Substitution + Elimination Reactions

·SN2 reaction

1. Kinetics
- rate = K[RX][:Nu], bimolecular
- concerted, one step rxn

2. Stereochemistry
- backside nucleophilic attack that caus an inversion of configuration. R→S
- endothermic, heterolytic

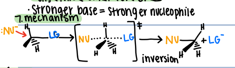
3. R-group identity
- smaller / less R groups react faster bc less steric hendrance

4. Who does SN2 rxns?
- methyl halide, 1° halide, 2° halides

5. Solvent type
- Polar aprotic solvents! Nu are not well solvated here, making them stronger + better for SN2 rxns. DMSO

6. Nucleophile
- Prefers strong nucleophile w/ (-) charge
- $-CH_3 < NH_2 < -OH, < F < Cl < Br < I$
- Stronger base = stronger nucleophile

7. mechanism



E1 reaction

★E1 + SN1 both deal w/ carbocations★

1. Kinetics
- rate = K[RX]
- first order, unimolecular, two step

2. The Base
- favored by weaker bases. H_2O / ROH

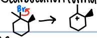
3. The leaving group
- Stronger LG = faster rxn

4. Solvent
- Polar protic, w/ O-H / N-H

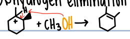
5. R group
- more substituted = faster rxn

6. Mechanism

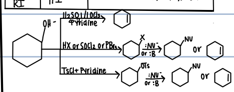
① carbocation formation - rate determining



② β hydrogen elimination



rxn	reagent	comment
ROH → RCl	HCl	all ROH. 2°/3° = SN1. 1°/methyl = SN2
	$SOCl_2$	SN2, best for methyl, 1° + 2°
ROH → RBr	HBr	all ROH. 2°/3° = SN1. 1°/methyl = SN2
	PBr_3	SN2, best for methyl, 1° + 2°
ROH → RI	HI	all ROH. 2°/3° = SN1. 1°/methyl = SN2



SN1 rxn

1: Kinetics
- rate = K[RX]
- two step, carbocation formation = rate determining
- nu⁻ does NOT effect rate, only carbocation!

2: Stereochemistry
- nu⁻ attacks fm. front + back, so 50% inversion + 50% retention, racemic mixture of enantiomers

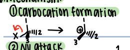
3: R-group identity
- more substituted = faster rxn. no methyl / 1°!!!

4: Solvent:
- Polar protic solvents, stabalize carbocation (OH / NH)

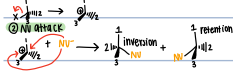
5: Nucleophile
- weak :Nu⁻, I < Br < Cl < F < OH < NH_2 < CH_3 strong

6. Mechanism:

① carbocation formation



② Nu attack



RX	rxn with	mechanism
1°	Strong nucleophile	SN2
	strong bulky base	E2
2°	Strong base/nu⁻	SN2/E2
	strong bulky base	E2
	weak base/nu⁻	SN1/E1
3°	weak base/nu⁻	SN1/E1
	strong base	E2

- Tertiary alkyl halide rxns: all mechanisms except SN2
  - 3° + weak Nu/base = SN1/E1 (maybe both)
  - 3° + strong base = E2
- Secondary alkyl halides: all mechanisms
  - 2° + strong base = SN2/E2 (maybe both)
  - 2° + bulky base = E2
  - 2° + weak nu/base = SN1/E1
- Primary alkyl halides: SN2 or E2 only
  - 1° + strong nu⁻: SN2
  - 1° + strong bulky base = E2

- hot → elimination; cold → substitution
- ⁻OR / ⁻OH = SN2/E2 ★bulky R = E2!!!!
- H_2O / ROH = SN1/E1
- polar protic: F < Cl < Br < I (best nu) have -OH/-NH!! acetone2
- polar aprotic: I < Br < Cl < F (best nu) THF, DMF, DMSO, no -OH/-NH!!

·E2 reaction

1. Kinetics
- rate = K[RX][:B] second order, bimolecular

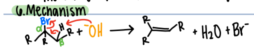
2. The Base
- stronger base = faster rxn
- VSU. strong bases (⁻OH / ⁻OR) or DBU/DBN

3. Leaving Group
- better leaving group = faster rxn
- (bad LG) F < Cl < Br < I (good)

4. Solvent
- polar aprotic - does not solvate base

5. R group
- more R groups = faster rxn, no methyl

6. Mechanism



alcohol Reactions

E1 dehydration of 2° + 3° alcohols

① Protonation of -OH → -OH₂, a good leaving group

② carbocation formation (rate determining)

③ HSO_4^- removes β proton + π bond formed

★H_2SO_4 is an acid-catalyst in this reaction

E2 dehydration of 1° alcohol

① Protonation of -OH → -OH₂, a good leaving group

② Base removes β + π bond is formed at the sametime

arbocation rearrangement: alkyl / hydride group shifts once to switch places with ⊕ to create a more stable carbocation

Dehydration of $POCl_3$: works better than H_2SO_4 w/ organic compound, acts as an acid catalyst happens through E2 mechanism, no rearrangements.

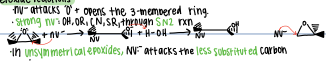
alcohol → alkyl halides using HX: H protonates OH, and X acts as nucleophile. HX are used to prepare alkyl halides. more substituted alcohols react more quickly w/ HX
- 1° alcohols → SN2 rxns
- 2°/3° alcohols → SN1 rxns
- 1° ROH + HX - SN2 mechanism
  - ① Protonation of -OH → -OH₂, a good leaving group
  - ② R-X σ bond forms as -OH₂ leaves
  - inversion of stereogenic center
- 2° ROH + HX - SN1 mechanism
  - ① Protonation of -OH → -OH₂, a good leaving group
  - ② carbocation formed (rate determining)
  - ③ Nu attack of X forming racemic product
  - racemization at stereogenic center!

ROH with $SOCl_2$ + Pyridine
- 1°/2° ROH + $SOCl_2$ + Pyridine react to form alkylchloride, HCl + SO_2

Tosylate and alcohols
- TsCl + alcohol, then H on OH leaves + O binds to Ts, making ⁻OTs which is a good leaving group, similar to I. retention of stereogenic center.

Rxns of Ethers with strong acids
- only HI and HBr can be used w/ ethers bc both C-O bonds are cleaved + two alkyl halides products
- two successive nu substitution, one for each alkyl
- 3° SN1 to break C-O bond
  - ① Protonation of ether O creates O⁺, good leaving group
  - ② cleavage of C-O bond → 3° carbocation (SN1)
  - ③ nu attack forms substitution product (+ CH_3OH (see next step))
- 1° CH_3-OH → alkyl halide by SN2 mechanism
  - ④ Protonation of OH to make good leaving group: $CH_3-OH + H-I \rightarrow CH_3-OH_2^+ + I^-$
  - ⑤ Nu attack by I⁻ forming second alkyl halide: $CH_3-OH_2 + I^- \rightarrow CH_3-I$

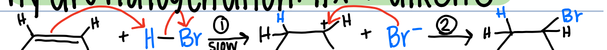
Epoxide reactions
- nu⁻ attacks 'O' + opens the 3-membered ring.
- strong nu⁻: OH, OR, CN, SR, through SN2 rxn



- In unsymmetrical epoxides, Nu⁻ attacks the less substituted carbon

alkene reactions

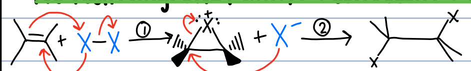
hydrohalogenation: HX + alkene



- 2 enantiomers produced, markinov's rule! syn + anti addition

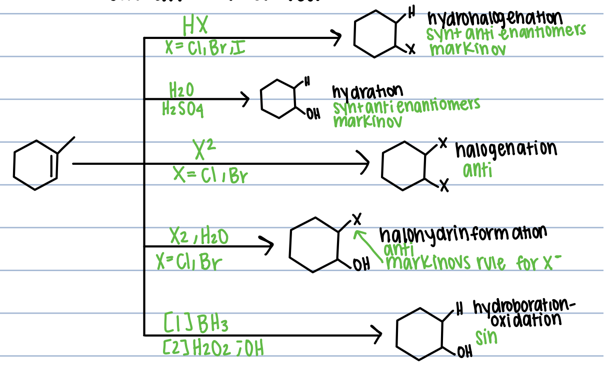
Halogenation - X_2 + alkene

No rearrang. ONLY anti, no carbocation, 2 steps



trans products ONLY!

- ★cis reactant → enantiomers
- ★trans reactant → identical

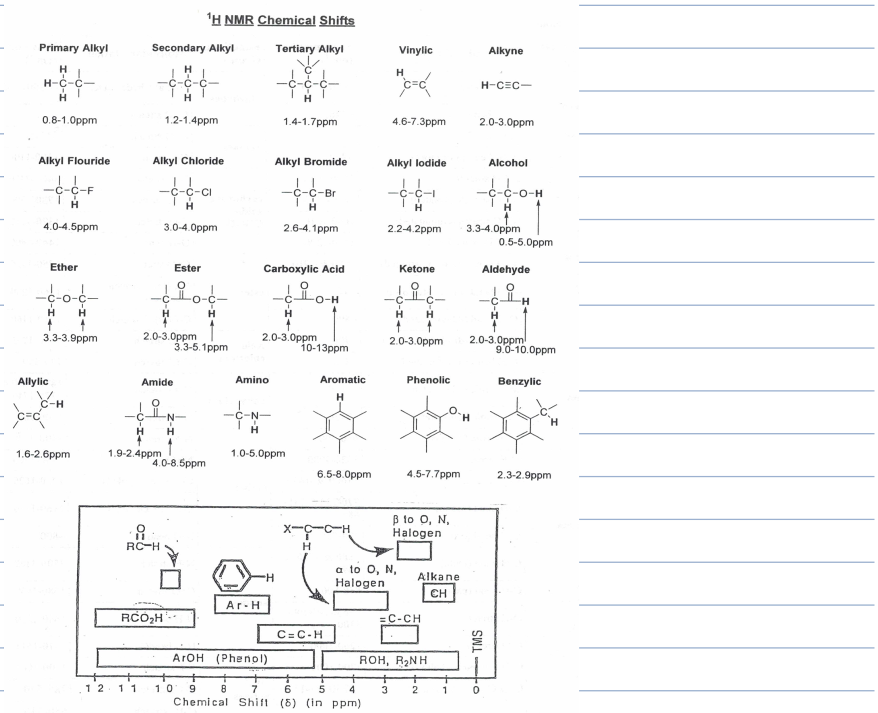


IR IDENTIFYING

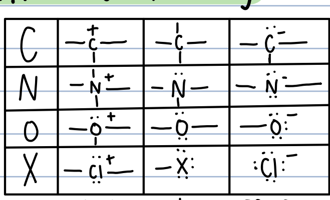
Functional Group	Molecular Motion	Wavenumber (cm^{-1})	Functional Group	Molecular Motion	Wavenumber (cm^{-1})
	C-H stretch	2950-2800	aldehydes	C-H aldehyde stretch	~2850 & ~2750
alkanes	CH_2 bend	~1465		C=O stretch	~1725
C_nH_{2n+2}	CH_3 bend	~1375	ketones	C=O stretch	~1715
	CH_2 bend (4 or more)	~720		C-C stretch	1300-1100
	=CH stretch	3100-3010	carboxylic acids-COOH	O-H stretch	3400-2400
	C=C stretch (isolated)	1690-1630		C=O stretch	1730-1700
	C=C stretch (conjugated)	1640-1610		C-O stretch	1320-1210
	C-H in-plane bend	1430-1290		O-H bend	1440-1400
alkenes	C-H bend (monosubstituted)	~990 & ~910		C=O stretch	1750-1735
C_nH_{2n}	C-H bend (disubstituted - E)	~970	esters	C-C(O)-C stretch (acetates)	1260-1230
	C-H bend (disubstituted - 1,1)	~890		C-C(O)-C stretch	1210-1160
	C-H bend (disubstituted - Z)	~700	Acid chlorides	C=O stretch	1810-1775
	C-H bend (trisubstituted)	~815		C-Cl stretch	730-550
alkynes	acetylenic C-H stretch	~3300	anhydrides	C=O stretch	1830-1800 & 1775-1740
C_nH_{2n-2}	C,C triple bond stretch	~2150		C-O stretch	1300-900
	acetylenic C-H bend	650-600		N-H stretch	3500-3300
	C-H stretch	3020-3000		N-H bend	1640-1500
	C=C stretch	~1600 & ~1475	amines	C-N Stretch (alkyl)	1200-1025
aromatics	C-H bend (mono)	770-730 & 715-685		C-N Stretch (aryl)	1360-1250
	C-H bend (ortho)	770-735		N-H bend	~800
	C-H bend (meta)	~880 & ~780 & ~690		N-H stretch	3500-3180
	C-H bend (para)	850-800	amides	C=O stretch	1680-1630
alcohols	O-H stretch	~3650 or 3400-3300		N-H bend	1640-1550
	C-O stretch	1260-1000		N-H bend(1°)	1570-1515
	C-O-C stretch (dialkyl)	1300-1000		C-F stretch	1400-1000
ethers	C-O-C stretch (diaryl)	~1250 & ~1120	alkyl halides	C-Cl stretch	785-540
				C-Br stretch	650-510

¹H NMR IDENTIFYING

NMR and IR Shift Table



Ch1: Struct + bonding



- bond length: decreases across a row + increases down a column. single bonds longest, triple shortest.
- as s% character increases, bonds get shorter + stronger
- lone pair in unhybridized orbital

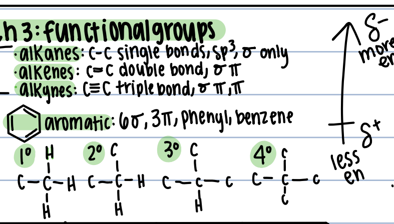
Ch2: acids + bases

- Brønsted acid: contain H, donates proton, (+)
- Brønsted Base: contains π / lone pair, accepts proton (-)
- Brønsted rxns: proton goes from acid to base!!
  - $NH_3 + H_2O \rightarrow OH^- + NH_4$ (base, acid, conj. base, conj. acid)
- strong acids have high Ka + low pKa
- $pKa = -\log(Ka)$ + $Ka = 10^{-pKa}$
- equillibrium favors weaker acid
- Determining acid strength
  - 1. Element: acidity incr. down a column (1st), then more en make stronger acid
    - weak acid - C-H < N-H < O-H strong acid
  - 2. Resonance: more resonance of conj. base (more lone pairs / π) mean stronger acid

Ch3: functional groups

aliphatic
- alkanes: C-C single bonds, sp^3, σ only
- alkenes: C=C double bond, σ π
- alkynes: C≡C triple bond, σ π, π

aromatic: 6σ, 3π, phenyl, benzene

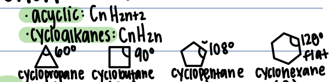


alkyl halide	R-X:	ester	R-C(=O)-OR
alcohol	R-OH	amide	R-C(=O)-N-H/R
ether	R-O-R	acid chloride	R-C(=O)-Cl
amine	R-NH / R_2NH / R_3N:	Intermolecular Forces	

- H bonded to O, N, F. Strong

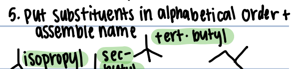
Chapter 4: Alkanes

- acyclic: C_nH_{2n+2}
- cycloalkanes: C_nH_{2n}



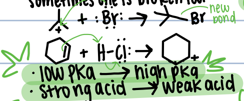
Strain: (Kcal-mol⁻¹)

- strain incr. reactivity
- Structural / constitutional isomers: same molec. formula, different atom arrangement
  - = diff. molecules, same molec. formula
- How to name acyclic alkanes
  1. identify + name longest carbon chain
     - 2 same length? choose chain w/ more substituents
  2. identify + name all substituents
  3. number carbon chain so the first substituent has lowest number
  4. add location + prefix of substituent
  5. put substituents in alphabetical order + assemble name



- π bond in p orbital # = pd. number!
- major contributor = more bonds + less charges
- resonance: only move π bonds/lone pairs, move π bonds towards (+) and draw in Hydrogens!!!
- major contributor:
  - B 1: bigger atom w/ charge = major
  - O 2: octet rule for all atoms = major
  - E 3: more en atom w/ charge = major
  - * if all carbon, then... major 3° > 2° > 1° minor
- σ: head-to-head/tail-to-tail orbital overlap of s/p orbital
- all hybridized orbitals are equivilent
- C w/ one double = sp^2, triple = sp^3

3. Inductive: acidity increases with presence + proximity of electron withdrawing groups similar to polarity.
4. Hybridization: acidity increases as % s-character increases. strong $sp > sp^2 > sp^3$ weakest
- lewis acid: e⁻ pair acceptor, partially positive, electrophile
- lewis base: e⁻ pair donor, must have π/lone pair, partially negative, nucleophile
- lewis acid/base rxns: electron transfer from base to acid. usually a bond is formed, sometimes one is broken too.



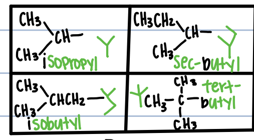
- low pKa → high pKa
- strong acid → weak acid

acids: HF, HCl, NH_4^+, H_3O^+, CH_3COOH

bases: F⁻, Cl⁻, OH⁻, NH_3, CH_3COO^-

Thiol	R-S-H
Sulfide	R-S-R
aldehyde	R-C(=O)-H
Ketone	R-C(=O)-R
carboxylic acid	R-C(=O)-OH

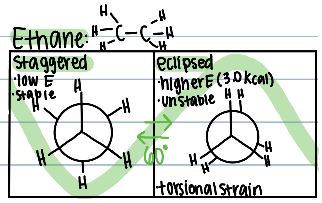
1. H-bond: H bonded to O/N/F, strong
2. Dipole-dipole: polar molecules
3. VDW: all molecules, weak!
- Boiling point: stronger imf = higher bp, bigger atom/more surface area = higher bp
- melting point: stronger imf + more symmetrical atoms = higher mp!
- Solubility: like dissolves like!!! organic molec. are usu. not soluble in water, unless there is at least one H-bond for every 5 carbons.



- naming cycloalkanes
  - more carbons in ring → name as cycloalkane w/ substituent chain
  - more carbons in chain → name as chain w/ cycloalkane substituent
  - * add cyclo- infront of parent name
- bp of butane ($CH_3CH_2CH_2CH_3$) is 0°C, the bp increases by ~33°C for every additional $-CH_2$

isobutyl

Ethane:



Staggered	eclipsed
low E, stable	higher E (3.0 kcal), unstable
	torsional strain

-5 kcal

pKa values

HCl	Cl⁻	-7
H_2SO_4	HSO_4^-	-5
H_3O^+	H_2O	-1
RCOOH (carboxylic acid!!!)	RCOO⁻	5
H_2CO_3	HCO_3^-	6.3
NH_4^+	NH_3	9.2
Phenol + alcohol (PhOH)	PhO⁻	10
RNH_3^+ (amine)	R-NH_2	~10
H_2O	OH⁻	15
ROH (alcohol)	RO⁻	15-17
R-C≡C-H (alkyne) (weakest base + hybrid!)	R-C≡C⁻	25
NH_3	NH_2^-	34
≥C-H (alkane)	≥C⁻	45-50

Strong acids + weak bases ↑ ... weak acids + strong base

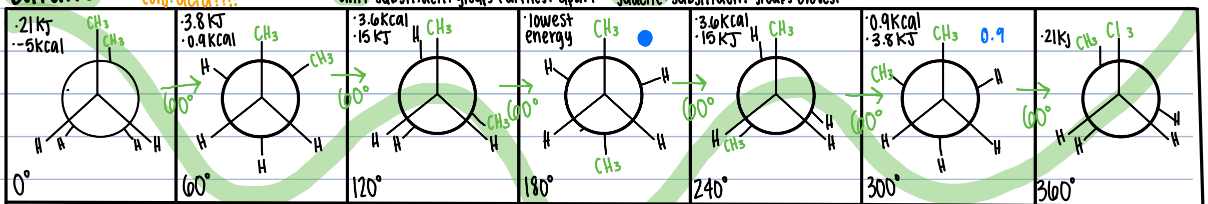
- Proton acidity: C-H < N-H < O-H (weak → strong)
  - if 2 H are bonded to the same element, draw both conj. bases + look for...
    1. e⁻ w/ drawing = stronger acid
    2. resonance = stronger acid
    3. hybridization $sp > sp^2 > sp^3$
  - → check elements bonded to H
  - 2 left? Make conj. base + go through here!
- Strong acid → weak acid; low pKa → high pKa
- * compare acid + conj. acid!!!!

- * more protons on product = base
- * more protons on reactant = acid] lewis

SP	50%	2 groups	σ	180°	linear/bent
Sp^2	33%	3 groups	σ π	120°	trigonal planar
Sp^3	25%	4 groups	σ π π	109.5°	tetrahedral

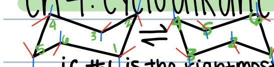
Butane

anti: substituent groups furthest apart. gauche: substituent groups closest

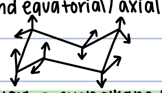


0°	60°	120°	180°	240°	300°	360°
21 kJ, ~5 kcal	3.8 kJ, 0.9 kcal	3.6 kcal, 15 kJ	lowest energy	3.6 kcal, 15 kJ	0.9 kcal, 3.8 kJ	21 kJ
Fully eclipsed, least stable, most energy	gauche, staggered	eclipsed	anti, staggered, most stable, least energy!	eclipsed	gauche, staggered	fully eclipsed, least stable, most energy

Ch 4: cycloalkane chairs



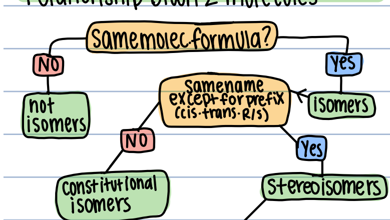
- if #1 is the rightmost carbon in one confirmation, it needs to be the rightmost carbon in all other confirmations
- substituents will switch from axial to equatorial as the confirmations switch and vice versa
- to determine cis/trans, look at what direction the substituents point
  - both point up/down: cis — cis = both up/down
  - one up + one down: trans — trans: one up/one down
- no correlation btwn cis/trans and equatorial/axial!!



- to convert a cycloalkane to a chair confirmation....
  1. # carbons in cycloalkane and chair going in the same direction
  2. add substituents correspondingly
     - if on a wedge in cycloalkane, it must point up on chair!
     - if on a dashed wedge in cycloalkane, it must point down on chair!
- equatorial is more stable than axial bc axial has steric hendrance!
- smaller substituents are more stable than larger substituents.
  - if needed, put larger substituents in the equatorial spot and smaller in axial

Isomers (Ch5)

Relationship btwn 2 molecules



Ch5: Stereoisomers

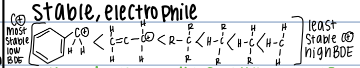
- constitutional isomer: same molecular formula, different connectivity
  - remember atoms can rotate!
- stereoisomers: same formula + connections but different spatial orientation
- chiral: have stereogenic center, mirror images do not match, sp^3, optically active, has enantiomers, not meso, no plane of symmetry in entire molec.
- achiral: no stereogenic center, mirror image aligns, optically inactive, has symmetry, can be meso, no enantiomers.
- one chiral carbon = 2 enantiomers only
- n stereogenic centers = 2^n stereoisomers max
- to draw enantiomers just draw the mirror image + check to see if they align. no align = enantiomers
- for cyclic compounds, double check to make sure it is a stereogenic center + the R-groups dont match — not chiral bc 2 groups match
- How to assign priority
  1. in order of decreasing atomic #
  2. priority is assigned at first point of difference!!
- How to assign (R) or (S) to enantiomers
  1. assign priority to each group
  2. use model (if needed) and orient the molecule so that 4th priority is away
  3. clockwise numerically = R; counterclockwise numerically = S

(R) (S)

- How to draw all possible stereoisomers
  1. Draw mirror image of original molecule to get its enantiomer
  2. switch positions of any 2 groups on one chiral carbon
  3. Draw mirror image of the molecule with the switched chiral carbon
  4. repeat steps 2 and 3 with different chiral carbons
     - A+B, C+D are enantiomers
     - A+C, B+D are diastereomers
- meso compounds: achiral compound with stereogenic centers usually has a plane of symmetry too
- enantiomers: completely opposite R,S conf.
- diastereomers: opposite R,S conf. for at least one chiral carbon
- optically active means only one plane of light is allowed through chiral compounds
  - R and S let diff. planes of light through
  - cw: d,+, dextratory
  - ccw: l,-, levorotatory

Ch6: Organic rxns

- Reaction Types
  - substitution: one group replaces another group. one σ bond broken + one σ formed
  - elimination: group is removed from the reactant. two σ bonds broke + one π forms
  - addition: group is added to the reactant. one π broken + 2 σ formed
- concerted rxn: one step rxn
- stepwise rxn: mult. steps + has an unstable reaction intermediate
- homolysis: bond breaks + each part gets one e⁻ A-B → A· + B· produces free radicals. endothermic. uncharged
- heterolysis: both e⁻ go to the more en part. A-B → A⁺ + B⁻ produces ions, endothermic, charged products
- carbocation stability: more R groups = more stable, electrophile



- * radicals have opposite stability from C⊕ *
- single bond has lowest BDE + triple has highest
- carboanions are nucleophiles.
- bond formation uses E and bond breaking releases E.
- ΔH° overall = (sum of bonds broken) + (-sum of bonds formed)
  - -ΔH° = exothermic → products favored
  - +ΔH° = endothermic → reactants favored

→	rxn arrow	btwn reactants + products
⇌	double rxn arrow	btwn reactants + products in equilibrium rxns
↔	double-headed arrow	btwn resonance structures
↷	full-headed arrow	shows e⁻ pair movement
↷	half-headed/fishhook	shows movement of only one e⁻

- Keq = [products]/[reactants]
  - Keq = 1 then ΔG = 0 → equilibrium
  - Keq > 1 then ΔG < 0 → products favored
  - Keq < 1 then ΔG > 0 → reactants favored
- ΔS < 0 → reactants favored
- ΔS > 0 → products favored
  - more molec. on products and cyclic to noncyclic = +ΔS
- ΔH, ΔS, ΔG and Keq do NOT effect the rate of rxn, only the equilibrium
- ΔG = ΔH - TΔS
- ΔG ≈ ΔH
- -ΔG = exergonic
- +ΔG = endergonic
- slowest step (highest Ea) is the rate determining step
- lower Ea and higher temp make the rxn faster, and have large 'k' values

Ch 7: alkyl halides

- alkyl halide: halogen attached to sp^3 carbon. reactive
- allylic halide: halogen attached to sp^3 carbon that is next to a C=C. reactive
- benzylic halide: halogen on sp^3 carbon adj. to benzene. reactive
- any halogen attached to an sp^2 carbon such as vinyl or aryl do NOT undergo S_N1/S_N2
- Properties of alkyl halides
  - higher bp/mp than alkanes w/ same carbon chain bc larger halide adds vdw forces
  - bp and mp increase as carbon chain increases and as halogen size increases
  - alkyl halides are soluble in organic solvents, but not soluble in water
- bottom left of periodic table = largest atoms
- top right of periodic table = smallest atoms
- alkyl halide + lewis base/nucleophile = substitution
- nucleophile (:Nu⁻): has lone pair/π bond + maybe (-) charge + replaces leaving group in subst. rxns
- nucleophilic substitution is heterolytic rxn
- The leaving group
  - better LG = weaker base (stronger acid)
  - LG strength increases left to right and down a column, opposite of bascity
  - good LG: Cl, Br, OH_2, I
  - bad LG: F, OH, NH_2, H, R
- equilibrium favors the product when the LG is a weaker base than the :Nu⁻, favors side with the stronger conj. acid (lower pKa)
- Nucleophilicity
  - same :Nu atom = stronger base = stronger Nu
  - :Nu with a (-) is always stronger than neutral Nu
  - right to left on pd table Nu increases
- Steric hendrance: more chunky R groups create steric hendrance, decreases Nu ability
- Polar protic solvents: has O-H or N-H, favors S_N1, solvates cations + anions. F < Cl < Br < I
- Polar aprotic solvents: no O-H or N-H, favors S_N2, I > Br > Cl > F. DSM, DMFC, acetone
- S_N2 reaction
  1. Kinetics
     - rate = K[RX][:Nu], bimolecular
     - concerted, one step rxn
  2. Stereochemistry
     - backside nucleophilic attack that causes an inversion of configuration. R → S endothermic, heterolytic
  3. R-group identity
     - smaller/less R groups react faster bc less steric hendrance
  4. Who does S_N2 rxns?
     - methyl halide, 1° halide, 2° halides
  5. Solvent type
     - Polar aprotic solvents! Nu are not well

are they mirror images?
Yes → enantiomers
NO → diastereomers

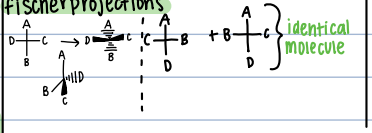
TO determine Stereoisomer type
- label ALL Stereogenic centers R/S
- if they are complete opposites: enantiomers
  - can check by drawing mirror image
- one or more but not all opposite: diastereomers
  - check by switching groups around
- none different: identical molecules

- achiral compounds are optically inactive and do not alter light
- Racemic mixtures: when 2 enantiomers are equally present so their rotations on light cancel out, making the solution optically inactive
- Diastereomers: not mirror images + not superimposable have diff. physical properties
- enantiomer physical properties: same chemical properties except how they interact w/ chiral non-racemic mixture
  - will fit differently into enzymes receptors + bend light different
- Plane of symmetry = achiral usually
- [α]D represents specific rotation

- rate = K[reactants in rate-determining]
  - unimolecular: rate = K[x], one reactant, first order
  - bimolecular: rate = K[x][Y], two reactants. second order
  - multi: conc. by x → rate increased by x. for bimolec. multi. both.
- Catalyst: lowers the E_A + speeds up the reaction. remains unchanged + can be recovered once rxn is over

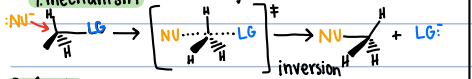
solvated here, making them stronger + better for SN2 rxns
6. Nucleophile
- Prefers strong nucleophile w/ (-) charge
- $-CH_3 < -NH_2 < -OH, -F < -Cl < -Br < -I$
- Stronger base = stronger nucleophile

Fischer projections

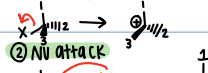


Ch7: SN1/SN2 rxns

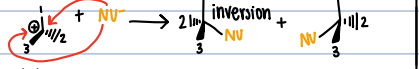
- SN2 reaction
1. Kinetics
- rate = K[RX][Nu], bimolecular
- concerted, one step rxn
2. Stereochemistry
- backside nucleophilic attack that causes an inversion of configuration. R→S
- endothermic, heterolytic
3. R-group identity
- smaller/less R groups react faster bc less steric hindrance
4. Who does SN2 rxns?
- methyl halide, 1° halides, 2° halides
5. Solvent type
- Polar aprotic solvents! Nu are not well solvated here, making them stronger + better for SN2 rxns. DMSO
6. Nucleophile
- Prefers strong nucleophile w/ (-) charge
- $-CH_3 < -NH_2 < -OH, -F < -Cl < -Br < -I$
- Stronger base = stronger nucleophile
7. mechanism



SN1 rxn
1. Kinetics
- rate = K[RX]
- two step, carbocation formation = rate determining
- Nu⁻ does NOT effect rate, only carbocation!
2. Stereochemistry
- Nu⁻ attacks from front + back, so 50% inversion + 50% retention, racemic mixture of enantiomers
3. R-group identity
- more substituted = faster rxn. no methyl!! 1°!!!
4. Solvent:
- Polar protic solvents, stabalize carbocation (OH/NH)
5. Nucleophile
- Weak: $Nu^-, I^- < Br^- < Cl^- < F^- < OH^- < NH_2^- < CH_3^-$ (weak → strong)
6. Mechanism:
① carbocation formation



② Nu attack



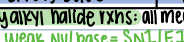
Nucleophilicity
- Same: Nu atom = stronger base = stronger Nu
- Nu with a (-) is always stronger than neutral Nu
- right to left on pd table Nu increases
- SN1 or SN2?

RX	mechanism	favored by...
methyl	SN2	· Strong: Nu⁻ · Polar aprotic
1°		
3°	SN1	· weak: Nu⁻ · Polar protic
2°	SN2/SN1	· Strong: Nu⁻: SN2 · Protic: SN1

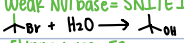
Elimination or substitution?
- good nucleophiles ($I^-, Br^-, SH^-, ^-CN$ + $CH_3CO_2^-$) usu. favor substitution.
- bulky bases ($^-OC(CH_3)_3$, DBU, DBN) favor elimination

RX	rxn with	mechanism
1°	Strong nucleophile	SN2
	strong bulky base	E2
2°	Strong base/Nu⁻	SN2/E2
	strong bulky base	E2
	weak base/ Nu⁻	SN1/E1
3°	weak base/Nu⁻	SN1/E1
	Strong base	E2

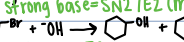
- Tertiary alkyl halide rxns: all mechanisms except SN2
- 3° + weak Nu/base = SN1/E1 (maybe both)



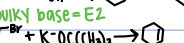
- 3° + strong base = E2



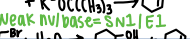
- Secondary alkyl halides: all mechanisms
- 2° + strong base = SN2/E2 (maybe both)



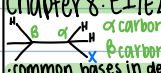
- 2° + bulky base = E2



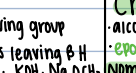
- 2° + weak Nu/base = SN1/E1



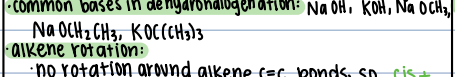
Chapter 8: E1/E2



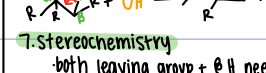
α carbon: directly connected to leaving group
β carbon: adjacent to α carbon. has leaving β H
- common bases in dehydrohalogenation: NaOH, KOH, $NaOCH_2CH_3$, $KOC(CH_3)_3$
- alkene rotation:
  - no rotation around alkene C=C bonds, so cis + trans are diastereomers



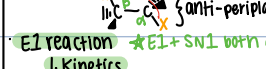
- Stability of alkenes:
  - trans more stable than cis isomers
  - less R groups = more stable



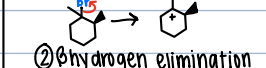
E2 reaction
1. Kinetics
- rate = K[RX][C:B] second order, bimolecular
2. The Base
- Stronger base = faster rxn
- VSU. strong bases (^-OH / ^-OR) or DBU/DBN
3. Leaving Group
- better leaving group = faster rxn
- (bad LG) F < Cl < Br < I (Good)
4. Solvent
- Polar aprotic - does not solvate base
5. R group
- more R groups = faster rxn, no methyl
6. Mechanism



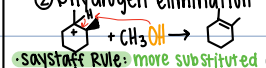
7. Stereochemistry
- both leaving group + β H need to be axial, one up + one down in chair confirmation
- 180° btwn leaving group + β Hydrogen (make models)



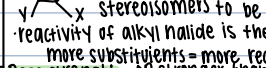
E1 reaction ★E1 + SN1 both deal w/ carbocations★
1. Kinetics
- rate = K[RX]
- first order, unimolecular, two step
2. The Base
- favored by weaker bases, H_2O/ ROH
3. The leaving group
- Stronger LG = faster rxn
4. Solvent
- Polar protic, w/ O-H / N-H
5. R group
- more substituted = faster rxn
6. Mechanism
① carbocation formation - rate determining



② β hydrogen elimination

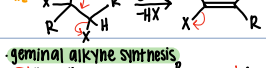


- Saytseff Rule: more substituted alkene C=C will be the major product bc it is more stable/zaisteck rule

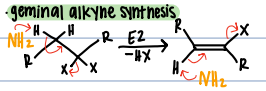


X'+X, Y'+Y must be different for stereoisomers to be possible!
- reactivity of alkyl halide is the same for E2 + E1, more substituents = more reactive

Base strength: ^-OR stronger than ^-OH, bigger R = stronger base. ROH
- Vicinal alkyne synthesis



- geminal alkyne synthesis



- dihalide: alkene w/ two halides, produces alkyne when w/ a strong base (NH_2 usu.) + DMSO solvent.

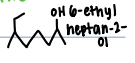
rxn	reagent	comment
ROH → RCl	HCl	all ROH. 2°/3° = SN1. 1°/methyl = SN2
	$SOCl_2$	SN2, best for methyl, 1° + 2°
ROH → RBr	HBr	all ROH. 2°/3° = SN1. 1°/methyl = SN2
	PBr_3	SN2, best for methyl, 1° + 2°
ROH → RI	HI	all ROH. 2°/3° = SN1. 1°/methyl = SN2

Ch 9: alcohols

alcohol: R-OH ether: epoxide: oxiranes 

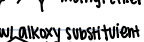
- alcohols, ethers and epoxides are tetrahedral + bent around oxygen!!
- epoxides have angle strain since they're in a ring, so they're more reactive

Nomenclature:
- alcohols: name longest carbon chain w/ OH group and add #-ol, then follow other nomenclature rules

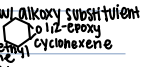


- diol: two -OH on alkyl, add -diol suffix instead of -ol
- simple ethers: name both alkyl groups + add 'ether' at end

- complex ethers: name simple ether (alkoxy) then name the rest normally w/ alkoxy substituent
- epoxyalkanes: name chain/ring attached to oxygen + use epoxy- prefix



- oxiranes: 2 C + one O in a ring. O at 1, substituent at 2



- alkene oxide: name like alkene, add 'oxide' at end

Properties
- boiling point/melting point: more -OH = higher bp/mp. Branching = lower mp/bp

Williamson ether synthesis: ethers synthesized through SN rxns. Pathway with less sterically hindered $:Nu^-$ is preferred bc SN rxns ♡ skinny
- alcohols need hydroxide nucleophile to be synthesized (NaOH, KOH)
- ethers need alkoxides to be synthesized ($NaOCH_3$)
- epoxides need an organic compound with a hydroxy + halogen on adjacent carbons to be synthesized
- alcohols, ethers + epoxides all have poor leaving groups that must be modified before they can undergo substitution/elimination rxns.

E1 dehydration of 2° + 3° alcohols
① Protonation of -OH → $-OH_2$, a good leaving group

② carbocation formation (rate determining)

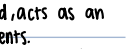
③ HSO_4 removes β proton + π bond formed

★H_2SO_4 is an acid-catalyst in this reaction

E2 dehydration of 1° alcohol
① Protonation of -OH → $-OH_2$, a good leaving group

② Base removes β + π bond is formed at the same time

carbocation rearrangement: alkyl/hydride group shifts once to switch places with ⊕ to create a more stable carbocation



Dehydration of $POCl_3$: works better than H_2SO_4 w/ organic compound, acts as an acid catalyst happens through E2 mechanism, no rearrangements.

alcohol → alkyl halides using HX: H Protonates OH, and X acts as nucleophile. HX are used to prepare alkyl halides. more substituted alcohols react more quickly w/ HX
- 1° alcohols → SN2 rxns
- 2°/3° alcohols → SN1 rxns
- 1° ROH + HX - SN2 mechanism
  ① Protonation of -OH → $-OH_2$, a good leaving group

  ② R-X σ bond forms as $-OH_2$ leaves

  - inversion of stereogenic center
- 2° ROH + HX - SN1 mechanism
  ① Protonation of -OH → $-OH_2$, a good leaving group

  ② carbocation formed (rate determining)

  ③ Nu attack of X forming racemic product

  - racemization at stereogenic center!

ROH with $SOCl_2$ + Pyridine
- 1°/2° ROH + $SOCl_2$ + Pyridine react to form alkylchloride, HCl + SO_2

Tosylate and alcohols
- TsCl + alcohol, then H on OH leaves + O binds to Ts, making ^-OTs which is a good leaving group, similar to I. retention of stereogenic center.

Rxns of Ethers with strong acids
- only HI and HBr can be used w/ ethers bc both C-O bonds are cleaved + two alkyl halides products
- two successive Nu substitution, one for each alkyl
- 3° SN1 to break C-O bond
  ① Protonation of ether O creates O^+, good leaving group

  ② Cleavage of C-O bond → 3° carbocation (SN1)

  ③ Nu attack forms substitution product

- 1° CH_3-OH → alkyl halide by SN2 mechanism
  ④ Protonation of OH to make good leaving group

$CH_3-OH + H-I \rightarrow CH_3-OH_2 + I^-$

  ⑤ Nu attack by I^- forming second alkyl halide

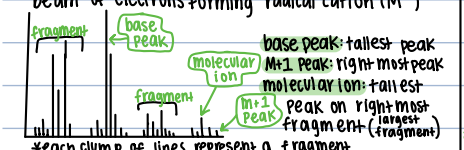
$CH_3-OH_2 + I^- \rightarrow CH_3-I$

Thiols R-S-H
- lower bp than alcohols
- Oxidized with Br_2 or I_2 to produce disulfides (RS-SR)

- Primary alkyl halides: SN2 or E2 only
  - 1° + Strong Nu⁻: SN2
  - 1° + Strong bulky base = E2
- not → elimination; cold → substitution
- -OR / -OH = SN1/E2 ★ bulky R = E2!!!!
- H2O/ROH = SN1/E1
- Polar protic: F<Cl<Br<I (best nu) have -OH/-NH!! acetone
- Polar aprotic: I<Br<Cl<F (best nu) THF, DMF, DMSO, no -OH/-NH!!

mass spectrometry: technique used for measuring the molecular weight to determine molec. formula.

- molecules are vaporized and ionized w/ high energy beam of electrons forming radical cation ($M^{+\cdot}$)



- base peak: tallest peak
- M+1 peak: right most peak
- molecular ion: tallest peak on right most fragment (largest fragment)

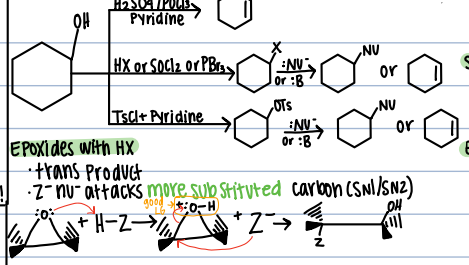
*each clump of lines represent a fragment

molecular ion → molecular formula C:12 N:14 O:16 H:1

1. divide mz value by 12 to determine max number of carbons
2. replace a carbon with 12 Hydrogens until you find a possible ratio of carbons + Hydrogens
3. add/subtract oxygen/Nitrogens as needed until you figure it out. Guess + Check

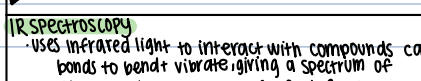
Isotopes

- Chlorine: ^{35}Cl and ^{37}Cl in a 3:1 ratio.
  - larger peak = 35Cl (M)
  - Smaller peak = 37Cl (M+2)
- Bromine: ^{79}Br and ^{81}Br in a 1:1 ratio. Graph will show two identical lines next to each other



Epoxides with HX

- trans Product
- Z⁻ Nu⁻ attacks more substituted carbon (SN1/SN2)



IR Spectroscopy

- uses infrared light to interact with compounds causing bonds to bend + vibrate, giving a spectrum of characteristic absorptions for each functional group

- Strong absorption = low % transmittance
- Stronger bonds have higher vibrational frequencies which means they absorb at higher wavenumbers C-C<C=C<C≡C
- lighter atoms vibrate at higher frequencies so they absorb at higher wavenumbers (X-H are always on left)
- molecules must have a dipole moment to show up on IR
- higher % s-character the stronger the bond and the higher the wavenumber! $sp^3 < sp^2 < sp$ (highest cm^{-1})

4000 — 2500

bonds to H	triple bond	double bond	single bonds
C-H	C≡C	C=C	C-C C-O
O-H	N≡N	C=O	C-N C-X
N-H		C=N	

Ch 10: Alkenes + additions

degrees of unsaturation:

1. calculate max. H atoms using C_nH_{2n+2} based on C
2. actual H − max H / 2 = degrees of unsaturation

★ O = ignored, N = Subtract H for each N; X = add H for each (halogen)

- number for degrees of unsaturation = number of π bonds AND rings in any combination!

Nomenclature

- OH gets numbered lower, then π bond on C chain!!
- add -ene ending + indicate location
- diene: 2 double bonds (-adiene ending)
- cycloalkene: assume double bond btwn C1 + C2, unless there is alcohol (which will be C1)

Stereoisomers

- cis: groups on same side
- trans: groups on different sides
- ★ cis + trans alkenes do NOT interconvert bc π bond!!

E/Z assignments

1. assign priority like normal to groups around double bond, seperate for each half
2. first priority on SAME side = Z; first priority on DIFFERENT side = E
- ★ in dia stereomers, R → S changes NOT E/Z!
- E + Z confirmations are stereoisomers

common names

methylene, vinyl, allyl

Preparation of alkenes

- fm. alkyl halides + alcohols via elimination
- See substitution + elimination rxns!

Addition reactions Basics

- alkenes act as nu⁻ bc π bond + rxt with electrophiles
- Syn addition: X + Y added to SAME side (cis: 1 product, trans: 2 enant.)
- anti addition: X + Y added fm OPPOSITE sides (cis: 2 enant., trans: 1 product)

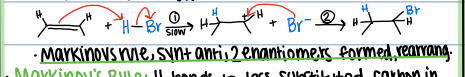
Hydrohalogenation - electrophilic addition of HX

- addition of H and X (Cl, Br or I) to an alkene

mechanism: alkene + HX

1. π bond attacks H to form C-H bond + carbocation (slow)
   - ★ H goes to the LESS substituted carbon
2. Nu⁻ attack of X⁻ on carbocation; C-X σ bond formed

-Br⁻ acts as lewis acid



- Markinovs rule, SynI anti; 2 enantiomers formed, rearrang.

Markinov's Rule: H bonds to less substituted carbon in unsymmetrical alkenes! forms more stable carbocation!

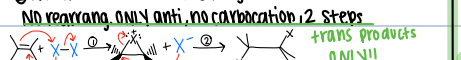
Halogenation - X_2 + alkene

- X_2 (Cl/Br) added to alkene forms vicinal dihalide

mechanism: alkene + X_2

1. bridged halonium ion formed using lone pair + e⁻ fm π bond X-X cleaved; C-X bond formed
2. Nu⁻ attack of X opens ring + makes new C-X σ bond

NO rearrang. ONLY anti, no carbocation, 2 steps



- ★ cis reactant → enantiomers
- ★ trans reactant → identical

Halonydrins: alkene + X_2 + H_2O

- add X and OH to alkene
- anti, trans product, X on less substituted C, NO rearrang

mechanism: alkene + H_2O + X_2

1. bridged halonium ion formed
2. Nu⁻ attack by H_2O opens ring + C-OH_2 added
3. OH_2 deprotonated by H_2O + halohydrin formed

-NBS + DMSO(aq) used for bromonydrin

Ch 12: redox reactions

Oxidation: increase of C-Z (usu. C-O) bonds OR decrease of C-H bonds

reduction: decrease of C-Z bonds (usu. C-O) OR increase of C-H bonds. alkyne → alkene → alkane is all reduction

- more C-O bonds → better oxidized
- more C-H bonds → better reduced

Reducing agents

- H_2
- dissolving metal reductions: NH_3 + Na
- metal hydride reagents: $LiAlH_4$, $NaBH_4$

catalytic Hydrogenation (alkene reduction)

- alkene + H_2 $\xrightarrow{Pd\text{-}C/Ni\text{-}C/Pt\text{-}C}$ alkane
- syn addition
- trans alkenes hydrogenate easier bc lower $\Delta H°$

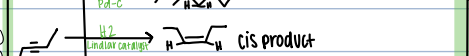
mechanism:

1. H_2 binds to metal catalyst, H-H bond breaks
2. π bond in alkene binds to metal catalyst
3. both H replace π bond + the now alkane decomplexes because no π bond to keep it complexed

- less subst. alkene = faster hydrogenation rxn
- degree of unsaturation after hydrogenation − degree of unsaturation before hydrogenation = # of rings in starting material

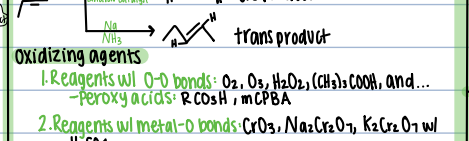
aldehyde + ketone hydrogenation

aldehyde + H_2 + Pd-C → 1° alcohol



Ketone + H_2 + Pd-C → 2° alcohol

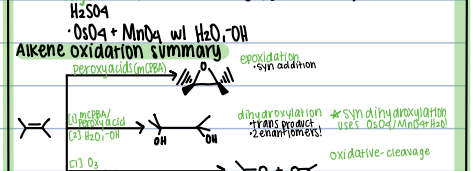
Alkyne reduction summary



Oxidizing agents

1. Reagents w/ O-O bonds: O_2, O_3, H_2O_2, $(CH_3)_3COOH$, and...
   - Peroxy acids: RCO3H, mCPBA
2. Reagents w/ metal-O bonds: CrO_3, $Na_2Cr_2O_7$, $K_2Cr_2O_7$ w/ H_2SO_4
   - OsO_4 + MnO_4 w/ H_2O, -OH

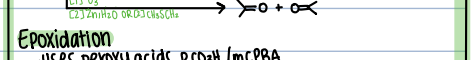
Alkene oxidation summary



Epoxidation

- uses peroxy acids RCO3H / mCPBA

mechanism

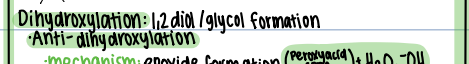


- one step rxn
- syn addition
- substituent positions retained

Dihydroxylation: 1,2 diol / glycol formation

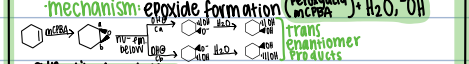
- Anti-dihydroxylation

mechanism: epoxide formation (peroxyacid mCPBA) + H_2O, -OH



- Syn-dihydroxylation

mechanism: alkene + $KMnO_4$ / OsO_4



oxidative cleavage of alkenes

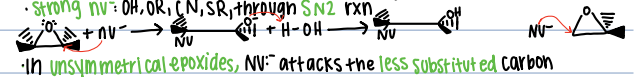
- Yeilds aldehyde if 3 groups, Ketone if 4 groups

Sulfides R-S-R

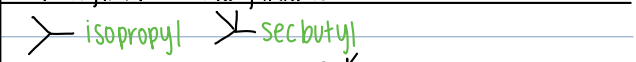
- name like ethers, but alkylthio instead of alkyloxide
- Prepared by SN2 similar to williamson ether synthesis like ethers.
- Nu⁻ sulfur atom that reacts with unhindered alkyl halides to form sulfonium ions

Epoxide reactions

- Nu⁻ attacks "O" + opens the 3-membered ring.
- Strong Nu⁻: OH, OR, CN, SR, through SN2 rxn



- In unsymmetrical epoxides, Nu⁻ attacks the less substituted carbon
- achiral reactant → meso products racemic mixture
- optically inactive → optically inactive



→ E+O⁻ = Strong skinny base (S_N2/E2)

heat = elimination!!

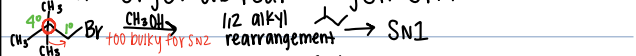
cold = substitution!!

Zaitsev → more stable / major

Hoffman → less stable / minor

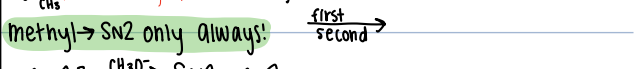
bulky reactant and bulky base = Hoffman

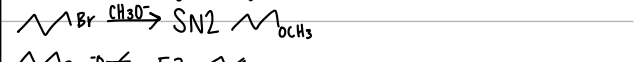
★ dont forget abrearrangement



methyl → SN2 only always!

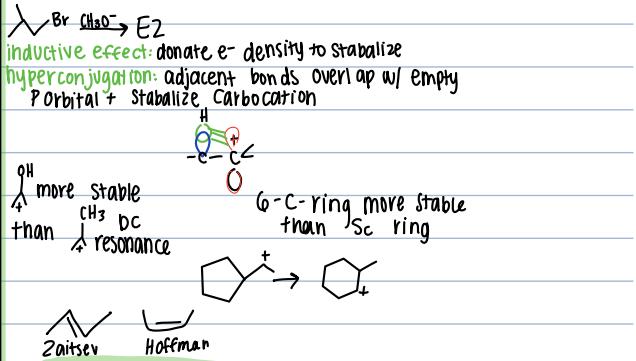
first > second





inductive effect: donate e⁻ density to stabalize

hyperconjugation: adjacent bonds overlap w/ empty P orbital + stabalize Carbocation



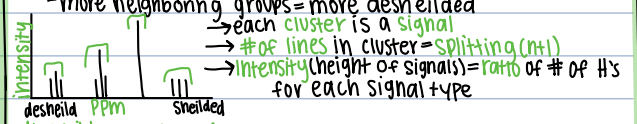
poor LG → Hoffman

good LG → Zaitsev

NMR Spectroscopy

^1H NMR signaling

- # of signals = # of protons in DIFFERENT environments
- equivalent protons are cis and trans to the same groups (left)
- deshielding effect: decreased e⁻ density, absorption shifts downfield
  - Protons near an electronegative atom are deshielded
  - more neighboring groups = more deshielded



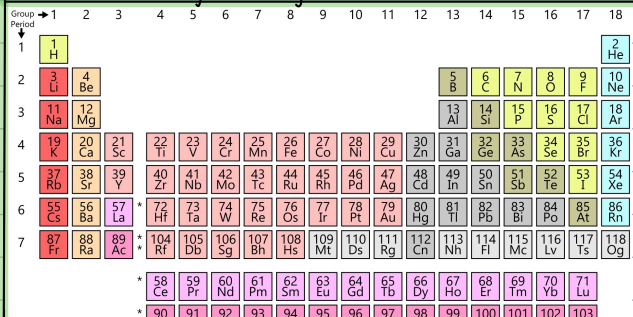
→ each cluster is a signal

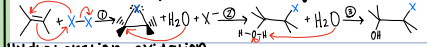
→ # of lines in cluster = splitting (n+1)

→ intensity (height of signals) = ratio of # of H's for each signal + type

^{13}C NMR

- signals show carbons in diff. environments, just like ^1H NMR
- ^{13}C NMR does NOT have splitting
- 300 MHz → weak signal bc only 1% of C is ^{13}C

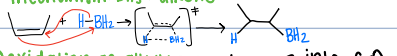




Hydroboration-oxidation

① hydroboration: add BH_3 to alkene → alkylborane, syn addition, no carbocation rearrangement, boron on less subst. carbon bc chunky Boron

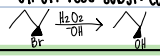
mechanism: BH_3 + alkene

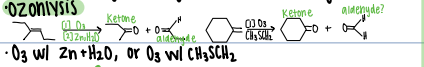


② oxidation of alkylborane: turn C-B into C-O

OH replaces BH_2 in the SAME configuration! syn addition

OH on less subst. carbon (same C as BH_2!)

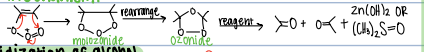




• ozonolysis

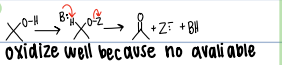
• O_3 w/ Zn + H_2O, or O_3 w/ CH_3SCH_2

mechanism?



Oxidization of alcohol

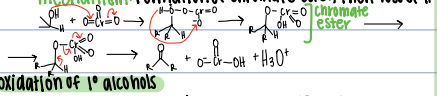
• basic mechanism:



• 3° alcohols: do not oxidize well because no available H on the carbon w/ the alcohol

• 2° alcohols: alcohol converted to a ketone using CrO_3, MnO_3, $K_2Cr_2O_7$, $Na_2Cr_2O_7$

• mechanism: formation of chromate ester, then loss of H^+

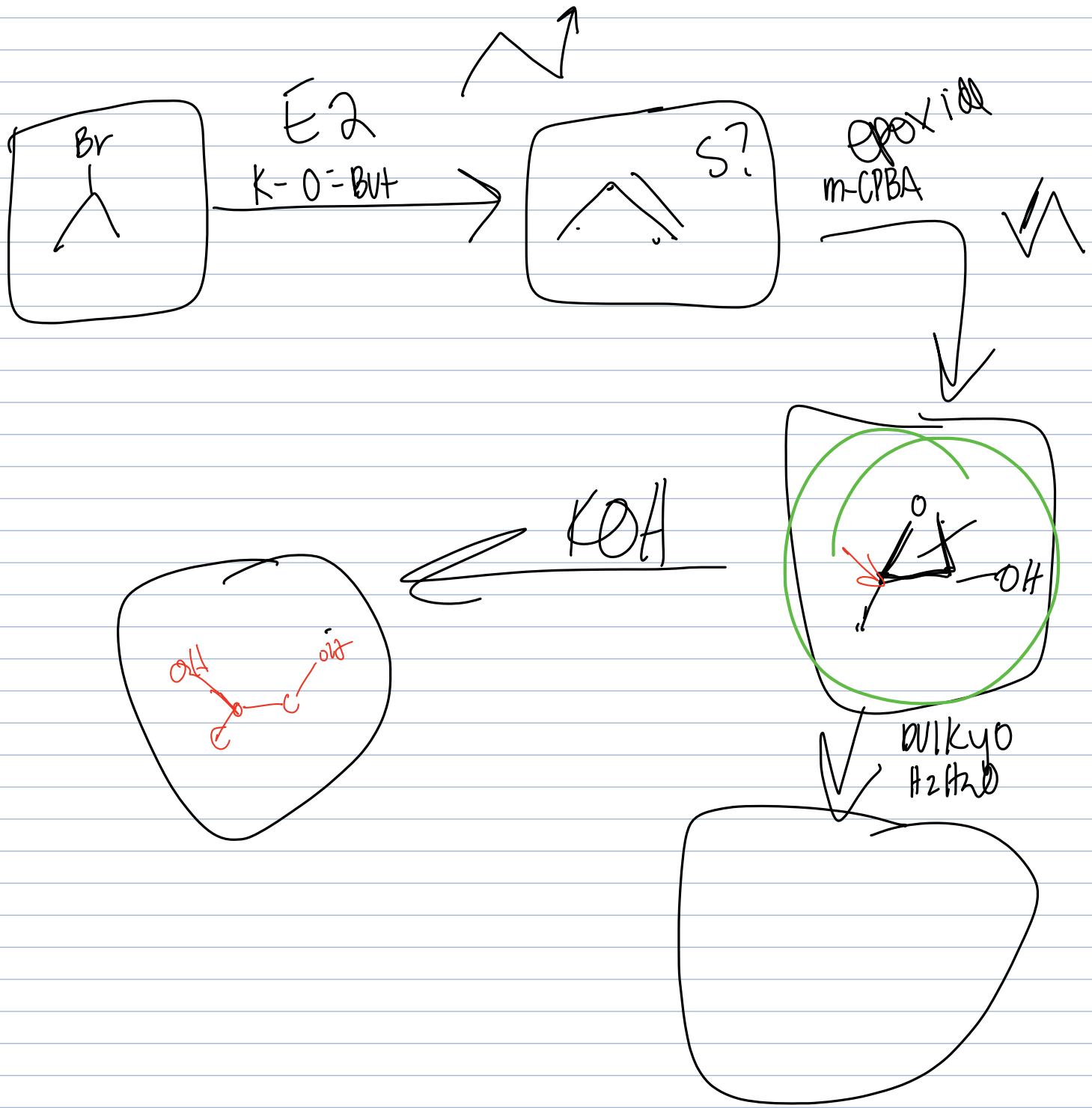


Oxidation of 1° alcohols

• 1° alcohols are oxidized to aldehydes (RCHO) under mild rxn conditions using PCC in CH_2Cl_2

• 1° alcohols are oxidized to carboxylic acids (RCOOH) using harsher rxn conditions: $Na_2Cr_2O_7$, $K_2Cr_2O_7$, or CrO_3 IN H_2SO_4 (aq.) and H_2O

— 3 steps: oxidation to form first aldehyde, rxn w/ water, oxidation to form carboxylic acid


Br
E2
K-O-BUt
S?
epoxide
m-CPBA
KOH
OH
OH
OH
Alkyo
H2H2O