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[DRUGS]

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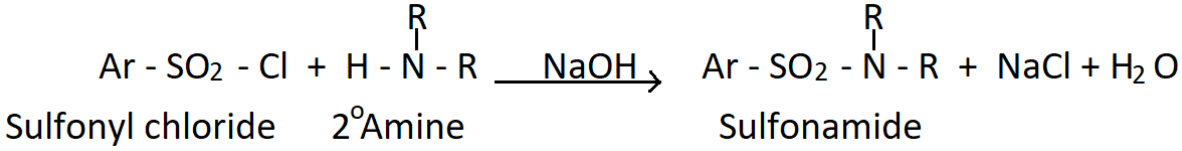
"DRUGS"

SULFONAMIDES, SULFA DRUGD:-

The sulfa drugs, which are derivatives of sulfonamide where the first effective chemotherapeutic agents to be widely used for the care of bacterial infection in humans. They are active against certain gram – positive and gram – negative cocci, certain gram – negative bacteria and protozoa.

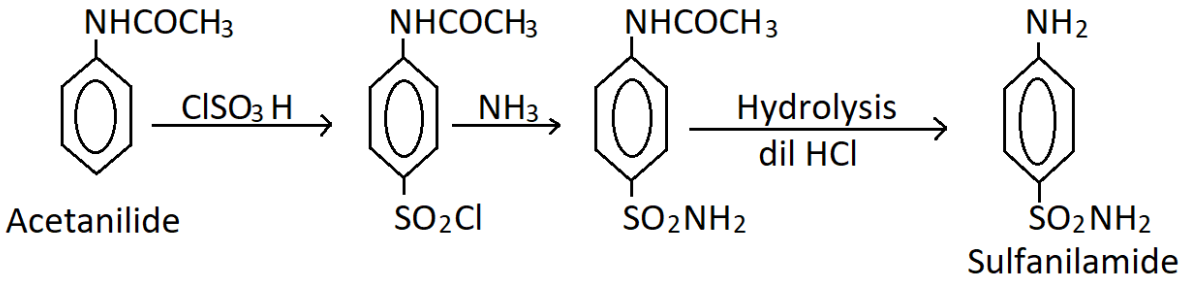
Sulfonation of amines play an important role in the pharmaceutical industry, especially in the formation of sulfa drugs.

Sulfa drugs were among the earliest synthetic antibiotics used to treat bacterial infections. The sulfonation of amines using aromatic. Sulfonyl chlorides ($Ar - SO_2 - Cl$) to form sulphonamides is closely related to the acylation of amines to form amides.



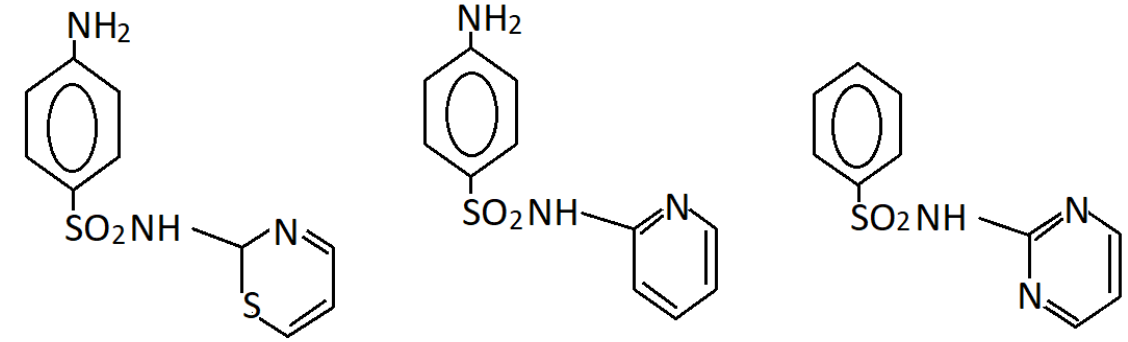
Sulfonamides are derivatives of sulfonic acids ($Ar - SO_3H$). like the acylation reaction, the sulfonation reaction occurs only with primary and secondary amines, in which a hydrogen is replaced with a sulfonyl group. ($R - SO_2 -$).

The parent compound for all sulfa drugs is sulphanilamide prepared from acetanilide by the following steps.



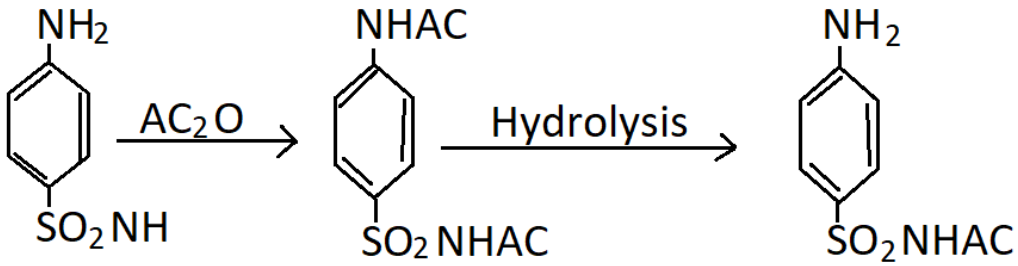
Sulphanilamide eventually was found to be too toxic for general use, but thousands of derivatives have been synthesized and tested. Most sulfa drugs used today have been derived from the sulfonation of primary amines rather than sulfonation of ammonia for example.

Sulfathiazole saved the lives of many people wounded in world war ii; sulfapyridine provided the first successful treatment for Pneumonia, and sulfadiazine is used to treat many different infections.



Sulfathiazole Sulfapyridine Sulfadiazine

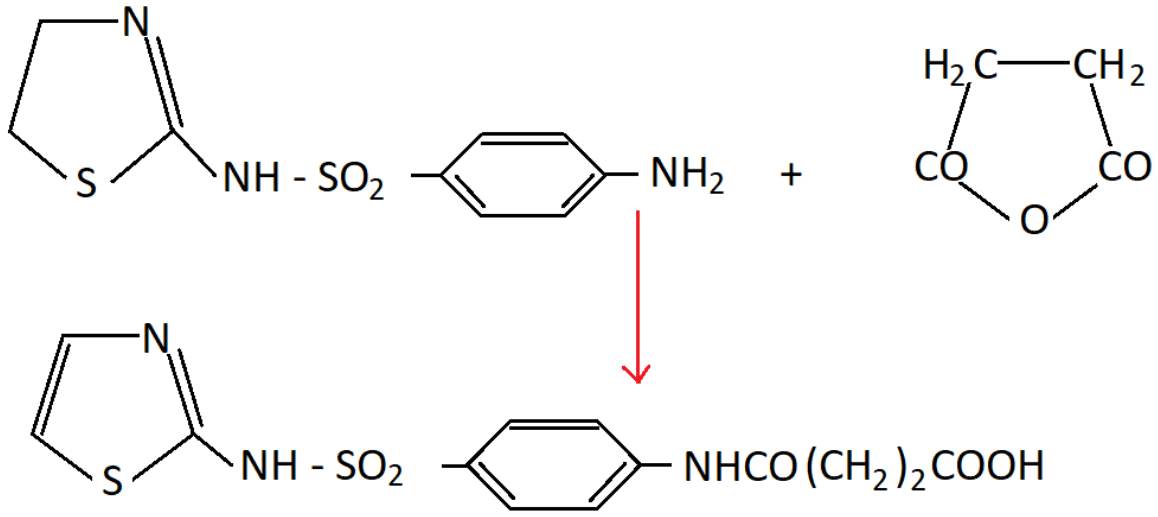
(1) Sulfacetamide:- It is prepared by the careful and of course. Controlled hydrolysis of the diacetyl derivative of sulfanilamide.



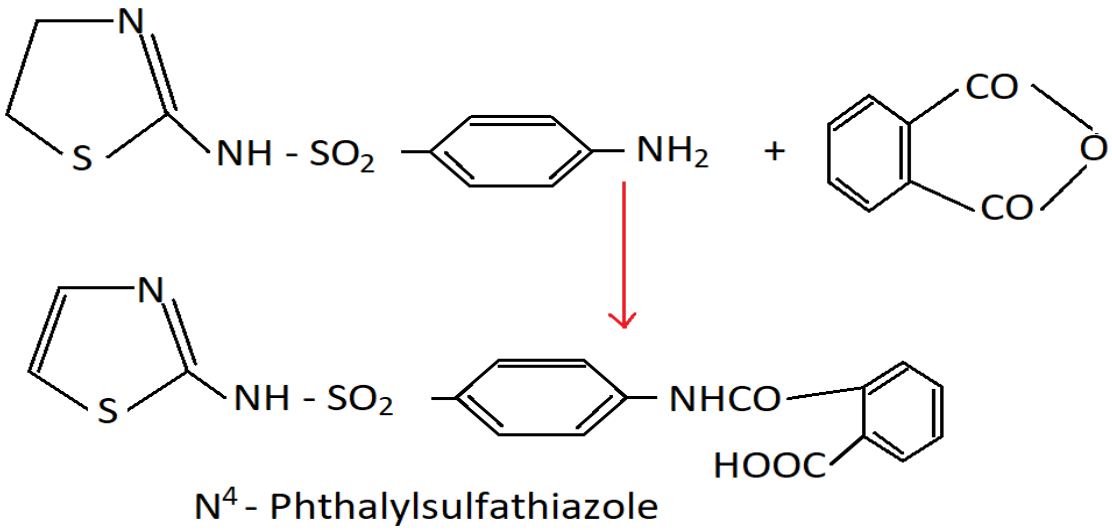
It is one of the highly soluble sulfonamide drugs and used for urinary tract infections. But due to its toxic nature it is replaced by other highly soluble sulfa drugs, viz sulfathiazole.

(2) Succinyl sulfathiazole:- (N – 2 – thiazolyl – N^4 – succinyl sulfanilamide or N^4 – succinyl sulfathiazole).

It is prepared by heating succinic anhydride with sulfathiazole.



(3) Phthalyl sulfathiazole :- (N – 2 – thiazolyl – N^4 – phthalyl sulfanilamide or N^4 – phthalylsulfathiazole). It is prepared by heating phthalic anhydride with sulfathiazole.

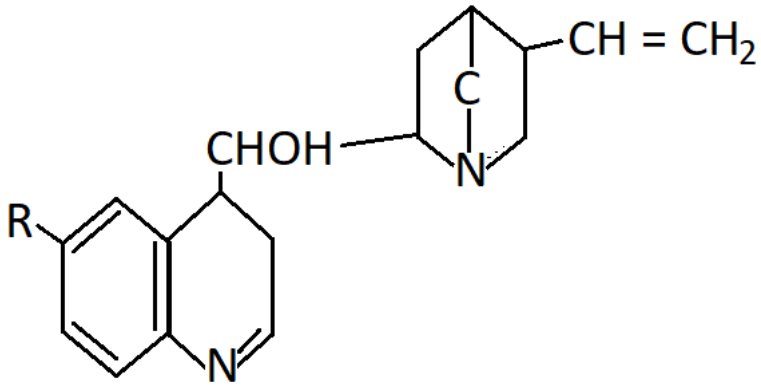


N^4 - Phthalylsulfathiazole

It has also similar medicinal value as succinyl sulfathiazole.

"ANTIMATERIALS"

Malaria is perhaps the most widespread of all the human diseases. In human being it is caused by the few species of plasmodium. When an infected female anopheles bites to the man, ie actually first of all the plasmodium protozoan infects female anopheles which then infect the human being. Earlierly cinchona bark was used as a remedy for malaria. The medicinal value of cinchona bark was found to be due to the presence of certain alkaloids, viz quinine cinchonine, quinidine, and cinchonidine, out of which quinine is the most important. Since that time malaria was treated by quinine extracted from the cinchona bark.

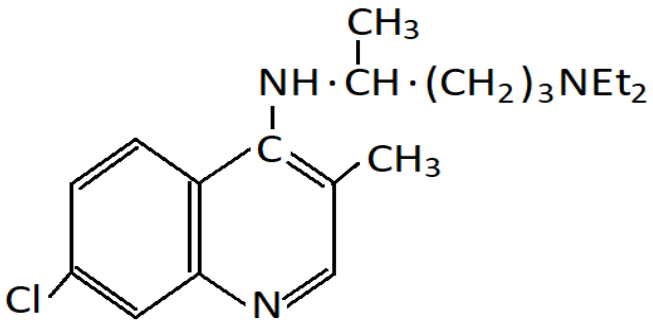


The important and most widely used synthetic antimalarials can be classified in to the following four groups.

(a) 8 – Aminoquinoline derivatives.
(b) 4 – Aminoquinoline derivative.
(c) Acridine derivative.
(d) Pyrimidine and biguanide derivative.

"4 – Aminoquinoline":-

(i) Santoquine:- Santoquine is having one additional methyl group in position 3 – in the quinoline ring of chloroquine. It is less reactive than chloroquine.



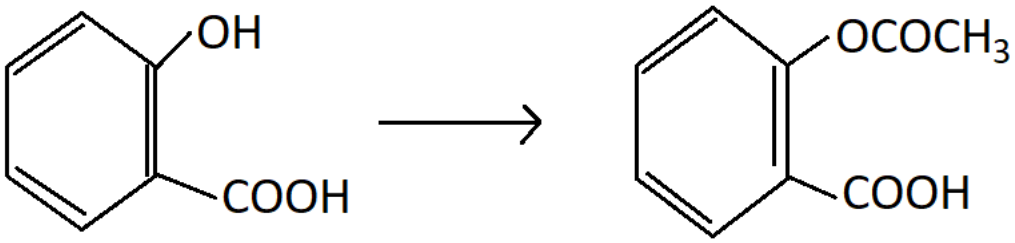
Santoquine

"Analgesics" or "Antipyretics" :-

Analgesics are defined as those substances which reduce body temperature in fevers whereas analgesics are the compounds which relieve pain. The antipyretic compounds studied and synthesised in the earlier days were also found to possess the analgesic properties and hence these two types of drugs are generally studied together, but now a days. Some compounds are known which possess only the antipyretic properties without any analgesic action. The antipyretic drug effects the hypothalamic centre which in turn activates the dilation of the peripheral blood vessels and increase the rate of perspiration which cause as the body to lose heat and subsequently lowers the body temperature. Antipyretic have no effect on body temperature. When it is in the normal range. The most commonly used antipyretics analgesics fall in to following groups.

Aspirin:- Aspirin as obtained by the acetylation of salicylic

acid acetylation can be executed either by a mixture of acetic acid and acetic anhydride in the presence of sulphuric acid or by acetic anhydride in the presence of pyridine.



The acetylation by diketone $(CH_2 = CO)_2$ has not proved industrially economical.

Aspirin has the property of salicylic acid against rheumatic fever, with the additional use against muscular aches and pain, headaches, colds, pain from arthritis, bursitis etc.

However, aspirin is effective as an analgesic only in cases in which the pain is mild, it is in effective in cases of severe pain. Aspirin is hydrolysed to salicylic acid by enzymatic reactions in the blood and it is the active component salicylic acid appears to block or interfere with the pain impulses being transmitted to the thalamus and to raise the threshold of the pain stimuli.

"Sedatives" :-

Sedatives are central nervous system depressants that reduce nervous tension and promote relaxation without producing sleep.

Eg;- Simple bromides are good sedatives and possess little or viz, thiopentone cannot be used as sedatives.

Some group use in sedatives:-

(a) Alcohols.
(b) Aldehydes, Ketones, and Phosphorus.
(c) Urethanes, Amides and Urea.
(d) Barbiturates.
(e) Hydantoin derivatives.
(f) Tranquilizers.

Alcohols:- Ethyl alcohol, the most important member of the series, was used as sedatives and hypnotic for a long time; but its continuous use leads to alcoholism and hence it is replaces by other alcohols (eg:- X – amyl alcohol) and their halogen derivatives.

Among the halogenated alcohols trichloro ethanol, tribromo – ethanol, and chloretone, have been used widely. The first two are prepared by the reduction of the chloral or bromal with aluminium isopropoxide and isopropyl alcohol.

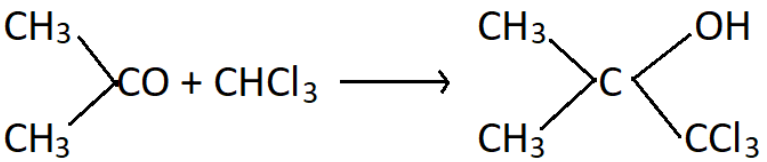
$CCl_3 \cdot CHO \longrightarrow CCl_3 \cdot CH_2OH$

Chloral — Trichloro ethanol

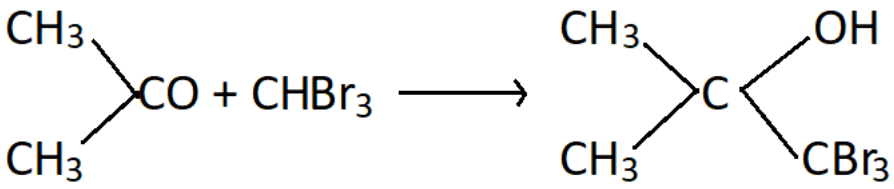
$CBr_3 \cdot CHO \longrightarrow CBr_3 \cdot CH_2OH$

Bromal — Tribromo ethanol

On the other hand, chloretone and analogous bromine compounds, bromoethane are prepared by the bong sensation of acetone with chloroform or bromoform.



Chloretone



Brometone

"Antiseptics" :-

Antiseptic are those chemical compounds which prevent the sepsis of wounds, ie. Stops the action of microorganism either by inhibiting their reproduction or causing their death. On the other hand the term disinfectant is used for the chemical compounds applied to inanimate objects although sometimes it is used not correctly, in certain combined terms such as skin disinfectant. The antiseptics power of a drug is generally measured in terms of phenol coefficient. Which is defined as the dilution at which it will kill bacteria in a given time (generally 10 metres) compared to the dilution required for phenol.

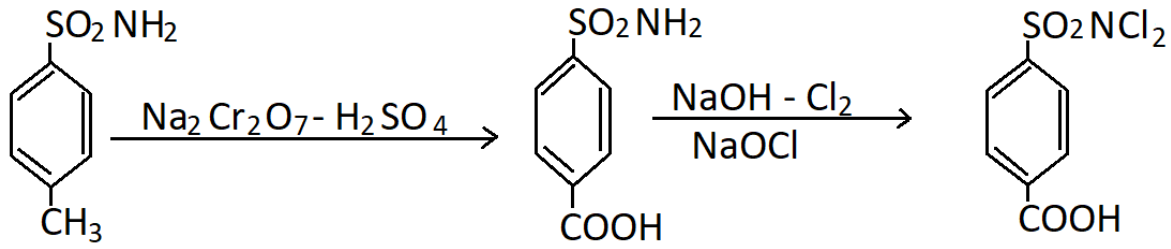
$$Phenol\ coefficient = \frac{Germicidal\ dilution\ of\ the\ compound}{Germicidal\ dilution\ of\ phenol}$$

The commonly used antiseptics may be studied under the following headings.

(a) Halogens and halogen compounds.
(b) Aromatic acids and esters.
(c) Phenols and related compounds.
(d) Synthetic dyestuffs.

Halogen (P – sulphone dichloro amine benzoic acid):-

It is prepared from P – toluene sulphonamide in the following manner.



Its soluble sodium salt is used for sterilisation of drinking water.

"Antibiotics" :-

There are substances produced by microorganism which selectively suppress the growth of or kill other microorganism at very low concentrations.

Now many antibiotics and their analogues have been synthesized. Both synthetic and microbiologically produced drugs need to be included together.

It would be more meaningful to use the term antimicrobial agent (AMA) to designate synthetic as well as naturally obtained drugs that to make something weather, smaller or less effective attenuate microorganisms.

Examples and uses:-

(1) Antibacterial:- Penicillin, Aminoglycoside, Erythromycin etc.

(2) Antifungal:- Griseofulvin, Amphotericin B, Ketoconazole etc.

(3) Antiviral:- Acyclovir, Amantadine, Zidovudine etc.

(4) Antiprotozoal:- Chloroquine, Pyrimethamine, Metronidazole, Diloxanide etc.

(5) Anthelmintic:- Mebendazole, Pyrantel, Diethylcarbamazine etc.

Antibiotics are obtained from:-

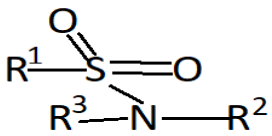
(a) From fungi:- Penicillin, Cephalosporins, Griseofulvin.

(b) From bacteria:- Polymyxin B, Tyrothricin, Colistin, Aztreonam, Bacitracin etc.

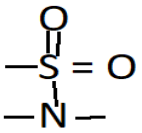
(c) From Actinomycetes:- Aminoglycosides, Macrolides, Tetracycline, Chloramphenicol.

(Q). What are sulpha drugs? Mention the synthesis of any two sulfa drugs. Mention the adverse effect of sulpha drugs.

Ans:– Sulpha drugs:- Sulpha drugs is a first antimicrobial agent is a synthetic compound in which sulphonamide function group is found.

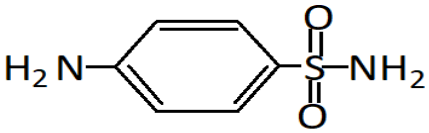


Sulfadrug



Sulphonamide function group

Example:- (1)



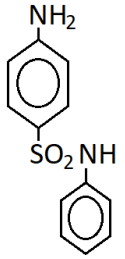
Sulphamilamide

Note:- It is first antimicrobial agent which is obtained by the breakdown of prontosil. It is too toxic for general use. So, other sulfa – drugs have been invented.

The best therapeutic result were obtained from compounds in which one hydrogen of -

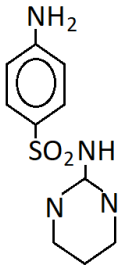
SO_2NH_2 is replaced by some other group usually a heterocyclic.

Example:- (2)



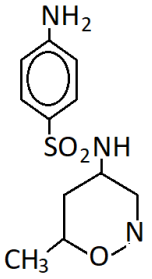
Sulphapyridine

(3)



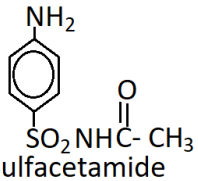
Sulphadiozine

(4)



Sulfamethoxazole

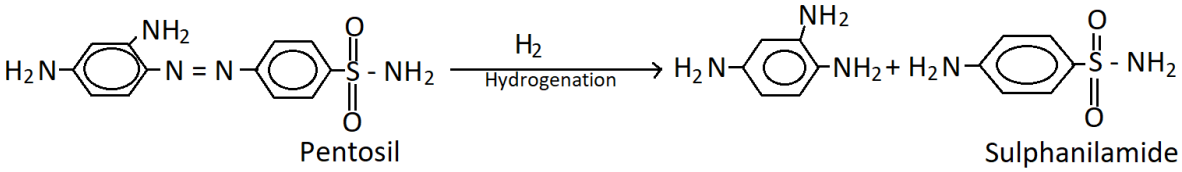
(5)



Sulfacetamide

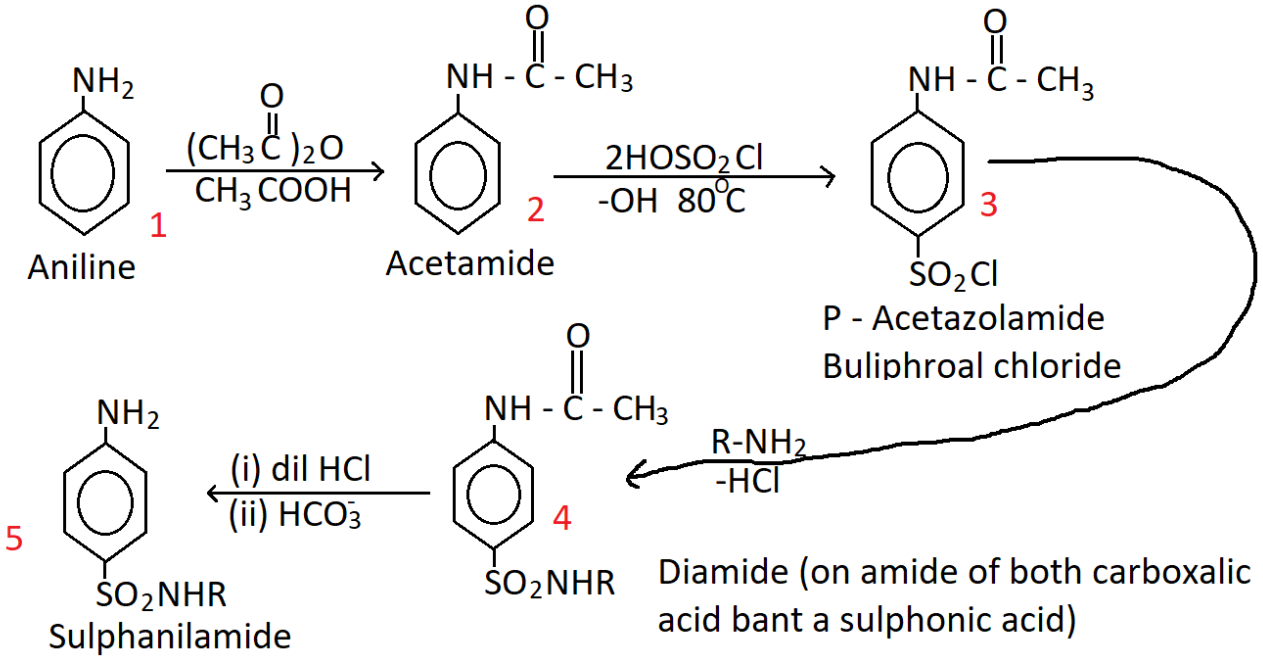
Synthesis of any two sulfa drugs:-

(a) Synthesis of sulfa drugs:-



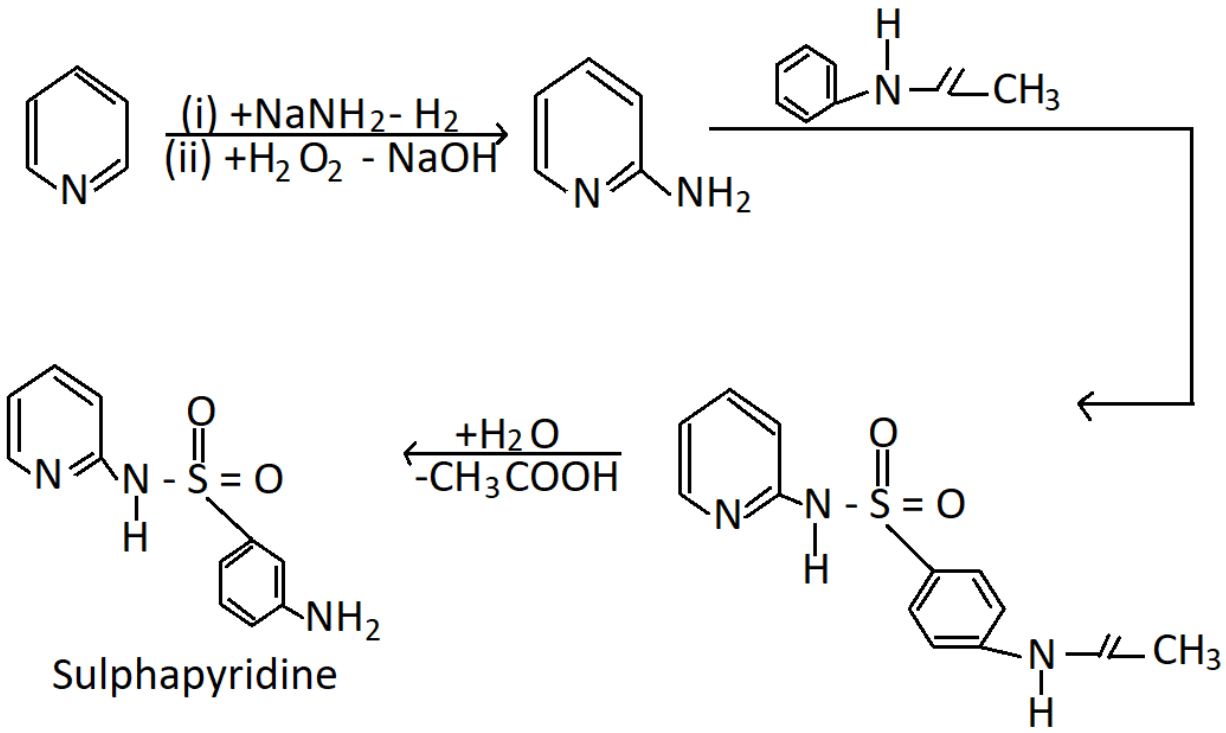
Pentosil — Sulphanilamide

Sulphanilamide can be synthesis from aniline through the following sequence of reactions.



Aniline — Acetamide — P - Acetazolamide Buliphroal chloride — Diamide (on amide of both carboxalic acid bant a sulphonic acid) — Sulphanilamide

(b) Synthesis of sulphapyridine :-



SULFAMIDE :-

Acetylation of aniline produces acetanilide (ii) and protects the amino group from the reagent to be used. Treatment of (ii) with HSO_3Cl beings about an electrophilic aromatic substituent reaction and yields (iii). Addition of ammonia or a primary amine gives (iv). Finally refluxing (iv) with dilute HCl selective by hydrolysis the carboxamide linkage and produces a sulfanilamide (Hydrolysis of carboxamides is much more rapid than that of sulphonamide).

Adverse effect of sulfa drugs :-

Adverse effect of sulphonamides are relatively common:

(a) Nausea (the feeling that are you going to vomit).

(b) Vomiting.

(c) Epigastric pain :- It is name for pain or discomfort right below your ribs in the area of your upper abdomen.

(d) Crystalluria :- It refera to doubly urine when the cause of cloudiness is due to crystals found in the urine when performing a urine lesl. Crystallization is considered as one of the side effects of sulphonamides as one of the side effects of sulphonamides and penicillins. It is dose related precipitation in urine can be minimized by taking plenty of fluids and by rationalizing the urine in which sulfonamides and their acetylated derivatives are more soluble.

(e) Hypersensitivity reaction occurs in 2 – 5% patients. These are mostly in the form of rashes, vertical and drug force.

(f) Hepatitis unrelated to does occurs in 0.1% patients.

(g) Topical use (application to body suspricls) of sulphonamides is not recommended because of risk of contact sensitization. However, outdoor use (connected with eurovision).

(h) Sulphonamides cause haemolysis (the rupture dissection of red blood cells) in does dependent manner.

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