

A Green Chemistry Module

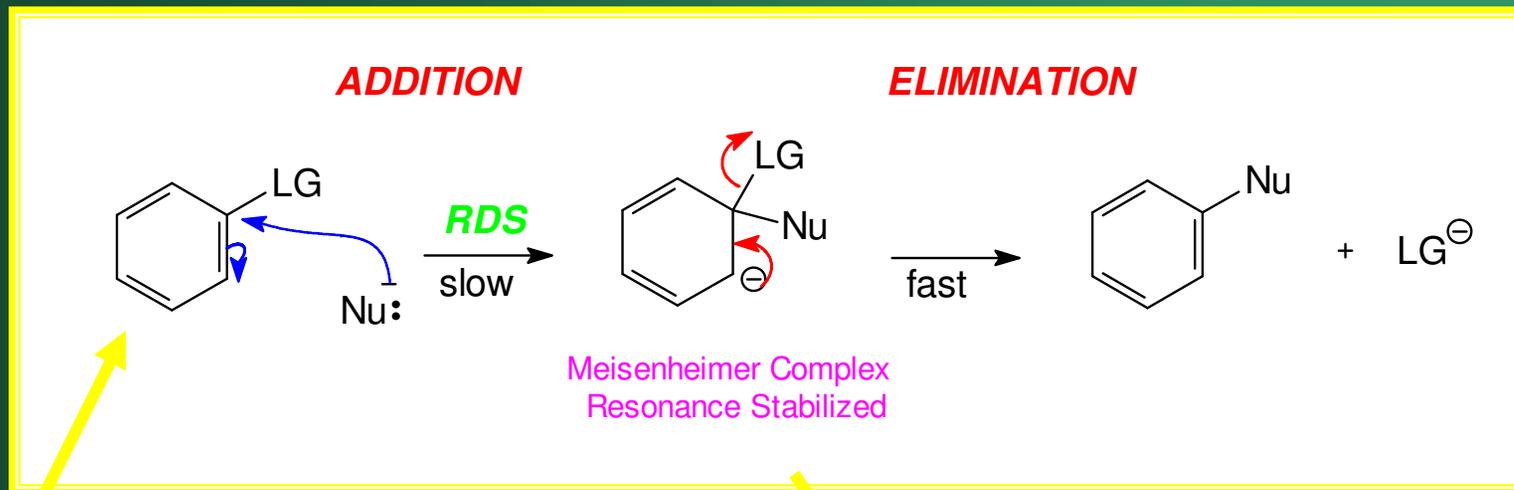


Nucleophilic Aromatic Substitution

Presidential Green Chemistry Challenge Award

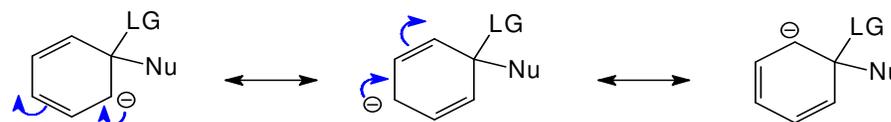
Elimination of Chlorine in the Synthesis of 4-Aminodiphenylamine.
A New Process Which Utilizes Nucleophilic Aromatic Substitution
for Hydrogen

S_NAr Mechanism - addition / elimination



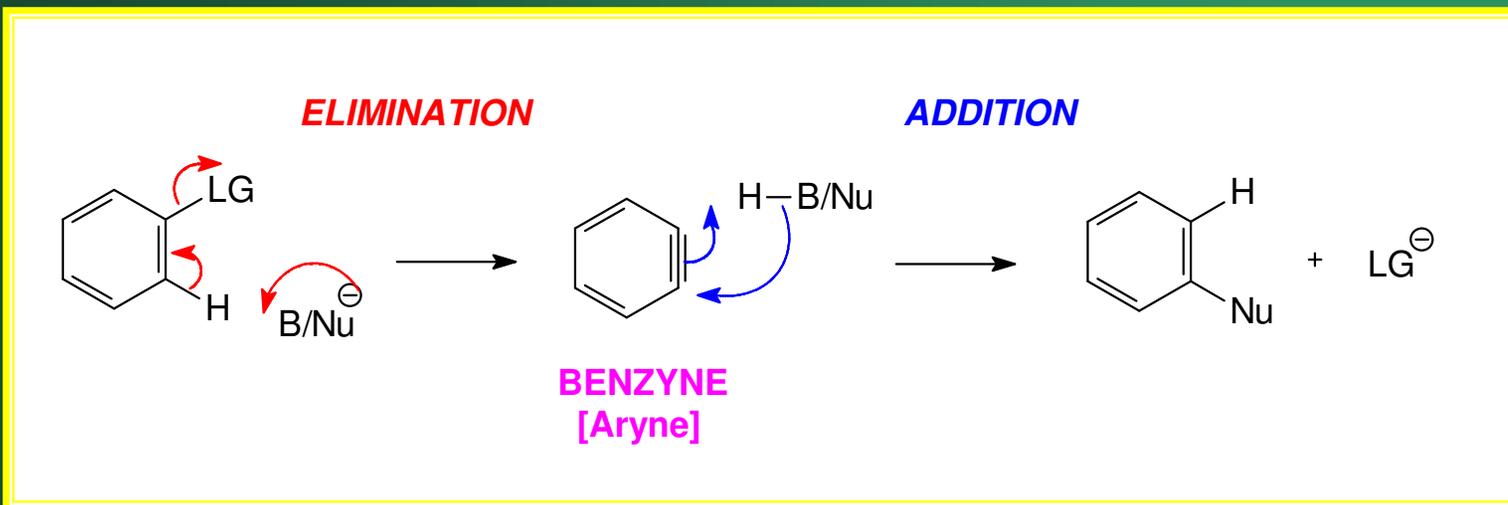
CF₃, CN, CHO, COR, COOH, Br, Cl, I

Common Activating Groups for NAS

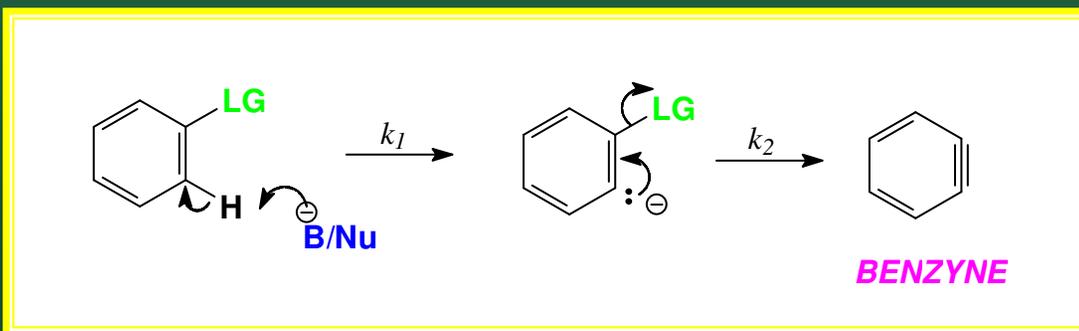


Resonance Stabilization of the Intermediate Anion
[The Meisenheimer Complex]

Benzyne Mechanism - elimination / addition

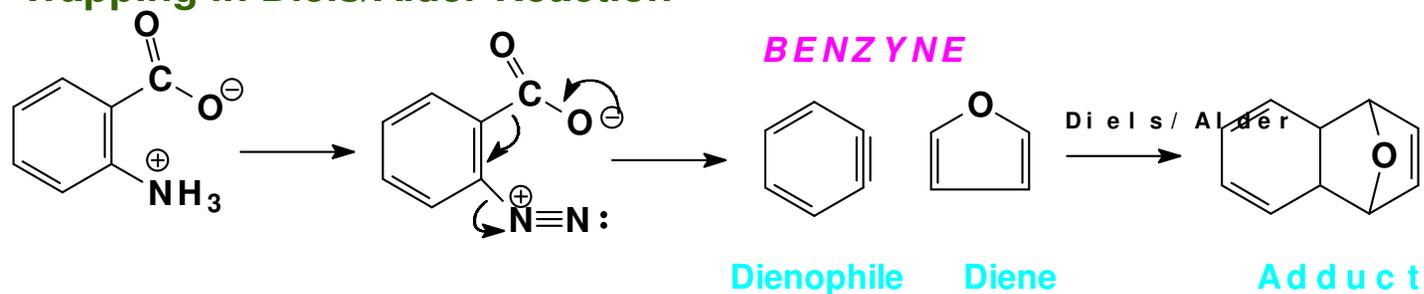


Step-wise formation of Benzyne

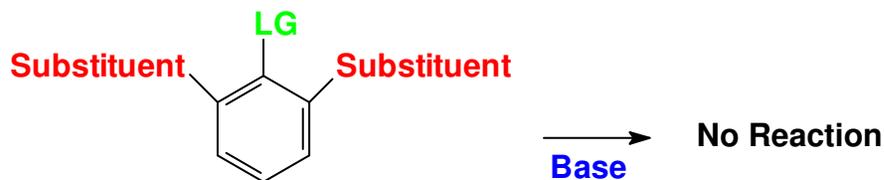


Evidence for the Benzyne Mechanism

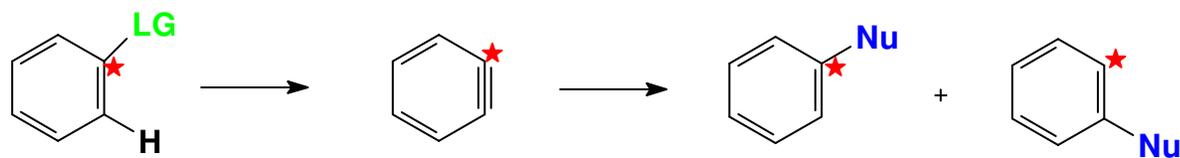
Trapping in Diels/Alder Reaction



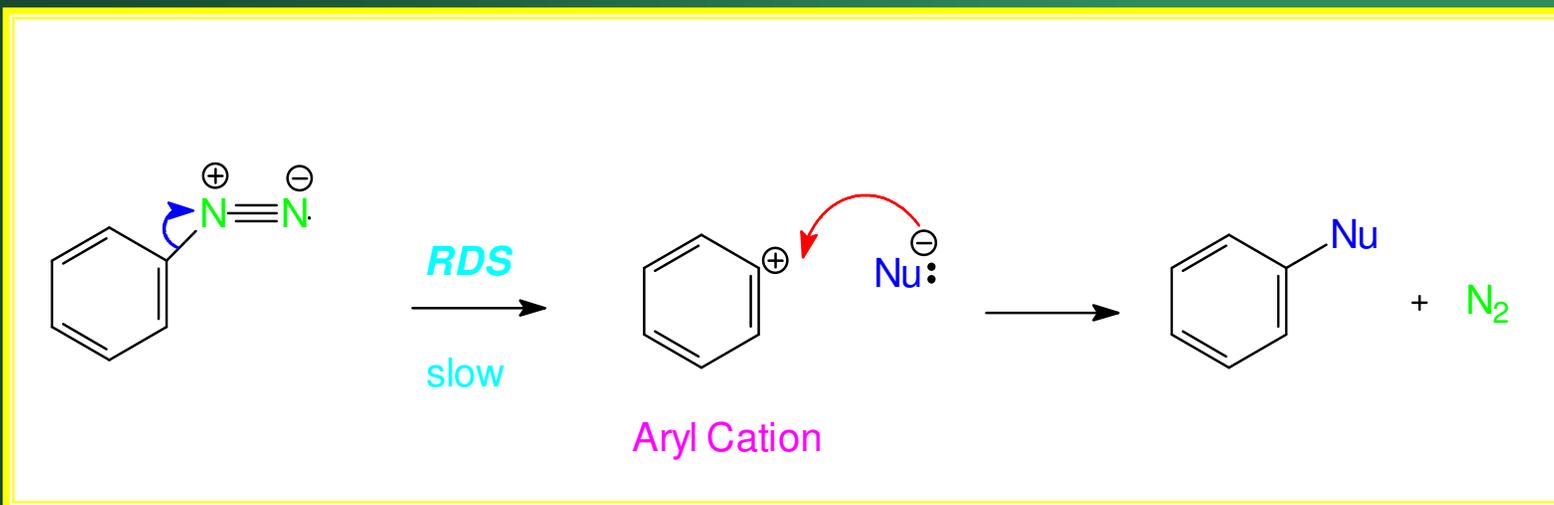
Substrate Modification – absence of α hydrogens



Isotopic Labeling

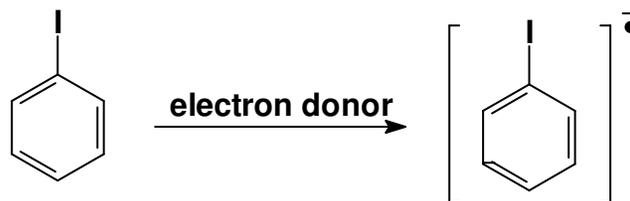


S_N1 Mechanism



$S_{NR}1$ Mechanism

Initiation

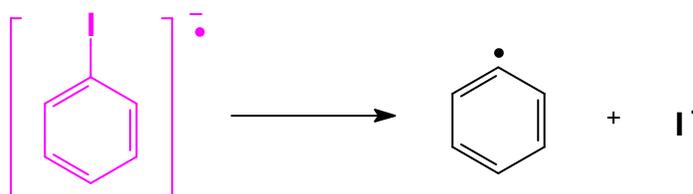


Chain

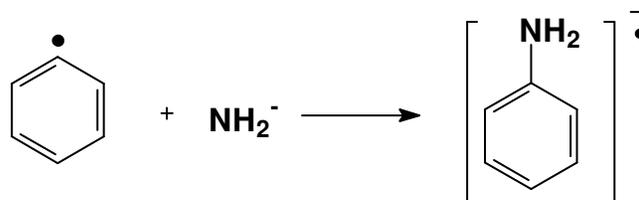
Propagation

Steps

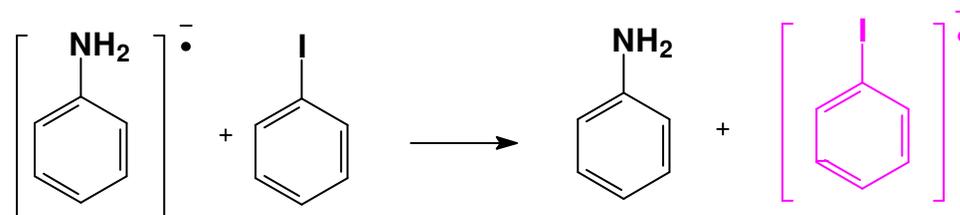
1



2

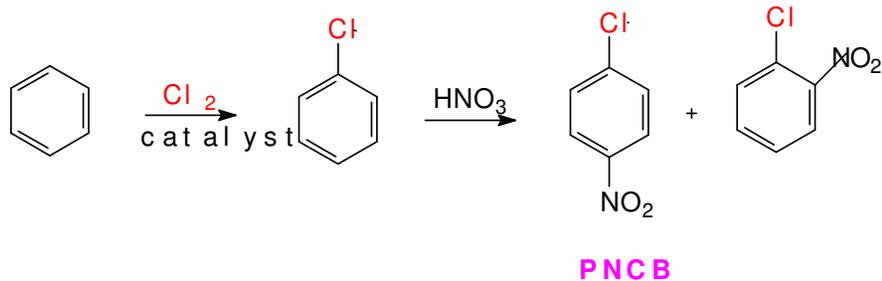


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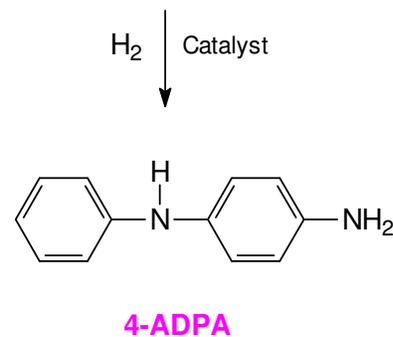
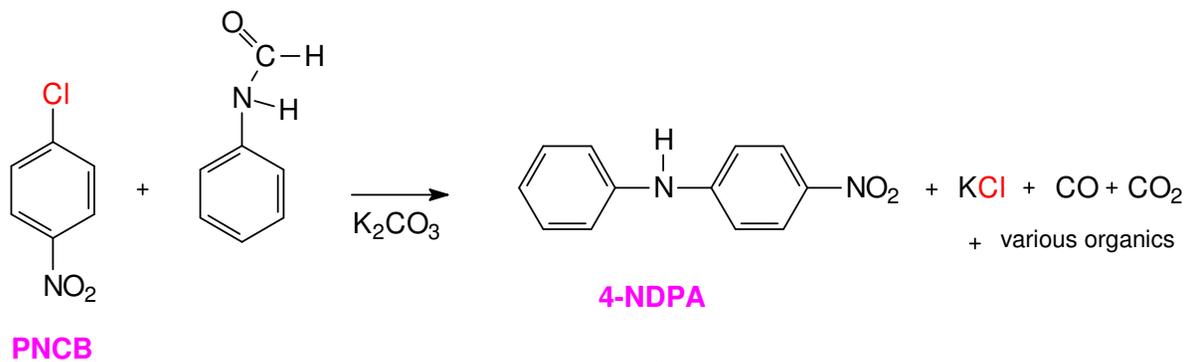


Brown Chemistry Route to 4-ADPA

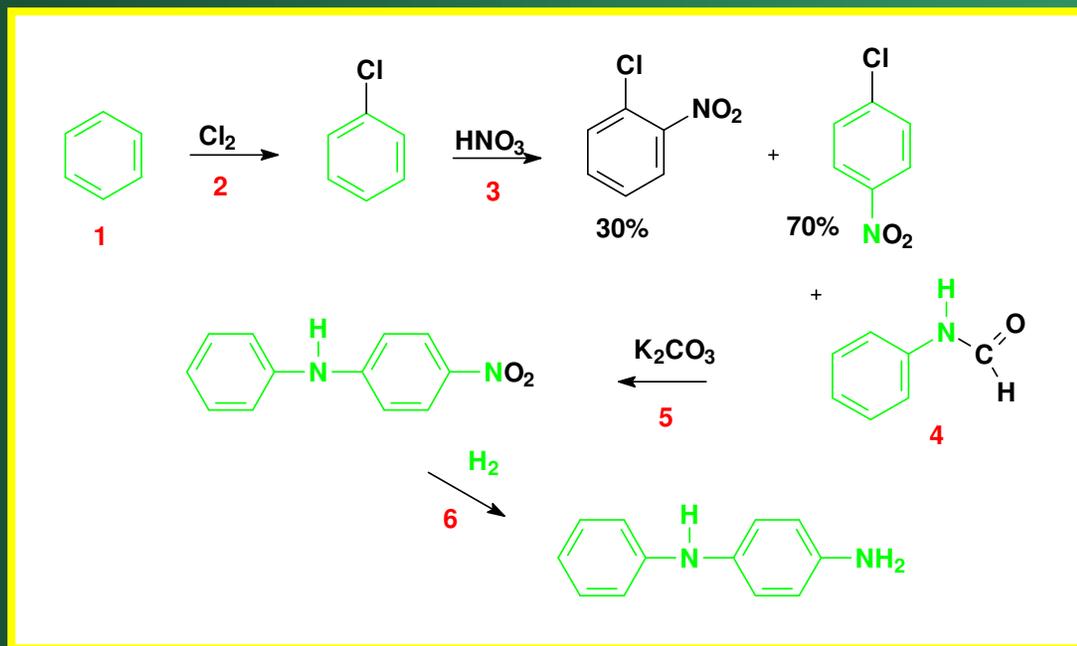
Electrophilic Aromatic Substitution



Nucleophilic Aromatic Substitution



Atom Economy of the Traditional Chemistry



Reagent formula	Reagent FW	Utilized Atoms	Wt	Unutilized Atoms	Wt
1 C_6H_6	78	6C, 4H	53	2 H	2
2 Cl_2	70	-----	0	2 Cl	70
3 HNO_3	63	1 N	14	1 H, 3 O	49
4 $\text{C}_7\text{H}_7\text{NO}$	121	6 C, 6 H, 1 N	92	1 C, 1 O, 1 H	29
5 K_2CO_3	98	-----	0	2 K, 1 C, 3 O	98
6 H_2	2	2 H	2	-----	0
TOTAL	432	12C, 12H, 2N	161	2C, 4H, 2C, 2K, 7O	248

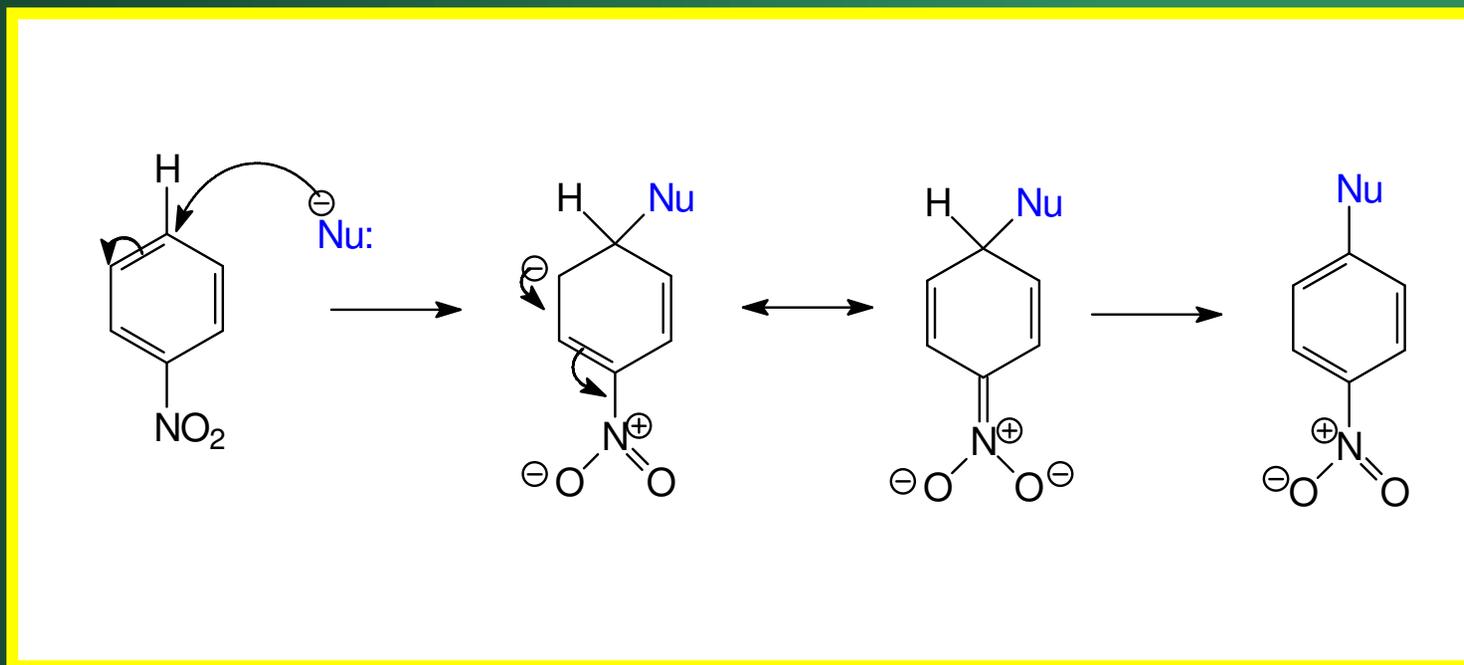
Brown Chemistry

Nucleophilic Aromatic Substitution for Chlorine

- *Large amount of chlorine*
storage
handling
- *Waste stream components*
inorganic salts
organics
- *Large amounts of water consumed*
- *Heavy metal catalyst*

Nucleophilic Aromatic Substitution for Hydrogen

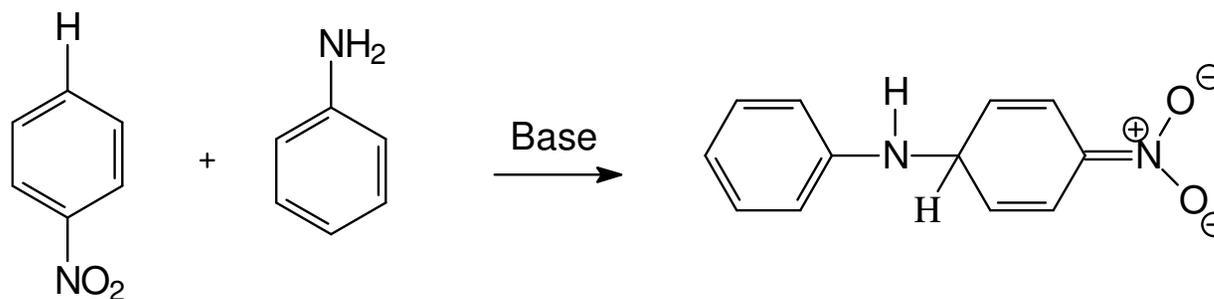
General Mechanism



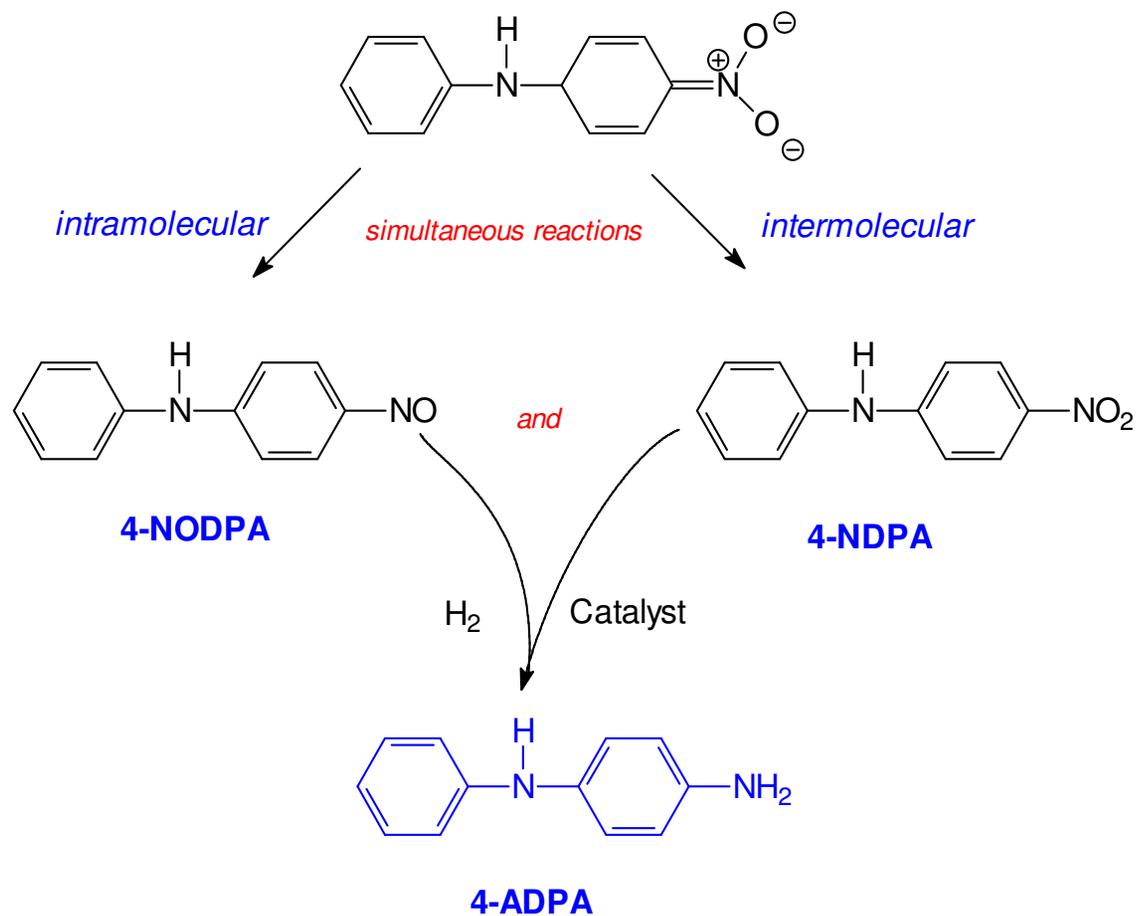
Flexsys Route to 4-ADPA

Base-Promoted Coupling Reaction

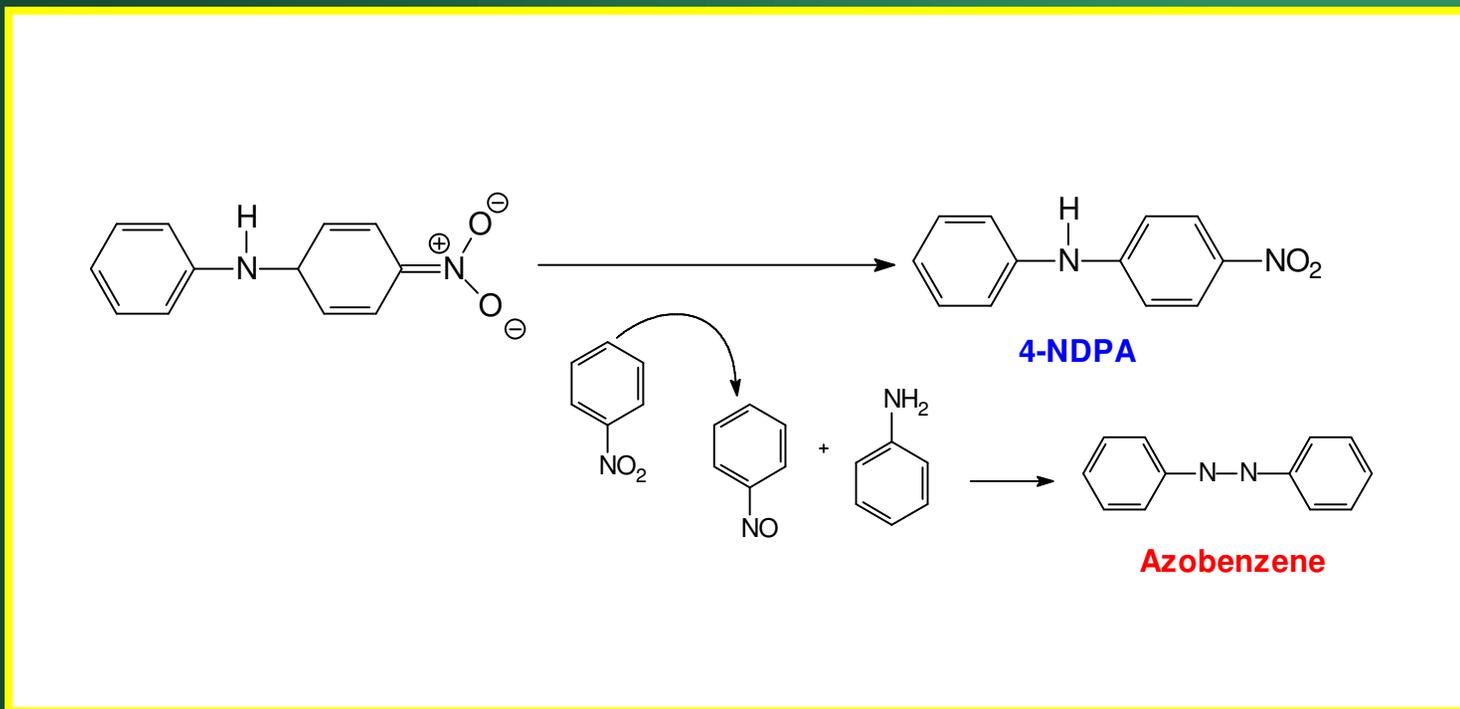
Base-Promoted Coupling Reaction



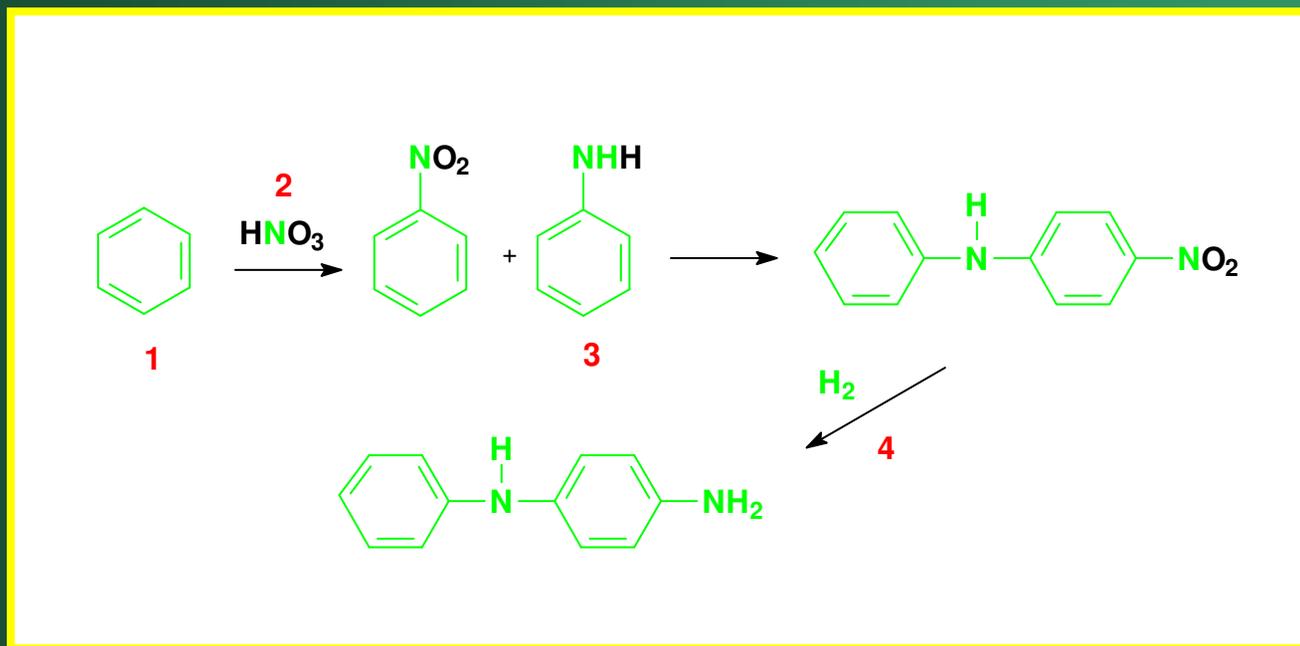
Flexsys - Anaerobic Oxidation to 4-NDPA



Flexsys - Intermolecular Oxidation Pathway



Atom Economy of the Flexsys Chemistry



Reagent Formula	Reagent FW	Utilized Atoms	Wt	Unutilized Atoms	Wt
1 C ₆ H ₆	78	6 C, 4 H	76	2 H	2
2 HNO ₃	63	1 N	14	1 H, 3 O	49
3 C ₆ H ₇ N	93	6 C, 6 H, N	92	1 H	1
4 H ₂	2	2 H	2	-----	0
TOTAL	236	12C, 12 h, 2 n	184	4H, 3O	52

Green Chemistry Advantages for Nucleophilic Aromatic Substitution for Hydrogen

- *Reduction in chemical waste generation*
 - elimination of
 - 74% of organic waste
 - 99% of inorganic waste
- *Eliminates use of chlorine*
- *Reduction in waste water*
 - more than 97% savings
- *Eliminates use of xylene*
 - a SARA chemical
- *Improves process safety*
 - lower reaction temperatures

