

① LECTURE 6: THERMODYNAMICS

- BENSON INCREMENT TABLES
- CONFORMATIONAL ANALYSIS
- STEREOCHEMISTRY & CHIRALITY
- ACYCLIC SYSTEMS

PS #3 DUE TUES, 9/22

HINI PLAN

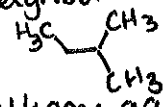
② BENSON INCREMENT TABLES ( $\Delta H_f^\circ$ )  
 Instead of considering bonds, @ 298) consider groups.

ex:

$C_B = C$  in benzene ring  
 $C_d = C$  in double bond.  
 $C_t =$  triple-bonded C.  
 $C_a =$  allenic C.

③ Corrections

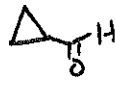
① Non-nearest neighbor



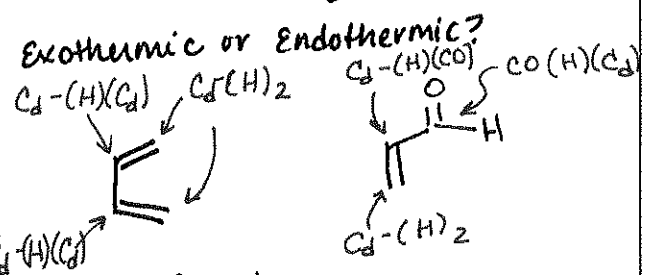
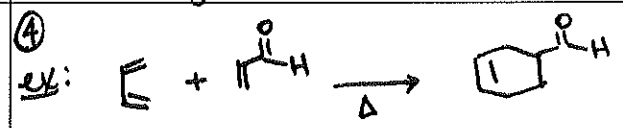
alkane gauche = +0.8 kcal/mol

③ Corrections- cont'd

② Ring Strain

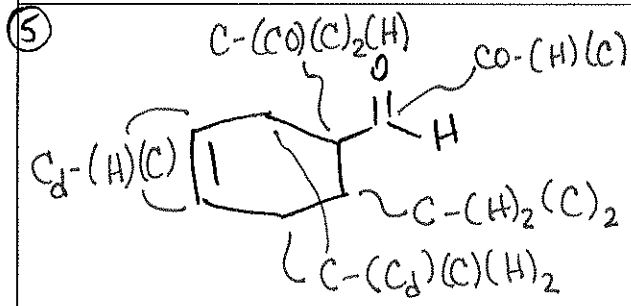


Correction = 27.6 kcal/mol



Group	$\Delta H_f^\circ(298)$
$C_d-(H)_2$	$6.26 \times 3$
$C_d-(H)(C_d)$	$6.78 \times 2$
$C_d-(H)(CO)$	5.0
$CO-(H)(C_d)$	-29.1

$\Delta H_f^\circ \approx 8.24 \text{ kcal/mol}$



GROUP  $\Delta H_f^\circ(298)$

$CO-(H)(C)$	-29.1
$C-(CO)(C)_2(H)$	-1.7
$C-(H)_2(C)_2$	-4.93
$C-(C_d)(C)(H)_2$	$-4.76 \times 2$
$C_d-(H)(C)$	$8.59 \times 2$

Correction: cyclohexene +1.4

$\Delta H_f^\circ \approx -26.67 \text{ kcal/mol}$

⑥ So, for this Diels-Alder rxn:

$\Delta H^\circ = -26.67 \text{ kcal/mol} - 8.24 \text{ kcal/mol}$

$\Delta H^\circ = -34.91 \text{ kcal/mol}$

⑦ CONFORMATIONAL ANALYSIS

→ Thermodynamics depends on conformation as well as connectivity.

Stereochemistry

Chirality = "handedness"

You should be able to

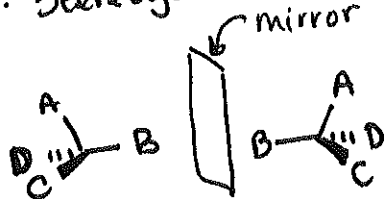
- (1) tell if something is chiral &
- (2) assign enantiomeric & diastereomeric relationships b/w molecules

BY VISUAL INSPECTION / QUICKLY.

BE ABLE TO SEE 3-D STRUCTURES IN YOUR HEAD!!  
PRACTICE THIS!!

⑧ Sometimes identifying chirality is easy...

ex: Stereogenic centers (4 different substituents)  $\equiv$  Stereocenter

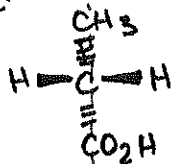


Enantiomers = Non-superimposable mirror image partners

Note: you should be able to assign R or S configuration to stereocenters.

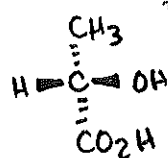
⑨

ex: symmetry plane ( $\sigma$ )



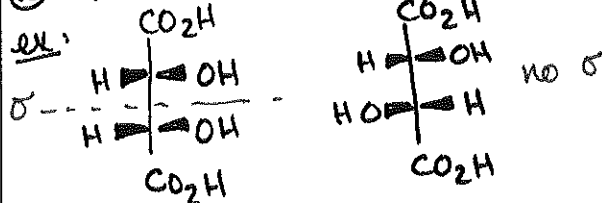
propanoic acid  
CHIRAL OR ACHIRAL?

no symmetry plane



lactic acid  
CHIRAL OR ACHIRAL?

⑩ TARTARIC ACID:

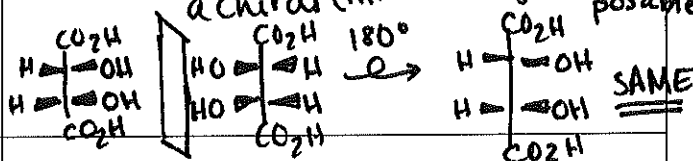


CHIRAL OR ACHIRAL?

CHIRAL OR ACHIRAL?

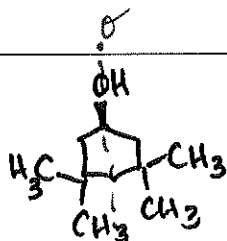
MESO-tartaric acid

↳  $> 1$  stereocenter but achiral (mirror image is superimposable)



⑪

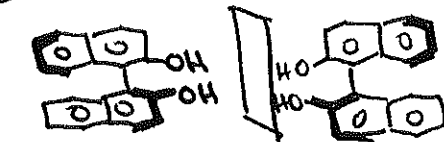
ex



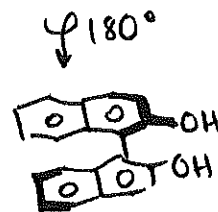
CHIRAL OR ACHIRAL?  
NOT MESO (only 1 stereocenter)

⑫

ex: BINOL (no stereogenic carbon)



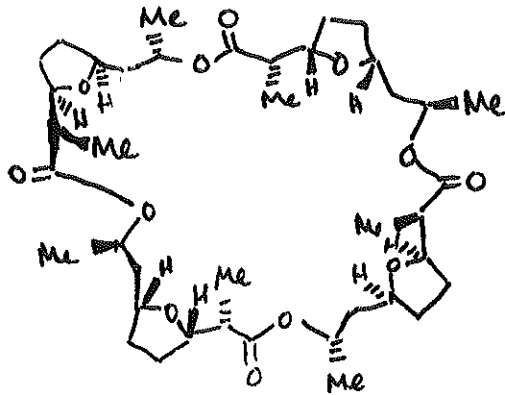
CHIRAL OR ACHIRAL?



non-superimposable

A molecule contains these symmetry elements if you do the symmetry operation & the result is superimposable on the starting molecule.

⑬ ex: Non actin



CHIRAL OR ACHIRAL?  
Initial report: Shocked that  $[\alpha] = 0!$

⑭ More analytical approach...

A molecule is chiral if it lacks improper axes of rotation ( $S_n$  symmetry).

Symmetry Operations:

$C_1 = E$  = identity operator (superimposable on itself)

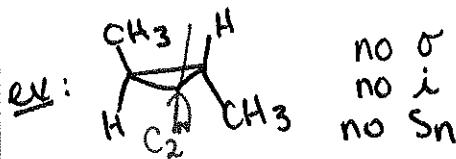
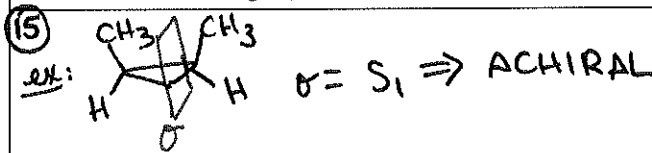
$C_n$  = rotation abt axis by  $\frac{360^\circ}{n}$

$S_1 = \sigma$  = plane of symmetry

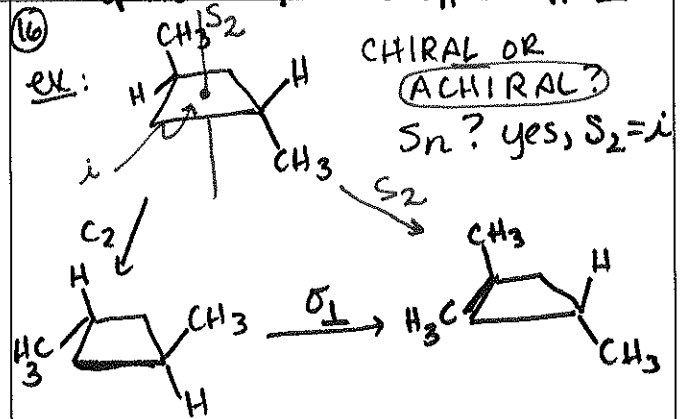
$S_2 = i$  = inversion through a point

$S_n$  = improper axis of rotation  
=  $C_n + \sigma_\perp$

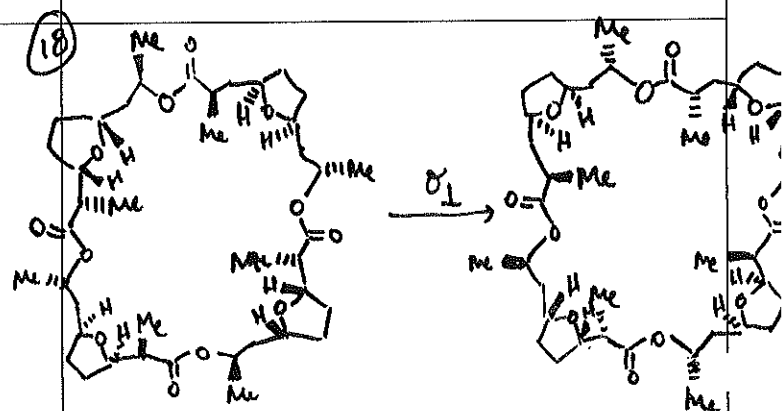
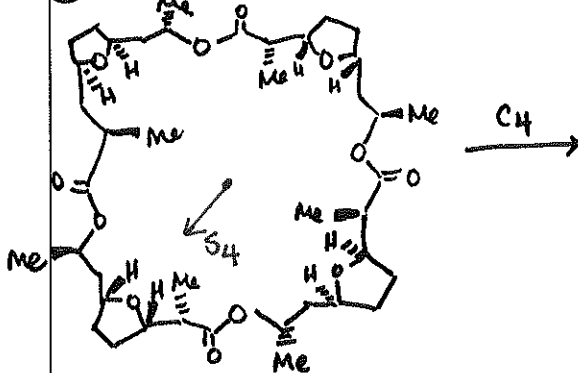
All operations fit into  $C_n$  or  $S_n$ .



$C_2$  symmetric  
 $\Rightarrow$  CHIRAL



⑰ Back to NONACTIN...



superimposable.

ACHIRAL.

① Measuring enantiomeric ratios?

POLARIMETRY (OLD SCHOOL)

"optically active"  $\equiv$  rotates plane polarized light.

$\hookrightarrow$  Enantiomerically enriched.

Report  $\alpha$  rotation  $\Rightarrow$  VERY sensitive to impurities!!

measure  $\alpha$  of enantiopure sample...  
measure  $\alpha$  of your enantioenriched sample...

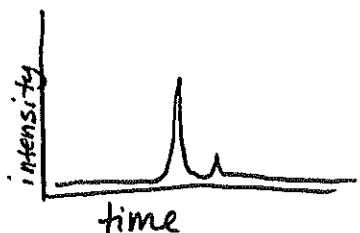
$$\frac{\text{obs } \alpha}{\text{max } \alpha} = \text{enantiomeric excess (ee)} = \frac{(\text{major enantiomer} - \text{minor enantiomer})}{(\text{major enantiomer} + \text{minor enantiomer})}$$

Often reported as %ee.

②

② "New" technology: Chromatography columns of chiral materials

(GC, LC, or SFC)  
 $\uparrow$  gas     $\uparrow$  liquid     $\uparrow$  supercritical fluid (CO<sub>2</sub>)



Ratio of peak areas = enantiomeric ratio (er)

② You will see both ee & er in publications.

Major	Minor	%ee	er
1	1	0	1 or 50:50
2	1	33.3	2 or 66:33
3	1	50	3 or 75:25
10	1	82	10 or 91:9
100	1	98	100 or 99:1
1000	1	99.8	1000 or 99.9:0.1

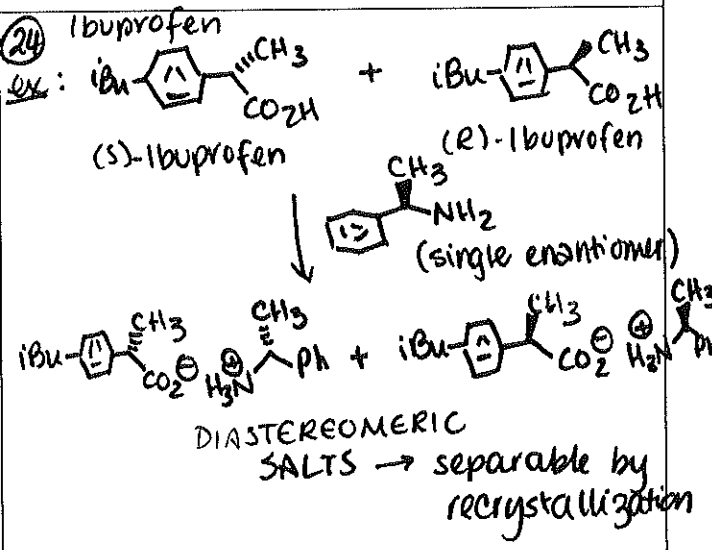
Racemic (still chiral, just not enantioenriched).

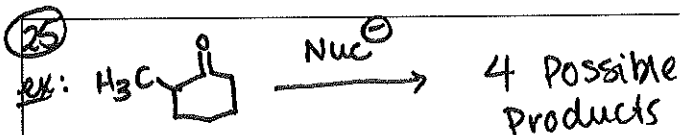
③

DIASTEREOMERS

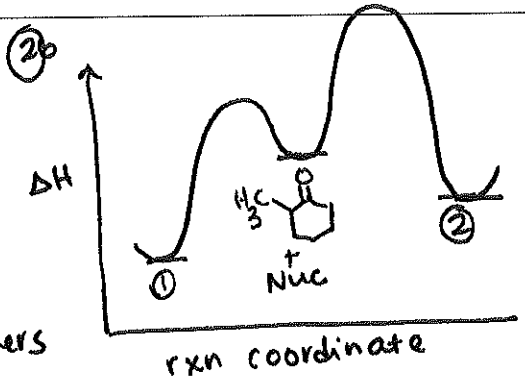
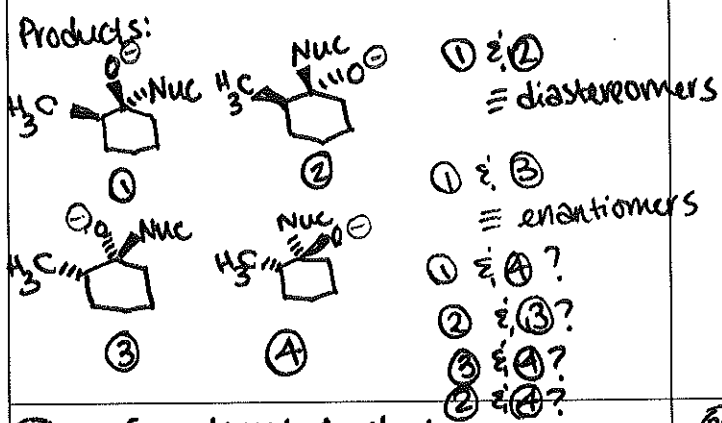
$\equiv$  Stereoisomers that are not enantiomers (same connectivity)  
Different energies, physical properties, reactivities, etc.

④





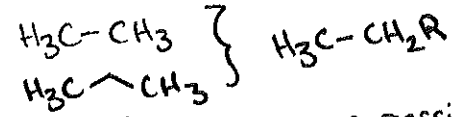
CHIRAL or ACHIRAL? racemic



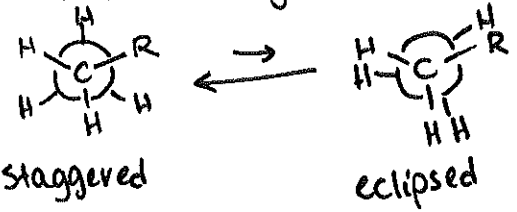
Diastereomers have different energies  $E^\ddagger$ , usually form at different rates.

27) Conformational Analysis of Acyclic Systems (C&EA, Ch 2 & 3)  
 Hoffmann Chem Rev 1989, 89, 1841.  
 Hoffmann ACIE 2000, 39, 2054.  
 Useful Reference: Eliel & Wilen (1994).  
Stereochemistry of Organic Compds.  
 New York: Wiley.

28) Ethane & Propane



What conformations are possible?  
 Relative energies?



$\Delta E = +3.0 \text{ kcal/mol (R=H)}$   
 $\Delta E = +3.4 \text{ kcal/mol (R=CH}_3)$

29) How much is each interaction worth?

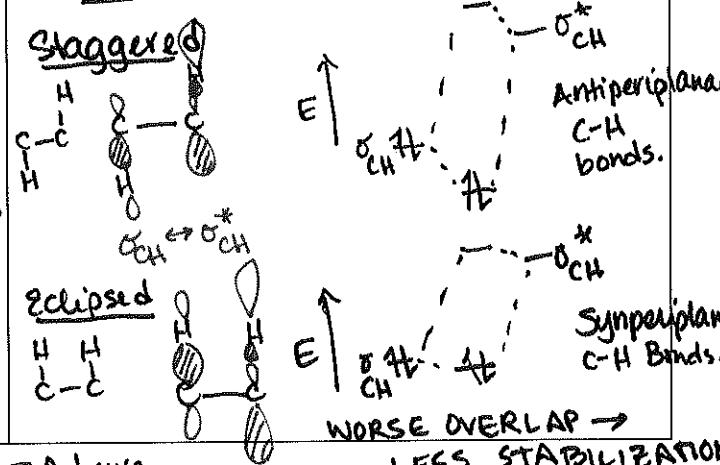
Structure	Eclipsed atoms	$\Delta E$ (kcal/mol)
ethane	3 (H $\leftrightarrow$ H)	$+3.0/3 = +1.0$ each
propane	{ 2 (H $\leftrightarrow$ H) 1 (H $\leftrightarrow$ Me)	+1.0 each +1.4

We can use these  $\Delta E$  to predict stability of conformations of other molecules w/ H  $\leftrightarrow$  H or H  $\leftrightarrow$  CH<sub>3</sub> eclipsing interactions.

30) Steric effect?

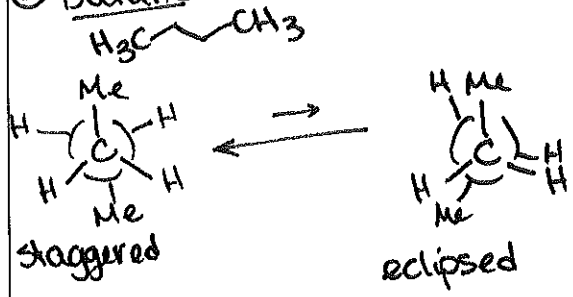
Ethane  $\rightarrow$  No overlap of van der Waals radii

Stereoelectronic effect?



J.P. Lowe JACS 1970, 92, 3799. LESS STABILIZATION Propane: Steric & Stereoelec

31) Butane



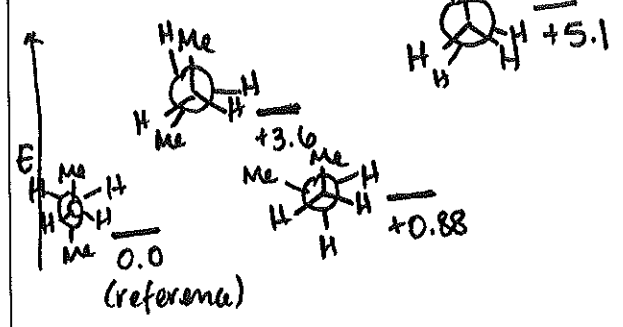
$\Delta E?$

Approximation:

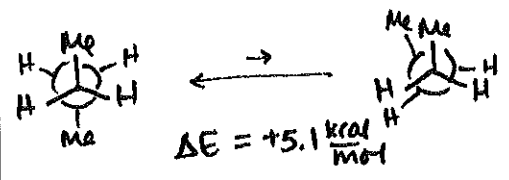
Eclipsed atoms	$\Delta E$ (kcal/mol)
1 x (H $\leftrightarrow$ H)	+1.0
2 x (H $\leftrightarrow$ Me)	+1.4 x 2 = +2.8
	<u>+3.8 kcal/mol</u>

Computed  $\Delta E = +3.6$  kcal/mol  $\Rightarrow$  Good agreement!  
 (Allinger J Chem Comp 1980, 1, 181.)

32) More conformations possible:  
 Torsional Energy Profile



33) How much does Me  $\leftrightarrow$  Me eclipsing interaction cost?



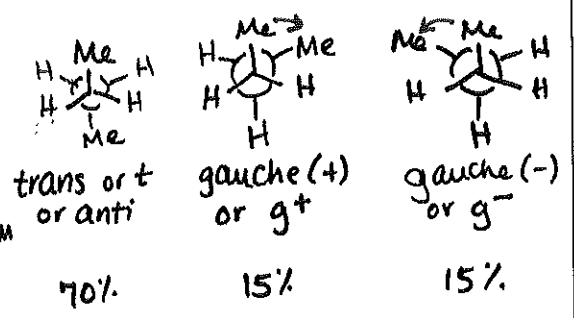
$$2(H \leftrightarrow H) + 1(Me \leftrightarrow Me) = +5.1 \text{ kcal/mol}$$

$$- 2(H \leftrightarrow H) \Rightarrow -2.0 \text{ kcal/mol}$$


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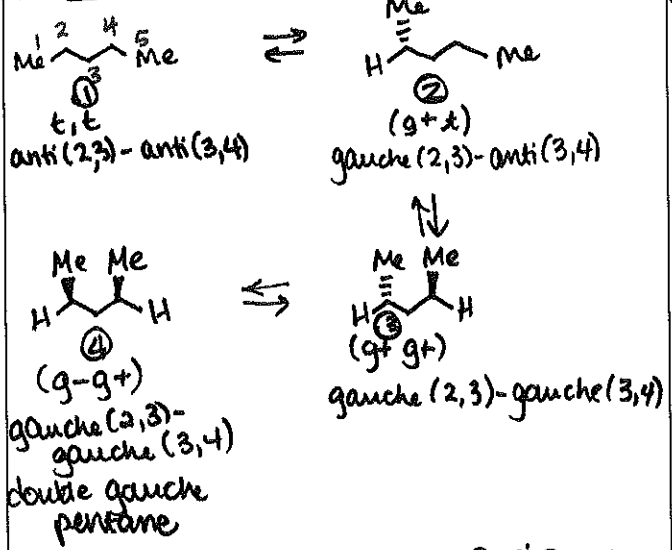

$$+3.1 \text{ kcal/mol}$$

34) Staggered conformations:



population @ 298K

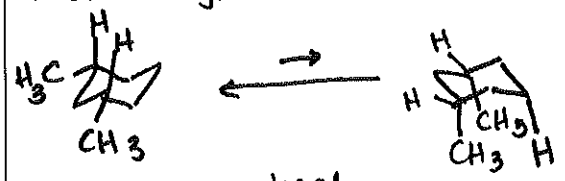
35) PENTANE (lots of conformations):



CHALLENGE: Estimate  $\Delta E$  of 2 & 3 relative to 1.

36) New interaction in  $\oplus$ :  
 1,3-dimethyl eclipsing interaction.  
 How much energy?

Model System:



$$\Delta G^\circ = +5.5 \text{ kcal/mol}$$

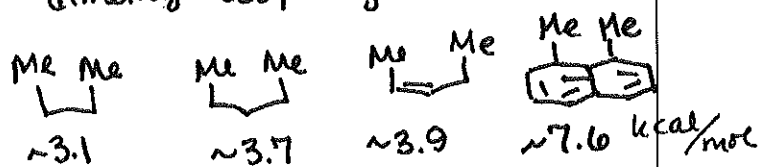
$$= 2(1,3\text{me} \leftrightarrow \text{H}) + 1(1,3\text{-Me} \leftrightarrow \text{Me})$$

skew-butane = 0.88 kcal/mol

$$+5.5 - (2)(0.88) = +3.7 \text{ kcal/mol}$$

37

Estimates of in-plane 1,2- & 1,3-  
dimethyl eclipsing interactions



In-plane 1,3 (Me $\leftrightarrow$ Me)  $\sim 4$  kcal/mol

In-plane 1,2 (Me $\leftrightarrow$ Me)  $\sim 3$  kcal/mol