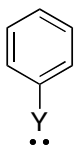
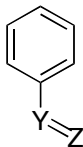


Review from last class

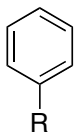
Aromatic compounds with a heteroatom attached to it with a lone pair of electrons is considered a resonance donating system and will direct the reaction to the ortho or para positions.



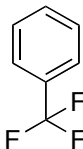
Aromatic compounds with a conjugated double bond conjugated to the aromatic ring are generally resonance withdrawing (especially if Z is electronegative) and will direct aromatic substitution to the meta position.



Aromatic compounds with an alkyl chain are considered inductively donating and will direct substitution to the ortho or para positions.



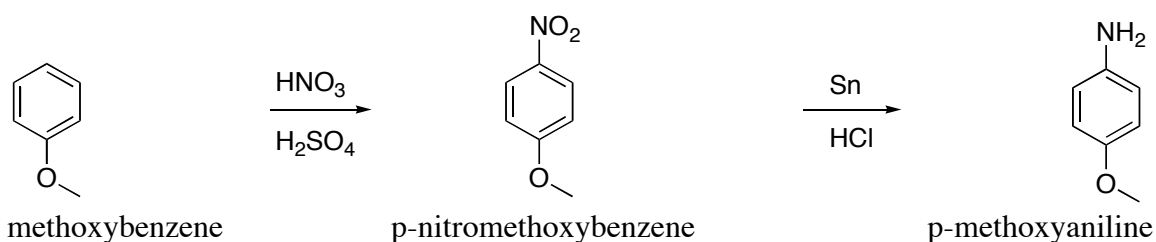
Aromatic compounds that have an electron withdrawing group attached but that do not fall into the above categories (eg. CF_3) are inductively withdrawing and direct substitution to the meta position.



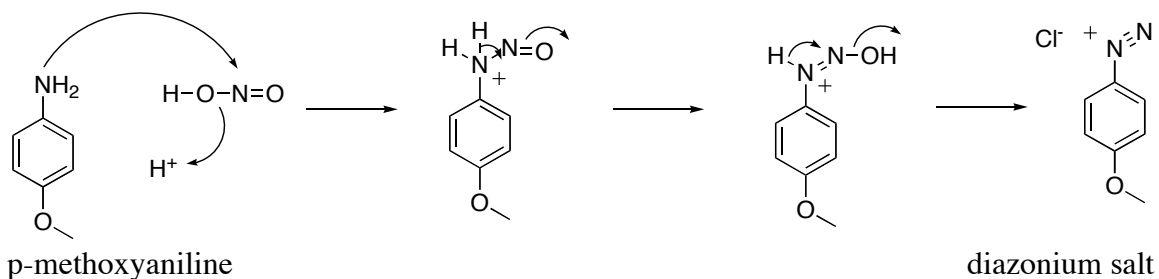
Reduction of Aryl Nitro Compounds to Anilines (from last class)

Examples

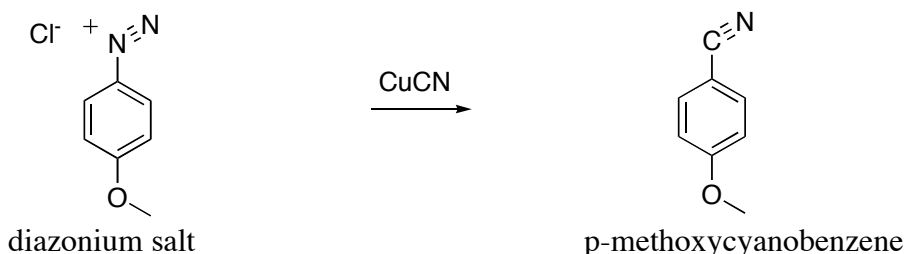
For example, 4-methoxyaniline can be formed from methoxybenzene (anisole) by nitration of the aromatic ring followed by reduction of the nitro group. The first step involves the nitration of methoxybenzene to form ortho-nitromethoxybenzene and para-nitromethoxybenzene. Shown is the formation of the para derivative. The ortho derivative forms analogously. The next step uses tin under acidic conditions to reduce the nitro group to an amine and form 4-methoxyaniline.



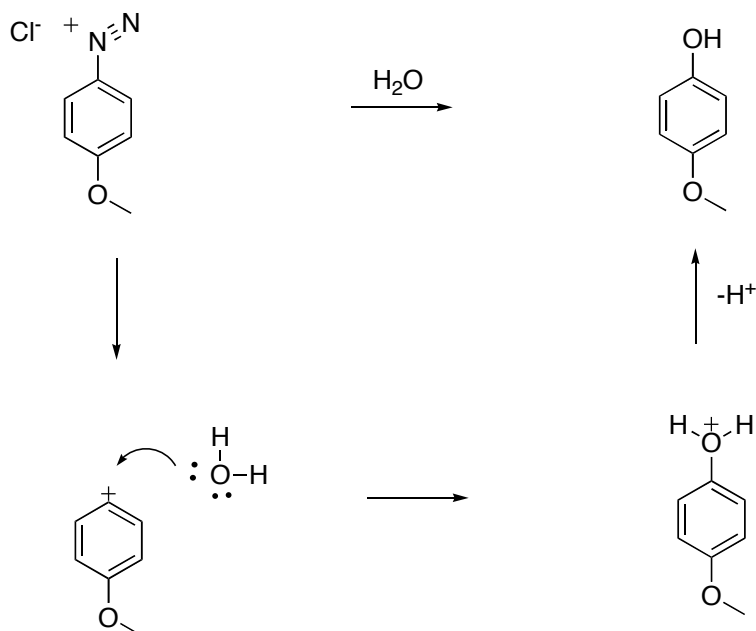
The aniline can then be reacted with nitrous acid to give the explosive diazonium salt. Nitrous acid is formed from the addition of sodium nitrite (NaNO_2) and hydrochloric acid (HCl). In a very abbreviated mechanism, first step of the mechanism is attack of the aniline on nitrous acid to form the new nitrogen-nitrogen bond. This is followed by deprotonation and reprotonation to make the nitrogen-nitrogen double bond. The loss of water then forms the diazonium species. The chloride counter ion is from the initial formation of nitrous acid with HCl .



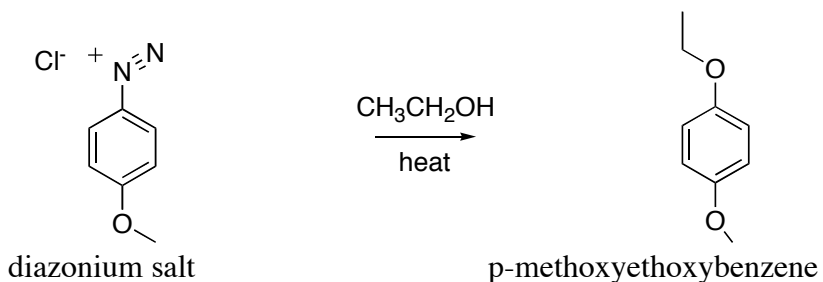
Treatment of the diazonium salt with cuprous cyanide (CuCN) yields the aryl nitrile, ArCN . Nitrogen gas is the leaving group. This reaction is useful because it allows replacement of the nitrogen substituent with by a carbon substituent. For example, treatment of the p-methoxy diazonium salt with CuCN forms p-methoxycyanobenzene (4-methoxybenzonitrile, 4-cyanoanisole).



The diazonium salt can also be replaced by a hydroxyl group to form phenols. This reaction is especially useful because few other general methods exist for introducing an -OH group onto an aromatic ring. For example, treatment of the p-methoxy diazonium salt with a hot water yields p-methoxyphenol. The mechanism of this reaction can be visualized as formation of the phenyl cation by loss of nitrogen gas (N_2). The lone pair of electrons on the water attacks the carbocation followed by deprotonation to yield p-methoxyphenol.

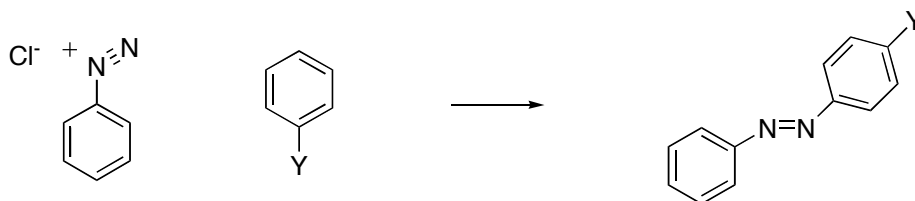


The diazonium salt can also be replaced by an ether functionality by addition of alcohols. For example, treatment of the p-methoxy diazonium salt with a hot ethanol forms p-methoxyethoxybenzene. The reaction mechanism is analogous to the formation of the phenol above.

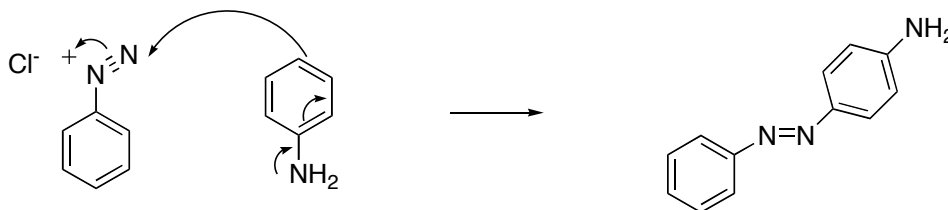


Diazonium Coupling

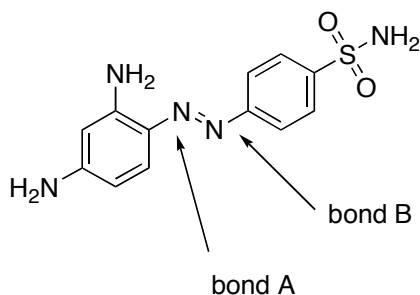
Diazonium salts undergo a coupling reaction with activated aromatic rings to yield very highly colored azo compounds with the general formula Ar-N=N-Ar as shown below. These azo coupled products are widely used as dyes because their extended conjugated pi (π) electron systems cause them to absorb in the visible region of the electromagnetic spectrum. As shown below, Y must be OH, NH_2 or NHR or the reaction will generally not work.



Diazonium couplings are typically electrophilic aromatic substitutions in which the positively charged diazonium ion is the electrophile that reacts with the electron rich ring of a phenol or arylamine. Diazonium coupling often takes place at the para position, although ortho attack can take place if the para position is blocked. An example is the formation of an azo aniline derivative. Attack of the aniline from para position on the diazonium salt, followed by loss of a proton forms the product.

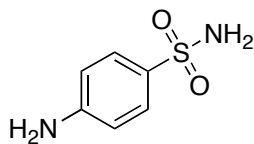


Aromatic azo compounds are valuable intermediates in the preparation of dyes and pharmaceuticals. For example, the sulfa drugs, such as Protosil, were the first useful antibiotics known and were found to have a broad range spectrum. Protosil is prepared commercially by a process that uses a diazonium ion. The diazonium coupling requires the use of a diazonium salt and a highly activated aromatic compound. For this reason, bond A (not bond B) is the bond formed in the diazonium coupling reaction. The aniline is highly reactive and would make a good coupling partner to the diazonium salt.

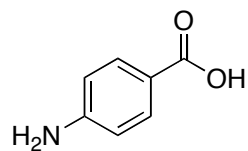


Protosil

Protosil is an effective antibacterial agent because the human body readily converts it to sulfanilamide, which is the active drug. Sulfanilamide resembles the structure of para-aminobenzoic acid, which bacteria use to make folic acid. The bacteria mistakenly tries to use sulfanilamide (an enzyme inhibitor) and eventually dies.



sulfanilamide

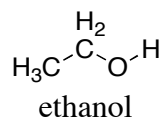


p-aminobenzoic acid

Review Topics

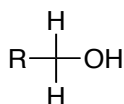
Nomenclature and Properties of Alcohols and Ethers

Alcohols are compounds that have a hydroxyl group (-OH) bonded to a carbon atom (but not a carbonyl C=O). Alcohols can be thought of as organic derivatives of water in which one of the hydrogens is replaced by an organic group: H-O-H versus R-O-H. Alcohols occur widely in nature and have many industrial and pharmaceutical applications. Ethanol is one of the simplest alcohols, finding use as a fuel additive, an industrial solvent, and key ingredient in many beverages (beer, wine etc).

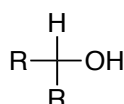


Naming Alcohols

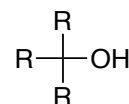
Alcohols are classified as primary (1°), secondary (2°), or tertiary (3°), depending on the number of organic groups bonded to the hydroxyl bearing carbon.



primary alcohol (1°)



secondary alcohol(2°)

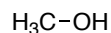


tertiary alcohol(3°)

Simple alcohols are named using the IUPAC system as derivatives of the parent alkane, using the suffix *ol*:

- 1) Select the longest carbon chain containing the alcohol, and derive the parent name by replacing the *-e* ending of the corresponding alkane with *-ol*.
- 2) Number the alkane chain, beginning at the end nearer the hydroxyl group.
- 3) Number the substituents according to their position on the chain.

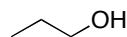
For example:



methanol



ethanol

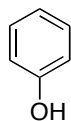
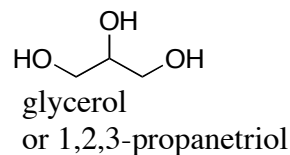
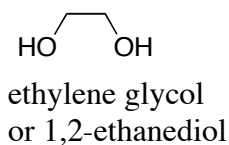


n-propanol
or 1-propanol

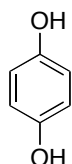


2-propanol
or isopropanol

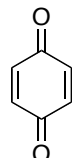
Some simple and widely occurring alcohols have common names that are accepted by IUPAC. For example:



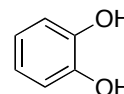
phenol



4-hydroxyphenol
or hydroquinone

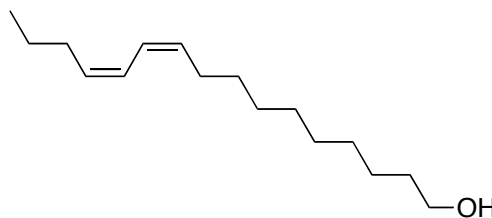


quinone



catechol

A more difficult example is the naming of the sex pheromone from the silk worm moth shown below.

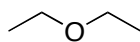


Z,Z-hexadeca-10,12-dien-1-ol.

The first step in naming this compound is to find the parent name of the longest chain. In this case it is 16 carbons long and therefore is a hexadecane. You then drop the *-e* ending, replacing it with *-ol* for the name to become hexadecane-1-ol. There are also two *cis* double bonds present in the molecule at positions 10 and 12. This information allows the compound to be named a 10,12-diene. Putting the overall name together then gives Z,Z-hexadeca-10,12-dien-1-ol.

Ethers

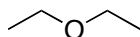
An ether is a substance that has two organic groups bonded to the same oxygen atom, R-O-R', where R and R' can be the same or different, but cannot be carbonyl (C=O) directly attached. The organic groups may be alkyl, aryl, or vinylic, and the oxygen atom can either be an open chain or a ring. Perhaps the most well known ether is diethyl ether, a familiar substance that has been used medically as an anesthetic, and is used industrially as a solvent.



diethyl ether

Naming Ethers

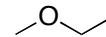
Two systems for naming ethers are allowed by IUPAC rules. Simple ethers with no functional groups are named by identifying the two organic substituents and adding the word *ether* as in the below examples.



diethyl ether
or ethyl ether
or ether

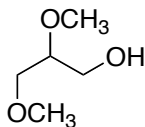


dimethyl ether
or methyl ether



ethyl methyl ether

If other functional groups are present, the ether part is considered to be an alkoxy substituent. For example, the parent name for the below structure is an alcohol.



2,3-dimethoxypropan-1-ol

The first step in naming this compound is to find the parent name of the longest chain. In this case it is 3 carbons long and therefore is a propane. You then drop the *-e* ending, replacing it with *-ol* for the name to become propan-1-ol. There are two methoxy groups in the molecule at positions 2 and 3. The name of this compound is 2,3-dimethoxypropan-1-ol.