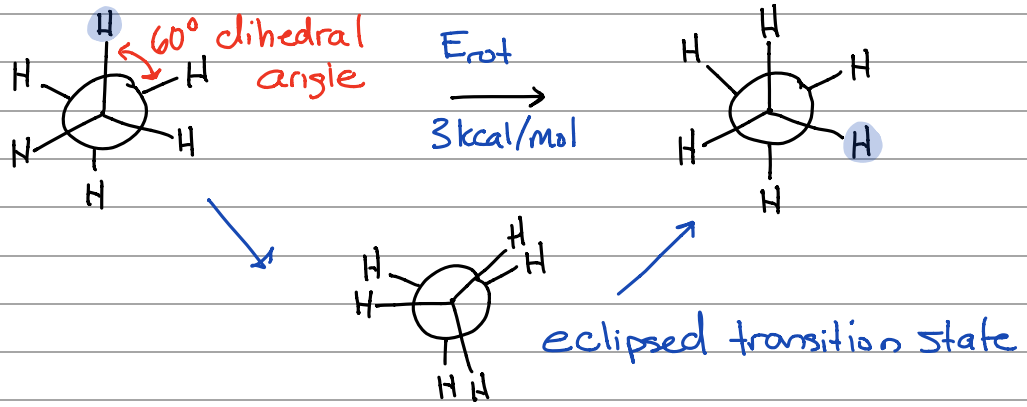
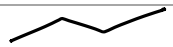
Part II - Conformational Analysis

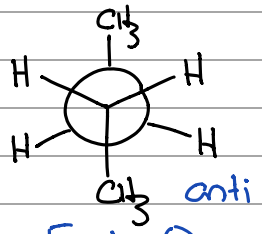
Acyclic Systems

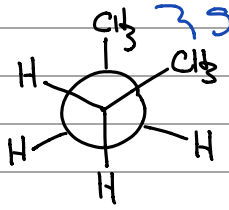


Torsional Strain - caused by eclipsing atoms separated by 3-bonds.
- as eclipsing occurs, there is a distortion of the C-C and C-H bonds (length + angles).

Butane



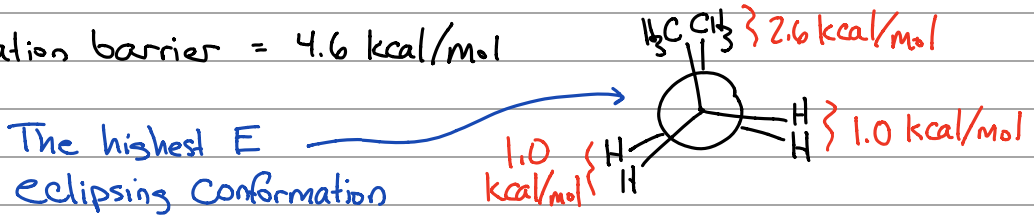




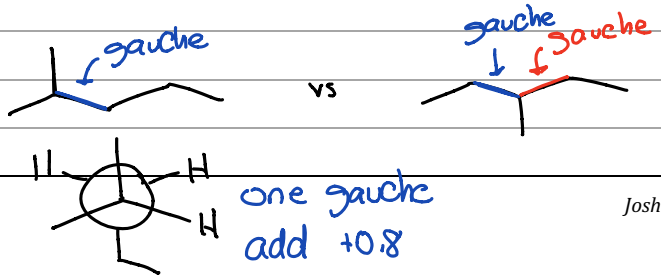
vicinal repulsion - b/t groups on adjacent carbons

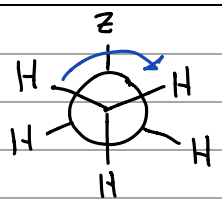
Steric Strain - buttressing of groups that destabilizes the molecule.

Butane rotation barrier = 4.6 kcal/mol



The Group Increment method accounts for Strain using "Corrections".
- Gauche +0.8 kcal/mol
- Cis alkene +1.0 kcal/mol
- ortho subs +0.6 kcal/mol





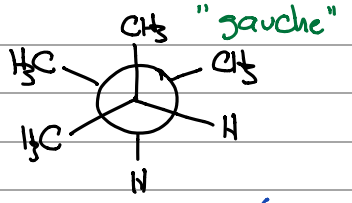
Z	E_{rot} (kcal/mol)	Z/H eclipse (kcal/mol)
H	3	1
CH_3	3.4	2.4
F	3.3	2.3
Cl	3.7	2.7
Br	3.7	2.7
I	3.2	2.2

inc Size ↓

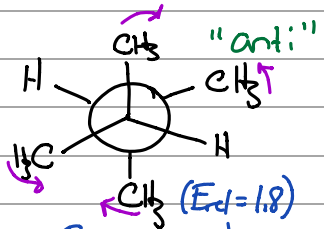
↳ But also ↑ C-X bond length which helps to offset the torsional Strain.

2,3-Dimethylbutane

Compare:



vs

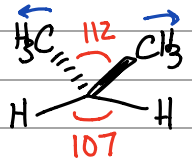


3 x gauche (E_{rel} = 2.7) 2 x gauche

Expected:	30%	⇌	70%	(See Calcs below)
Actual:	66%	⇌	33%	

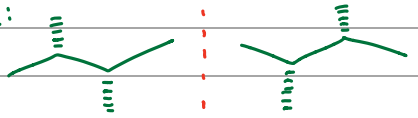
Geminal repulsions ↑E of the CH_3/CH_3 gauches making the "anti" form less stable than expected.

Geminal repulsion = steric interaction between methyls on the same C.



An Aside: The 66/33 2:1 ratio is a Statistical ratio making $\Delta H \approx 0$ between the anti + gauche 2,3-dimethylbutane forms

Gauche:

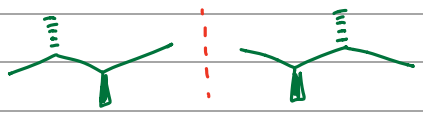


↳ enant ↲

2

vs

anti:



↳ identical ↲

1

$\Delta G = \Delta H - T\Delta S$

$= 0.9 - T(R\ln 2)$ @ 298 K $\Rightarrow$ $\Delta G = 0.9 - 298 \cdot 1.987 \cdot 10^{-3} \frac{kcal}{mol \cdot K} \cdot \ln 2$ (R)

For conformations of the same energy, the entropy increases $R\ln(n) = 0.490 \frac{kcal}{mol}$

n = # identical conformers.

$\Delta G = -RT \ln K_{eq} \Rightarrow K_{eq} = e^{-\Delta G/RT}$

$= e^{-0.490 \frac{kcal}{mol} \Big/ \left(1.987 \cdot 10^{-3} \frac{kcal}{mol \cdot K} \cdot 298\ K\right)}$

$= 0.437$

$K_{eq} = 0.437 = \frac{[B]}{[A]} \Rightarrow 0.437[A] = [B] \Rightarrow 0.437[A] = 100 - [A]$

$0.437[A] + [A] = 100$

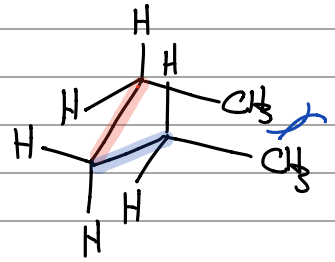
$1.437[A] = 100$

$[A] = 70$

So... $[B] = 30$

"An Aside"

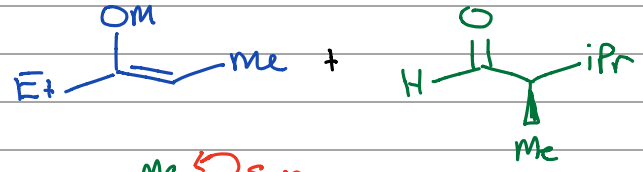
Syn-pentane

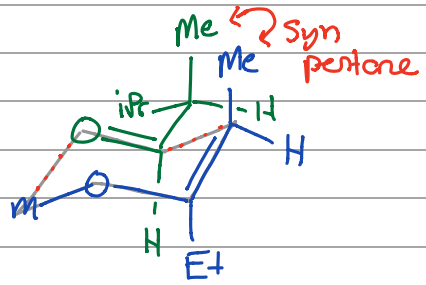


a gauche + / gauche − conformation that gives adverse H···H steric repulsions between the methyl groups

↑ E ~ 3.7 kcal/mol

Example Aldol Rxn



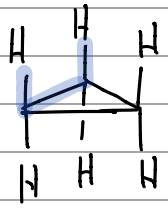


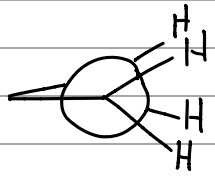
"Zimmerman - Traxler"

Cyclic Systems

Cyclopropane

Stuck in planer form





Strain Energy = 27.5 kcal/mol

ΔS = -7.7 eu

forced eclipses

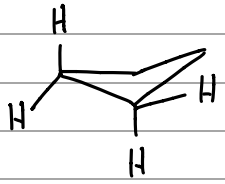
Cyclobutane

26.3 kcal/mol

-10.9 eu

additional bond "frozen"

Distorts from planarity to minimize torsional strain



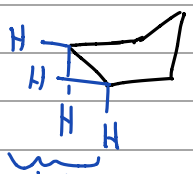
Cyclopentane

6.2 kcal/mol

-13.3 eu

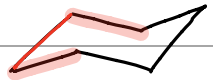
Mobile envelope conformation minimizes torsional strain

↳ always moving



Still some eclipsing

Cyclohexane

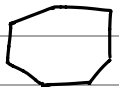


0 kcal/mol

-21.2 eu (extra jump due to chair stability)

Still has some gauche interactions

Cycloheptane

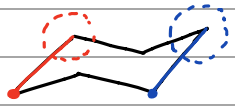


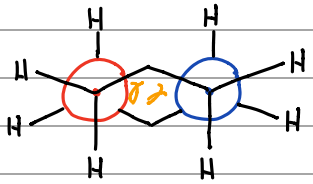
0.9 kcal/mol

-19.8 eu (more mobility)

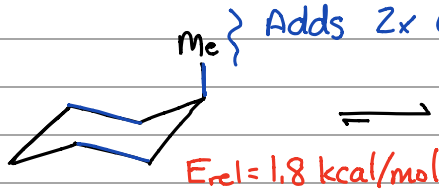
Pg 108 = group increment corrections for ring strain

Cyclohexane Conformational Analysis





unavoidable gauche



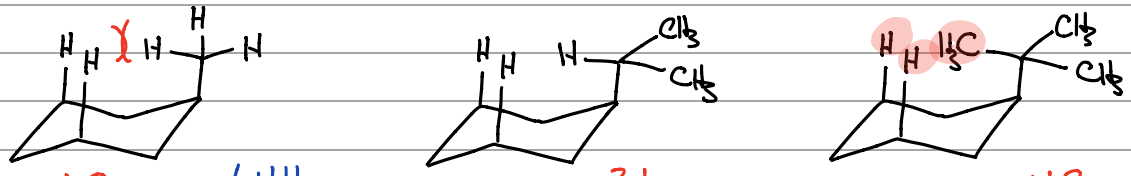
A-Value - Magnitude of the E difference of a substituent going from equatorial to axial.

A-Values

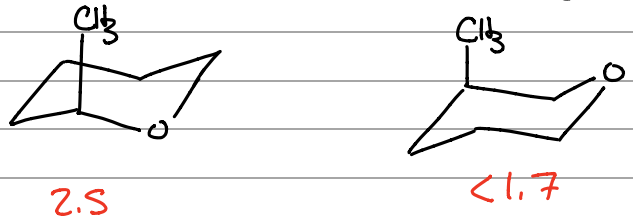
F	0.25	↑ size, but	OH	0.7	-C≡CH	0.4	increasing bulkiness
Cl	0.52	also ↑	OMe	0.75	$-CH_3$	1.8	
Br	0.56	bond length		0.71	-iPr	2.1	
I	0.46				-Ph	2.8	
					-tBu	4.8	

Transannular Origin of Strain "Axial 1,3-Repulsion"

↳ Unfavorable interactions of substituent on nonadjacent C's of ring.



Magnitude of A-Value Depends on the ring:

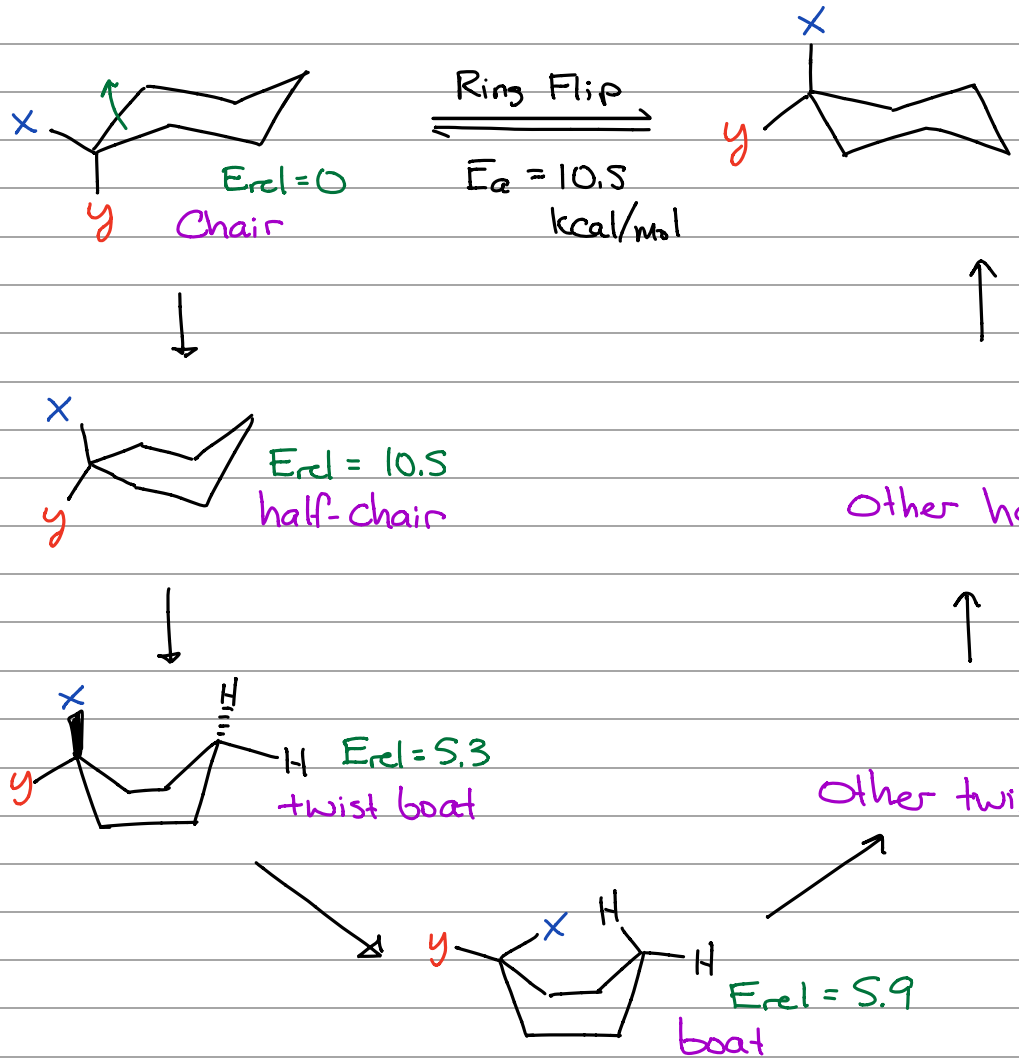


Explain Why

C-C 1.54 Å

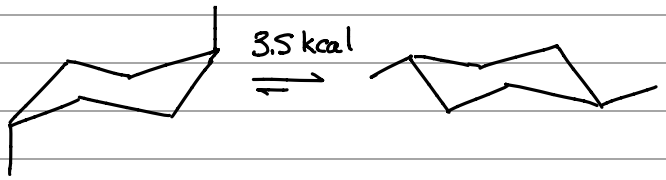
C-O 1.43 Å

Chair Interconversion

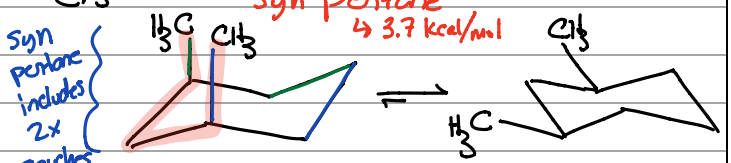


Disubstituted Cyclohexane

A-Values are nearly additive for trans substituents



This breaks down when groups are cis

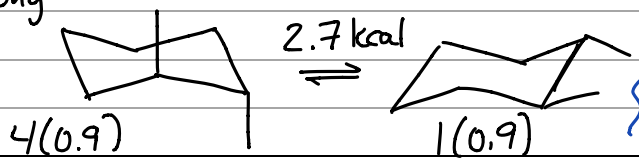


2(0.9) = 1.8

+ 3.7

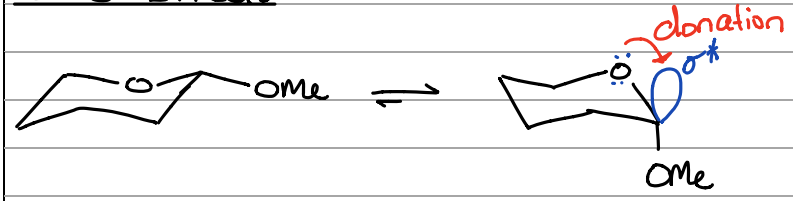
Erel = 5.5 kcal/mol

Consider Why:

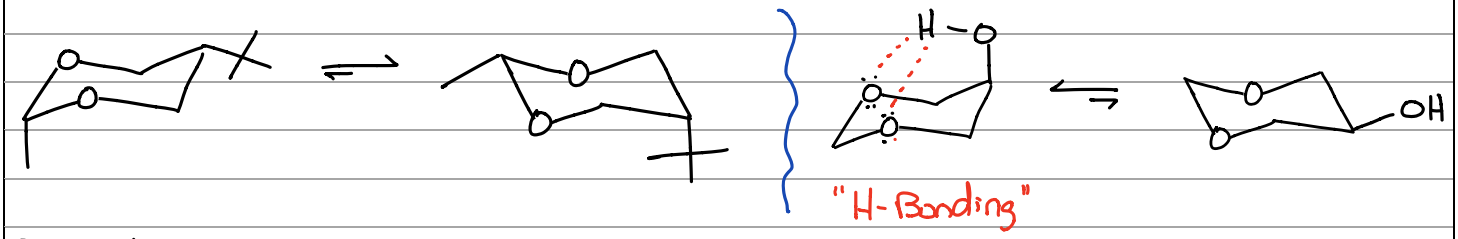


has an additional gauche

Other Effects

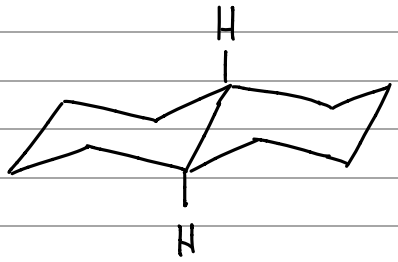


Anomeric Effect = preference for axial OR group at the anomeric carbon



Decalin

trans-decalin



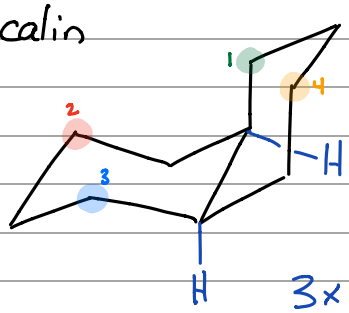
locked... can't ring flip

cis-decalin

C1 → C2

same [C1 → C3, C3 → C1]

C3 → C4



~2.7 kcal/mol higher E than trans

3x Gauche

Can undergo ring flip

π-Bonds in Rings

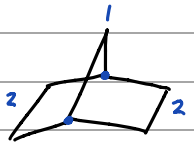
Cis is favored until ring becomes very large 7|12

trans can't be isolated for <8 membered rings.

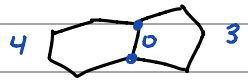
—≡— linear Cyclooctyne is the smallest that has been isolated.

Bred't Rule - Bridgehead olefins are unstable and inaccessible for smaller rings

↑ bridgehead olefin



bicyclo[2.2.1]heptane



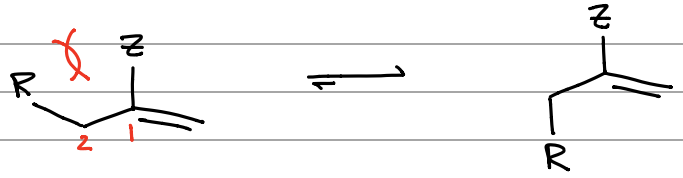
bicyclo[4.3.0]nonane

Allylic Strain

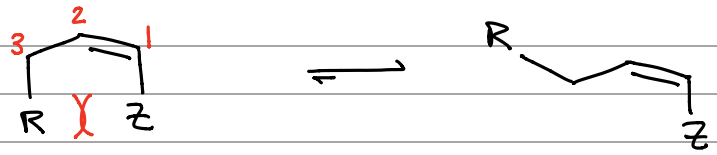
- torsional strain between an allylic and vinyl substituent.
- relevant for planar structures

Chem Rev 1989 89 1841

$A^{1,2}$-Strain

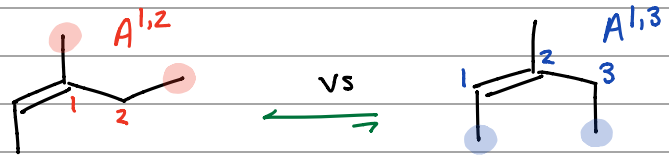


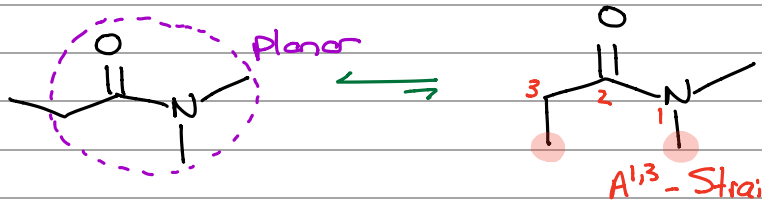
$A^{1,3}$-Strain



essentially syn pentane

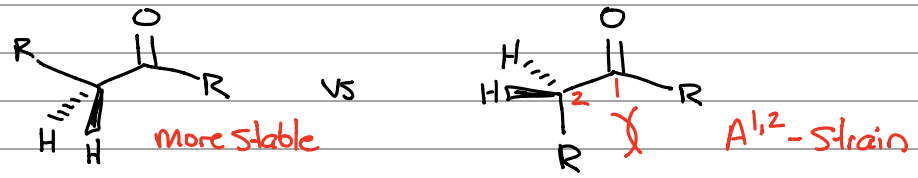
Generally $A^{1,3}$ is worse than $A^{1,2}$ (especially with big R-groups)



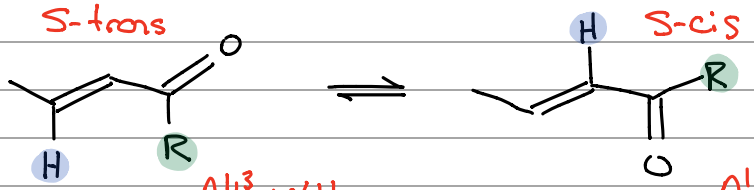


$A^{1,3}$-Strain

[Good Example or Test Q in P.F. notes]

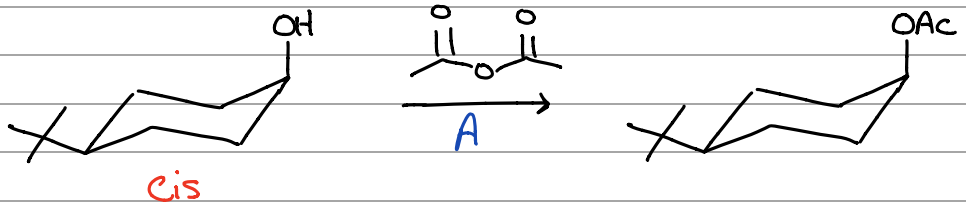


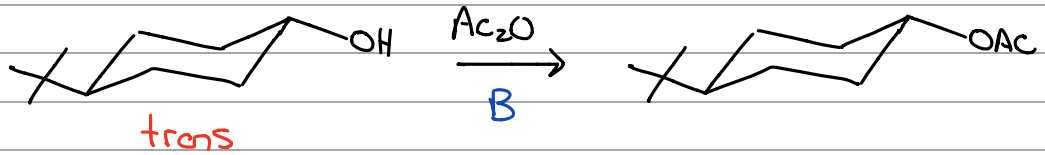
$A^{1,2}$-Strain



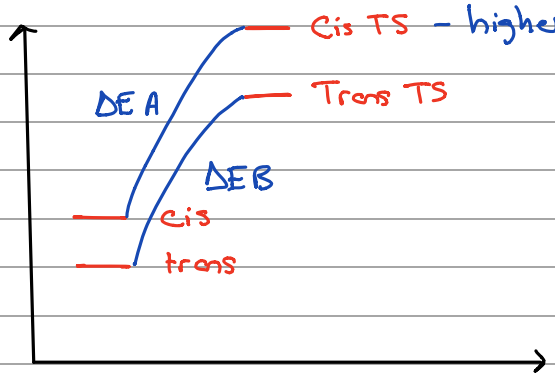
R = CH_3	70	30	% of S-cis form increases as size of "R" increases.
= Et	55	45	
= iPr	30	70	
= tBu	0	100	

Extra: Conformational Effects on Reactivity [C+S 3.7]





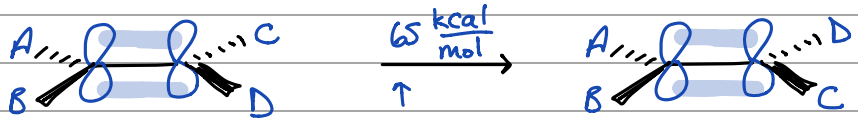
Rate: Evaluate the ΔE in the RDS



$\Delta E_A > \Delta E_B$

↑ faster rxn

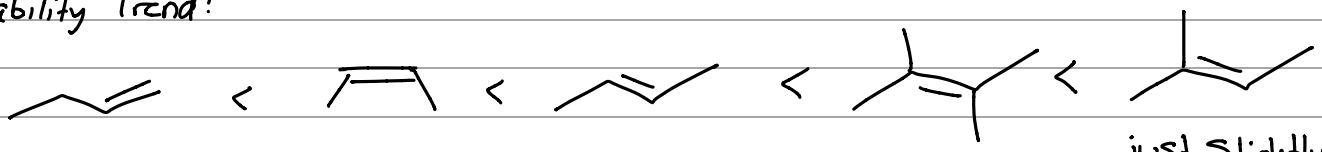
Alkenes



↑ Ethylene π-bond strength

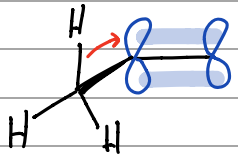
Heat is necessary for >50 kcal/mol barrier

Stability Trend:



just slightly more stable

Substitution Stabilizes alkenes



Donation to π* stabilizes the system

Understanding C=C rotation:
J. Chem. Ed. 2005, 82, 1329