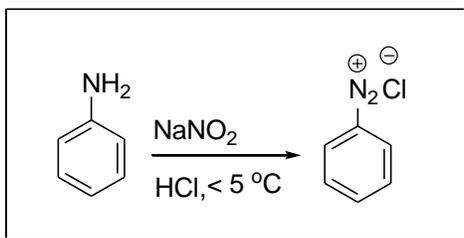


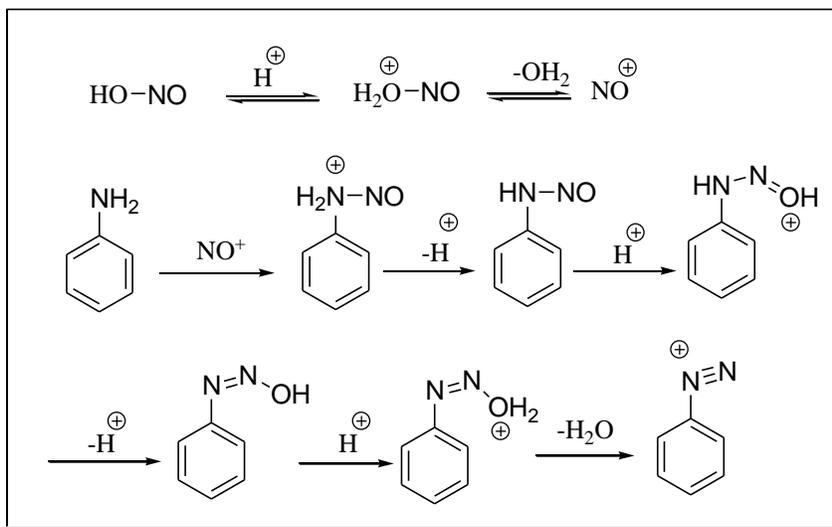
Lecture 16 Aromatic Diazonium Salts

7.1.1 The Formation of Diazonium Salts

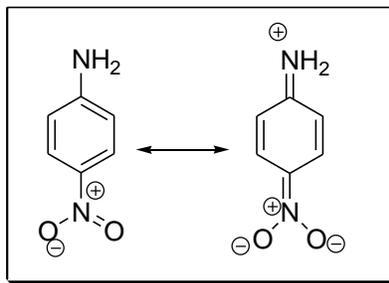
Addition of aqueous solution of NaNO_2 to a solution of amine hydrochloride in presence of excess of HCl which is cooled by an ice-bath such that the temperature of the reaction remains below 5°C diazotization of primary aromatic amine occurs.



Mechanism



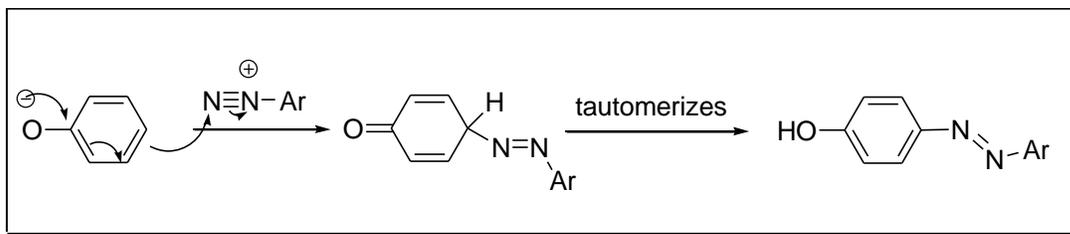
If electron withdrawing groups are attached to aromatic nucleus then the aromatic amines are difficult to diazotize because the nucleophilicity of the amino-nitrogen is reduced by the partial withdrawal of the unshared electron pair into the nucleus.



7.1.2 The Reaction of Diazonium Salts

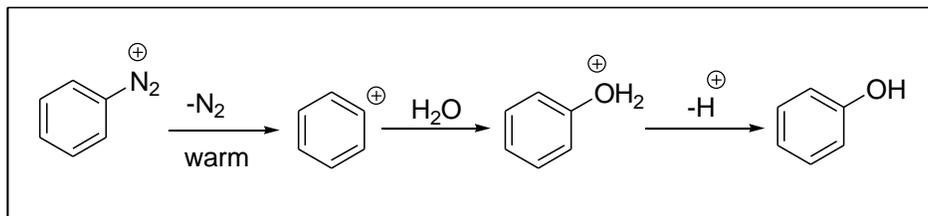
7.1.2.1 Reactions of nucleophiles at nitrogen

Nucleophiles react with diazonium ions to give covalent diazo-compounds. For example, phenol *via* phenoxide ion couples with diazonium salt at pH 9-10 to afford *para*-azophenols in good yield.



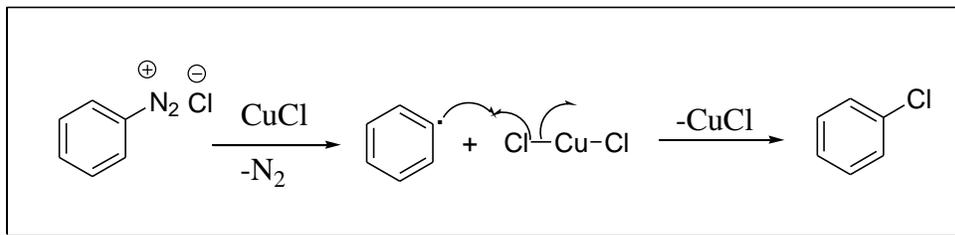
7.1.2.2 S_N1 Reaction

Diazonium salts decompose on warming into nitrogen and aryl cation which is highly reactive and could be attacked by any nucleophile in its vicinity.



7.1.2.3 One Electron Reductions

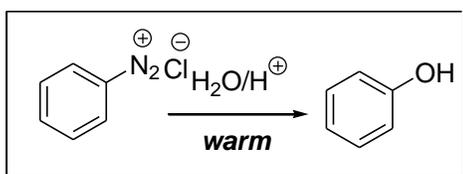
Diazonium ions could be reduced by single electron transfer to give an aryl radical and nitrogen. Copper(I) is frequently used for this purpose and the aryl radical is highly reactive capable of abstracting a ligand from the transition metal ion or a hydrogen atom from a covalent bond.



7.2 Reactions in which Nitrogen Eliminated

7.2.1 Replacement by Hydroxyl

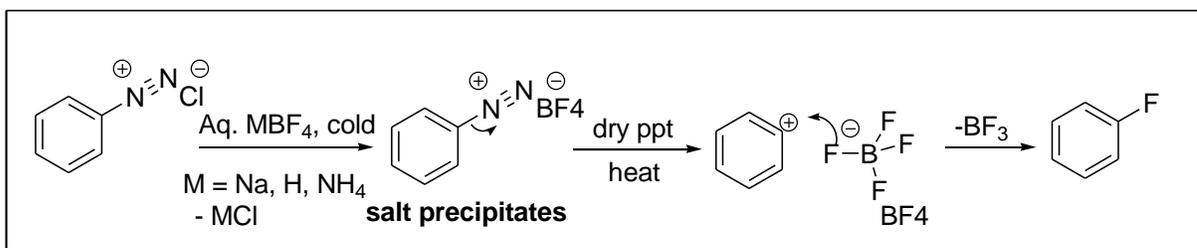
Diazonium salt on warming in water gives phenol via $\text{S}_{\text{N}}1$ mechanism. The reaction is generally performed in acidic solution to preserve phenol in its unionized form.

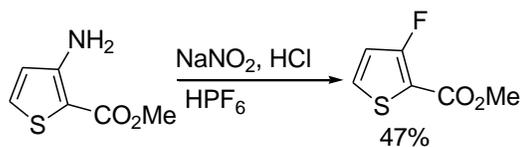


7.2.2 Replacement by Halogen

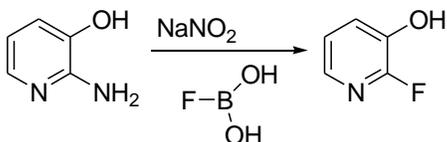
7.2.2.1 Schiemann Reaction

Treatment of an aqueous solution of diazonium salt with fluoroboric acid under cold conditions gives diazonium fluoroborate as precipitate, which could be dried and gently heated to afford the fluorene by decomposition. The reaction involves $\text{S}_{\text{N}}1$ mechanism.

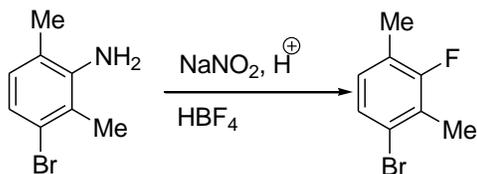


Examples:

A. Kiryanov, A. Seed, P. Sampson, *Tetrahedron Lett.* **2001**, 42, 8797.



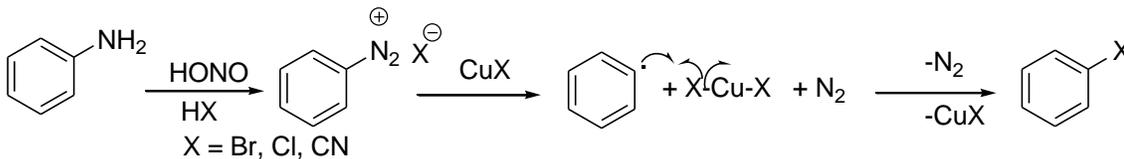
F. Dolle, L. Dolei, H. Valette, F. Hinnen, F. Vaufrey, H. Guenther, C. Fuseasu, C. Coulon, M. Buttalender, C. Crouzel, *J. Med. Chem.* **1999**, 42, 2251.



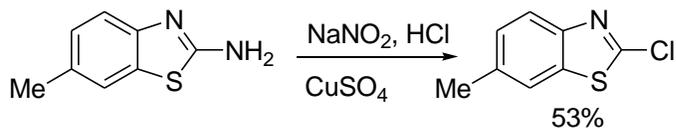
H. Hart, J. F. Janssen, *J. Org. Chem.* **1970**, 35, 3637.

7.2.2.2 Sandmeyer Reaction

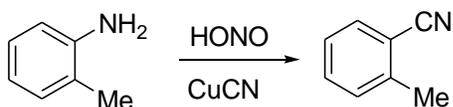
This method provides an effective route for the preparation of aromatic bromides and chlorides. Addition of cold aqueous solution of diazonium chloride to a solution of CuCl in HCl medium gives a sparingly soluble complex which is separated and heated to give aryl chloride or bromide by decomposition.



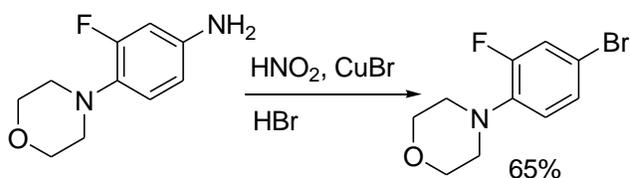
Examples:



N. Zou, J.-F. Liu, B. Jiang, *J. Combin. Chem.* **2003**, 5, 754.



H. T. Clarke, R. R. Reed, *Org. Synth.* 1941, 1, 514.



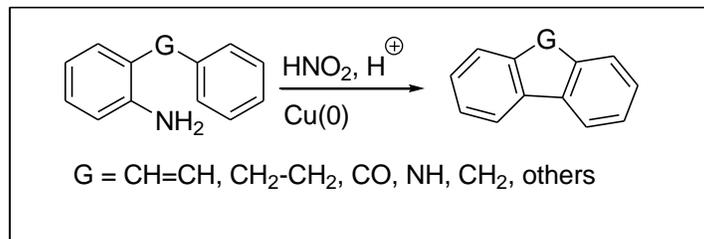
B. Mallesham, B. M. Rajesh, P. R. Reddy, D. Srinivas, S. Trehan, *Org. Lett.* **2003**, 5, 7963.

7.2.3 Replacement by Aromatic Carbon

A number of methods lead to arylation of aromatic carbon by diazonium salts.

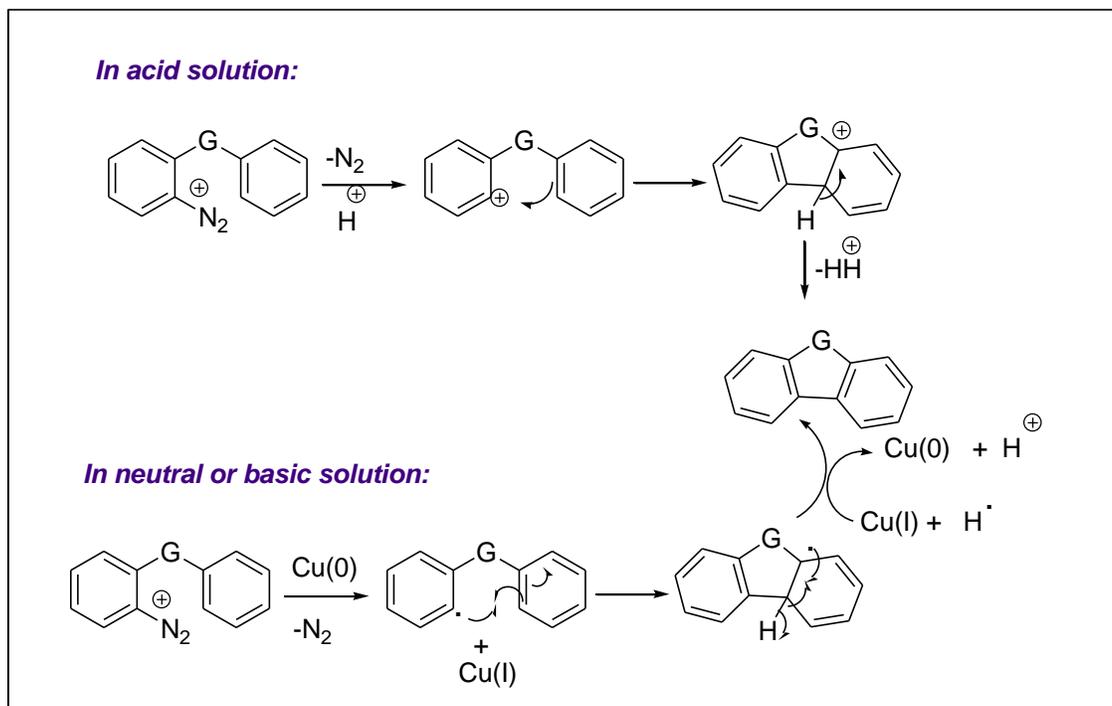
7.2.3.1 Pschorr Reaction

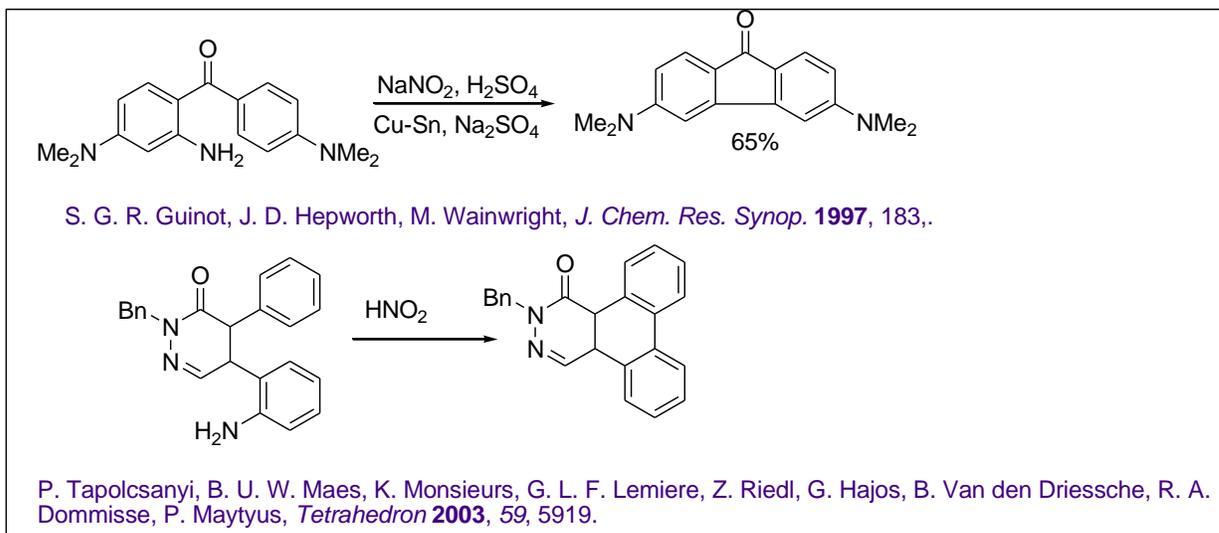
This reaction describes the synthesis of phenanthrene and its derivatives via diazotation followed by intramolecular cyclization using copper powder.



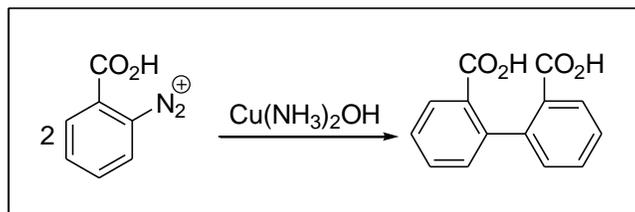
Mechanism

The reactive intermediate depends on the reaction conditions. Under acidic conditions, the diazonium salt is believed to decompose into aryl cation and nitrogen. The aryl cation is highly reactive and attacked by the aryl ring that leads to cyclization. On the other hand, under neutral and basic conditions, the diazonium salt is reduced by single electron transfer to give aryl radical which proceeds reaction intramolecularly with benzene ring to give the cyclized product.



Examples:**7.2.3.2 Reduction by Copper(I) Ammonium Ion**

Diazotized anthranilic acid with copper(I) ammonium hydroxide gives diphenic acid in 90% yield.



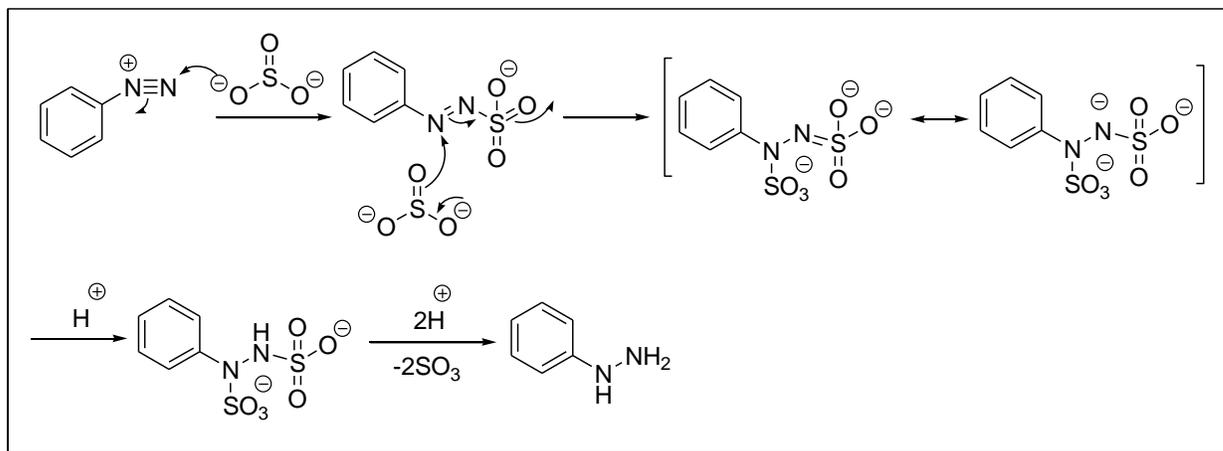
The process probably takes place via one-electron reduction of the diazonium ion followed by dimerization of the resulting aryl radicals.

7.3 Reactions in which Nitrogen is Retained

The reaction of the terminal nitrogen of a diazonium salt with nucleophile affords a covalent azo-compound.

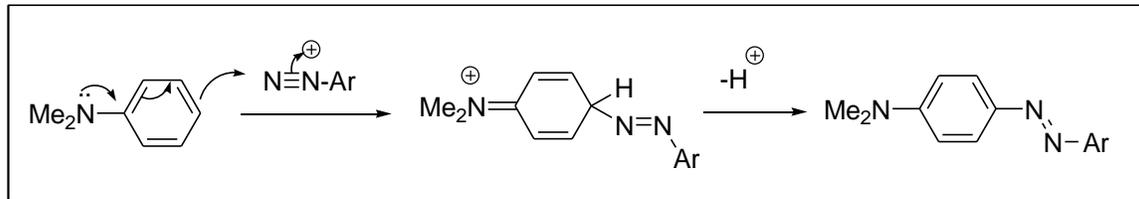
7.3.1 Reduction to Arylhydrazones

The reduction of aromatic diazonium salts can be accomplished with sodium sulfite or SnCl_2 or electrolysis to provide arylhydrazines. In case of sodium sulfite based reduction, the diazonium ion with a sulfite anion may give a covalent azo-sulfite that, having a double bond conjugated to an electron-accepting group, may add to a second nucleophilic sulfite ion which on hydrolysis provides the hydrazine.

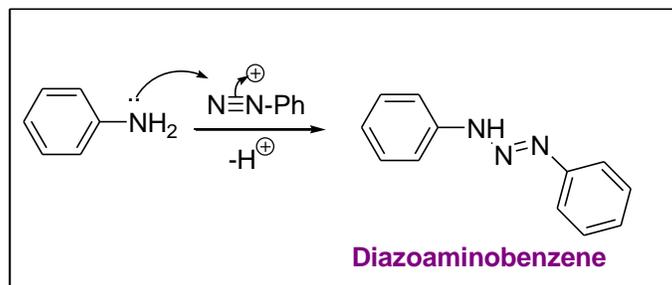


7.3.2 Coupling Reactions

Diazonium ions are weak electrophiles, however, they undergo coupling with activated aromatic nuclei such as aryl amines, phenols and aromatic heterocyclic compounds. For example, N,N-dimethylaniline reacts with diazonium ion almost at the *para*-position. However, the careful control of the pH of the reaction medium is necessary for the success of the process.



In case of primary and secondary aromatic amines, the reaction preferentially takes place at the nitrogen atoms of the diazonium ions. For example, aniline adds to the aromatic diazonium salt to give diazoaminobenzene.

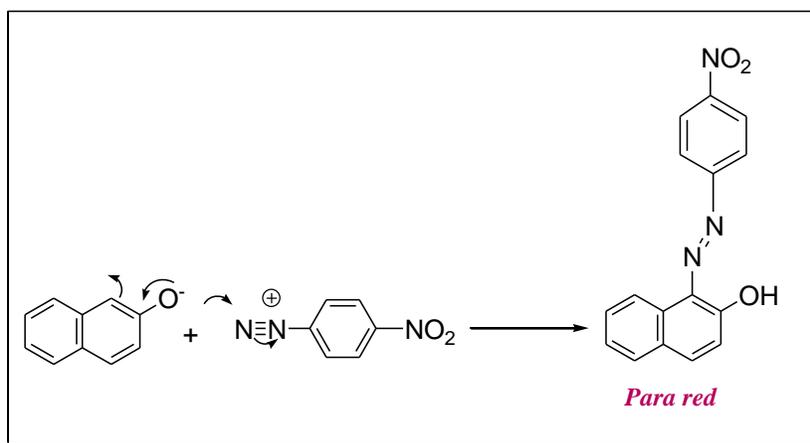


7.4 The Synthetic Value of Diazo-Coupling

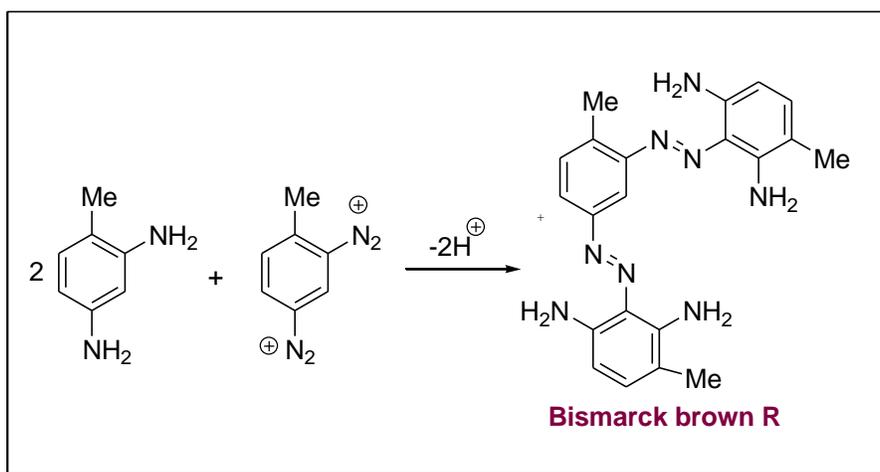
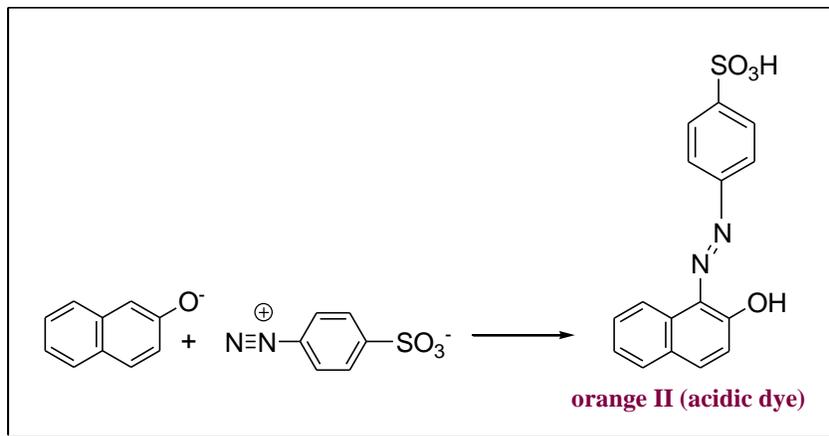
7.4.1 Dye-stuffs

Aromatic azo-compounds are coloured. Several of those compounds synthesized by the diazo-coupling are employed as dye-stuffs. These compounds can be classified into three groups.

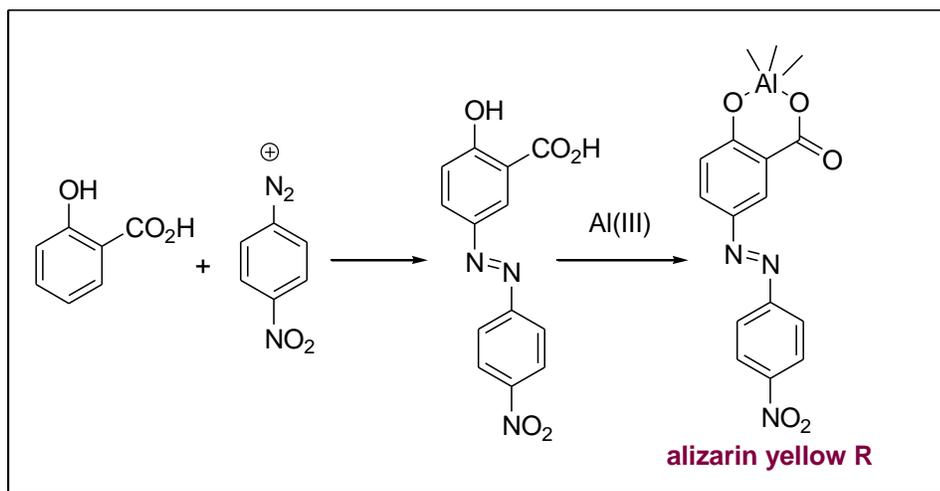
- First group of azo-compounds are neutral which are used as *azoic combination* (or ingrain) dyes. An example is *para red* which is prepared by coupling of 2-naphthol with *p*-nitrobenzenediazonium salt.



- The second group of azo-compounds possess either a sulfonic acid group or an amino group which are generally adsorbed directly on the fiber from aqueous solution. Examples are orange II (an acidic dye) and Bismarck brown R (a basic dye).

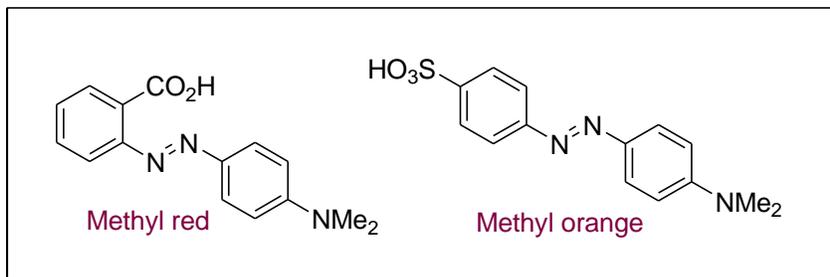


- Azo-compounds that contain chelating groups to bind with a metal ions such as Al(III) are used a mordant dyes. An example is alizarin yellow R, which contains phenolic and carboxyl chelating groups.



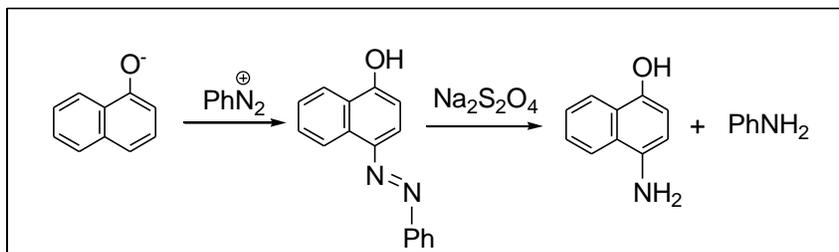
7.4.2 Indicators

Azo-compounds that contain both an acidic and a basic group can be utilized as indicators since the colours of the conjugate acid and the conjugate base are different. Examples are methyl orange and methyl red which are prepared by coupling of dimethylaniline with diazotized sulfanilic acid and diazotized anthranilic acid, respectively.



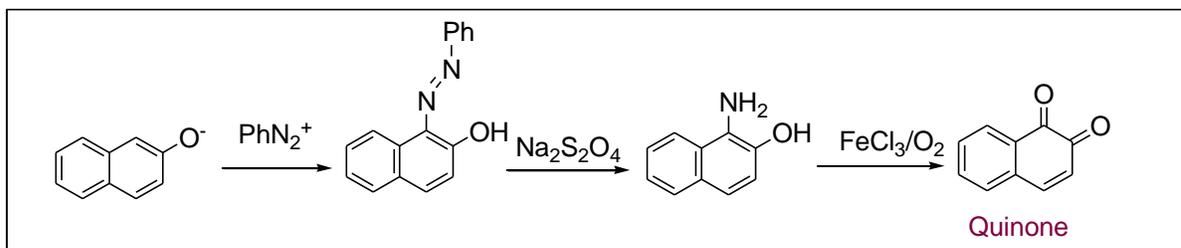
7.4.3 Synthesis of Amines

Azo-compounds are susceptible to hydrogenolysis to give amines. For example, the coupling of 1-naphthol with benzenediazonium chloride gives azo-compound which could be reduced to 4-amino-1-naphthol in the presence of dithionite.



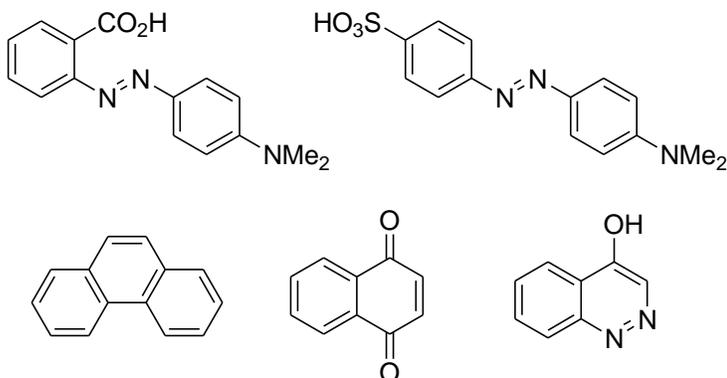
7.4.4 Synthesis of Quinones

The *ortho* and *para* diamines and aminophenols readily oxidize to give quinones. Both classes of compounds can be readily prepared by diazo-coupling followed by reduction.

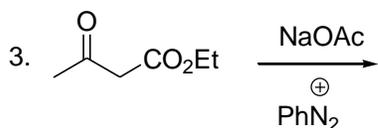
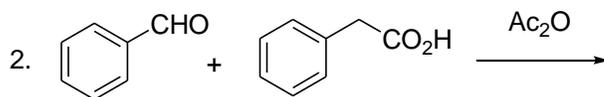
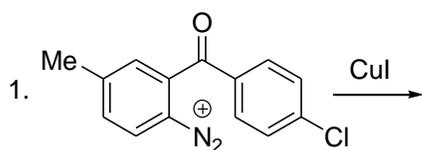


Problems:

A. How would you obtain the following compounds?



B. Complete the following reactions.



Text Books:

R.O.C. Norman and C. M. Coxon, *Principles of Organic Synthesis*, CRC Press, New York, 2009.

B. P. Mundy, M. G. Ellerd, F. G. Favalaro Jr, *Name Reactions and Reagents in Organic Synthesis*, Wiley Interscience, New Jersey, 2005.