ORGANIC CHEMISTRY.

- BASED ON C.
  - ALSO HAS H, O, N, HALOGENS, S OR P

C - RULE # 4 BONDS.

- MAY HAVE SINGLE, DOUBLE AND/OR TRIPLE BONDS.

- REACTIVE INTERMEDIATES MAY HAVE 3 BONDS

- CARBOCATIONS, CARBANIONS, FREE RADICALS

- ARE A FEW COMPOUNDS WITH 2 BONDS
  CARBENES

BONDING

- ELECTRONEGATIVITY = EN

  OF C = 2.5 MID RANGE

SO IF

$\Delta E_N < 0.5$ COVALENT

ΔE_N $0.5 < \Delta E_N < 1.7$ POLAR COVALENT

$\Delta E_N > 1.7$ IONIC

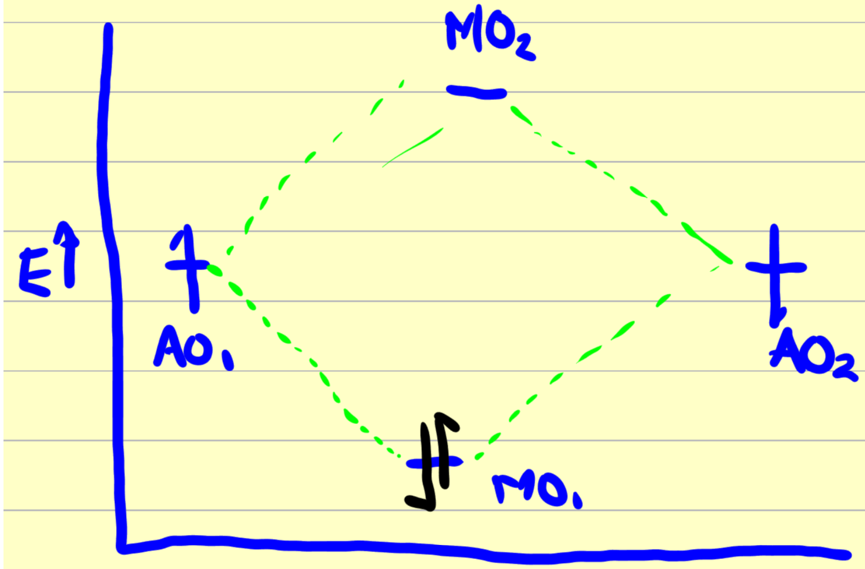
"ALWAYS" COVALENT OR POLAR COVALENT.

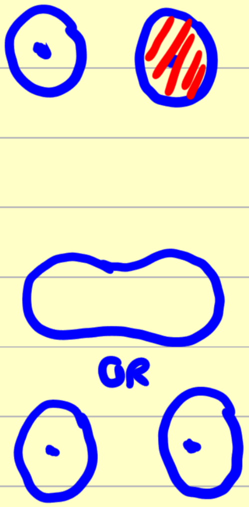
- IF COVALENT, BONDING BEST EXPLAINED BY OVERLAP OF ORBITALS.

- DEVELOP MOLECULAR ORBITALS (MO'S) BY COMBINING ATOMIC ORBITALS

LCAO / MO APPROACH

$H\cdot + H\cdot \longrightarrow H-H$

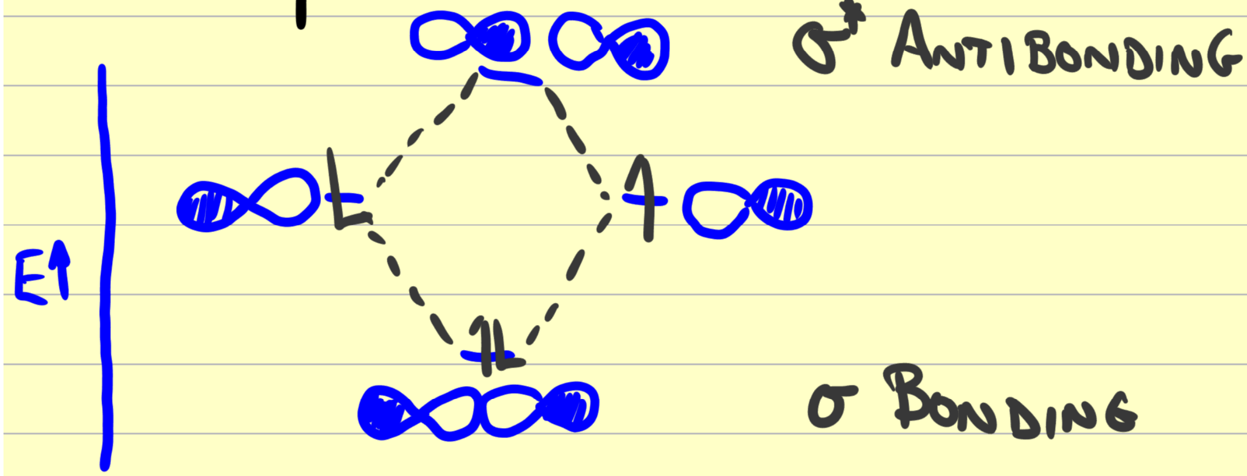




MO_1 - BONDING - σ BOND
(NO PHASE CHANGE)

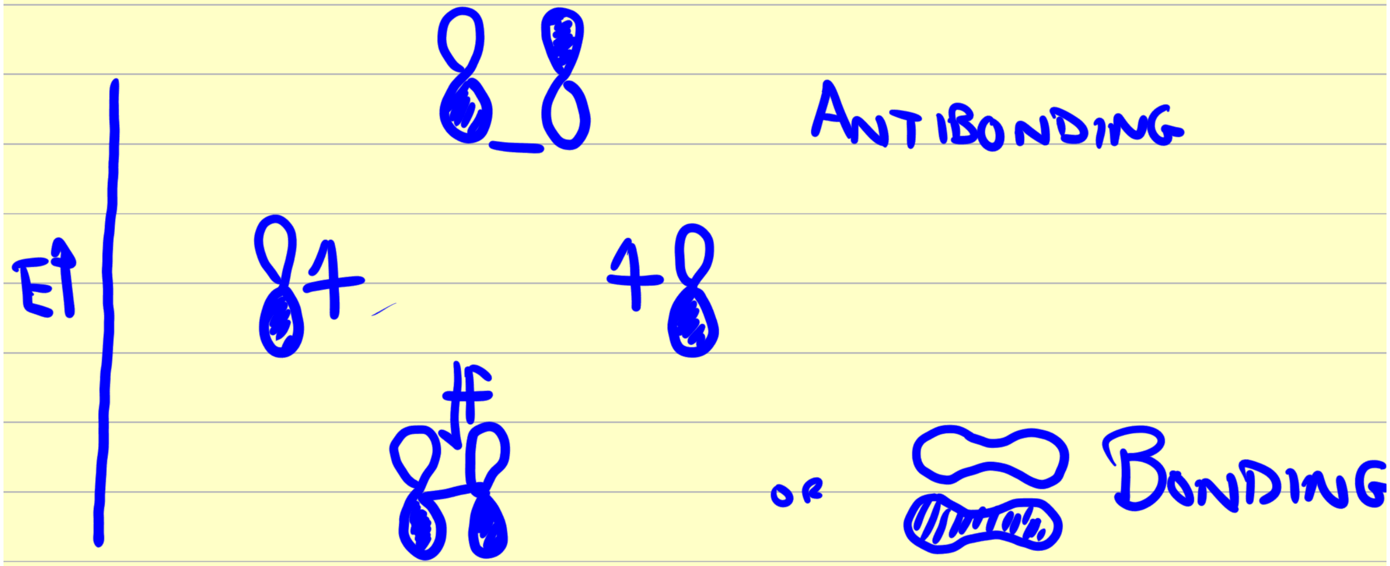
MO_2 - ANTIBONDING σ^*

FOR p- ORBITALS.



2ND ARRANGEMENT POSSIBLE

- SIDE ON INTERACTION



- CALLED π (PI) AND π* RESPECTIVELY.

(1 PHASE CHANGE)

- IF YOU HAVE d ORBITALS, CAN HAVE δ BONDS (2 PHASE CHANGES)

HYBRIDIZATION

- HOW DO WE GET 4 EQUIVALENT BONDS - SAME LENGTHS IN CH_4
  SAME ANGLES

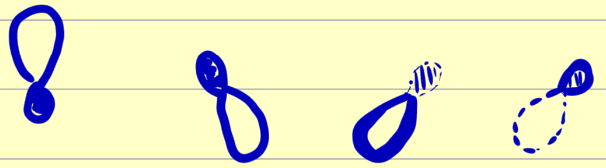
IF C HAS $1s^2\ 2s^2\ 2p_x^1\ 2p_y^1\ 2p_z^0$

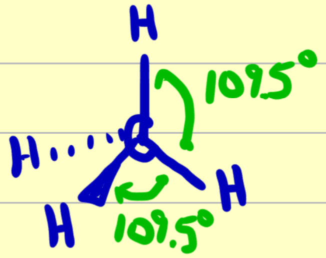
- MODEL THAT'S USED CREATES HYBRIDS OF s + p ELECTRONS (e^-'s)
- DEPENDS ON ATOMS AVAILABLE.

IF WE HAVE CH_4.

p ↑ ↑ — --> ↑ ↑ ↑ ↑ sp^3 HYBRID.

s ↑↓



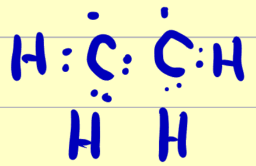


SHAPE: TETRAHEDRON

∴ sp^3 HYBRIDIZED C IS TETRAHEDRAL.

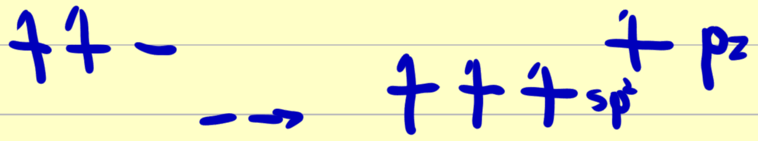
- CREATE 4 EQUIVALENTS BONDS AT ~ 109.5° ANGLES TO EACH OTHER.

CONSIDER C_2H_4

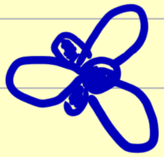


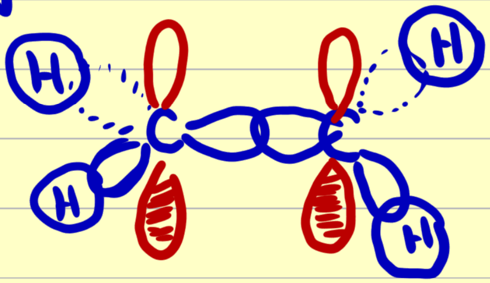
- DIRADICAL - Yuk! in sp^3

HOW ABOUT sp^2 HYBRID, WITH ONE p UNAFFECTED



sp² HYBRIDIZATION





- CARBON CAN FORM 3 σ BONDS
  + ONE π BOND.

- σ BONDS ARE 120° FROM EACH OTHER.

- CARBON IS TRIGONAL.

AND C_2H_2 ?

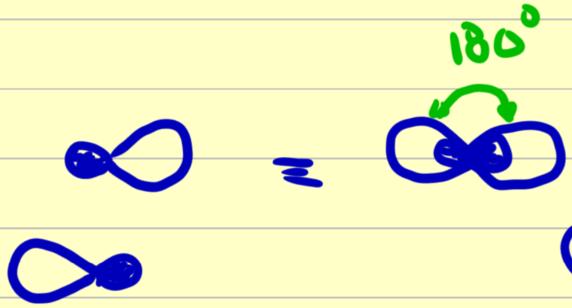
- REQUIRES sp HYBRIDIZATION.

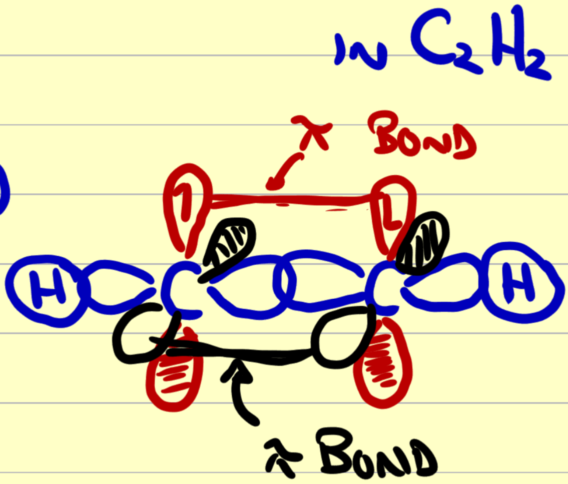
↿ ↿ – 2p p_x ↿ ↿ p_z

-- →   ↿ ↿ sp

⥮ 2s

sp HYBRID HAS TWO ORBITALS, AT 180° FROM EACH OTHER





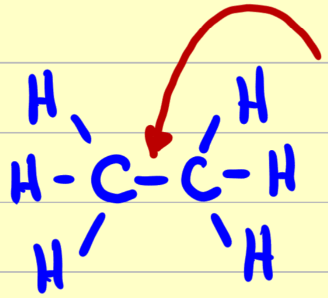
2 σ BONDS - AT 180°
2 π BONDS

BONDING.

- ALL OF sp^3, sp^2, sp POSSIBLE
- RESPONDS TO ATOMS PRESENT TO MAKE MOST STABLE COMPOUND.

C_2H_6

$2\cdot\dot{\underset{\cdot}{C}}\cdot + 6H\cdot \rightarrow$



85 kcal/mol (350 kJ/mol)

4σ BONDS FOR CARBON - sp^3 HYBRIDIZED.

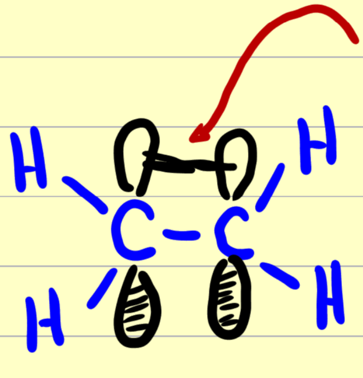
CH_4, C_3H_8, C_4H_{10}

C_nH_{2n+2}

---

sp^2 C_2H_4

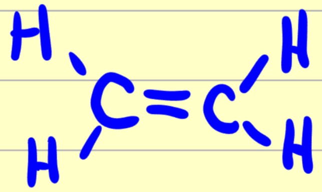
$2\cdot\dot{\underset{\cdot}{C}}\cdot + 4H\cdot \longrightarrow$



148 kcal/mol (620 kJ/mol)

(DIFF ~65 kcal)

≡



EACH C HAS 3σ BONDS, 1π BOND.

- DOUBLE BOND IS COMPRISED OF 1σ, 1π BOND.

APPLIES TO C_3H_6, C_4H_8, C_5H_{10}

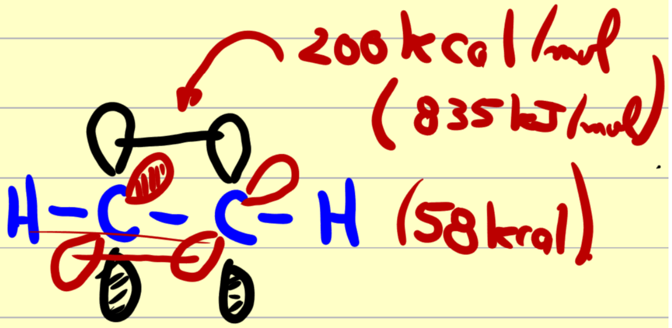
(C_nH_{2n})

—

SP HYBRIDIZATION

C_2H_2

$2\ \cdot\dot{\underset{\cdot}{C}}\colon + 2H\cdot \longrightarrow$



TRIPLE BOND COMPRISED OF $\left.\begin{matrix}1\ \sigma\\ 2\ \pi\end{matrix}\right\}$ BONDS

To be consistent, the carbon atom has two sigma bonds and two pi bonds

APPLIES TO C_2H_2, C_3H_4, C_4H_6, C_5H_8........

C_nH_{2n-2}

CH 2 HYDROCARBONS.

- ONLY HAVE CARBON AND HYDROGEN ATOMS.

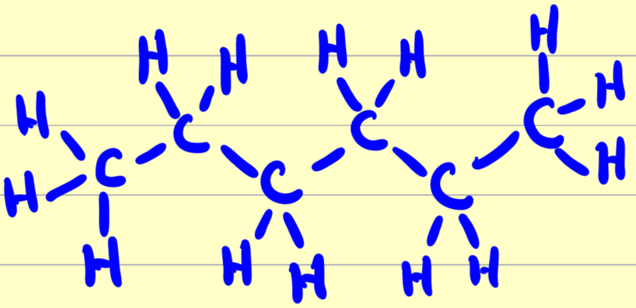
THREE TYPES

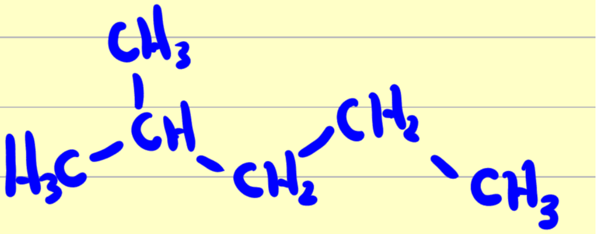
ALKANES, ALKENES, ALKYNES (ARENES)

arenes (benzenes) for this purpose (only) can be considered as a type of alkene

1. ALKANES.

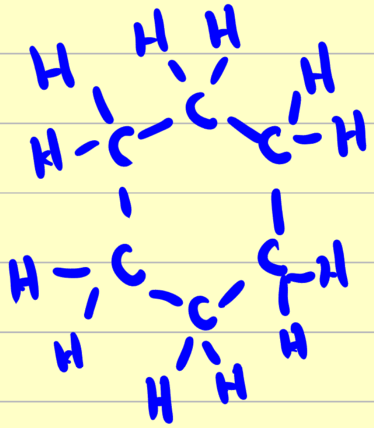
- ONLY SINGLE BONDS





ALSO CALLED

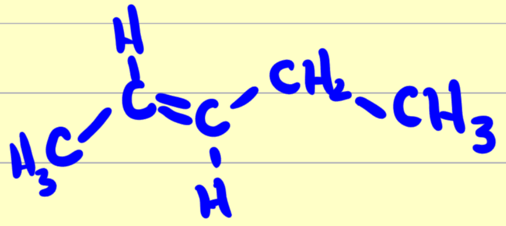
- SATURATED HYDROCARBONS.

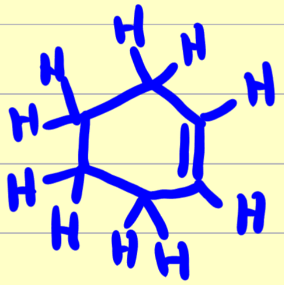


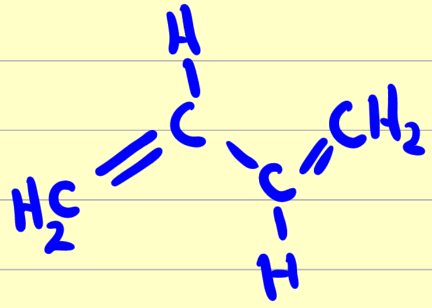
- ALL C'S sp^3 HYBRIDIZED

2) ALKENES

- AT LEAST ONE $C=C$







AT LEAST TWO C'S ARE SP^{2}

SYNONYN = OLEFIN

That's synonym

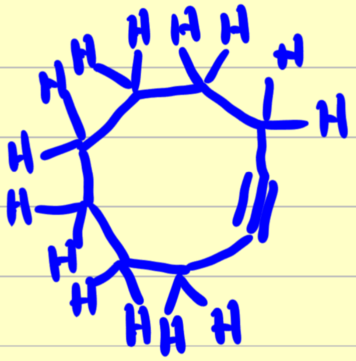
ALKENES & ALKYNES ARE CALLED UNSATURATED.

3) ALKYNES

TRIPLE

- AT LEAST 1 $C\equiv C$ BOND

$H-C\equiv C-CH_2-CH_2-CH_3$



CYCLIC, BUT ONLY IF
IF RING ≥ 8 C ATOMS

AT LEAST 2 C'S ARE <u>Sp</u>

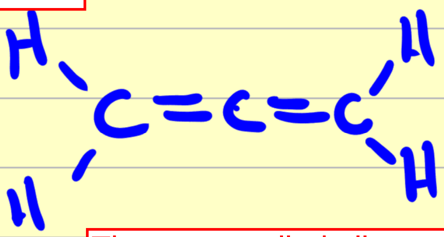
- OLDER NAME = ACETYLENES

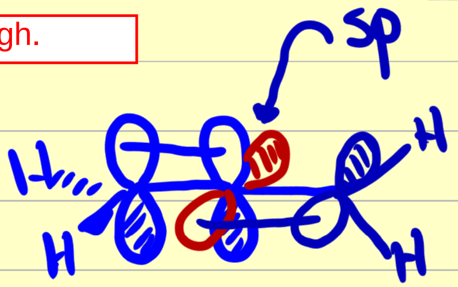
ARE Sp HYBRID CARBONS IN ALKYNES <u>ONLY</u>?

NO.

It is >90% of the cases, though.

The exception..





These are called allenes or cumulenes; they are a type of alkene

ISOMERISM.

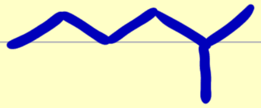
- MOLECULAR FORMULA

C_2H_6 - GIVES INFO ABOUT # AND TYPES OF ATOMS, BUT NO INFO ABOUT HOW THEY'RE CONNECTED. C-1ST H-2ND OTHERS ALBABETKALLY

$C_8H_{16}BrClO$

- STRUCTURAL FORMULA

$$CH_3-CH_2-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_3$$



- FORMULA INDICATING CONNECTIVITY (WHAT IS BONDED TO WHAT) - MAY OR MAY NOT INDICATE STEREOCHEMISTRY.

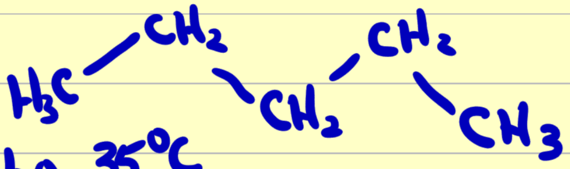
ISOMERS -

TWO OR MORE COMPOUNDS WITH SAME MOLECULAR FORMULA, DIFF. STRUCTURAL FORMULA.

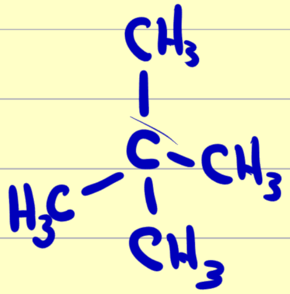
1ST TYPE - STRUCTURAL ISOMERS (POSITIONAL, CONSTITUTIONAL)

- SIMPLEST.

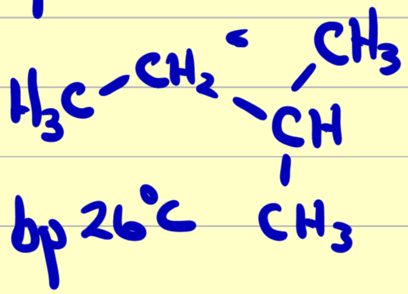
C_5H_{12}



bp 35°C



bp 7.2 °C



bp 26°C

- ATOMS ARE NOT CONNECTED TO SAME POSITIONS
- DIFFERENT COMPOUNDS (CPDS)
  - DIFF. mp, bp, DENSITY, REFRACTIVE INDEX, NMR SPECTRA.

NAMING ORGANIC COMPOUNDS

- IUPAC INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY HAS ACCEPTED RULES FOR HOW TO NAME CPDS.

GENERALITIES.

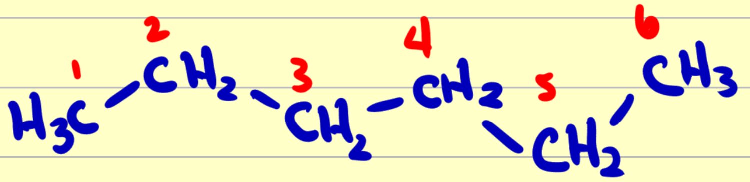
PREFIX + ROOT + SUFFIX. = NAME

ROOT - # ATOMS IN THE LONGEST CARBON CHAIN.

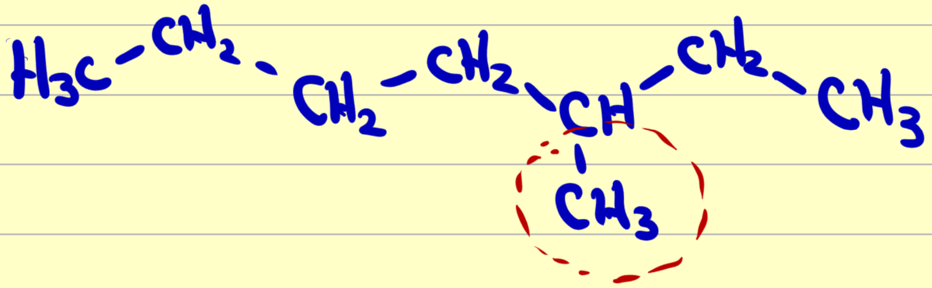
# C'S	NAME (ROOT)	C'S	ROOT
1	METH	7	HEPT
2	ETH	8	OCT
3	PROP	9	NON
4	BUT	10	DEC
5	PENT	11	UNDEC
6	HEX	12	DODEC

SUFFIX - TELLS WHAT KIND OF COMPOUND IT IS (WHAT FUNCTIONAL GROUP)

- ALKANE	- ANE
- ALKENE	- ENE
- ALKYNE	- YNE



HEXANE



HEPTANE

PREFIX - WHAT IS SUBSTITUTED ON THE MAIN CHAIN, AND WHERE

- 1 CARBON - METH - BUT BECAUSE IT'S A SUBSTITUENT, WE USE METH<u>YL</u>

(OR ETHYL OR BUTYL)

- COULD BE ON 5th OR 3RD C
  - USE LOWER #

3- METHYLHEPTANE

- OTHER SUBSTITUENTS - HALOGENS

F - FLUORO	Br - BROMO
Cl - CHLORO	I - IODO

SPACING - WORDS NORMALLY NOT SEPARATED.

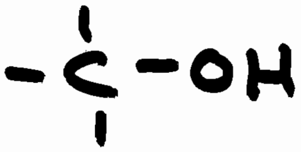
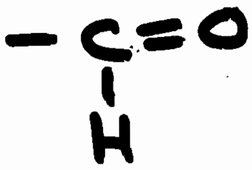
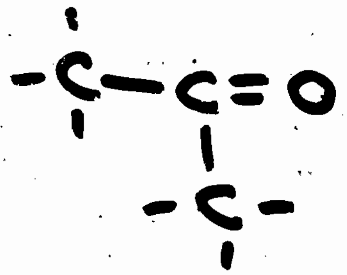
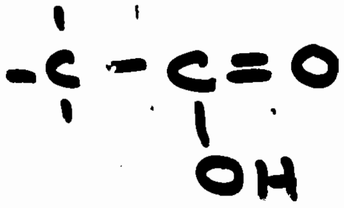
- NUMBERS SEPARATED FROM WORDS BY HYPHENS

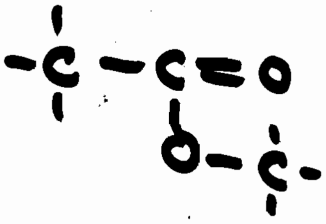
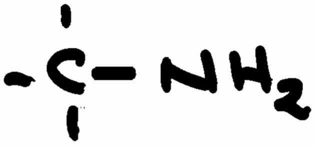
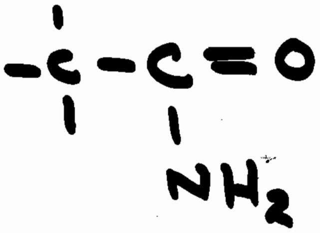
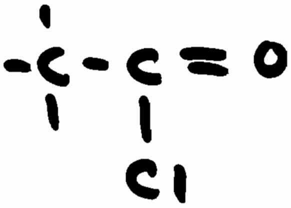
- NUMBERS AND NUMBERS SEPARATED BY COMMAS.

FUNCTIONAL GROUP CONCEPT.

- HALIDES ARE EXCEPTIONS
- EVERY OTHER COMMON FUNCTIONAL GROUP IS IN SUFFIX, SINCE COMPOUND IS NAMED AS A KETONE, ETC.

or as an aldehyde, or as an ester, or as an alcohol, etc.

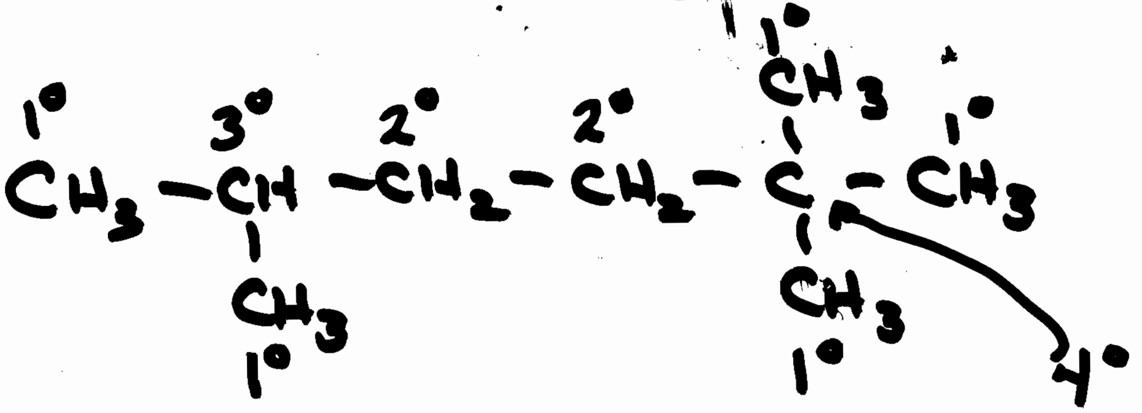
FUNCTIONAL GROUP		SUFFIX.
ALCOHOL	 $-\overset{\vert}{\underset{\vert}{C}}-OH$	-OL
ALDEHYDE	 $-\underset{\substack{\vert\\H}}{C}=O$	-AL
KETONE	 $-\overset{\vert}{\underset{\vert}{C}}-\underset{\substack{\vert\\-\underset{\vert}{C}-}}{C}=O$	-ONE
CARBOXYLIC ACID	 $-\overset{\vert}{\underset{\vert}{C}}-\underset{\substack{\vert\\OH}}{C}=O$	-OIC ACID.

ESTER		ALKYL -OATE
ETHER		ALKYL ALKYL ETHER
AMINE		-AMINE
AMIDE		-AMIDE
NITRILE		-(E)NITRILE
ACYL HALIDE OR ACID HALIDE		-OYL CHLORIDE

yes, acid bromides and acid fluorides do exist, but are so much less common than acid chlorides that we'll just focus on acid chlorides

SOME ADDITIONAL TERMS.

- PRIMARY, SECONDARY, TERTIARY, QUATERNARY



- PRIMARY (1°) - CARBON BOUND TO ONE OTHER CARBON

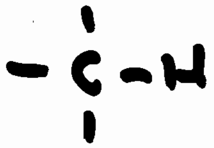
- SECONDARY (2°) - BOUND TO TWO OTHER CARBONS.

- TERTIARY (3°) - BOUND TO THREE OTHER CARBONS

- QUATERNARY (4°) - BOUND TO FOUR OTHER CARBONS.

OTHER TERMS

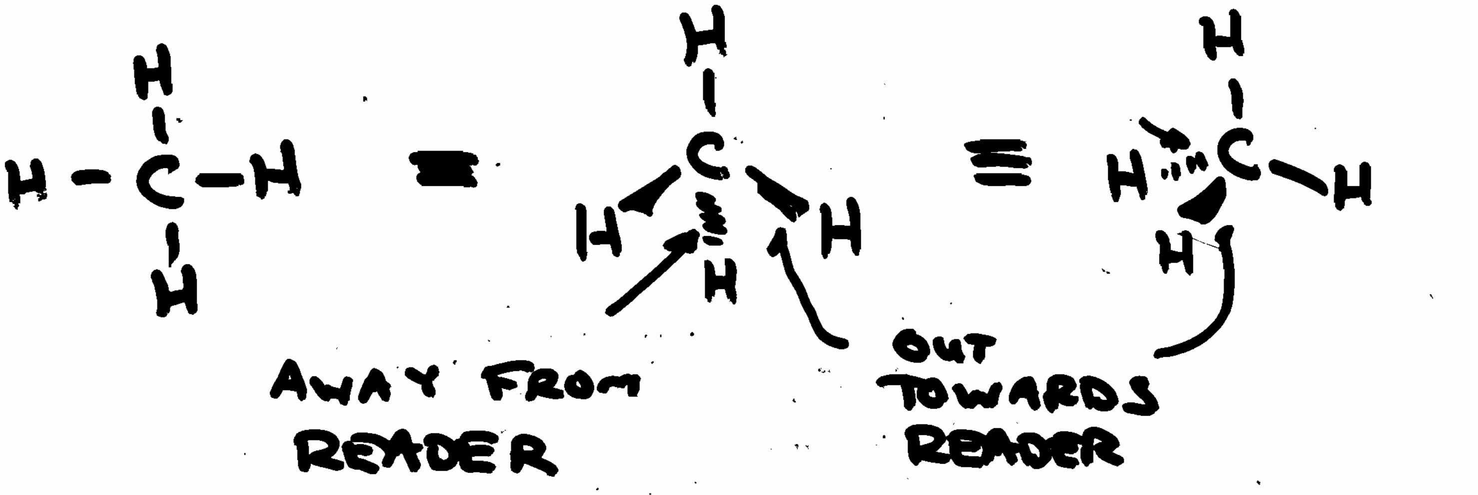
- METHYL $-CH_3$
- METHYLENE $-CH_2-$
- METHINE



$-\overset{|}{\underset{|}{C}}-H$

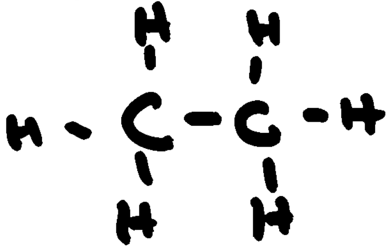
CH 3 STEREOCHEMISTRY.

- DISCUSSION OF DIFFERENCES IN MOLECULE AS THEY EXISTI IN SPACE - CAN BE 2-D OR 3-D.

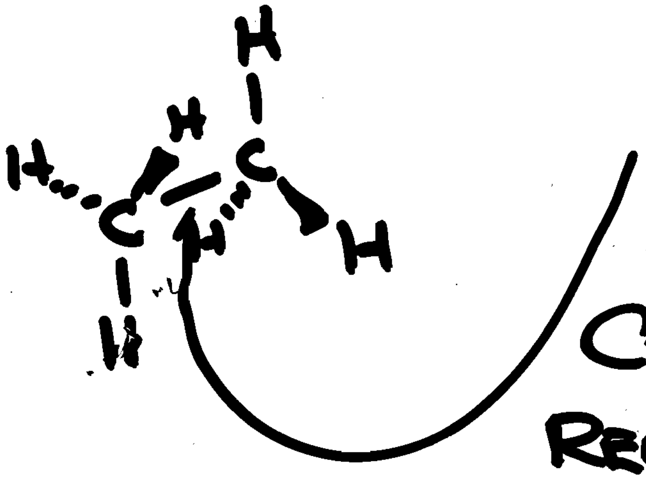


- ALL FOUR C-H'S IDENTICAL.

ONCE YOU GET TO ETHANE



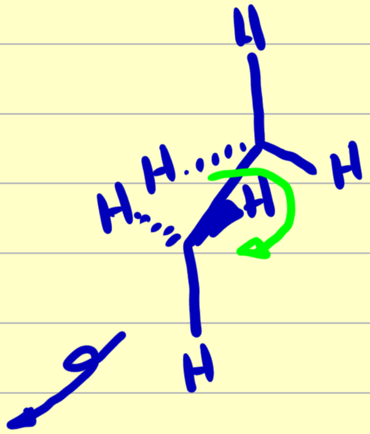
NOT ALL OF THE RELATIONSHIPS ARE THE SAME



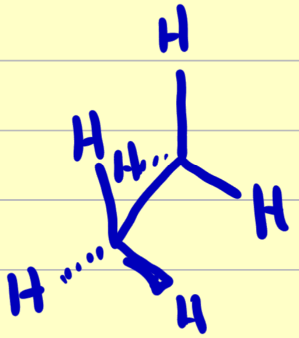
THAT BOND CAN ROTATE

CHANGES THE RELATIONSHIPS OF THE C-H BONDS.

ETHANE-



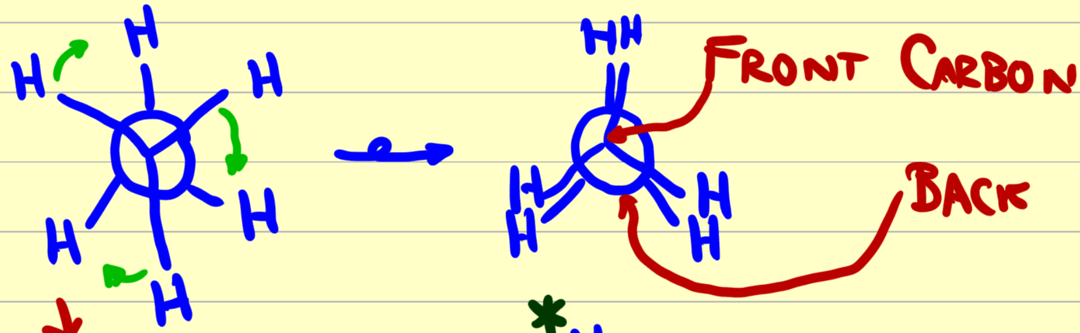
ROTATION OF C-C BOND IS PRETTY EASY.



- A BIT HIGHER IN ENERGY
- BUT NOT MUCH (3kcal, 12kJ/mol) HIGHER

NEWMAN PROJECTION-

- BETTER WAY TO LOOK AT A CARBON-CARBON SINGLE BOND - AND ROTATION

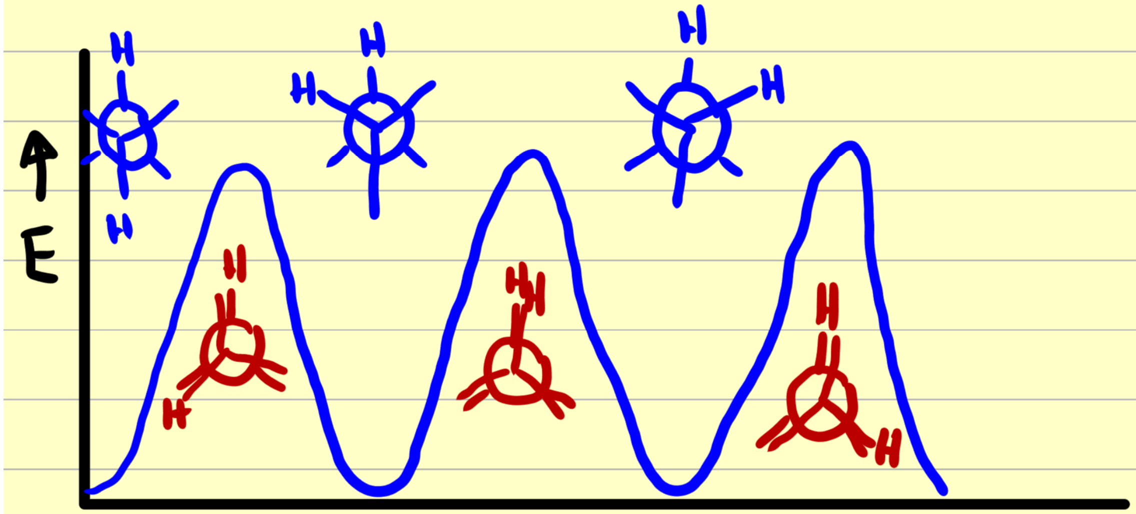


* LOWEST ENERGY CONFORMATION

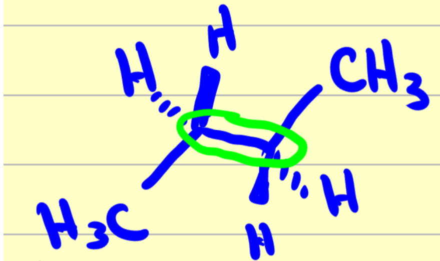
* HIGHER, BY CA. 3kcal.

NAMES- BETTER ONE IS CALLED STAGGERED *

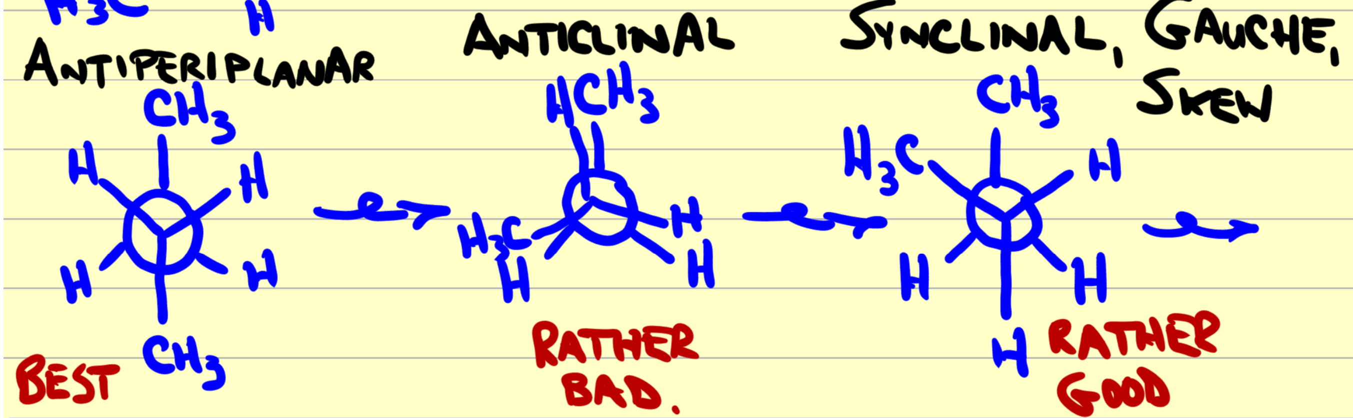
-WORSE ONE IS CALLED ECLIPSED *



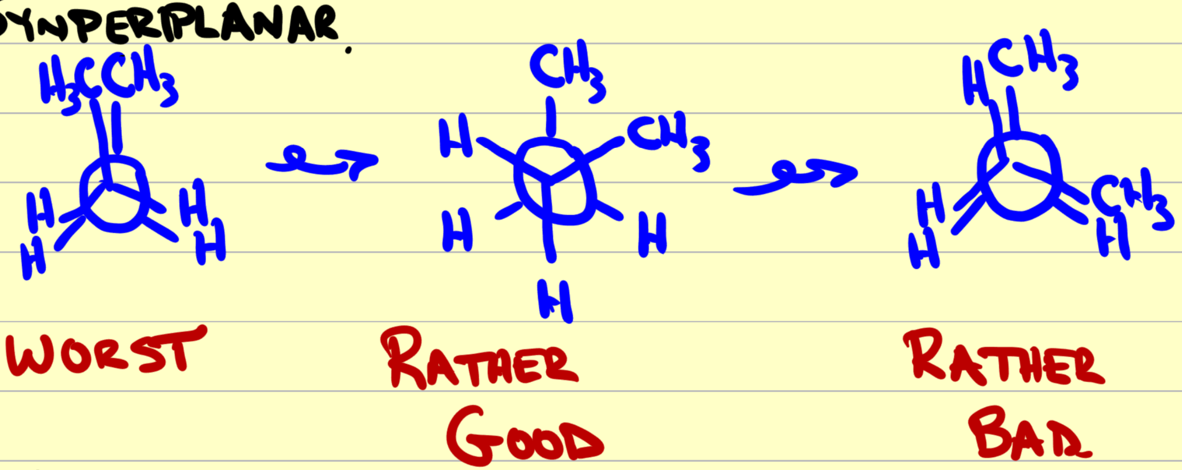
-WHAT ABOUT BUTANE?

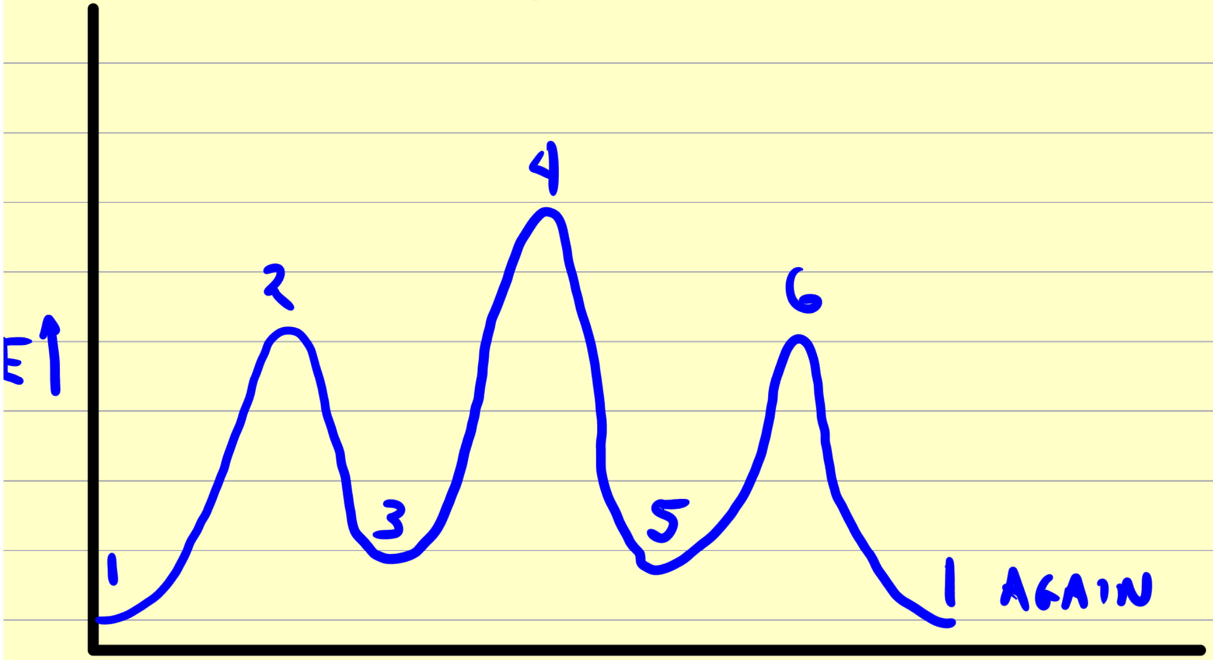


C$_2$-C$_3$ BOND



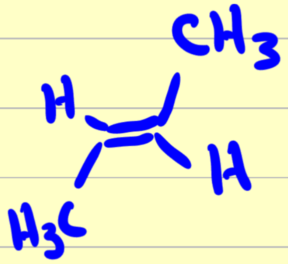
SYNPERIPLANAR.

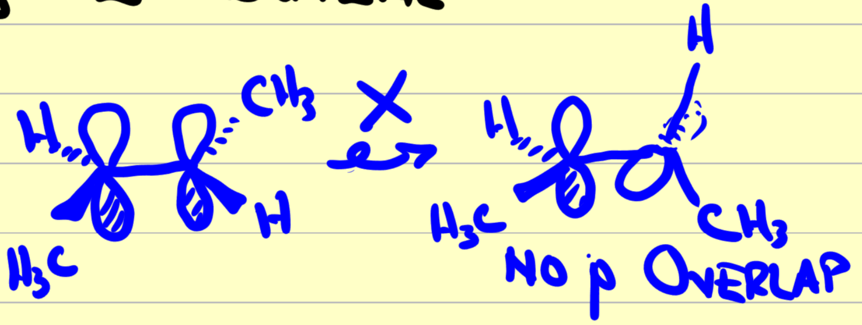




CONFORMATIONS - ROTATIONS ABOUT SINGLE BONDS, MOLECULE CAN DO THIS AT NORMAL TEMPERATURE

COMPARE TO 2-BUTENE

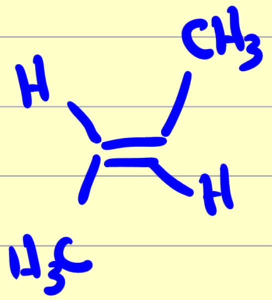




COSTS 60 kcal/mol

- MOLECULE WON'T DO THIS

SO



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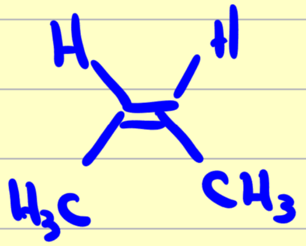
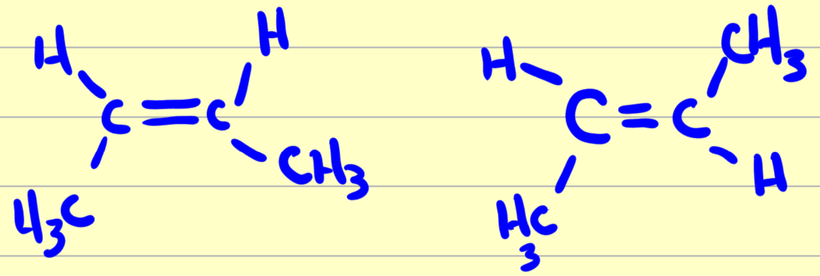


ARE DIFFERENT MOLECULES

- DON'T INTERCONVERT AT REASONABLE T.



THESE ARE **STEREOISOMERS.**

DEFN - ISOMERS WHICH DIFFER ONLY IN HOW THE ATOMS ARE ARRANGED IN SPACE (NOT WHERE THEY'RE CONNECTED)

a) GEOMETRIC ISOMERS (CIS-TRANS ISOMERS)

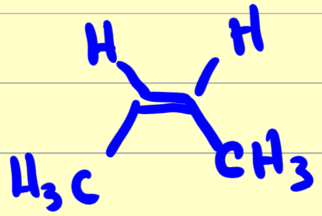
- ISOMERS DUE TO (VERY) RESTRICTED ROTATION OF A DOUBLE BOND
- THESE ARE DIFFERENT CONFIGURATIONS

(AS OPPOSED TO CONFORMATIONS, WHICH CAN INTERCONVERT)

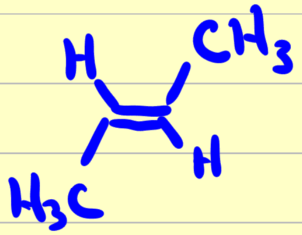
HOW TO NAME THEM?

- OLD NAMES

not IUPAC approved, but so common they can't be ignored



cis



trans

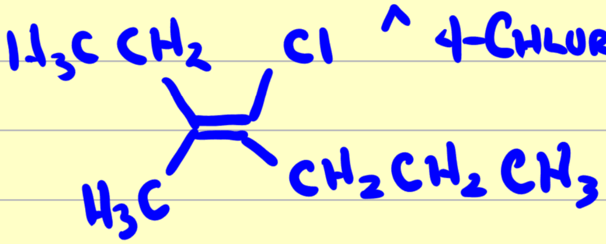
HOW YOU ASSIGN cis/trans

1) FIND THE MAIN CARBON CHAIN AS IT RUNS THROUGH THE DOUBLE BOND.

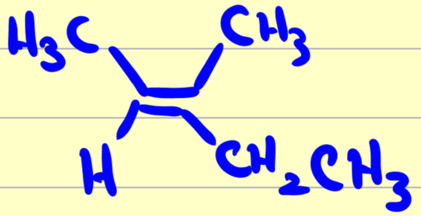
2) - IF CHAIN CONTINUES ON SAME SIDE (C SHAPE) - IT'S CIS

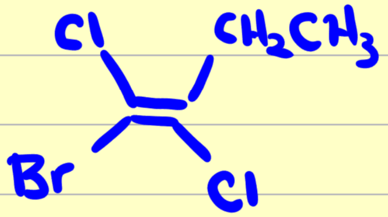
3) - IF IT CONTINUES ON OPPOSITE SIDES (S-SHAPE) - IT'S TRANS-

Note: normally written as lower case (trans-) in names trans ^ 4-CHLURO-3-METHYL-3-HEPTENE



PROBLEM-





WHAT IS THIS?

-DOESN'T FIT CIS OR TRANS, SINCE THERE'S NOTHING THAT CAN BE CALLED "MAIN CHAIN"

The following is the IUPAC approved way to name alkenes

SOLUTION- CAHN-INGOLD-PRELOG SEQUENCE RULES FOR PRIORITY.

a) ASSIGN HIGHEST PRIORITY GROUP FOR ATOMS DIRECTLY ATTACHED TO sp^2 HYBRIDIZED "C" ATOMS.

b) IF THE 2 HIGHEST PRIORITY GROUPS

ARE ON SAME SIDE ⇒ (Z)-

c) IF THEY'RE ARE ON OPPOSITE SIDES ⇒ (E)-

ASSIGNING PRIORITIES.

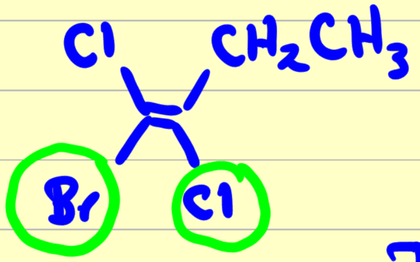
#1. ATOM WITH HIGHER ATOMIC # HAS HIGHER PRIORITY.

*- HIGHER ATOMIC MASS PRECEDES LOWER

* - NON BONDED ELECTRONS (i.e. LONE PAIR) ARE LOWER THAN H.

#2. IF 1ST SET OF ATOMS ARE TIED, MOVE DOWN CHAIN, ATOM BY ATOM, UNTIL 'YOU' FIND A DIFFERENCE

#3 - IF THERE'S A BRANCH POINT, CHOOSE THE PATH SUCH THAT THE EARLIEST POSSIBLE DISTINCTION IS MADE.

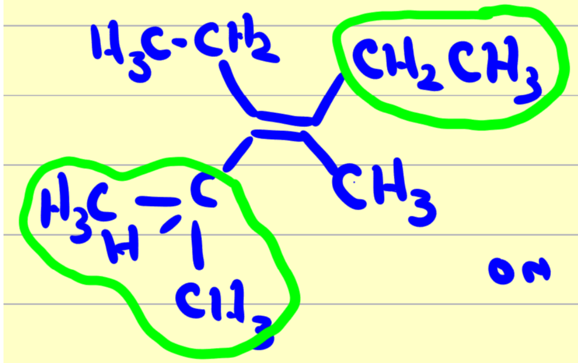


LEFT Br 'BEATS' Cl

RIGHT Cl 'BEATS' C

THIS IS (Z)-

here we *do* use the capital letter



RIGHT SIDE

C vs C TIE

ON IT... ⇓ ⇓

~~H~~, H, H   C, H, H

(E)-

again, *capital* E

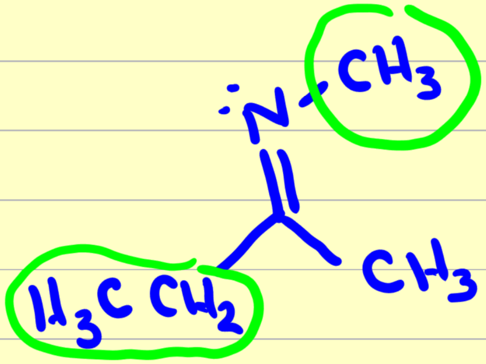
LEFT SIDE

1ST ATOM C vs C TIE

ON IT.... ⇓ ⇓

C, C, H   C, ~~H~~, H

The (Z)- and (E)- naming is not just for C=C double bonds.......



IMINE

(E)-

BOTTOM

C vs C

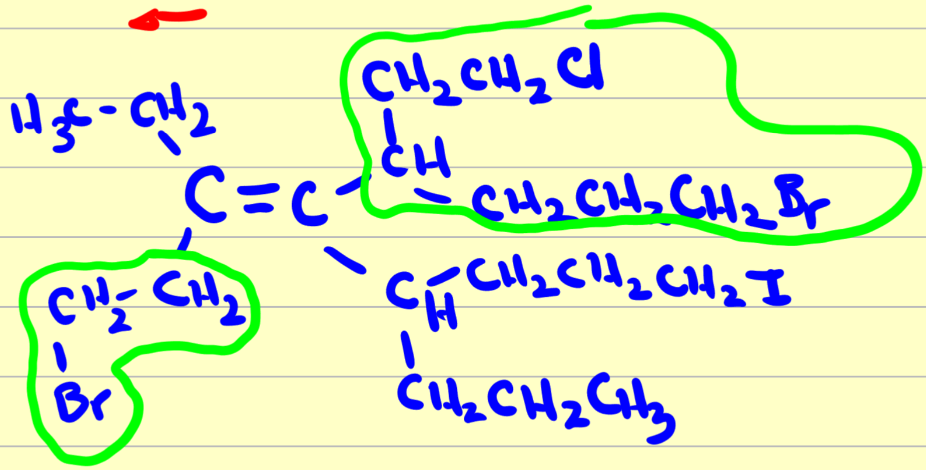
⇓ ⇓

C,H,H H,H,H

TOP ,

: vs C

A more complicated example on Z- vs. E- stereochemistry



LEFT HALF

TOP 1ST C ⇒ C, H, H ⇒ ~~H~~, H, H

BOT. C ⇒ C, H, H ⇒ Br, H, H

RIGHT HALF

TOP C ⇒ C, C, H ⇒ C, H, H ⇒ Cl, H, H

vs.

BOT C ⇒ C, C, H ⇒ C, H, H ⇒ ~~C~~, H, H

∴ THIS IS (E)-

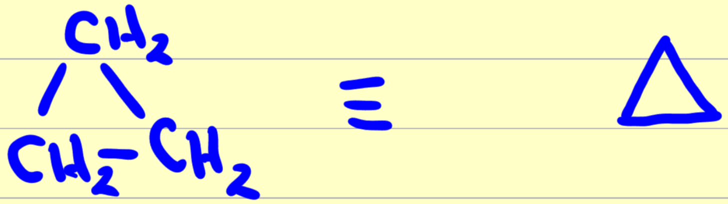
ALICYCLIC COMPOUNDS.

- MANY EXAMPLES OF HYDROCARBONS WHICH ARE CYCLIC

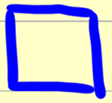
- sp^3, sp^2 VERY COMMON
- sp NOT SO MUCH. - 180° ANGLE IS TOUGH IN SMALL RINGS.

impossible for triple bonds to exist (and be stable) for anything smaller than a cyclooctyne

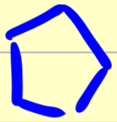
CONSIDER SMALLEST ONE:



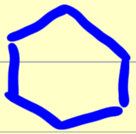
CYCLOPROPANE



CYCLOBUTANE



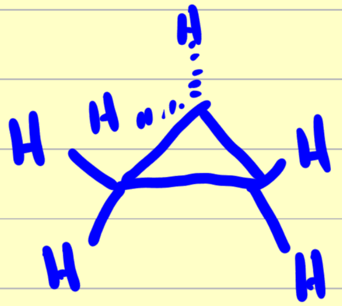
CYCLOPENTANE



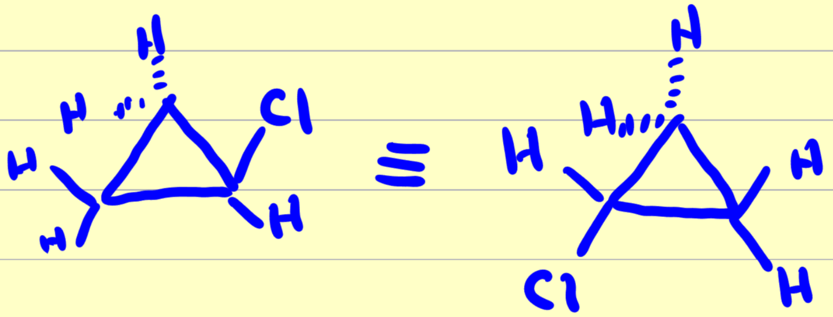
CYCLO- HEXANE

CYCLOPROPANE - KNOWN BUT STRAINED. SINCE sp^3 C'S ARE FORCED TO HAVE C-C-C ANGLES OF 60°

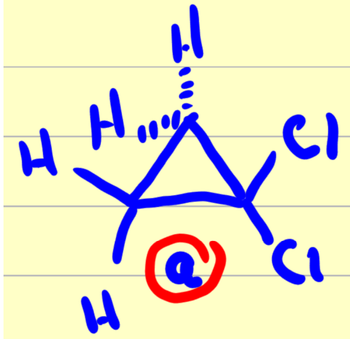
- ALL C ATOMS ARE IN A PLANE



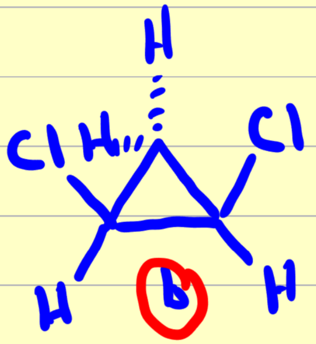
- IF ONE SUBSTITUENT, JUST ONE CPD.



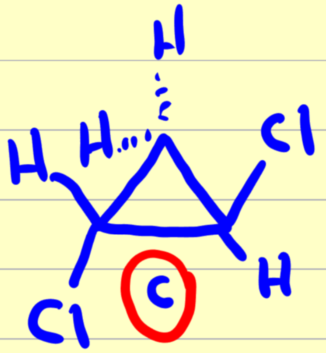
- BUT IF 2-CHLORO GROUPS, 3- POSSIBILITIES



ⓐ



ⓑ



ⓒ

ⓐ IS A STRUCTURAL ISOMER OF THE OTHER TWO (POSITIONAL)

ⓑ, ⓒ ARE STEREOISOMERS OF EACH OTHER

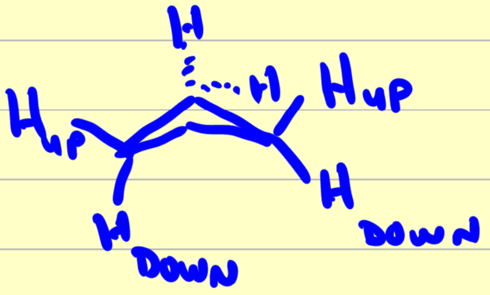
NAMING - THE OLD CIS- AND trans- NAMES ARE USUALLY USED FOR THESE

ⓑ - TWO Cl'S ARE BOTH ABOVE THE PLANE OF THE RING ∴ CIS-

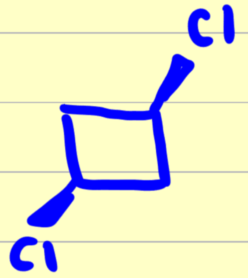
ⓒ - ONE Cl ABOVE, ONE Cl BELOW PLANE ∴ trans-

CYCLOBUTANE, CYCLOPENTANE

- NOT QUITE PLANAR, BUT CONFORMATION CHANGES ARE ESOTERIC



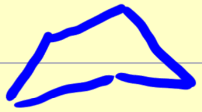
trans- 1,2-



CIS - 1,3-

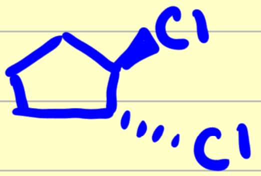
STRAINED ~~&~~ but LESS SO.

C-C-C angles about 88º , so not *as* bad as cyclopropane

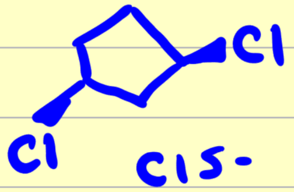


ALMOST UNSTRAINED.

C-C-C bond angles at ca. 104º, only 5.5º off perfection



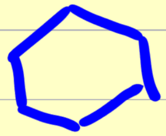
trans-1,2-



cis-1,3-

CYCLOHEXANES

- CONFORMATION WELL UNDERSTOOD, RELIABLE



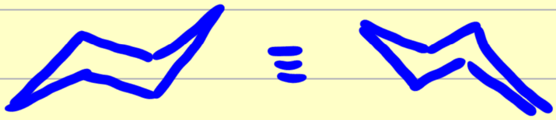
- IF FLAT, 120° BOND ANGLES FOR sp^3 CARBONS.

- MOLECULE CAN DO BETTER

AT CLOSE TO 109.5° (~111° FOR REAL)

- TWO LIMITING POSSIBILITIES

so <u>no</u> angle strain to speak of in simple cyclohexanes



CHAIR

BOAT

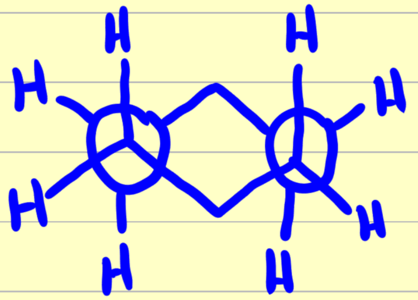
IS IT

CHAIR

OR

BOAT

??



STAGGERED

∴ FAVOURED

ECLIPSED

∴ DISFAVOURED

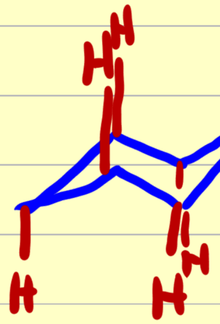
DIFFERENCE IS ~ 6.5 kcal/mol (27 kJ/mol)

- IN FACT, THERE'S A TWISTED BOAT STRUCTURE ACTUALLY BETTER THAN THE BOAT BY ~ 1.5 kcal

- CONCLUSION - WE ONLY HAVE TO WORRY ABOUT CHAIR CONFORMATIONS OF CYCLOHEXANES

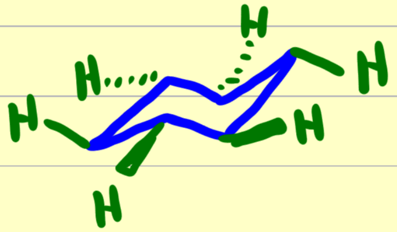
- BOAT WILL EXIST TRANSIENTLY, BUT IT WON'T STAY.

- SUBSTITUENTS ON CYCLOHEXANE
  - TWO TYPES



- ALTERNATE STRAIGHT UP, AND STRAIGHT DOWN.

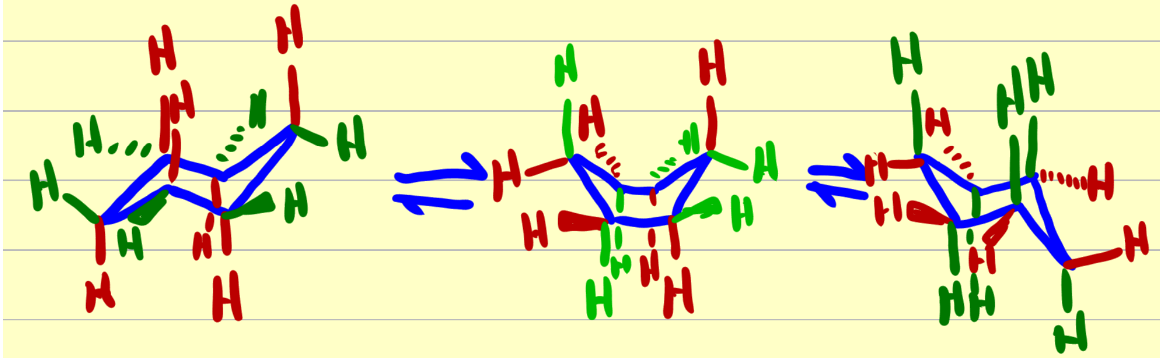
CALLED AXIAL



- ALTERNATING A BIT UP AND A BIT DOWN, BUT MOSTLY NEAR THE AVERAGE 'PLANE' OF CYCLOHEXANE

- CALLED EQUATORIAL.

- THESE ARE EXCHANGING AT ROOM TEMP
  - AXIAL ONES BECOMING EQUATORIAL AND VICE-VERSA

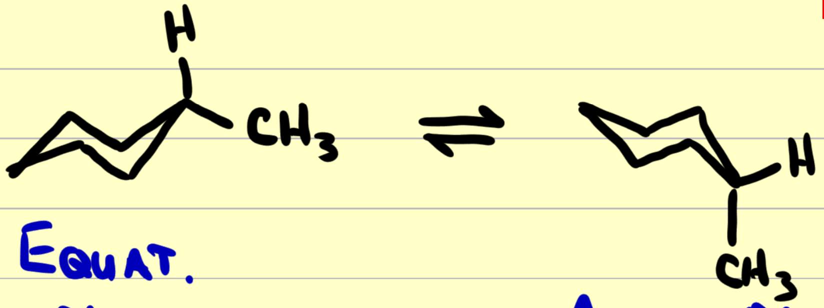


∴ ALL 12 H's IDENTICAL.

(BARRIER 10-11 kcal, 45 kJ/mol)

molecule can easily overcome this at room temperature, so this equilibration is happening >100 times per second

MONOSUBSTITUTED CASES.



EQUAT. METHYL

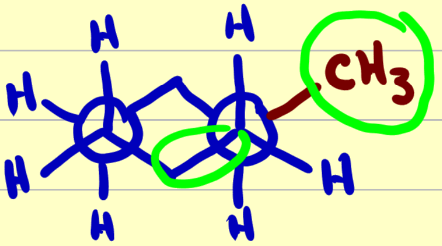
AXIAL METHYL

that's 1.7 kcal/mol

THIS ONE IS MORE STABLE BY 1.7 kcal/mol
(7 kJ/mol) ~20:1 AT RT.

- TWO REASONS.

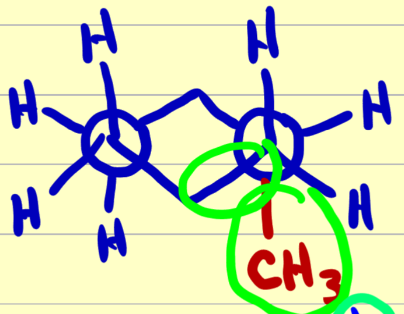
1)



- ANTIPERIPLANAR RELATIONSHIP
  - BEST POSSIBLE

in equatorial conformation

but, in the axial conformation



- SYNCLINAL (OR GAUCHE) RELATIONSHIP
- NOT QUITE AS STABLE

2)

- THERE ARE SLIGHT REPULSIVE 1,3-DIAXIAL INTERACTIONS

-all groups >H in size favour being equatorial, but not to the same degree

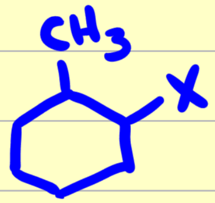
· DIRECTION IS THE SAME, BUT ENERGY DIFFERENCE DEPENDS ON GROUP SIZE

- Br (0.5 kcal/mol) about 2.3:1 at room temp

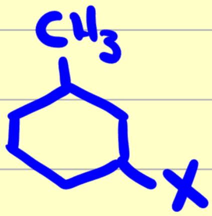
- $C(CH_3)_3$ (4.5 kcal/mol) > 3000:1

∴ THE LARGER THE GROUP, THE MORE IT 'WANTS' TO BE EQUATORIAL.

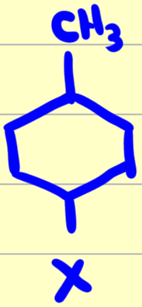
DISUBSTITUTED CYCLOHEXANES



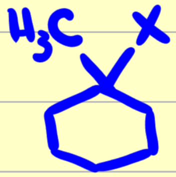
1,2-



1,3-



1,4-



1,1-

2 STEREO-ISOMERS.

2-

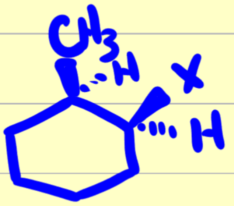
2-

1-

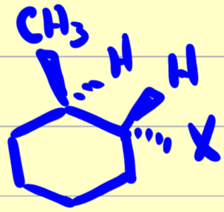
2 stereoisomers each

just one

1,2-DISUBSTITUTED

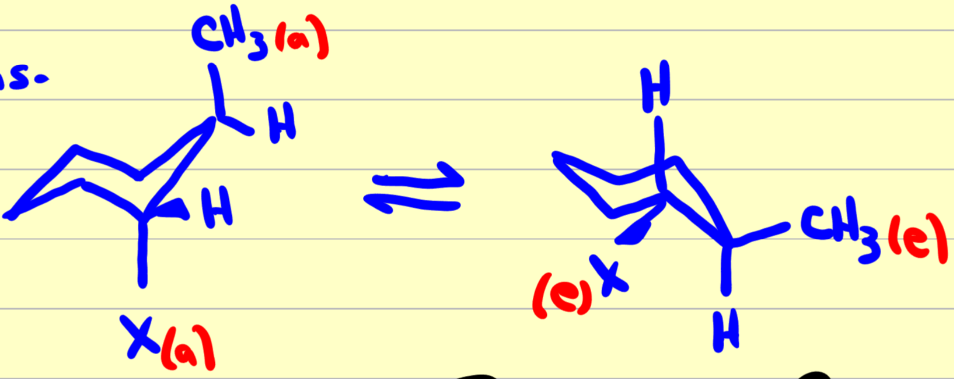


cis 1,2-



trans 1,2-

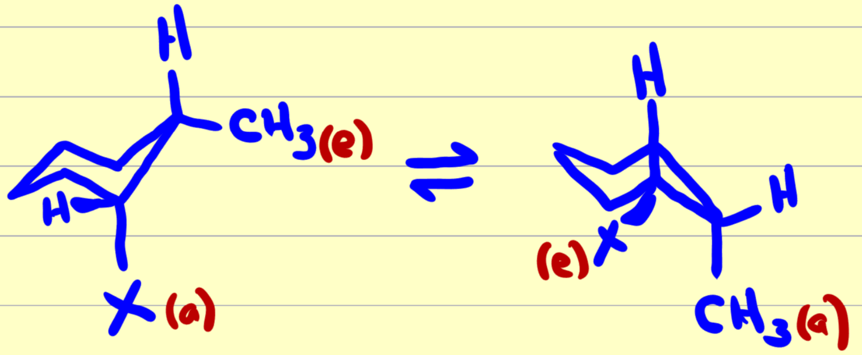
trans-



PREFERRED CONFORMATION

-BOTH GROUPS GET TO BE EQUATORIAL.

CIS-



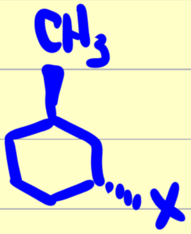
PREFERRED IF $X < CH_3$ IN SIZE

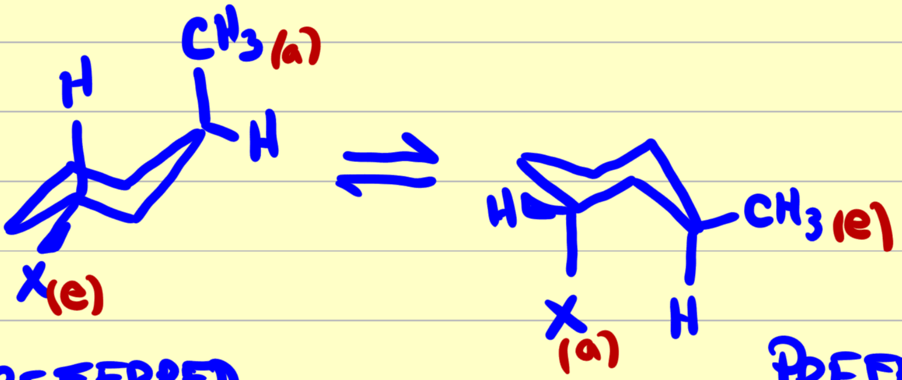
PREFERRED IF $X > CH_3$ IN SIZE

trans- ISOMER IS MORE THERMODYNAMICALLY STABLE, SINCE BOTH CH_3 AND X GET TO BE EQUATORIAL.

1,3-

trans-



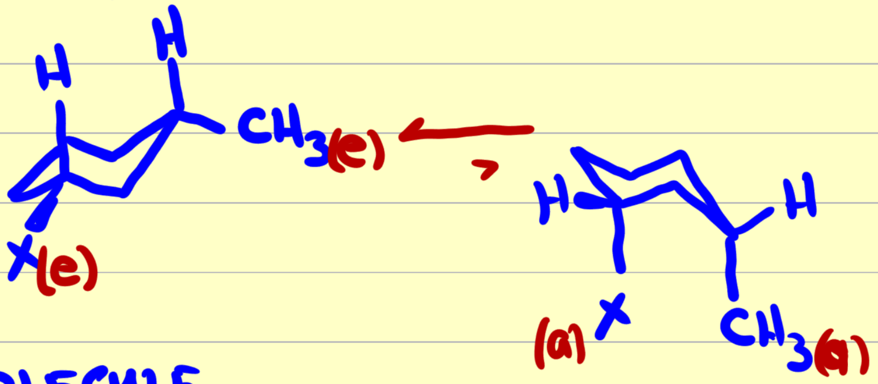


PREFERRED IF $X > CH_3$

PREFERRED IF $X < CH_3$

in size - has nothing to do with 'priority'

1,3- CIS.

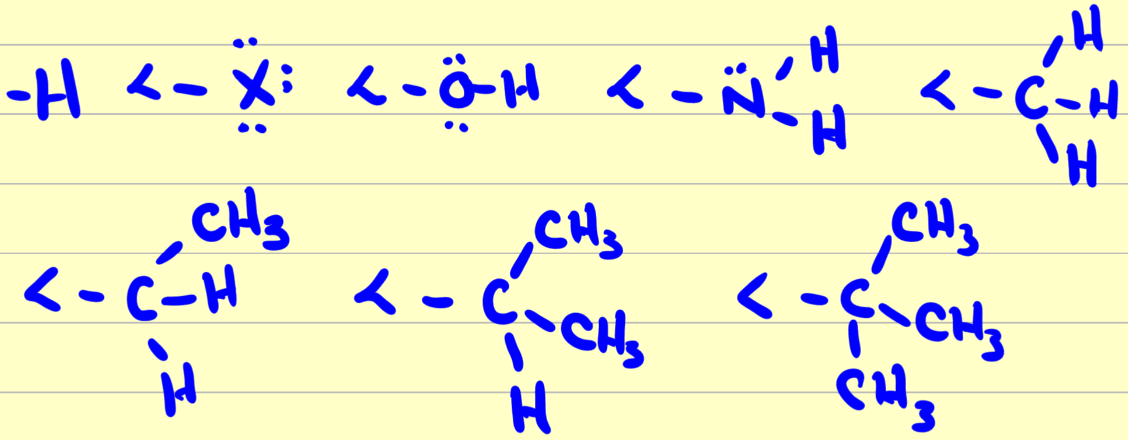


MOLECULE SPENDS "ALL" IT'S TIME HERE (>99.9%)

ACTUALLY MORE STABLE THAN TRANS. ISOMER

1,4- ANALOGOUS TO 1,2-

SO WHAT'S BIG? WHAT'S NOT?



$$-H < -\ddot{X}: < -\ddot{O}-H < -\ddot{N}H_2 < -CH_3 < -CH_2CH_3 < -CH(CH_3)_2 < -C(CH_3)_3$$

-in general, the more groups on the atom, the larger it is

- axial, equatorial - different CONFORMATIONS - CAN INTERCHANGE THESE

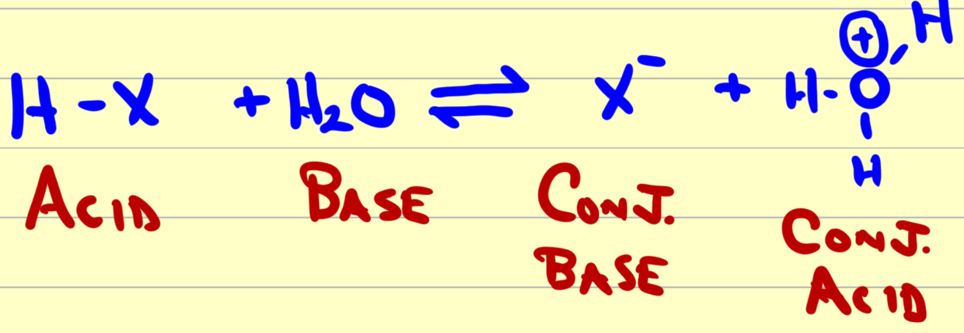
- cis-, trans- different CONFIGURATIONS
  - DO NOT INTERCHANGE

END OF TEST #1.

CHAPTER 4 - SOME FUNDAMENTALS.

ACIDITY

BRONSTED



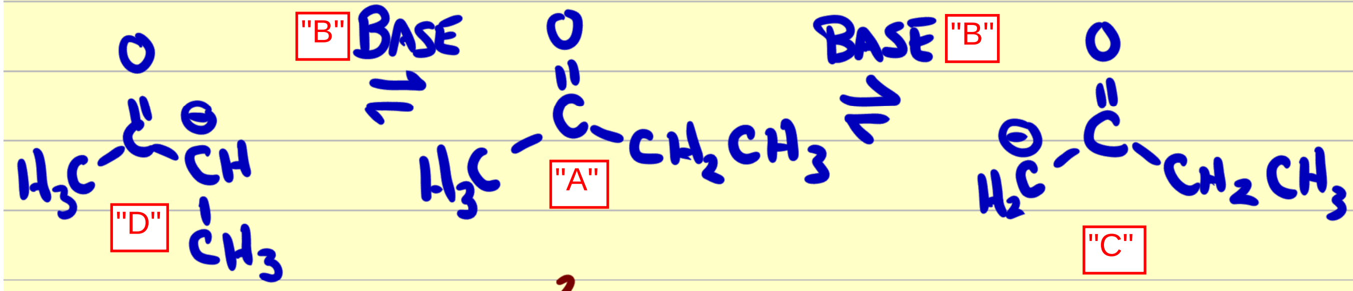
$$H{-}X + H_2O \rightleftharpoons X^- + H{-}\overset{+}{O}H_2$$

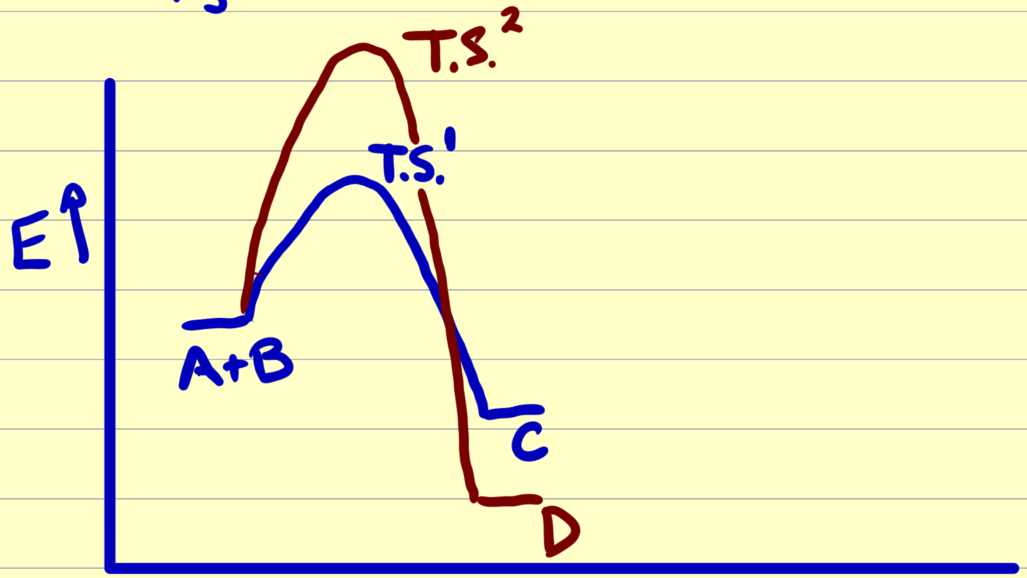
KINETIC CONTROL VS. THERMODYNAMIC CONTROL.

Consider the following generic reaction

$$D \rightleftharpoons A+B \rightleftharpoons C$$

In fact, a real-world example is the alpha deprotonation of ketones, i.e........





TWO SITUATIONS.

1) IF USE MINIMUM CONDITIONS TO GET ANY RXN TO GO. - RXN WILL BE ABLE GET OVER TS' (LOWEST BARRIER) - YOU WILL

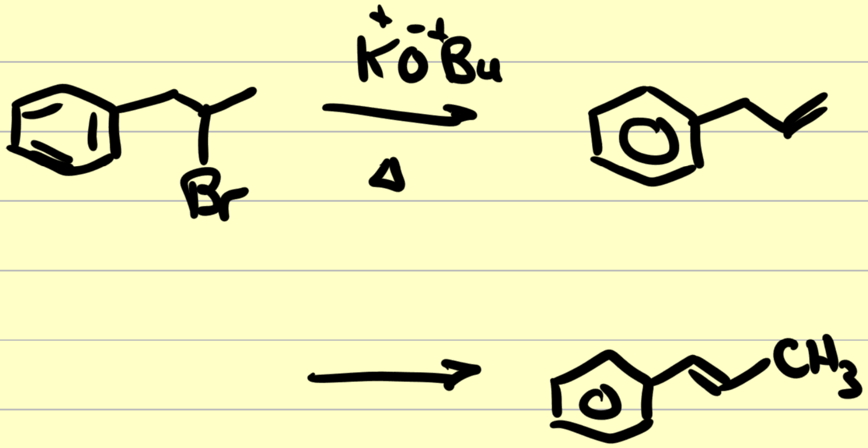
MAKE (MOSTLY) C - OPERATING UNDER

KINETIC CONTROL

ii) IF YOU USE HIGHER T, LONGER RXN TIME, YOU CAN GET BACK OVER T.S.$^{-1}$ TO A+B, AND OVER T.S.^{2}, TO GET D

∴ PRODUCTS WILL SIMPLY REFLECT ENERGIES OF MATERIALS - WILL GET D MOSTLY

THERMODYNAMIC CONTROL



OK, come to think of it, this pair isn't a perfect example

RATE DETERMINING STEP

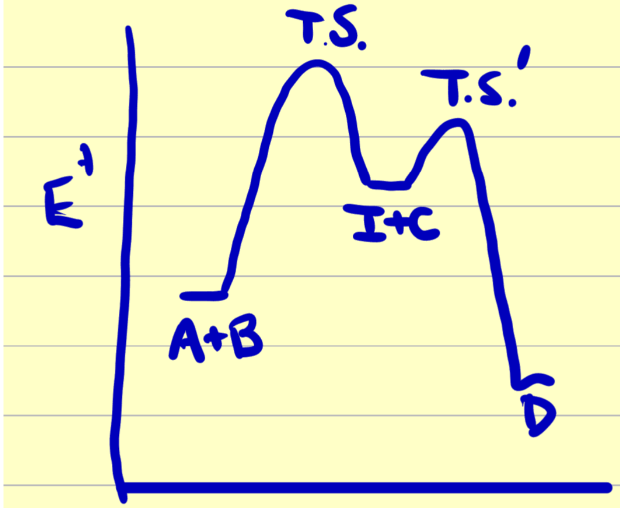
$A + B + C \longrightarrow D.$

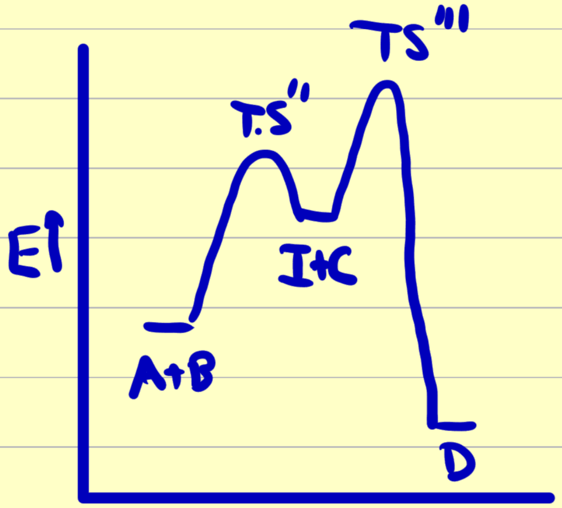
MECH There is >1 possible mechanism for this process, but a reasonable one would be......

$A + B \rightleftharpoons I$ (INTERMEDIATE)

$I + C \rightleftharpoons D.$

-possible energy profiles could be....





$\text{rate} = k[A][B]$

2^{ND} ORDER OVERALL

1^{ST} STEP IS SLOW

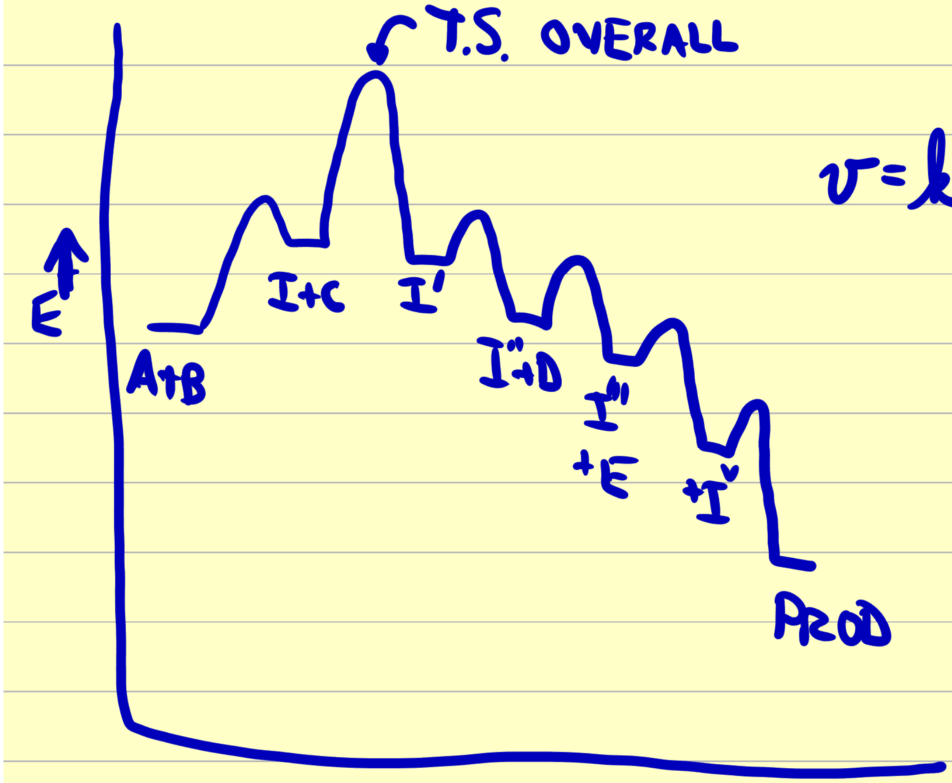
(RATE DETERMINING)

$\text{rate} = k'[A][B][C]$

3^{RD} ORDER OVERALL

2^{ND} STEP (r.d.s)

-situations can be far more complex, than above, i.e.,



$$v = k[A][B][C]$$

ONLY REAGENTS APPEARING BEFORE SLOWEST STEP APPEAR IN RATE EQN.

NUCLEOPHILES, ELECTROPHILES.

NUCLEOPHILE- ATOM OR GROUP OF ATOMS THAT BRING AN ELECTRON PAIR INTO A REACTION - EMPHASIS IS ON KINETICS

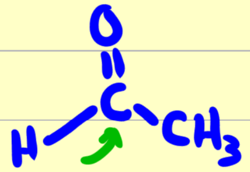
$Br^{\ominus}$, $I^{\ominus}$, , $Cl^{\ominus}$, $HO^{\ominus}$, $H_3N:$, 

- ALWAYS A POTENTIAL BASE, BUT NOT NECESSARILY A GOOD BASE

ELECTROPHILE - ATOM OR GROUP OF ATOMS THAT IS ATTACKED BY A NUCLEOPHILE

- e^- DEFICIENT IN SOME WAY.

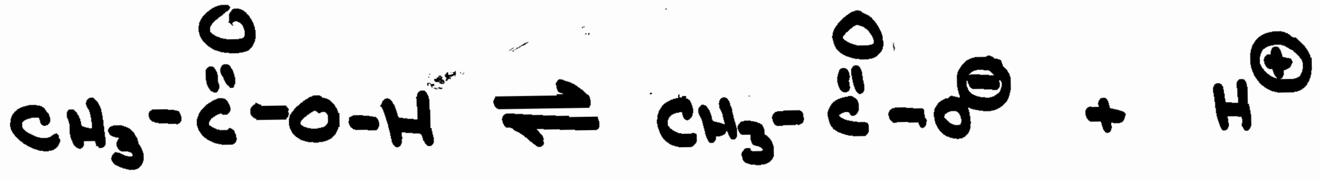
Br^+, $^+CH_3$, CH_3-Cl,



ELECTRONIC EFFECTS.

- EFFECT OF GROUPS ON STABILITY, OF ANIONS, CATIONS, RADICALS.

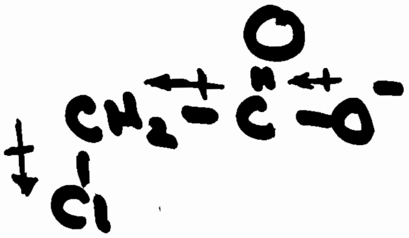
FOR EXAMPLE



$$CH_3-\overset{\overset{O}{\|}}{C}-O-H \rightleftharpoons CH_3-\overset{\overset{O}{\|}}{C}-O^{\ominus} + H^{\oplus}$$

$pK_a \approx 4.8$

IF WE REPLACED ONE H BY AN ELECTRONEGATIVE GROUP.

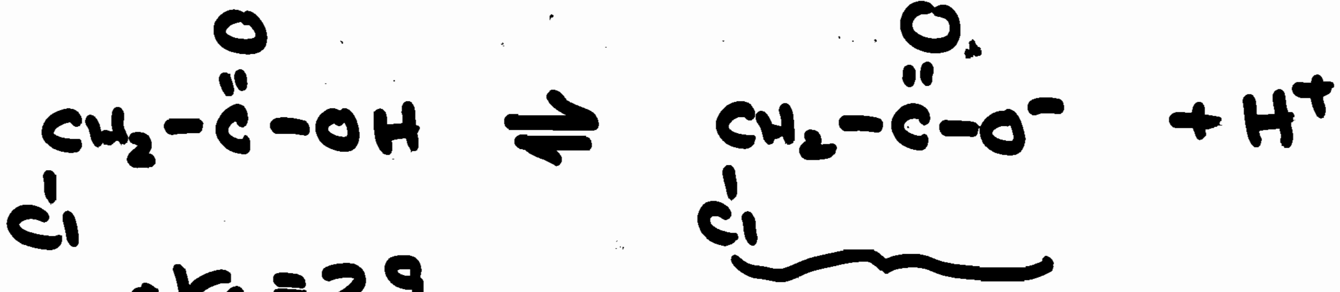


$$\underset{Cl}{\underset{|}{CH_2}}\leftarrow\overset{\overset{O}{\|}}{C}\leftarrow O^-$$

- ELECTRONEG. GROUP IS PULLING ELECTRON DENSITY FROM THE ADJACENT CARBON

- THAT CARBON IS ∴ A BIT e^- DEFICIENT, SO *IT* PULLS e^- DENSITY FROM CARBON ATTACHED

ULTIMATELY, THAT O^- IS HAVING ITS "−" CHARGE RELIEVED A BIT — THAT IS STABILIZING



$$\underset{Cl}{CH_2}-\overset{\overset{O}{\|}}{C}-OH \rightleftharpoons \underbrace{\underset{Cl}{CH_2}-\overset{\overset{O}{\|}}{C}-O^-}_{\text{STABILIZED.}} + H^+$$

$pK_a = 2.9$

STABILIZED.

OCCURS THROUGH σ BONDS

CALLED INDUCTIVE (THROUGH BOND) EFFECT −I

↑ WITHDRAWING e^- DENSITY INDUCTIVELY

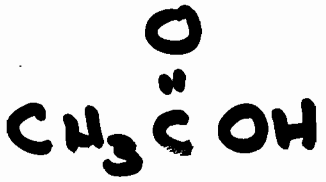
−I GROUPS F, Cl, OH, NH_2

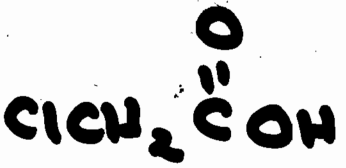
STABILIZE ANIONS.

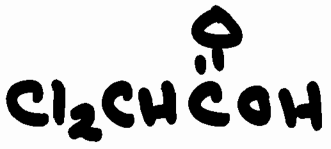
DESTABILIZE CATIONS.

(+I GROUPS ALKYL GROUPS $-CH_3$, CH_2CH)

↳ DONATING INDUCTIVELY.

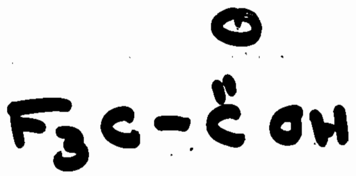

$CH_3C(=O)OH$


$ClCH_2C(=O)OH$


$Cl_2CHC(=O)OH$

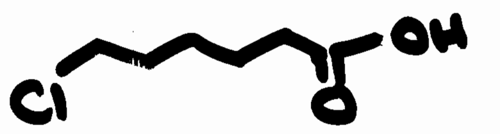
pKa 4.8 2.9 1.3

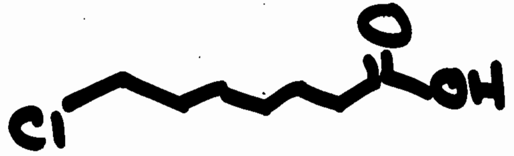

$Cl_3C-C(=O)-OH$


$F_3C-C(=O)OH$

0.5 0.2

EFFECT DOES DROP OFF RAPIDLY THROUGH 4 σ BONDS MAXIMUM.





NOT MUCH CHANGE IN THESE

- ALSO CALLED <u>FIELD</u> EFFECTS.

RESONANCE EFFECTS.

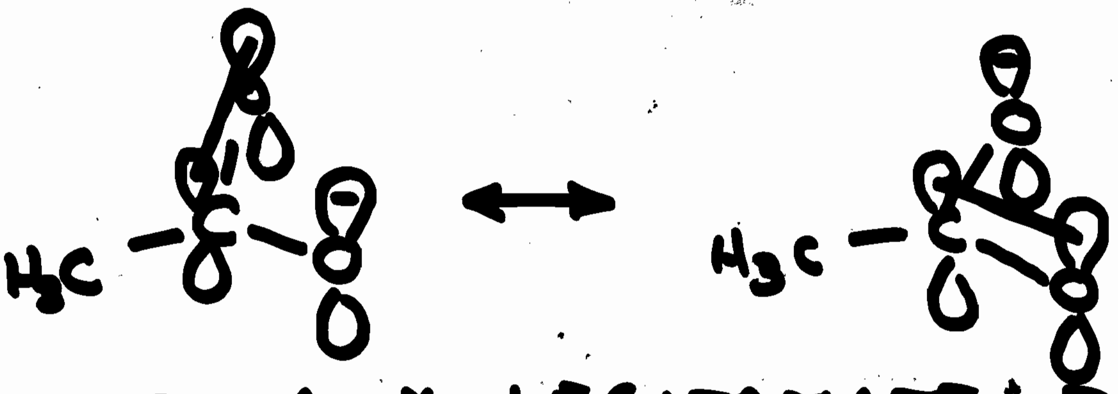

$CH_3C(=O)-OH$

CH_3CH_2OH

pKa ≈ 4.8 pKa ≈ 16.5

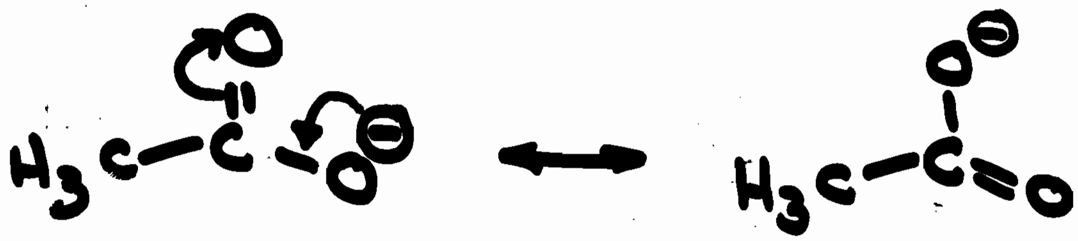
HUGE DIFFERENCE

- DUE TO π SYSTEM OF CARBONYL



EQUALLY LEGITAMATE DESCRIPTIONS OF ELECTRONIC DISTRIBUTION

p- ORBITAL OVERLAP PERFECTLY



EACH O ATOM IS − ½ CHARGED

- TREMENDOUSLY STABILIZING

- OFTEN MUCH MORE POWERFUL THAN INDUCTIVE EFFECT

POINTS.

1) THESE ARE NOT TWO RAPIDLY EQUILIBRATING SPECIES, IT'S ONE SPECIES WHOSE ELECTRONIC DESCRIPTION IS A WEIGHTED AVERAGE

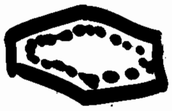
2) ↔ ARROW IS RESERVED FOR RESONANCE FORMS.

→	⇌	⇆	⇝	↔
RXN	RXN	RXN	INFORMAL	RESONANCE FORMS

ULTIMATE CASE

BENZENE

REALLY



36 kcal/mol STABILIZATION.

RULES:

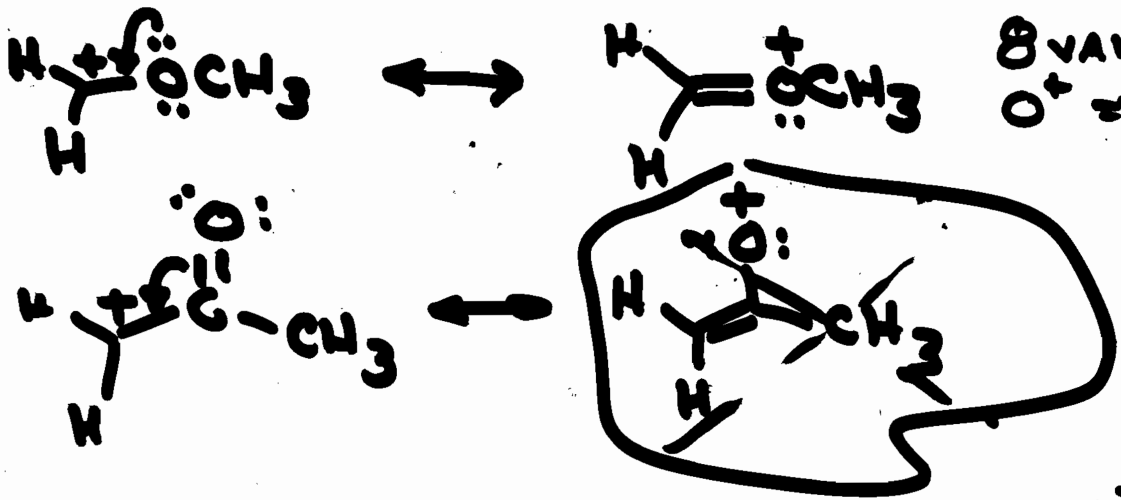
1) INVOLVES π- SYSTEM.

2) -IF YOU CAN PUT A "−" CHARGE ON AN ELECTRONEGATIVE ATOM, THAT'S ESPECIALLY GOOD.

3) -IF YOU PUT A "+" CHARGE ON AN ELECTRONEGATIVE ATOM

-IF 8 VALENCE e^-'S $\Rightarrow$ OK

-IF 6 VALENCE e^-S ⇒ NO WAY



8 VALENCE e^-
O^+ ⇒ OK

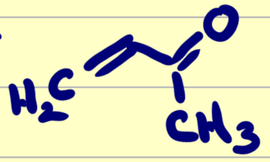
No!

6 VALENCE e^- O^+
NO!!!

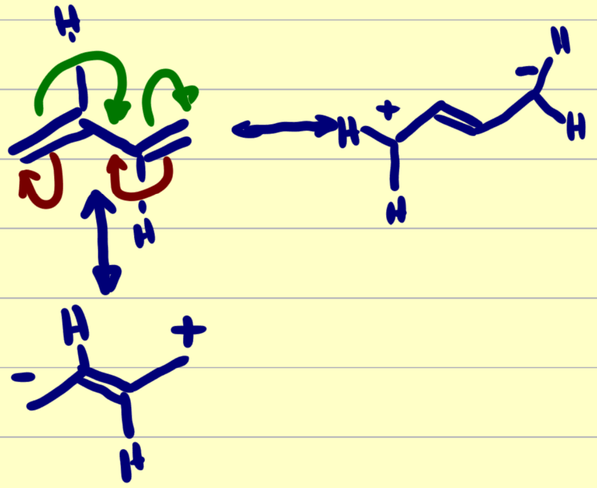
RESONANCE FORMS

- WHEN ARE THEY DRAWN?

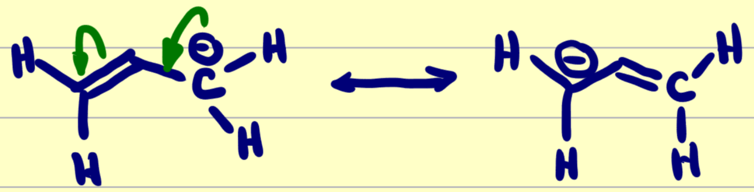
1)



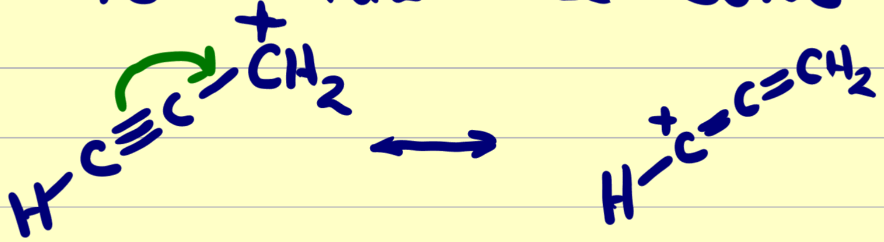
- TWO MULTIPLE BONDS SEPARATED BY A SINGLE BOND.



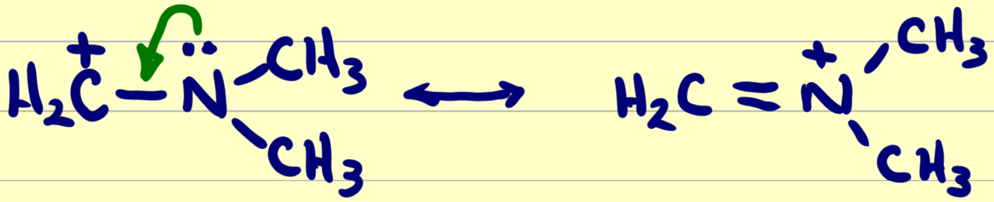
2) IF YOU HAVE A (LONE) PAIR OF ELECTRONS ON AN ATOM NEXT TO A MULTIPLE BOND

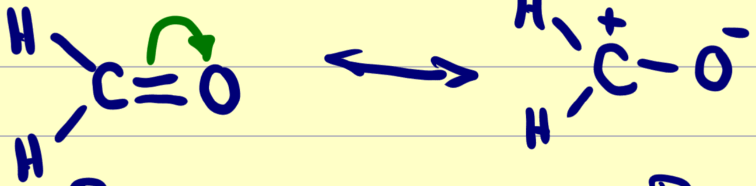


3) WHERE YOU HAVE AN ATOM WITH AN EMPTY p-ORBITAL (CATION) NEXT TO A MULTIPLE BOND



4) WHERE THERE'S A CATION IMMEDIATELY NEXT TO A LONE PAIR





POLARIZED MULTIPLE BOND

CHAPTER 5 - CHEMISTRY OF HYDROCARBONS.

ALKANES	ALKENES	ALKYNES
ALMOST 0	A WHOLE LOT	A FEW LESS

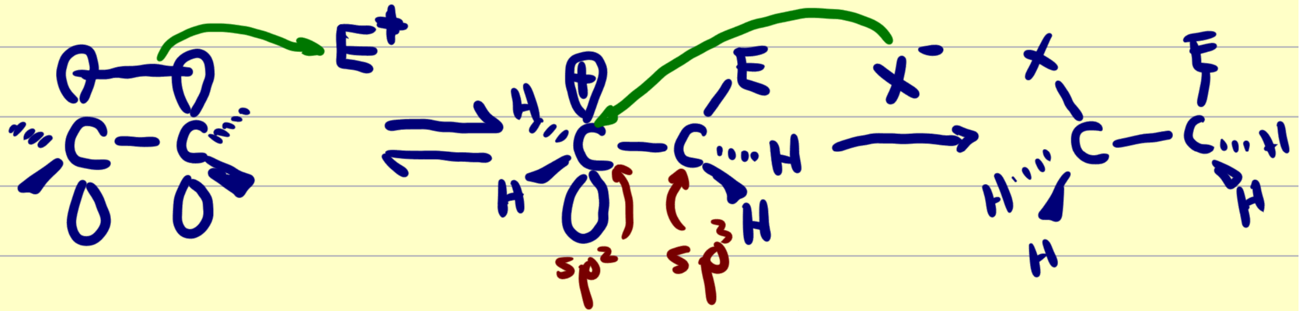
ALKENES - A BUNCH OF σ BOND AT ~ 84 kcal/mol

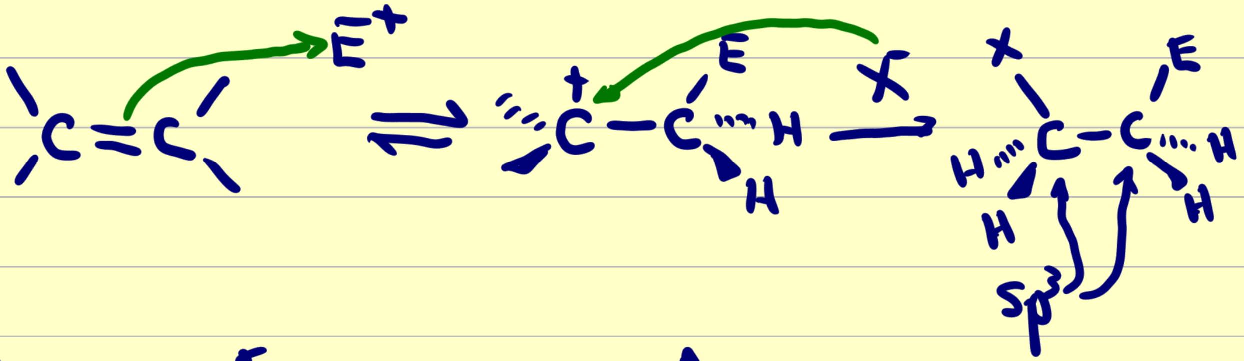
\+ ONE BOND AT ~64 kcal/mol

π BOND. - e^-'S ARE EASIER TO "GET AT"

- THIS MEANS "NUCLEOPHILE"

- SO LIKELY TO REACT WITH ELECTROPHILES

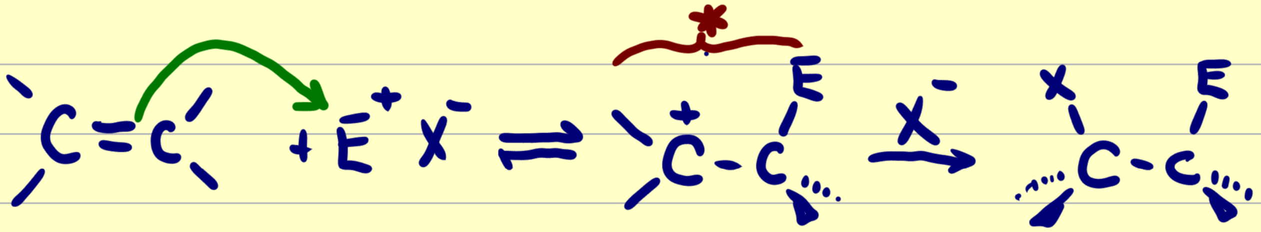




CALLED ELECTROPHILIC ADDITION REACTION

WHAT'S E^+X^- ?

HBr HCl Br_2 Cl_2 I-Cl H_2O^*



ELECTROPHILIC ADDITION

*- CALLED A CARBOCATION

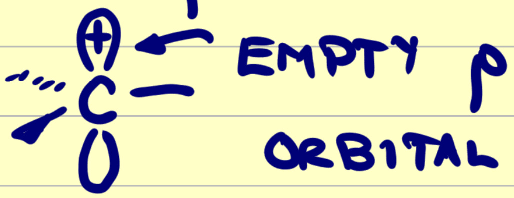
(CARBENIUM ION)

~~(CARBONIUM ION)~~ - OUTDATED

there is another species that is now properly called a carbonium ion

· 6 VALENCE e^-, C^+, sp^2 HYBRIDIZED

∴ PLANAR



E^+X^- $\overset{+}{H}\overset{-}{Cl}$, HBr, Br_2, Cl_2, ICl, H_2O^*

WHY NOT $\overset{+}{Na}\overset{-}{Cl}$ - TOTALLY UNREACTIVE

Na^+ - SIMPLY TOO STABLE AS THE CATION

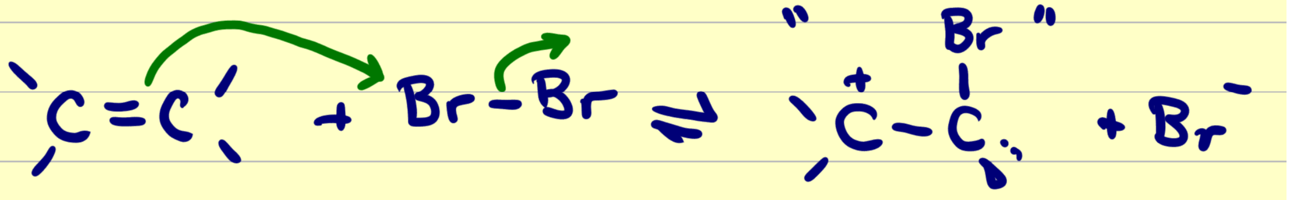
WHY NOT CH_3-Cl ON ITS OWN?

- $\overset{+}{C}H_3$ NOT STABLE ENOUGH,

NO AMOUNT OF IT IN SOLUTION

H^+ - VERY GOOD - BOTH REASONABLE CONCENTRATION. AND REACTIVE ENOUGH TO DO SOMETHING.

Br_2 AND Cl_2 REAL ANSWER FOR HOW THESE ARE E^+



OK TO WRITE

$$Br-Br \longleftrightarrow Br^+ \, Br^-$$

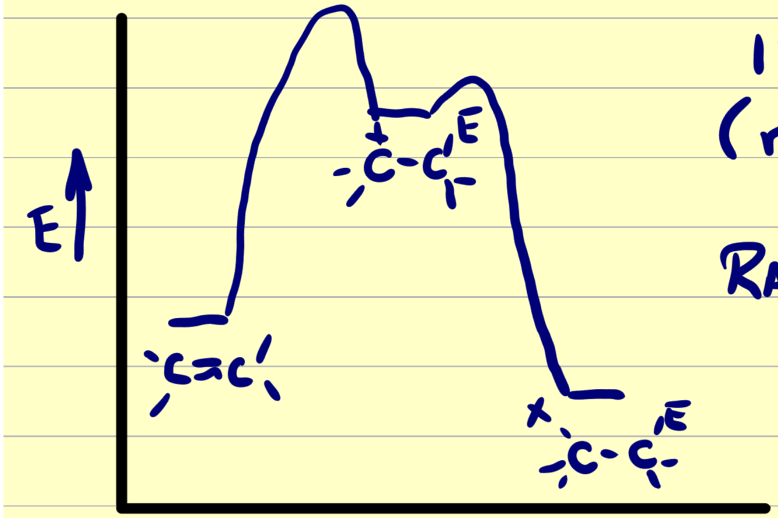
TWO STEPS - WHICH IS RATE DETERMINING (?

1^{ST} - STEP - DOING THE TOUGH THING - MAKING A PRETTY HIGH ENERGY CARBOCATION - SLOW STEP.

2^{ND} STEP - $-\overset{|}{\underset{|}{C}}{}^{+} + X^- \longrightarrow -\overset{|}{\underset{|}{C}}-X$

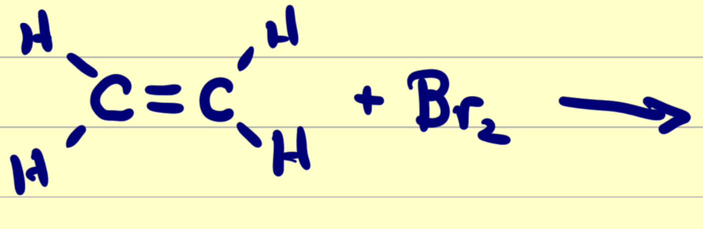
- OPPOSITELY CHARGED SPECIES

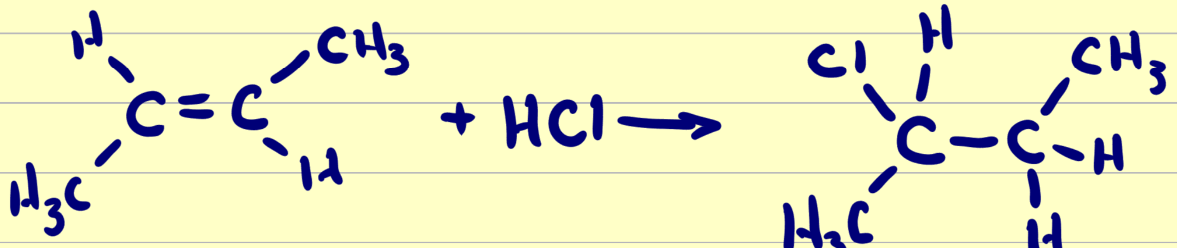
COMBINING TO GET A NEUTRAL - SHOULD BE REALLY FAST

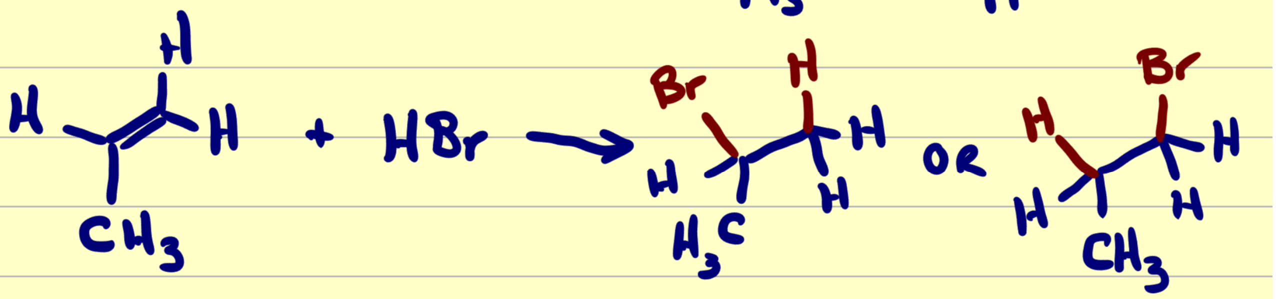


1ST STEP IS SLOW (rds)

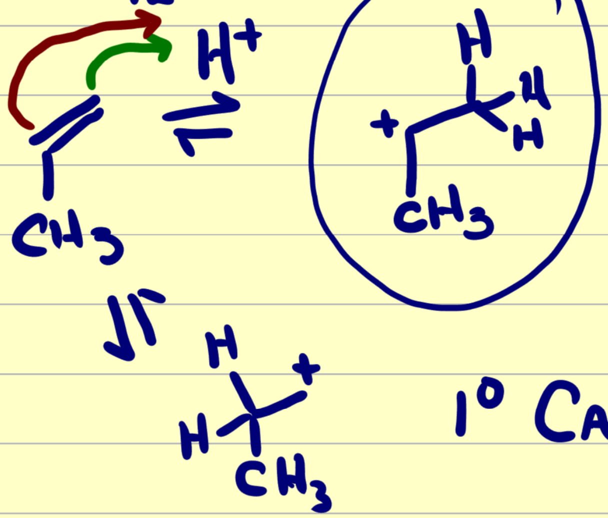
RATE $v = k[E^+][C=C]$







1ST STEP



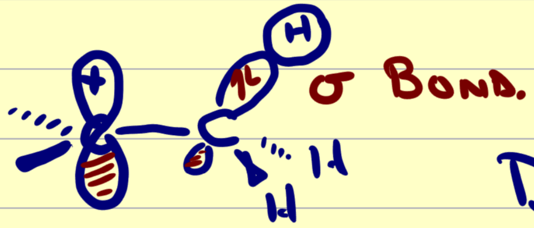
2° CARBOCATION

1° CARBOCATION

- WHICH IS MORE STABLE ?

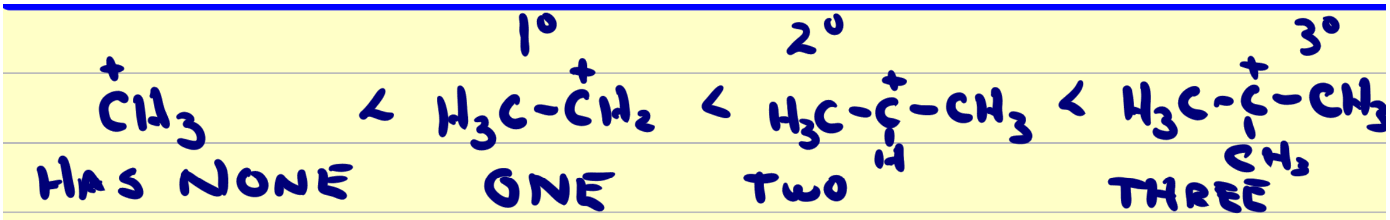
1) ALKYL GROUPS ARE +I
∴ STABILIZE CATION.

2)



- THIS σ BOND IS ALIGNED TO DONATE e^- DENSITY TO THE CATION
∴ STABILIZATION

CALLED HYPERCONJUGATION.

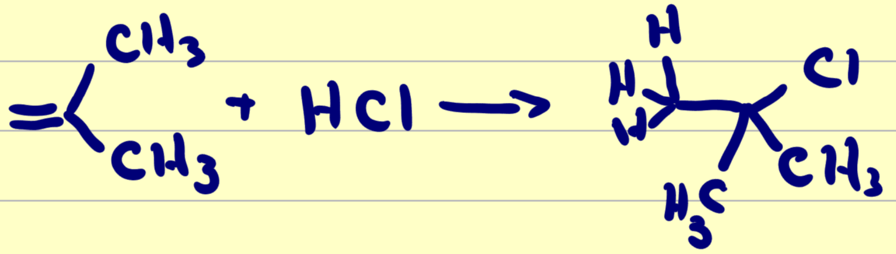


$\overset{+}{C}H_3 < H_3C-\overset{+}{C}H_2 < H_3C-\underset{H}{\overset{+}{C}}-CH_3 < H_3C-\underset{CH_3}{\overset{+}{C}}-CH_3$

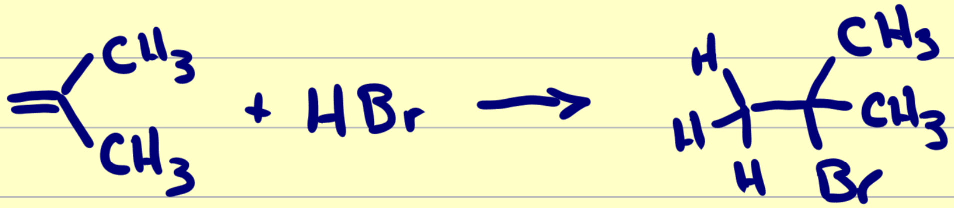
WE MUST ADD THIS TO HAMMOND POSTULATE

- TRANSITION STATE MOST CLOSELY RESEMBLES THE SPECIES IT'S CLOSEST TO IN ENERGY

∴ RATE OF FORMATION 3° > 2° > 1°



MARKOVNIKOV'S RULE



MARKOVNIKOV'S RULE

DEFN: THE POSITIVE PORTION OF THE REAGENT GOES TO THE SIDE OF MULTIPLE BOND THAT HAS THE MOST HYDROGENS

- IN SIMPLE CASES FOR E^+X^- ADDN.

E ENDS UP ON LESS SUBSTIT. C

X ENDS UP ON MORE SUBSTIT. C

ADDITION OF H_2O, AND CATALYSIS.

 + H_2O ⟶ NOTHING.

PROBLEM E^+ IS H^+

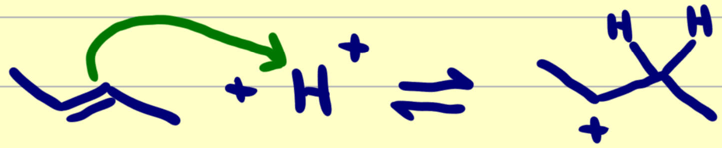
$H_2O \rightleftarrows H^+ + {}^-OH$

$[H^+] = 10^{-7}$ M TINY.

∴ TOO SLOW

- FIX THIS BY ADDING H^+

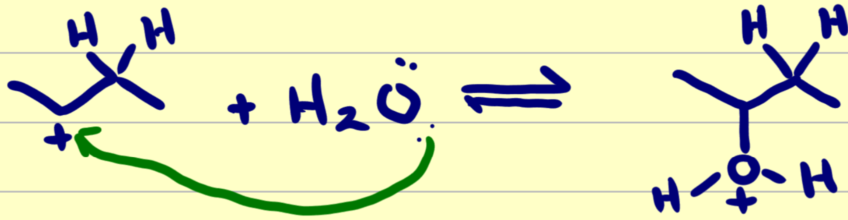
- WILL USE 10% H_2SO_4 (1.9 M)



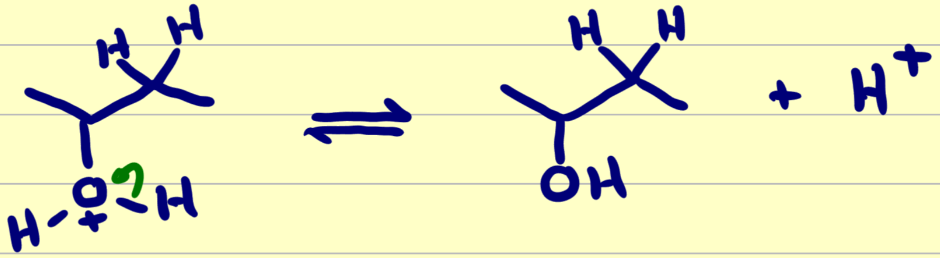
NOW $[HO^-]$ IS SMALL 5.3×10^{-15} M

BUT WE HAVE $H_2\ddot{O}$ PRESENT

- NOT A GREAT NUCLEOPHILE, BUT GOOD ENOUGH AND IT'S 55 M



AND THEN THIS LOSES H^+



POINTS 1) H^+ IS A CATALYST

- SPED UP THE REACTION BY GIVING THE PROCESS A DIFFERENT, 'EASIER' MECH.

2) REGENERATED AT THE END.

WHY NOT HSO_4^- AS X^- ?

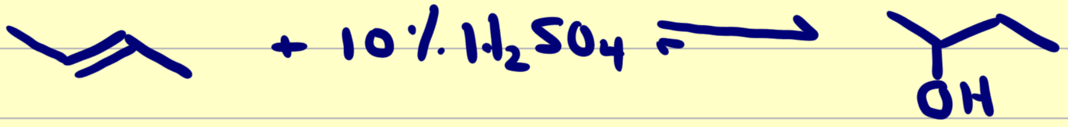
- IT'S SO STABLE THAT IT'S A POOR NUCLEOPHILE.

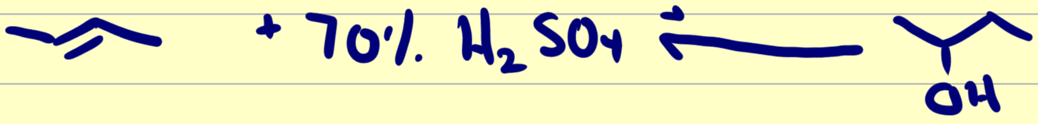
3) 10% H_2SO_4, NOT 70% H_2SO_4

BECAUSE

$$H_2\ddot{O}{:} + H_2SO_4 \rightleftharpoons H{-}\overset{+}{O}H_2 + HSO_4^-$$

YOU'RE NUCLEOPHILE IS GONE

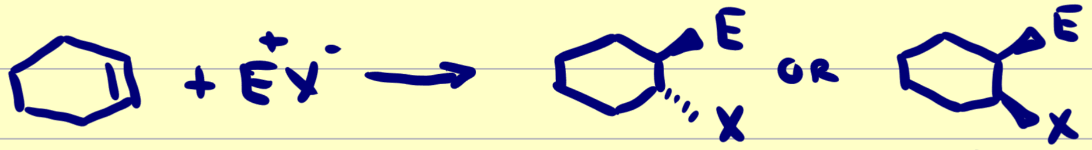




- 70% H_2SO_4 DOES ELIMINATION RXN. OF THE ALCOHOL.

- SAME MECHANISM, OPPOSITE ORDER OF STEPS.
  - PRINCIPLE OF MICROSCOPIC REVERSIBILIT

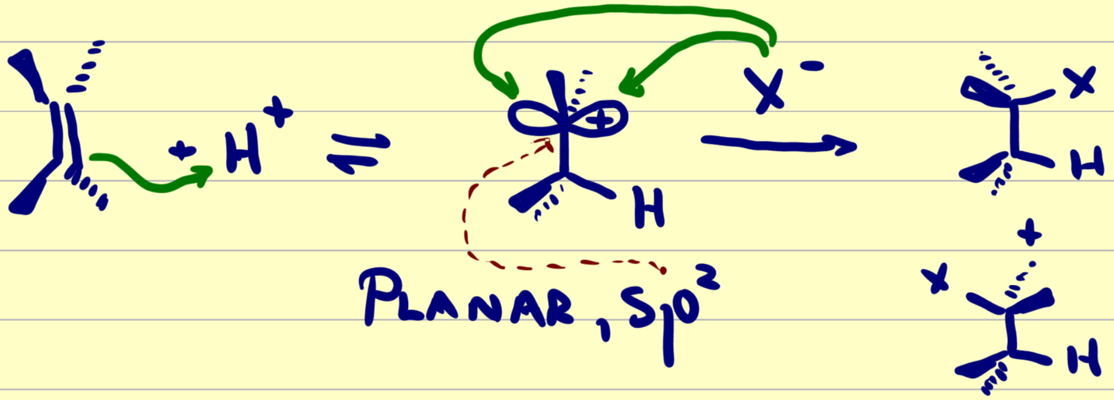
STEREOCHEMISTRY OF ADDITION



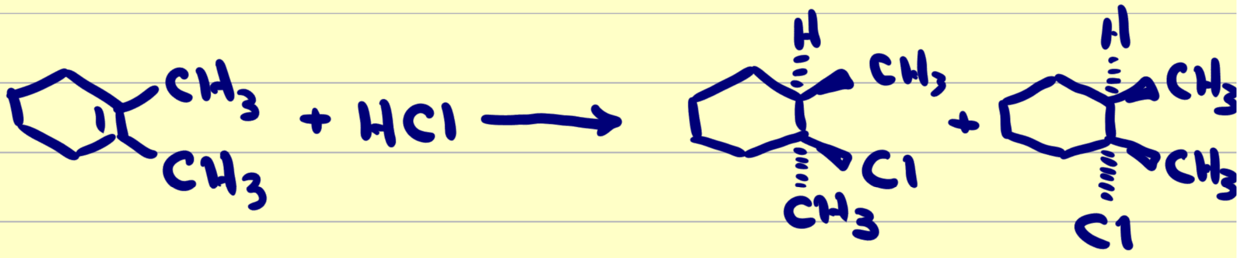
OR BOTH?

ANSWER - IT DEPENDS. - TWO SITUATIONS.

1) MOST COMMON - WHEN $E^+ = H^+$



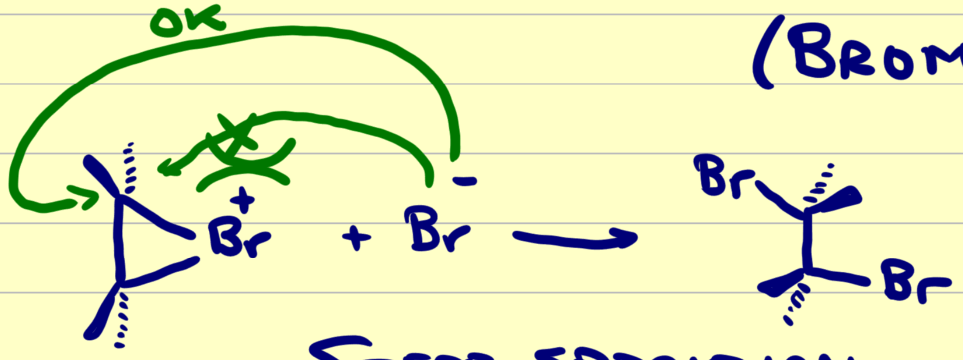
EITHER FACE OF CATIONIC CENTRE IS ACCESSIBLE - GET STEREOCHEMICAL MIXTURE OF CIS + TRANS- ADDN



- MIX OF BOTH.

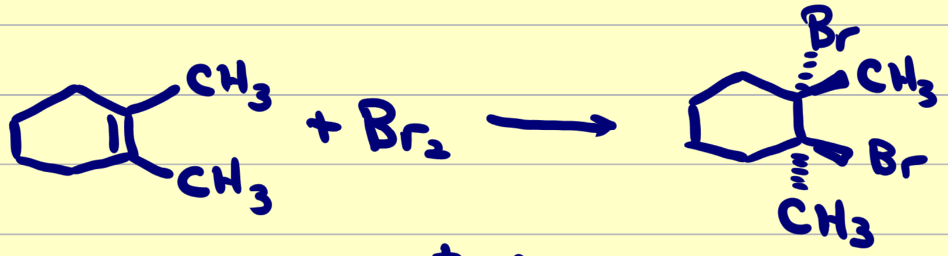
2) IF E^+ IS "Br^+", "Cl^+", "I^+"
(Br_2), (Cl_2), (ICl)

HALONIUM ION
(BROMONIUM)



TRANS ADDN.

STEREOSPECIFICALLY TRANS



- REASON - E^+ HAS A LONE PAIR

∴ CATION IS ACTUALLY CYCLIC

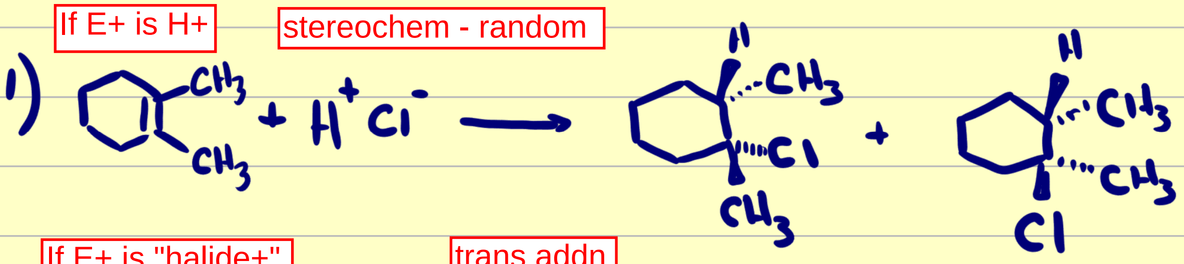
∴ ONLY ONE 'FACE' OF CATION IS UNBLOCKED FOR ATTACK BY X^-

Quick review - stereochemistry of electrophilic addition reactions

If E+ is H+

stereochem - random

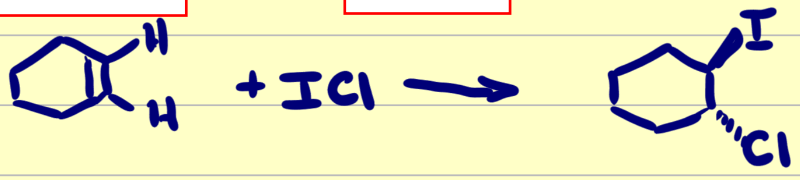
1)



If E+ is "halide+"

trans addn

2)

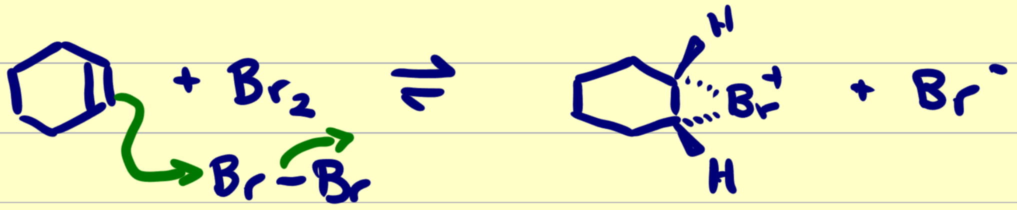


INTERVENTION OF SOLVENT.

- TRADITIONAL SOLVENTS CCl_4, CH_2Cl_2
  - GOOD SOLVENTS, NOT AT ALL NUCLEOPHILIC - DON'T INTERFERE

- WHAT IF SOLVENT IS NUCLEOPHILIC? i.e. H_2O (OR CH_3OH).

1)



2) 2 NUCLEOPHILES PRESENT a) Br^-

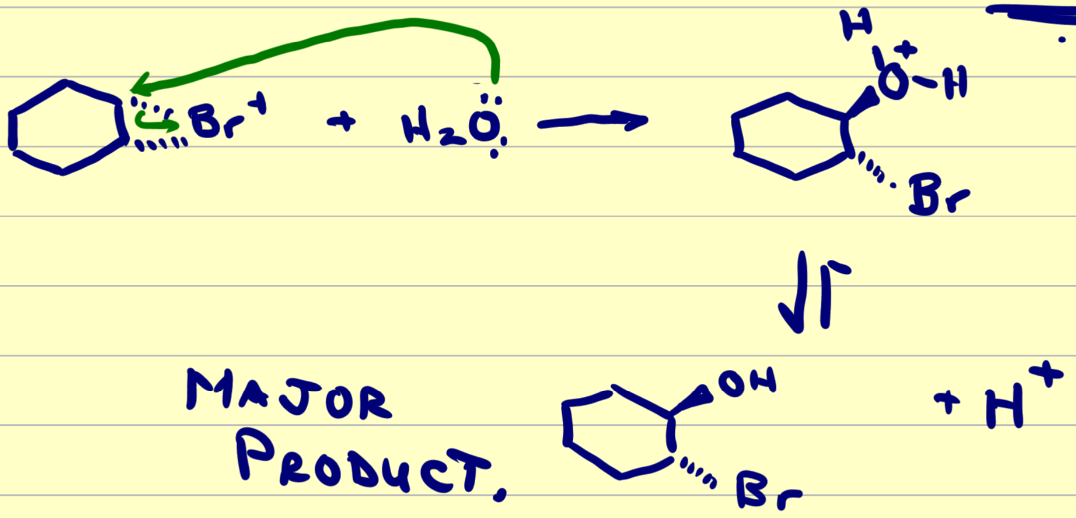
b) $H_2\ddot{O}$:

CONSIDERATIONS

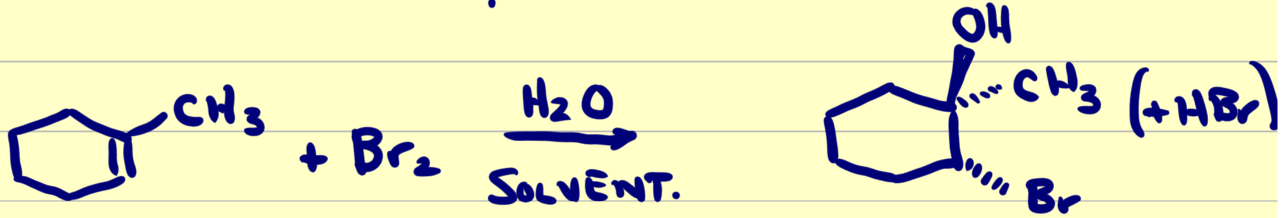
i) REACTIVITY OF X^- $Br^- > H_2\ddot{O}$

ii) CONCENTRATION OF X^- $[H_2O]/[Br^-] > 500$

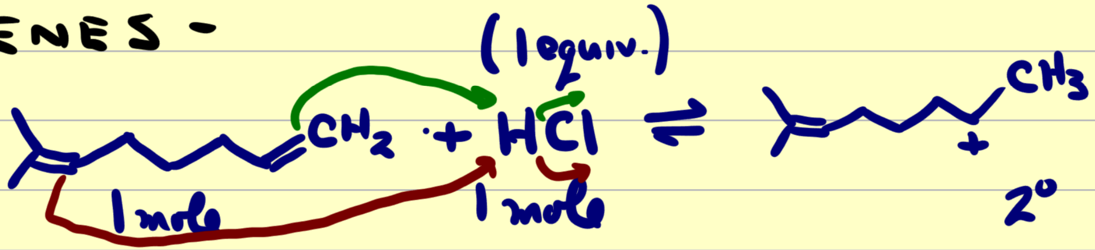
iii) REACTIVITY OF CATION - VERY HIGH, LOOKING FOR ANYTHING. - $\underline{H_2O}$

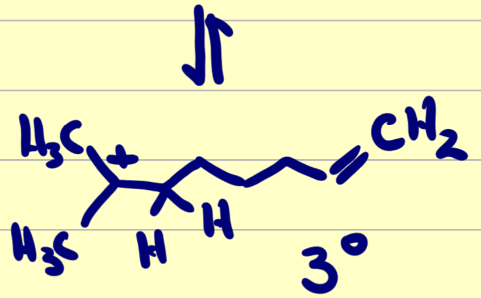


NOTE: MARKOVNIKOV'S RULE DOES STILL HOLD.

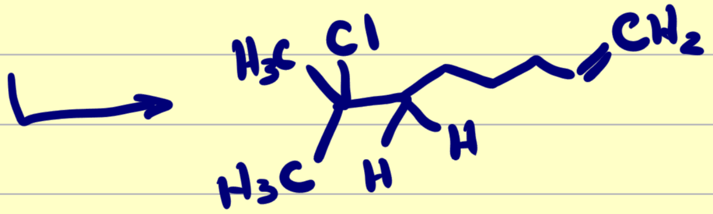


DIENES -

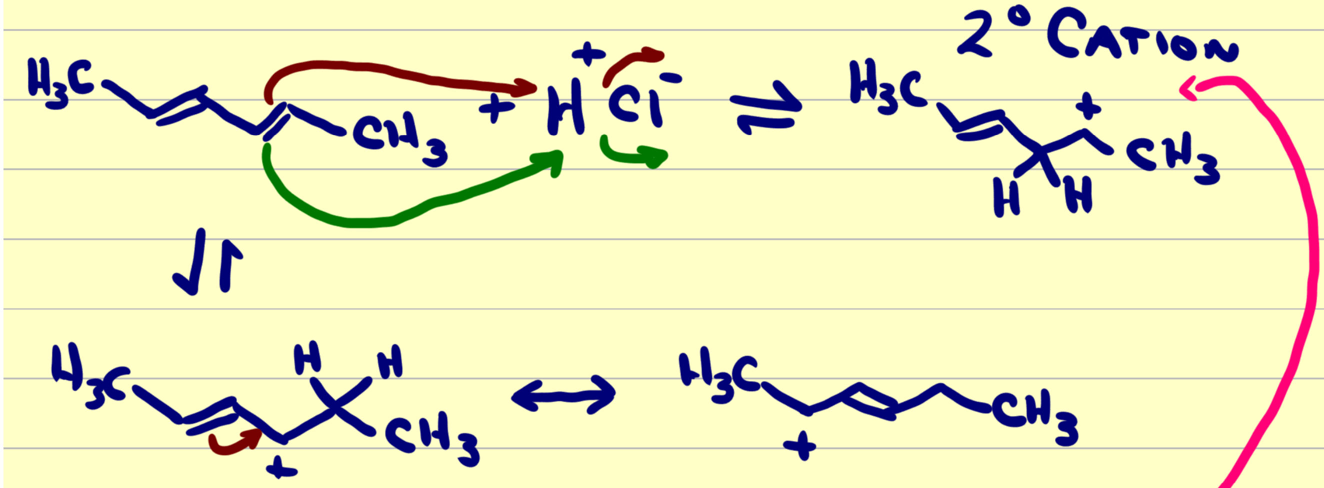




THIS IS FORMED PREFERENTIALLY



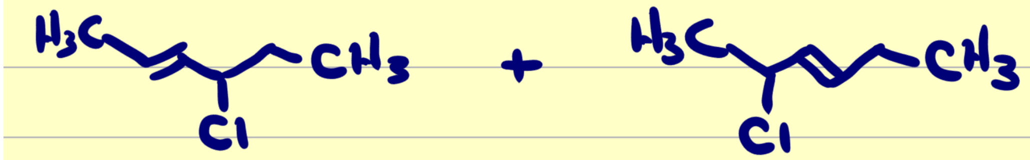
CONJUGATED DIENES.



2° + ALLYLIC - FAR MORE STABLE THAN

- ONLY ONE FORMED

Cl⁻ - BUT IT HAS 2 ATTACK SITES



- AT LEAST 2 ADDITION PRODUCTS

OTHER RXNS OF ALKENES.

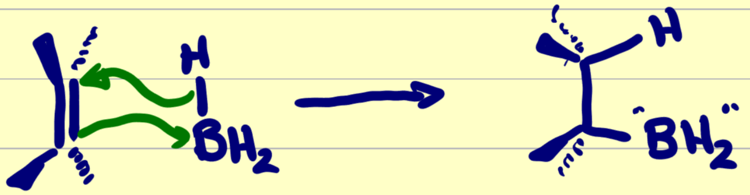
1) HYDROBORATION

"BH_3" - BORANE (EXISTS AS B_2H_6)

- ADDS ACROSS ALKENE C=C BONDS SOMEWHAT LIKE H-Br

- SOME DIFFERENCES.

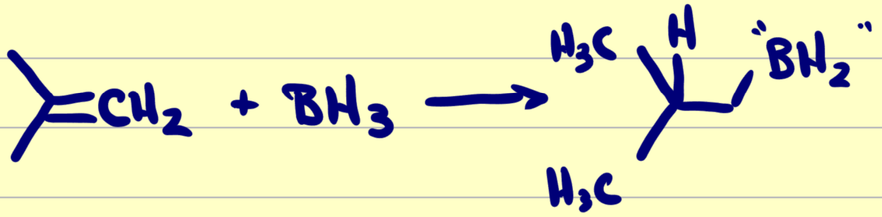
1)



CIS ADDITION.

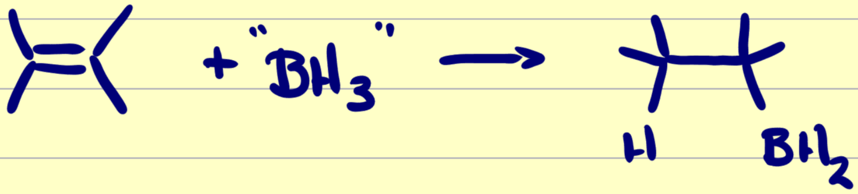
BECAUSE ALL BOND MAKING & BREAKING IS CONCERTED

2) $\overset{\delta-}{H} - \overset{\delta+}{BH_2}$



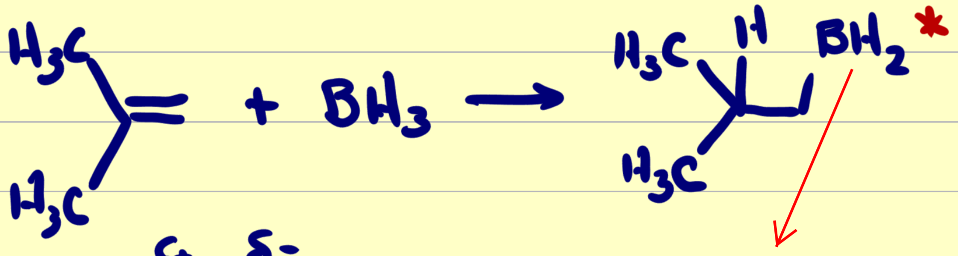
H GOES TO MORE SUBST. SIDE

∴ CALLED ANTI-MARKOVNIKOV ADDN.



i) CONCERTED, SO ADDN IS CIS.

ii) ANTI-MARKOVNIKOV

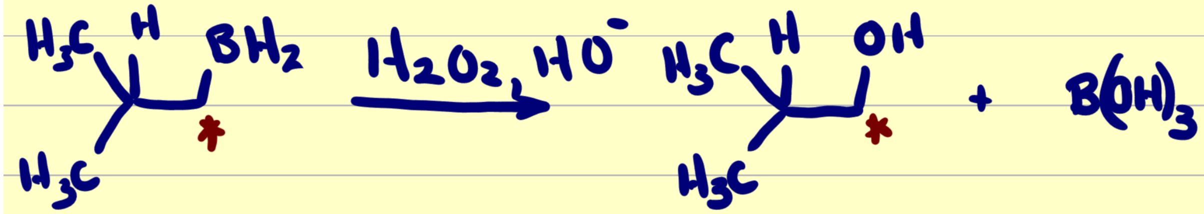


a) $>\overset{\delta+}{B}-\overset{\delta-}{H}$

b) "BH_2" LARGER THAN H
∴ BH_2 AVOIDS THE more
SUBSTITUTED END.

iii) - DON'T ISOLATE THE ORGANOBORON PRODUCTS. - ADD HO^- + H_2O_2

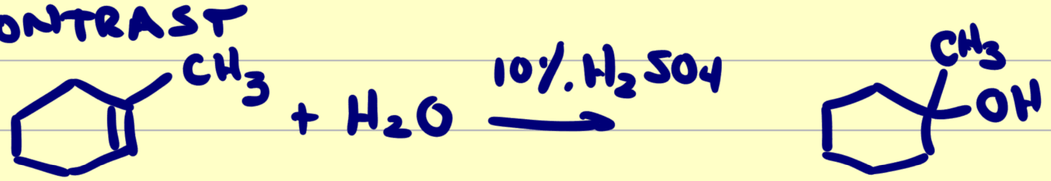
- REPLACES $/\overset{H}{\overset{|}{B}}-H$ BY AN ALCOHOL.

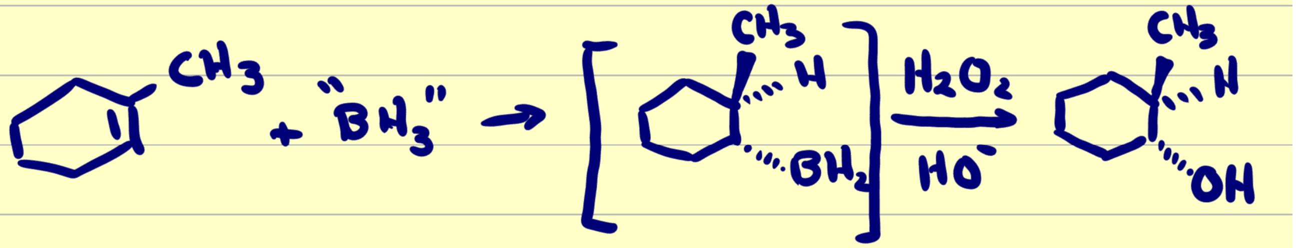


- ANY STEREOCHEMICAL INFO * IS RETAINED

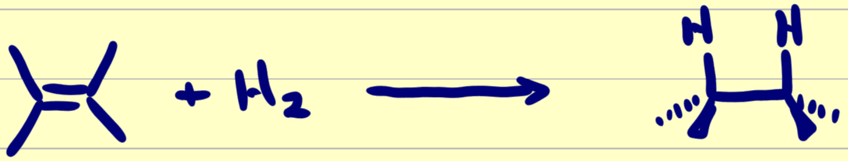
Usefulness: can get complementary product to acid catalyzed water addn reaction

CONTRAST





CATALYTIC HYDROGENATION



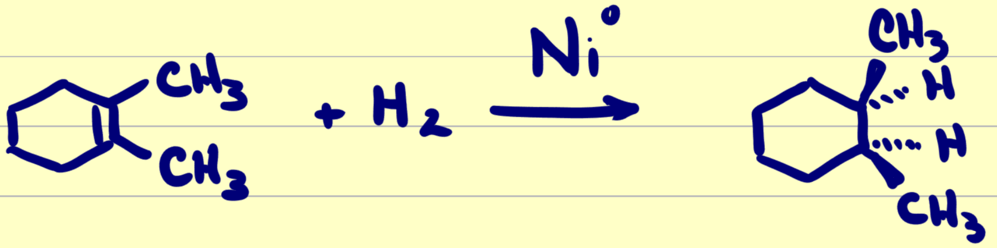
SLOW AS IS.

- BUT IF YOU ADD A SMALL AMOUNT OF A FINELY DIVIDED METAL POWDER (Ni, Pd, Pt); THIS REACTION GOES RAPIDLY AT ROOM TEMPERATURE, NORMAL H_2 PRESSURES

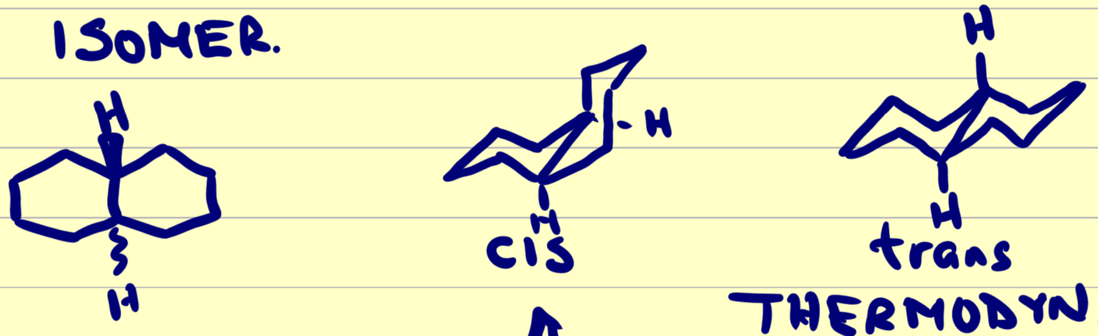
- CALLED CATALYTIC HYDROGENATION

  - CONSIDERED A <u>REDUCTION</u> OR AN ADDITION REACTION

REDUCTION - DEFINITION - ADDN OF H ATOMS, OR LOSS OF OXYGEN ATOMS



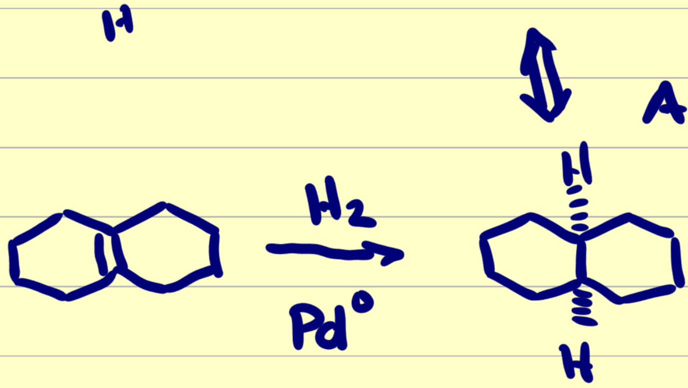
H2 ADDN IS CIS, EVEN IF THE PRODUCT ISN'T THE MOST STABLE ISOMER.



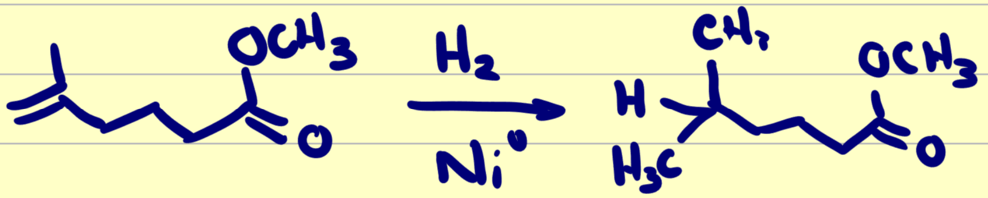
cis

trans

THERMODYNAMICALLY MORE STABLE



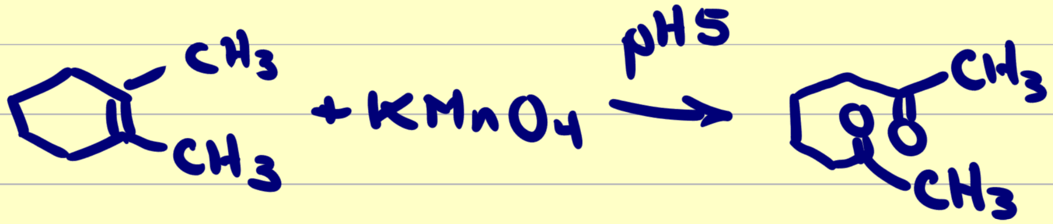
CIS is the one 'you' get



ALKENES REACT BEFORE MOST OTHER

ii) IF pH ≤ 7, REACTION GOES FURTHER

- σ BOND ALSO GETS CLEAVED



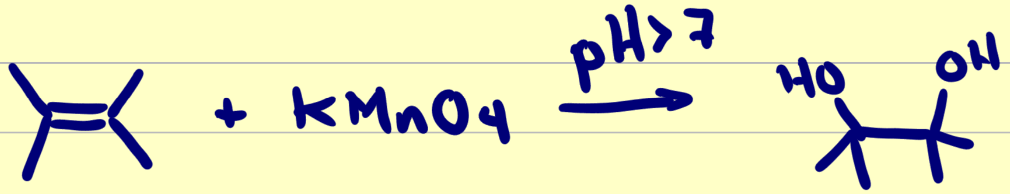
GROUPS. ketones, acids, esters, amides, all less reactive to catalytic hydrogenation

OXIDATION OF ALKENES.

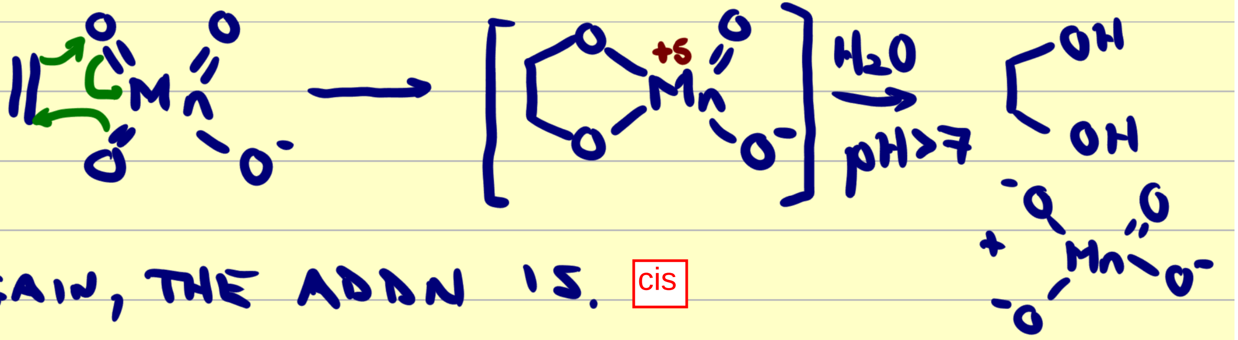
DEFN - ADDITION OF OXYGEN ATOMS, OR LOSS OF H ATOMS

COMMON REAGENT $KMnO_4$ (Mn^{+7})

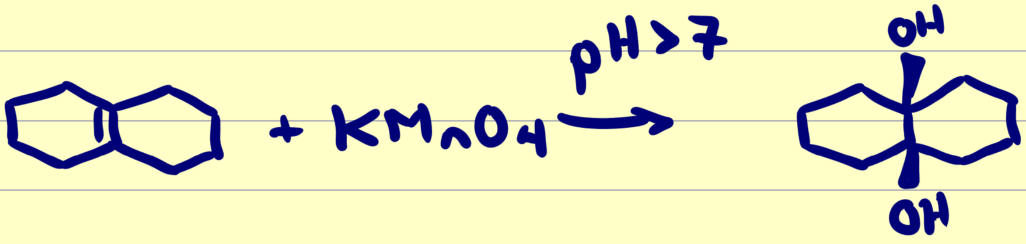
i) IF SOLUTION IS BASIC pH > 7



Mn now +5 oxidation state

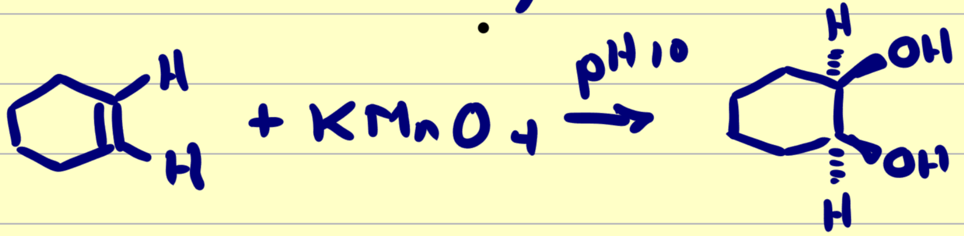


AGAIN, THE ADDN IS. cis

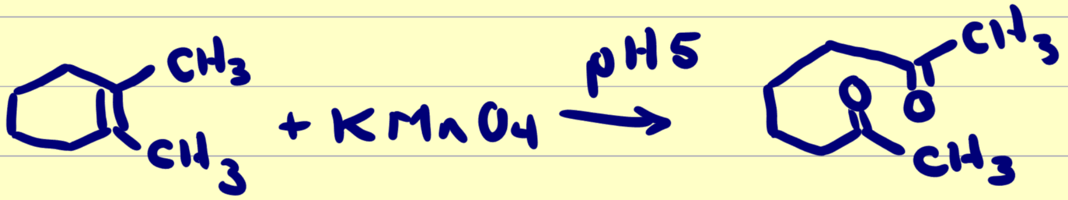


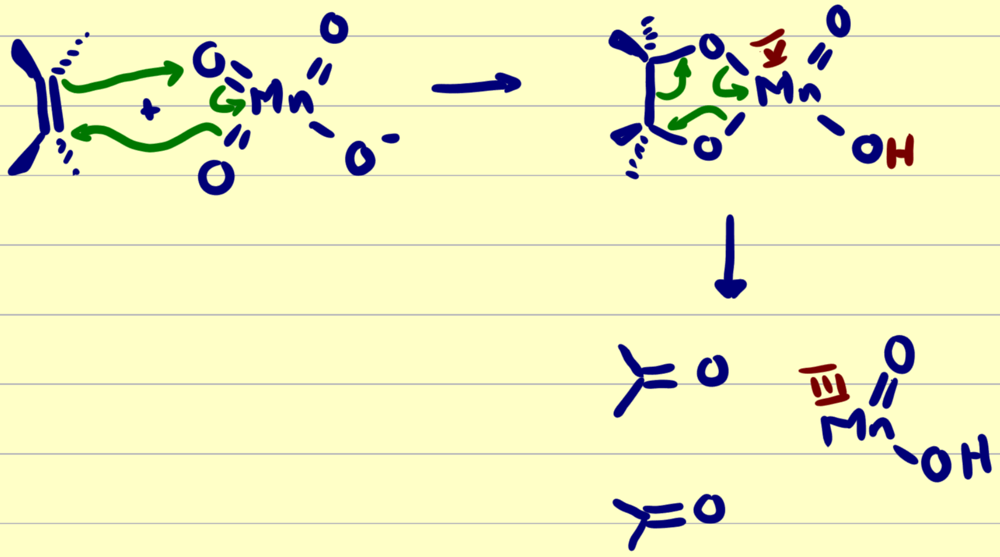
ALKENE OXIDATIONS.

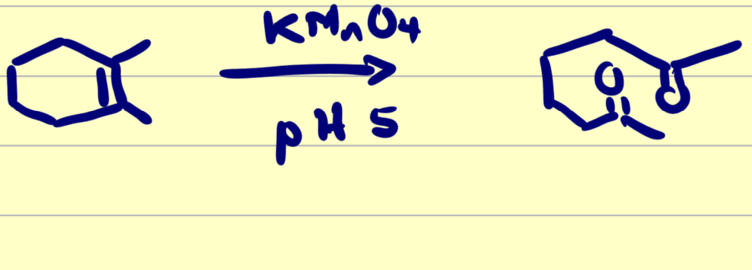
1) KMnO$_4$ (BASIC)



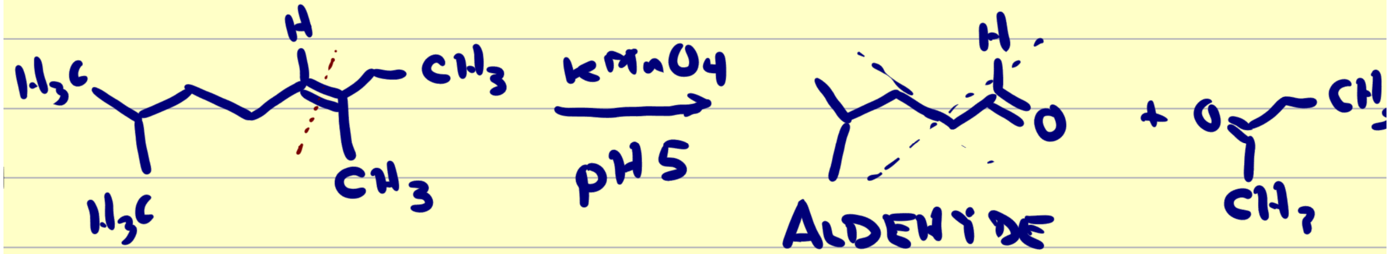
2) KMnO$_4$ (ACIDIC OR NEUTRAL)





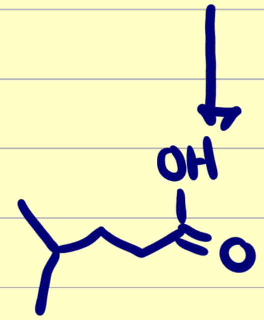


2 KETONES

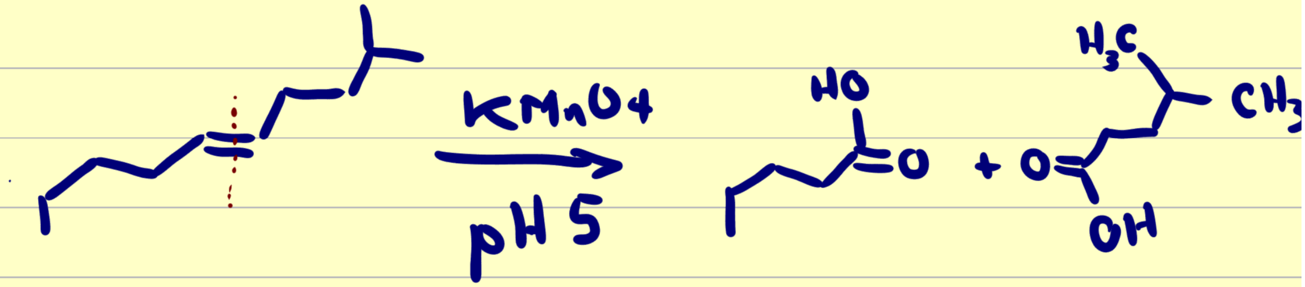


ALDEHYDE
OXIDIZED UNDER
THESE CONDS

You don't get an aldehyde under acidic KMnO4 conditions, because it's immediately oxidized to the carboxylic acid



CARBOXYLIC
ACID

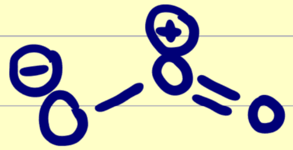


OTHER REAGENTS MORE COMMONLY USED

KMnO4 BASIC ⇒ OsO_4 MORE COMMON
KMnO4 ACIDIC ⇒ Na_2WO_4
$Na_2Cr_2O_7$ - MORE COMMON

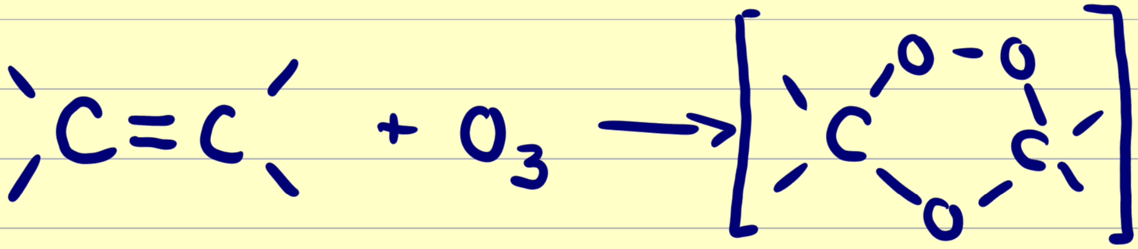
OZONE O_3

- WHAT IF YOU WANT AN ALDEHYDE

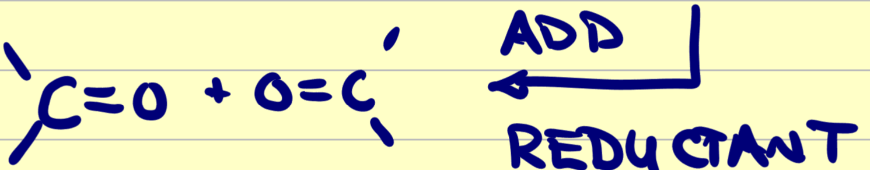


INCREDIBLY REACTIVE OXIDANT

IMMEDIATELY CLEAVES BOTH THE π AND σ BONDS OF A DOUBLE BOND



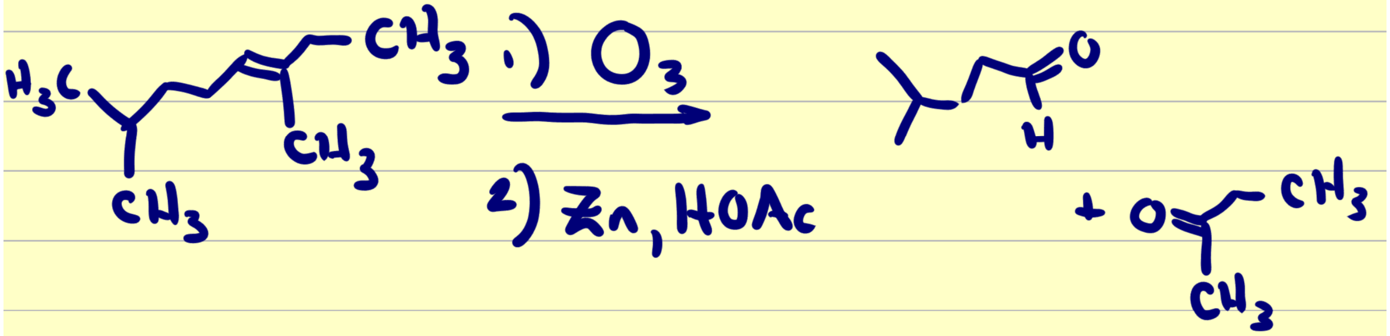
OZONIDE

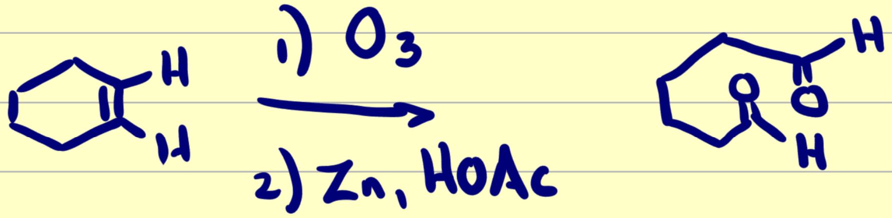


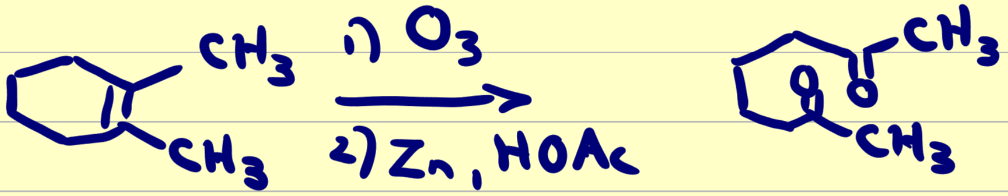
ADD REDUCTANT

Zn, $CH_3\overset{O}{\overset{\|}{C}}-OH$

SINCE CARBONYLS THEMSELVES ARE NOT FORMED UNTIL ALL OXIDANT IS GONE, 'YOU' CAN GET ALDEHYDES







ALKYNES.

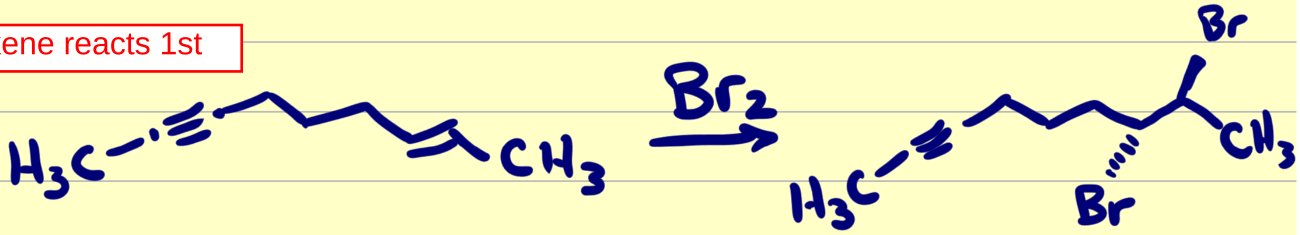
- THEY DO ELECTROPHILIC ADDN. RXNS, PRETTY MUCH LIKE ALKENES, BUT MORE SLOWLY.
- REASON - sp CARBONS HAVE e^- DENSITY HELD MORE CLOSELY TO NUCLEUS THAN sp^2 CARBONS

–≡ MORE ELECTRONEGATIVE

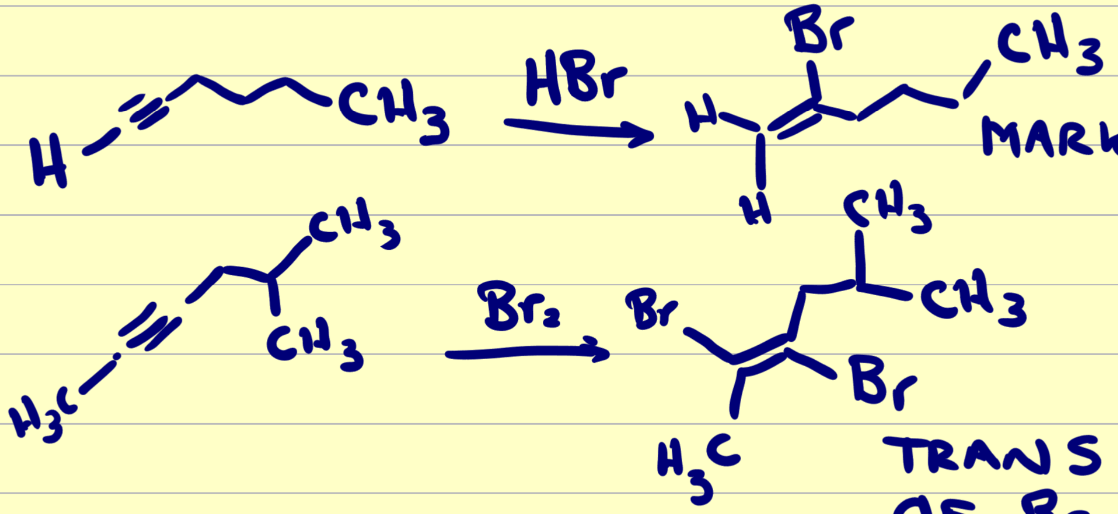
∴ LESS WILLING TO DONATE e^-'S

IN ELECTROPHILIC ADDN RXN.

alkene reacts 1st



OTHER WISE, CHEMISTRY IS ANALOGOUS



MARKOVNIKOV

TRANS ADDN OF Br_2

One difference in acid catalyzed addn of H2O

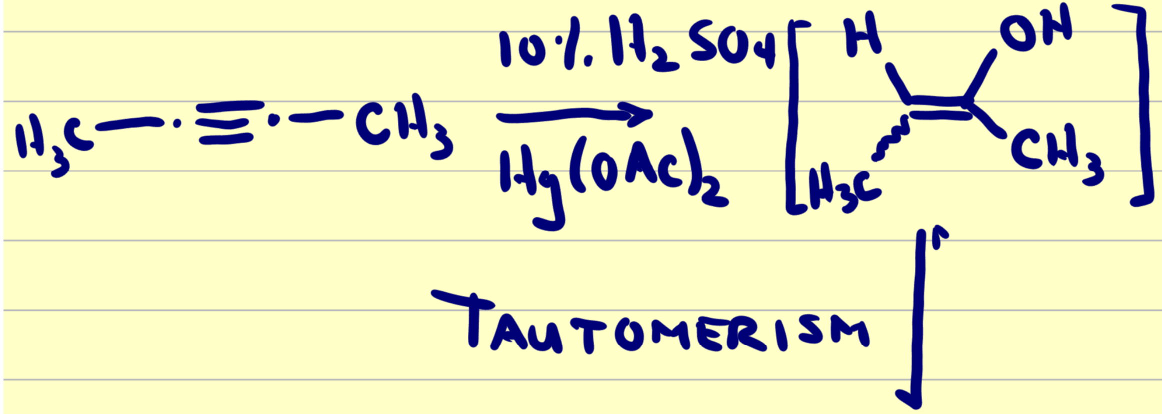
ADDN OF $H_2O + H_2SO_4$ – TOO SLOW.

- NEEDS Hg^{2+} SALT $Hg(-O-\overset{O}{\overset{\|}{C}}-CH_3)_2$

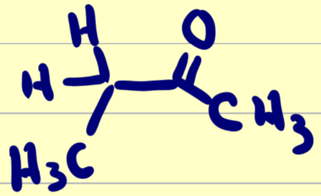
$(Hg(OAc)_2)$

CHANGES MECH., BUT PRODUCT IS ODD.

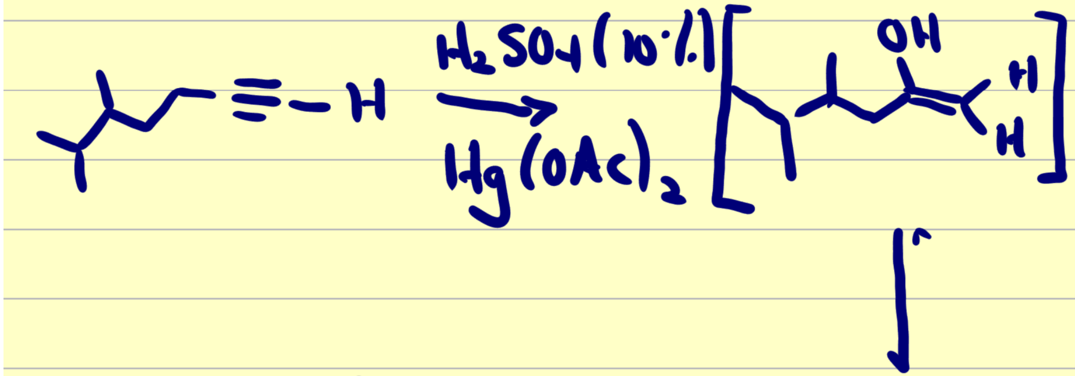
(or at least different from alkene addn product



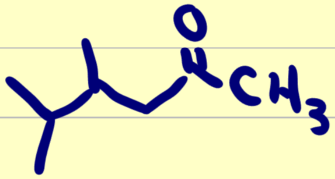
The equilibrium constant for this 'tautomerism' is about 1000000:1 in favour of the ketone - so that's all you see



USUALLY USED FOR 1-ALKYNES



GET A METHYL KETONE



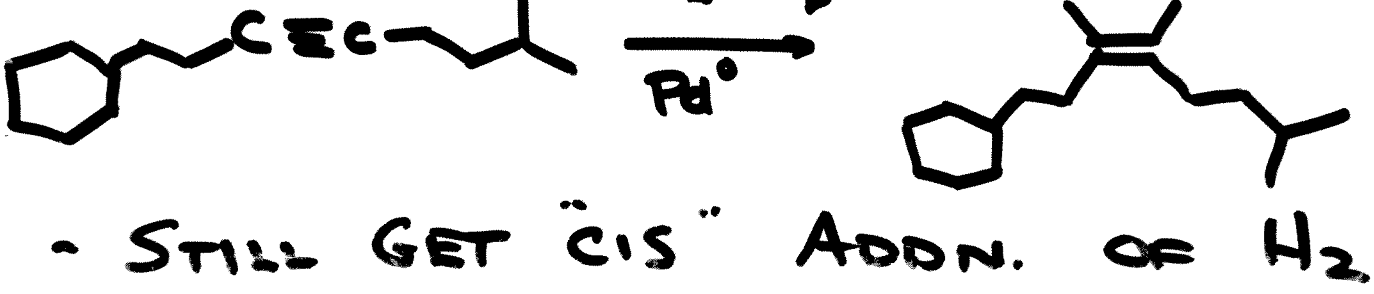
best in these cases because Markovnikov addn means only one product is obtained

ALKYNES. AND ELECTROPHILIC ADDN RXNS.

1) YES, BUT SLOWER THAN ALKENES
2) MOST OF RULES STILL APPLY
   a) MARKOVNIKOV RULE
   b) STEREOCHEMISTRY
3) H^+/H_2O NEEDED Hg^{2+} AND GIVES KETONE.

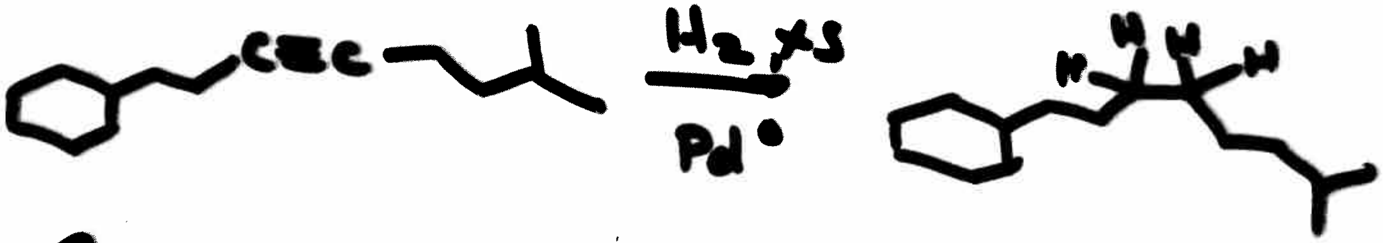
CATALYTIC HYDROGENATION.

- ALKYNES DO THIS REACTION
- REACTION IS A BIT <u>FASTER</u> THAN ALKENES.



- STILL GET "CIS" ADDN. OF H_2
- BEST WAY TO MAKE Z- ALKENE

- BUT - ALKENES AREN'T THAT MUCH SLOWER, SO IF ONE IS SLOPPY.



- COMMON TO USE A DEACTIVATED Pd° CATALYST - LINDLAR CATALYST.

CHAPTER 6.

NUCLEOPHILIC SUBSTITUTIONS. CHIRALITY.

CHIRALITY & CHIRAL CENTRES.

- HANDS ARE MIRROR IMAGES, BUT ARE NOT SUPERIMPOSABLE
- NOT IDENTICAL.

CONSIDE

there's an 'R' in 'consider'

CARBON WITH 4 DIFF. GROUPS SUBSTITUTED

- MIRROR IMAGES BUT NOT SUPERIMPOSABLE

∴ ENANTIOMERS

definition

- A COMPOUND WHICH HAS THIS PROPERTY IS SAID TO BE <u>CHIRAL</u>

- THE CENTRE WITH 4 DIFFERENT GROUPS IS A CHIRAL OR ASYMMETRIC CENTRE.

- MOST PHYSICAL PROPERTIES WILL BE IDENTICAL.

mp, bp, IR, NMR, Rf refractive index

- ROTATE PLANE POLARIZED LIGHT TO EXACTLY THE SAME

DEGREE, BUT IN OPPOSITE DIRECTIONS.

- OLD NAMES - ENANTIOMER THAT ROTATES LIGHT CLOCKWISE IS CALLED 'd' or '+' ENANTIOMER.

- THE ONE THAT ROTATES IT COUNTERCLOCKWISE, 'l' OR '−' ENANTIOMER

- MEASURE VALUE $[\alpha]_D$ "SPECIFIC ROTATION"

$$[\alpha]_D^T = \frac{100\,\alpha}{l \times c}$$

'D' is the wavelength of light used (589 nm), T is the temperature it is recorded at

α - OBSERVED ROTATION

l - PATH LENGTH (1 dm)

not the same 'l' as above

c - CONCENTRATION g per 100 mL SOLN

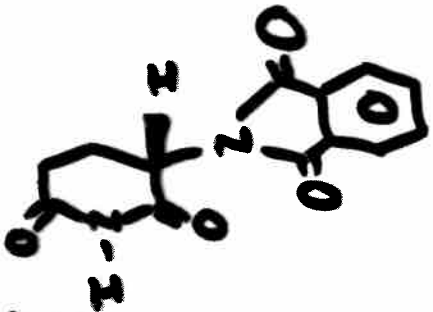
COMPOUNDS WHICH ARE CHIRAL AND ENANTIOMERICALLY PURE ARE "OPTICALLY ACTIVE"

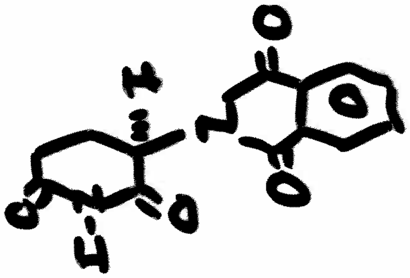
- COMMON TO HAVE A 50:50 MIXTURE OF ENANTIOMERS

$[\alpha]_D^T = 0$

because optical rotation of individual enantiomers cancel out exactly

- RACEMIC MIXTURE (RACEMATE)





(S)- THALIDOMIDE (R)-

SEDATIVE
ANTI MORNING SICKNESS

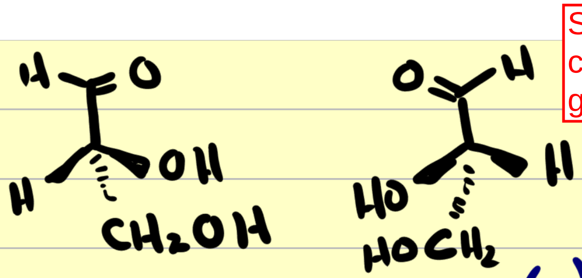
TERATOGEN
(BIRTH DEFECTS)

- HOW DO WE KNOW WHICH IS '+' OR '−' ?

- HOW DO WE NAME THEM IN A LOGICAL FASHION.

So how can one relate structure to optical rotation? The realtionship is *so* complex, that until ca. 1950, one could only guess....

So here's the guess; glyceraldehyde is easy to convert to many other compounds, so it was a great starting point



(+)-   (-)-

GLYCERALDEHYDE

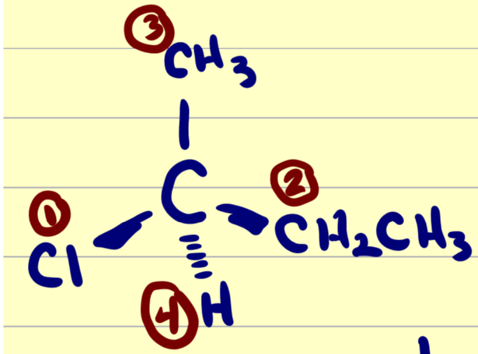
GUESS.

1951- XRAY CRYSTALLOGRAPHY PROVED THIS GUESS CORRECT.

'd', or 'l' or '+' or '-' will still be seen occasionally, but it is not systematic

SYSTEMATIC WAY OF NAMING ENANTIOMERS

CIP SYSTEM, SIMILAR TO ALKENES, IS USED TO BE RIGOUROUS



(S)-

a) RANK THE 4 GROUPS 1,2,3,4 IN ORDER OF PRIORITY.

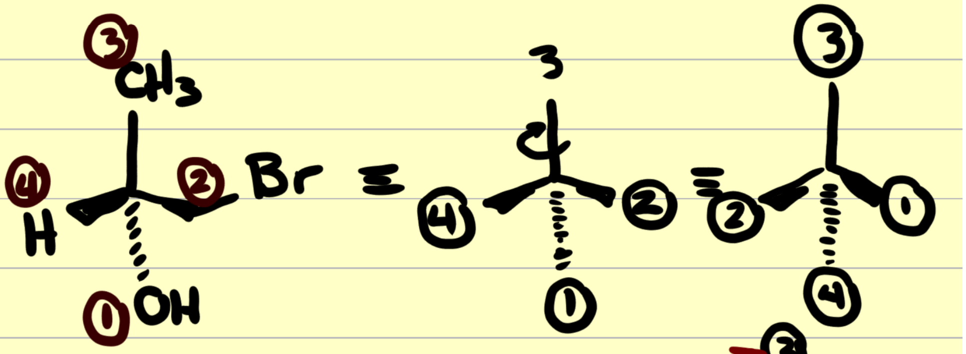
b) ORIENT MOLECULE SUCH THAT LOWEST PRIORITY GROUP IS DIRECTED AWAY FROM READER ④

c) TRACE 1 → 2 → 3

d) IF TRACE IS CLOCKWISE, IT'S (R)-
ENANTIOMER
IF TRACE IS COUNTERCLOCKWISE, IT'S
THE (S)- ENANTIOMER

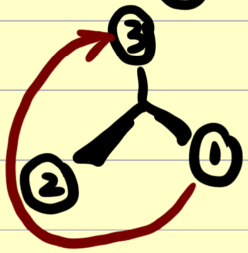
(S)- 2-CHLOROBUTANE

CONSIDER



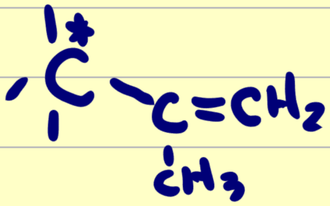
CLOCKWISE

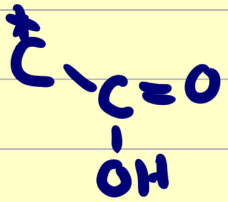
(R)-



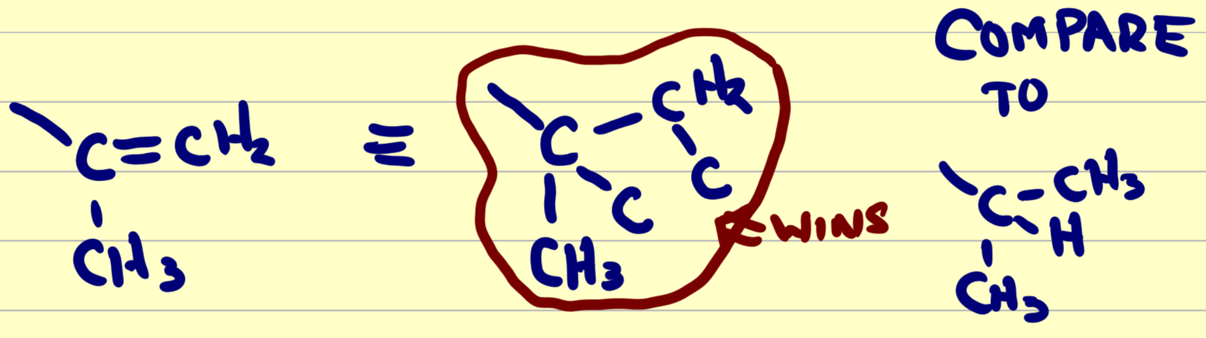
(R)- 1-BROMO-2-PROPANOL

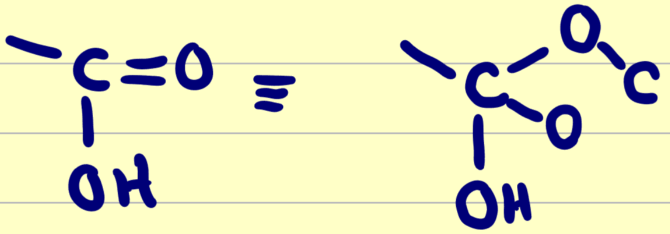
ADDENDUM ON PRIORITY RULES
- MULTIPLY BONDED FUNCTIONAL GROUPS

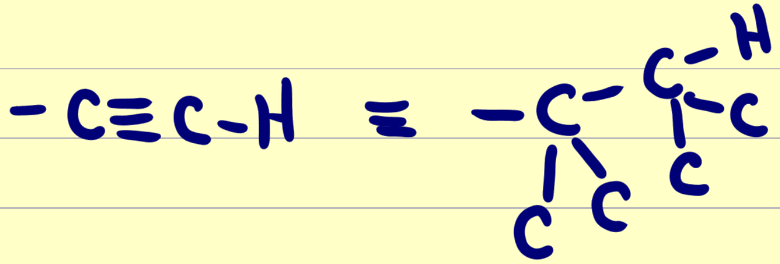




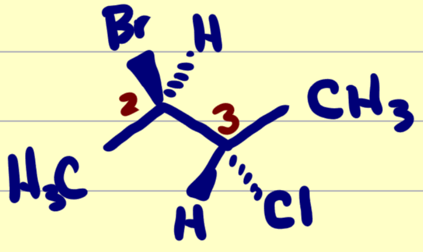
- FOR PRIORITY PURPOSES ONLY, REPLACE MULTIPLY BONDED ATOMS BY A EQUAL # OF SINGLY BONDED ATOMS







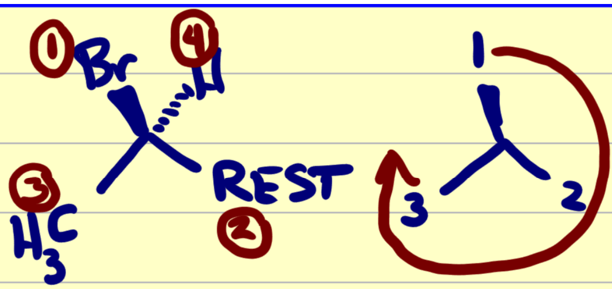
WITH 2 CHIRAL CENTRES - HOW DO YOU DO THIS?



2-BROMO-3-CHLOROBUTANE

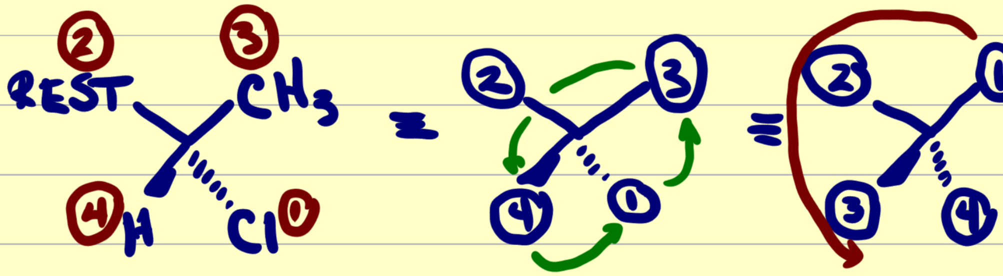
- CONSIDER THE CHIRALS ONE AT A TIME

C-2



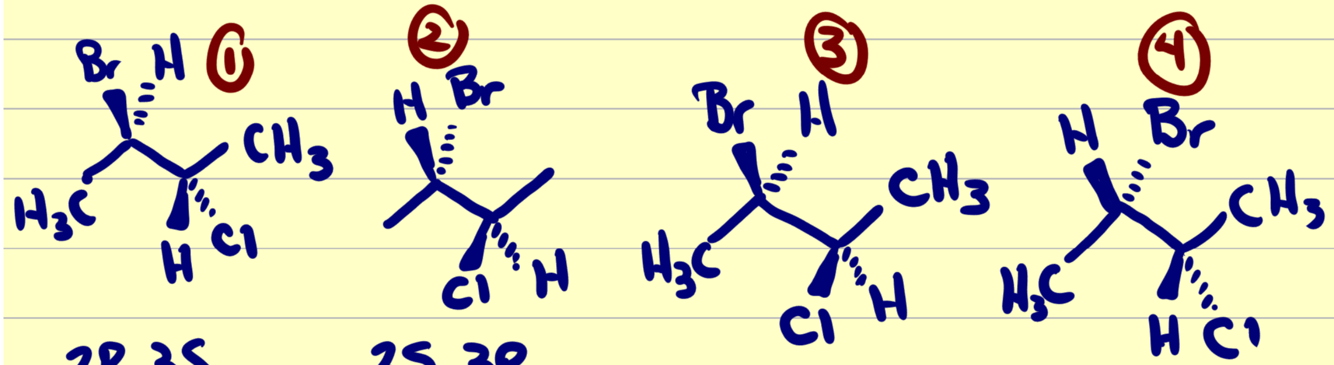
(R)-

C-3



(S)-

(2R,3S)- 2-BROMO-3-CHLOROBUTANE



2R,3S 2S,3R

ENANTIOMERS

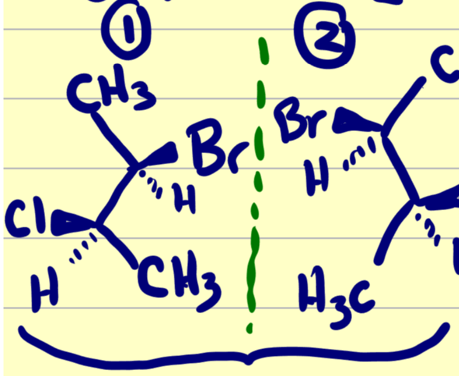
2R, 3R 2S,3S

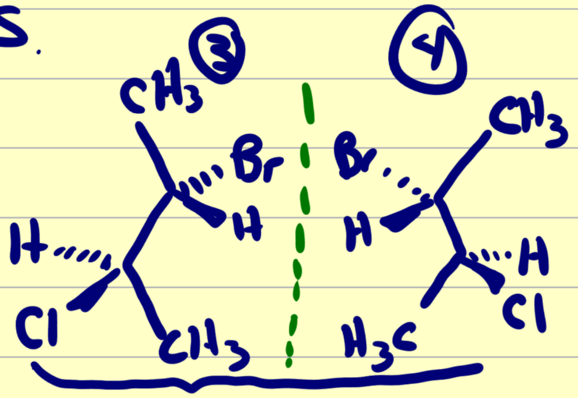
ENANTIOMERS

HOW ABOUT ① & ③ OR ② & ④

- NOT ENANTIOMERS, BUT RATHER DIASTEREOMERS.

DIASTEREOMERS





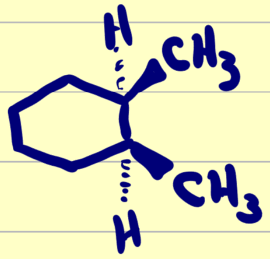
ENANTIOMERS ENANTIOMERS

1 & 3 OR 2 & 3 OR 2 & 4 OR 1 & 4.
DIASTEREOMERS

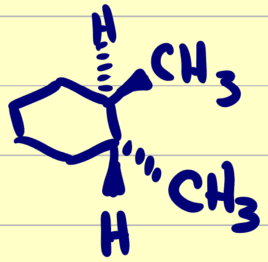
- OCCURS WHEN YOU HAVE ≥ 2 CHIRAL CENTRES - AND SOME CENTRES HAVE THE SAME CHIRALITY, OTHERS ARE OPPOSITE.

OFFICIAL DEFINITION- STEREOISOMER THAT ARE NOT ENANTIOMERS

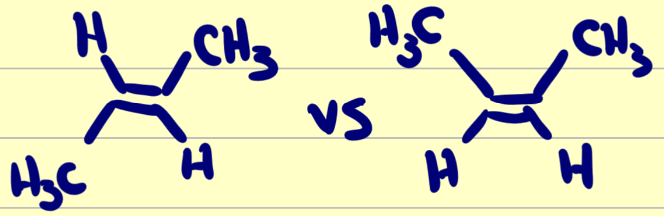
SO



VS



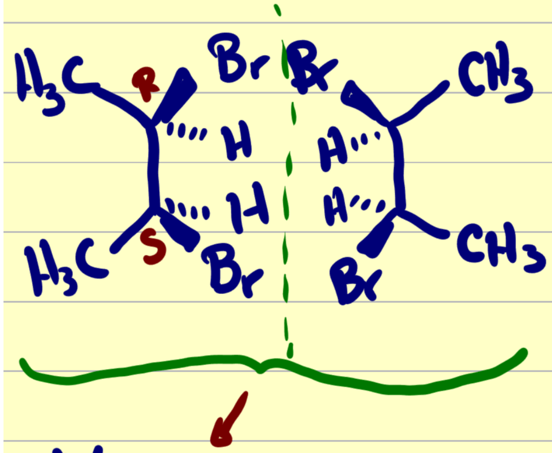
ARE DIASTEREOMERS

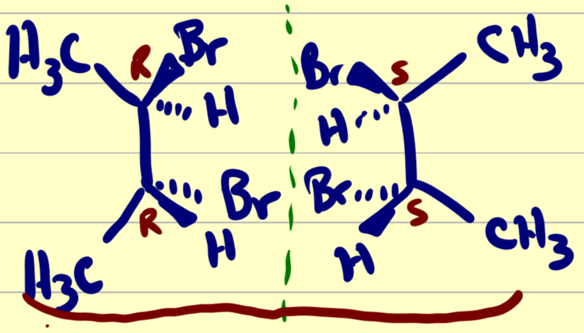


CAN ALSO BE CALLED DIASTEREOMERS

DIASTEREOMERS HAVE DIFFERENT PHYSICAL & SPECTROSCOPIC PROPERTIES; CAN SEPARATED BY CONVENTIONAL MEANS

BEWARE





ENANTIOMERS

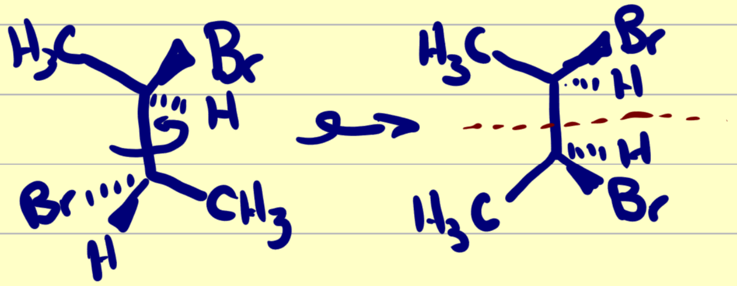
MESO FORMS - HAVE CHIRAL CENTRES, BUT <u>ARE</u> SUPERIMPOSABLE

∴ NOT ENANTIOMERS, NOT A CHIRAL COMPOUND - THEY ARE IDENTICAL.

- WHEN MOLECULE HAS AN INTERAL MIRROR PLANE (TOP HALF + BOTTOM HALF HAVE SAME SUBSTITUENTS).

- WHEN THE CHIRAL CENTRES ARE EXACTLY OPPOSITE IN THE OTHER HALF OF THE MOLECULE

WATCH OUT

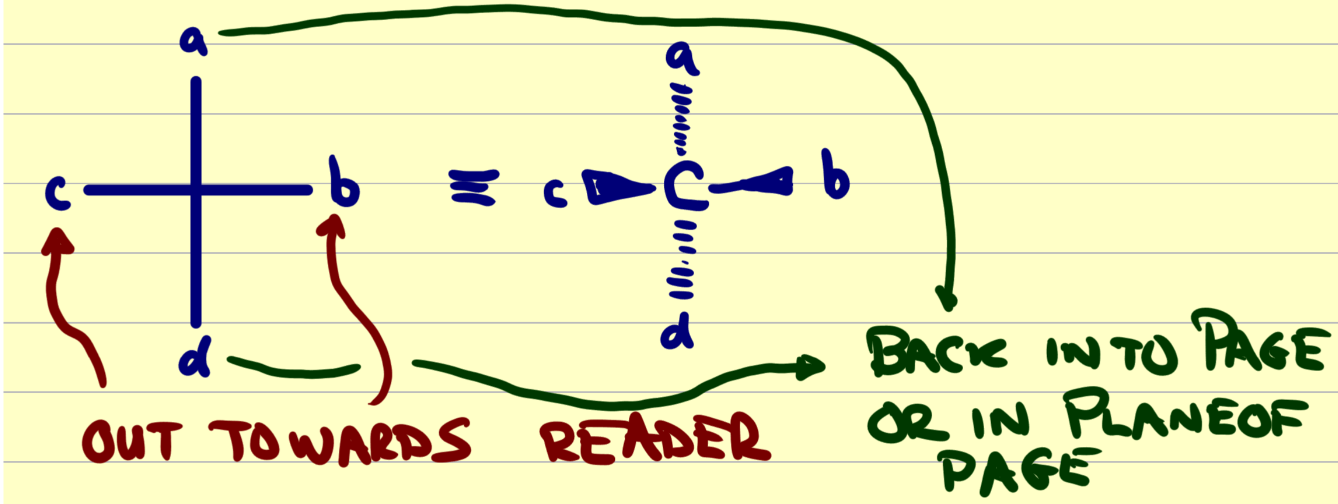


END OF TEST II MATERIAL

FISCHER PROJECTIONS.

- A WAY OF DRAWING CHIRAL CENTRES IN 2-DIMENSIONS

∴ A SERIES OF ARTIFICIAL RULES



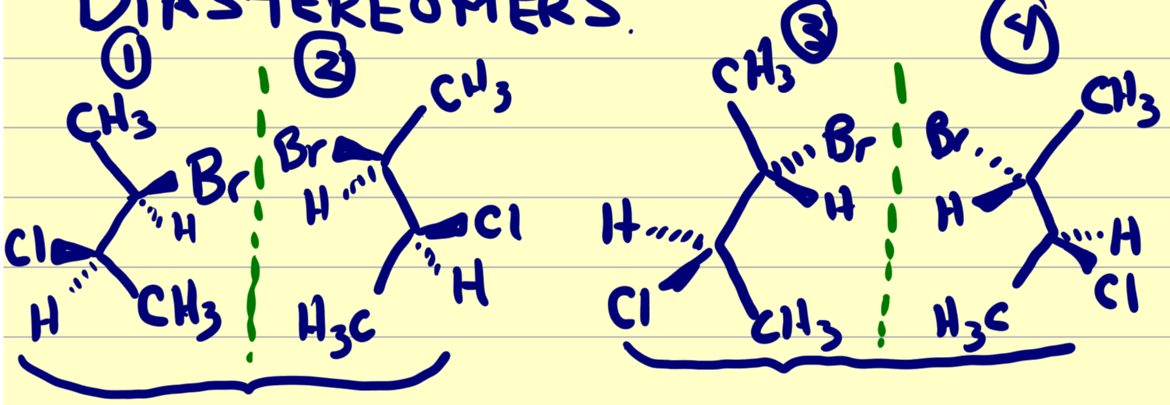
TO DETERMINE CHIRALITY, GET LOWEST PRIORITY GROUP STRAIGHT DOWN OR STRAIGHT UP

- THEN a → b → c CLOCKWISE ⇒ (R).
  COUNTERCLOCKWISE ⇒ (S).

SERIES OF ARTIFICIAL RULES

1) ROTATE BY 90°
2) ROTATE BY 180°
3) EXCHANGE 2 GROUPS
4) 3 SITE EXCHANGE

DIASTEREOMERS.



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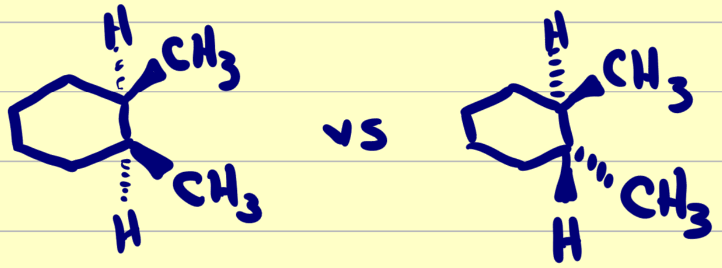
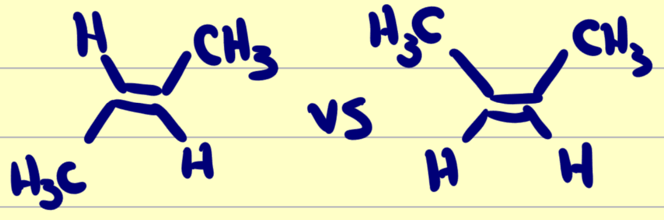
OFFICIAL DEFINITION - STEREOISOMER THAT ARE NOT ENANTIOMERS

SO



ARE DIASTEREOMERS



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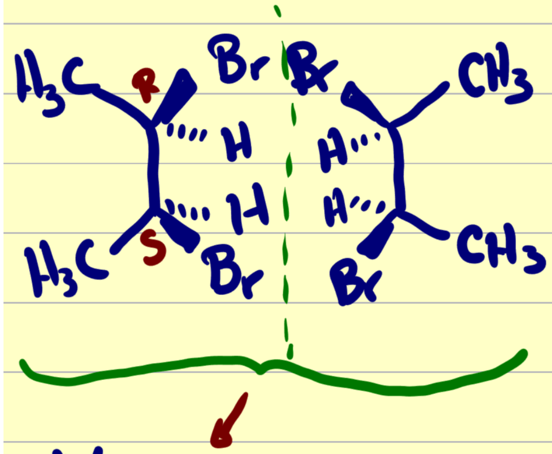

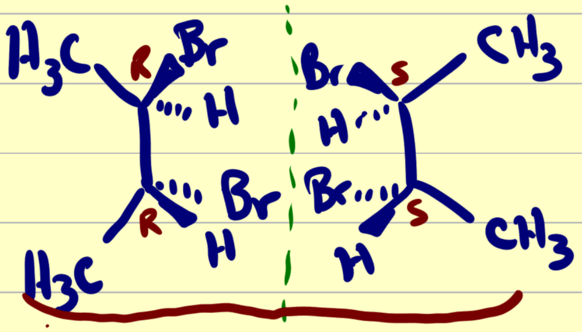

ENANTIOMERS

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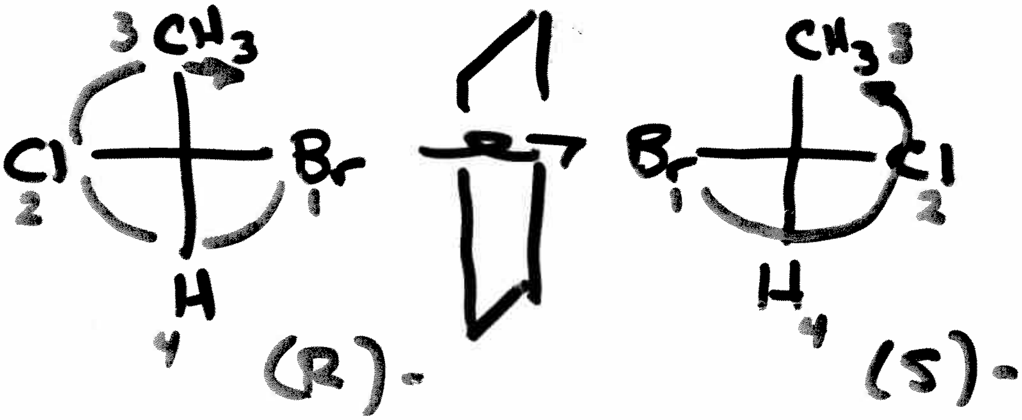
∴ NOT ENANTIOMERS, NOT A CHIRAL COMPOUND - THEY ARE IDENTICAL.

FISCHER PROJECTIONS.

WHAT HAPPENS IF?

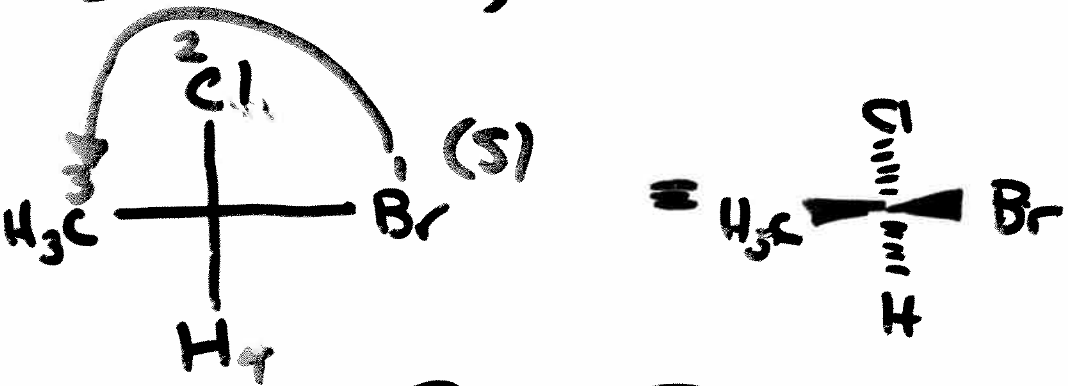
1) SWITCH 2 GROUPS.
   - ENANTIOMER
2) 3 SITE XCHANGE
   - SAME
3) ROTATE BY 90°
   - ENANTIOMER
4) ROTATE BY 180°
   - SAME.

1)

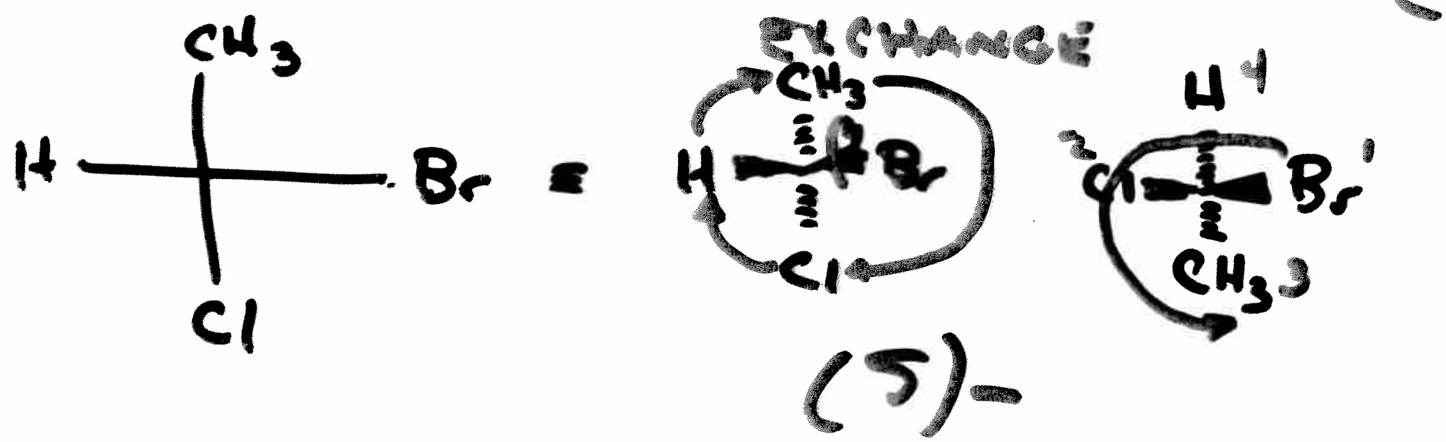


∴ ENANTI

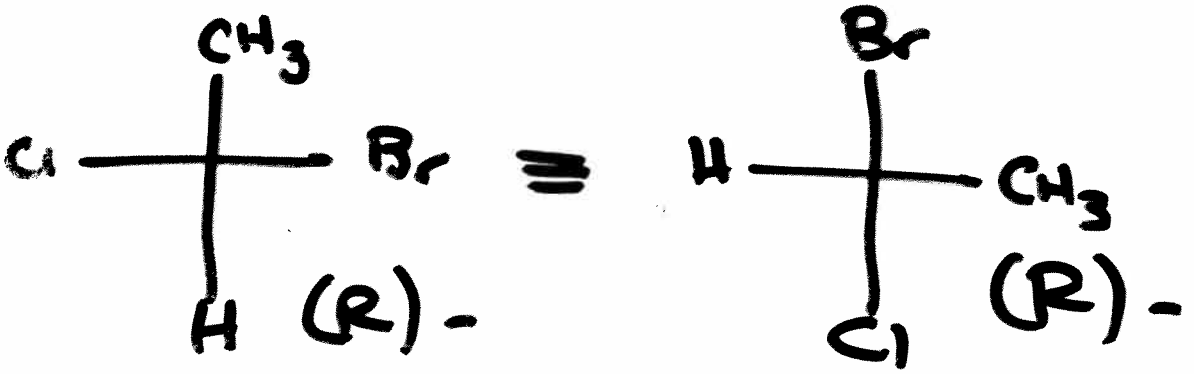
SWITCH 2&3



SWITCH ④ + ②



COROLLARY - IF YOU DO 2 SWITCHES OF 2, GET ORIGINAL BACK.



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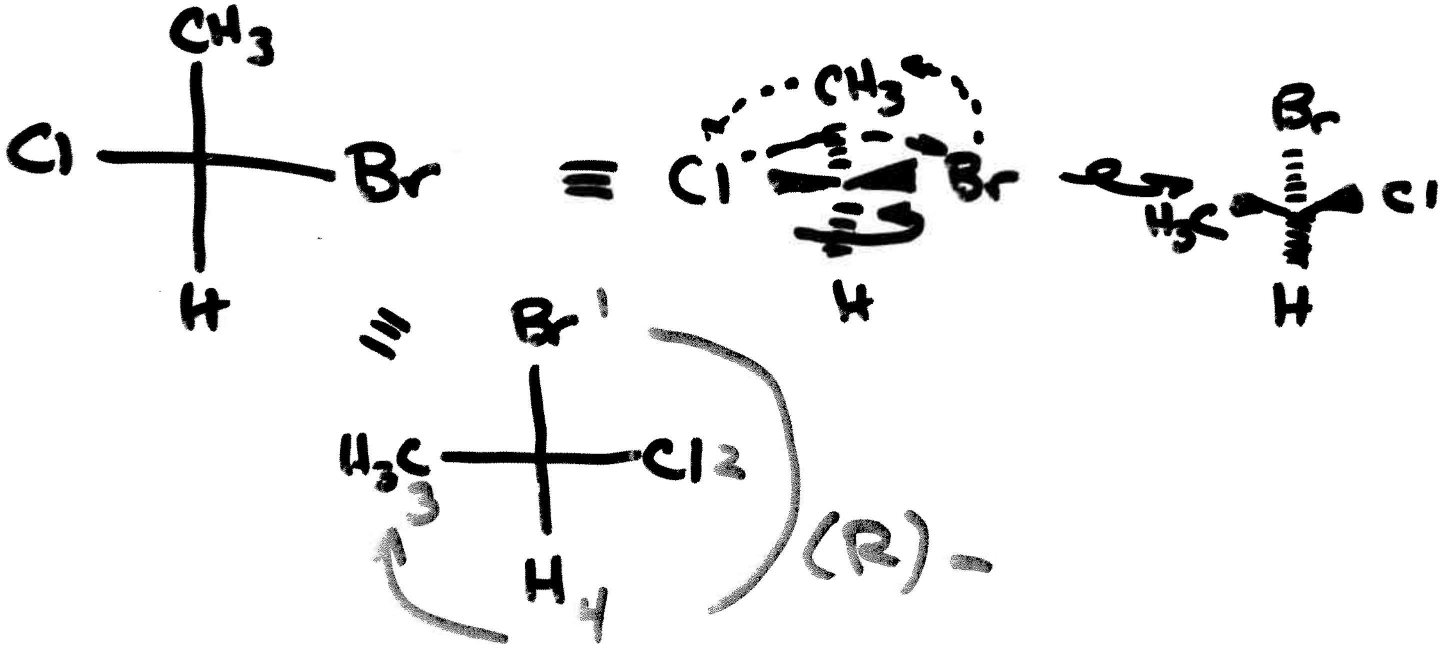
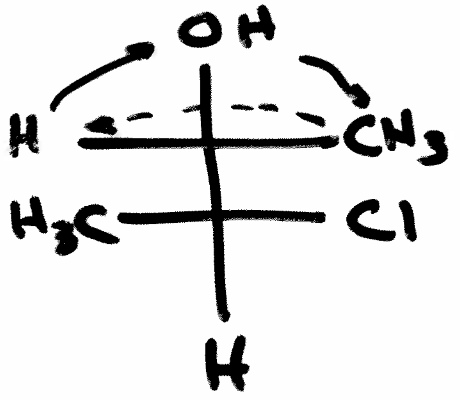
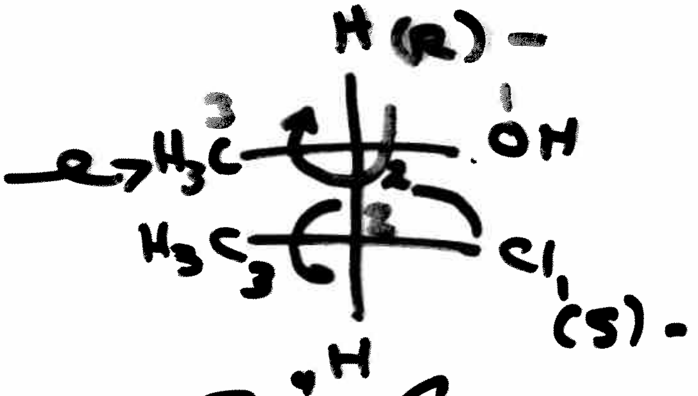
2) 3 SITE EXCHANGE



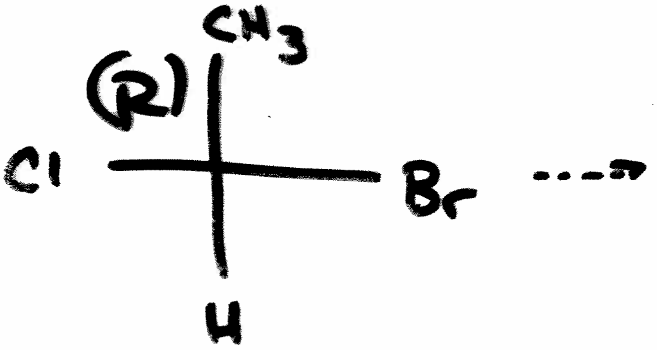


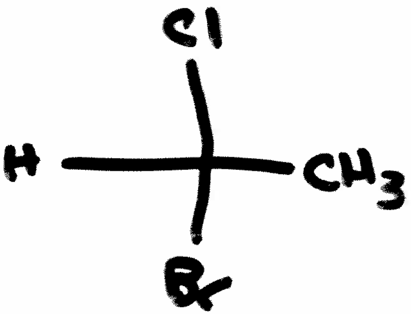


SAME CHIRALITY

∴ GIVES SAME ENANTIOMER

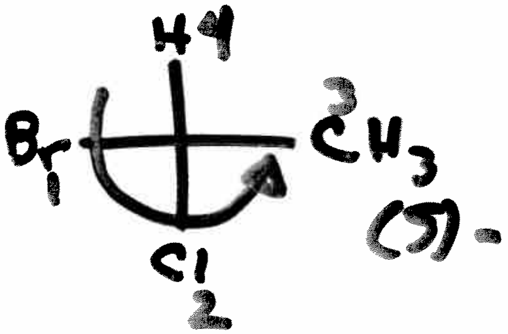
3) 90° ROTATION.





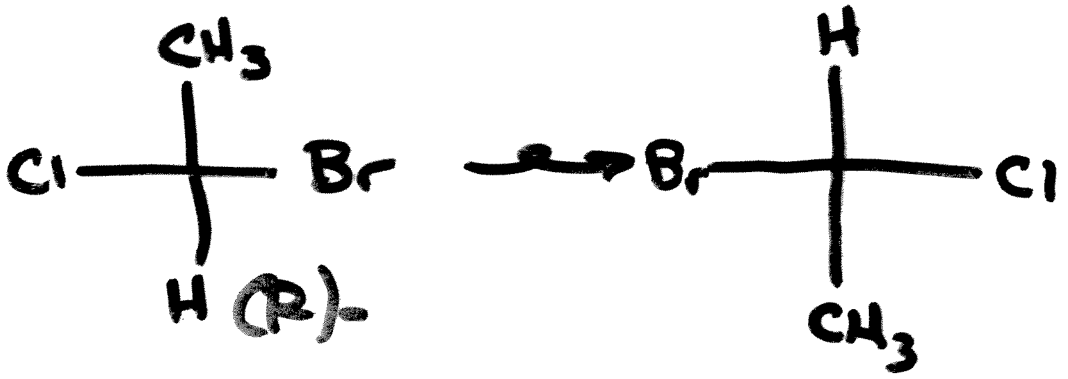
WHAT IS THIS?

≡

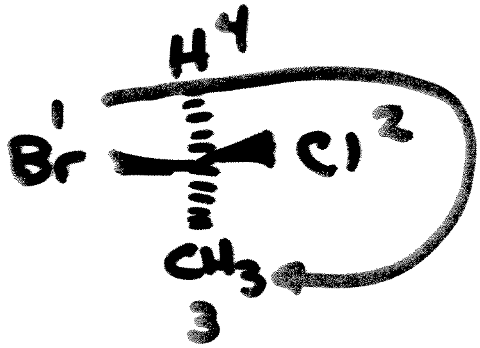


∴ A 90°
ROTATION
INVERTS THE
ENANTIOMER YOU
ARE DRAWING

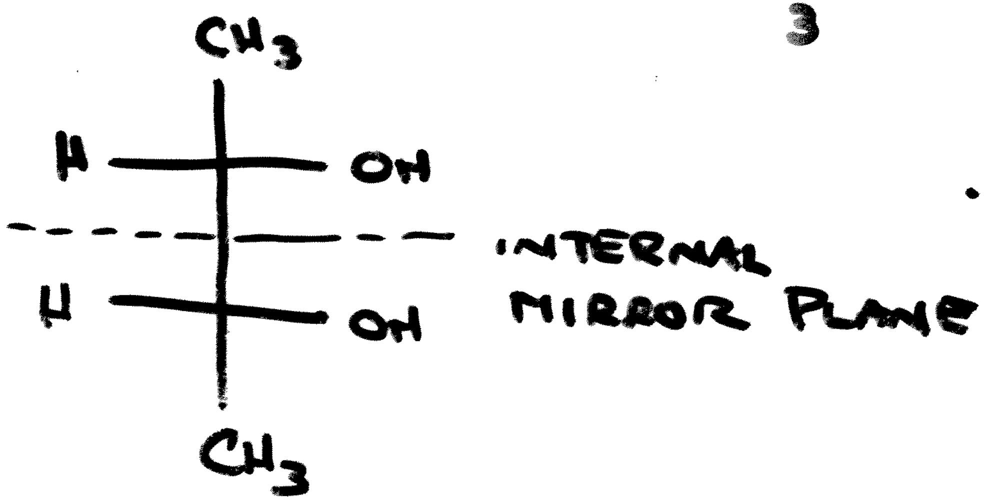
4) 180° ROTATION - SAME ENANT.



SAME AS
2 EXCHANGES
OF TWO
∴ SAME.



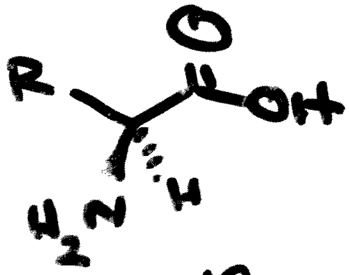
(R)-



∴ MESO
FORM.

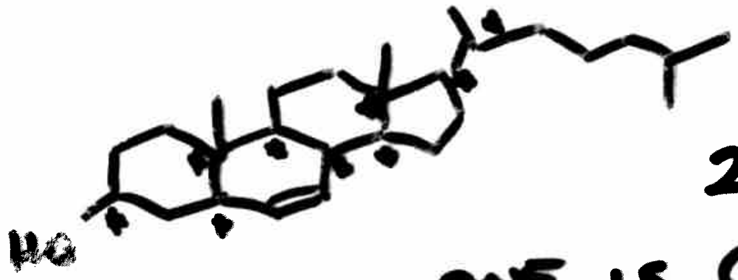
WHO CARES?

- MANY NATURAL MOLECULES ARE
1 ENANTIOMER



AMINO ACIDS.
BUILDING BLOCK OF
PROTEINS.

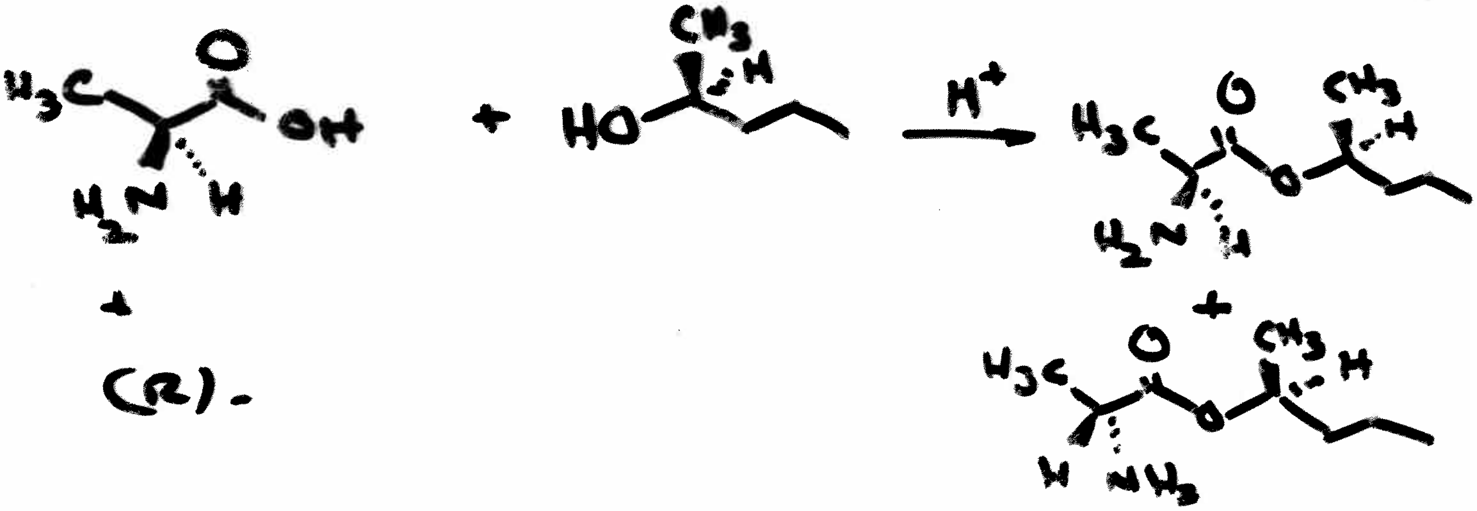
19 OF 20 ARE CHIRAL. 18 ARE (S)-



2^9 = 512 CPDS.

ONE IS CHOLESTEROL.

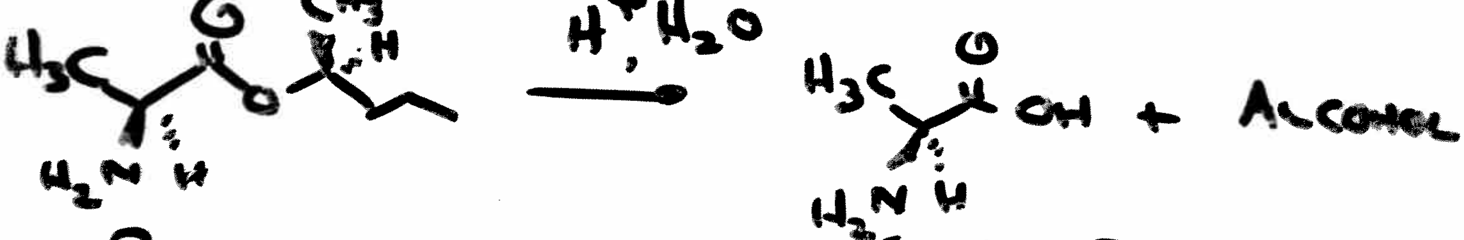
HOW DO YOU SEPARATE ENANTIOMERS



DIASTEREOMERS.

∴ CAN SEPARATE THEM.

GET



PURE

(S)- PURE.

CALLED.....

CLASSICAL RESOLUTION.

SUBSTITUTION REACTIONS

$$CH_3-Br + I^- \longrightarrow I-CH_3 + Br^-$$

SUBSTITUTION

- REPLACING Br WITH I

HOW DOES THIS OCCUR?

TWO MAJOR, DOMINANT, LIMITING MECHANISMS.

1) S_N1 MECHANISM

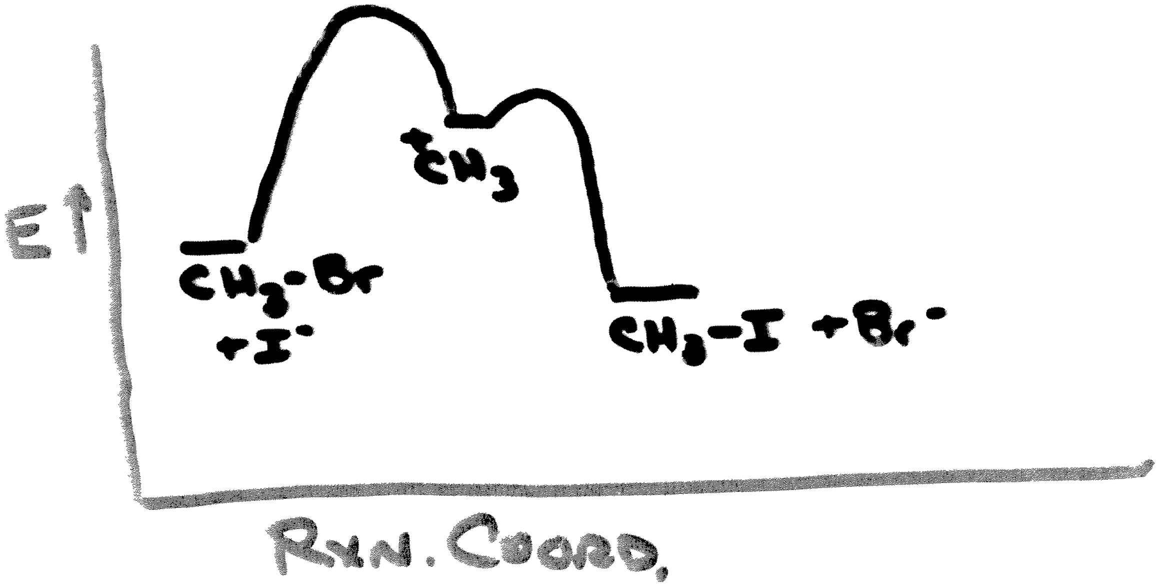
- CARBOCATION ROUTE

a)

$$CH_3-Br \rightleftharpoons \left[\overset{+}{C}H_3 + Br^- \right] \xrightarrow{I^-} CH_3-I + Br^-$$

- HAS A CARBOCATION <u>INTERMEDIATE</u>
- TWO STEPS.
- TOUGH ONE - SEPARATING A NEUTRAL SPECIES INTO A PAIR AN ION PAIR.

- EASY ONE - RECOMBING A PAIR OF IONS INTO A NEUTRAL CPD.



1ST STEP IS SLOWEST

RATE $v = k[CH_3-Br]$

$\therefore$ 1ST ORDER.

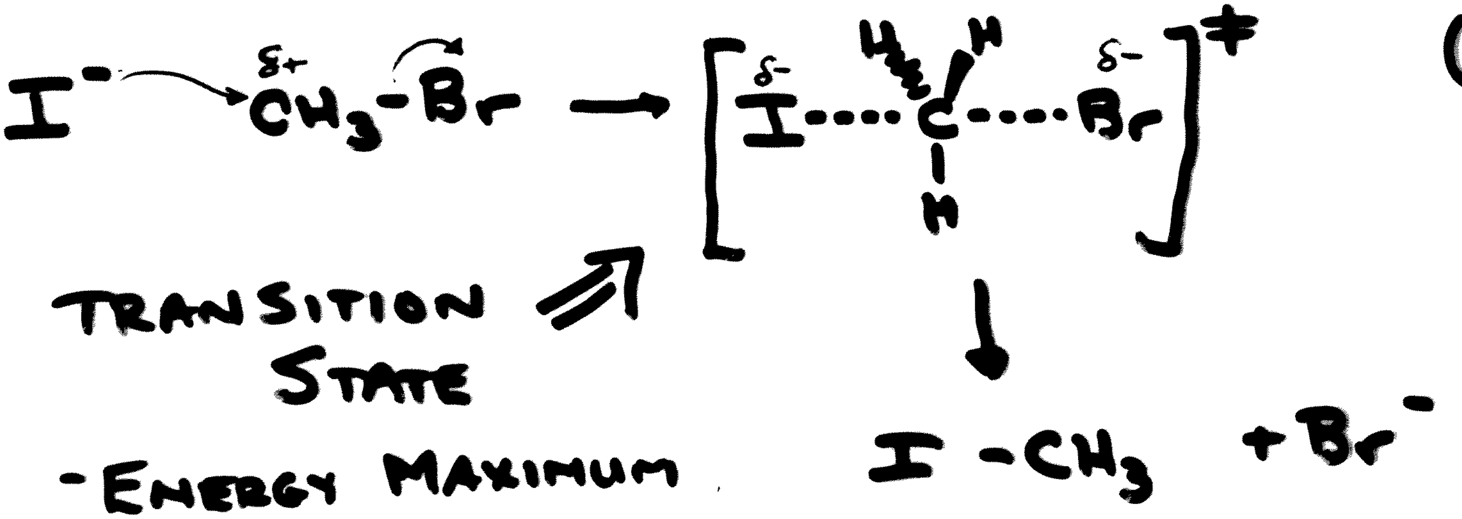
S_N1 S - SUBSTITUTION

N - NUCLEOPHILIC

1 - 1ST ORDER

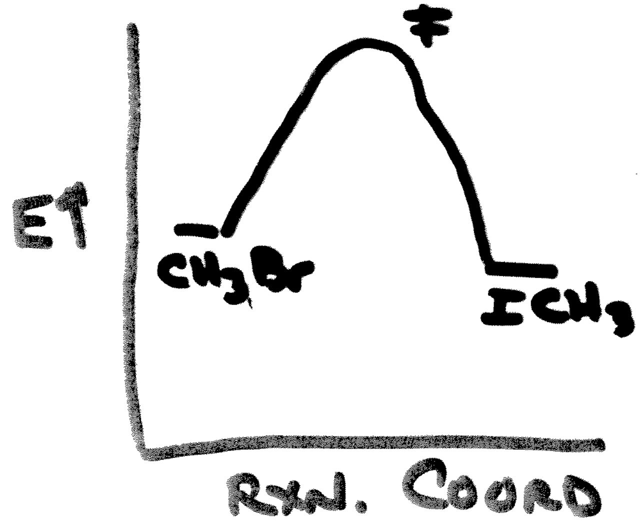
2) S_N2 SUBSTITUTION.

- CONCERTED.
- ALL BOND MAKING, BOND BREAKING EVENTS OCCUR AT THE SAME TIME



TRANSITION STATE

- ENERGY MAXIMUM
- NO LIFETIME
- ONLY ONE STEP.



- BOTH I^- AND CH_3-Br ARE CONSUMED IN SLOW STEP

RATE $v = k[CH_3Br][I^-]$

2ND ORDER OVERALL.

S_N2

S - SUBSTITUTION
N - NUCLEOPHILIC
2 - 2ND ORDER.

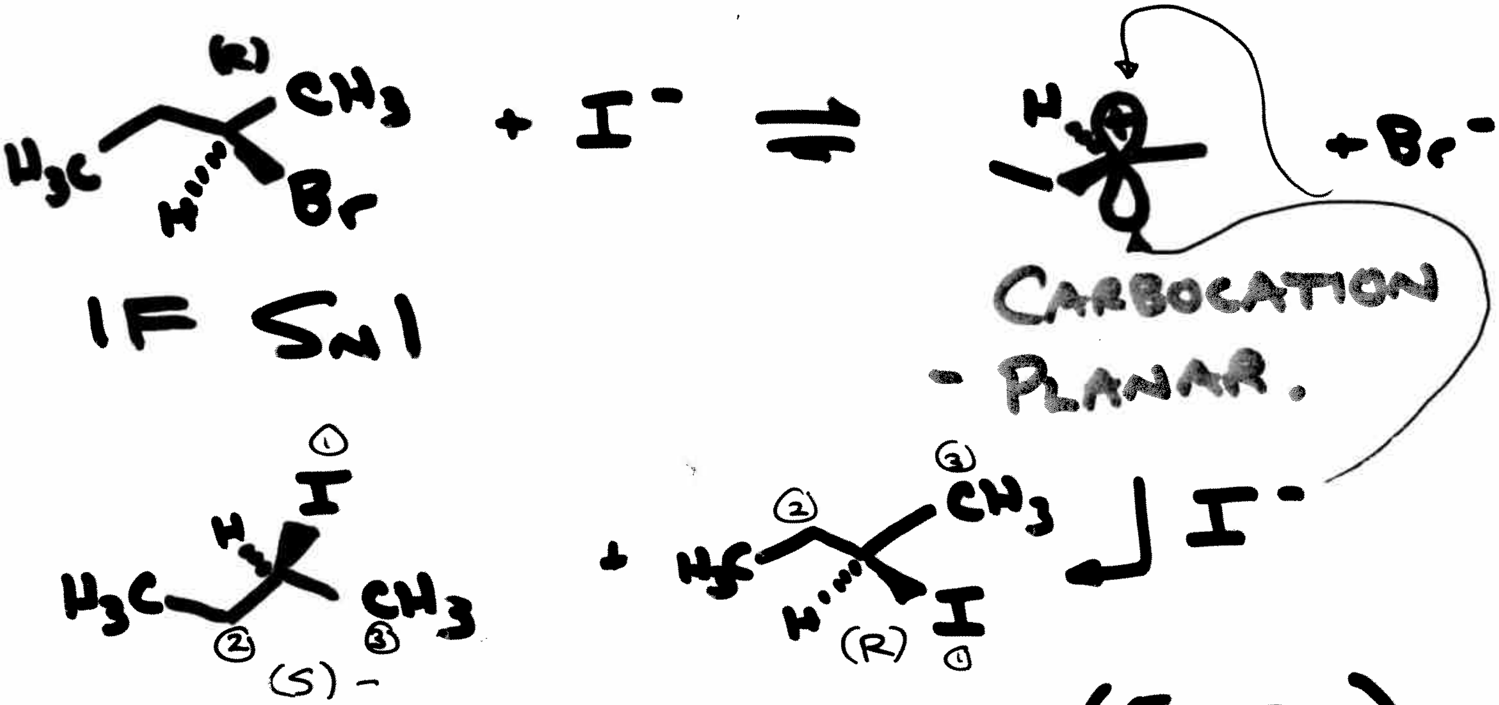
NOTE - THERE ARE CASES THAT ARE MOST ONE MECHANISM, BUT A BIT OF THE OTHER.

- THERE ARE A COUPLE OF MINOR ALTERNATIVE S_Ni

STEREOCHEMISTRY.

- WHAT HAPPENS FOR S_N1, S_N2.

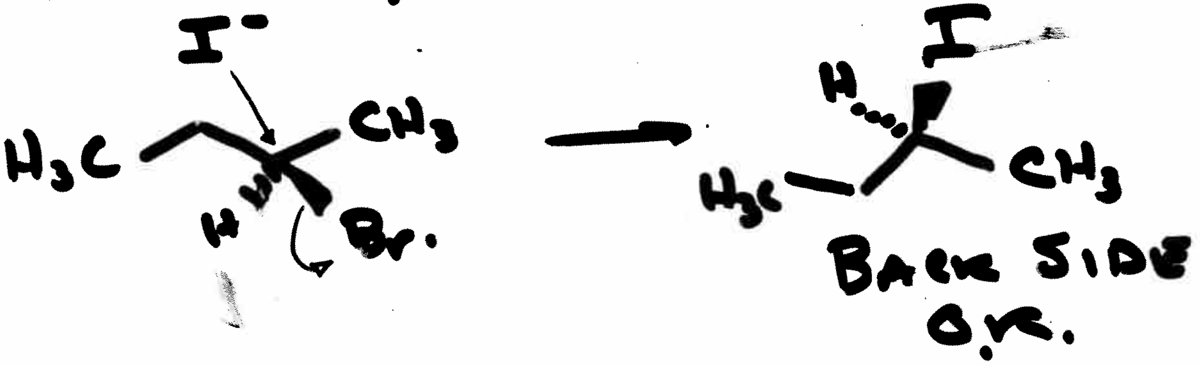
IF S_N1



CARBOCATION
- PLANAR.

∴ RACEMIC MIXTURE (50:50)
LOSS OF STEREOCHEMICAL INFO.
- RACEMIZATION.

IF S_N2.



O.K.

BACK SIDE
O.K.

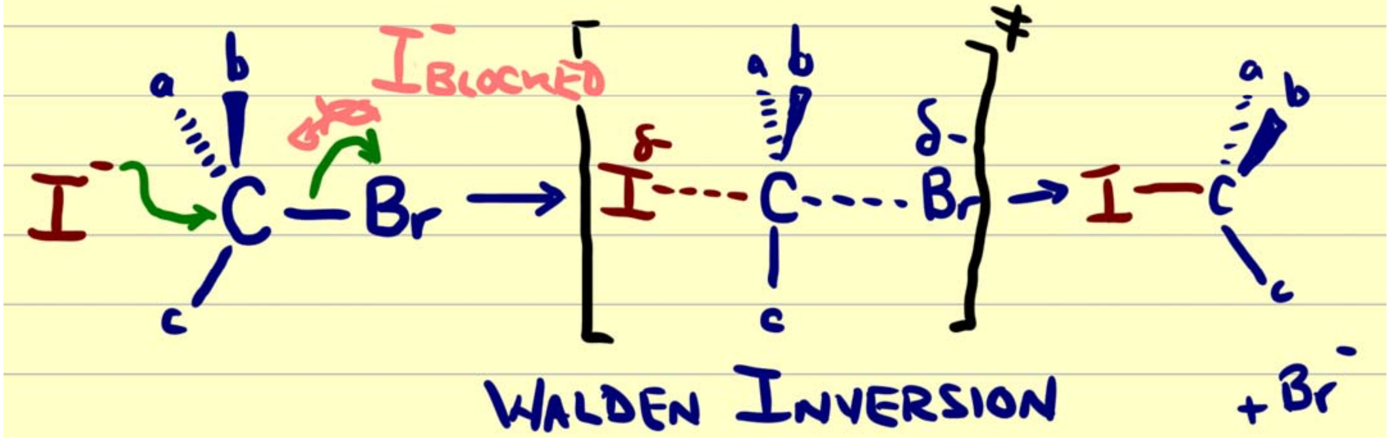
FRONT SIDE BLOCKED

SINCE FRONT IS BLOCKED, GET 100% INVERSION OF CONFIGURATION AT CHIRAL CENTRE.

NOT ALWAYS (R) TO (S)- OR (S) TO (R)-, BECAUSE INCOMING GROUP MAY HAVE DIFFERENT PRIORITY THAN LEAVING GROUP.

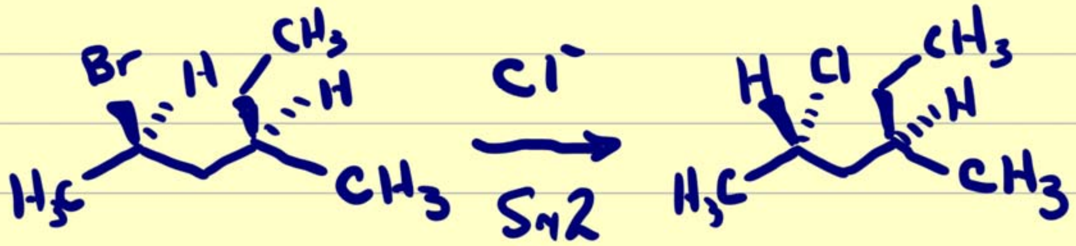
STEREOCHEM. OF SUBST., CONT'D.

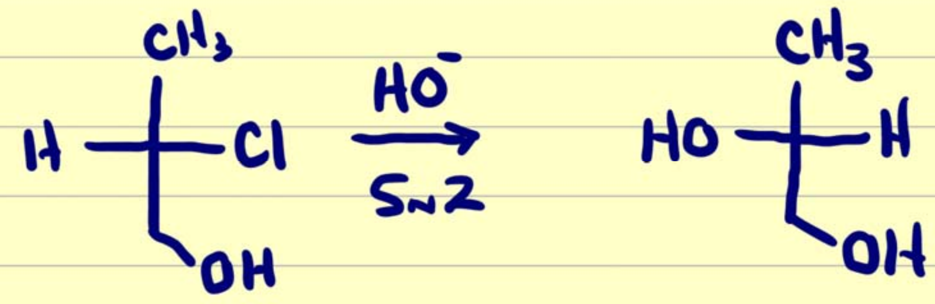
S_N2 - INVERSION OF CONFIGURATION AT C UNDER ATTACK



WALDEN INVERSION

IF PRIORITIES ARE I/Br > c > b > a
THAT (R) → (S).





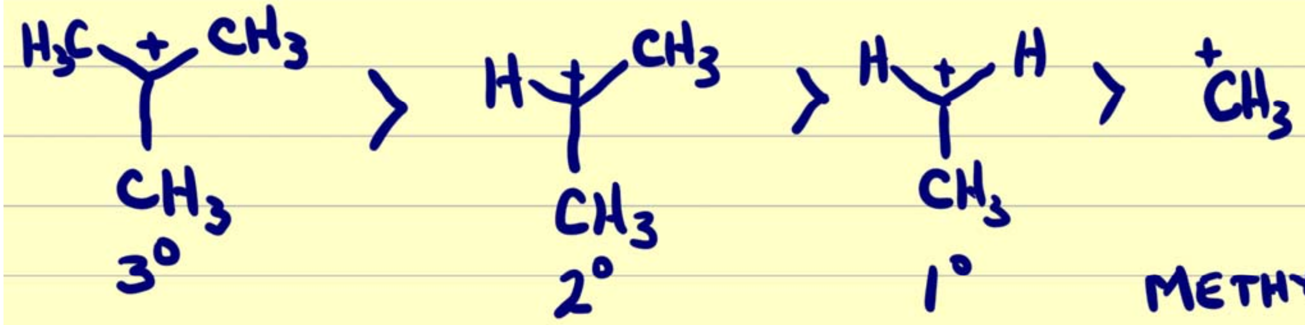
IS IT S_N1 OR S_N2 – HOW DO YOU TELL?

4 CRITERIA TO CONSIDER

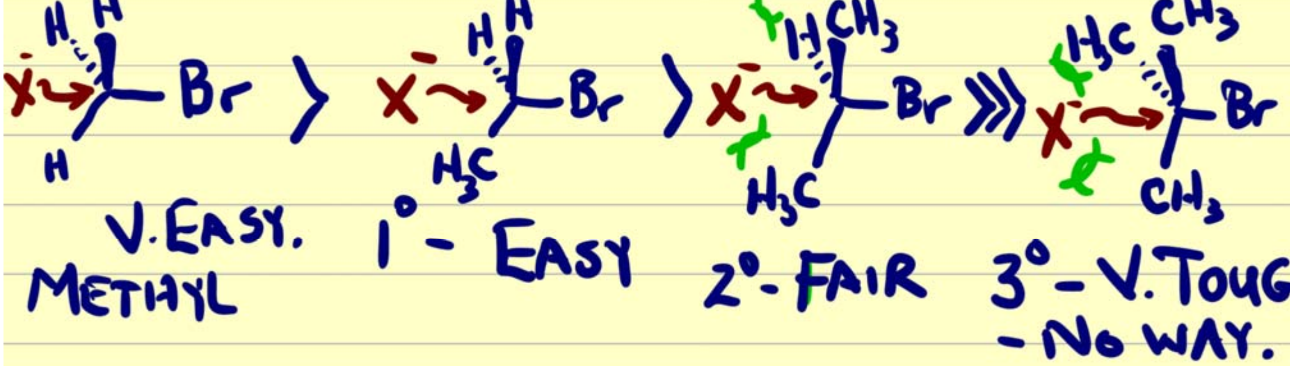
1) CENTRE UNDER ATTACK.

- S_N1 - CRITICAL STEP (SLOW) IS FORM OF CARBOCATION

- CARBOCATION STABILITIES



S_N2 - 1 STEP, BACKSIDE ATTACK
- STERICALLY LESS HINDERED = BETTER

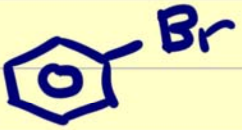


1°, METHYL - USUALLY S_N2

3° - ALWAYS S_N1

TERRIBLE FOR BOTH.

, R-C≡C-Br, OR



S_N2 - BACKSIDE ATTACK IS BLOCKED

S_N1 - CARBOCATIONS JUST TOO UNSTABLE

- USUALLY NO REACTION.

GOOD FOR BOTH

BENZYL

ALLYLIC

2) NUCLEOPHILE:

S_N1 - DOESN'T HAVE TO BE THAT GOOD.

- BECAUSE IT'S NOT IN R.D.S.
- GOING FROM GOOD TO A MEDIOCRE NUCLEOPHILE DOESN'T MATTER

SN2 - Nu^- MATTERS A LOT

- IT'S IN R.D.S.

- GOING FROM MEDIOCRE TO GOOD Nu^- SPEED US SN2 A LOT.

Recall from last lecture - importance of nucleophile to S_N1 vs S_N2 reactions

Nu: - NOT SO CRITICAL FOR S_N1

- QUITE IMPORTANT FOR S_N2

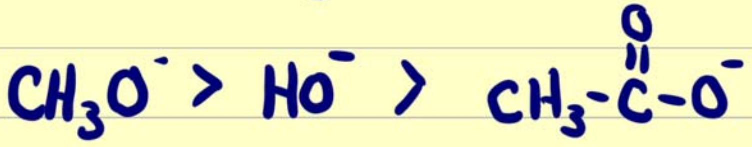
Q - WHAT MAKES A GOOD NUCLEOPHILE?

- NEEDS e^- PAIR, OFTEN ANIONIC

i) IN SAME ROW OF PERIODIC TABLE, NUCLEOPHILICITY PARALLELS BASICITY

$$H_2N^- > HO^- > F^-$$

$$H_3N: > H_2\ddot{O}:$$



$$CH_3O^- > HO^- > CH_3-\overset{O}{\overset{\|}{C}}-O^-$$

(BY A BIT)

ii) AS YOU GO DOWN A COLUMN IN PERIODI NUCLEOPHILES GET BETTER

$$I^- > Br^- > Cl^- > F^-$$

$$HS^- > HO^-$$

- REASON - SOLVENT EFFECTS; DETAILS BEYOND SCOPE OF COURSE

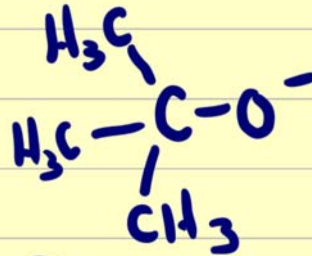
iii) NEGATIVELY CHARGED ~~S~~ Nu^- IS STRONGER THAN A NEUTRAL Nu:

$HO^- > H_2O$

$H_2N^- > H_3N:$

iv) STERIC EFFECTS CAN HINDER A NUCLEOPHILE

$CH_3O^- \gg$

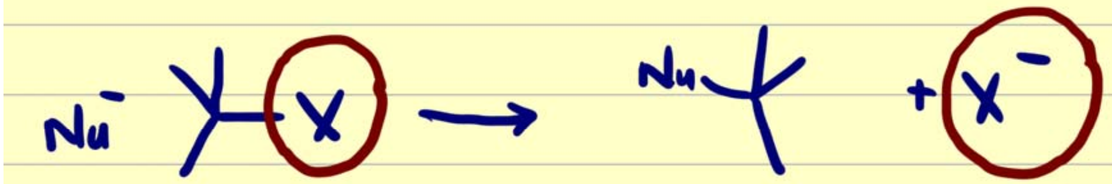


$(H_3C)_3C-O^-$

V. GOOD

POOR - TOO STERICALLY HINDERED

LEAVING GROUP.



IMPORTANT FOR BOTH S_N1 & S_N2, BUT ESP. <u>S_N1</u>

- USUALLY, S_N1'S HAVE EXCELLENT LEAVING GROUPS

- TREND - LOOK AT ACID STRENGTH

IF HX IS A STRONG ACID, X^- IS A GOOD LEAVING GRP.

ACIDITY

$HI > HBr > HCl > HF > H_2O > NH_3$

∴ L.G. ABILITY

$I^- > Br^- > Cl^- > F^- > HO^- > {}^-NH_2$

NOTE: H_2O IS EXCELLENT NEUTRAL L.G.

SOLVENT

POLARITY OF SOLVENT HAS AN IMPORTANT EFFECT

LOW POLARITY, = LOW DIELECTRIC CONSTANT

HEXANE, BENZENE, TOLUENE, CH_2Cl_2

HIGH POLARITY

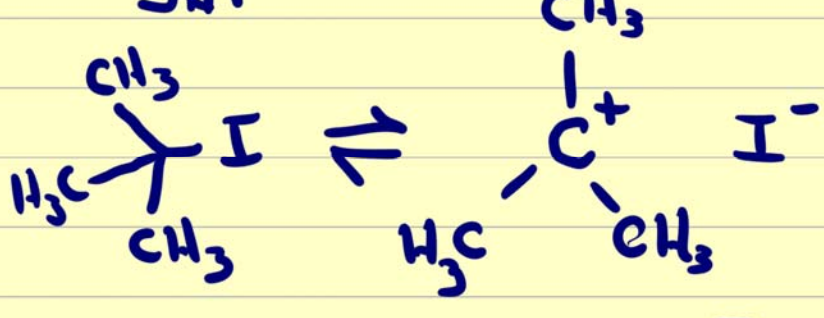
H_2O, CH_3OH, $CH_3C{\equiv}N$

ACETONE - MEDIUM POLARITY.

HIGH POLARITY SOLVENTS
- STABILIZE CHARGED SPECIES.

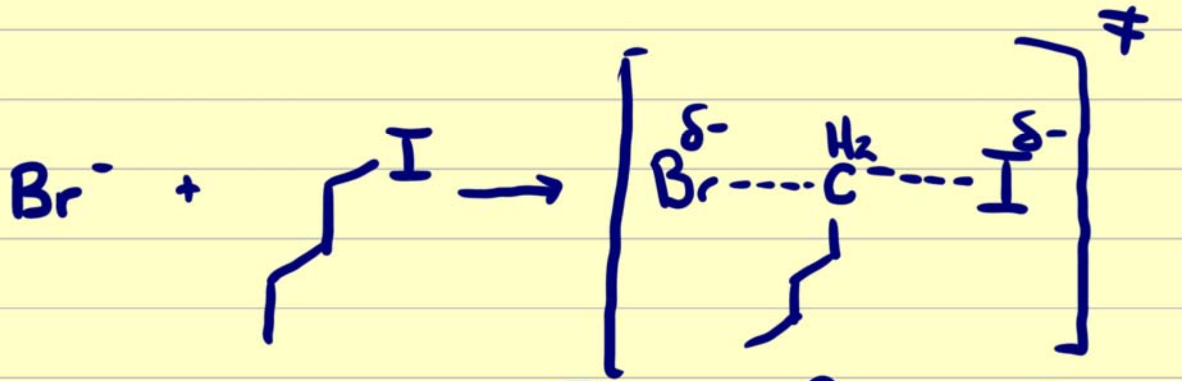
LOW POLARITY SOLVENTS
- DESTABILIZE CHARGED SPECIES

S_N1



SLOW STEP.

POLAR SOLVENT STABILIZES THIS, SPEEDS UP S_N1.



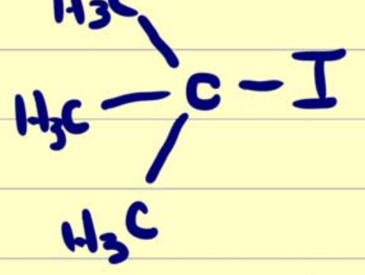
IN TRANSITION STATE, CHARGE DENSITY IS LOWER

∴ SLOWED IN POLAR SOLVENTS.

PUTTING THEM ALL TOGETHER

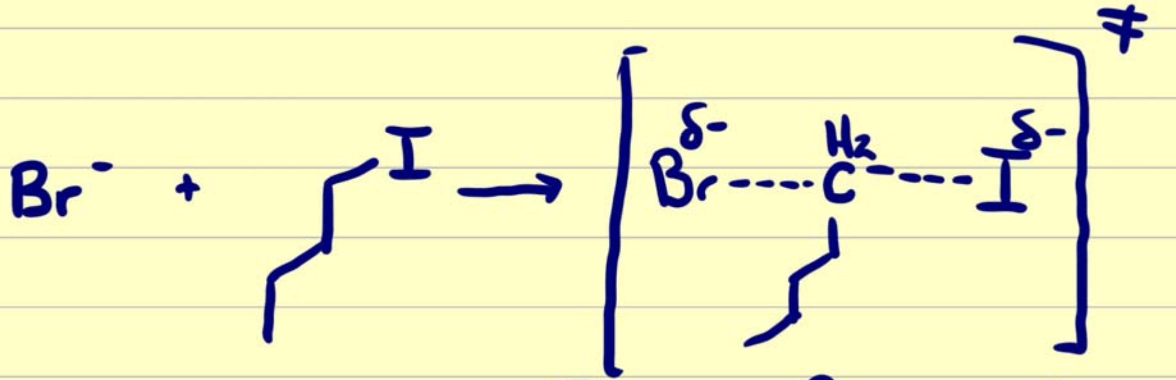
$CH_3CH_2CH_2\text{-}Br + H_2O \longrightarrow$?

$CH_3CH_2CH_2\text{-}Br + H_3N \longrightarrow$?



$+ H_2O \longrightarrow$?

$CH_3CH_2CH_2\text{-}I + H_2O \longrightarrow$?



IN TRANSITION STATE, CHARGE DENSITY IS LOWER

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$CH_3CH_2CH_2{-}Br + H_2O \longrightarrow$?

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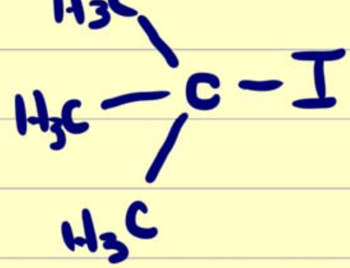


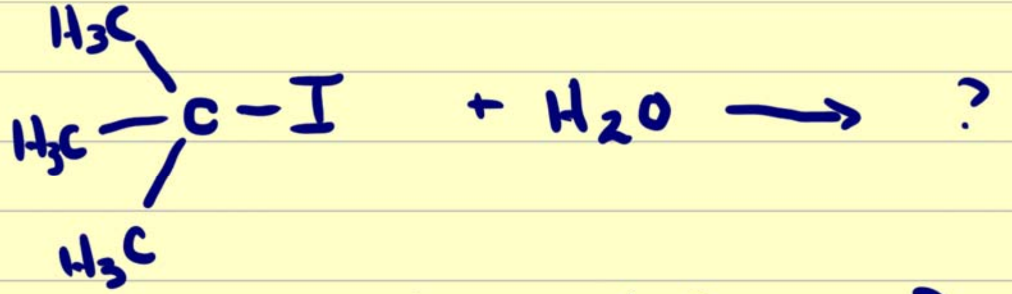
$+ H_2O \longrightarrow$?

$CH_3CH_2CH_2{-}I + H_2O \longrightarrow$?

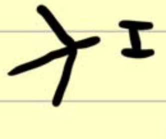
PROBLEM - GIVE PRODUCTS AND RANK, S_N1 vs S_N2

$CH_3CH_2CH_2-Br + H_2O \longrightarrow$?

$CH_3CH_2CH_2-Br + H_3N \longrightarrow$?



$CH_3CH_2CH_2-I + H_2O \longrightarrow$?

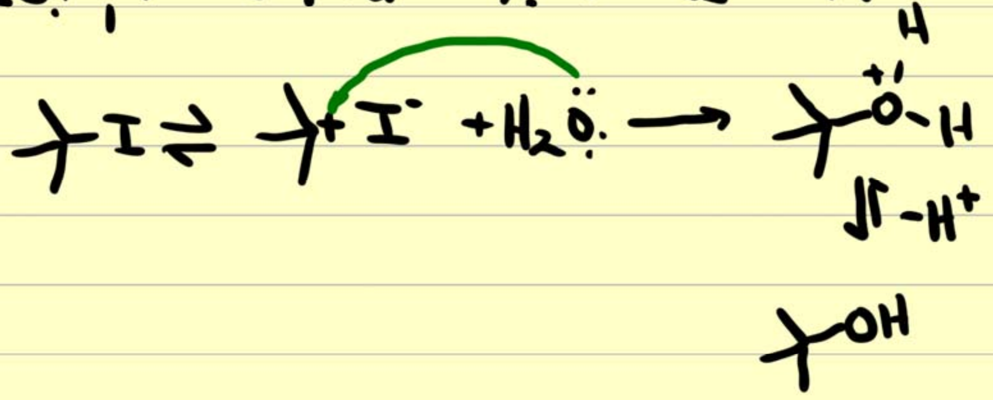


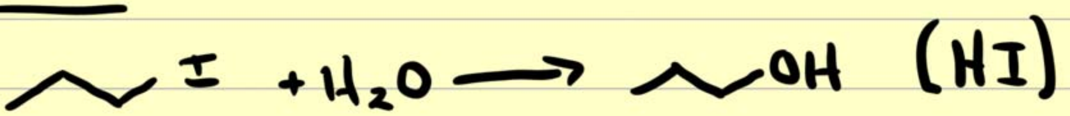
3° HALIDE - S_N1

I^- - EXCELLENT L.G. - S_N1 OR S_N2

$H_2\ddot{O}$:, POOR Nü ∴ MORE S_N1

∴ S_N1





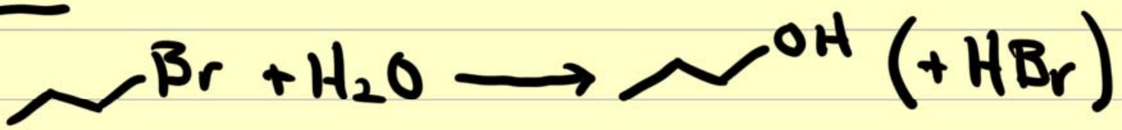
1° ALKYL HALIDE - S_N2

HALIDE I^- (L.G.) - EXCELLENT - S_N1 OR S_N2

NÜ - H_2O - POOR ∴ S_N1 TENDENCY.

∴ 50/50 S_N1 / S_N2

—



1° ALKYL HALIDE - S_N2

L.G. IS Br^- - NOT QUITE AS GOOD AS I^-
A BIT MORE S_N2 THAN I^-

NÜ - $H_2O:$ - POOR ∴ S_N1 TENDENCY.

∴ A BIT MORE S_N2 CHARACTER

—

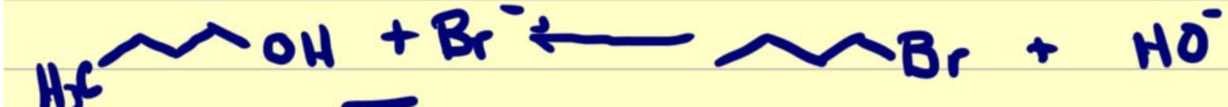
1° HALIDE - S_N2

L.G. - Br^- - A BIT MORE S_N2 THAN I^-

NH_3 - GOOD NÜ - TENDS TOWARDS S_N2
(MORE THAN H_2O)

∴ ALMOST 100% S_N2 CHARACTER.

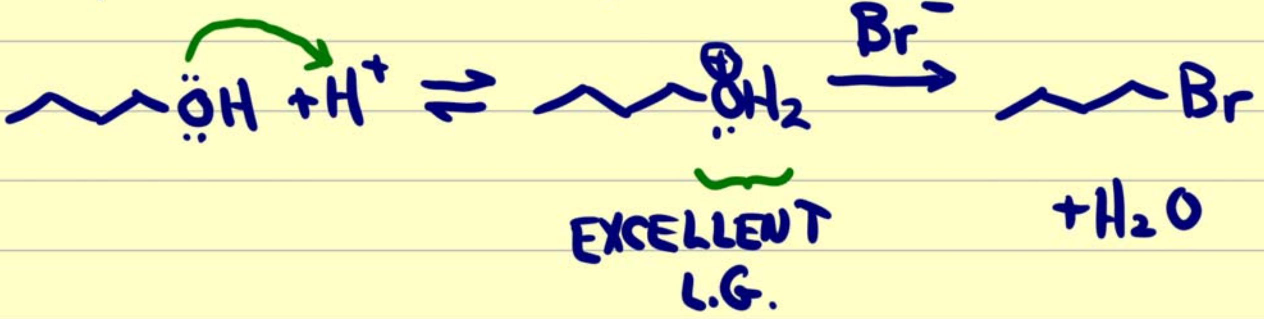
ALCOHOLS AS SUBSTRATES FOR S_N1 OR 2



FAILS

PROBLEMS - ⊖OH IS A POOR LEAVING GROUP.
- K_{eqm} IS HORRIBLE

BUT, IF YOU ADD H^+, THIS BECOMES FEASIBLE



OFTEN USE EXCESS HBr, SO THAT

$HBr + H_2O \rightleftharpoons H_3O^+ \; Br^-$

90% OF TIME, THIS IS S_N1.

CH 7. - ALCOHOLS, ETHERS, HALIDES, AMINES.

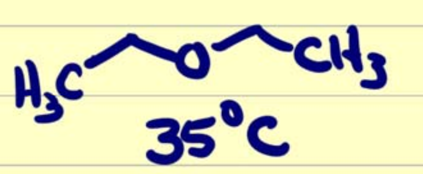
ALCOHOLS- R-OH - RULED BY OH

THEY'RE A BIT LIKE H_2O

- PARTICPATE IN HYDROGEN BONDING.
- BPT - UNUSUALLY HIGH
- TEND TO BE WATER SOLUBLE UP TO C_5

BPT. DIETHYL ETHER BUTANOL

36°C



35°C

BPT 117°C

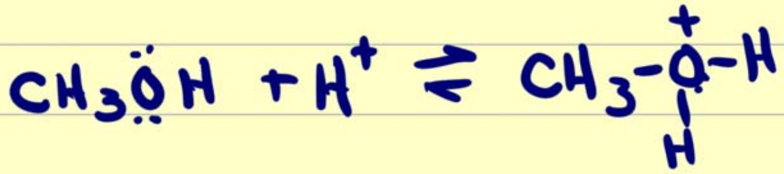
ETHERS R-O-R
- NOT H_2O SOLUBLE
- NOT ESPECIALLY BOILING.

ALCOHOLS- CHEMISTRY LIKE H_2O - ACIDIC

$$H_2O + BASE \rightleftharpoons HO^- + BASE-H^+$$

$$H_3C-OH + BASE \rightleftharpoons H_3C-O^- + BASE-H^+$$

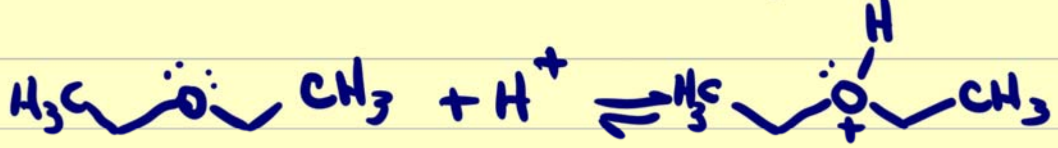
ALSO BASIC.



$$CH_3\underset{\cdot\cdot}{\ddot{O}}H + H^+ \rightleftharpoons CH_3-\underset{H}{\overset{+}{O}}-H$$

ETHERS - NOT ACIDIC - NO OH

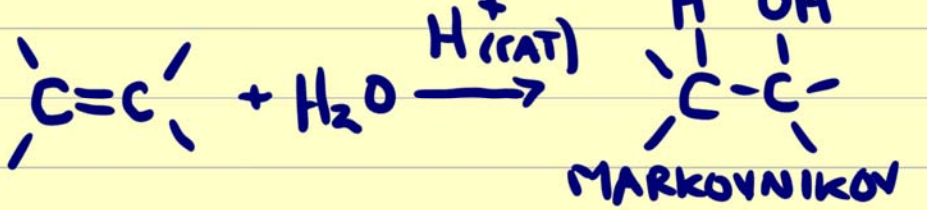
- THEY ARE BASIC, THOUGH



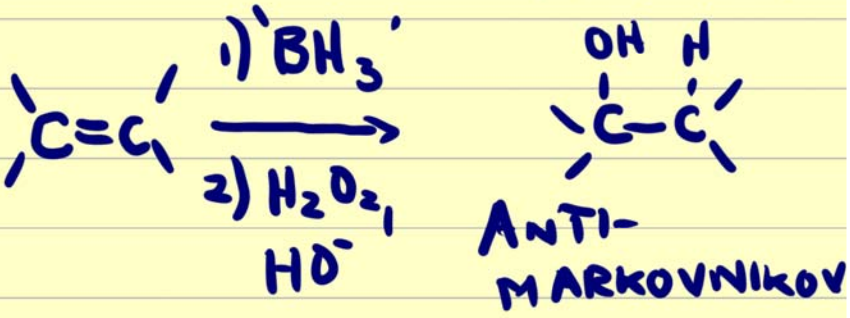
PREPARATION OF ALCOHOLS, ETHERS.

ALCOHOLS

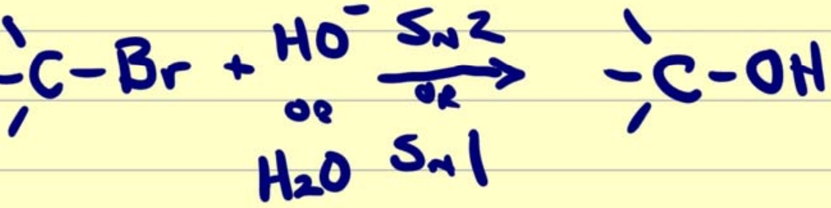
ADDN OF H_2O TO ALKENES.



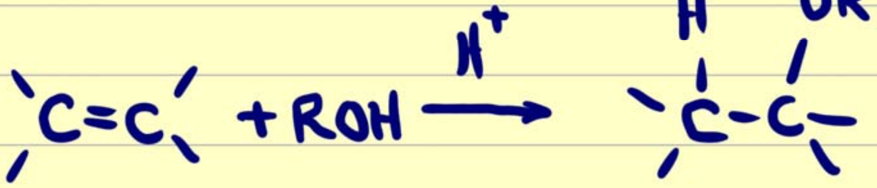
HYDROBORATION OF ALKENES

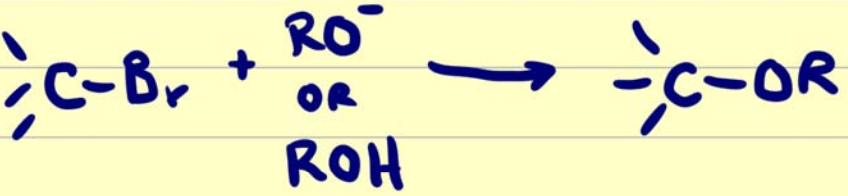


NUCLEOPHILIC SUBST.



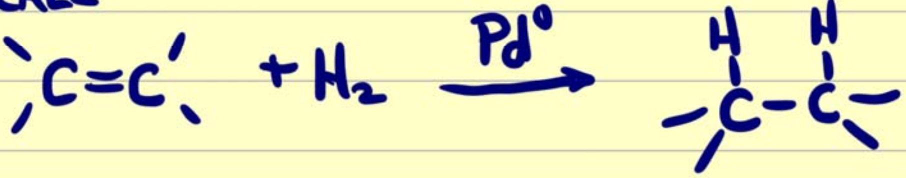
ETHERS



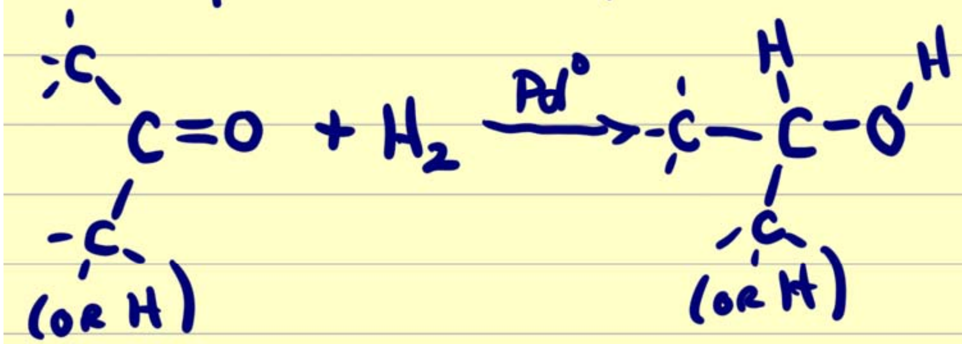


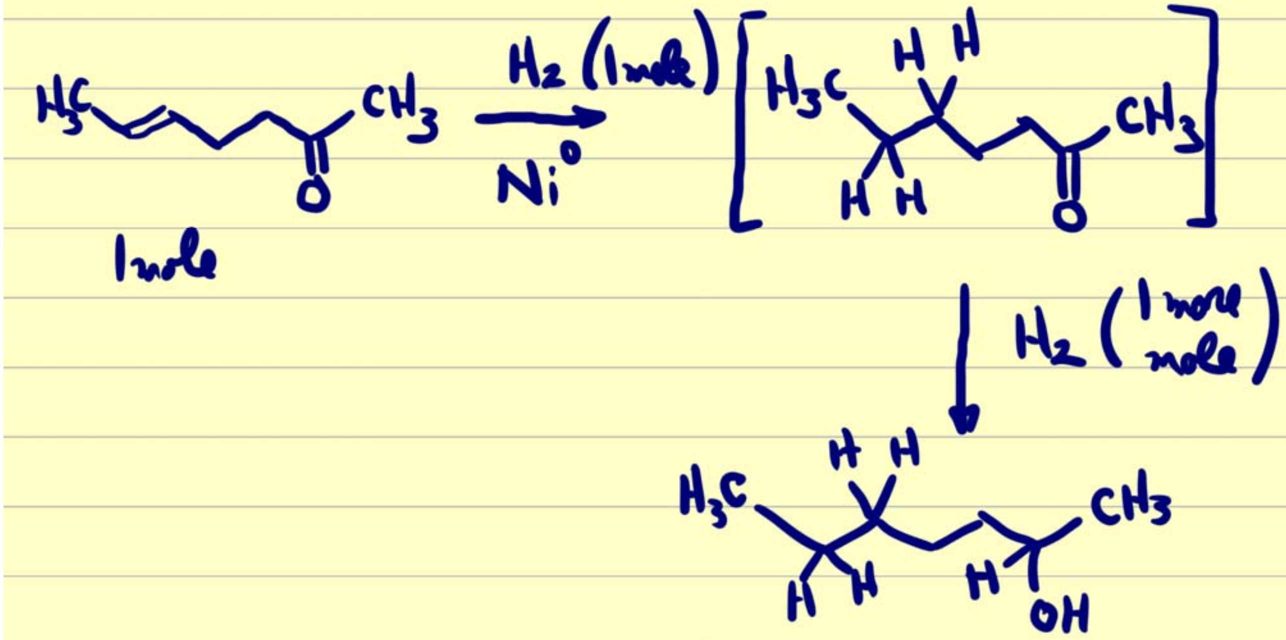
NEW ONE - CATALYTIC HYDROGENATION.

RECALL



WELL, IT'S SLOWER, BUT.....





REACTIONS OF ALCOHOLS.

1) - ACIDIC 'OH' DOMINATES

(STRONG BASE)

EXCELLENT NUCLEOPHILE

2) PREPARATION OF HALIDES.

$R{-}OH + H{-}Br \longrightarrow R{-}Br + H_2O$

(USUALLY S_N1)

$R{-}OH + H{-}Cl \xrightarrow{ZnCl_2 (CAT)} R{-}Cl + H_2O$

(NOT QUITE AS REACTIVE, $ZnCl_2$ USUALLY NEEDED AS CATALYST)

MORE COMMON IN SYNTHESIS IS TO USE $SOCl_2$ OR PBr_3


$R{-}OH + Cl{-}\overset{\overset{O}{\|}}{S}{-}Cl \longrightarrow R{-}Cl + SO_2 + HCl$

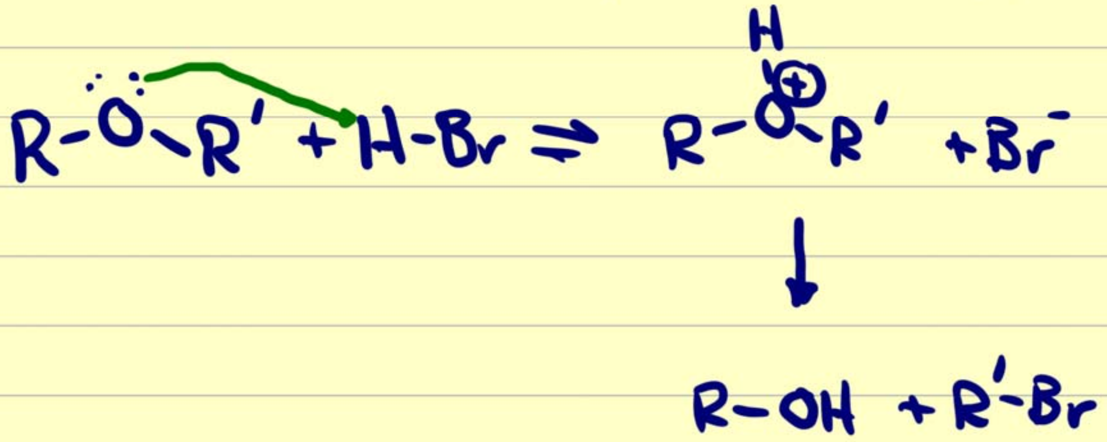
(THIONYL CHLORIDE)

RARE S_Ni MECH

$R-OH + PBr_3 \longrightarrow R-Br + H_3PO_3$

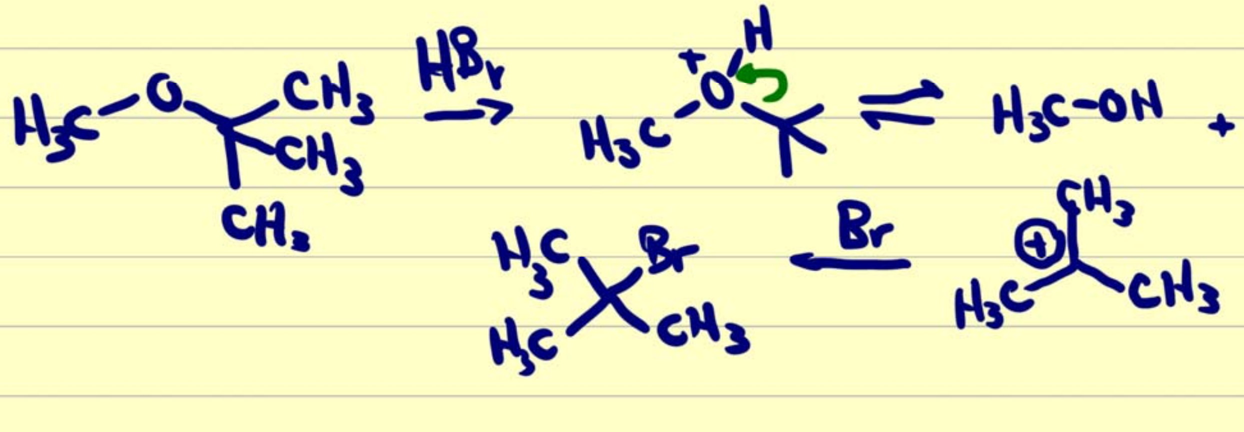
ETHERS

- NOT ACIDS
- BUT THEY WILL REACT WITH STRONG ACIDS (i.e. HBr)



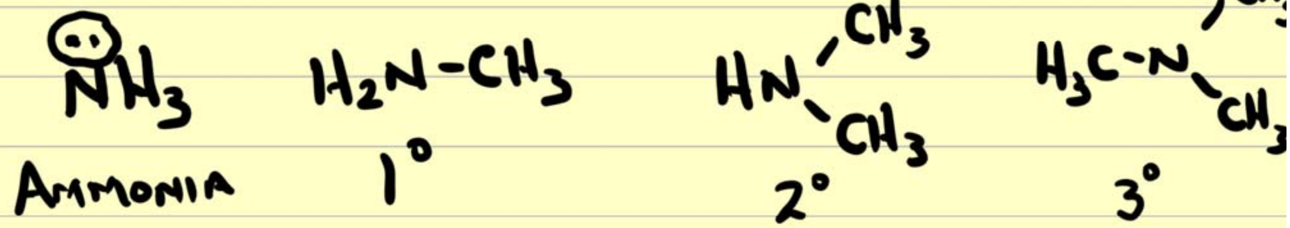
$$R-\ddot{O}-R' + H-Br \rightleftharpoons R-\overset{H}{\overset{\oplus}{O}}-R' + Br^- \longrightarrow R-OH + R'-Br$$

SELECTIVE FOR SUBSTITUTED R



HCl - NOT REACTIVE ENOUGH.

AMINES



RULED BY LONE PAIR.

$$\ddot{N}H_3 + H^+X^- \longrightarrow \overset{+}{N}H_4\ X^-$$

BASIC

ALSO VERY SOLID NUCLEOPHILES.

$$\ddot{N}H_3 + CH_3-I \longrightarrow H_3\overset{\oplus}{N}-CH_3\ I^-$$

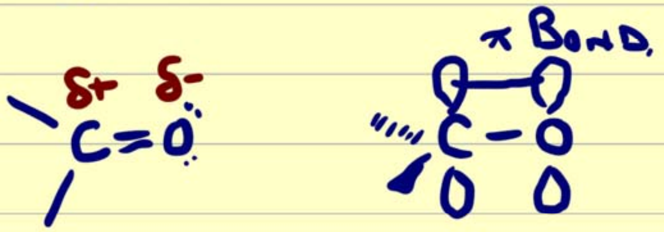
$$\Big\downarrow HO^-$$

$$H_2N-CH_3 + H_2O$$

USED IN
AMINE
SYNTHESIS - OFTEN.

Not in latest versions of 230. Moved to 235; replaced by eliminations.

CARBONYL COMPOUNDS.

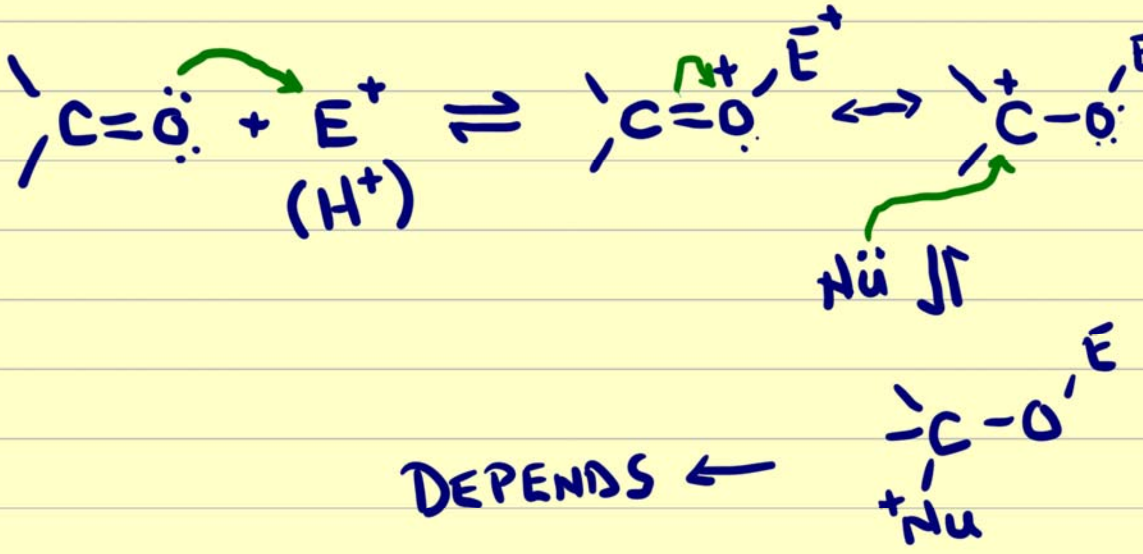


O En 3.5

C En 2.5

∴ MOST OF REACTIVITY IS.

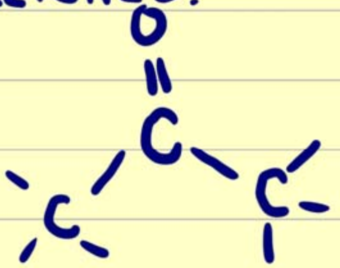
OR



USUALLY CALLED NUCLEOPHILIC ADDITION

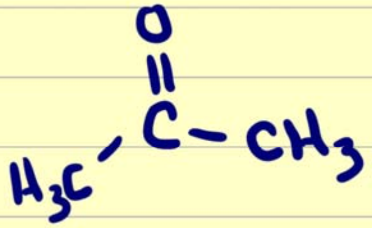
GROUP TOGETHER ALDEHYDES & KETONES

KETONES.



CARBONYL C HAS TWO ADDNAL C'S BOUND.

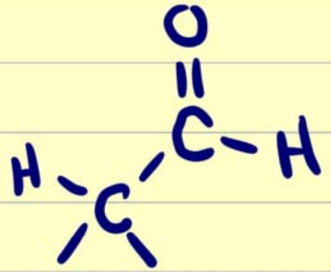
<u>ONE</u>



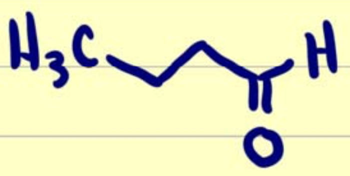
2-PROPANONE (ACETONE)

ALDEHYDES

CARBONYL CARBON HAS ONE H & ONE C (EXCEPT METHANAL)



"AL"



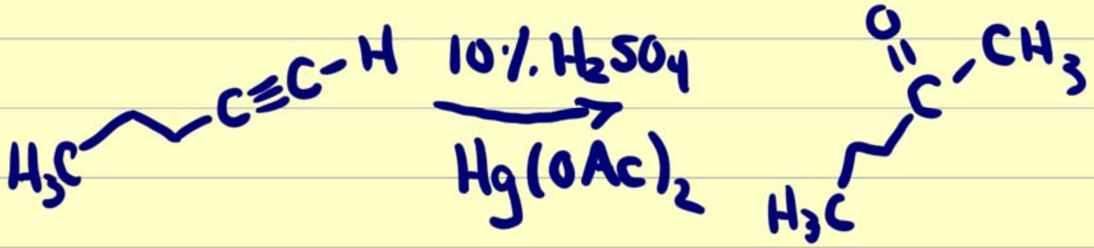
BUTANAL

KEY

NO LEAVING GROUPS ON CARBONYL C

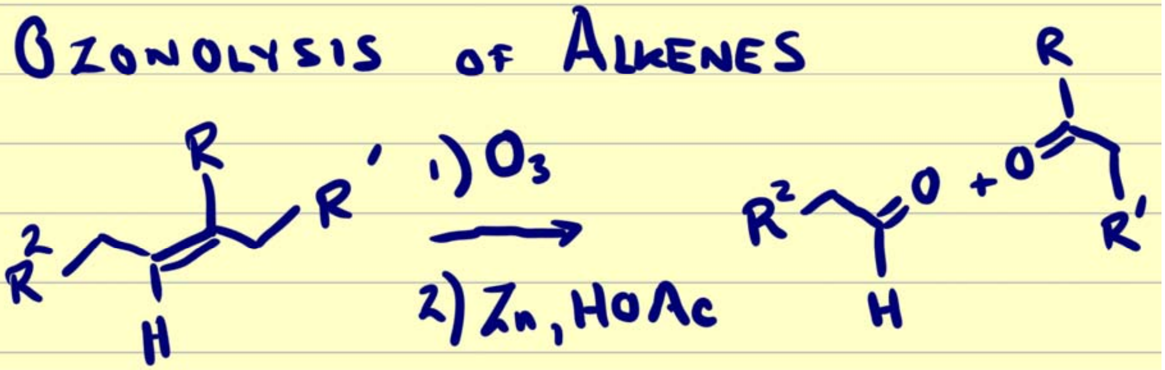
PREPARATION
- 3 TYPES (1 NEW)

a)

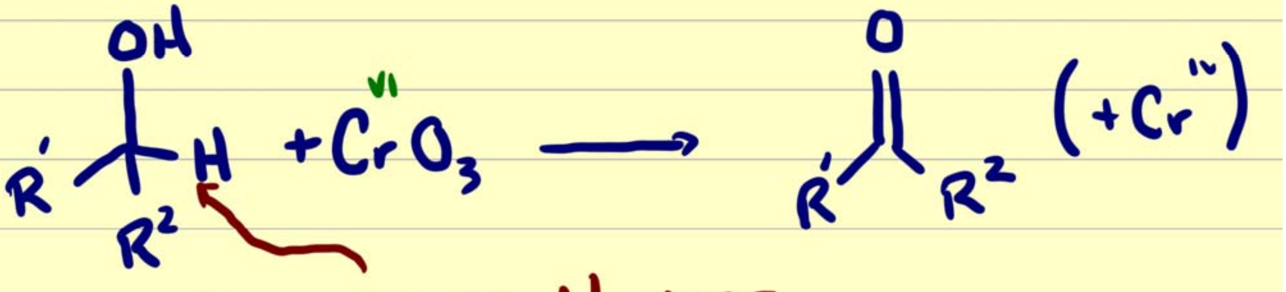


ADDN OF H_2O ALKYNE

b) OZONOLYSIS OF ALKENES

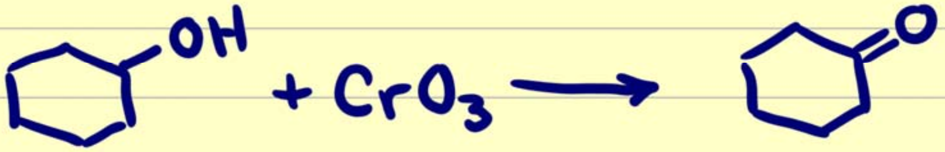


c) OXIDATION OF ALCOHOLS

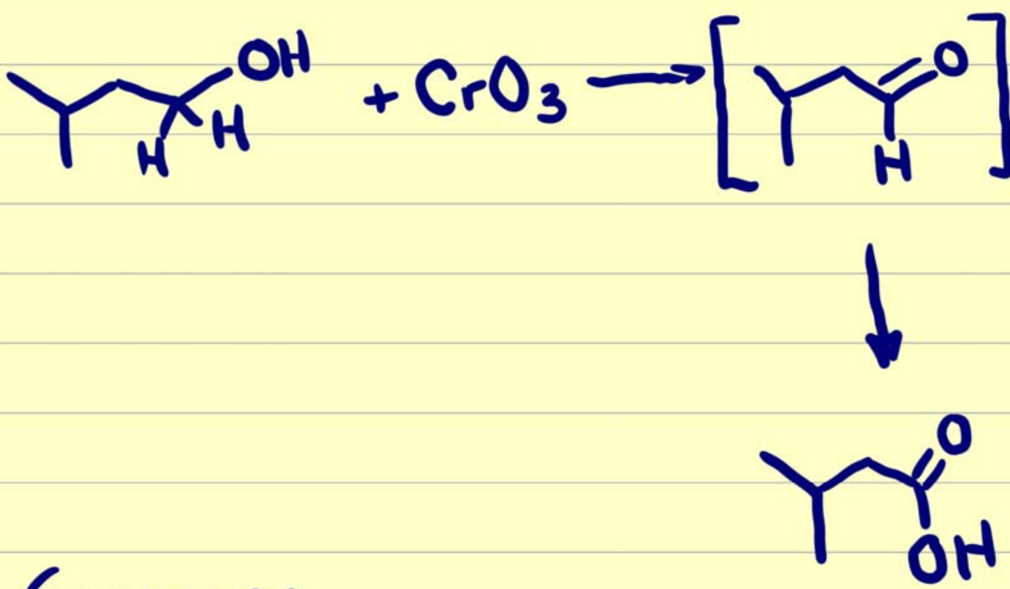


MUST BE >1 H HERE

FOR 2° ALCOHOL → KETONE PROCESS,
IT'S VERY SIMPLE



FOR 1° ALCOHOLS → ALDEHYDES, THIS IS TRICKIER

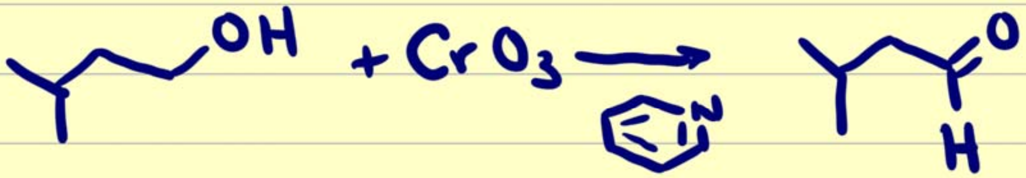


DOESN'T STOP

GET ACID

SOLUTION

- ADD  (PYRIDINE), LOWERS CrO3 REACTIVITY



REACTIONS.

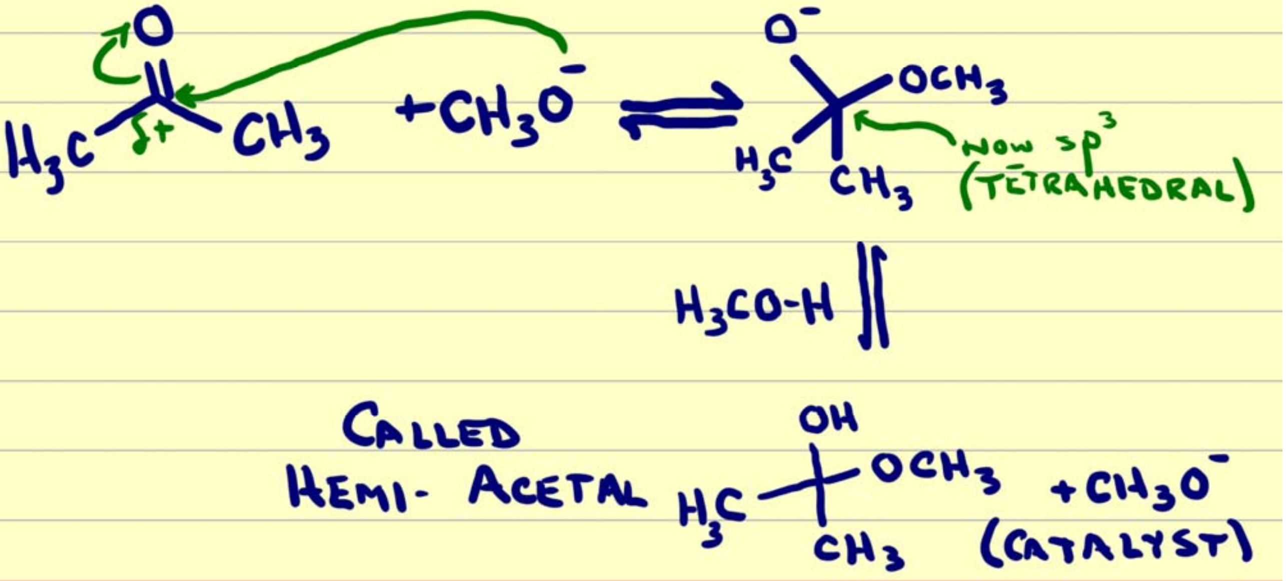
- ALL NUCLEOPHILIC ADDNS.
- TWO GROUPS
  - "O" NUCLEOPHILES.
  - C OR H NUCLEOPHILES

i) OXYGEN NUCLEOPHILES.

- H_2O, ROH ARE JUST NOT STRONG ENOUGH ON THEIR OWN

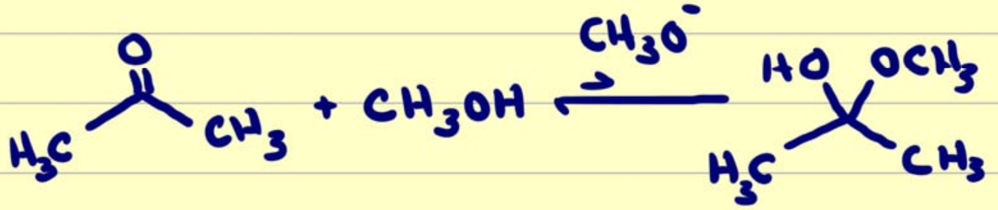
- CAN ADD H^+ OR BASE

i) BASE $CH_3\cancel{OH}$ $\underline{\underline{CH_3O^-}}$



CALLED HEMI-ACETAL

BUT THERE'S A SIGNIFICANT PROBLEM.

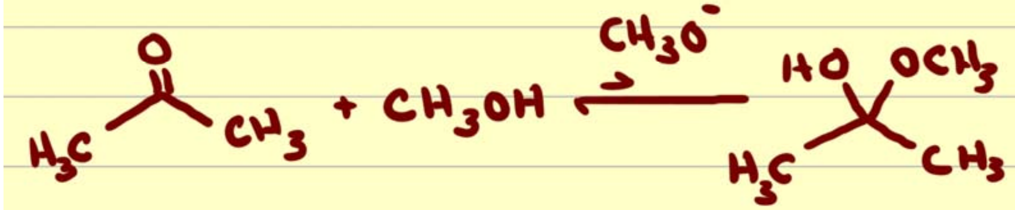


THE K_{eqn} (EQUILIBRIUM CONSTANT) IS $<< 1$

- IN OTHER WORDS, IN THE VAST MAJORITY OF CASES, THIS DOESN'T YIELD PRODUCT.

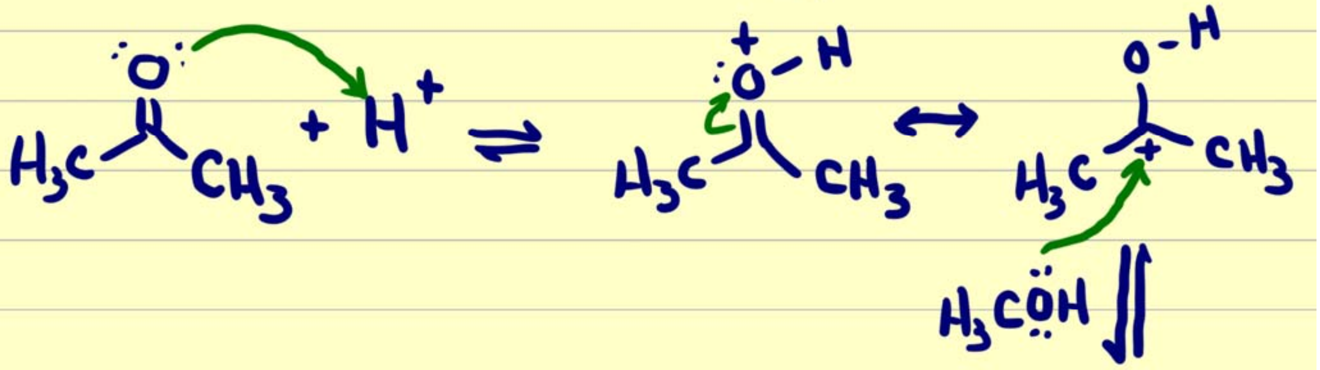
So here's how we ended Monday's lecture - the 'failure' of basic catalysts

BUT THERE'S A SIGNIFICANT PROBLEM.

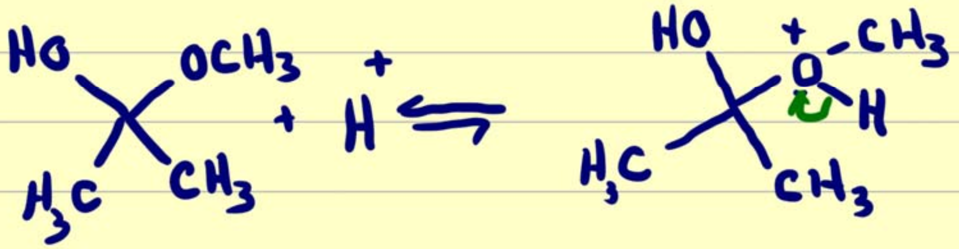


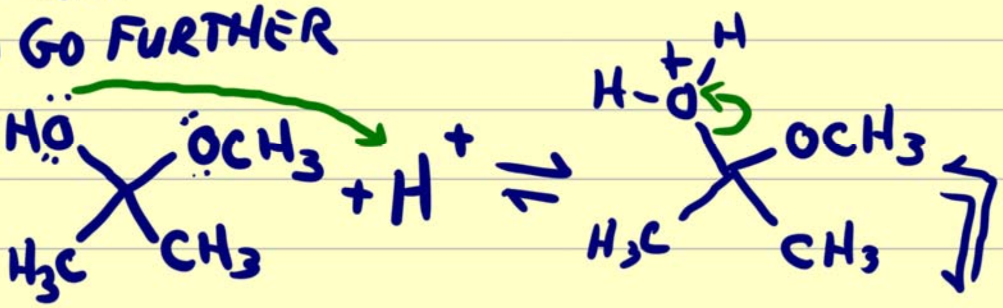
THE K_{eqn} (EQUILIBRIUM CONSTANT) IS <<1
- IN OTHER WORDS, IN THE VAST MAJORITY OF CASES, THIS DOESN'T YIELD PRODUCT.

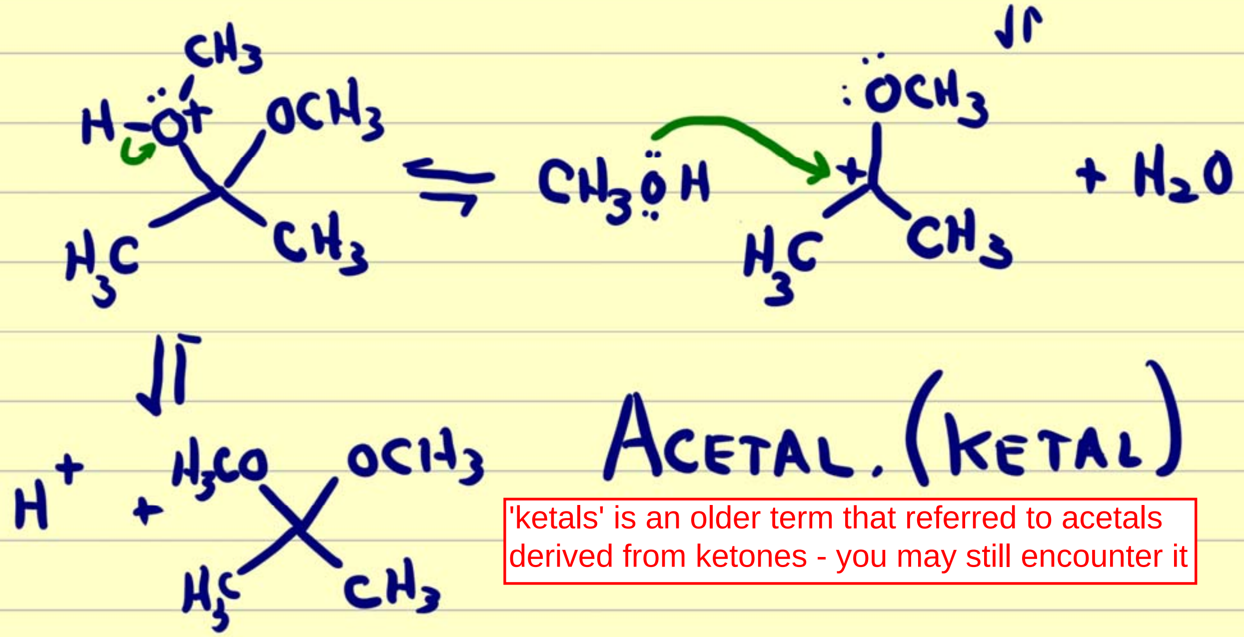
HOW ABOUT IN ACID $\underline{H^+}$



TO HERE
K_{eqn} IS
STILL BAD
BUT RXN
CAN GO FURTHER

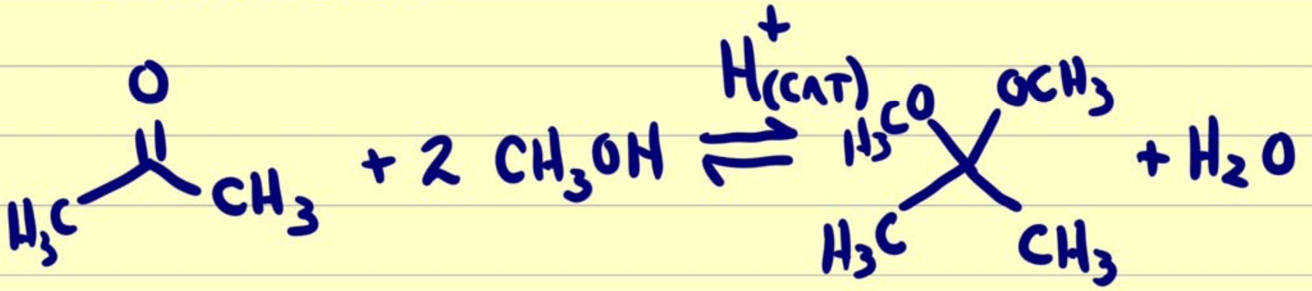





ACETAL. (KETAL)

'ketals' is an older term that referred to acetals derived from ketones - you may still encounter it

OVERALL...



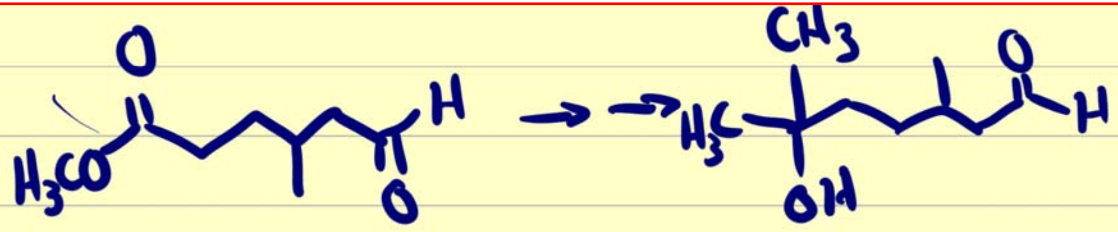
water can be removed by a drying agent or by azeotropic distillation

BY REMOVING H_2O, OR USING THE ALCOHOL IN XS, YOU CAN GET EXCELLENT YIELDS OF THE ACETAL

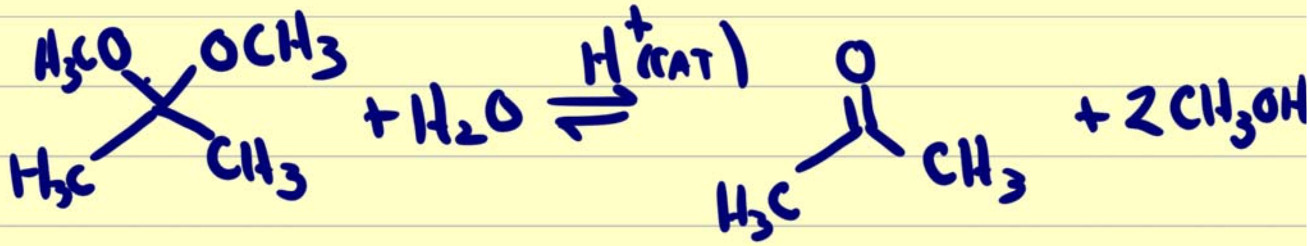
USE - ACETALS ARE ETHERS
∴ INERT TO BASES, NUCLEOPHILES, GRIGNARD REAGENTS, "H^-" SOURCES

∴ PROTECTING GROUP FOR KETONES, ALDEHYDES

i.e., what if you want to do a Grigard reaction with an ester, but not the aldehyde? You could 'protect' the aldehyde as an acetal, and get it back at the end....



IF WE TAKE ACETAL, ADD $H_2O + H^+$



get back the ketone (or aldehyde)

CARBON NUCLEOPHILES

- HOW DO WE GET $>\!C^{\ominus}$?

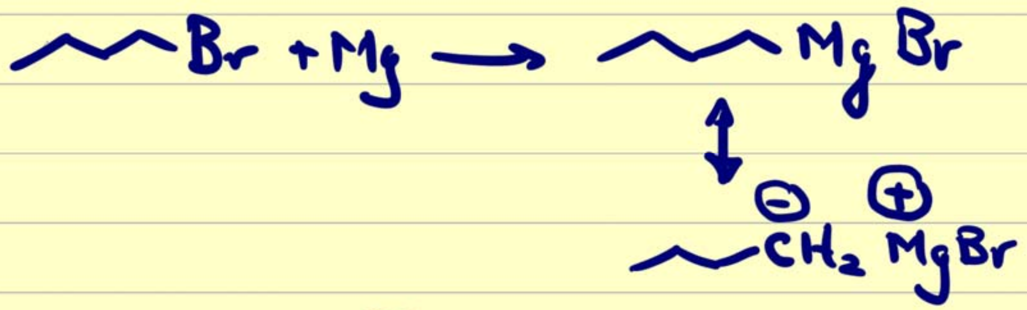
GRIGNARD REAGENT.

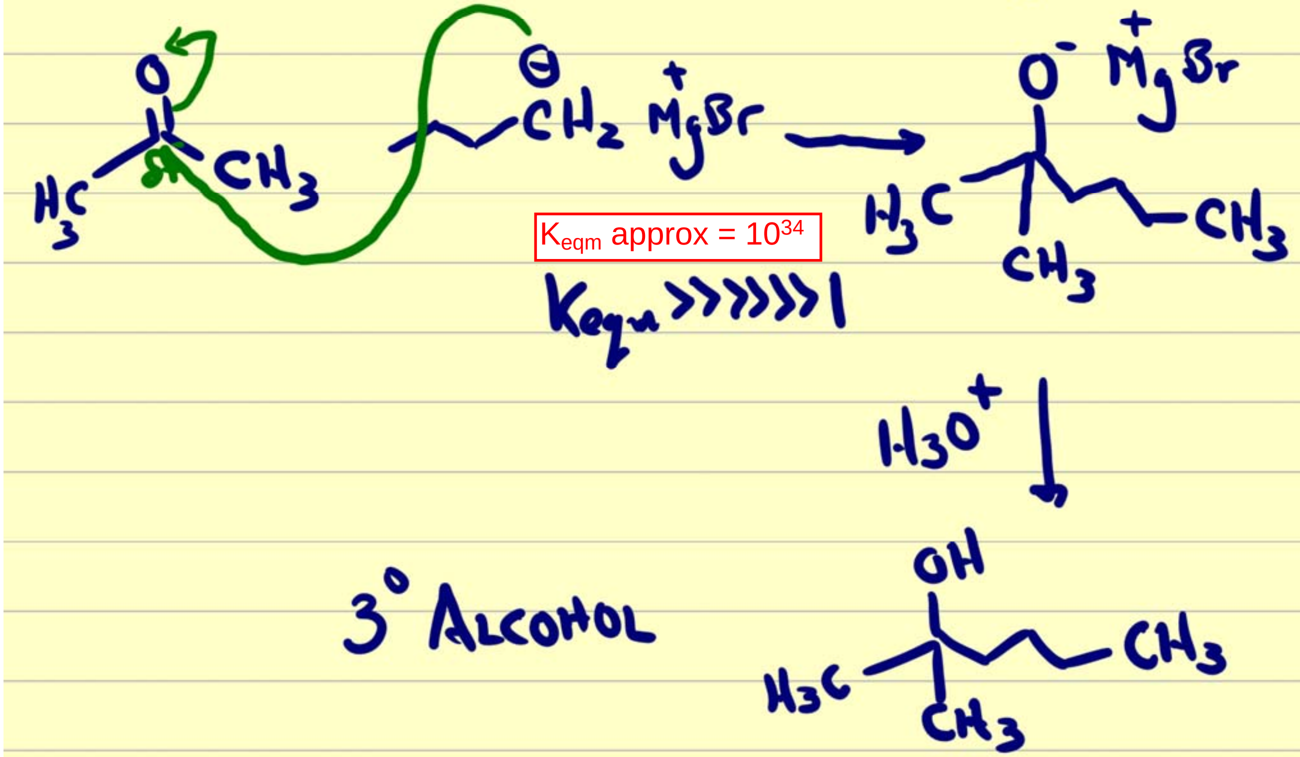
it's really polar covalent, but we'll consider it ionic for simplicity

$$R{-}Br + Mg^{\circ} \xrightarrow[\text{ADDN.}]{\text{OXID.}} R{-}MgBr \updownarrow R^{\ominus}\ \overset{+}{Mg}Br$$

(CAN BE R-I, R-Cl)

- EXTREMELY NUCLEOPHILIC



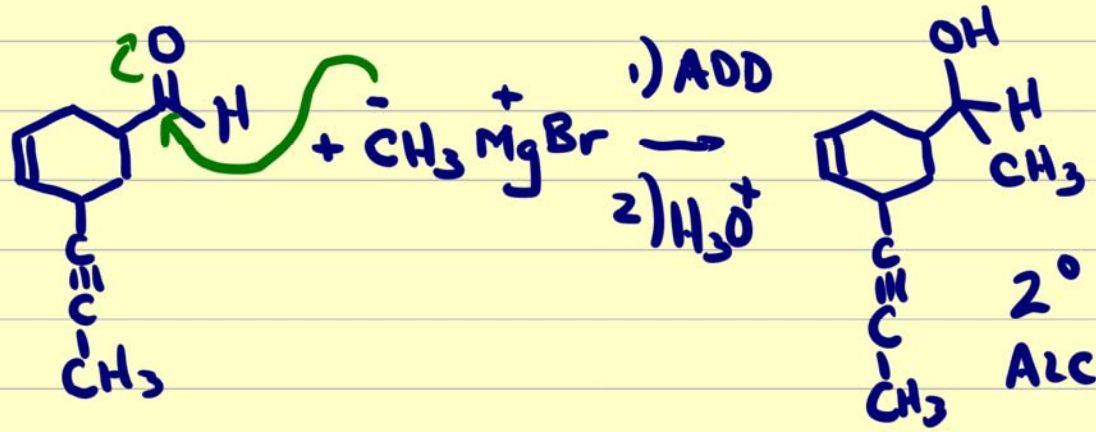


K_{eqm} approx = 10^{34}

$K_{eqm} >>>>>>> 1$

3° ALCOHOL

- VERY POLAR REAGENT, SO NON POLAR C=C'S, C-C≡C-C ARE INERT

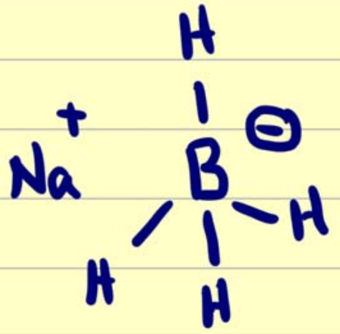


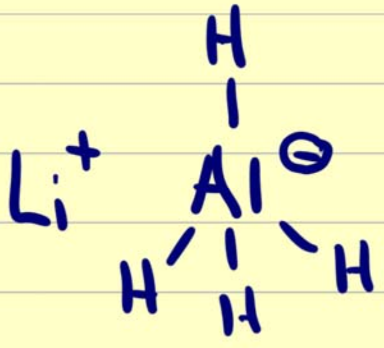
2° ALCOHOL.

$$H_3C-C\equiv C-H + CH_3MgBr \longrightarrow H_3C-C\equiv C^{\ominus}\,\overset{+}{Mg}Br + CH_4$$

HOW ABOUT "H^-" NUCLEOPHILES?

TWO REAGENTS ARE USED





$NaBH_4$

SODIUM BOROHYDRIDE

MILD, ALDEHYDES & KETONES ONLY.

$LiAlH_4$

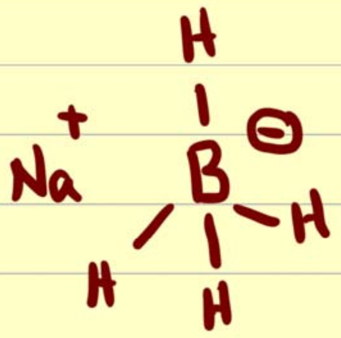
LITHIUM ALUMINUM HYDRIDE

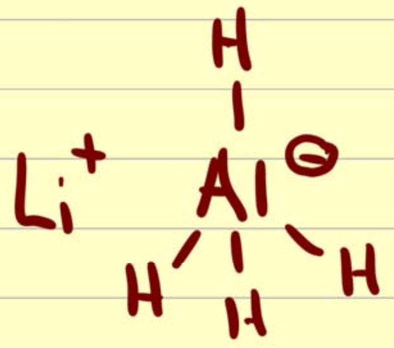
V. REACTIVE - POOF!

Where we left off - H^- sources; the 'hydride' equivalent of Grignard reagents - two common ones

HOW ABOUT "H^-" NUCLEOPHILES?

TWO REAGENTS ARE USED





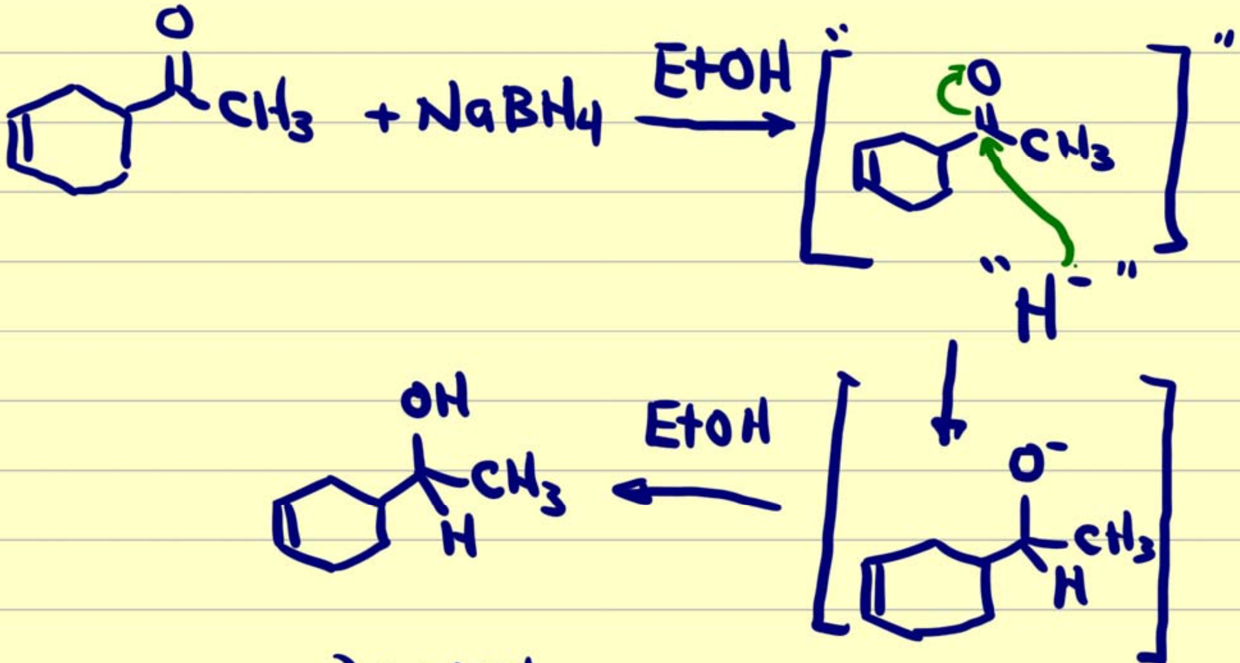
$NaBH_4$	$LiAlH_4$
SODIUM BOROHYDRIDE	LITHIUM ALUMINUM HYDRIDE
MILD, ALDEHYDES & KETONES ONLY.	V. REACTIVE-POOF!

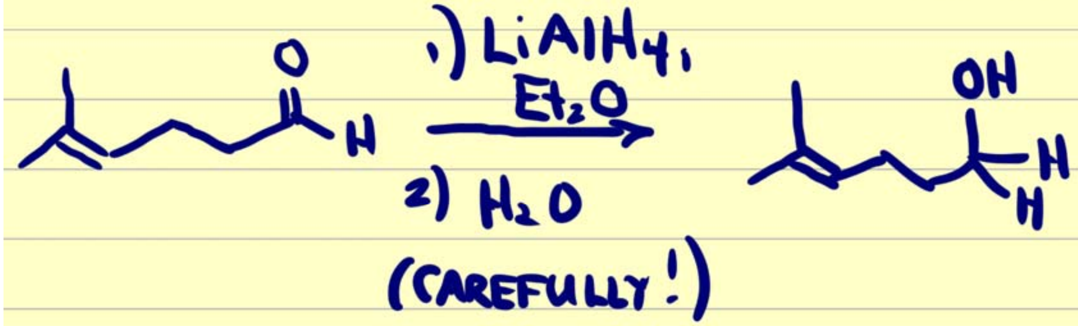
REACTIVITY - GIVE SAME THING WITH ALDEHYDES OR KETONES

$NaBH_4$ CAN BE USED IN PROTIC SOLVENTS

$LiAlH_4$ MUST BE USED IN APROTIC SOLVENTS I.E. $H_3CCH_2OCH_2CH_3$ (Et_2O)

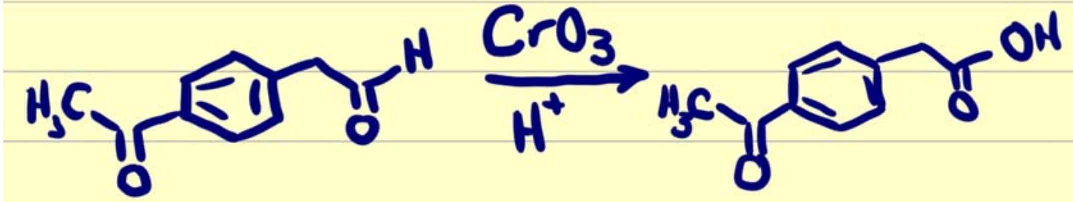
new abbreviation - 'Et' for CH_3CH_2- (ethyl)





FINALLY - OXIDATION.

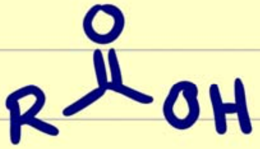
- ALDEHYDE ARE EASILY OXIDIZED TO CARBOXYLIC ACIDS



MILDER REAGENTS Ag_2O, EVEN AIR WILL DO THIS

KETONES ARE INERT TO THIS.

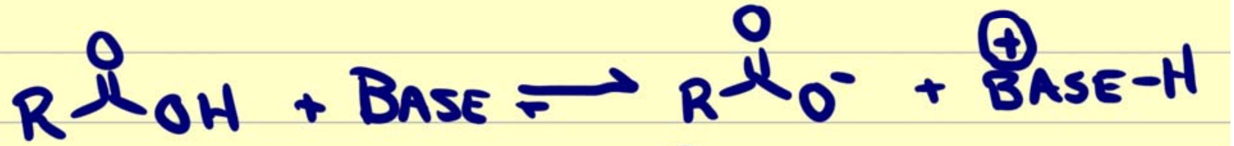
CHAPTER 8. CARBOXYLIC ACIDS + DERIVATIVES



CARBOXYLIC ACID.

- OH - RULES MUCH OF ITS CHEMISTRY

PROPERTY #1 IT'S ACIDIC.



pKa ~4-5

CARBOXYLATE SALT

- CARBOXYLATES ARE H_2O SOLUBLE
- PRETTY MUCH ONLY ORGANIC GROUP THAT ARE H_2O SOLUBLE REGARDLESS OF R.

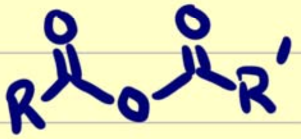
WHY IT'S ACIDIC

RESONANCE FORMS

give great stability to anion

DERIVATIVES.

ACID (ACYL) CHLORIDES



ANHYDRIDE

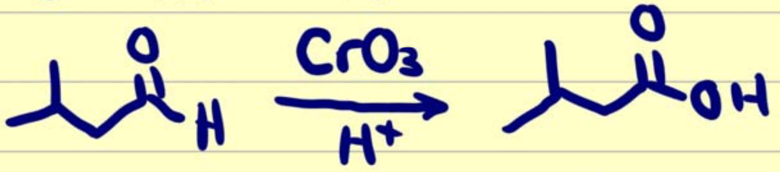
ESTERS

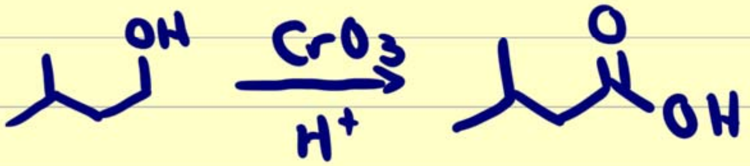
AMIDES

DECREASING REACTIVITY. →

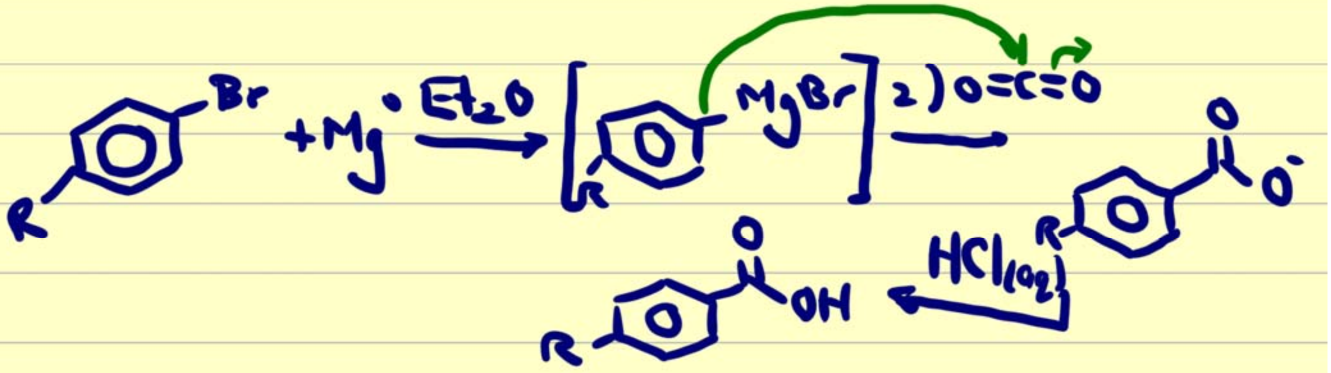
PREPARATIONS OF CARBOXYLIC ACIDS

1) OXIDATION.





2) GRIGNARD REAGENT WITH CO_2



REACTIONS.

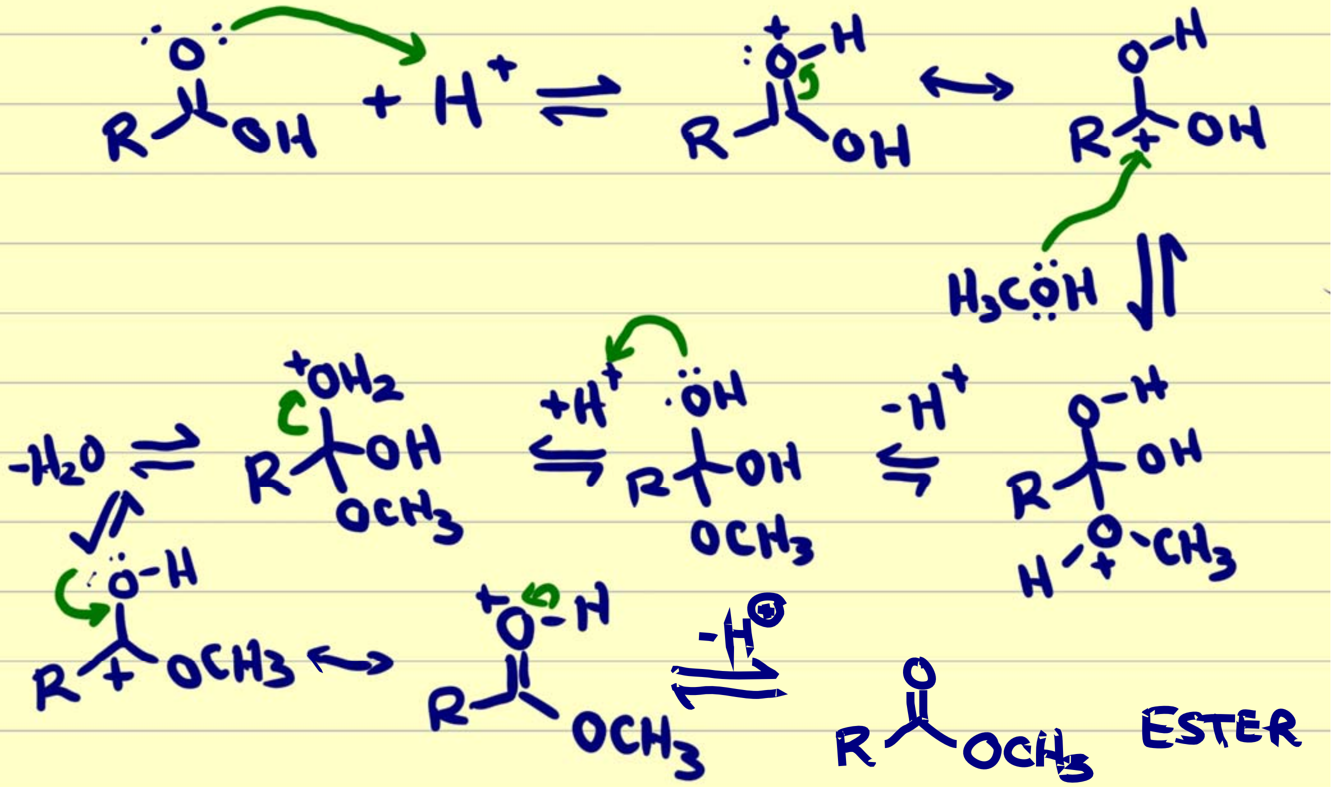
1) ESTERIFICATION.

a) w̄ BASE CATALYST? NO WAY.

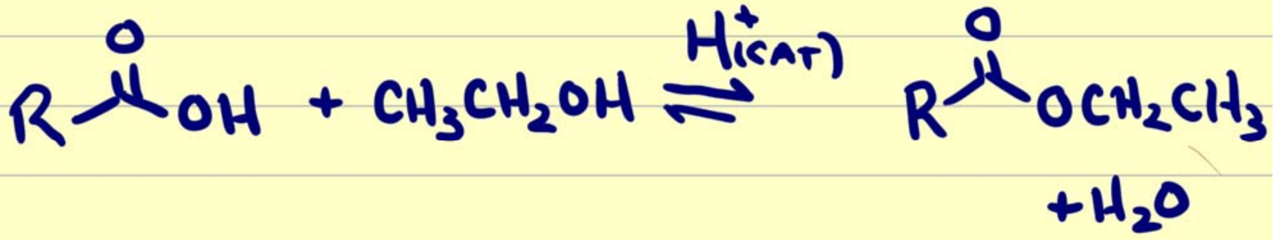
AND NOTHING ELSE.

base simply deprotonates the acid; no further reaction occurs

b) ACID CATALYST? ~YES. (H^+)



-very easy to push this equilibrium to either side
-use excess alcohol if you want ester
-use excess water of you want the carboxylic acid



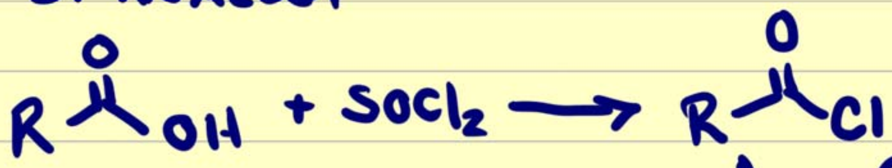
OTHER RXNS OF CARBOXYLIC ACIDS.

FORMATION OF ACID CHLORIDES.

RECALL

$R{-}OH + SOCl_2 \longrightarrow R{-}Cl + SO_2 + HCl$

BY ANALOGY



ACID CHLORIDE

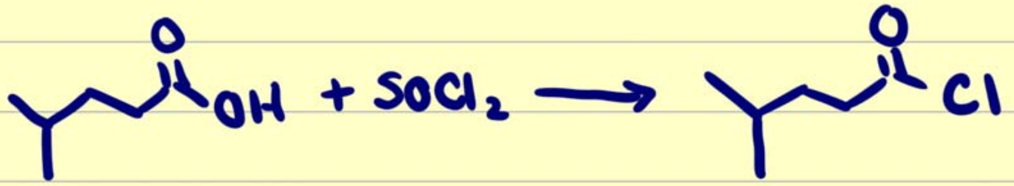
(ACYL)

VERY REACTIVE TO NUCLEOPHILIC SUBST.

- DON'T NEED H^+ OR BASE AS CAT.

- REASON - Cl^- IS EXCELLENT L.G.

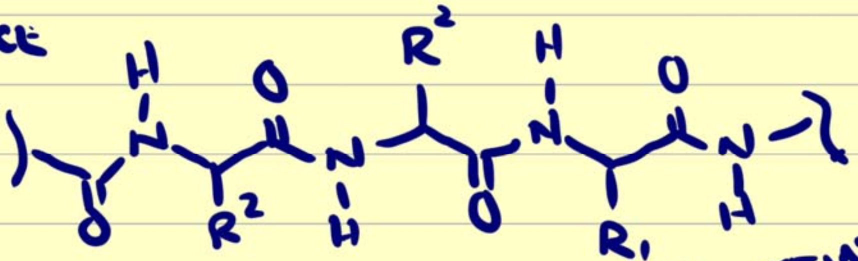
- ALSO COMMONLY USED TO MAKE AMIDES



AMIDE. (+HCl)

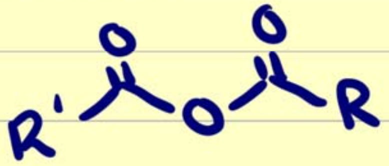
IMPORTANCE

59-261



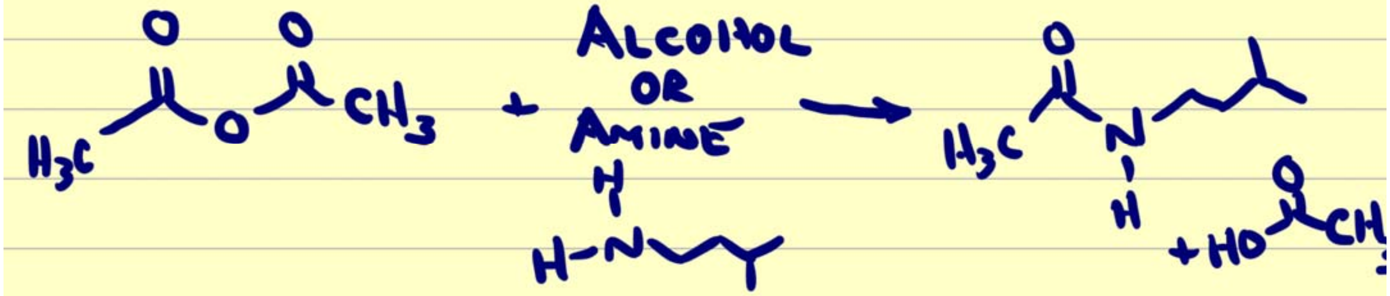
PROTEINS.

ANHYDRIDES.



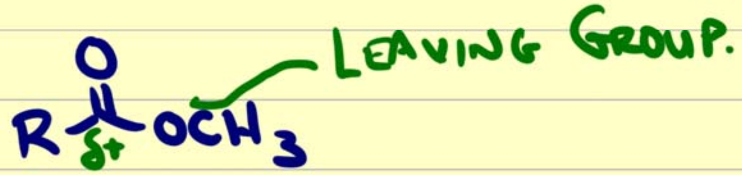
- TWO CARBOXYLIC ACIDS WITH H_2O REMOVED

SIMILAR TO ACID CHLORIDES BUT NOT QUITE AS REACTIVE (2ND MOST)



REACTIONS OF ESTERS.

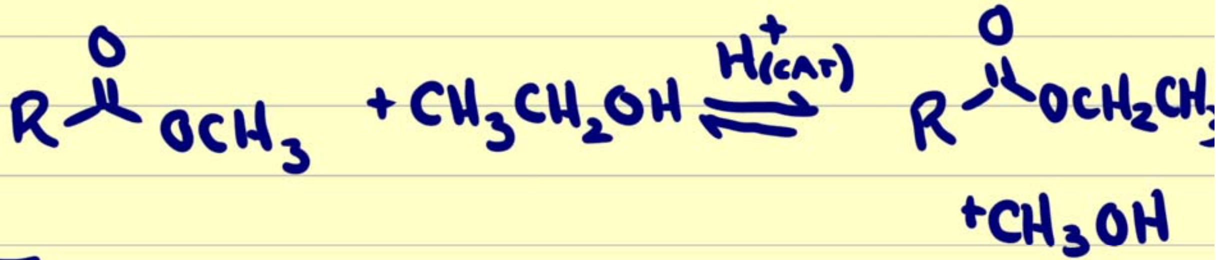
- REACTIONS OF ESTERS PARALLEL OTHER ACID DERIVATIVES



$\mathrm{RC(=O)OCH_3}$

NUCLEOPHILIC SUBSTITUTION / ADDITION RXNS.

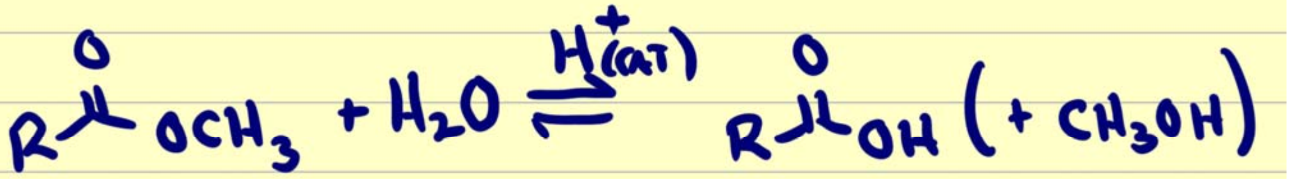
- a) ACIDIC CATALYSIS - YES



$$\mathrm{RC(=O)OCH_3 + CH_3CH_2OH \xrightleftharpoons{H^+(CAT)} RC(=O)OCH_2CH_3 + CH_3OH}$$

- TRANSESTERIFICATION
  - EASY IF YOU USE THE INCOMING ALCOHOL (CH_3CH_2OH) IN EXCESS

ACID SYNTHESIS JUST AS SIMPLE

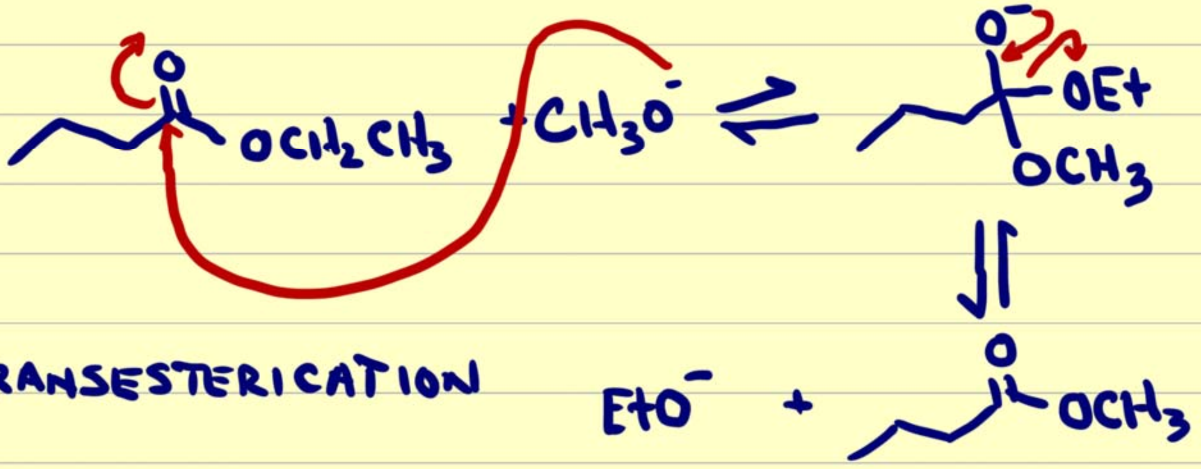


$$\mathrm{RC(=O)OCH_3 + H_2O \xrightleftharpoons{H^+(CAT)} RC(=O)OH\ (+\ CH_3OH)}$$

b) HOW ABOUT BASE CATALYSIS?

-YES

FOR EXAMPLE

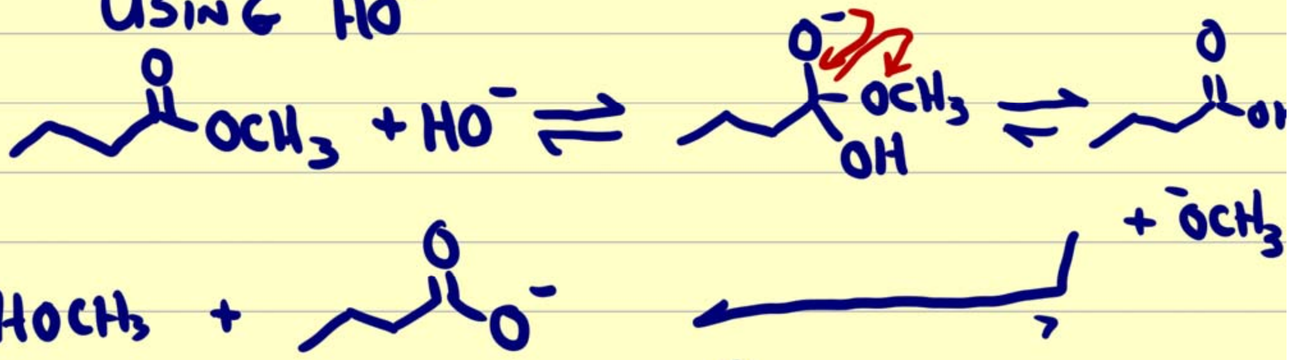


TRANSESTERICATION

$EtO^- + CH_3OH \rightleftharpoons CH_3O^- + EtOH$

- WOULD USE MeOH AS SOLVENT TO PUSH EQM. TO PRODUCT SIDE

PARTICULARLY GOOD FOR MAKING ACIDS USING HO⁻



- EQUILIBRIUM FAVOURS CARBOXYLATE

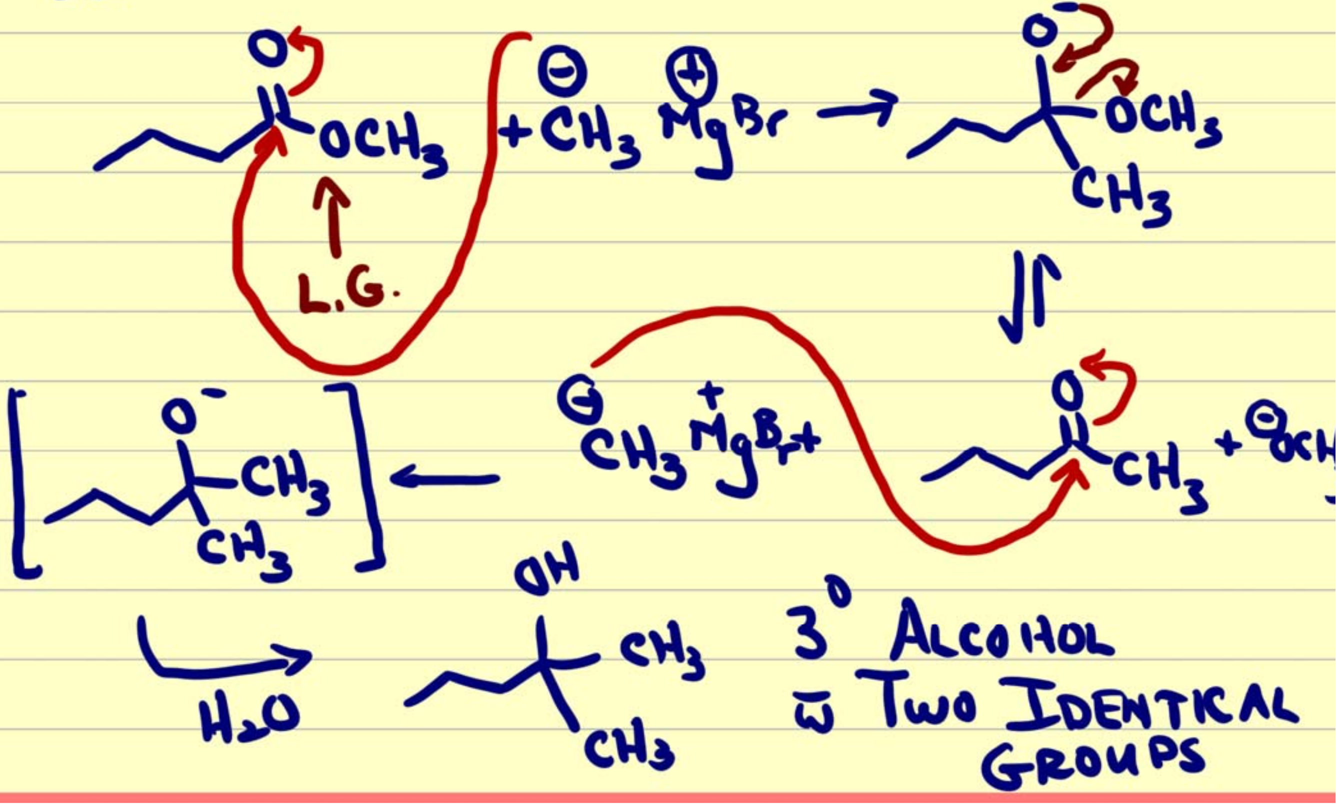
WHEN REACTION IS DONE, POUR EVERYTHING INTO H_3O^+ TO GET CARBOXYLIC ACID

V. EASY; OFTEN CALLED SAPONIFICATION

CARBON, H^- NUCLEOPHILES WITH ESTERS.

$CH_3MgBr \leftrightarrow \overset{\ominus}{C}H_3 \; \overset{\oplus}{M}gBr$ GRIGNARD

So.

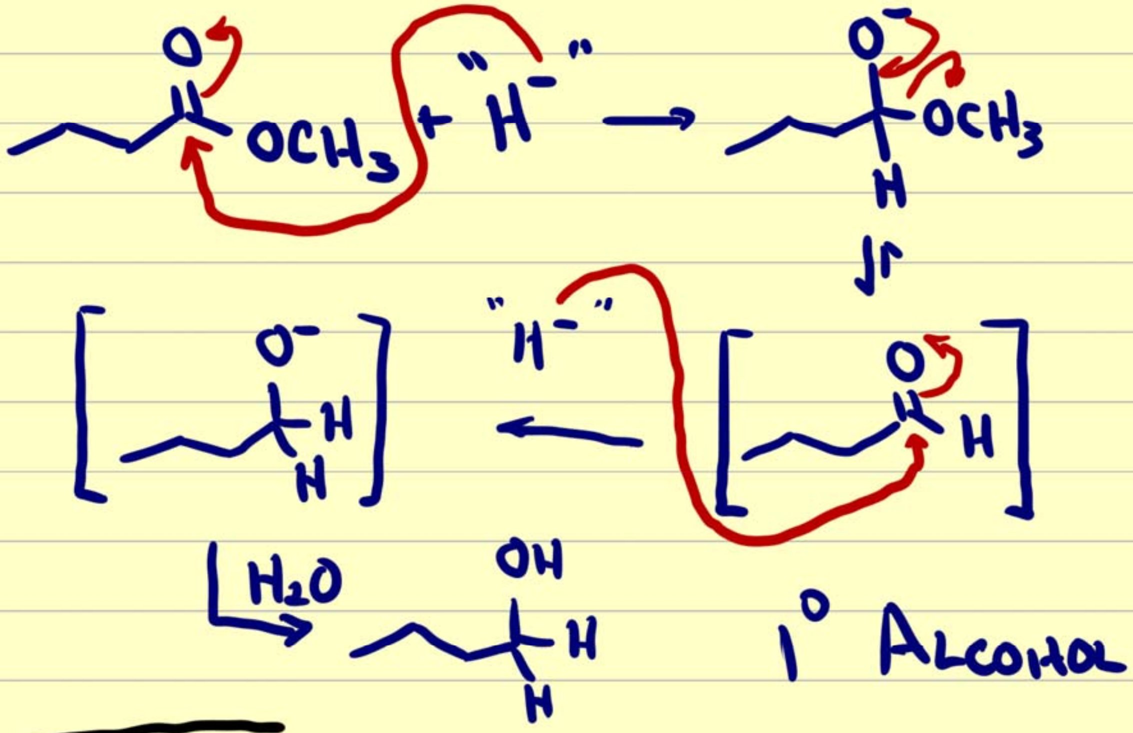


3° ALCOHOL
w̄ TWO IDENTICAL GROUPS

BECAUSE
KETONE IS MORE REACTIVE TO ADDN
THAN ESTER

HYDRIDE (H^-) ↳ $NaBH_4$ MILD
↳ NOT REACTIVE ENOUGH

↳ $LiAlH_4$ REACTIVE
↳ OH YES.

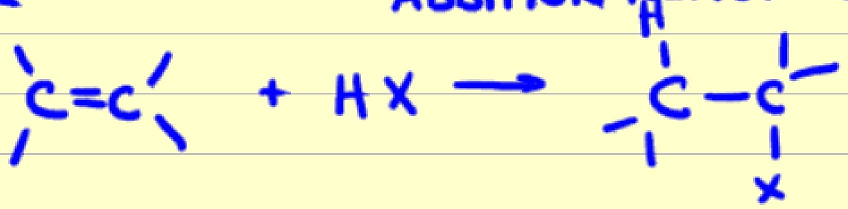


THE END.

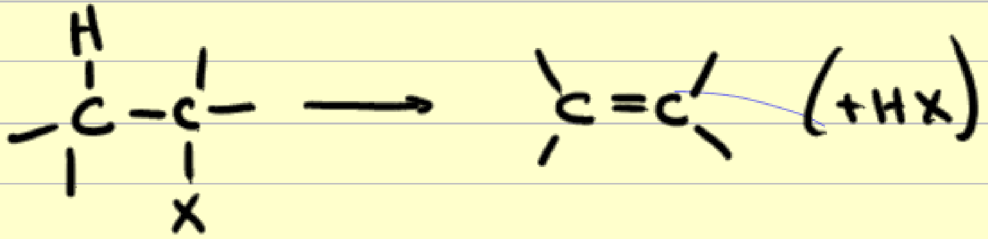
Now in latest version of 230. Moved from 235 course, replacing carbonyl chemistry.

ELIMINATION REACTIONS

RECALL 230 ADDITION REACTION



NOW



ELIMINATION RXNS.

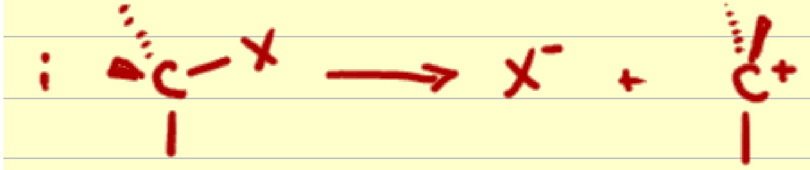
- MOST IMPORTANT ALKENE PREP METHOD
- PROBABLY FOR ALKYNES TOO

MECHANISMS - 3 IMPORTANT ONES

2 VERY WELL STUDIED

E1 AND E2 MECHANISMS

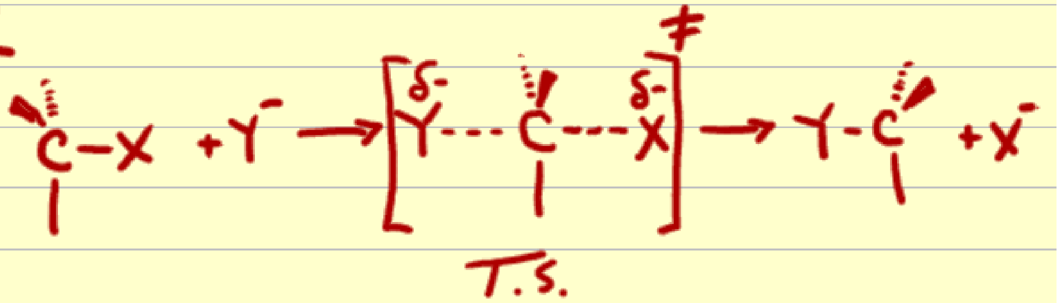
RECALL S_N1



SLOW (rds)

ii

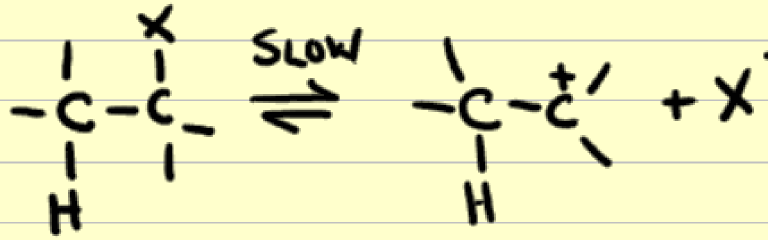
SN2



E1 ELIMINATION

- TWO STEP PROCESS

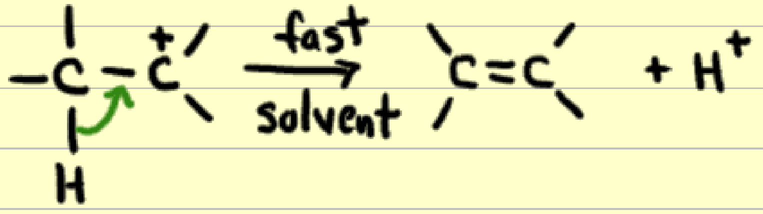
STEP 1



r.d.s.

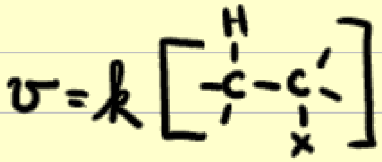
IONIZATION TO GIVE CARBOCATION

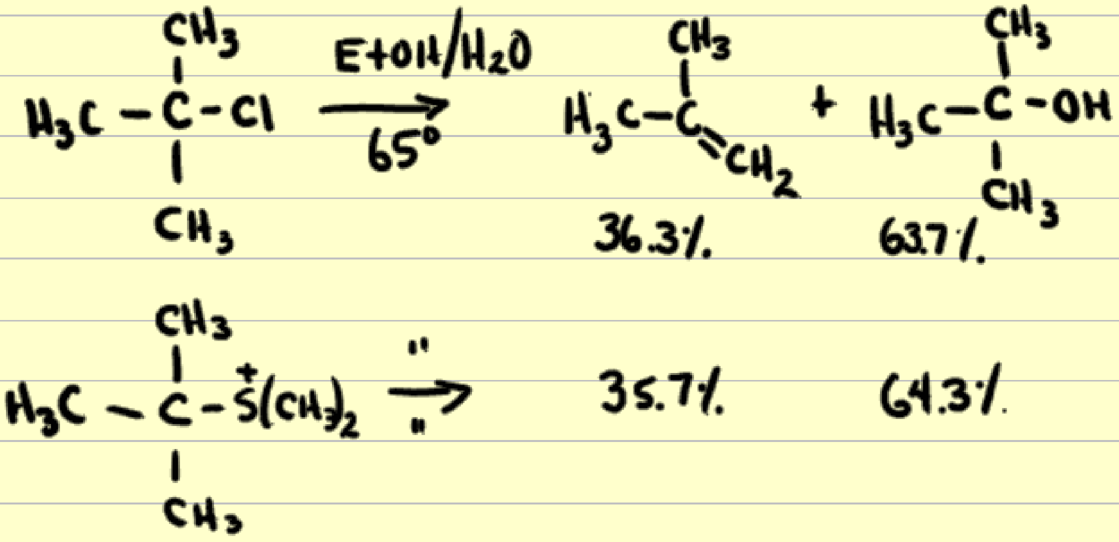
STEP 2



FEATURES

- TWO STEPS

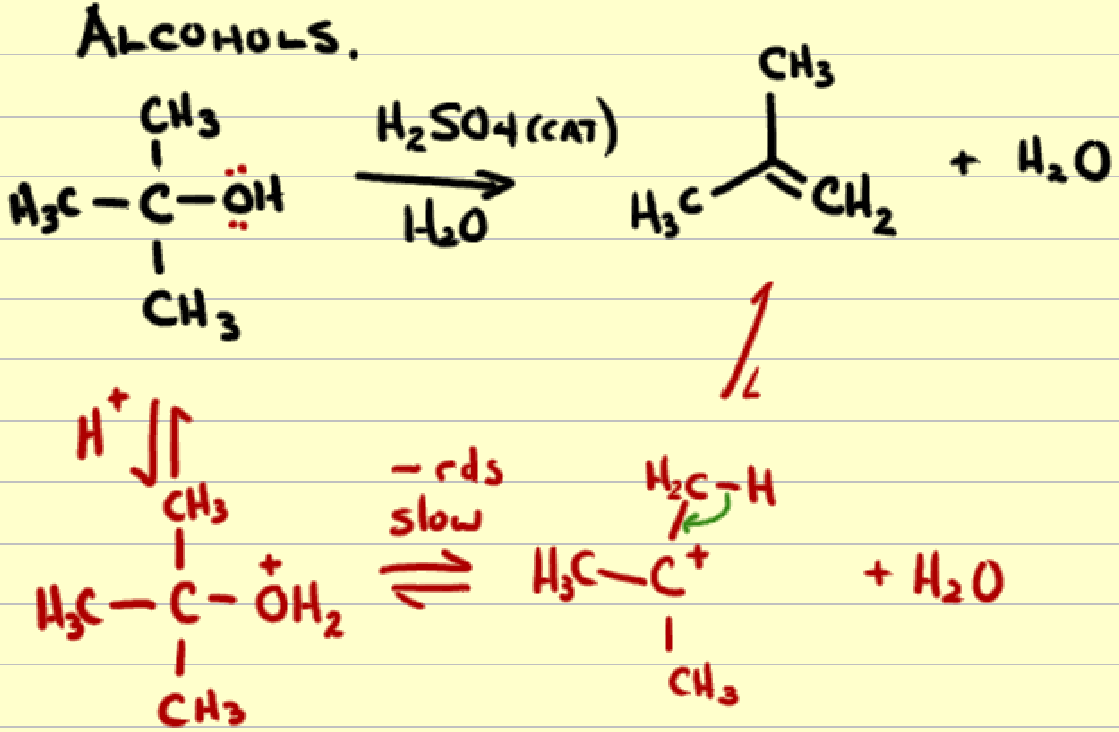
- 1ST STEP SLOW
- 1ST ORDER KINETICS 
$v = k\left[\overset{H}{-C}-\underset{X}{C}-\right]$
- 1ST STEP IDENTICAL TO S_N1 1ST STEP
- NO ADDED BASE (SOLVENT ACTS A BASE)



- TWO POINTS.
  - E1 ELIMINATIONS & S_N1 SUBSTITUTIONS OFTEN COMPETE.
  - IF YOU CHANGE LEAVING GROUP, AND THE SUBST./ELIMINATION RATIO STAYS THE SAME - EXCELLENT EVIDENCE THAT ELIMINATION WAS E1

PROTOTYPICAL E1 ELIMINATION

- ACID CATALYZED ELIMINATION OF ALCOHOLS.



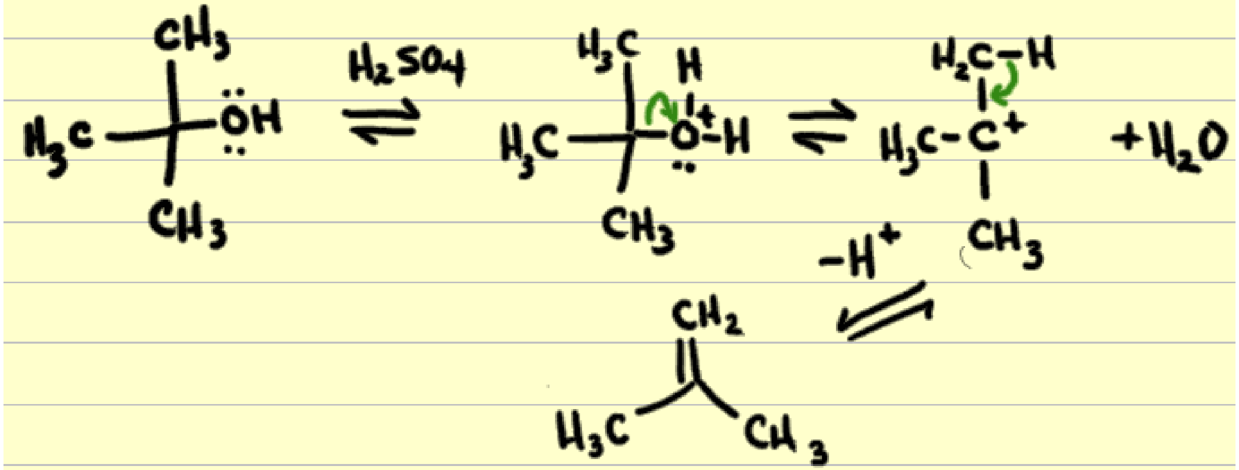
235 Notes

Notebook: jgreen1263's notebook
Created: 11/13/2009 2:45 PM **Updated:** 3/5/2013 11:24 AM

CHEM. ~~235~~ 230 - LECTURE 14

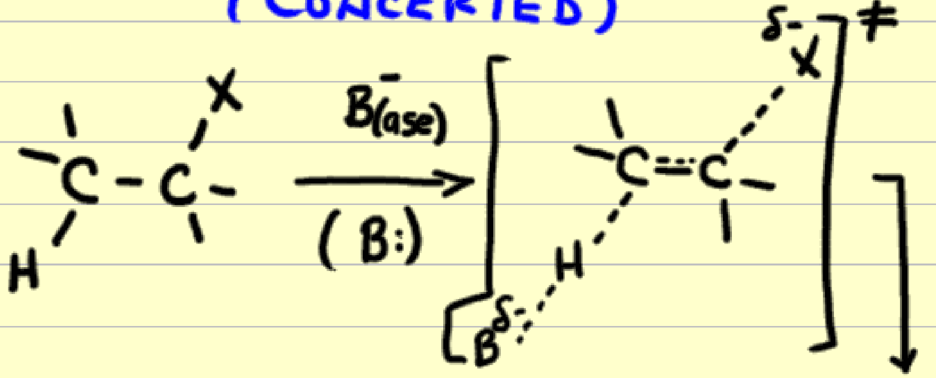
PROTOTYPICAL E1 ELIMIN.

- ACID INDUCED (CATALYZED) ELIMINATION OF H_2O FROM ALCOHOL



E2 MECHANISM

- ONE STEP - ALL BOND MAKING AND BREAKING AT THE SAME TIME (CONCERTED)



↓

$$X^- + B{-}H + \;{>}C{=}C{<}$$

(or $\overset{+}{B}{-}H$)

- FEATURES
  1) CONCERTED IN ONE STEP
     - PROTON ABSTRACTION BY BASE
     - DOUBLE BOND FORMATION
     - LOSS OF X^-

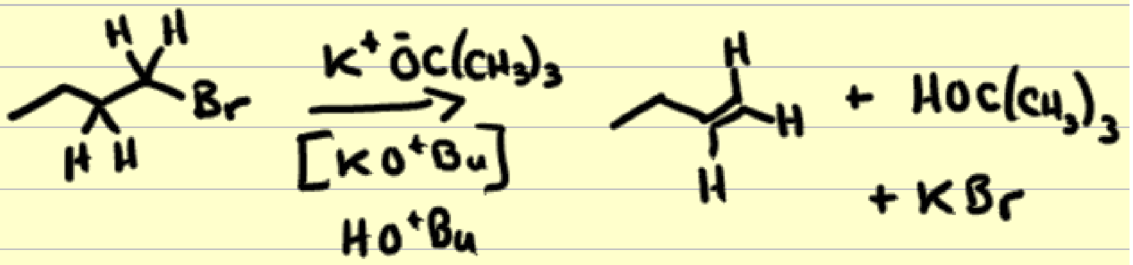
  2) SECOND ORDER KINETICS

$$v = k\,[B^-]\left[\,-\underset{H}{\overset{|}{C}}-\overset{X}{\underset{|}{C}}-\,\right]$$

E 2

ELIMINATION ↗ ↑ BIMOLECULAR

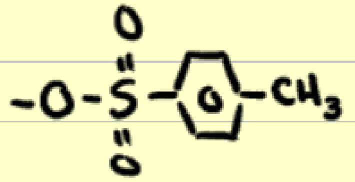
PROTOTYPICAL E2 EXAMPLE



- BASE INDUCED ELIMINATION OF ALKYL HALIDES

X OFTEN HALIDE

$I > Br > Cl >> F$

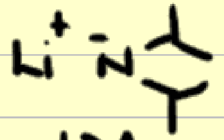
X ALSO CAN BE  = $-OTs$

ROUGHLY ≈ Br

BASE: MOST COMMON ARE THINGS LIKE

ALKOXIDES $^{\ominus}OR$ ($KO^{t}Bu$, $NaOEt$)

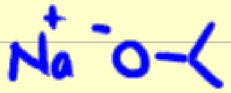
HYDROXIDE $^{\ominus}OH$

AMIDE ION $^{\ominus}NR_2$ ()

LDA

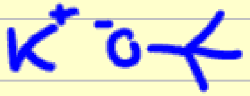
AMINES $:NR_3$

ASIDE



SODIUM ISOPROPOXIDE

$NaO^{i}Pr$



POTASSIUM tert-BUTOXIDE

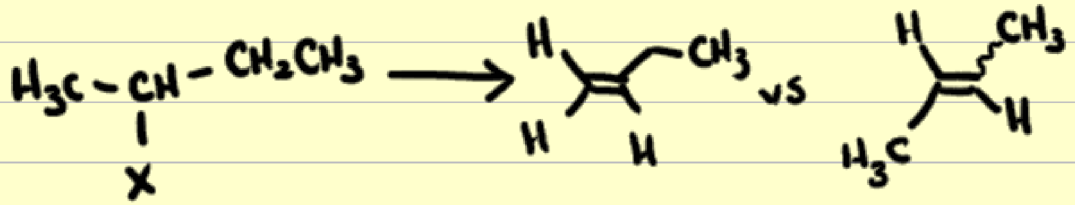
$KOBu\text{-}t$

OR

$KO^{t}Bu$

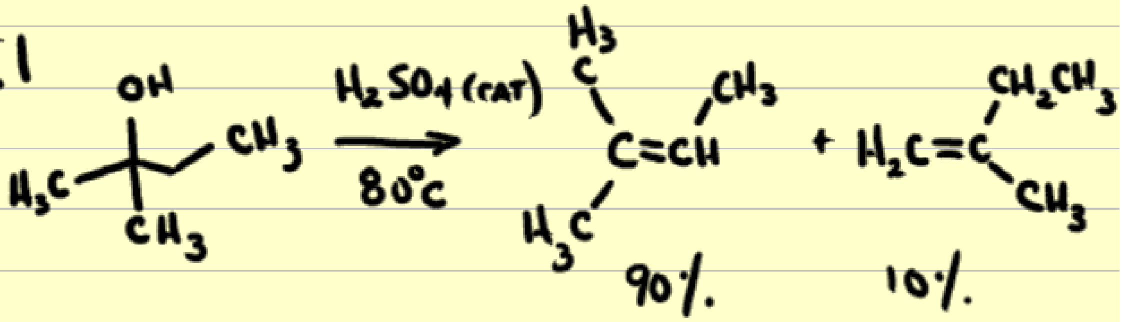
REGIOCHEMISTRY.

- TWO POSSIBLE SITES OFTEN



2 ISOMERS

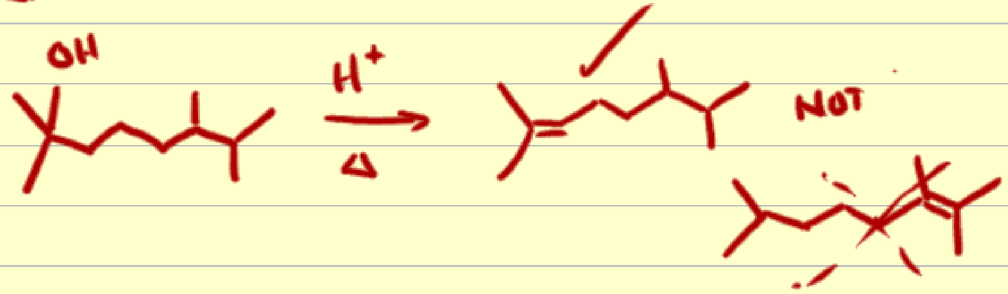
E1



- CATIONIC INTERMEDIATE ELIMINATES TO FORM THE MORE STABLE ALKENE POSSIBLE
  - MORE SUBSTITUTED ALKENE NORMALLY

- OPERATING UNDER ZATSEV RULE

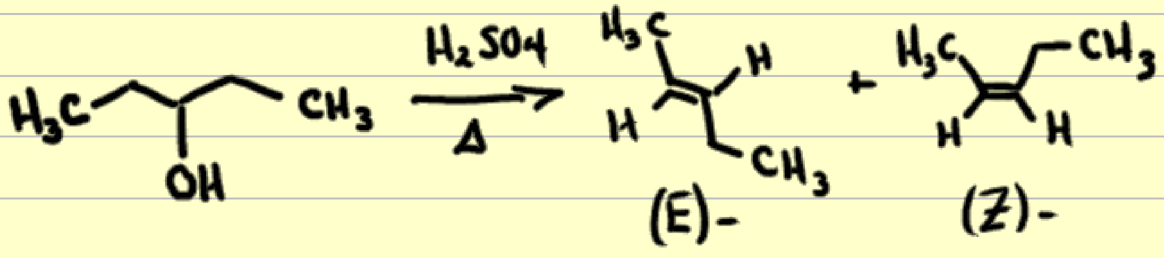
MEANS



- ALSO ANSWERS THE STEREOCHEMISTRY QUESTION - SINCE MOST STABLE ALKENE IS FORMED.

I.E. WHERE LARGEST GROUPS ARE TRANS- TO EACH OTHER

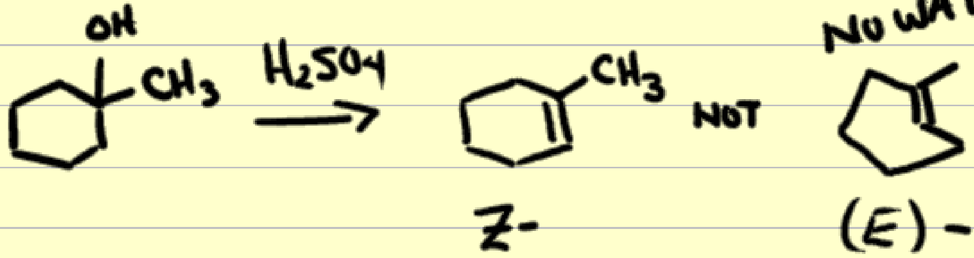
∴ (E)- ISOMER USUALLY



87 : 13

- CALLED STEREOSELECTIVE BECAUSE ONE STEREOISOMER IS FORMED MOSTLY

- MUST USE WITH SOME CARE



NO WAY.

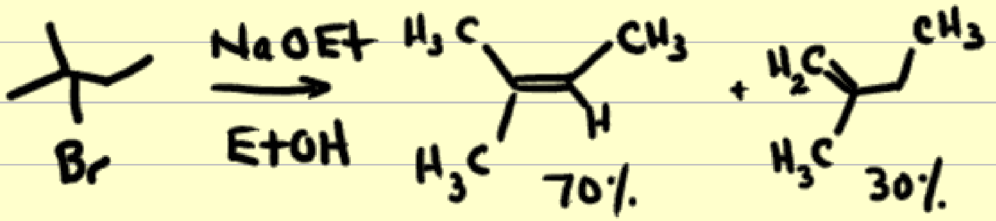
NOT IF < 10 MEMB. RING

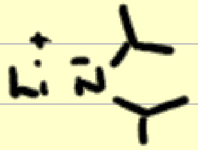
E2 - NOT A CLEAR CUT

- Depends on Leaving Group X
- Especially Depends on Base

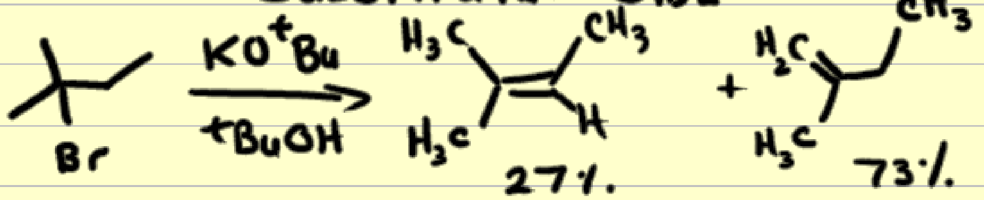
Less Bulky Base HO$^-$, MeO$^-$, EtO$^-$

- More Towards Zaitsev
  (More Substituted Side)



- Bulky Bases KO^{t}Bu or 

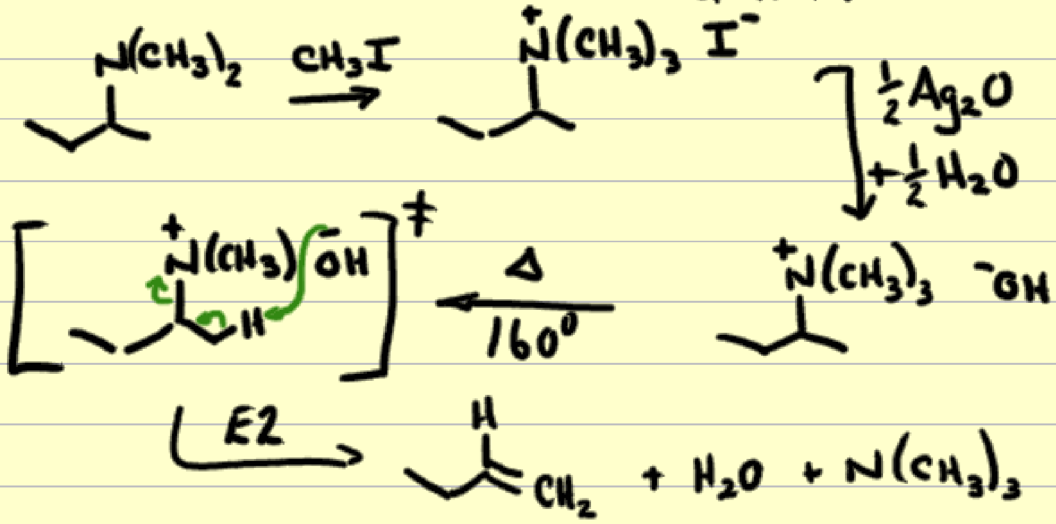
Elimination Prefers Less Substituted Side



- Reason - Approach to More Subst. Side is Getting Too Sterically Hindered

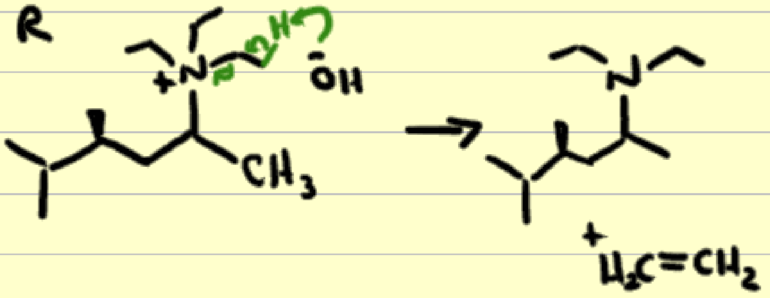
- These Eliminations are Said to Be Operating Under the <u>Hofmann</u> Rule

- SPECIAL ELIMINATION PROTOCOL TO GIVE LESS SUBST. ALKENE
  - CALLED HOFMANN ELIMINATION



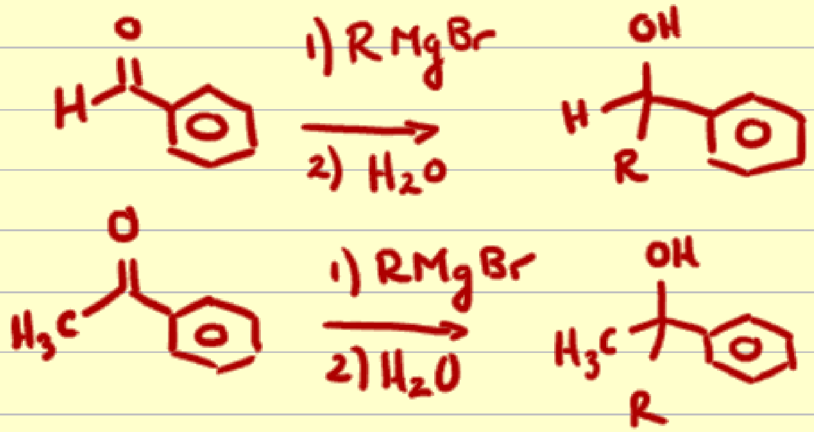
LESS SUBST. ALKENE RELIABLY

- ALWAYS $\underset{R}{\overset{+}{N}Me_3}$ BECAUSE .....



CHEM. ~~235~~ 230 - LECTURE 15

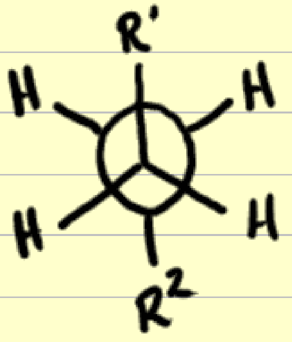
ASIDE



MAYBE TEST #2

E2 ELIMINATIONS - STEREOCHEMISTRY OF THE ELIMINATION

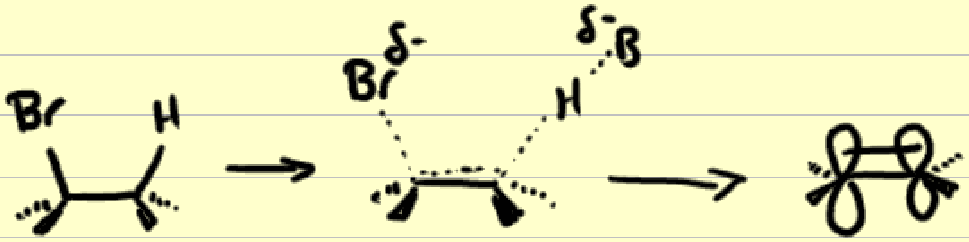
- VERY DISTINCT RELATIONSHIP BETWEEN THE TWO GROUPS BEING ELIMINATED (i.e. THE H + THE Br)
- HAVE AN ANTIPERIPLANAR ORIENTATION



- WHY? - sp^3 HYBRID C-H + C-Br BONDS ARE BECOMING p- ORIBTALS FORMING THE π-BOND

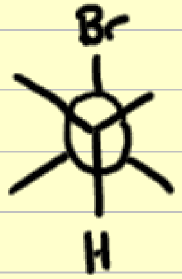
∴ MUST BE LINED UP

ANTIPERIPLANAR

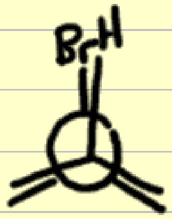


SYNPERIPLANAR ALSO POSSIBLE, BUT

1)

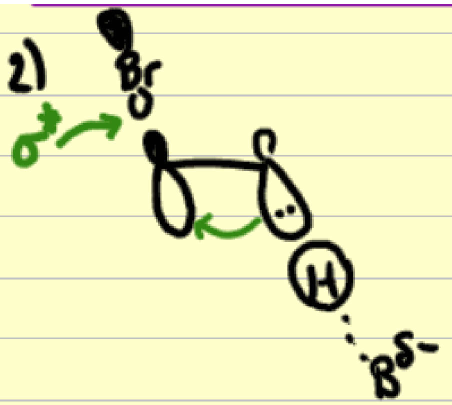


ANTIPERIPLANAR
- STAGGERED
LOWER E.



SYNPERIPLANAR
- ECLIPSED
HIGHER E.

2)

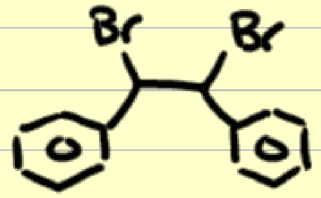


DONATION OF e^- DENSITY TO THE σ* (ANTIBONDING) ORBITAL OF C-Br WEAKENS THE BOND
- ASSISTS IN BREAKING THE BOND

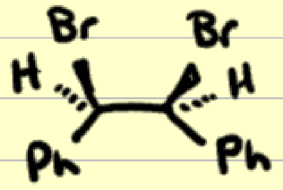
THIS MEANS LOWER $\Delta G^{\ddagger}$ TRANSITION STATE

- NOT AVAILABLE FOR SYNPERIPLANAR ELIMINATION

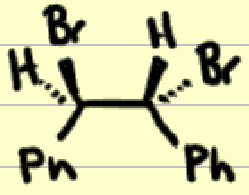
IMPLICATIONS



IS ACTUALLY 2 DIASTEREOMERS

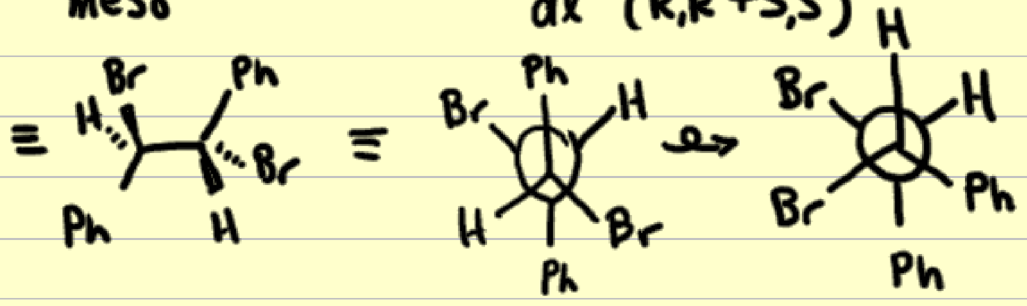


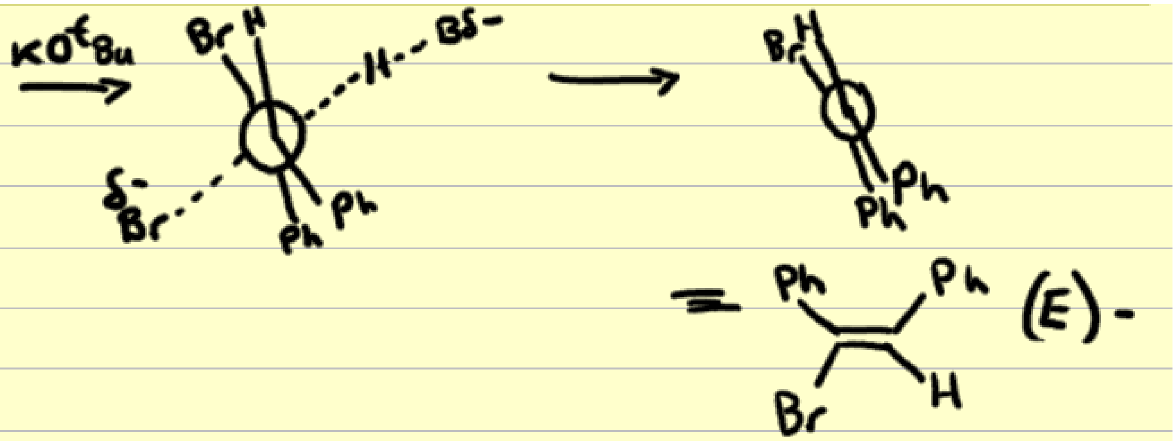
meso



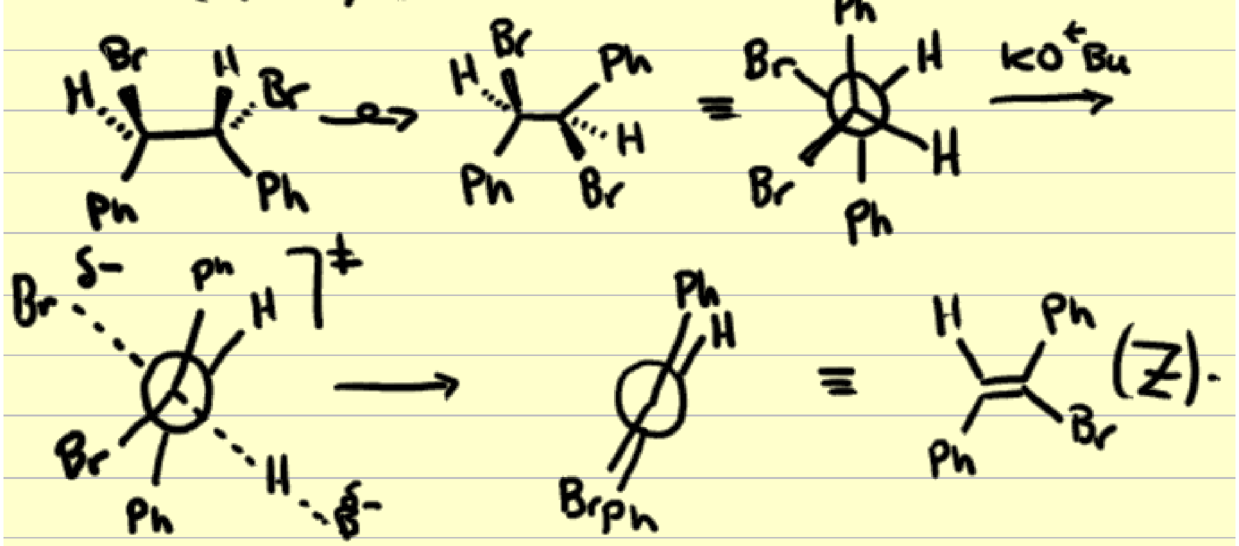
dl (R,R + S,S)

MESO





dl or (R,R + S,S)



∴ ONE DIASTEREOMER → (E)-
(meso, r,s)

OTHER DIASTEREOMER → (Z)-
(R,R or S,S)

- RXNS LIKE THESE ARE CALLED } STEREOSPECIFIC

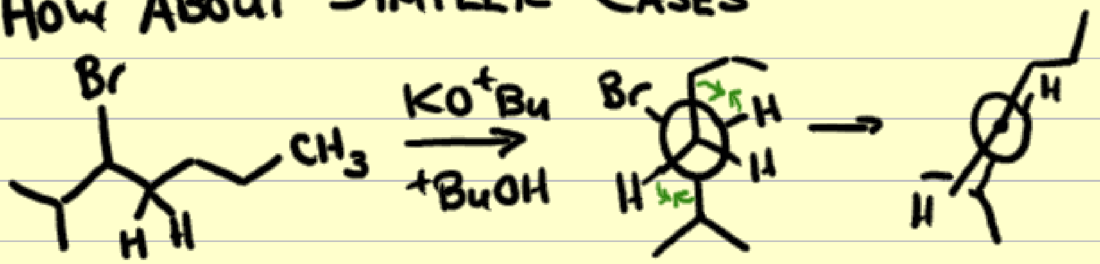
STEREOSPECIFIC MEANS THERE'S A PAIR (OR MORE) OF S.M. STEREOISOMERS AND A PAIR (OR MORE) OF PRODUCT STEREOISOMERS – AND –

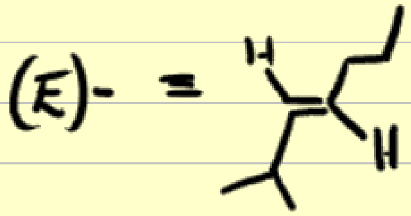
ONE S.M. STEREOISOMER FORMS ONE PRODUCT STEREOISOMER

OTHER S.M. STEREOISOMER FORMS OTHER PRODUCT STEREOISOMER

COMPARE TO STEREOSELECTIVE
– JUST MEANS THAT ONE PRODUCT STEREOISOMER IS FORMED MOSTLY

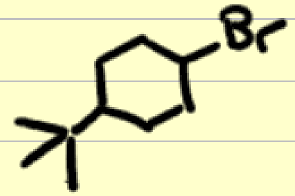
HOW ABOUT SIMPLER CASES



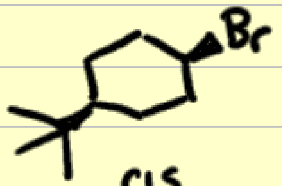


IN SIMPLER CASES
MOST STABLE ALKENE STEREOCHEMISTRY WINS OUT.

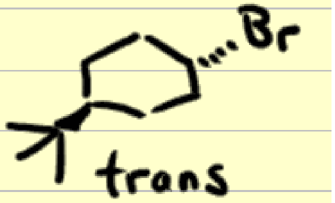
IN CYCLIC SYSTEMS (CYCLOHEXANES)



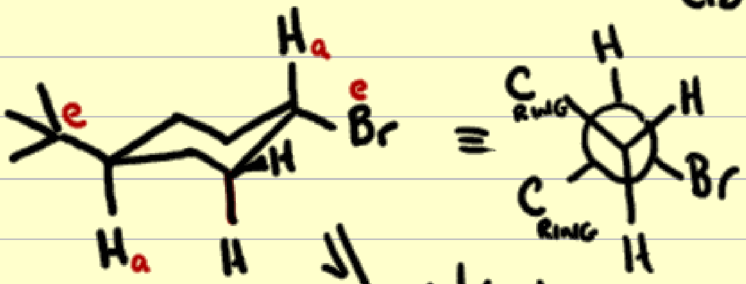
2 CPDS



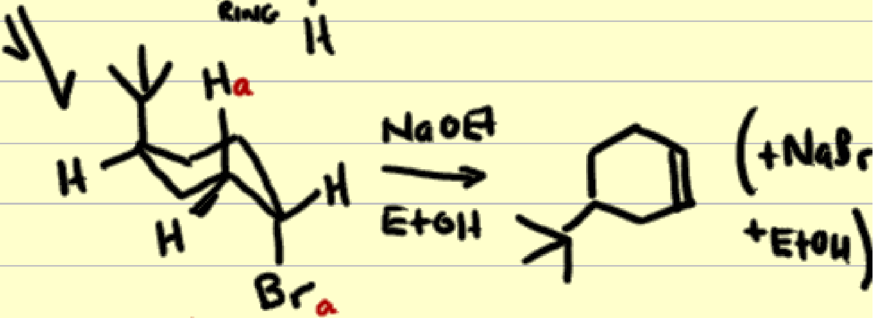
CIS



trans



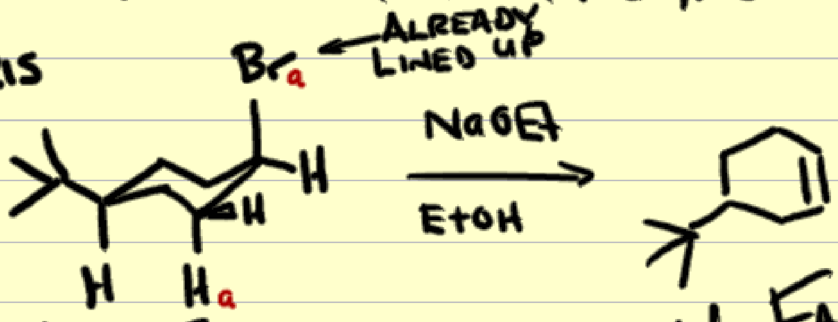
BR NOT ANTI TO ANY H



NOW H_a & Br_a ARE ANTI

V. SLOW ELIMINATION, SINCE Br IS AXIAL ONLY A SMALL % OF TIME

CIS



MOST STABLE CONFORMER

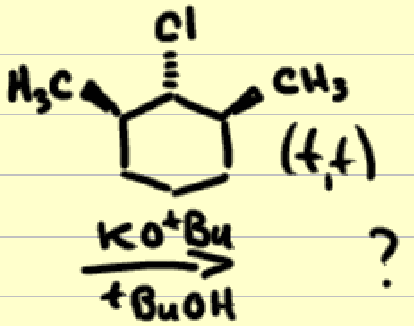
V. FAST

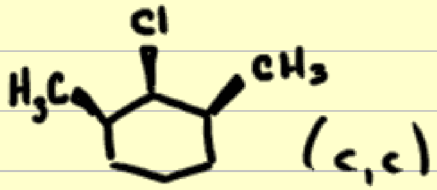
235 Notes

Notebook: igreen1263's notebook
Created: 11/13/2009 3:45 PM **Updated:** 3/12/2013 11:21 AM

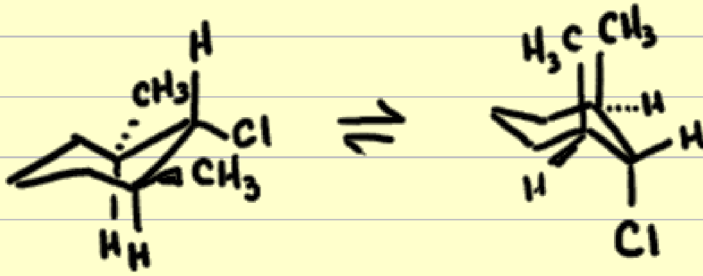
CHEM. ~~235~~ 230 - LECTURE 16

A COUPLE MORE CASES





t,t

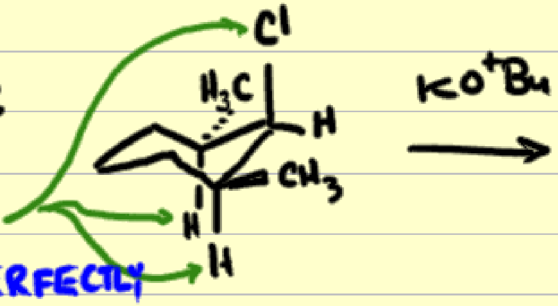


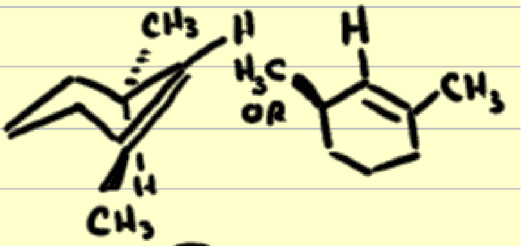
RXN. WILL BE V.V.V. SLUGGISH

Cl NOT AXIAL

NO AXIAL H ANTIPERIPLANAR TO Cl

c,c





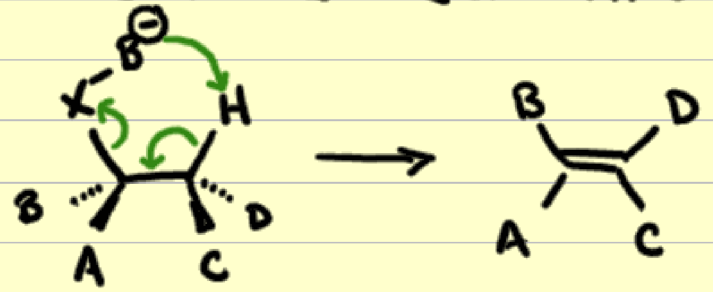
PERFECTLY ANTI PERIPLANAR
- ELIMINATES (E2) FAST

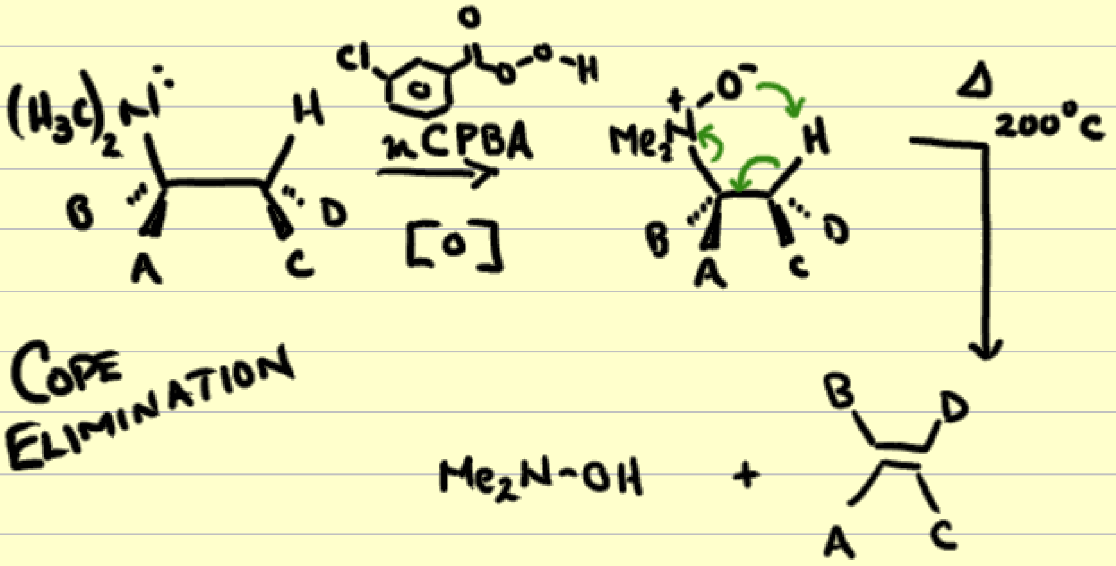
RAPID

CAN AN E2 EVER BE SYN (PERIPLAR)?

– YES

SPECIALIZED ELIMINATIONS.





COPE ELIMINATION

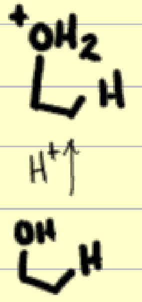
END OF TEST #2 MATERIAL

E1 VS. E2 ELIMINATIONS

- OFTEN COMPETITIVE, OFTEN CASES WHICH HAVE SOME E1 <u>AND</u> SOME E2
  - HOW DO WE EVALUATE?
- CONSIDER A NUMBER OF FACTORS.

LEAVING GROUP

E1 – $\ddot{X}$ MUST LEAVE ALL ON ITS OWN!
$\therefore$ MUST BE VERY GOOD OR BETTER



- LEAVING GROUP IS H_2O
$\therefore$ ALCOHOLS NEVER E2

- I^-, Br^-, Cl^-, NR_3, ^-OTs CERTAINLY CAN DO E1

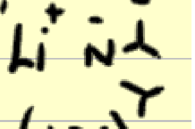
E2 - HAS TO BE A DECENT LEAVING GROUP BUT BASE IS HELPING

- NEVER AN ALCOHOL

BASE - E1 NO BASE (SOLVENT ACTING AS BASE)

E2 - MODERATE OR STRONG BASES

NR_3, ^{-}OH, ^{-}OR (NaOEt, KO^{t}Bu), $\overset{\ominus}{N}R_2$



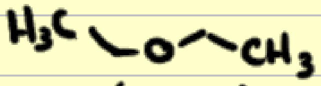
(LDA)

SOLVENT - E1 CATIONIC INTERMEDIATE STABILIZED BY POLAR SOLVENT

H_2O, CH_3OH, EtOH, MAYBE CH_3CN

- E2 - NOT SO CRITICAL
  - POLAR SOLVENTS FINE
  - NON-POLAR SOLVENTS FINE

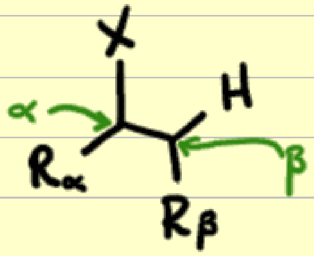
MAY BE MORE APPROPRIATE FOR THE BASE



(Et_2O)

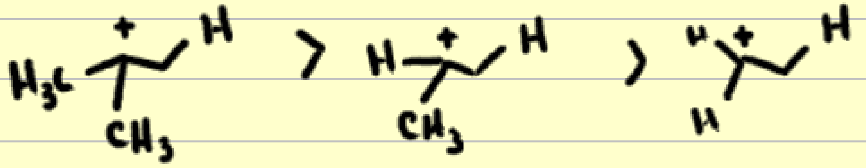
THF

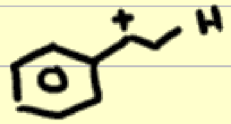
SUBSTRATE:



α- SITE - ADDITIONAL R_α'S TEND TO FAVOUR E1

- STABILIZE CARBOCATION

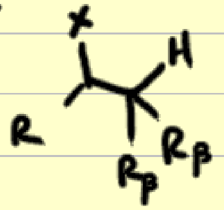




IS ALSO V. STABILIZED

SO R_α = ARYL ALSO FAVOURS E1

β- SITE

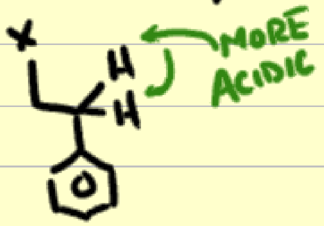


IF R_β IS ALKYL GROUP, WE HINDER BASE APPROACH TO THE H

∴ SLOW E2

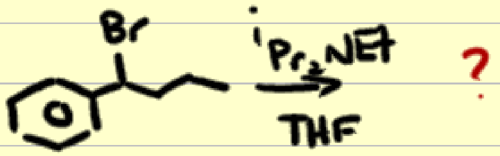
(∴ MORE E1 BY DEFAULT)

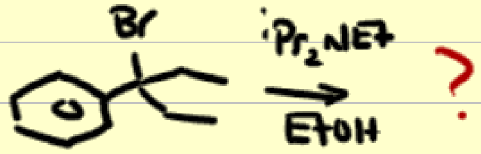
IF THE R_β'S ARE ARYLS.

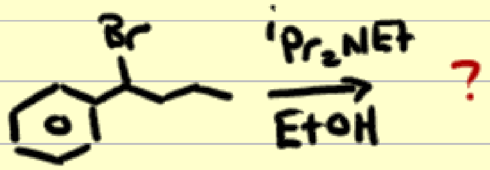


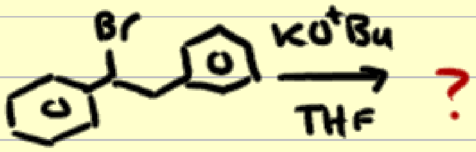
- H IS ACIDIFIED
  ∴ EASIER TO ABSTRACT
  ∴ SPEED UP <u>E2</u>

TYPICAL QUESTION



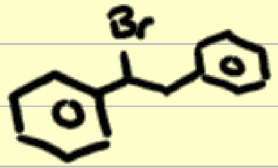






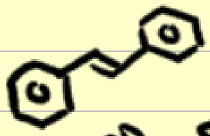
RANK THESE E1 vs E2 & WHY ?

- GIVE THE PRODUCTS



Ph GROUP α - MORE E1 TENDING, BUT THEY ALL HAVE THIS

Br^- L.G. - E1 OR E2 V.G. L.G.



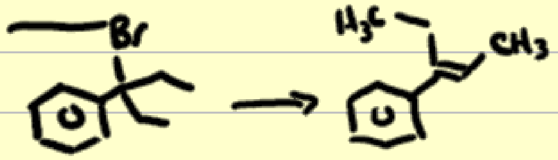
PROD.

BASE - KO^tBu IS STRONG BASE → E2 FAVOURING

SOLVENT - NONPOLAR ∴ E2 FAVOURING

β-ARYL - SPEEDS UP E2

∴ PRETTY HIGHLY E2 - MOST OF ALL

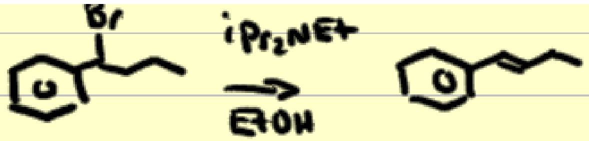


MOST E1 CHARACTER

3° & BENZYLIC HALIDE ∴ V. CATION FAVOURING
⇒ E1

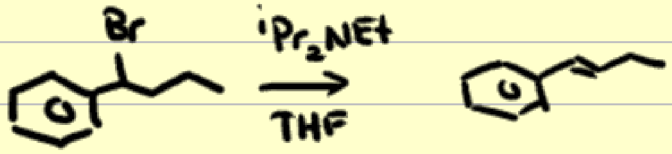
POLAR SOLVENT (EtOH) ⇒ CATION STABILIZING
⇒ E1

BASE NOT SO STRONG ∴ LESS E2 THAN ABOVE



- 2° + BENZYLIC ∴ NOT AS E1 AS 3° CASE
- BASE - MODERATE TO WEAK - E1 OR E2
- NO β-ARYL - NOT AS E2 AS KO^{t}BU CASE
- BUT POLAR SOLVENT ∴ MORE E1 THAN THF CASE

2ND MOST E1 CHARACTER



2° + BENZYLIC - NOT AS E1 AS 3° CASE
- NO β-ARYL ; NO STRONG BASE
  ∴ NOT AS E2 AS KO^{t}BU CASE
- SOLVENT (THF) NON-POLAR
  ∴ LESS E1, MORE E2 THAN CASE w̄ EtOH

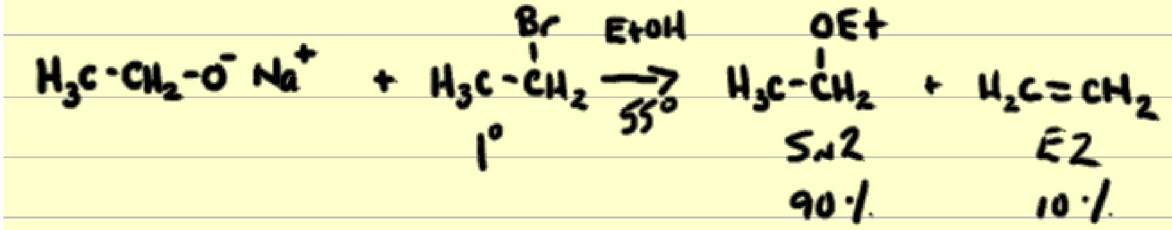
∴ 2ND MOST E2 CHARACTER

CHEM. ~~235~~ 230 - LECTURE 17

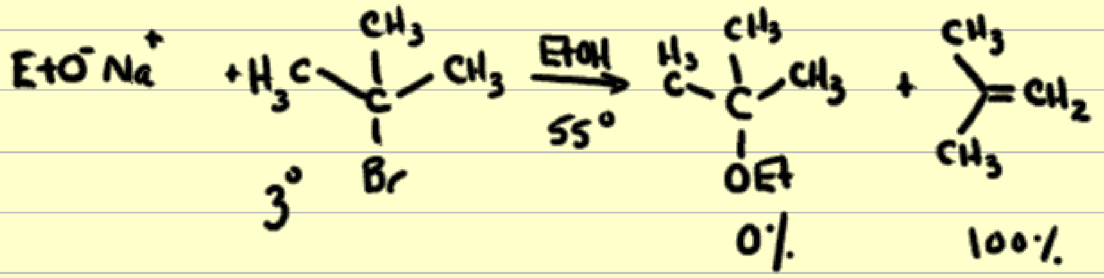
ELIMINATION VS SUBSTITUTION
E2 SN2

- STERICS OF RXN
- BASICITY OF Nu⁻ / BASE
- TEMPERATURE

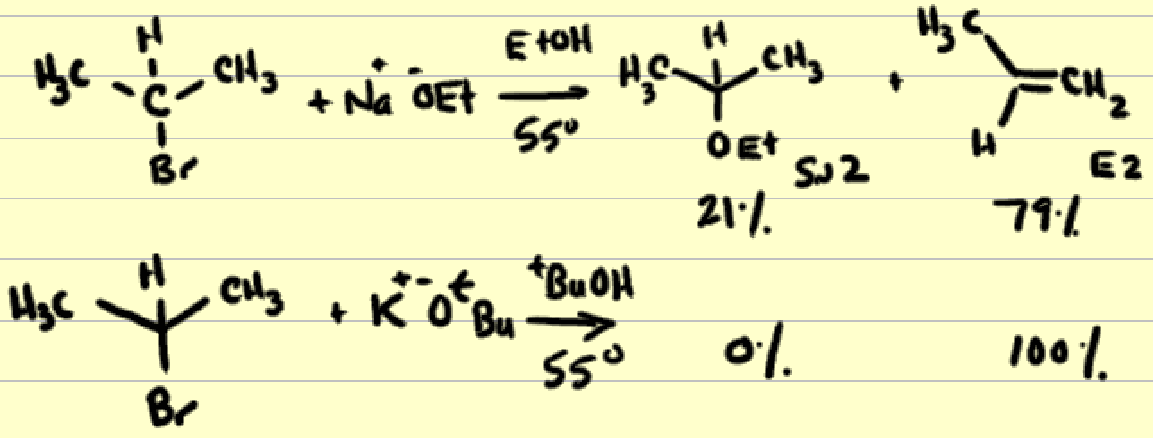
- SN2 HATES STERIC CROWED REAGENTS
  ∴ BULKIER SUBSTRATES 3°>2°>1°
  WILL TEND TO FAVOUR E2



$$H_3C-CH_2-O^- Na^+ + H_3C-\overset{Br}{C}H_2 \xrightarrow[55°]{EtOH} H_3C-\overset{OEt}{C}H_2 + H_2C=CH_2$$

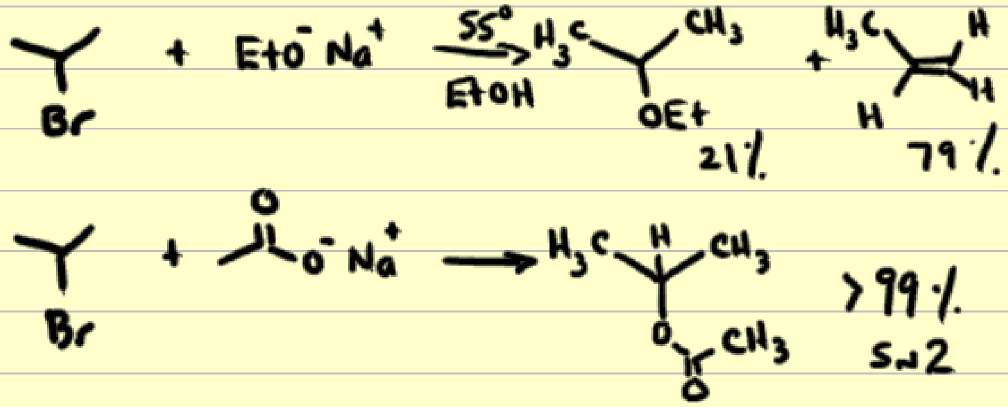


SAME FOR BASE / Nu⁻



BASICITY OF BASE / Nu⁻

$EtO^- Na^+$	$H_3C\text{-}C(=O)O^- Na^+$	$H_3C\text{-}CH_2\text{-}S^- Na^+$
V. BASIC	NOT V. BASIC	NOT V. BASIC
V. GOOD Nu⁻	DECENT Nu⁻	V. GOOD Nu⁻



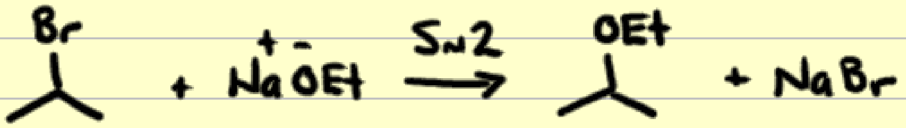
- MORE BASIC ⟹ E2
LESS BASIC ⟹ S_N2

TEMPERATURE

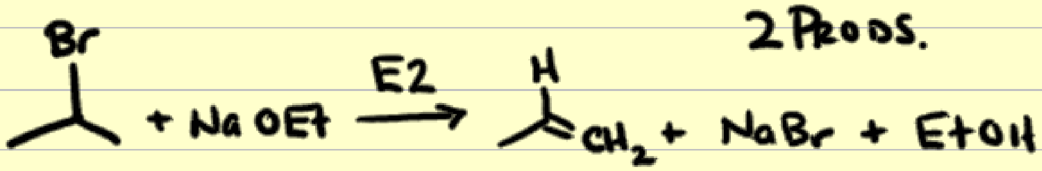
- HIGHER TEMPS TEND TO ENCOURAGE ELIMINATION (E1 OR E2) OVER SUBSTITUTION

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

ΔS IS RANDOMNESS - IF RXN PRODUCES MORE PRODUCTS, ΔS IS HIGHER
- SHOULD GET MORE FAVOURABLE AT HIGH T



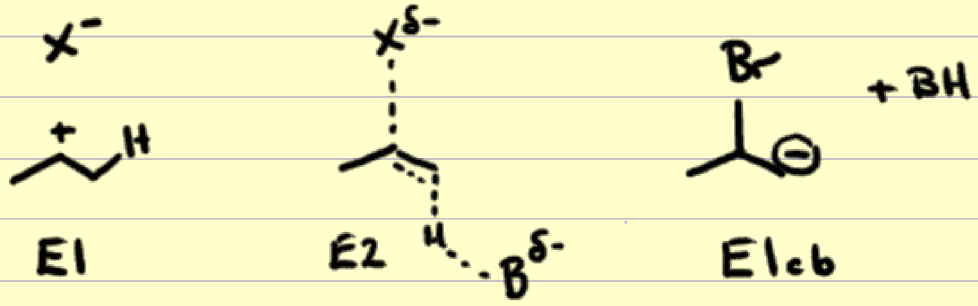
2 PRODS.



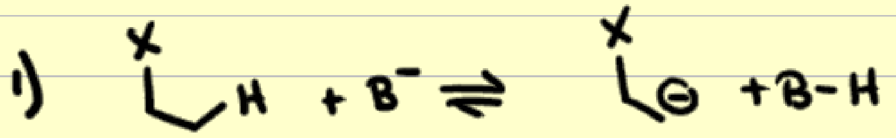
3 PRODS

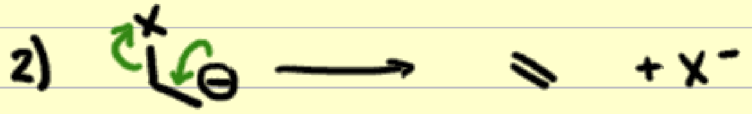
∴ FAVOURED MORE AT HIGH T.

FINAL MECH E1cb



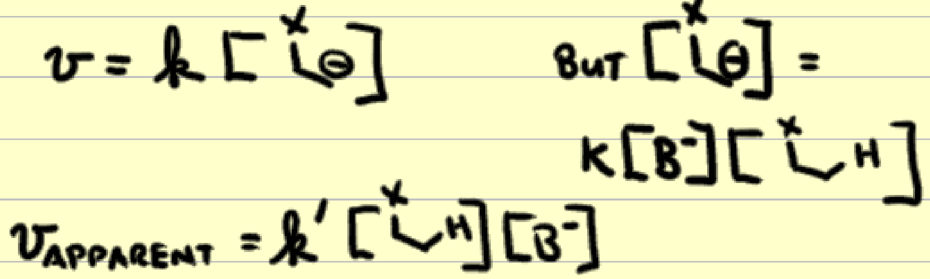
TWO STEPS.



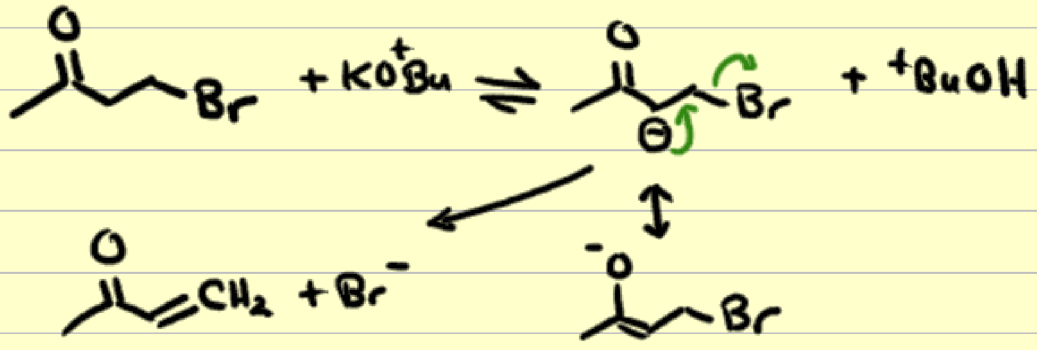


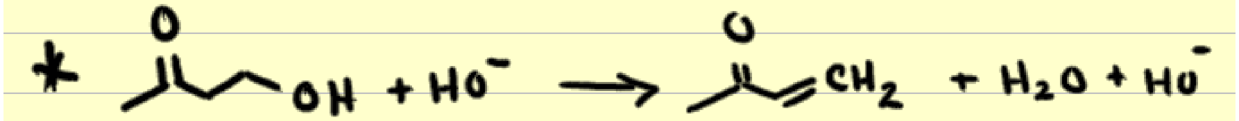
E1 CONJUGATE BASE

USUALLY 2^{ND} STEP IS SLOW ONE



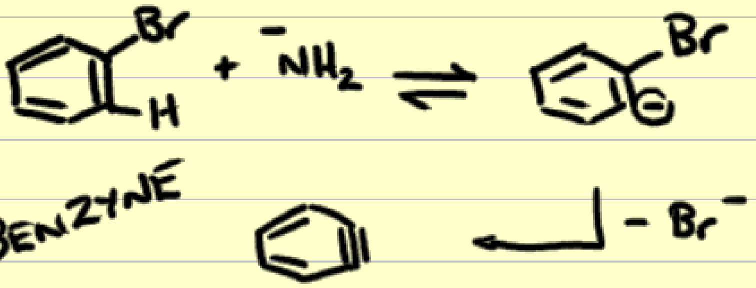
95% OF TIME, THERE'S A REAL ACIDIFYING GROUP





ALDOL CONDENSATION

EXCEPTION (5%)



BENZYNE

E1cb