From Last Time

– can think about from perspective of dipole moment

- **nucleophiles** are neutral or anionic species that donate high energy electrons from a filled orbital (HOMO) to an electrophile
- **electrophiles** are neutral or cationic species with low energy vacant or anti-bonding orbitals (LUMO) that can accept electrons

nucleophile

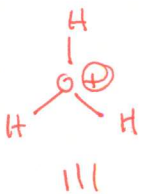
lone pairs: electron pairs available for donation

what is more nucleophilic? SH vs S⊖

electrophile:

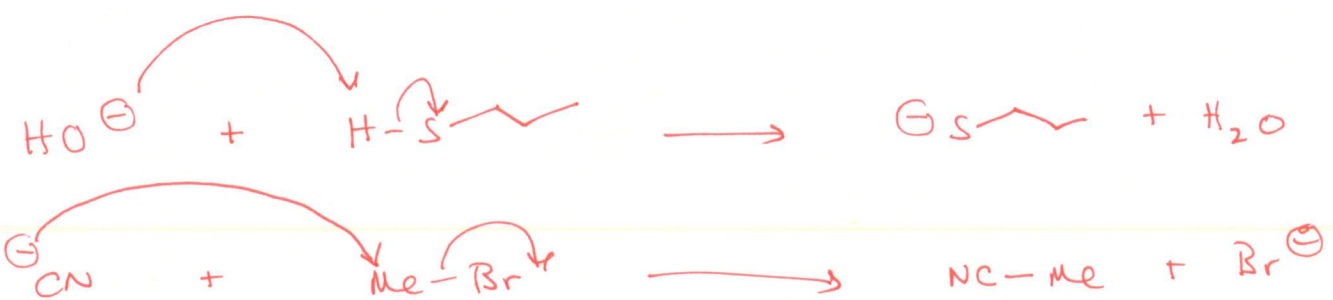
vacant 1s orbital!

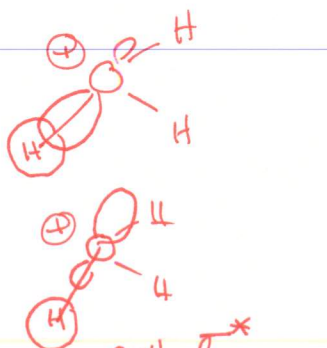
typically we see:



III

- organic chemists use curved arrows to show reaction mechanisms
- curved arrows indicate the flow of electrons





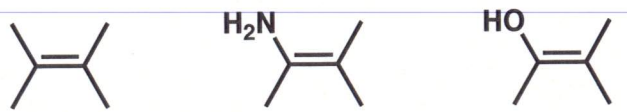
– the functional groups do the reacting

Nucleophiles

neutral lone pair nucleophiles:

anionic lone pair nucleophiles:

neutral π-nucleophiles:

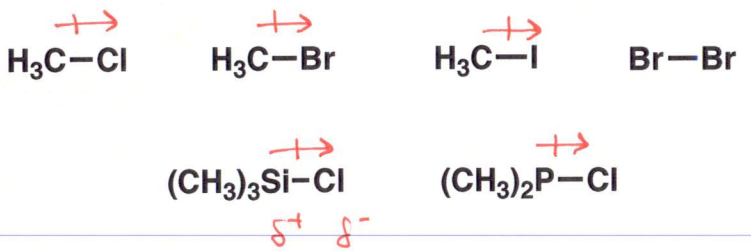


organometallic reagents:

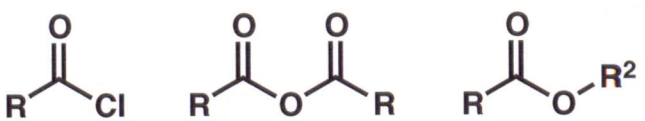
Electrophiles

protic and Lewis acids:

halides or other compounds with weak σ-bonds:

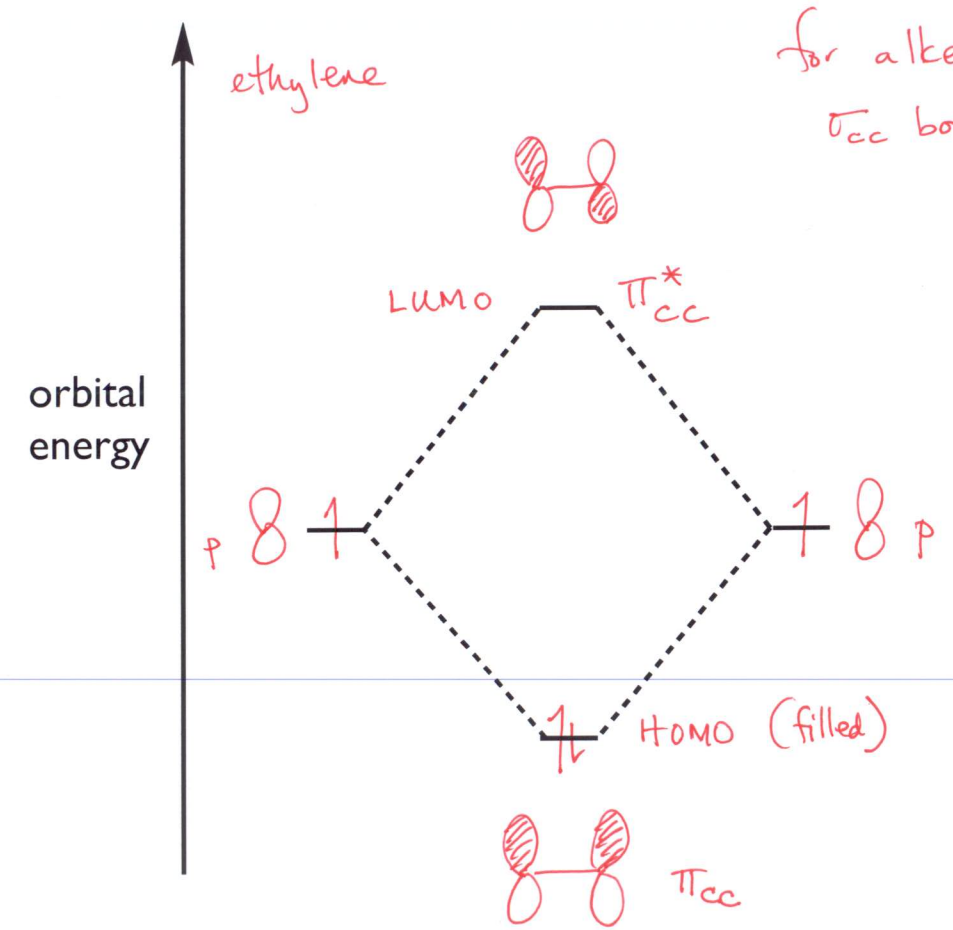


carbonyl compounds:



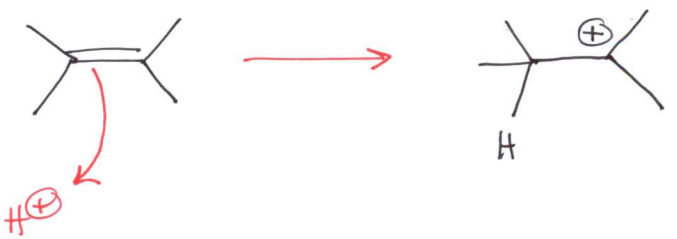
Why are Alkenes Nucleophilic?

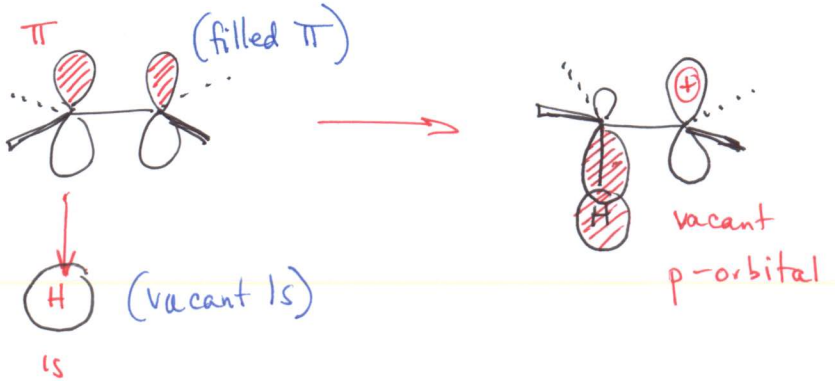
- the filled π-bonding orbital is the highest occupied molecular orbital (HOMO)
- alkenes are weak nucleophiles, but will react with strong electrophiles (H^+, Br_2)



for alkenes, π bond is higher in energy than σ_{cc} bond, π bond is HOMO

arrow pushing:





Why are Alkyl Halides Good Electrophiles?

alkyl halides have low-lying vacant σ^* orbitals that can accept electrons

other important factors:

- bond strength of breaking σ-bond
- orbital overlap
- ability of "leaving group" to stabilize negative charge

	BE (kcal/mol)		BE (kcal/mol)
H_3C-CH_3	83	C–OH	86
Cl–Cl	58	C–Cl	81
Br–Br	46	C–Br	68
I–I	36	C–I	51

poor leaving group

v. poor electrophile

increasing electrophilicity

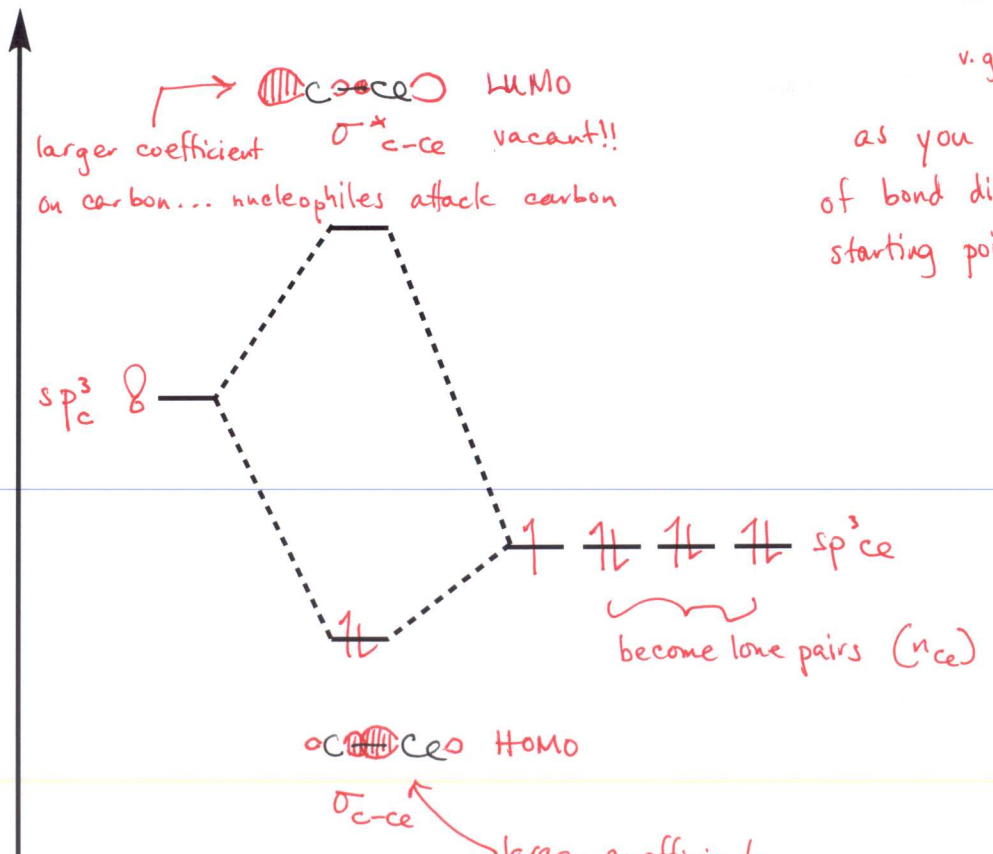
decreasing efficiency of orbital overlap

v. good electrophile

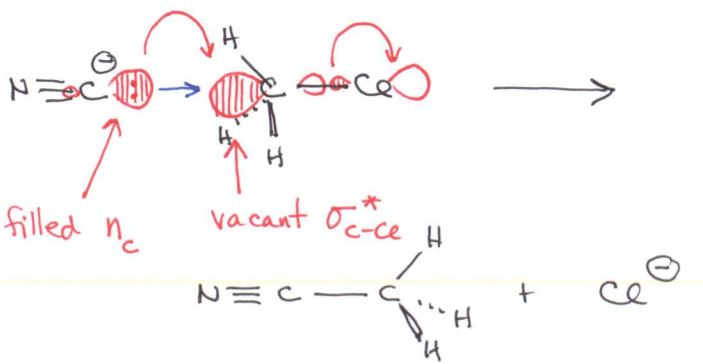
good leaving group

orbital overlap is best between two orbitals of similar size and energy

as you can see, analysis of bond dipoles can be a good starting point, but it isn't the whole picture



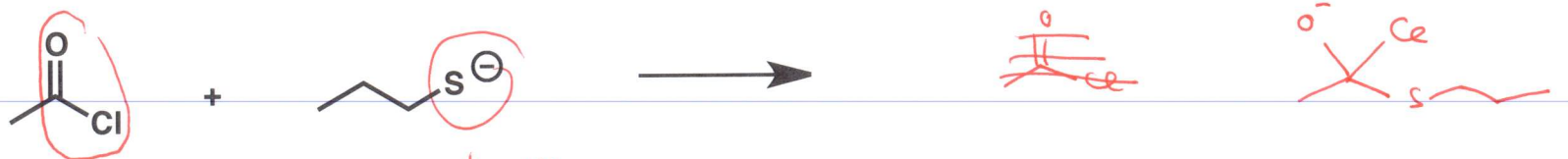
mechanism of NaCN + H_3C-Ce in terms of molecular orbitals:



Identify the Nucleophile and Electrophile

nuc

electroplic



electrophile

nucleophile

some guidelines: - we don't break C-C bonds

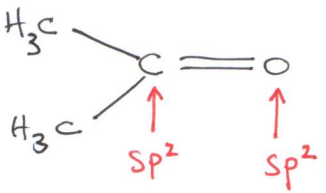
- we don't break simple alkane C-H bonds

The Carbonyl: The Most Important Functional Group

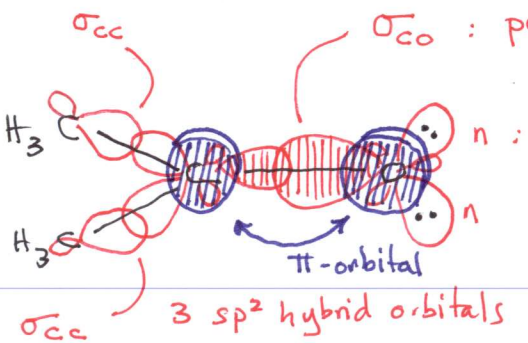
- the relatively low-energy vacant π^* orbital makes the carbonyl a good electrophile
- the relatively high-energy filled n orbitals (lone pairs) also allow the carbonyl to act as a nucleophile (a weak one)

rule of thumbs:
- bonding orbitals are lower in energy than non-bonding orbitals
- σ orbitals tend to be lower in energy than π-orbitals

acetone :



consider the molecular orbitals

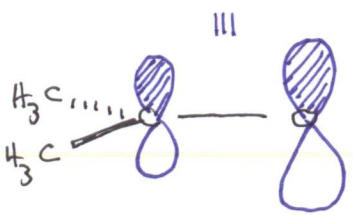


σ_{CO} : polarized towards oxygen

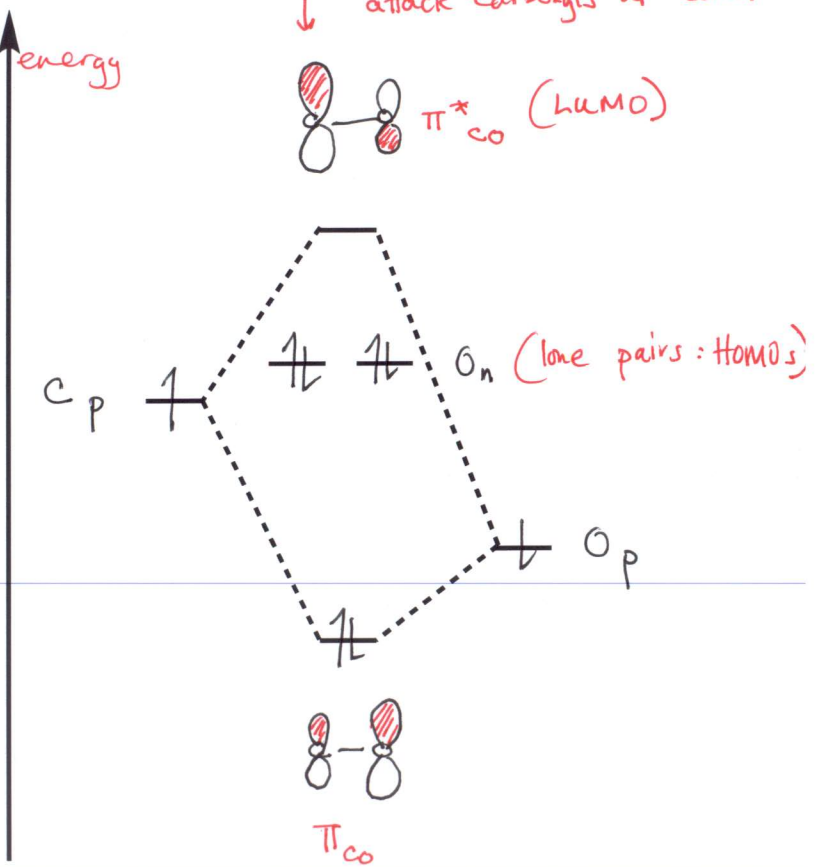
n : sp^2 hybrid orbital with non-bonding electrons : lone pair

3 sp^2 hybrid orbitals

1 p orbital



π_{CO} : polarized towards oxygen



larger coefficient on carbon in LUMO... nucleophiles ↓ attack carbonyls at carbon

- the carbon has the larger 'coefficient' in the π^* orbital, so nucleophiles attack the carbonyl at carbon

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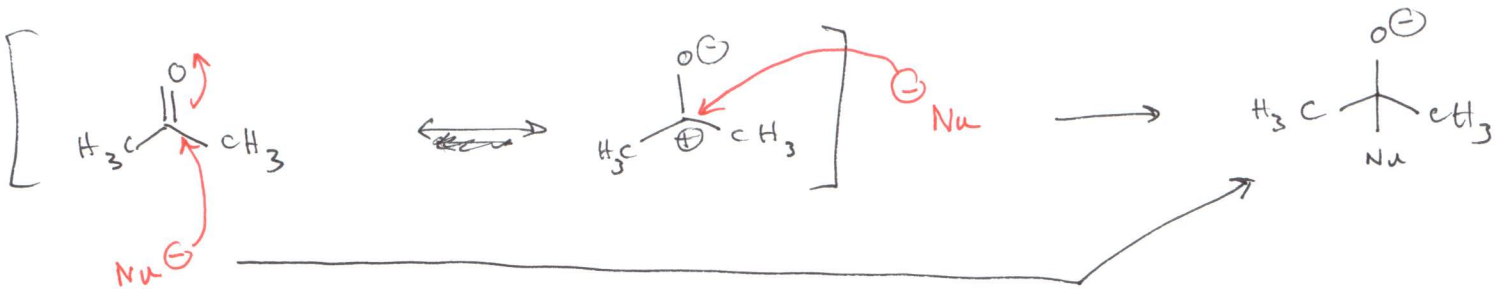
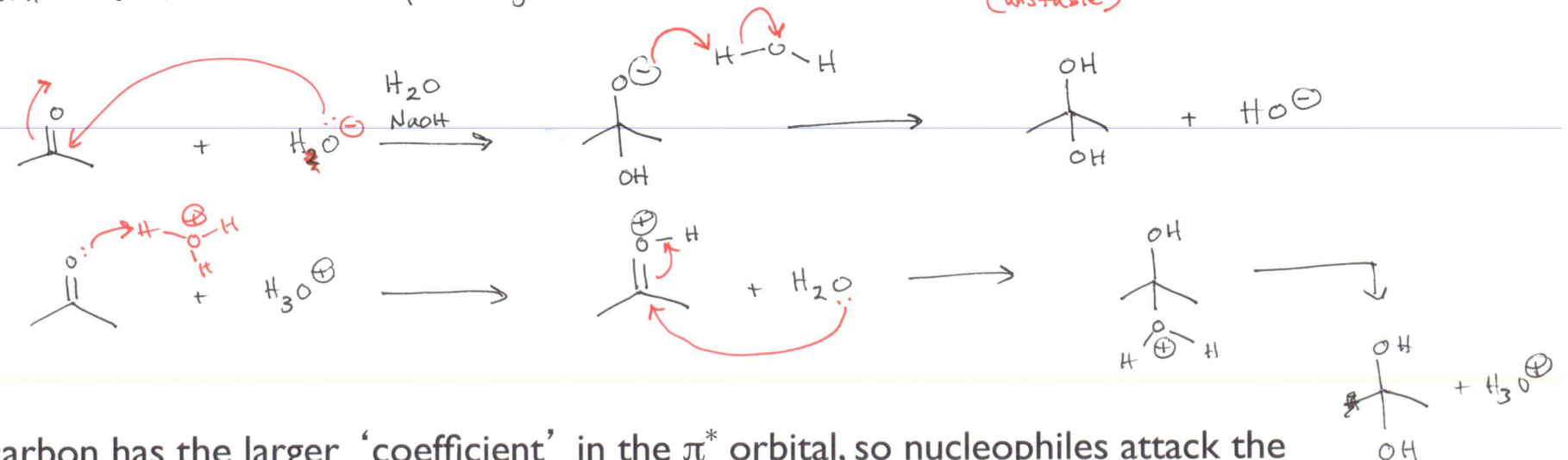


we can also tie several steps together in one mechanism:

(unstable)



- the carbon has the larger 'coefficient' in the π^* orbital, so nucleophiles attack the carbonyl at carbon

what is more electrophilic?  vs  ?

The Carbonyl: The Most Important Functional Group

- the relatively low-energy vacant π^* orbital makes the carbonyl a good electrophile
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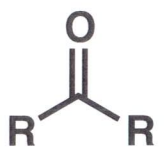
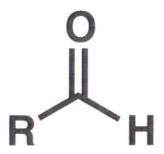
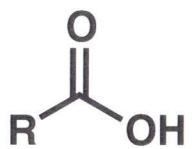
Examples of carbonyl compounds:



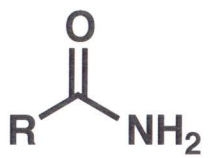
ketone



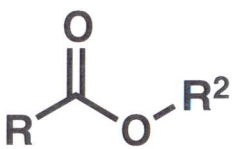
aldehyde



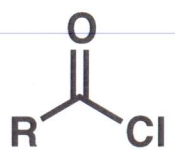
carboxylic acid



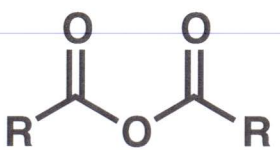
amide



ester



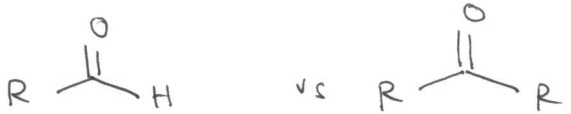
acid chloride



anhydride

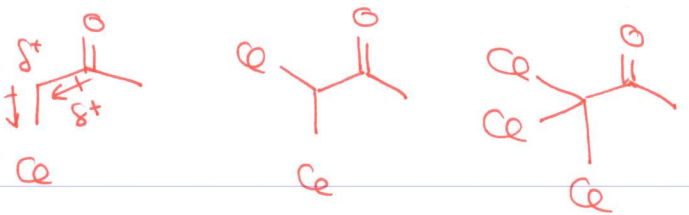
Aldehydes and Ketones

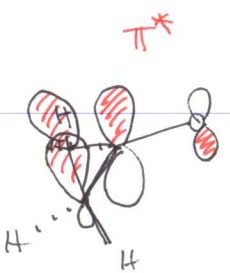
- both functional groups are in the same oxidation level
- aldehydes are more reactive the ketones
- substitution of adjacent carbons with electron-withdrawing groups increases the electrophilicity



more electrophilic, more reactive

substituents that with draw electron density enhance the electrophilicity





$\sigma_{CH} \rightarrow \pi^*_{CO}$

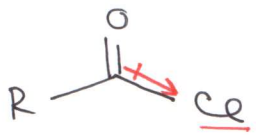
donation

"hyper conjugation"

Carbonyl Derivatives: Variations in Reactivity

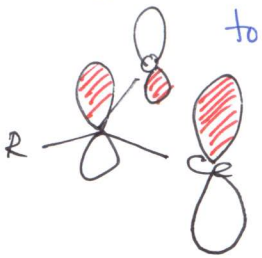
- the electronic nature of the group attached to the carbonyl carbon greatly influences the reactivity
- the effects can be categorized as inductive or resonance

most electrophilic



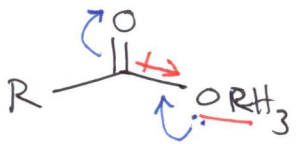
inductive effects : the pull of charge through bonds; is electrostatically driven

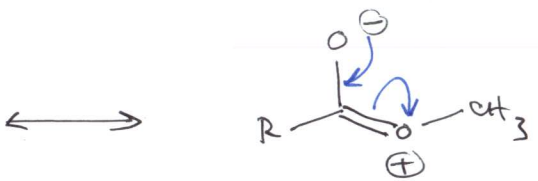
resonance effects : ability of substituent to donate electron density : ability to donate by resonance depends on orbital overlap and EN

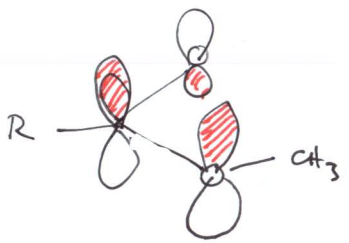


Cℓ is down one row in the periodic table, overlap of orbitals is not as good ... very little resonance donation

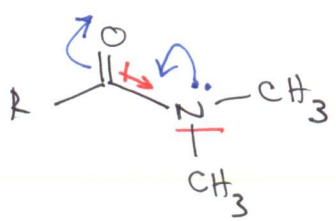
decreasing EN of attached group



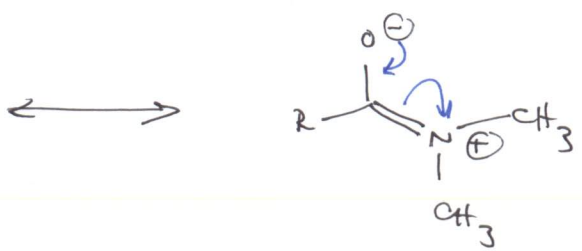


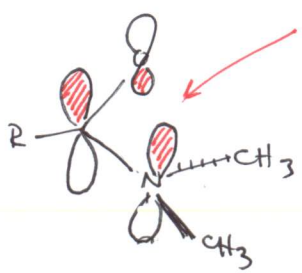


less prominent than amide, but still possible



least electrophilic





good orbital overlap, can donate into the π^*

lowers the energy of the p_π orbital, raises the energy of the π^*