Summary Sheet: Two Key Concepts for Nucleophilic Substitution on Carbonyls

Prefixing the nate of injurior at a contract and the Main of the recursing settentials intermediate departs or understanding too key concepts. 1. The electrons returns of the storms indicating the contract. 2. Storm build except the contract.

Ray Concept #1: The importance of electronic factors

Take the simplest cultoring formulatingle.

Eurobergoes one type of reaction: nucleophilic addition.



What happens when poly autostilute one of the hydrogene on formadethyte for a different functional group?

O BLOH OR CALLAN, NHR ME, NHALL

The late of the respitors will depend on two key factors.

 Elemonogativa functional groups make the carbony carbon more electropositive, artist increases the rate of reaction with numericals.

Primaring reaction rate or nucleightine

 Donatum of a attentions by the if group mates the partnersh carbon less electropositive, which decreases the late of machine with numbershape.



Even this discussion seem familiar from electrophilic aromatic automitation? It should! It's the same principle:

Pacual from attempedito promote substitution

MIL MIR NA, Dr. O

Moderately activating sercook, sercost down on

Wealty activating ON, CAL R CAL

Westly Descripting

deschineting the to another againsty but are a distorts Moderately describeding CDJH, CDJA, Ch CHO, COR

Strongly Describeting

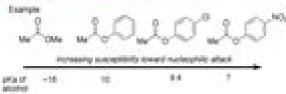
"I raft off INGs and SOsyn, which are important in electrosphile accreated automatic but not have in-parteral, carbony groups attached to these functions groups are too yestellar treatment inydicity in the architecture useful.

Note: tors at the position of DH prot O. They are entremely strong a discord. There why carboxylic apole are receitant to affact under basic conditions, strong a disreption by OC 1910 the pathonyl makes it extremely receitant literate inclinion/fell strains.

And the aith playinghile promote publishers, a denoted having electrologistry. The bronger the s-dance, the more resistant the perbodyl will be brownite had legalitic affects. The presence of directing groups makes the carbonyl carbon less associativits and the carbonyl support more numbers to Result freez resonance forms.

The carbonyl is the most nucleogratic part Lewis basis) plus. Therefore, it is protonated find

A good prony for domating storing is plf.a, especially when the atom attached to the carbony' is the same.



The total activated intermediate can undergo turber reaction

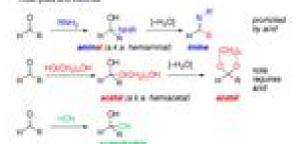
How can you predict what will happen?

Leaving group ability is directly related to the pKa of the conjugate acid.

pro of collegate and *remember, forevers. That under basic conditions (3H will be C* which means it would have to reason as C**, an extremely that become provi-

Advice: Know your pita's cold. They are a great measure of learning group ability and also of the obstron storating ability of the conjugate base, which colors up again and again when discussing chamical reactivity.

- Automorphics and Entoneous

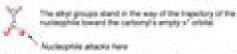


Key concept Kit. The importance of steric factors

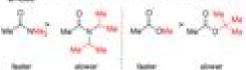
Formattehyde again, as the hydrogens are rigitated eith progressively bulker groups, the reaction rate goes street.

increasing attent fundamor adjacent to the carbony

18hy? Recall the artificiniting (x*) printing of the carbonyl group.



The same concept applies for the rate of reaction of multiciphties with eaters and articles.



A first important concept. Levils acids make carbonyls more electrophilic

For example, in the Fruction extentication, the find play is protonation of the surface/fit and

The protonated carbonyl, which is now more electrophilic, reacts with the relatively weak nucleochies. The attacket

Note in this example that the reaction between the Laws and InCit and nucleophile (EICH) is reverable under the reaction-conditions, whereas using , say, a Dirighest respect would require in increasible proteination of the nucleophile is a no reaction. Compatibility between Laws acids and nucleophiles is treated with more detail in advanced level properly charmetry counters.

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more hurlegable a less electrophic a factor rate of reaction with electrophics a higher electron density a more (units basis) in less Lesis acids" a more electron rich a less electropositive more electrophic a less electrophic in test electrophic

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Julia Schneider

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