Ministry of Health of the Russian Federation
Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

CHEMICAL METHODS OF PHARMACOPOEIAL ANALYSIS - IDENTIFICATION OF DRUGS OF ORGANIC NATURE (IDENTIFICATION OF FUNCTIONAL GROUPS)

Lesson 3
(part 1)
V term

Volgograd, 2022

Medicinal products of organic origin constitute the majority of medicinal products. The analysis of these pharmaceutical substances is mainly confined to the examination of the functional groups that make up the compound.

A functional group is a reactive atom or group of atoms that determines the chemical properties of a substance, its pharmacological activity and its belonging to a certain class of organic compounds.

The analysis of drugs by functional groups makes it possible

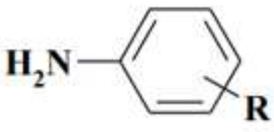
- to unify the methods of identification and quantification reactions;
- to predict test methods according to their structure.

Medicinal substances are usually polyfunctional compounds, i.e. they contain several functional groups.

In the identification, reactions are usually conducted for all functional groups, which makes it possible to correctly identify the drug substance.

For each functional group several methods of quantification are proposed, which makes it possible to select the optimal method of analysis in the study of medicinal substances in different objects (substance, medicinal product).

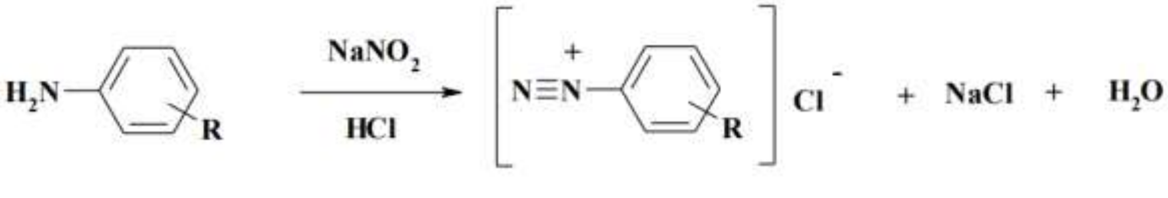
Identification of primary aromatic aminogroup



1. Azo dye formation

Azo dyes are coloured (red, brown and orange) products produced in two stages:

1) Diazotization (production of a diazonium salt):



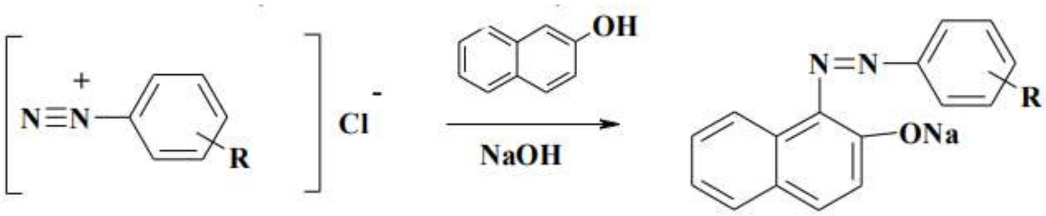
Positive charge on this nitrogen atom and negative charge on chlorine

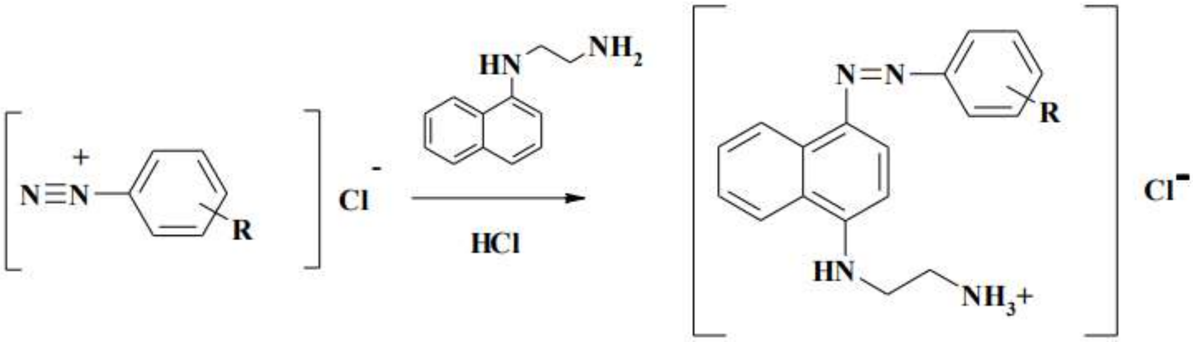
2) Azo coupling (interaction of a diazonium salt with a phenol or aromatic amine).

The reaction takes place in the ortho- or para-position with respect to the hydroxyl or amino group, but goes more easily to the para-position.

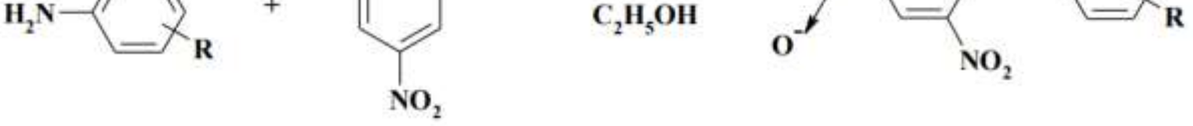
Azo coupling with phenols (naphthols) takes place in a slightly alkaline (pH 9.0-10.0) solution, and with amines in a slightly acidic solution.

In practice, β-naphthol (in an alkaline solution) or α-naphthylethylenediamine (in an acidic solution) are the most commonly used components for azo coupling:

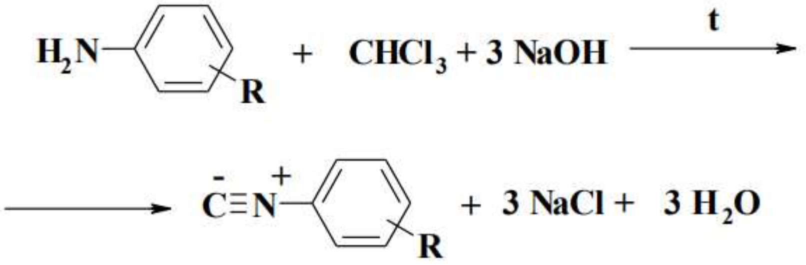




2. Interaction with 2,4-dinitrochlorobenzene. A sodium acisol dinitrophenyl derivative (yellow) is formed.

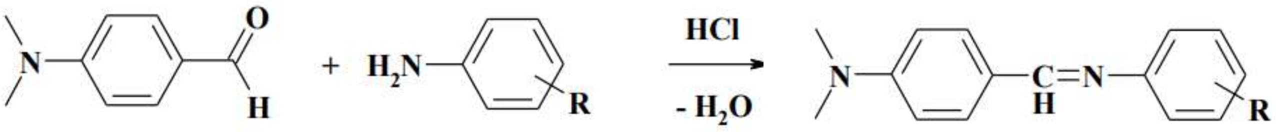


3. Isonitrile test. The reaction consists of the interaction of a primary aromatic amine with chloroform in an alkaline medium under heating. The resulting isonitriles are detected by the characteristic nauseating smell.

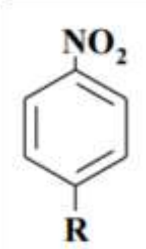


4. Condensation reaction with aromatic aldehydes (formation of Schiff bases). The reaction products of primary amines with 4-dimethylaminobenzaldehyde or vanillin in hydrochloric acid solution are usually colored yellow-orange.

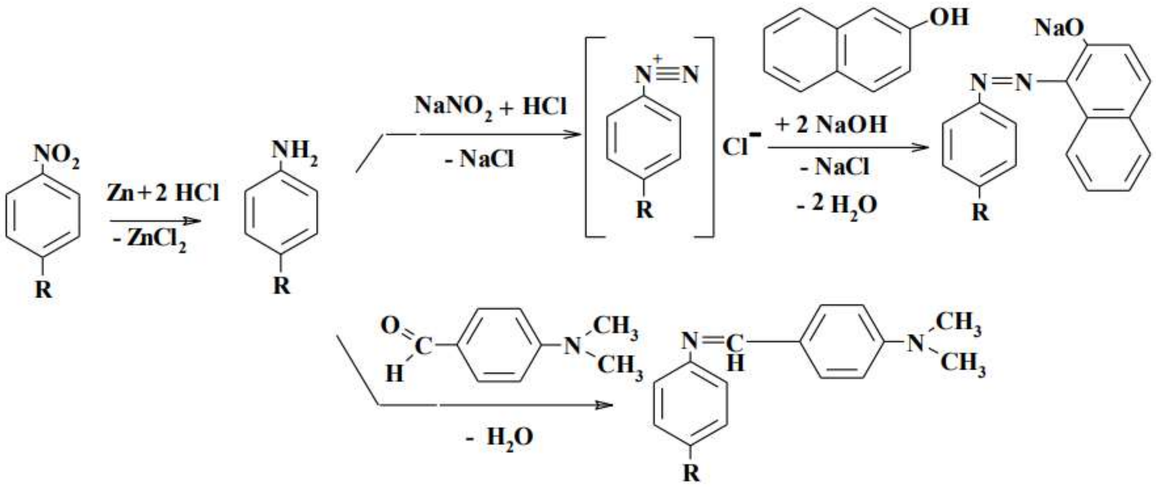
In express analysis this reaction is carried out in a drop version (lignin test, Ovchinnikov reaction).



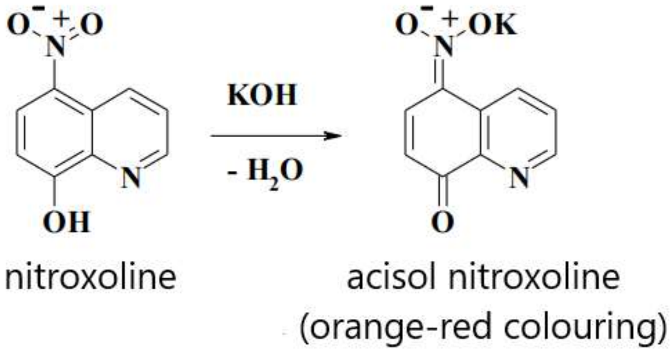
Identification of aromatic nitrogroup



1. Reduction reaction of an aromatic nitro group to a primary aromatic amino group (followed by determination). Reagent - metallic zinc in an acidic medium when heated. The formation of the primary aromatic amine is proved by the reaction of the formation of the azo dye or Schiff bases.



2. The acisol formation reaction. Conducted for aromatic compounds containing a group with a mobile hydrogen atom (OH, NH_2, CH_2, CH) in ortho- or para-position relative to the nitro group. When alkalis are acted upon, potassium or sodium acisols are formed, which have respectively an ortho- or para-quinoid structure and are coloured bright yellow, orange or red.

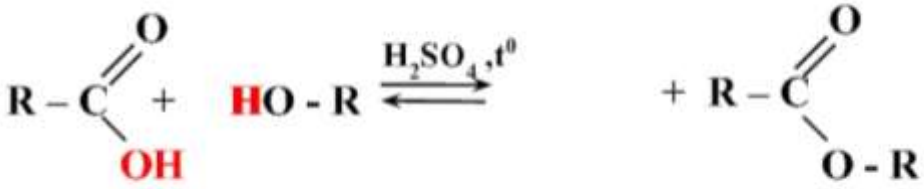


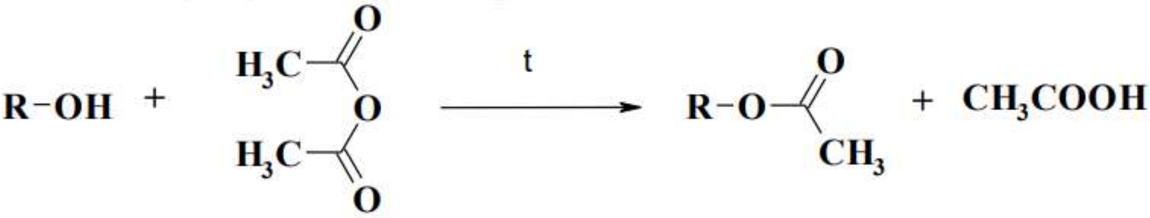
Hydroxyl group identification

Identification of monobasic alcohols

1. Monobasic alcohols can be detected by the esterification reaction or by acetylation with using acetic anhydride:

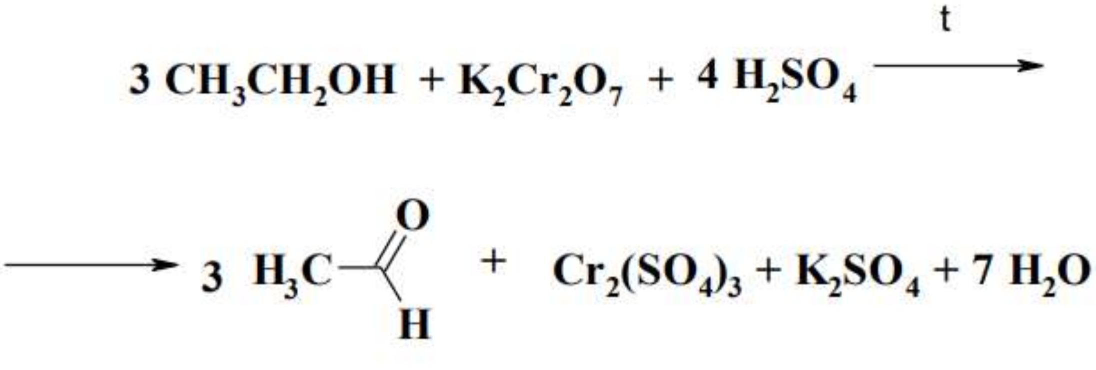
The reactions are carried out in the presence of water-removing agents under heating.





The esters derived from low molecular weight alcohols have a characteristic odour and the esters derived from high molecular weight alcohols are crystalline substances, and have a distinct melting point.

2. Oxidation reactions. Oxidised only by strong oxidants ($K_2Cr_2O_7$, $KMnO_4$, HIO_4, KIO_4) in an acidic medium. The mechanism of the oxidation reaction is different, depending on the nature of the hydroxyl. For example, ethanol is oxidised to acetaldehyde by potassium dichromate in the presence of sulphuric acid, which is detectable by smell:



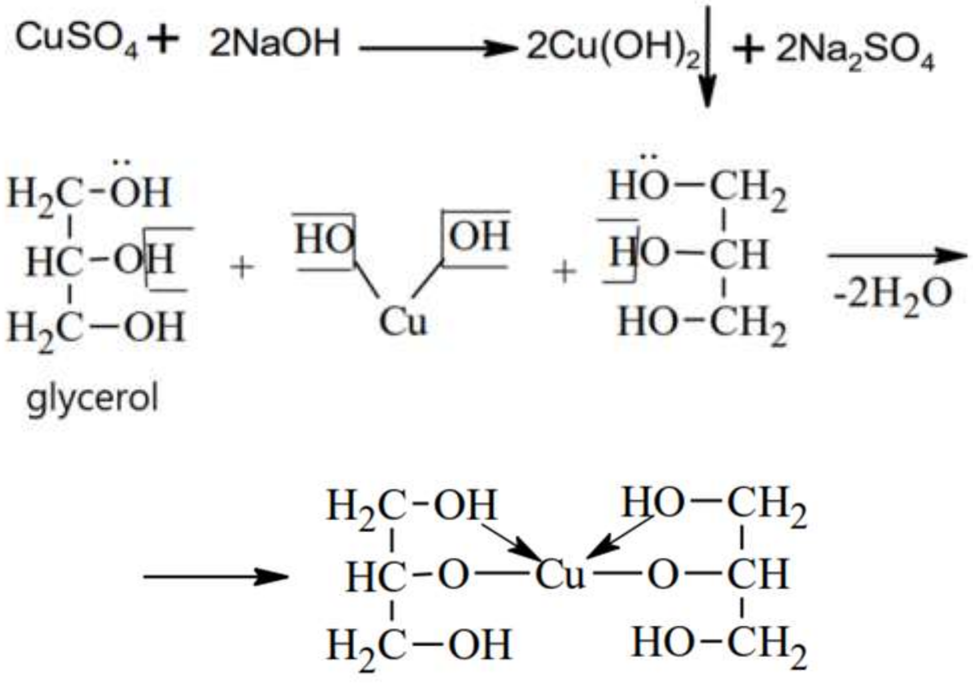
$$3\ CH_3CH_2OH + K_2Cr_2O_7 + 4\ H_2SO_4 \xrightarrow{t} 3\ H_3C{-}CHO + Cr_2(SO_4)_3 + K_2SO_4 + 7\ H_2O$$

Secondary alcohols under these conditions give ketones. Tertiary alcohols oxidise difficultly, breaking the hydrocarbon chain.

Identification of polybasic alcohols

Reactions of complex compound formation.

The strength of the acidic properties is affected by the number of hydroxyl groups in the compound: as the number of groups increases, the acidic properties increase. Due to this, polybasic alcohols are capable of forming intracomplex (chelate) compounds with metal salts (copper, cobalt) in strongly alkaline media. The reaction with copper (II) sulphate in sodium hydroxide medium is of most interest.



soluble blue chelate