

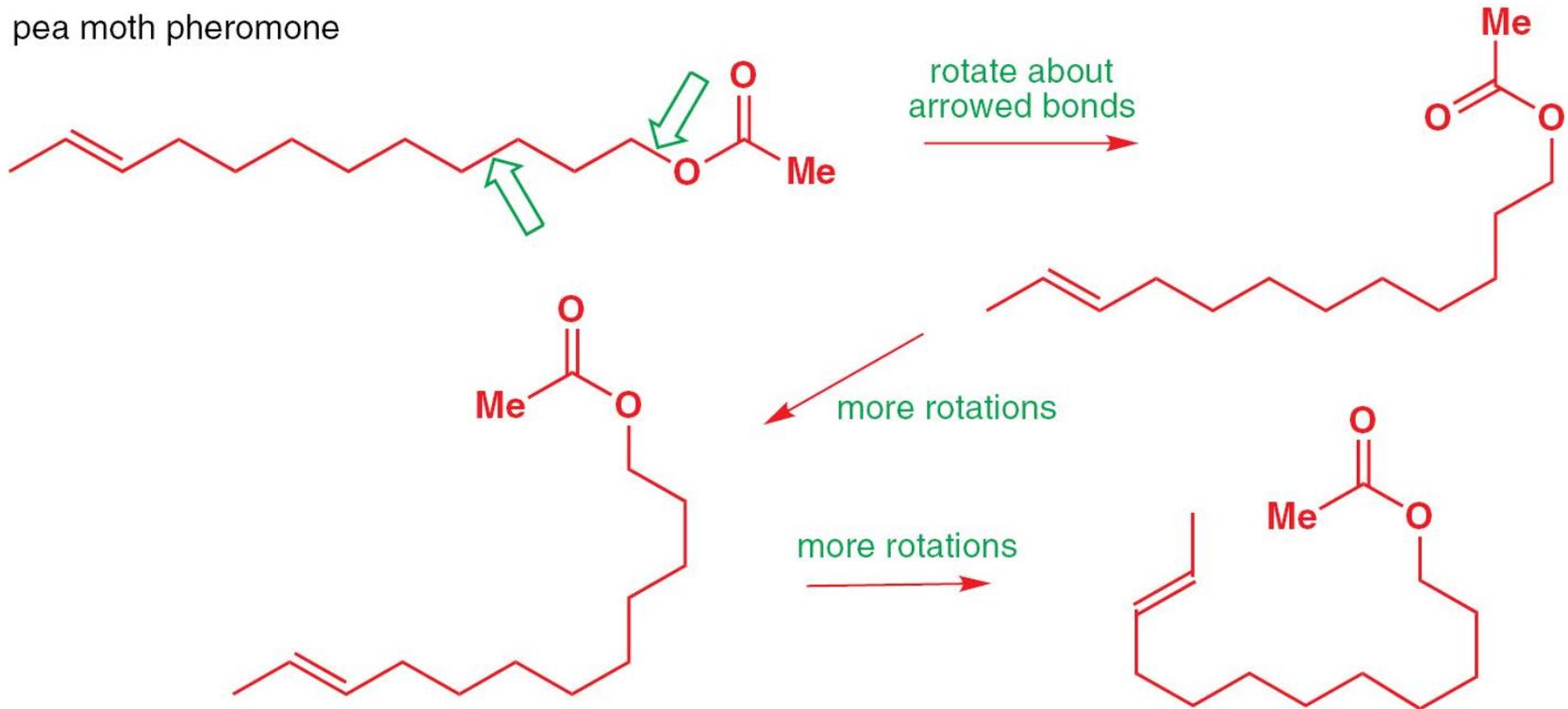
QFL-0341 Estrutura e reatividade de compostos orgânicos

2019 (25/outubro e 01/novembro)

Análise conformacional

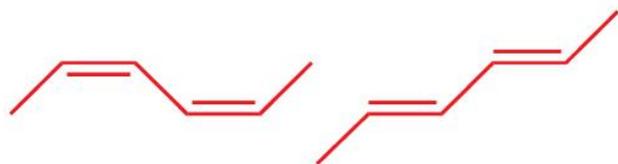
Análise conformacional

pea moth pheromone



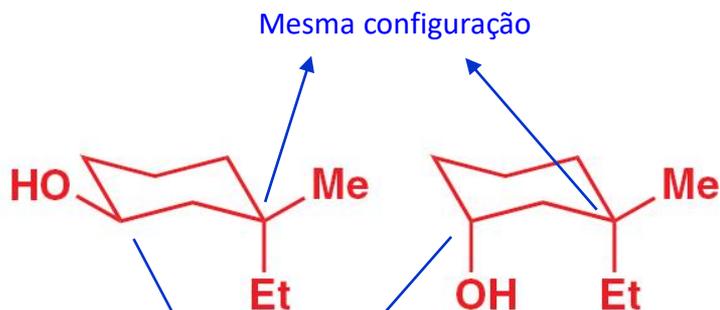
Conformação: forma adotada por moléculas envolvendo rotações de uma ou mais ligações sigma.

three pairs of stereoisomers: each member of a pair has a different configuration



cis cis trans trans

diferentes configurações

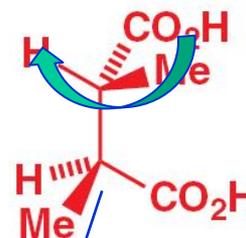
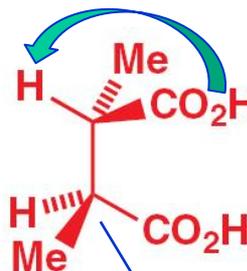


diferentes configurações

diferentes configurações

Sequencia carboxila, metila e hidrogênio

Sequencia carboxila, metila e hidrogênio

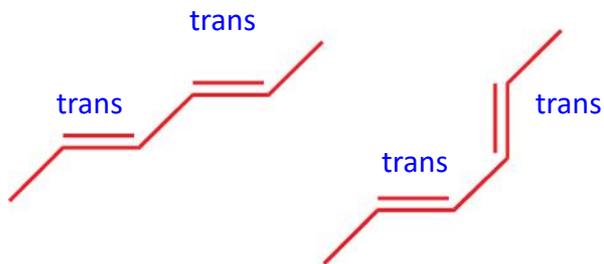


Mesma configuração

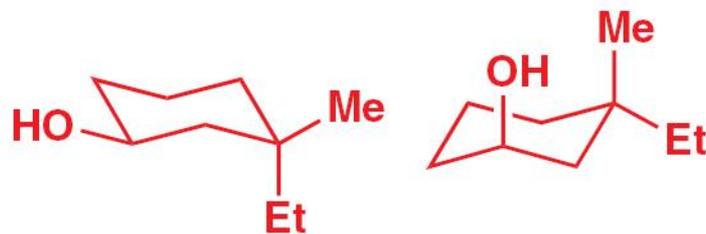
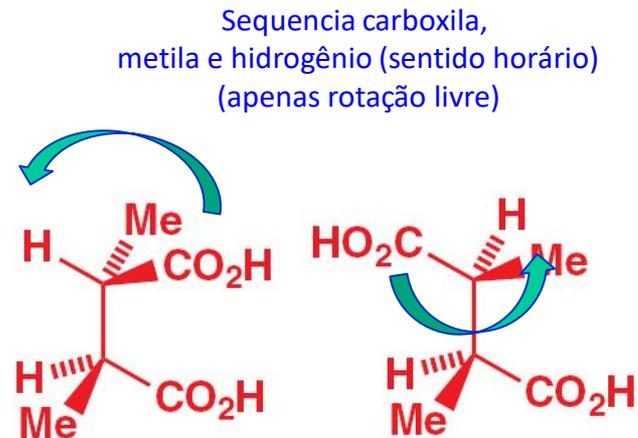
Configuração: disposição de um carbono e seus substituintes com relação aos demais grupos nos quais se encontra ligado.

Não podem ser interconvertidos por rotação mas apenas quebrando-se as ligações.

three compounds, each shown in two conformations

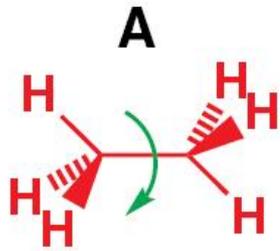


Mesmas configurações
Mas com diferentes conformações



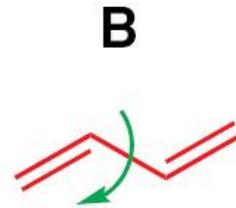
Hidroxilas acima do plano

Mesmas configurações
Mas com diferentes conformações

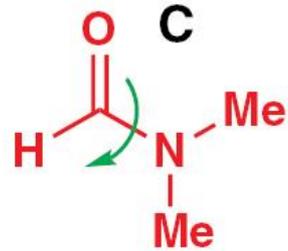


12 kJ mol⁻¹

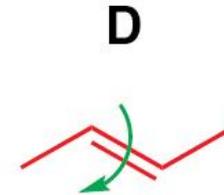
Rotações permitidas



30 kJ mol⁻¹

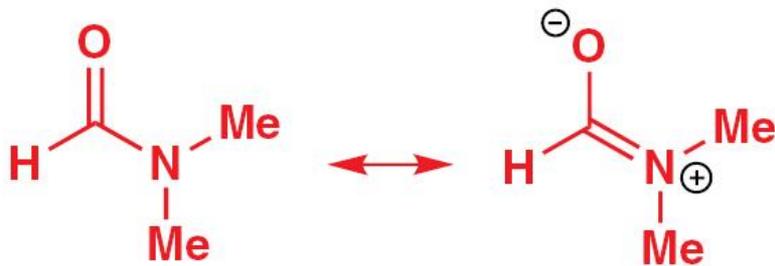


85 kJ mol⁻¹



260 kJ mol⁻¹

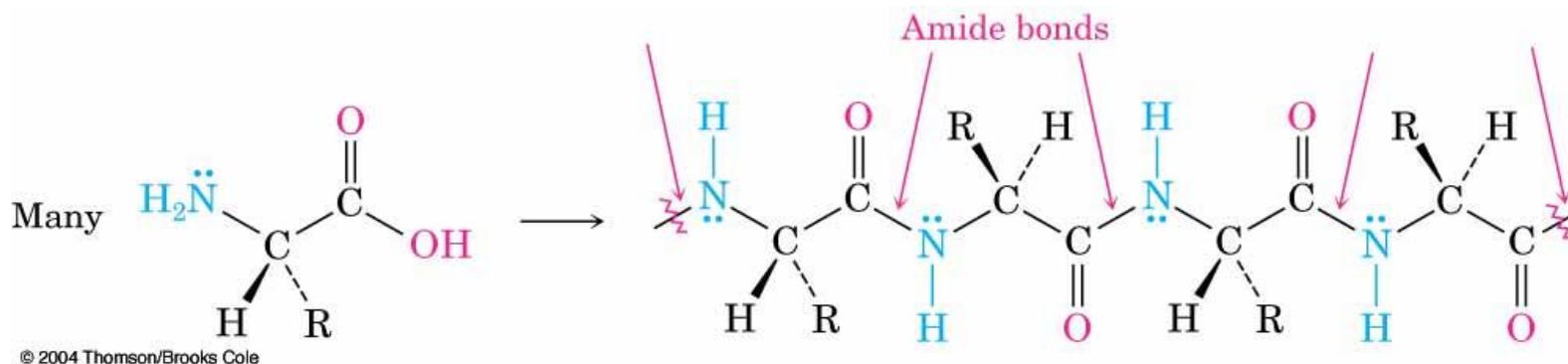
Rotação não permitida



A barreira rotacional em ligações amidicas é limitada pelo caráter de ligação dupla

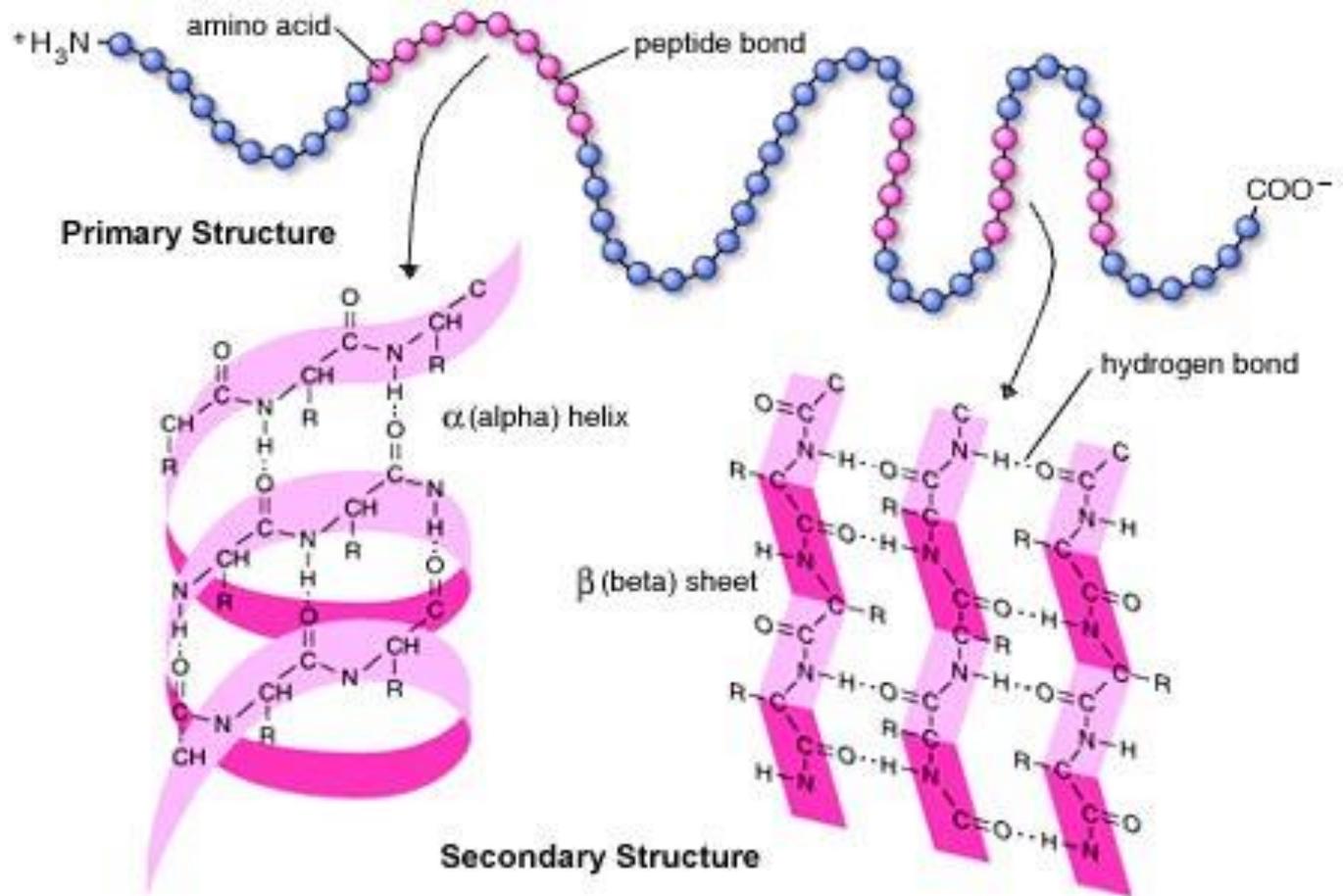
Proteins – Amides from Amino Acids

- Amino acids contain a basic amino group and an acidic carboxyl group
- Joined as amides between the —NH₂ of one amino acid and the —CO₂H the next
- Chains with fewer than 50 units are called peptides
- Protein: large chains that have structural or catalytic functions in biology



Protein Structures

- The **primary structure of a protein** is simply the amino acid sequence.
- The **secondary structure** of a protein describes how segments of the peptide backbone orient into a regular pattern.
- The **tertiary structure** describes how the entire protein molecule coils into an overall three-dimensional shape.
- The quaternary structure describes how different protein molecules come together to yield large aggregate structures

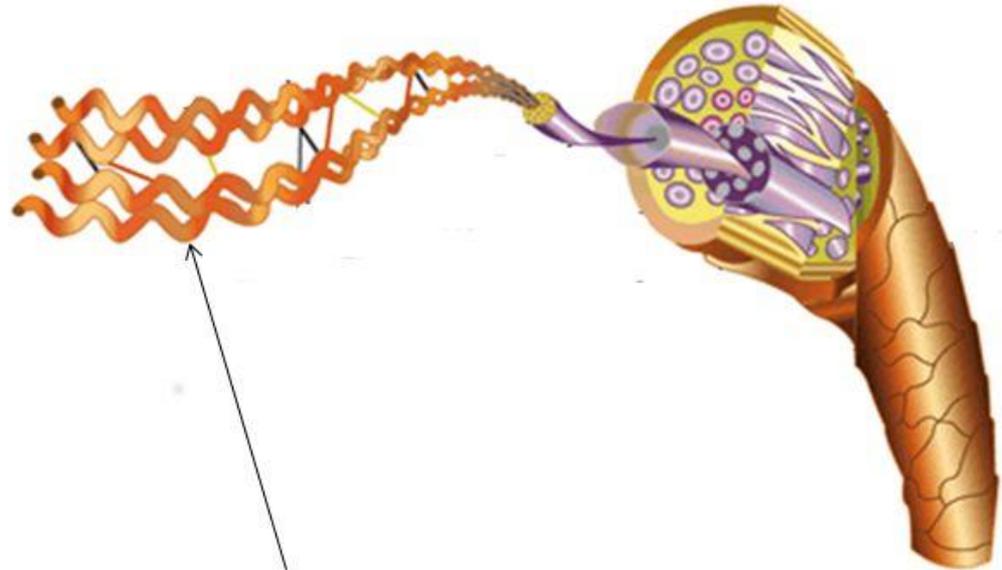


α -helix and β sheet: different conformation of proteins

Protein Structure



Structural proteins give hair and horns their toughness.



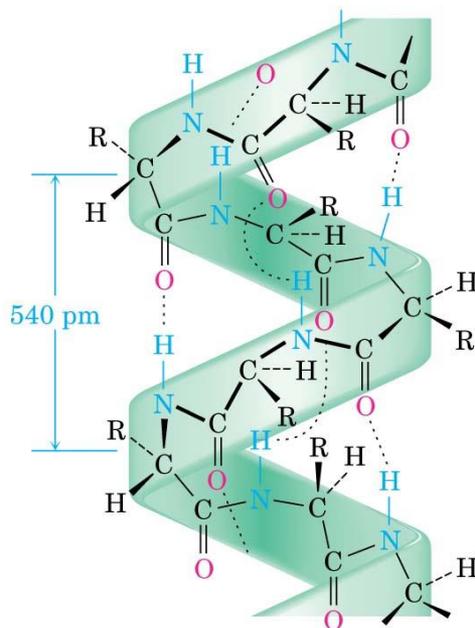
Strands of the protein *keratin*.

Let's zoom in even closer... what are these helices (corkscrews) made out of? What holds them together?

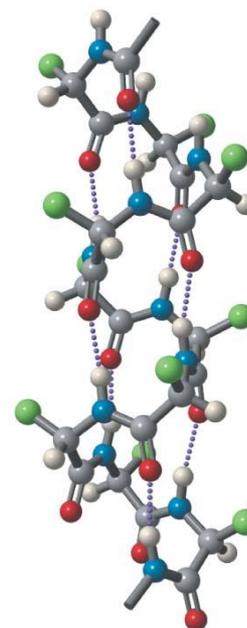
α -Keratin

- A fibrous structural protein coiled into a right-handed helical secondary structure, α -helix stabilized by H-bonds between amide N–H groups and C=O groups four residues away α -helical segments in their chains

Estabilização de conformações α -hélice por ligações de H entre N-H e C=O

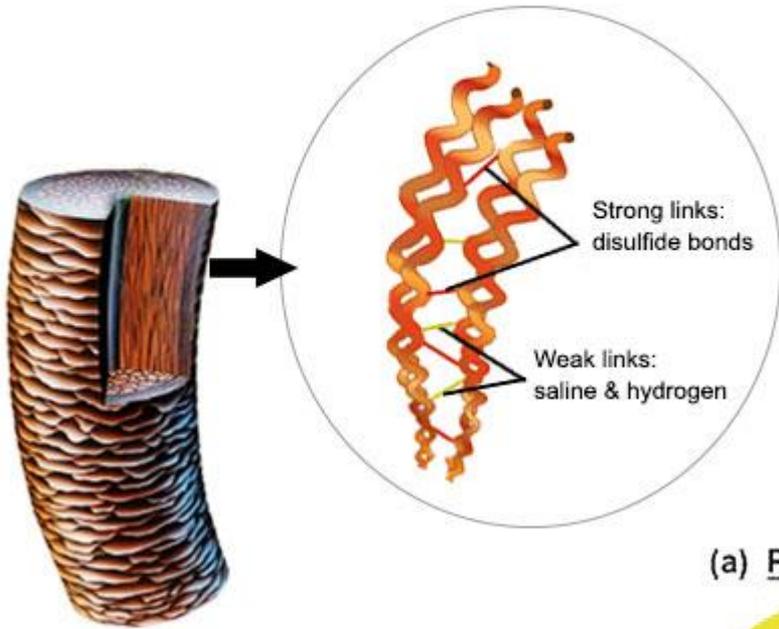


© 2004 Thomson/Brooks Cole



Based on McMurry, Organic Chemistry, Chapter 26, 6th edition, (c) 2003

Hair structure, strong links and weak links

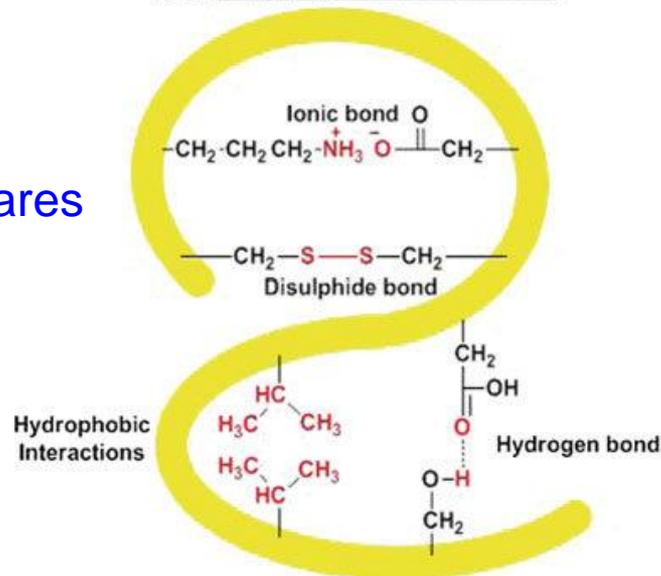


Estabilização de cadeias proteicas por ligações dissulfídicas (intramoleculares e intermoleculares) entre duas cadeias

intermoleculares

intramoleculares

(a) Polypeptide backbone

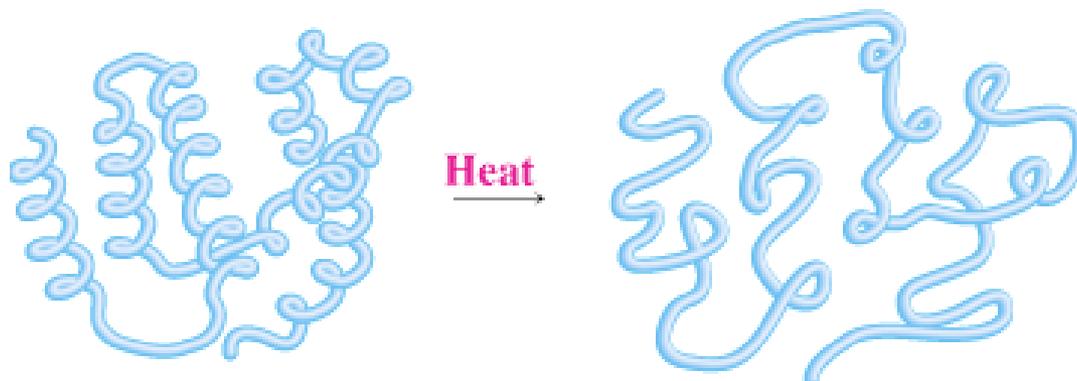


(b) Disulphide bond



Protein Denaturation

- The tertiary structure of a globular protein is the result of many intramolecular attractions that can be disrupted by a change of the environment, causing the protein to become denatured
- Solubility is drastically decreased as in heating egg white, where the albumins unfold and coagulate
- Enzymes also lose all catalytic activity when denatured

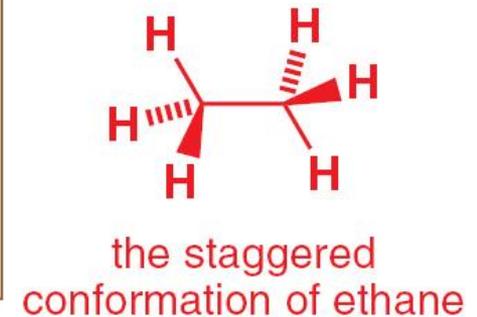
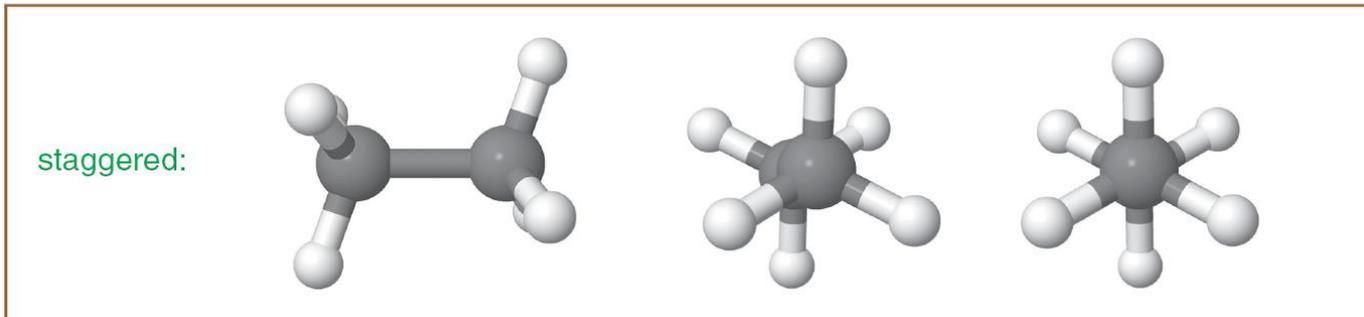


Perturbação da conformação intramolecular

Confôrmeros no etano

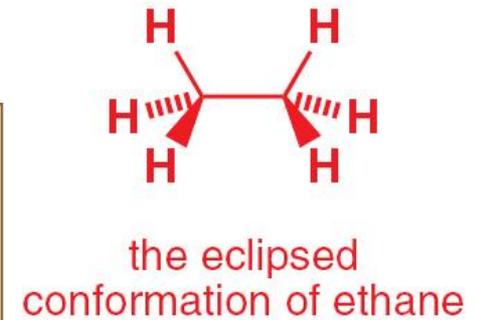
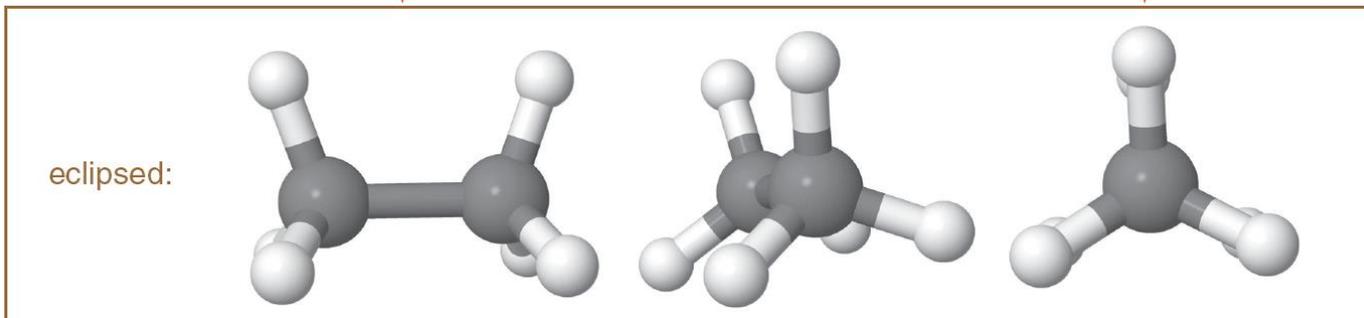
Representação de Newman

the two extreme conformations of ethane, staggered and eclipsed, each shown from three different viewpoints

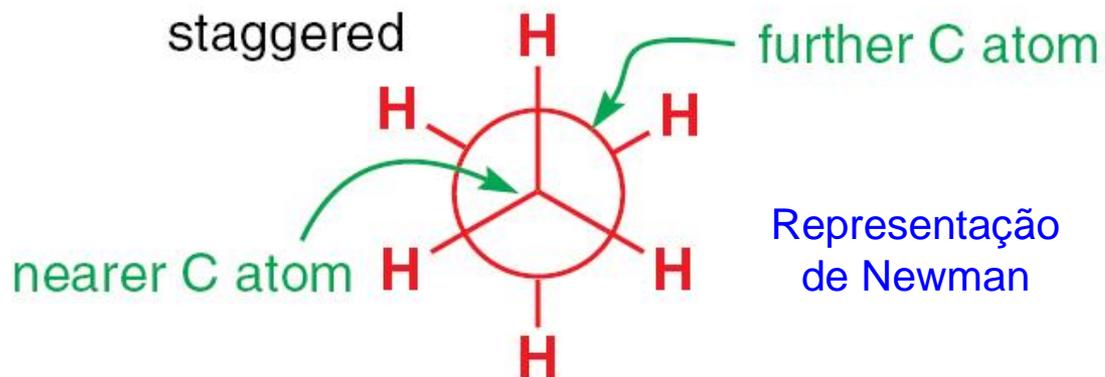


side view

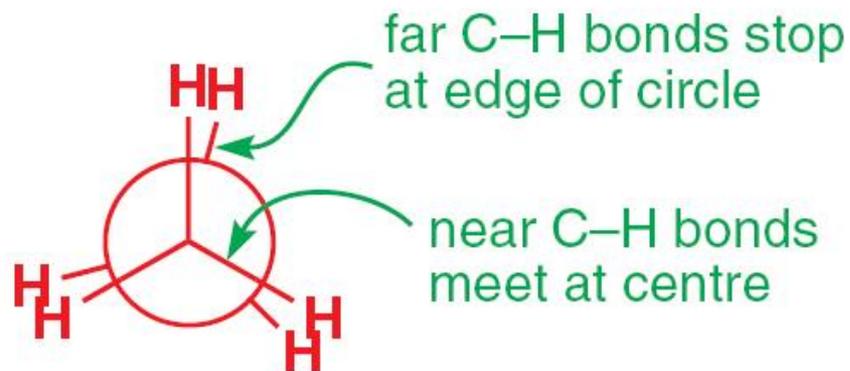
end-on view



Newman projections of the staggered and eclipsed conformations of ethane

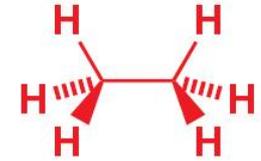
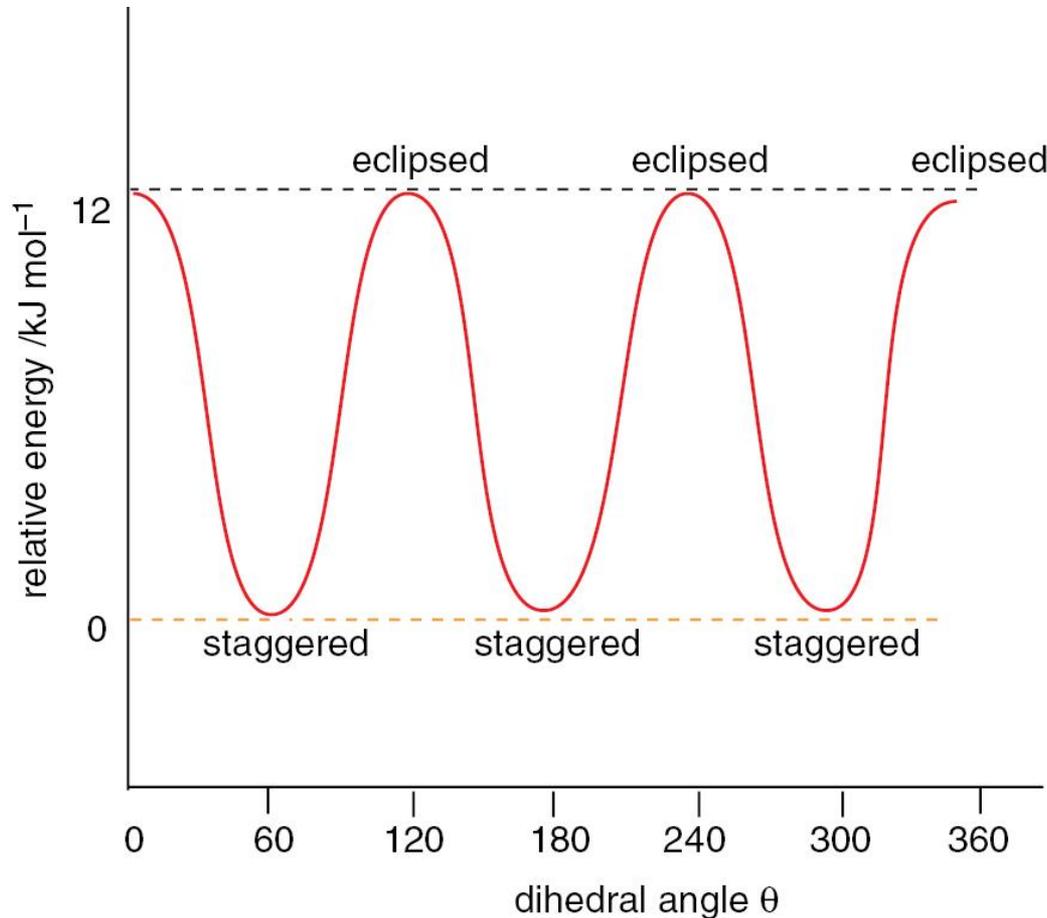


eclipsed

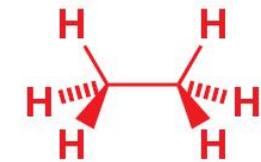
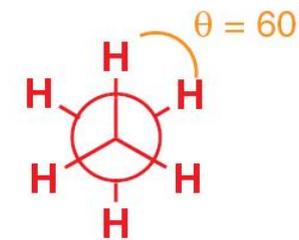


Qual confômero é mais estável?

Barreiras rotacionais para o etano

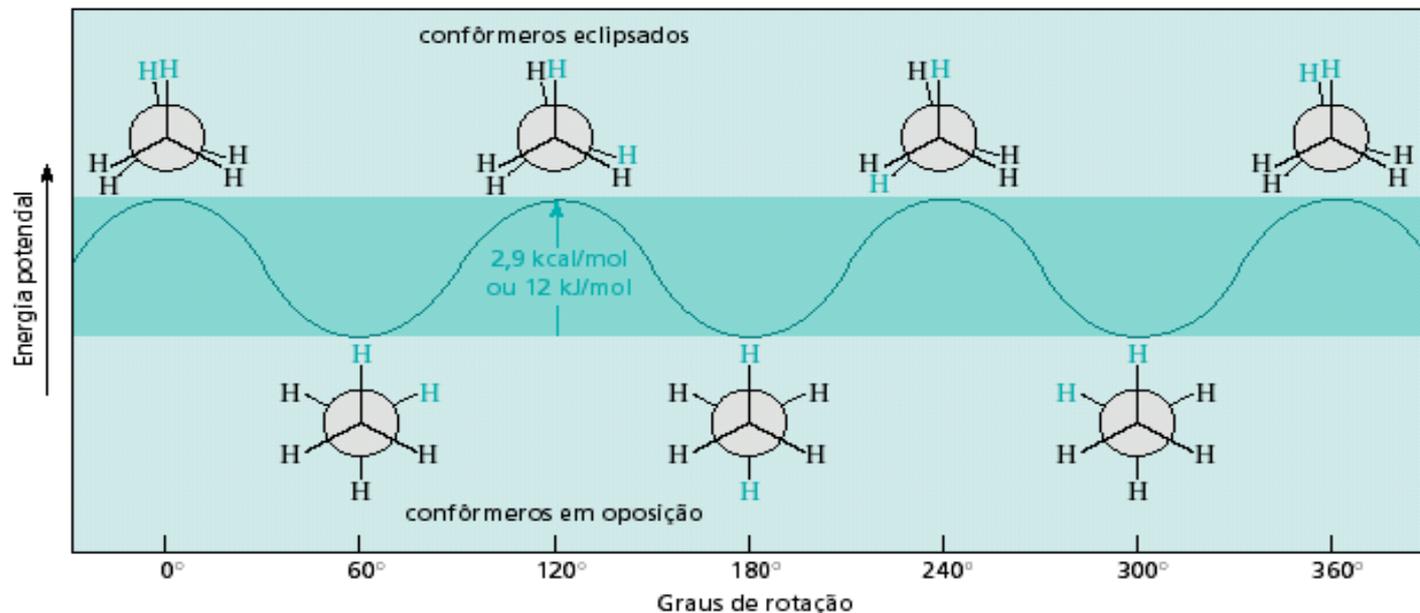


in the eclipsed conformation,
 $\theta = 0, 120, \text{ or } 240^\circ$



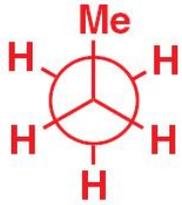
in the staggered conformation,
 $\theta = 60, 180, \text{ or } 300^\circ$

Diferentes Conformações do Etano

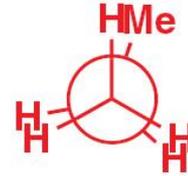
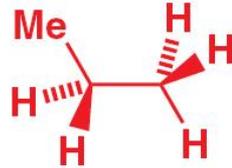


- Um conformero em oposição é mais estável que um conformero eclipsado.
- Tensão torsional: repulsão entre pares de elétrons ligantes.

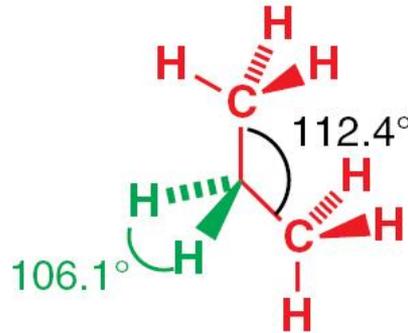
Confôrmeros para o propano



the staggered conformation of propane



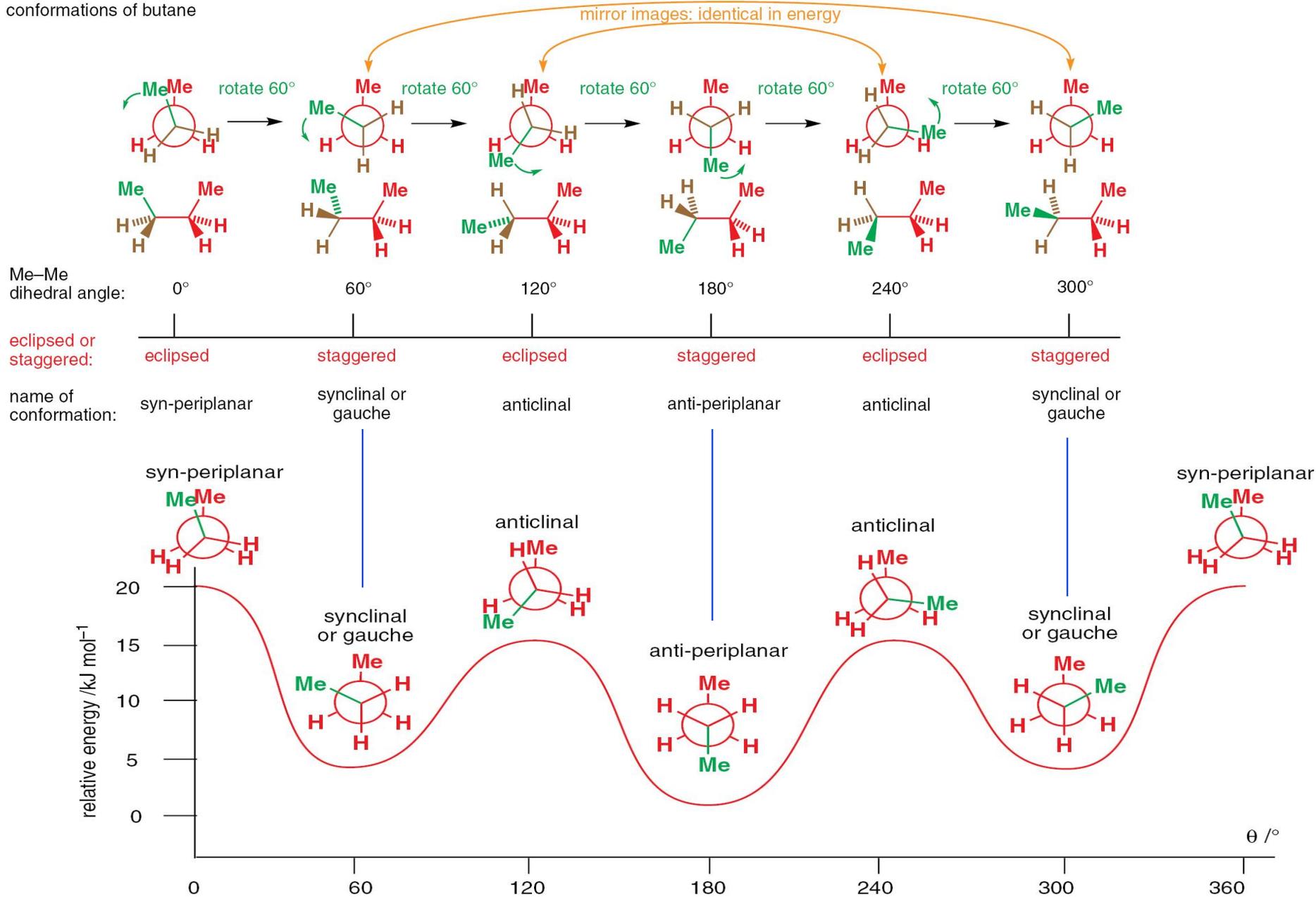
the eclipsed conformation of propane



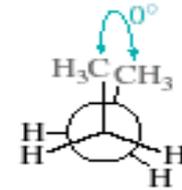
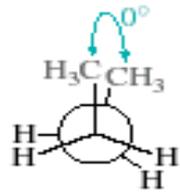
there is greater repulsion
between two C-C bonds
than between
two C-H bonds

Conformations of *n*-butane

conformations of butane

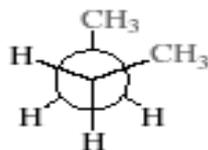
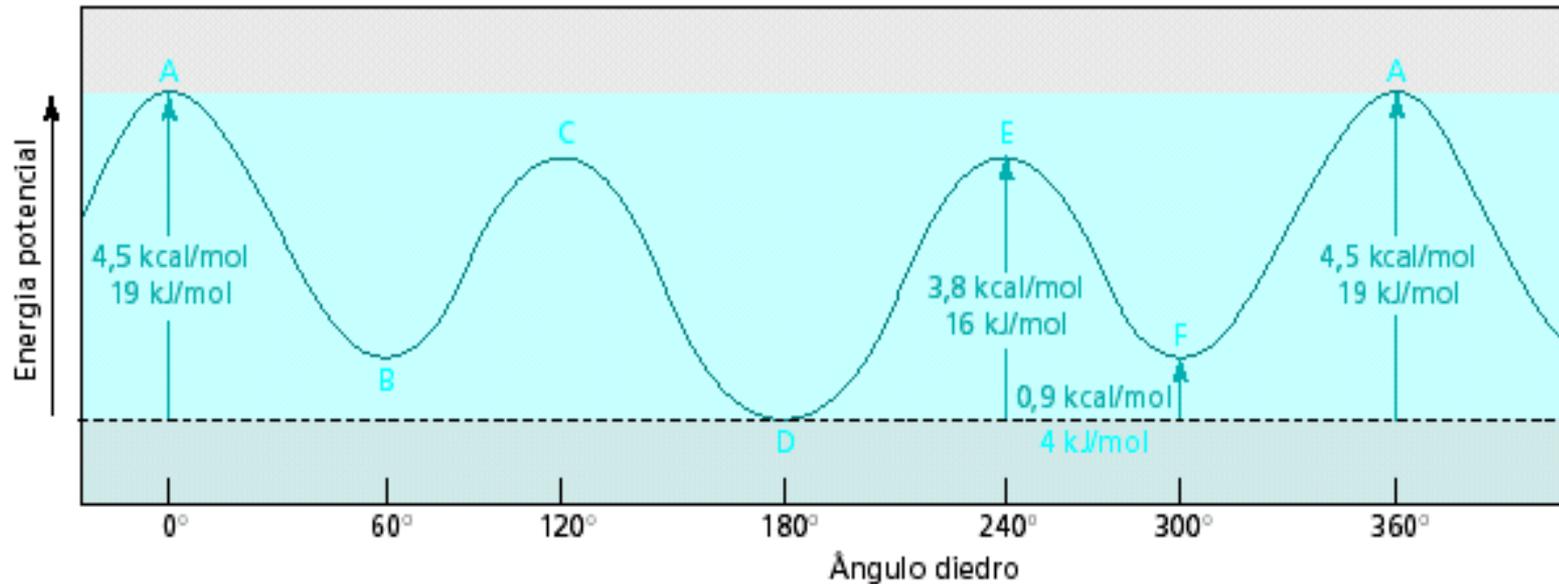


Conformações do *n*-Butano



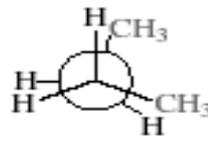
A

A

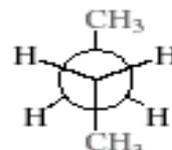


gauche

B

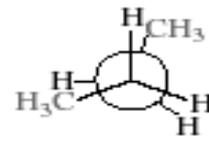


C

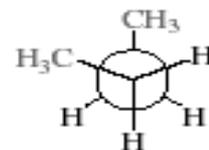


anti

D



E

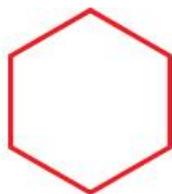


gauche

F

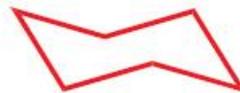
Representações do cicloexano

A



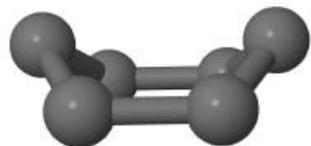
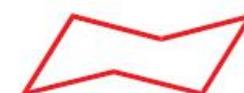
No plano

B



cadeira

C

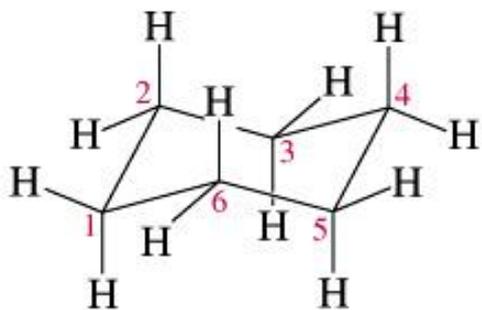


D

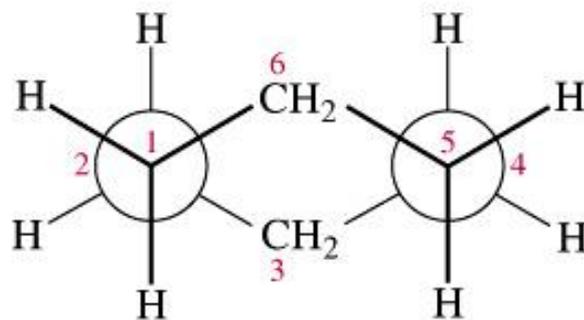
bote



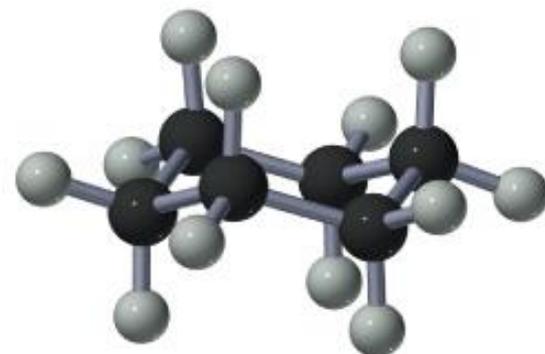
- A conformação cadeira do ciclo-hexano



chair conformer of cyclohexane

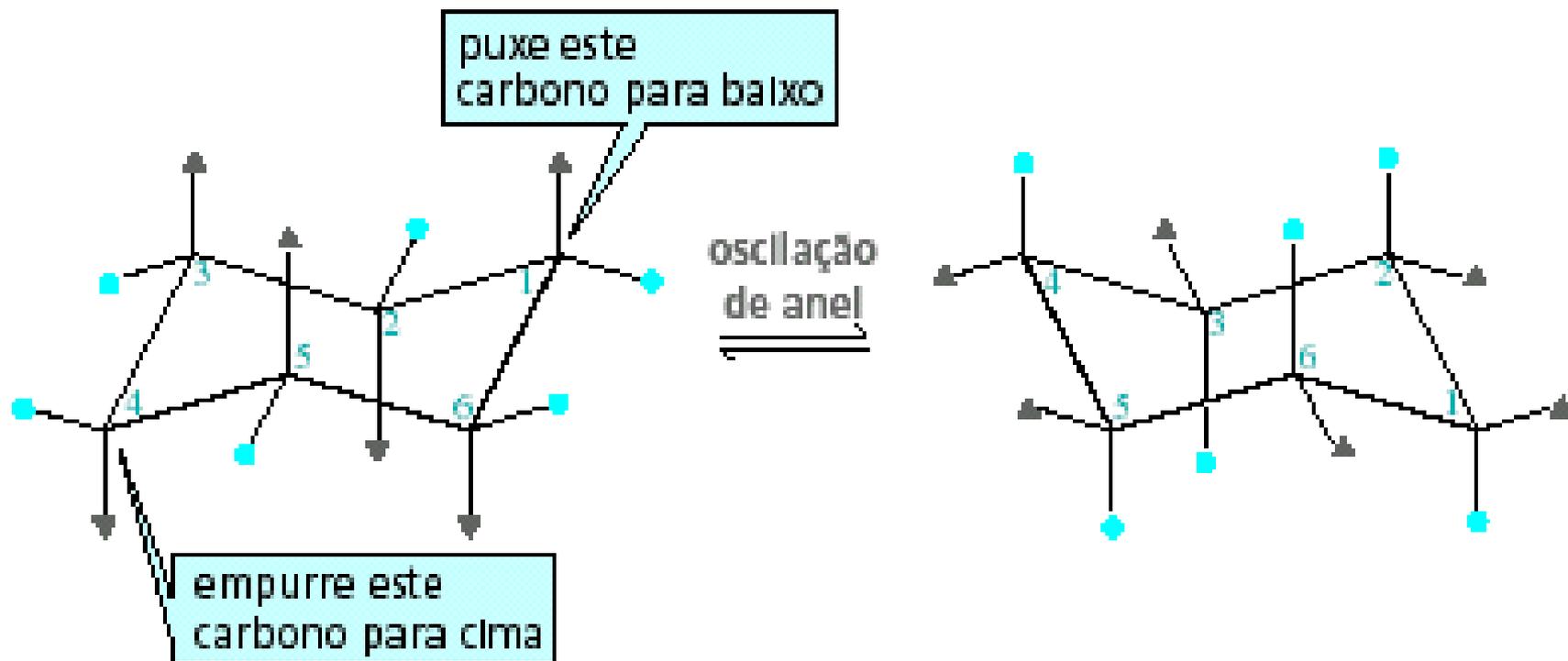


Newman projection of the chair conformer

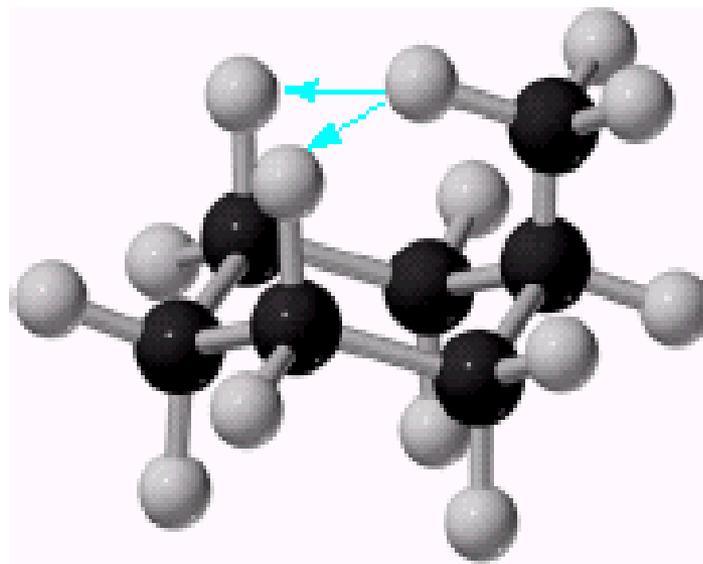
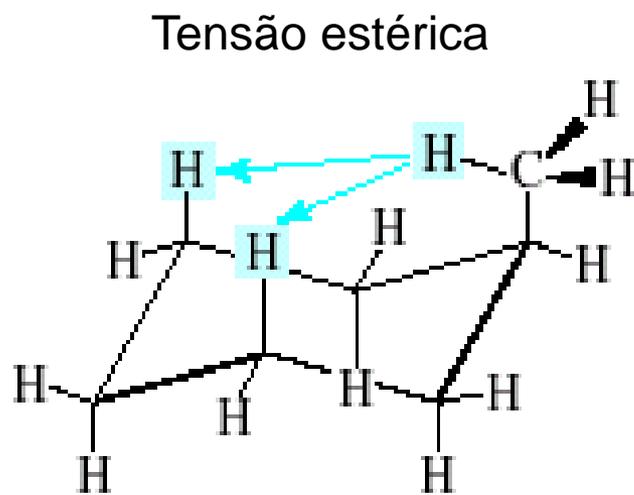


ball-and-stick model of the chair conformer of cyclohexane

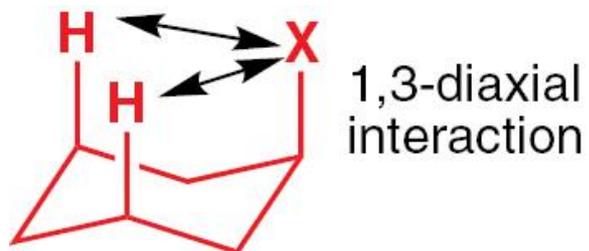
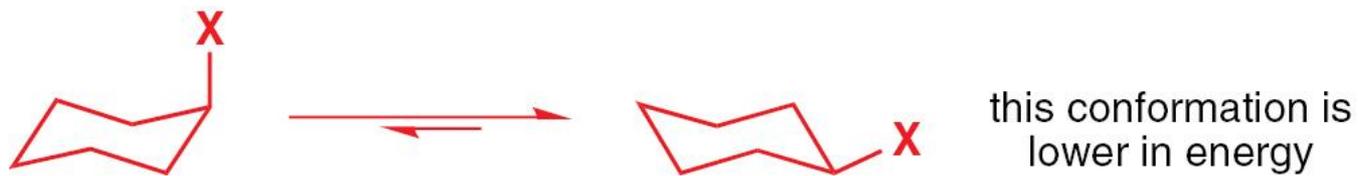
Interconversão de anel no ciclo-hexano

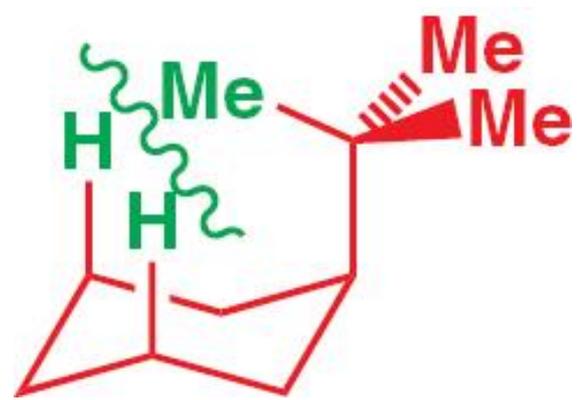
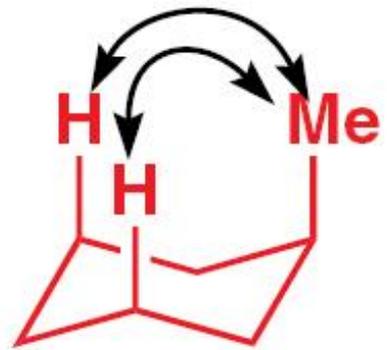


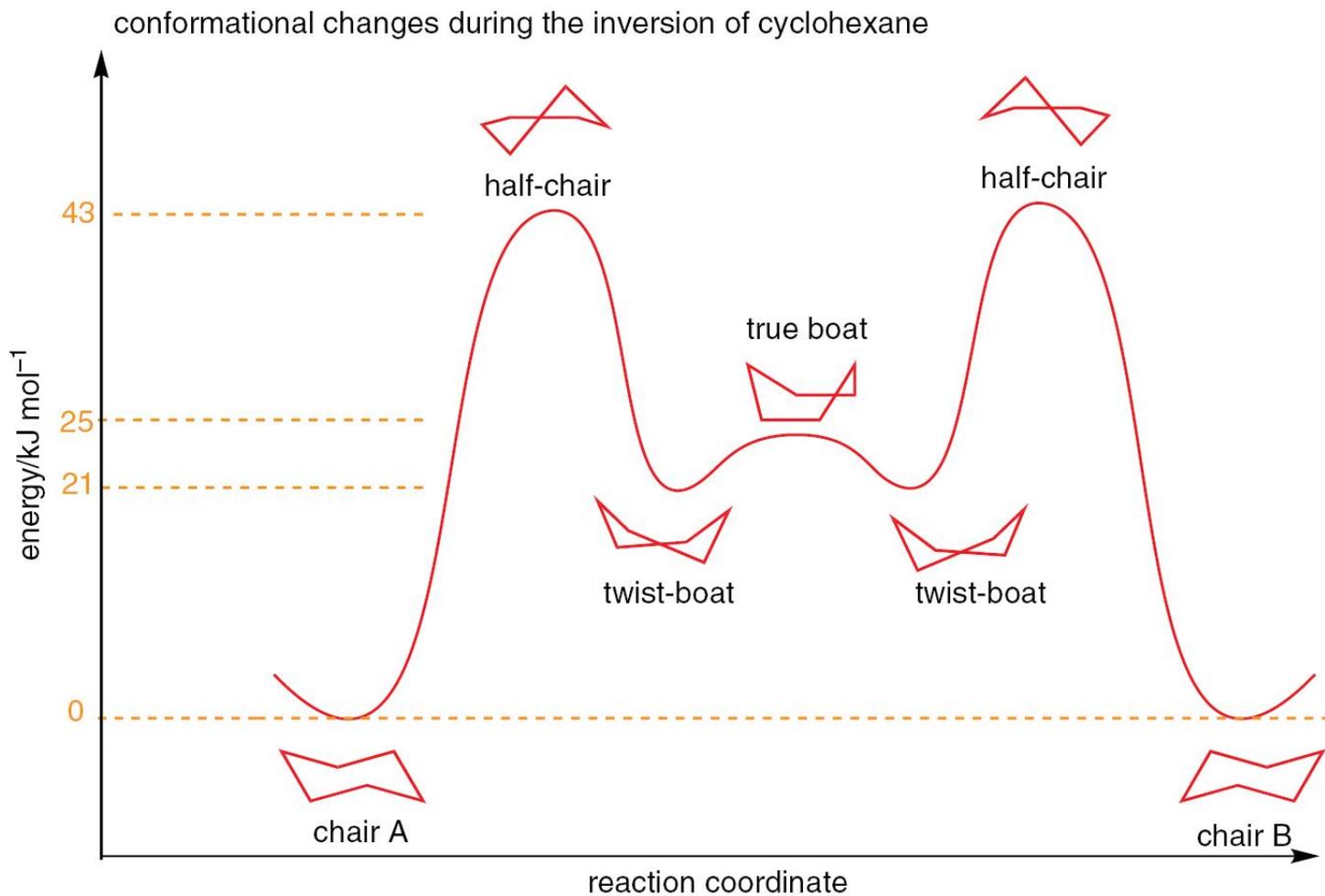
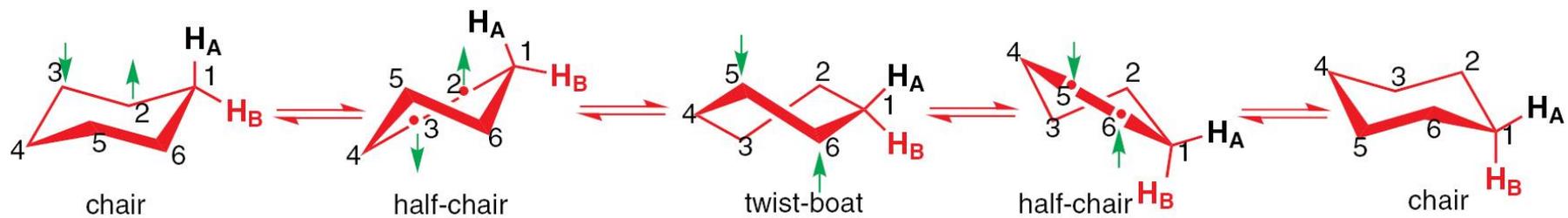
Interação 1,3-diaxial no metil-ciclo-hexano



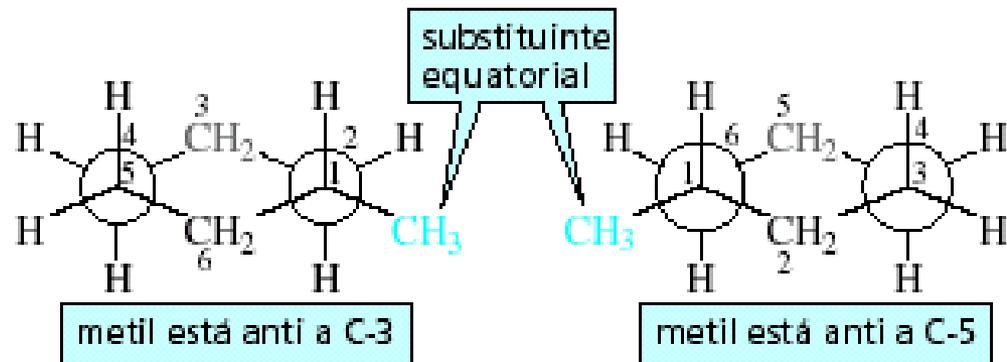
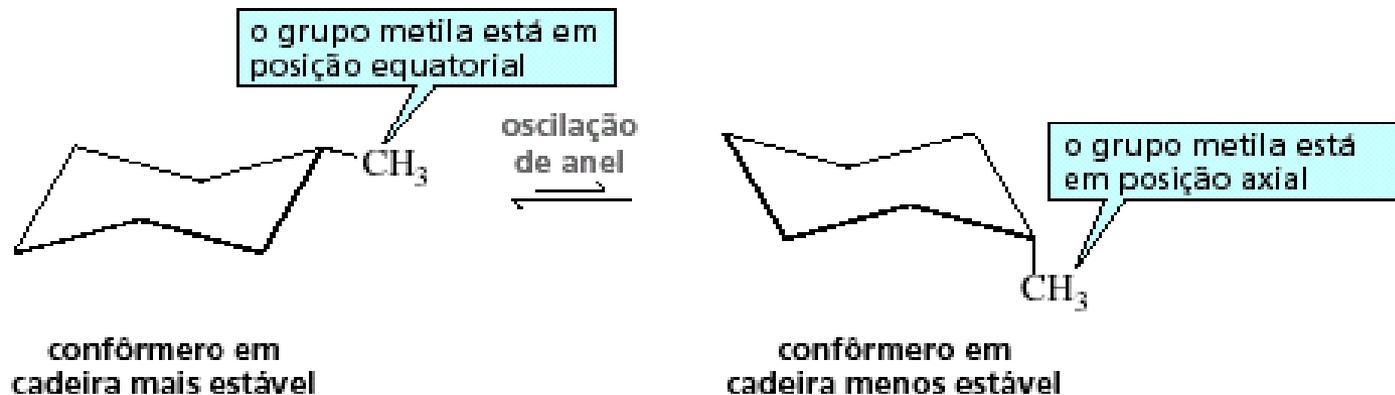
modelo bola e vareta



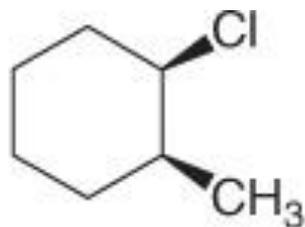




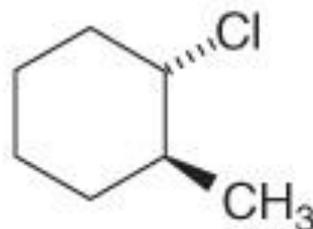
Conformações de ciclo-hexanos monossubstituídos



- E2 dehydrohalogenation of *cis*- and *trans*-1-chloro-2-methylcyclohexane.

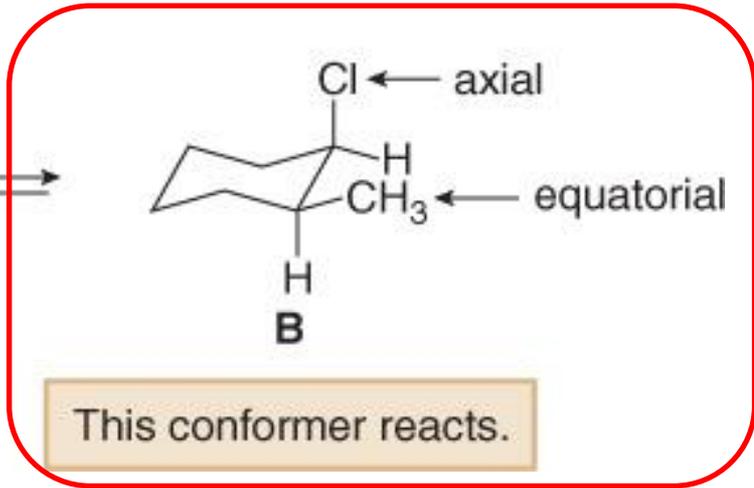
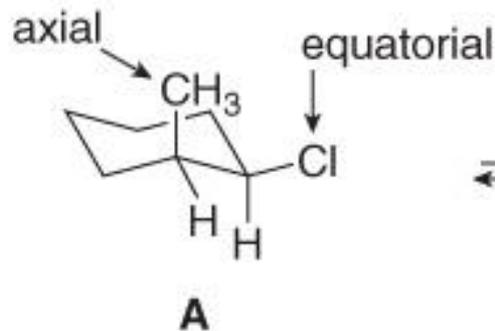


cis-1-chloro-2-methylcyclohexane

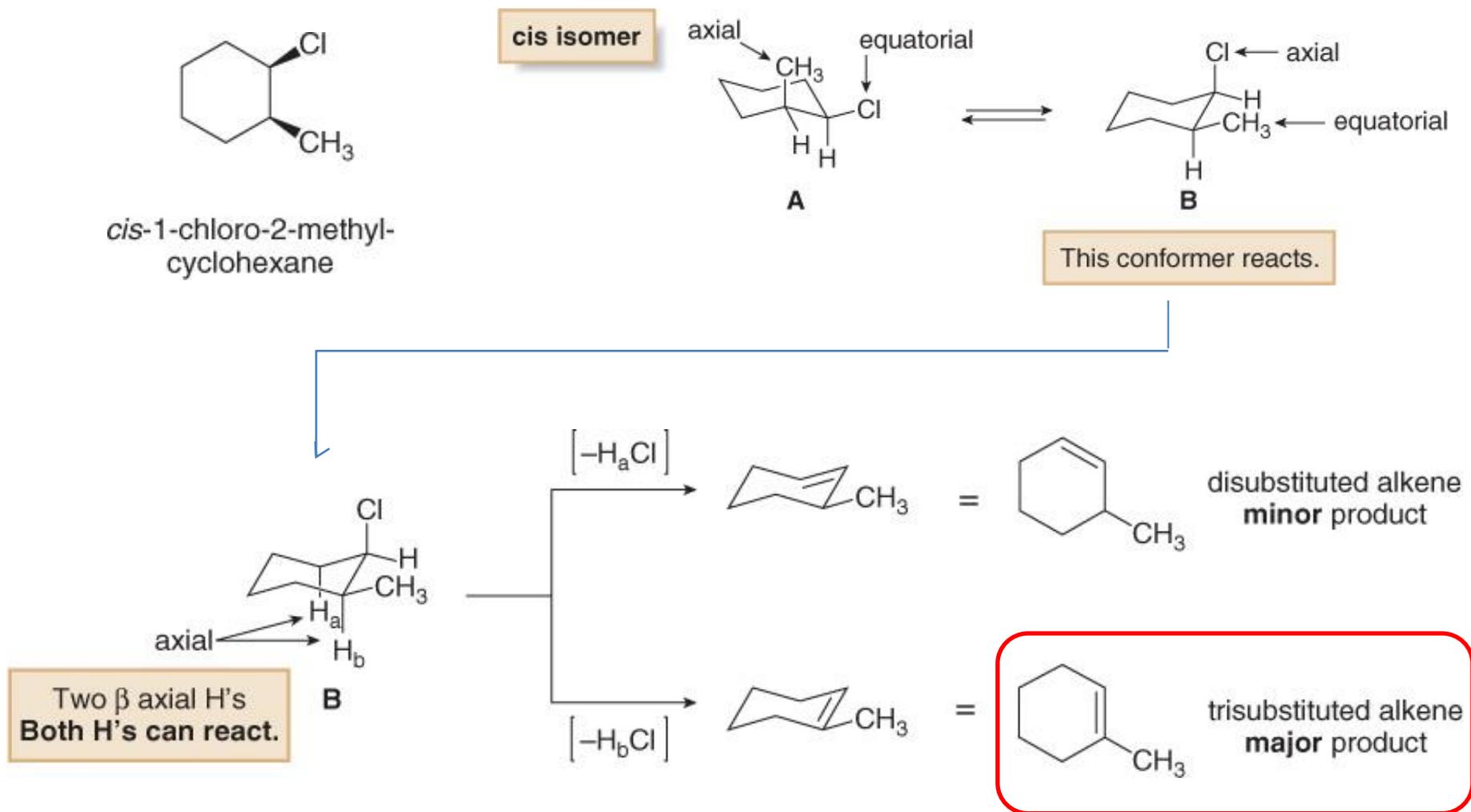


trans-1-chloro-2-methylcyclohexane

cis isomer



- E2 dehydrohalogenation of *cis*-1-chloro-2-methylcyclohexane.



- The major product contains the more stable trisubstituted double bond, as predicted by the Zaitsev rule.

Efeito do tamanho do substituinte sobre as constantes de equilíbrio para ciclo-hexanos substituídos

Tabela 2.10 Constantes de equilíbrio para vários ciclo-hexanos monossustituídos a 25 °C

| Substituinte | Axial $\xrightleftharpoons{K_{eq}}$ Equatorial | Substituinte | Axial $\xrightleftharpoons{K_{eq}}$ Equatorial |
|--|--|--------------|--|
| H | 1 | CN | 1,4 |
| CH ₃ | 18 | F | 1,5 |
| CH ₃ CH ₂ | 21 | Cl | 2,4 |
| $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{CH} \end{array}$ | 35 | Br | 2,2 |
| $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{C} \\ \\ \text{CH}_3 \end{array}$ | 4.800 | I | 2,2 |
| | | HO | 5,4 |

Efeito do tamanho do substituinte

$$K_{eq} = [\text{confômero equatorial}]/[\text{confômero axial}]$$

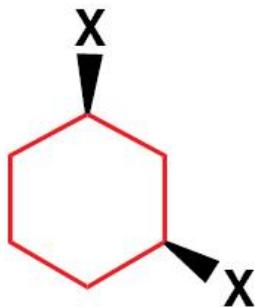
Quais são os confôrmeros mais estáveis para o

cis-1,4-dimetil-ciclo-hexano

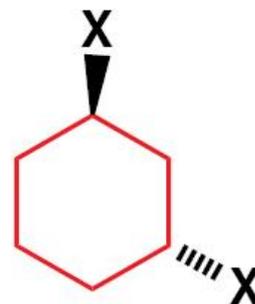
trans-1,4-dimetil-ciclo-hexano

trans-1-*terc*-butil-3-metil-ciclo-hexano

Quais devem ser os confôrmeros mais estáveis em cada um dos casos?

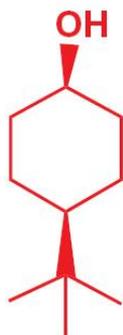


cis-1,3-disubstituted cyclohexane



trans-1,3-disubstituted cyclohexane

cis-4-*t*-butylcyclohexanol



in the *cis* diastereoisomer,
the hydroxyl group is forced
into an axial position

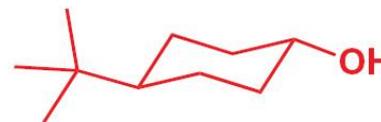


in both compounds, the *t*-butyl
group is equatorial

trans-4-*t*-butylcyclohexanol



in the *trans* diastereoisomer,
the hydroxyl group is forced
into an equatorial position

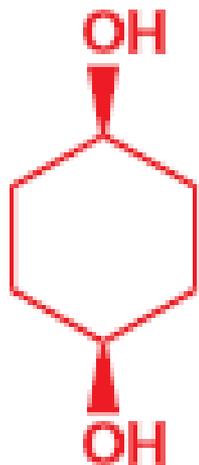


in both compounds, the *t*-butyl
group is equatorial

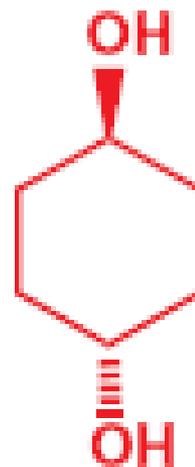
Consequencias das conformações

- Efeitos sobre propriedades físicas (pontos de fusão)
- Atividade catalítica de enzimas
- Estereoseletividade nas reações de eliminação bimolecular
- Estereoespecificidade em reações de substituição nucleofílica bimolecular

Explique essa diferença
nos pontos de fusão para os dois álcoois
isoméricos



m.p. 113–114 °C

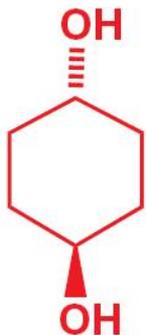
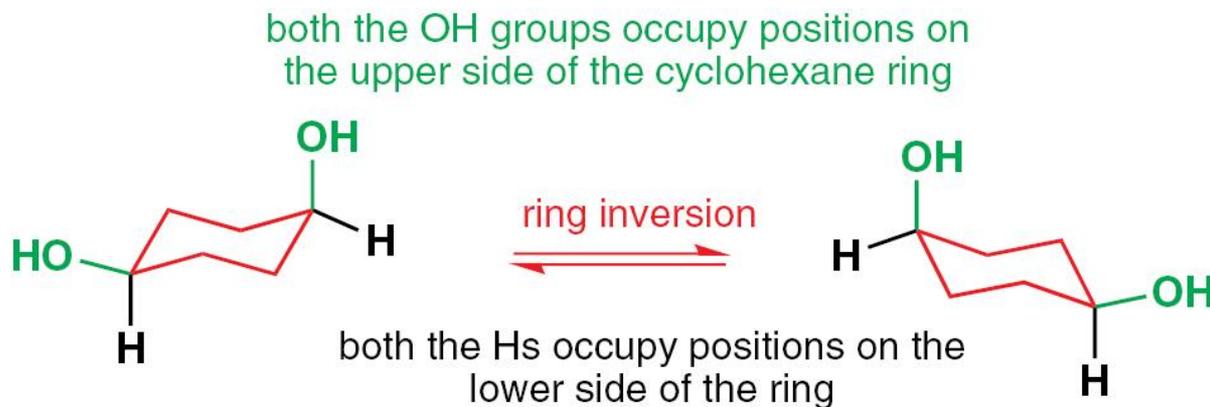


m.p. 143–144 °C



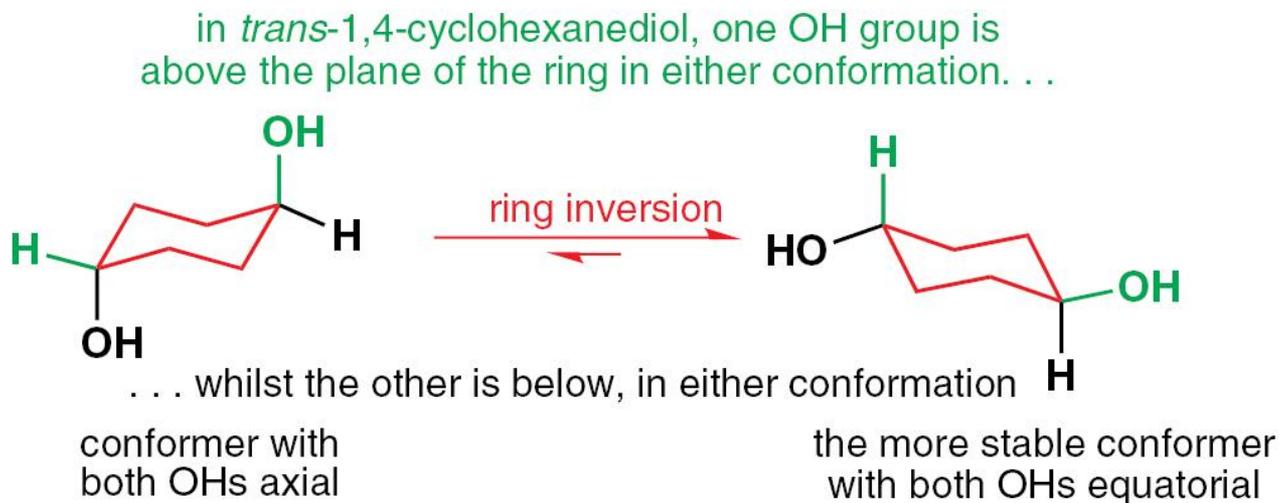
cis-1,4-cyclohexanediol

m.p. 113–114 °C



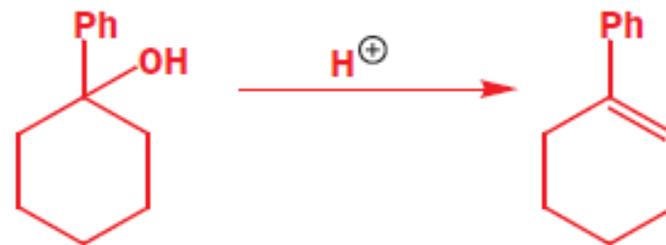
trans-1,4-cyclohexanediol

m.p. 143–144 °C

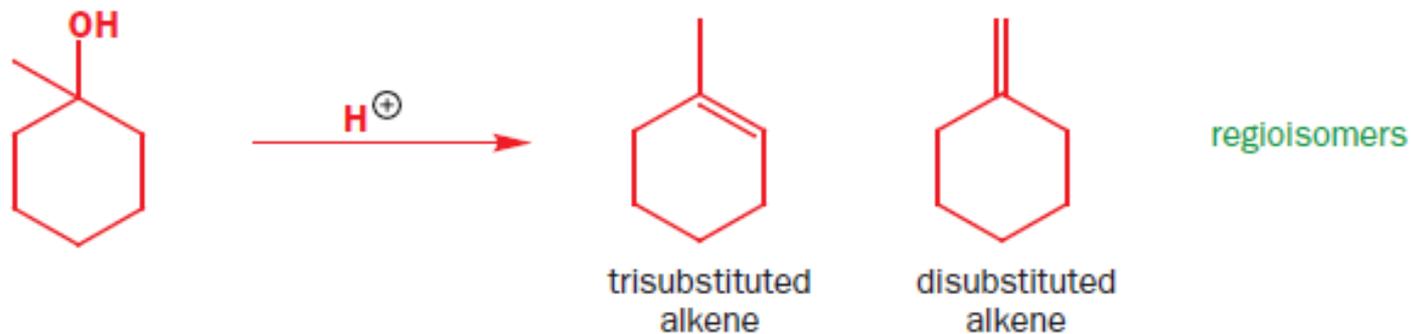


Reações de eliminação

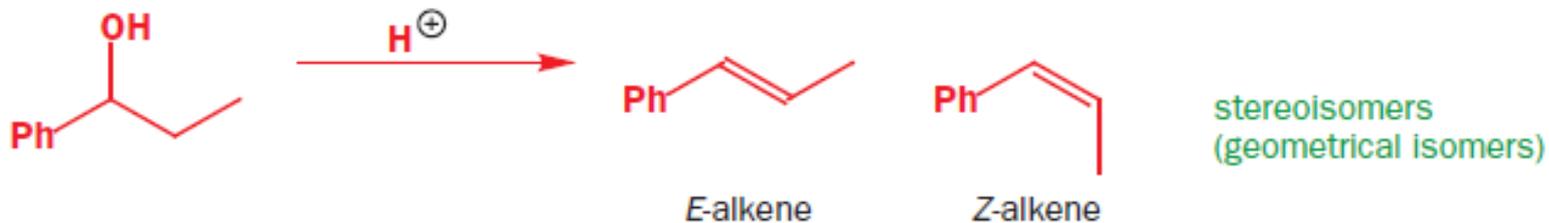
only one alkene possible



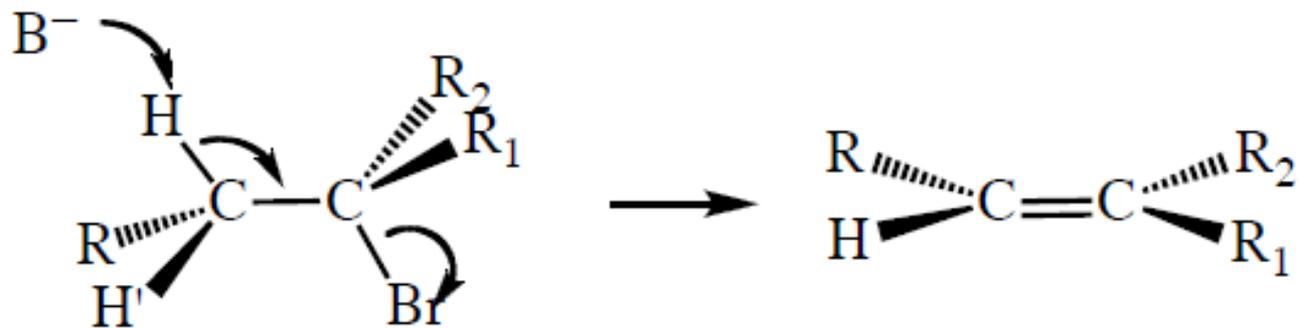
two regioisomeric alkenes possible



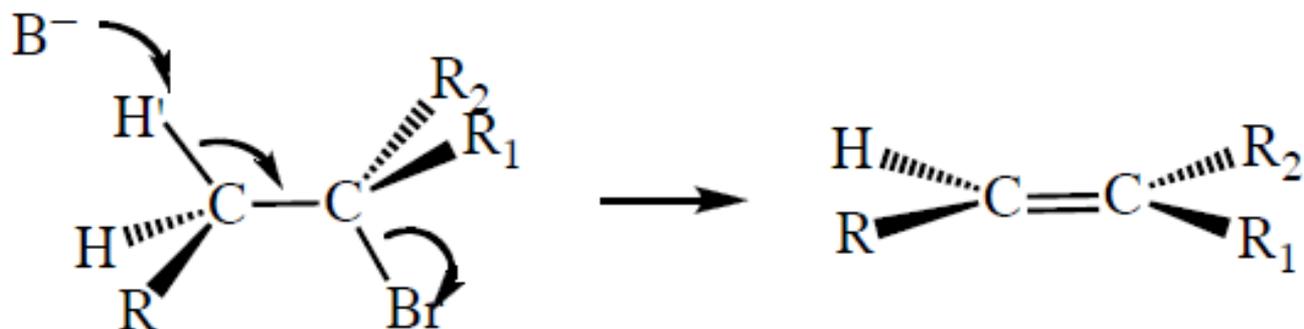
two stereoisomeric alkenes possible

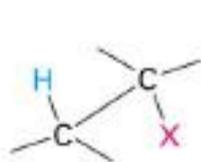


Reações de eliminação E2 (grupos envolvidos devem estar em *anti*)

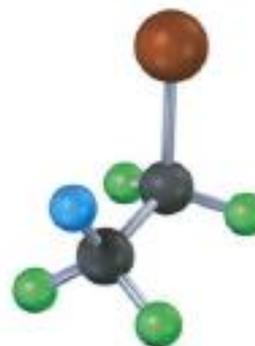
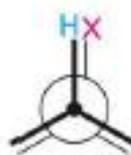
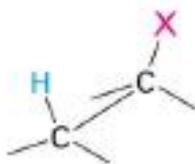


rotate around C-C by 120°





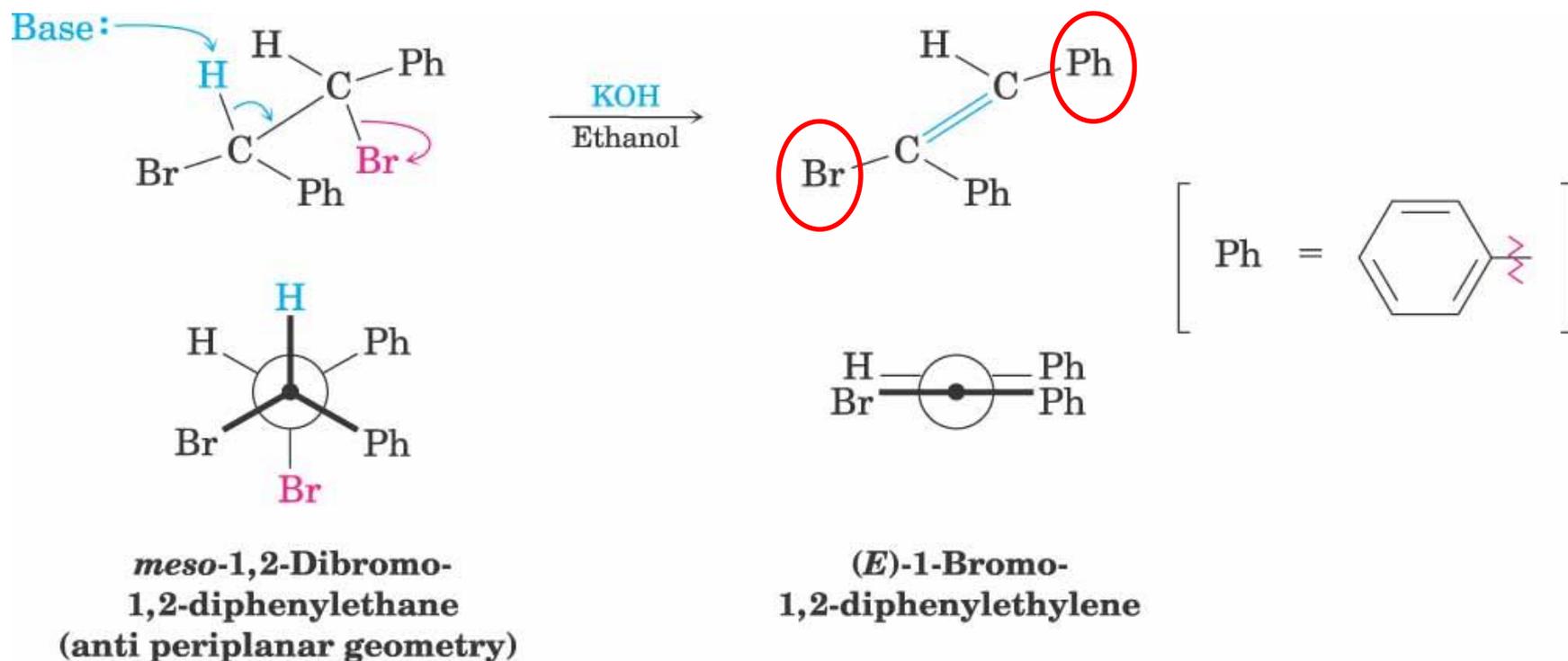
**Anti periplanar geometry
(staggered, lower energy)**



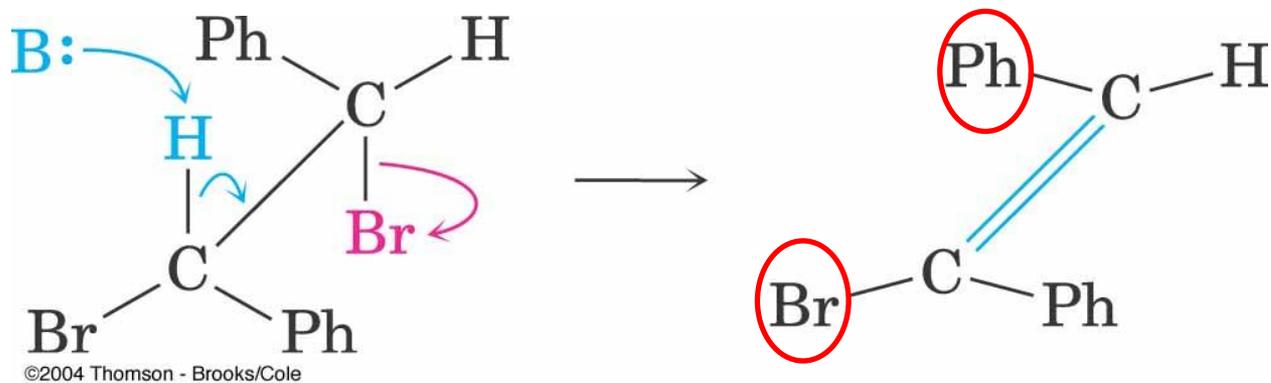
**Syn periplanar geometry
(eclipsed, higher energy)**

Consequencias das conformações

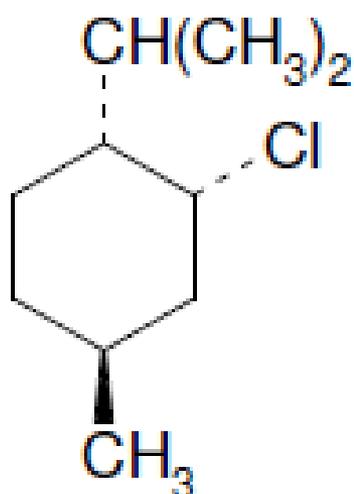
- E2 (bimolecular elimination reaction) is stereospecific
- **Meso**-1,2-dibromo-1,2-diphenylethane with base gives (*E*)-1,2-diphenylethylene



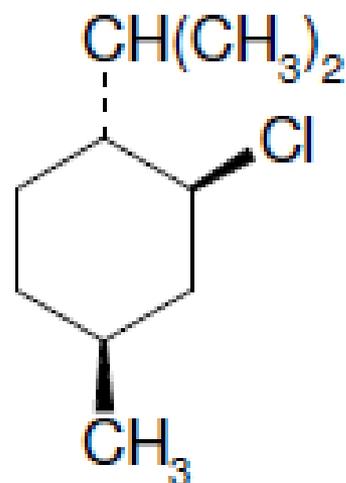
(*RR*) or (*SS*)-1,2-dibromo-1,2-diphenylethane with base gives (*Z*)-1,2-diphenylethylene



Dehydrochlorination of Neomenthyl Chloride And Menthyl Chloride

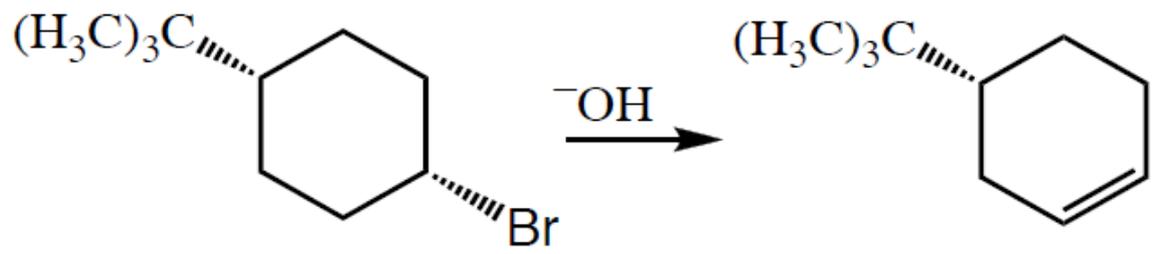
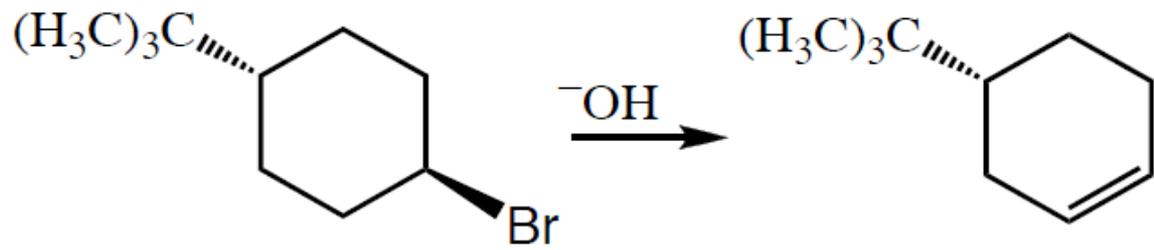


Neomenthyl Chloride



Menthyl Chloride

Elimination from neomenthyl chloride with ethoxide
200 faster than from menthyl chloride.



E2 eliminations have anti-periplanar transition states



O que explica esse resultado?

O produto formado depende da conformação



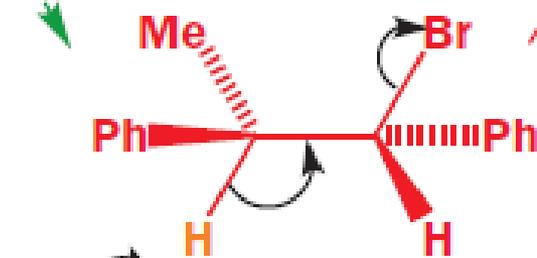
A repulsão entre as metilas
leva esse confôrmero a ser
Menos abundante

this diastereoisomer

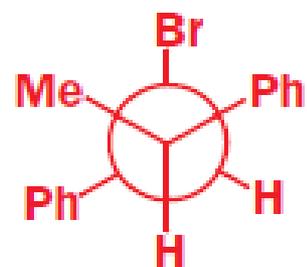
eliminates to give this alkene (*E*)



redraw



only this proton can
be attacked by HO⁻



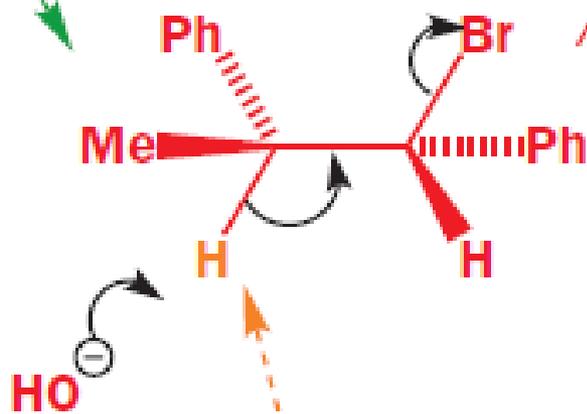
H and Br must be
anti-periplanar

this diastereoisomer

eliminates to give this alkene (Z)

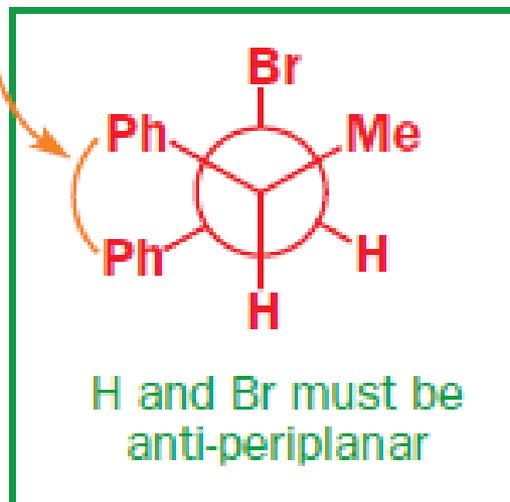


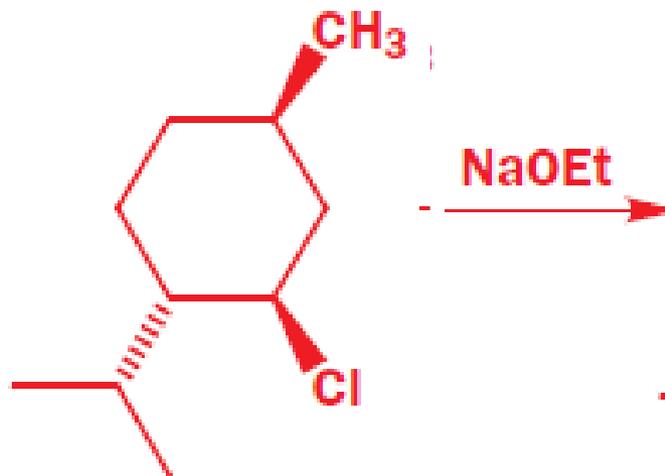
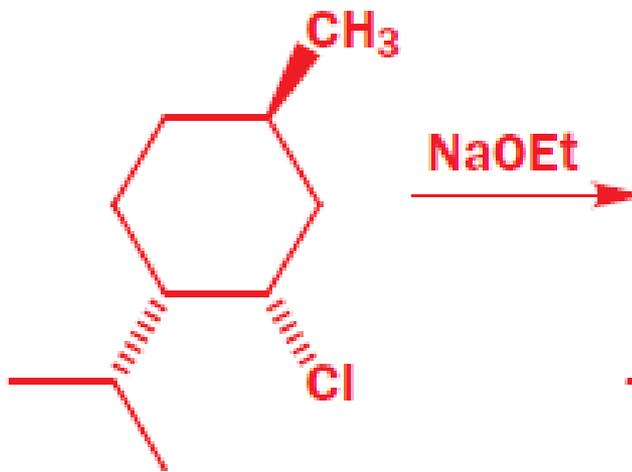
redraw



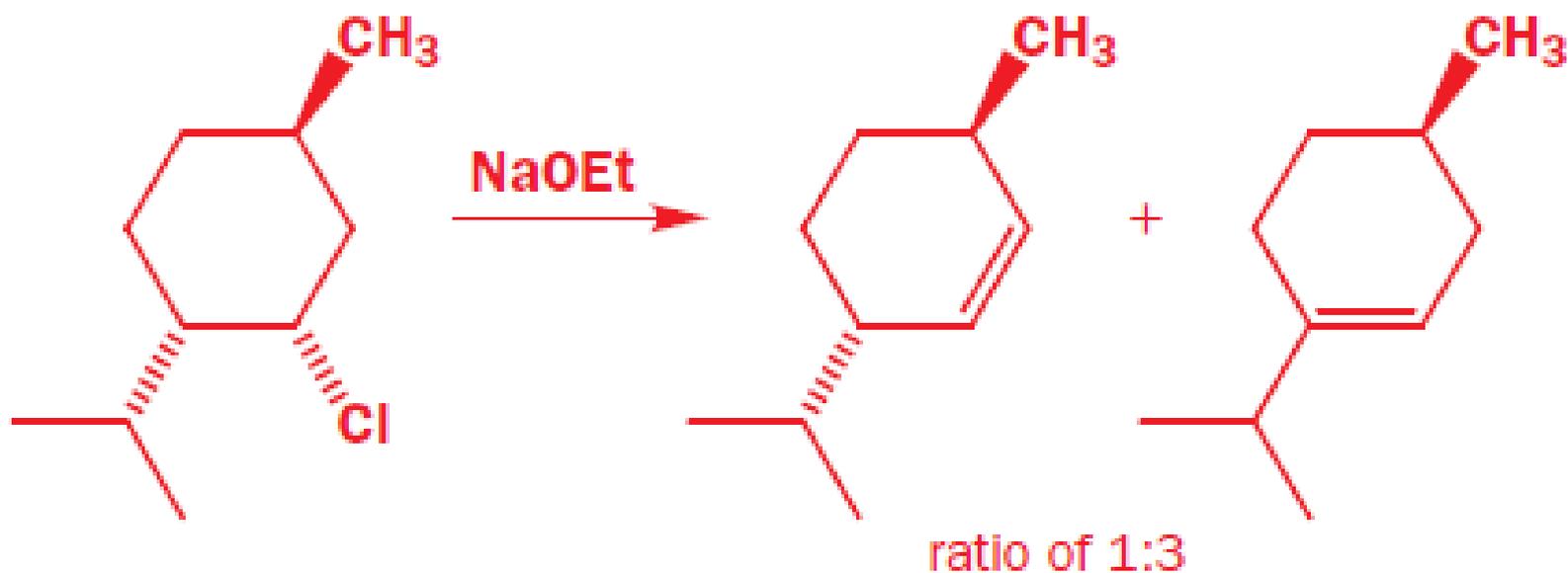
only this proton can be attacked by HO⁻

slower reaction because of gauche interactions in reactive conformation

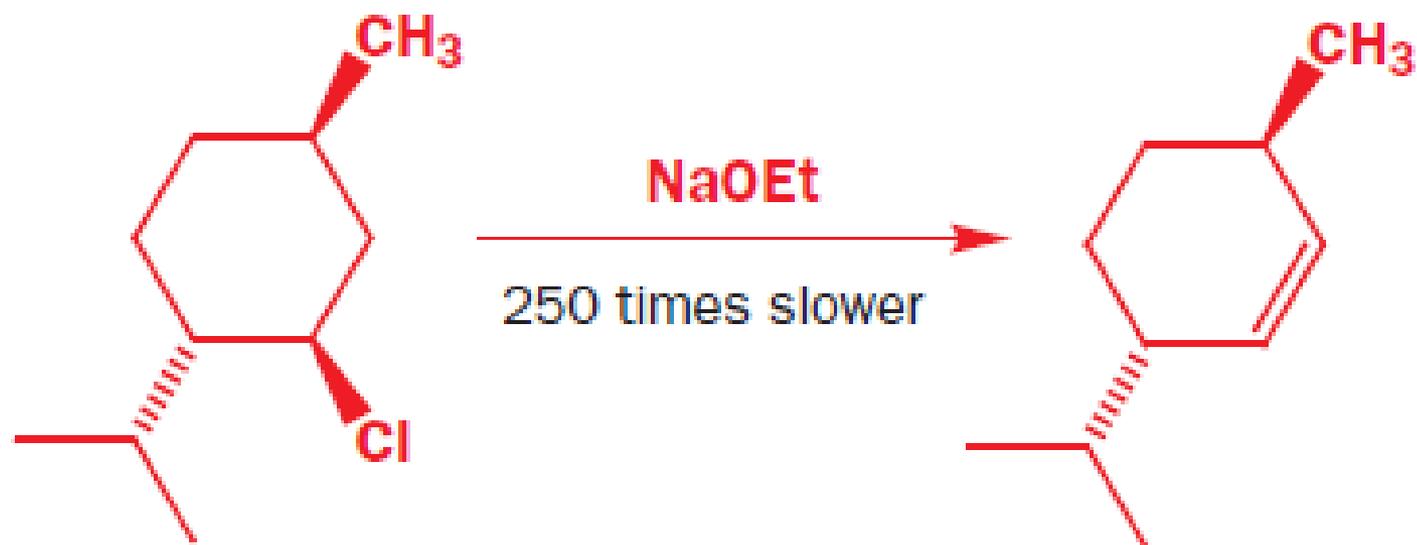




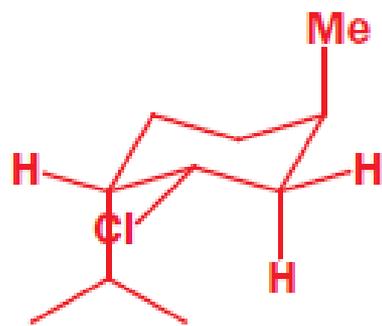
elimination of diastereoisomer A



elimination of diastereoisomer B

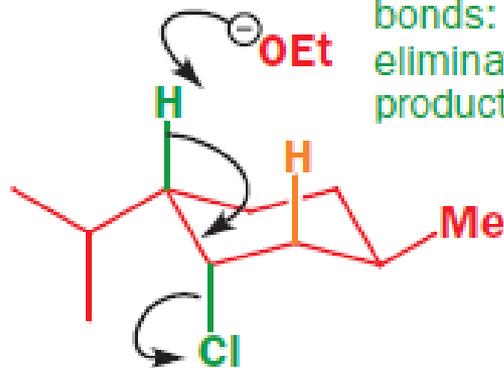


conformation of diastereoisomer A



disfavoured; axial *iPr*
can't eliminate (no
anti-periplanar C–H bonds)

ring
inversion



favoured; equatorial *iPr*

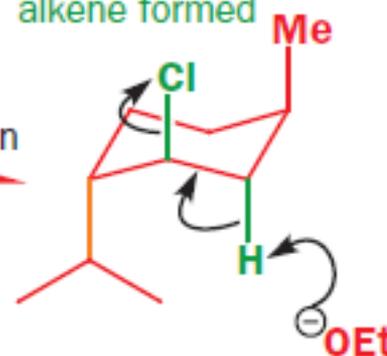
two anti-periplanar C–H
bonds: either can be
eliminated to give different
products

conformation of diastereoisomer B



favoured; equatorial *iPr*
can't eliminate (no
anti-periplanar C–H bonds)

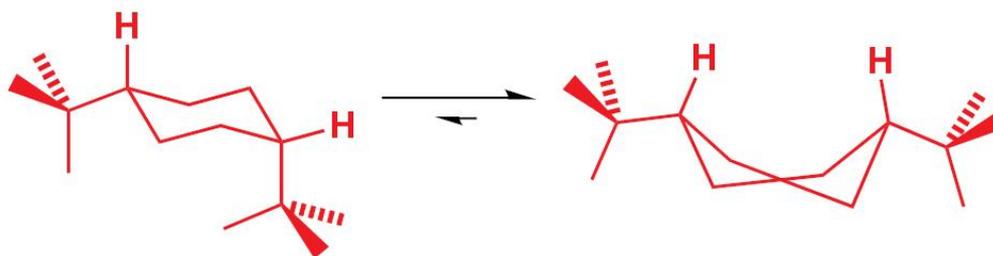
ring
inversion



disfavoured: axial *iPr*

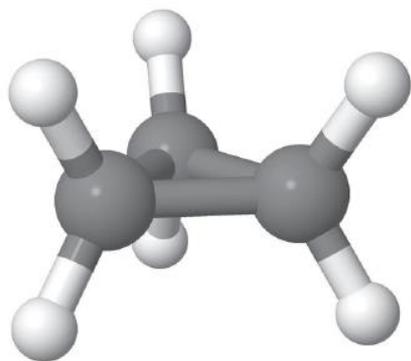
one anti-
periplanar C–H
bond: single
alkene formed

cis-1,4-
di-*t*-butyl-
cyclo-
hexane



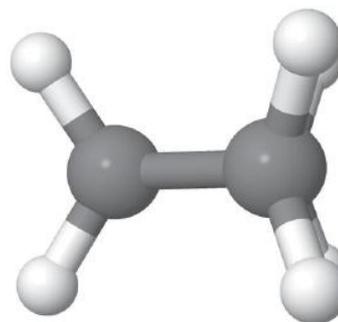
the twist-boat conformer (with both *t*-butyl groups in pseudoequatorial positions) is lower in energy than the chair conformer.

Conformações em ciclopropanos

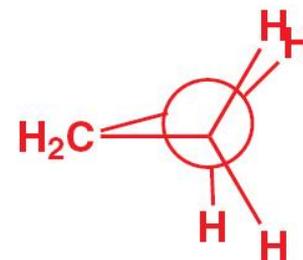


a side-on view of
cyclopropane

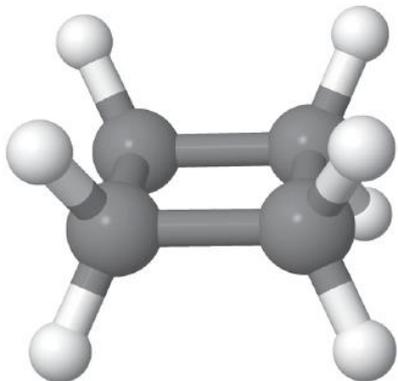
view along C–C
→



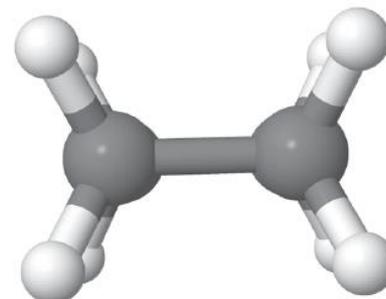
viewing cyclopropane along a C–C bond
shows that all the C–H bonds are eclipsed



Conformações em ciclobutanos

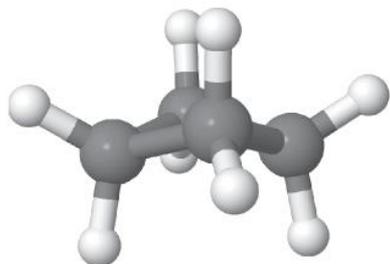


view along C-C

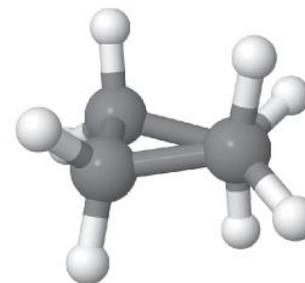


planar cyclobutane (not the real conformation)

side-on view of planar cyclobutane shows eclipsing C-H bonds



view along C-C



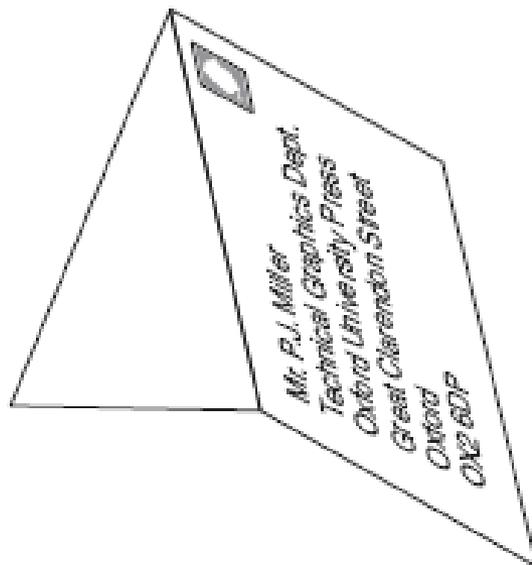
the puckered 'wing' conformation of cyclobutane

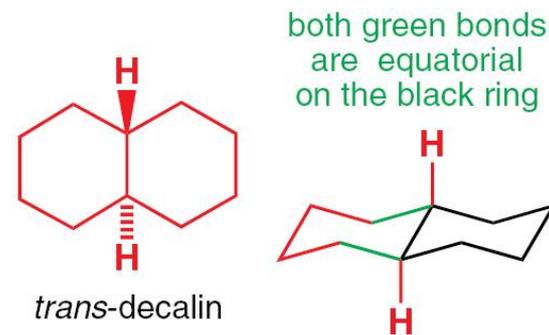
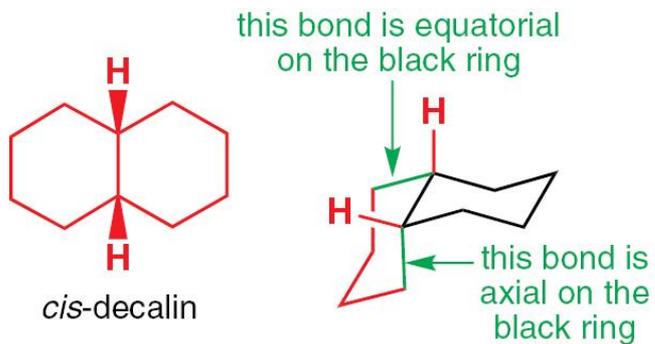
C-H bonds no longer fully eclipsed

Conformações em ciclopentanos

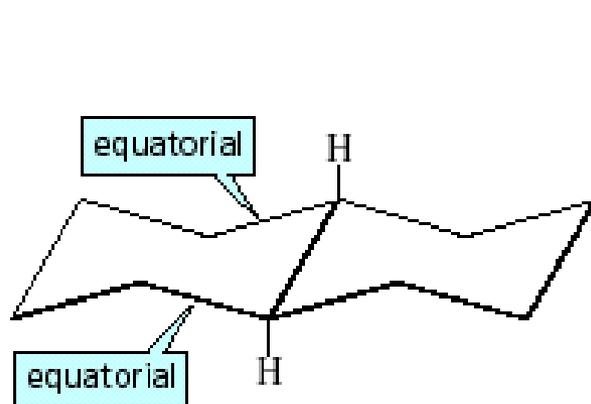


'open envelope'
conformation of
cyclopentane

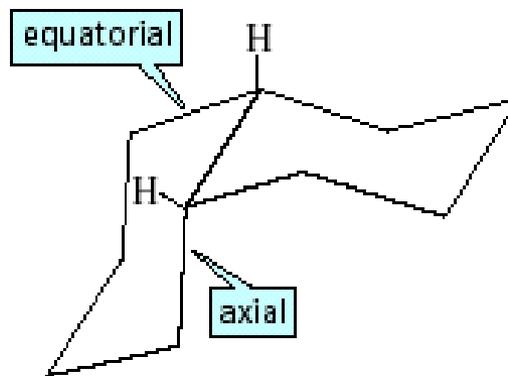




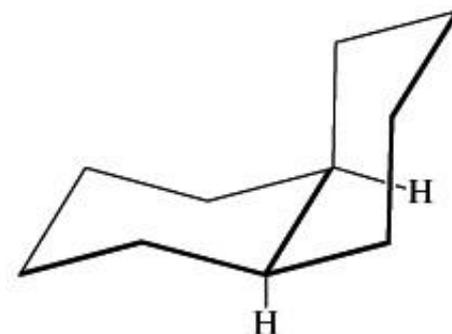
Conformações em anéis fundidos



trans-decalina
anéis fundidos em *trans*
mais estável

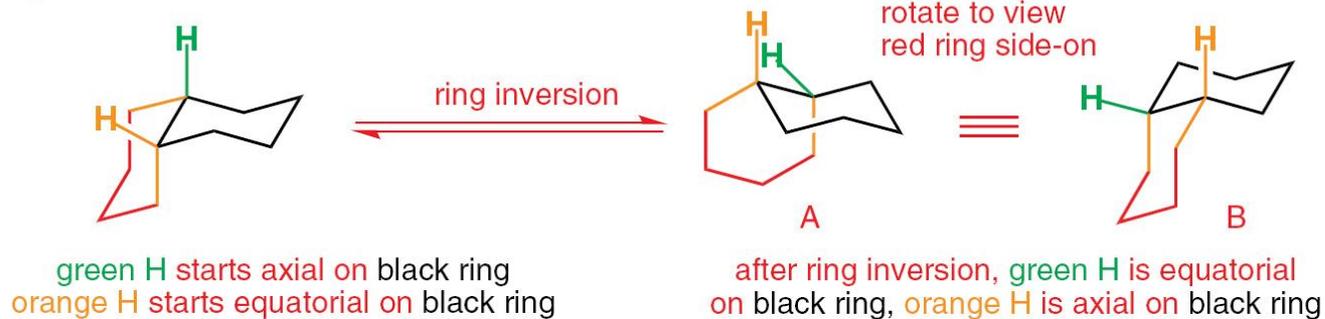


cis-decalina
anéis fundidos em *cis*
menos estável

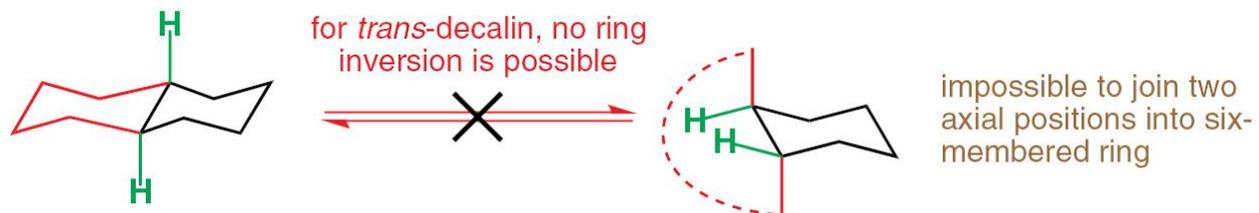


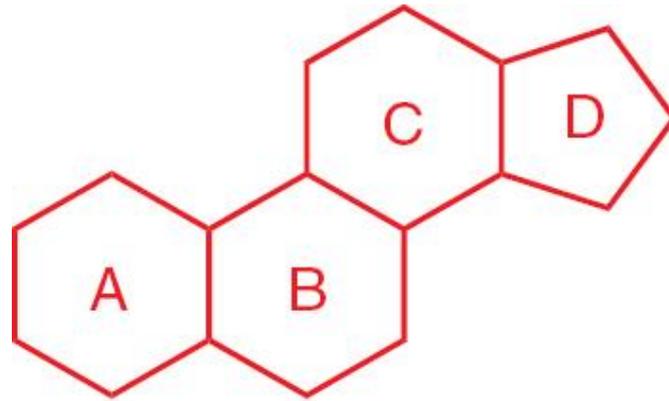
- Anéis de ciclo-hexano fundidos em *trans* são mais estáveis que anéis de ciclo-hexano fundidos em *cis*.

ring inversion of *cis*-decalin



no ring inversion in *trans*-decalin





the steroid skeleton

