Aromatic Electrophilc Substitution

I. arenium ion mechanism - AE + DE



A. first step is usually rate determining

B. evidence -

1. usually no primary deuterium isotope effect (X = H)

2. arenium ions observed by NMR in superacid solutions

3. mechanism is consistent with distribution of products

II. -complex

A. probably forms prior to arenium ion

B. may be rate determining step certain cases

III. electron-transfer mechanism



oxidation of anisole and other electron rich aromatic in presence of NO2 gave same product distribution as direct nitration (common intermediate)

IV. DE + AE (SE1)



V. single directing and activating groups

A. rationalized using arenium ion

B. electron donating groups accelerate versus H and direct toward ortho and para positions



C. electron withdrawing groups slow down versus H and direct toward meta

D. Cl, Br, and I deactivate but are ortho and para directors



E. ipso attack - five possible fates: electrophile migration, ipso group migration, ipso group loss, electrophile loss, nucleophile addition

1. known groups displaced after ipso attack: stable alkyl cations, electro positive groups (SiR3 and SnR3)



1. silicon and tin are good ipso directors because of stabilization of -carbocation (hyperconjugation)



VI. Multiple groups

A. strongest activating group controls position of substitution

B. position between meta goups disfavored

C. ortho effect: meta and ortho-para directors meta to each other - substitution occurs ortho to meta director. Initial attack is ipso which does not place charge at NO2 carbon

VII. structure/reactivity

1. Partial rate factors – rate relative to single benzene position
2. 
3. for example: if nitration of trichloromethylbenzene were 15 times slower than benzene and 29% of product is para then 
4. reactive electrophiles have early transition state, rates and product distribution are less sensitive to substitutents:

|  |  |  |  |
| --- | --- | --- | --- |
| Partial rates factors for toluene | | | |
|  |  | fm | fp |
| alkylation (RBr, GaBr3) | -2.4 | 1.4 | 5.0 |
| bromination (Br2, AcOH) | -13.1 | 5.5 | 2420 |

1. early versus late transition state



1. late transition state structure is like intermediate: using perturbation theory o,p substituents overlap with MO at positions with non-zero coefficients, m substituents have limited interactions due to node



1. early transition state structure is like reactant – determined by electron density



III. other ring systems

A. multiple rings

1. more reactive than benzene

2. form intermediate with most stable resonance forms (1 substitution is kinetically preferred, 2 substitution is thermodynamically preferred) 

B. heterocyclic

1. five membered rings- heteroatom donates a pair of electrons to aromatic ring: more reactive than benzene and directs  (2) substitution (pyrrole)



2. six member ring: heteroatom donates only single electron to aromatic ring: less reactive than benzene and directs to 3 position (pyridine) avoiding charge on heteroatom

# 

# IX. electrophiles

A. NO2+ (AcONO2 or HNO3/H2SO4), *i*-Pr+ (iPrCl/GaCl3), SO3 (H2SO4), NO+ (HNO2, HCl), Cl2, H+, RCO+ (RCOCl/AlCl3)

X. selected reactions

A. deuteration - general-acid catalyzed

B. nitration -

 

product

1. reaction is zero order in aromatic compound if aromatic is very reactive indicating formation of nitronium ion is rate determining or formation of nitronium ion is slow.
2. Reaction is first order in aromatic if aromatic is moderately reactive.
3. Freidel Crafts Acylation either goes by acylium or complexed acid halide

1.Other Lewis acids include SbF5, TiCl4, SnCl4, BF3

2. F-C acylation is more selective than alkylation indicating acylium ions are less reactive than alkyl cation toward aromatic



1. Halogenation
2. halogenation with I2 < Br2 < Cl2 (order of reactivity) occurs directly only with more reactive aromatics
3. Lewis acid catalysts are often used, for example AlCl3, FeBr3
4. Other reagents are used HOCl, HOBr, HOI, ICl, CH3CO2Cl, CF3CO2Br
5. Note that rate laws are often complex

E. Kolbe-Schmitt



F. deacylation and dealkylation (lone pair on CO)



G. protonate oxygen first? Other mechanisms? Distinguish by experiment?



.H. Formylation with chloroform



Aromatic Nucleophilic Substitution

I. SNAr (AN + DN), bimolecular kinetics

A. electron-withdrawing groups ortho and para, ussually requires 2 or more activating groups



B. first step is usually rate determining so rate shows little dependence on L

C. replacement of halogens: F > Cl > Br > I because first step is rate determining.

II. SN1 (DN + AN)

A. usually with diazonium group



B. first-order in diazonium, independent of nucleophile

C. tight-ion pair probably occurs

D. normally occurs by radical process in the presence of Cu salts (Sandmeyer)

III. benzyne (AxhDH + DN + AN + AHDxh) - favored by strong base

A. 

B. first or second step is rate determing depending on leaving group

1. proton loss is rate determining for Br and I

2. leaving group loss is rate determining for F and Cl

C. formation of most stable carbanion intermediate determines position of nucleophile attack



IV. SRN1 - favored by reducing agents

A. 







B. initiated by electron transfer

V. leaving groups

A. for SNAr: F > NO2 > OTs > SOPh > Cl, Br, I > N3 > NR3 > OR, SR, NH2 (*ipso* activation)

B. for SRN1: N2, halide, SPh, NMe3+, OPO(OEt)2 ????

VI. selected reactions???

A. Bucherer reactions: enamine hydroylsis



B. von Richter reaction: http://www.answers.com/topic/list-of-organic-reactions#wp-V



C. Sommelet-Hauser rearrangement (start from more stable anion) http://books.google.com/books?id=w9lTxIaPCQIC&pg=PA438&lpg=PA438&dq=%22sommelet+hauser%22+rearrangement+mechanism&source=web&ots=Kve7pICAT1&sig=Dt5xzAwfRzCT2B\_w71yiYKcp-F0



note most stable anion is not reactive.