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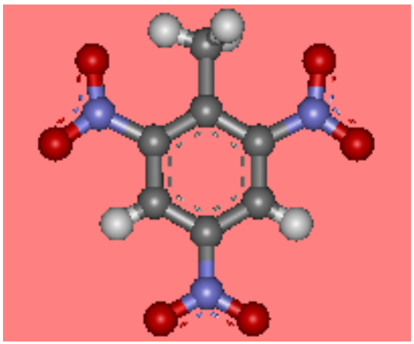


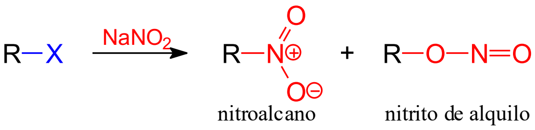
Nitrogen compounds

1. NITRO COMPOUNDS

1.1. SYNTHESIS

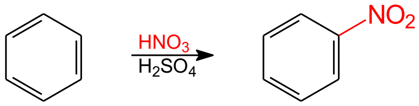
1.1.1. Bimolecular nucleophilic substitution (SN2)

The use of sodium nitrite as a nucleophile against alkyl halides forms mostly nitro compounds and alkyl nitrites as side products.



1.1.2. Aromatic Electrophilic Substitution (SEAr)

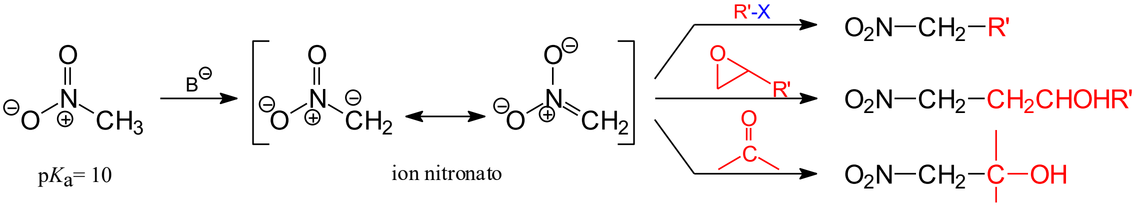
Benzene (and most aromatic compounds) can be nitrated with a mixture of concentrated nitric acid and sulfuric acid. Nitric acid alone can be used for reactive aromatic compounds, or in water, acetic acid or acetic anhydride.



1.2. REACTIVITY

1.2.1. ALKYLATION AND HYDROXYALKYLATION

Nitroalkanes can be rented and hydroxyalkylated by a process similar to that of aldehydes and ketones. Nitroalkanes dehydronate relatively easily to form nitronate ions (analogous to enolate ions), which react with haloalkanes, epoxides and carbonyls:



1.2.2. Reduction

Nitro compounds are easily reduced to primary amines with many reducers. Since the most affordable nitro compounds are aromatics, this reaction is often used to synthesize anilines.

$$R{-}NO_2 \xrightarrow{[H]} R{-}NH_2$$

[H] = H2/cat., M/HCl M = Sn, Zn, Fe.

2. ISOCYANATES

2.1. SYNTHESIS

2.1.1. Bimolecular nucleophilic substitution (SN2)

The alkylation of the cyanate ion undergoes almost exclusively N-alkylation giving alkyl isocyanates.

$$R{-}X \xrightarrow{NaNCO} R{-}N{=}C{=}O + R{-}O{-}C{\equiv}N$$

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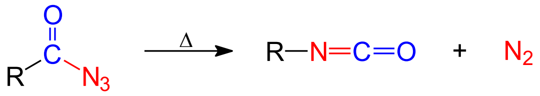
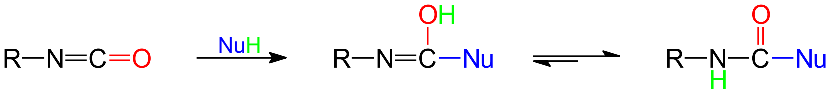
2.1.2. Curtius rearrangement

Pyrolysis of acyl azides produces isocyanates in good yields. The reaction occurs through a rearrangement called *the Curtius rearrangement* (see section **18.3.6**.).



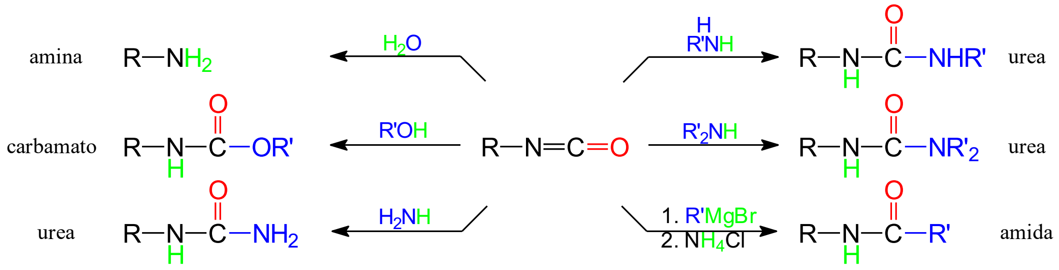
2.2. REACTIVITY

Isocyanates are highly reactive species as electrophiles and readily give nucleophilic addition reactions.



$$R{-}N{=}C{=}O \xrightarrow{NuH} R{-}N{=}\overset{OH}{C}{-}Nu \rightleftharpoons R{-}\underset{H}{N}{-}\overset{O}{\overset{\|}{C}}{-}Nu$$

Primary amines, carbamates, ureas and amides can be obtained from alkyl isocyanates:

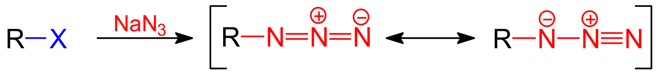


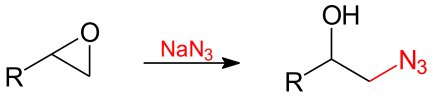
AZIDES

3.1. SYNTHESIS

3.1.1. Bimolecular nucleophilic substitution (SN2)

The reaction of alkyl halides or sulfonates with alkaline azides, usually NaN_3, is a simple method to form alkyl azides in good yields. If the reaction is carried out with epoxides, the products are β-azido alcohols:

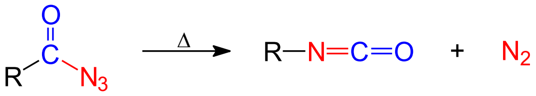




3.2. REACTIVITY

3.2.1. Curtius rearrangement

Azides undergo a rearrangement with loss of dinitrogen when heated. The only rearrangement that is synthetically useful of acil azides is the Curtius rearrangement.



3.2.2. Reduction

The reduction of alkyl azides produces primary amines without contamination of secondary or tertiary amines.

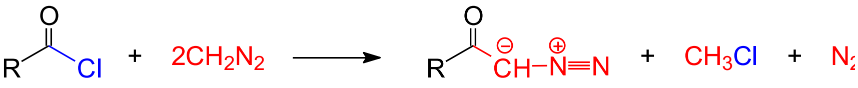
$$R{-}N_3 \xrightarrow{[H]} R{-}NH_2 + N_2$$

[H] = H2/cat., LiAlH4.

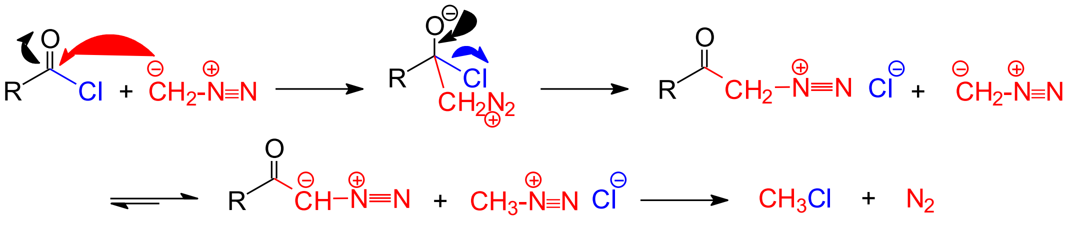
4. DIAZO COMPOUNDS

4.1. SYNTHESIS OF DIAZO KETONES

If an acyl chloride is treated with two equivalents of diazomethane, or one equivalent and one equivalent of a base, it is transformed into a diazo ketone.



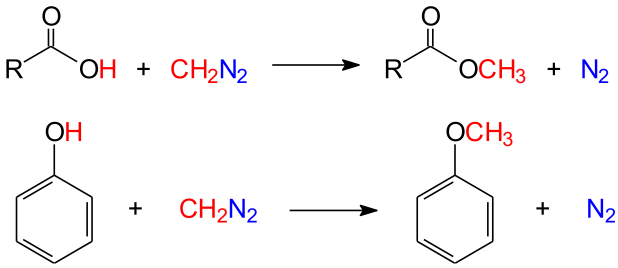
This reaction begins with the substitution of chloride for the diazomethane molecule by an addition-elimination mechanism. The resulting product has an acidity similar to that of acetic acid and undergoes dehydronation, by another diazomethane molecule or by the base, to form a diazo ketone:



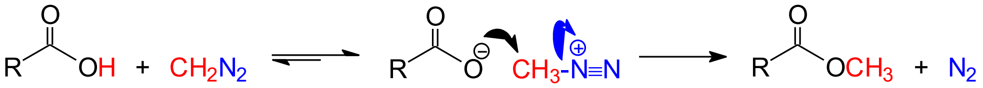
4.2. REACTIVITY

4.2.1. Methylation of carboxylic acids and phenols

Diazo compounds are reagents used for the alkylation of carboxylic acids and phenols. The most widely used of these is diazomethane.

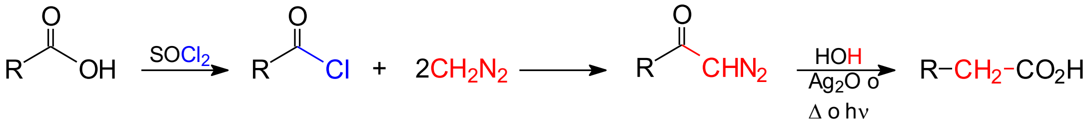


Diazo compounds are slightly basic molecules and are capable of dehydronating the most acidic functional groups (carboxylic acids and phenols). When a diazo compound is hydronated, it is transformed into an alkanediazonio salt, which undergoes a nucleophilic substitution by the anion resulting from dehydronation:

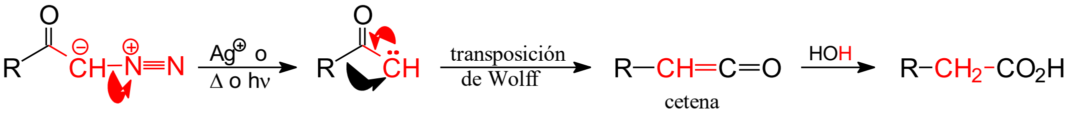


4.2.2. Arndt-Eistert reaction

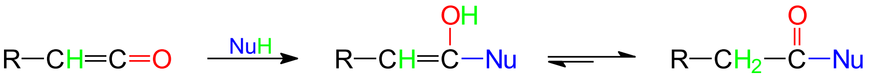
Carboxylic acids (and their derivatives) can be homologated by adding a carbon by the *Arndt-Eistert reaction*. The transformation begins with the formation of a diazo ketone from an acyl chloride. If diazo ketone is heated, irradiated, or added silver salts in an aqueous medium, it is transformed into a carboxylic acid with one carbon higher than the initial one:



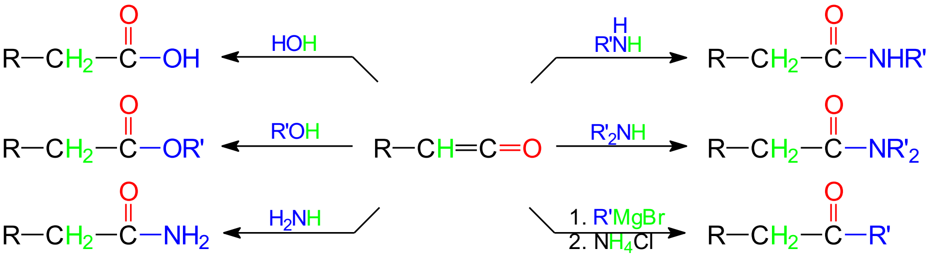
Under these conditions, diazo ketone is transposed (*Wolff rearrangement*) into a ketene, which adds water and forms a carboxylic acid:



Ketenes have a similar reactivity to isocyanates. They also give the nucleophile addition products.



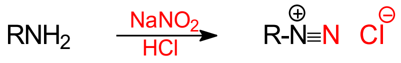
Carboxylic acids, esters, amides and ketones can be formed from a keten:



5. DIAZONIUM SALTS

5.1. SYNTHESIS

Diazonium salts are synthesized from primary amines with nitrous acid (see section **18.4.5**):



$$RNH_2 \xrightarrow[HCl]{NaNO_2} R\text{-}\overset{\oplus}{N}\equiv N \;\; Cl^{\ominus}$$

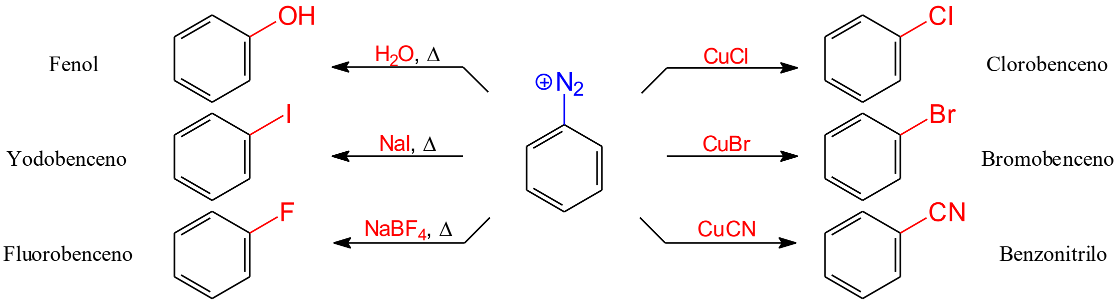
Aliphatic diazonium salts are very unstable and have little synthetic utility. Aromatic diazonium salts are usually stable below 5 °C.

5.2. REACTIVITY

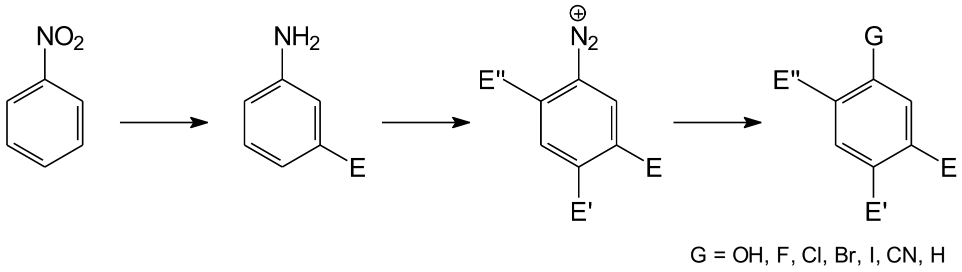
The reactions that aromatic diazonium salts can undergo can be divided into two groups: reactions in which the diazonium group is substituted and reactions in which a nucleophile is added to the diazonium group.

5.2.1. Substitution Reactions

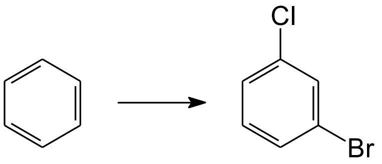
Aromatic diazonium salts can be replaced by numerous functional groups:

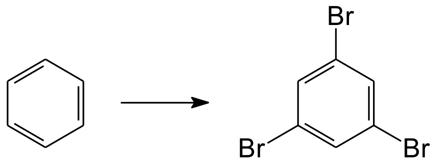


Diazonium salts are very important for the synthesis of aromatic molecules. Apart from being able to form molecules with groups that are difficult to access by other methods, they can be used to synthesize the so-called "impossible benzenes". A diazonium salt can be considered as the universal orienting substituent. For its formation, it is necessary to form nitrobenzene (meta orientator), then aniline (*ortho*/*para* orienter) and, finally, it can be replaced by a wide variety of groups:



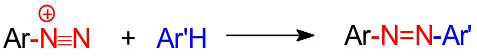
Thus, molecules such as the following can be synthesized:



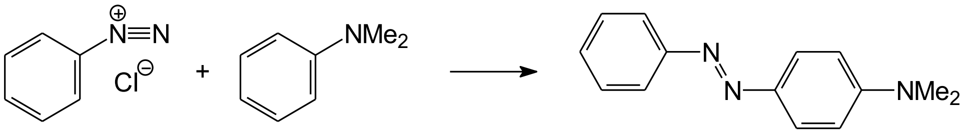


5.2.2. Addition reactions. Synthesis of azo dyes

The diazonium group behaves as an electrophile against certain nucleophiles. Of particular interest are aromatic molecules with activating groups (phenols and anilines), since the products are used as dyes.

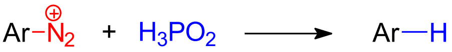


$$Ar\text{-}\overset{\oplus}{N}{\equiv}N + Ar'H \longrightarrow Ar\text{-}N{=}N\text{-}Ar'$$



5.2.3. Reduction

Diazonium salts can be reduced with H_3PO_2 or $NaBH_4$.



$$Ar-\overset{\oplus}{N_2} + H_3PO_2 \longrightarrow Ar-H$$