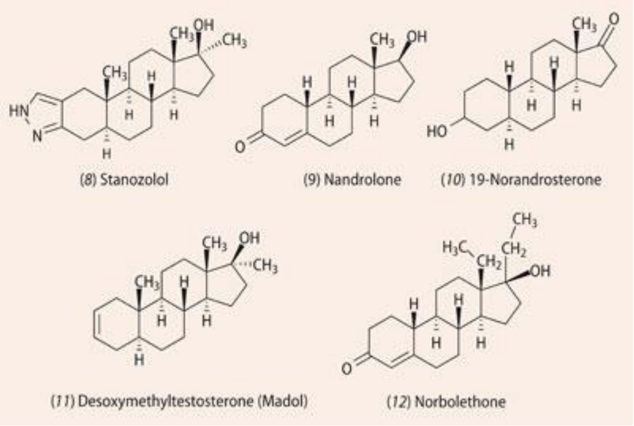
FIVE RINGS GOOD, FOUR RINGS BAD



See **2010** *Education in Chemistry* (March)

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WHAT'S NEXT

This Week

- **Chapters 3/4 required OWL homework: available W 9pm; due Sat 11:59pm**
- **more Chapters 3/4 practice: optional OWL homework, EOC Qs, MyLS links**

Next Week

Chapter 5: Stereochemistry

5.9	A Review of Isomerism
5.1	Enantiomers and Tetrahedral Carbon
5.2, 5.10	Chirality
5.12	Chirality in Nature
5.5	Sequence Rules for Specifying Configuration
5.3, 5.4	Optical Activity

BEFORE MONDAY 11:59 pm

NO EXTENSIONS THIS WEEK!!

- **Chapters 5 (Part I) resources (learning tasks, video lectures, PP slides) 12:01am on Sunday**

MUST COMPLETE "CHAPTERS 3 AND 4 LEARNING TASKS INVENTORY" (UNDER SURVEYS) FIRST

- **required OWL Homework released 12:01am on Sunday; due Wednesday at 12:01pm**
- **optional OWL Homework released 12:01am on Sunday; available for term**
- **extensions and applications in class next Wednesday**

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