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UNIT-II: Phenols: Acidity of phenols, effect of substituents on acidity, qualitative tests, Structure and uses of phenol, cresols, resorcinol, naphthols

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Presentation · June 2018

DOI: 10.13140/RG.2.2.24895.41120

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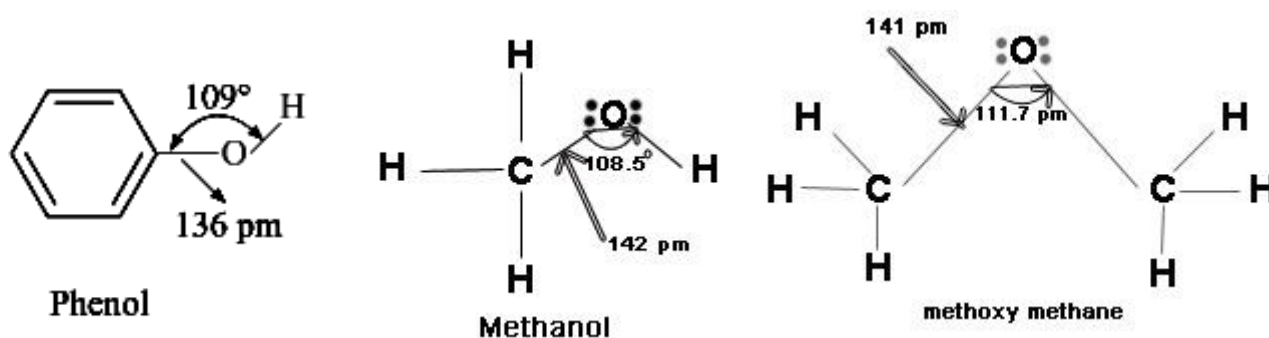
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❖ Introduction

- Phenols are molecules that have a hydroxyl group attached to the carbon atom of an aromatic ring.
- In phenol, hydroxy functional group is directly attached to the **sp² hybridized** carbon atom of the benzene ring. The interaction of six unhybridized **2pz orbitals** of carbon atoms of the benzene ring leads to the formation of delocalized pi-electron clouds.
- The **C-O-H bond angle** in phenol is **109°**. The carbon-oxygen bond length (**136 pm**)
- In **phenol** carbon-oxygen bond length is slightly less than that in **methanol** (142 pm). This is due to partial double bond character on account of the conjugation of unshared electron pair of oxygen with the aromatic ring.
- Similarly, In **ethers**, the four electron pairs, ie; the two bond pairs and two lone pairs of electrons around oxygen are arranged approximately in a tetrahedral arrangement. The **C-O-C bond angle** (**111.7°** in methoxy methane) is slightly greater than the tetrahedral angle (**109°28'**) due to the repulsive **C-O bond length** (**141 pm**) in ethers is almost the same as in alcohols (**142 pm** in methanol).



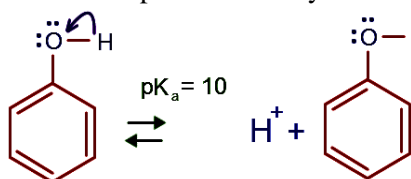
<i>Preferred IUPAC name</i>	Phenol
<i>Systematic IUPAC name</i>	Benzenol
<i>Other names</i>	Carbolic acid; Phenylic acid; Hydroxybenzene; Phenic acid
<i>Chemical formula</i>	C ₆ H ₆ O
<i>Molar mass</i>	94.11 g·mol ⁻¹
<i>Appearance</i>	Transparent crystalline solid
<i>Odor</i>	Sweet and tarry
<i>Density</i>	1.07 g/cm ³
<i>Melting point</i>	40.5 °C
<i>Boiling point</i>	181.7 °C
<i>Solubility in water</i>	8.3 g/100 mL (20 °C)

Note by: If the **pKa** value is increased what happens to the acidic strength and basic strength?

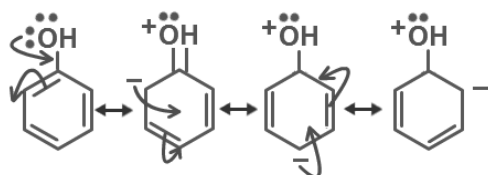
Answer: If the **pKa** value increased, the value of **Ka** decreased by the formula **pKa = - logKa**. And if **Ka** value is decreased, the number of **H⁺** ions in the solution will also be decreased as **Ka** is directly proportional to **[H⁺]** so acidity will decrease. So, if the **Pka** value is increased, acidic strength decreases and vice versa for basic strength.

❖ Acidity of Phenols

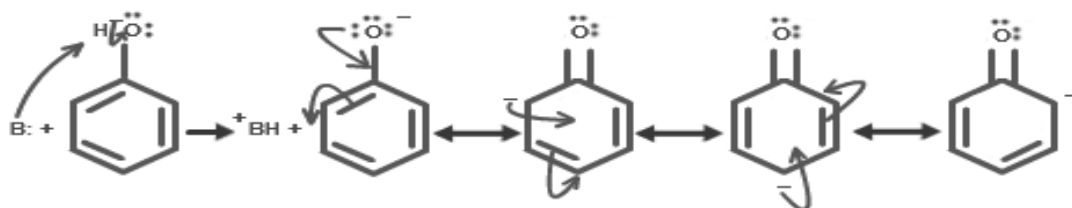
- Compare to alcohols, phenols are stronger acid as the **pK_a value for phenol is 10** while for **alcohols it's close to 16**. Because of acidic nature, phenols can turn blue litmus red and react with aqueous alkali to form phenate. Both reactions are not shown by alcohols. Compare to carboxylic acids, phenols are weaker acid.



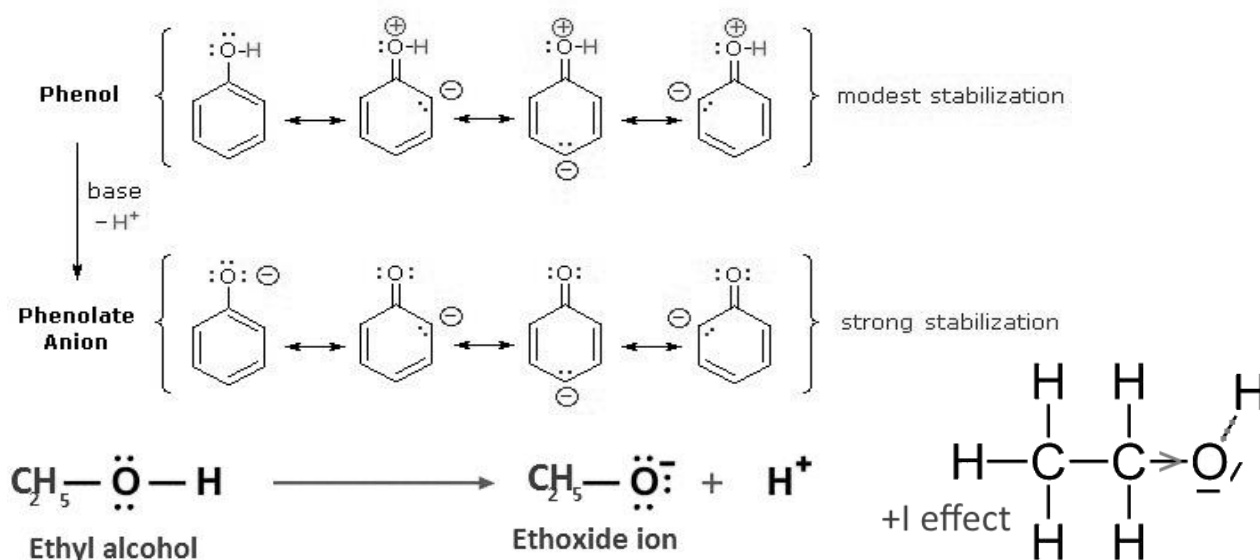
- Hence hydroxy group bonded to benzene ring is much more acidic than hydroxy group to alcohol. This is because of the resonance in phenol. Because of the resonance in phenol, the oxygen atom acquires a positive charge which weakens the oxygen-hydrogen bond and facilitates the release of a proton.



- The deprotonation of phenol forms phenoxide ion or phenate which also exists as a resonance.

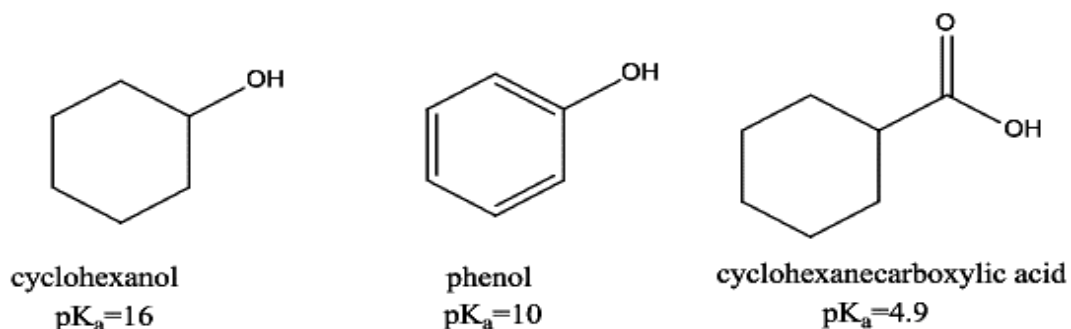


- Hence both phenol and phenoxide ion are stabilized by resonance. Compare to phenol, phenoxide ion is more stable as the negative charge gets delocalized over benzene ring. But the resonating structure of phenol involves the separation of negative and positive charges. Therefore phenol has greater tendency to form phenate by releasing the proton. The deprotonation of alcohol forms alkoxide ion which is not stable due to negative inductive effect of alkyl group and alcohols become less acidic than phenol.



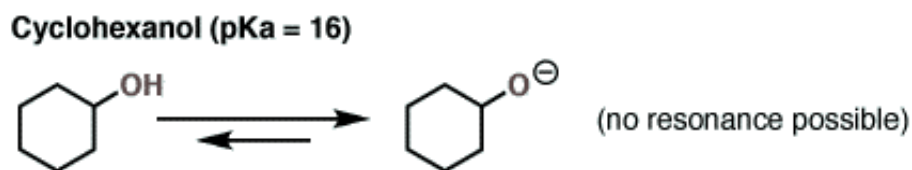
- In **Ethoxide**, the resonance is not possible and The **+ I effect** of the hydrocarbon chain increases the electron density between **O** and **H** and decreases the chances of **H⁺** to leave the alcohol. The more the chain is long and branched the greater the effect, the less will the alcohol be acidic.

❖ **What is the reasoning behind the increasing pKa for organic compounds?**

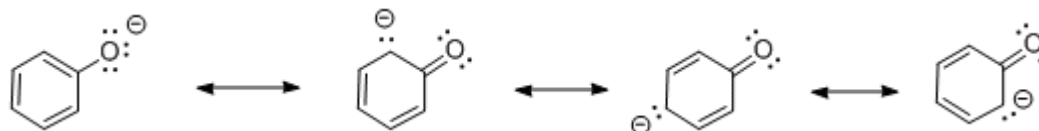


- *Cyclohexanol* is an alcohol. An alcohol contains an **OH group** connected to a **tetrahedral carbon**. *Phenol* is slightly different; it contains an **OH group** connected to a **trigonal planar carbon** that is part of an aromatic ring. *Cyclohexane carboxylic acid* contains a very different functional group, carboxylic acid.
- *Cyclohexanol* has a **pKa** of about **16**. It is less acidic than water. It can give up a proton, but the proton is much more likely to be bound to the oxygen than dissociated. *Phenol* has a **pKa** of about **10** and is considered mildly acidic. *Cyclohexane carboxylic acid* has a **pKa** of about **4.9**; its acidity is similar to **hydrofluoric acid**.
- Compare stability of the conjugate bases of *Cyclohexanol*, *Phenol* and *Cyclohexane carboxylic acid*:

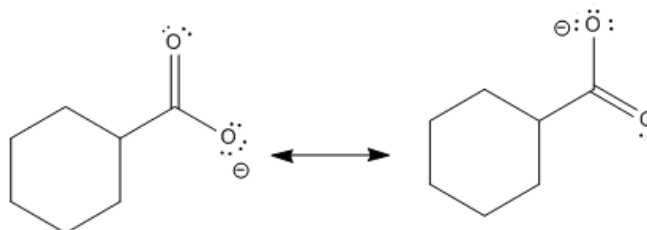
- o In *cyclohexanol*, the anion formed by loss of a proton is localized on the oxygen. There is no resonance stabilization.



- o In *phenol*, the anion formed by loss of a proton is delocalized. Resonance structures show the negative charge can be shared between the oxygen atom and three of the carbons in the benzene ring.



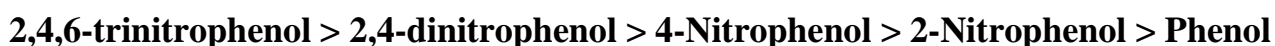
- o In *cyclohexane carboxylic acid*, the anion is also delocalized. This time the negative charge is shared between two different oxygen atoms.



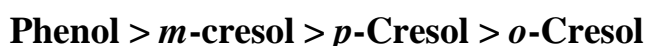
- Resonance delocalization plays a clear role in stabilizing the conjugate base formed after loss of a proton. Despite the similar bond polarity in **cyclohexanol** and **phenol**, the proton is much more tightly bound in cyclohexanol. The greater stability of the **phenolate anion** compared to the **cyclohexanoxide anion** makes it easier to remove a proton from phenol than cyclohexanol.
- The atom onto which the charge is delocalized still plays a major role in determining stability. Delocalization onto an additional oxygen atom may be more stabilizing than delocalization onto several carbons.

❖ Effect of Substituent on Acidity of Phenol

- As the acidic nature of phenol is due to the resonance stabilization of phenate compare to phenol. Therefore the presence of any substituent on aromatic ring which can stabilized the phenoxide ion will tend to increases the acidity of phenol. While any substituent which destabilized the phenate ion by increasing the negative charge will decrease the acidic nature of phenol.
- In other words; the presence of **electron withdrawing group** on benzene ring in phenol **increase the acidity** of phenol and **electron releasing group** will **decrease the acidity**. For example; if there is a **nitro group** substituted on phenol, it will increase the acidic nature of phenol. Hence **nitrophenol** will be more acidic than **phenol** as **nitro group imparts negative mesomeric effect and negative inductive effect**, hence acts as **electron withdrawing group**.
- The position of **nitro group** on **phenol** will affect the acidity of **phenol**. A nitro group at **-ortho** and **para**-position withdraws electrons from **hydroxy group** of **phenol** by stronger **-M effect** while nitro group at **-meta** position withdraws electrons by **weaker -I effect** only, as **meta** position cannot involve in resonance with **hydroxy group**. Hence **o-** and **p-nitrophenols** are more acidic than **m-nitrophenol**. Similarly as the number of nitro groups increases on phenol, the acidic nature of phenol increases. The decreasing order of acidity of **nitrophenols** is as given below.



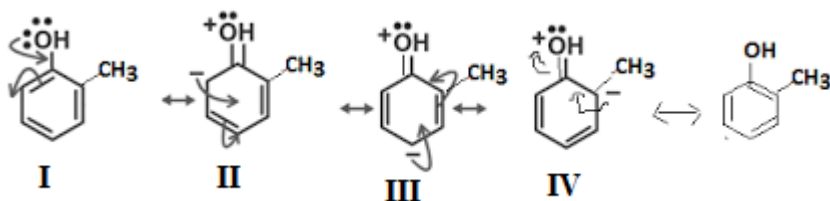
- **Electron donating groups** like amino (-NH₂), alkyl (-R) decreases the acidity of phenol. For example, cresol or methylphenols are less acidic compare to phenol due to positive inductive effect as well as hyperconjugation of methyl group. As both of these effects increases the electron density on hydroxy group and results in low acidity of phenols. Hyperconjugation can operate only at ortho and para position while inductive effect operates at all the three positions. Therefore o-cresol is least acidic. The decreasing order of acidity is as follow.



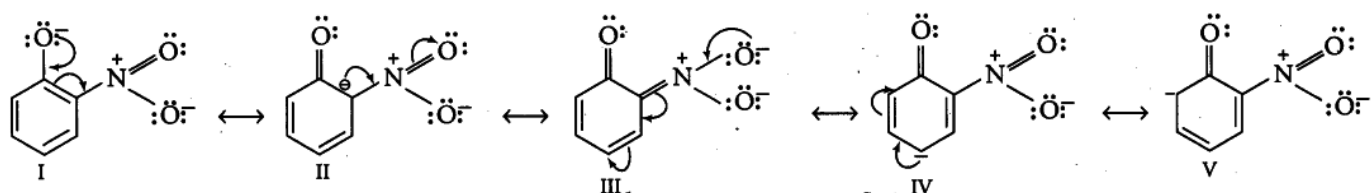
- Some of the substituted phenols with their pKa values are as follow.

Compound	pKa	Substituent	Effect of substituent
Phenol	10.0	-	-
o-Methoxyphenol	10.0	-OCH ₃	+M and -I
o-Methylphenol	10.3	-CH ₃	+I and hyperconjugation
o-Chlorophenol	8.6	-Cl	-I and +M
o-Nitrophenol	7.2	-NO ₂	-M and -I
m-nitrophenol	8.4	-NO ₂	-M and -I
p-Methoxyphenol	10.2	-OCH ₃	+M and -I
p-Methylphenol	10.3	-CH ₃	+I and hyperconjugation
p-Chlorophenol	9.4	-Cl	-I and +M
p-Nitrophenol	7.2	-NO ₂	-M and -I

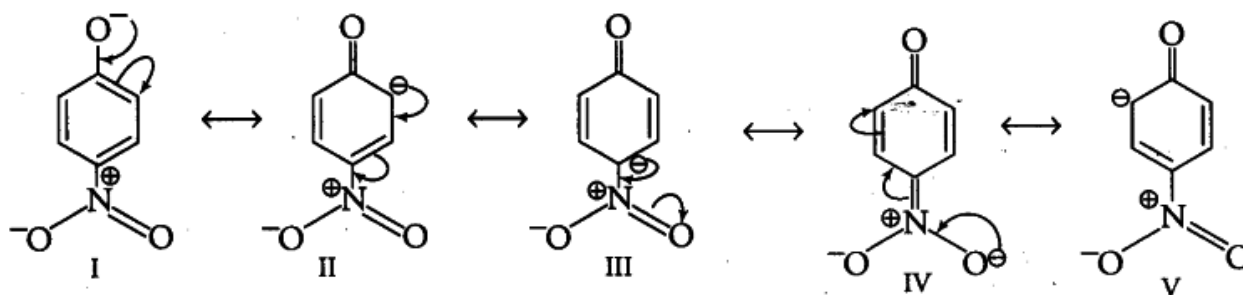
▪ **Resonating structures of ortho Cresol**



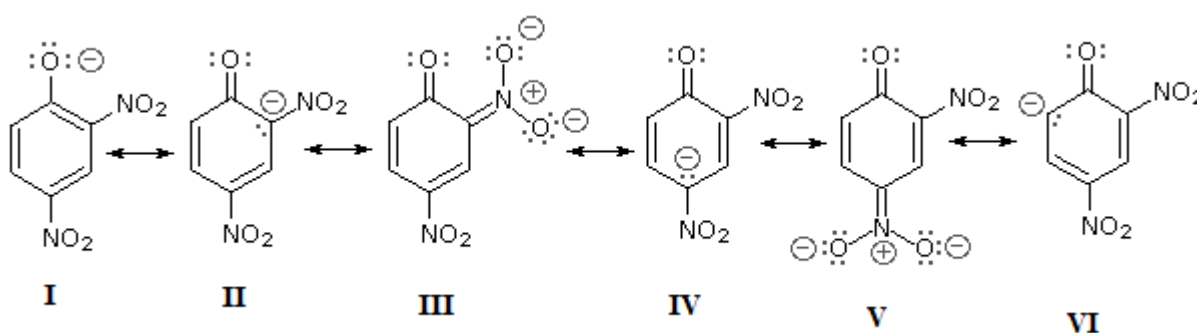
▪ **Resonating structures of o-nitrophenoxide ions (o-nitro phenol)**



▪ **Resonating structures of p-nitrophenoxide ions (p-nitro phenol)**

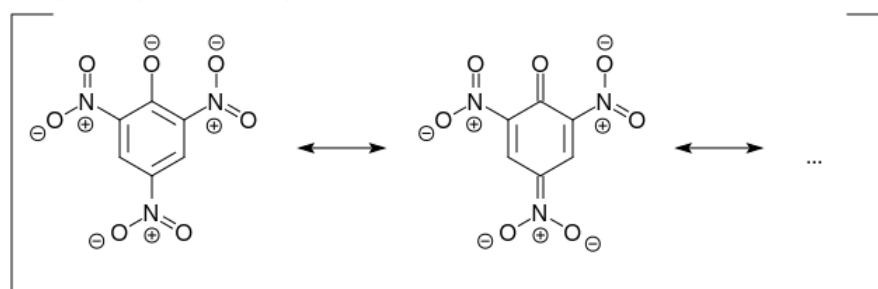


▪ **Resonating structures of 2,4 dinitro phenol**



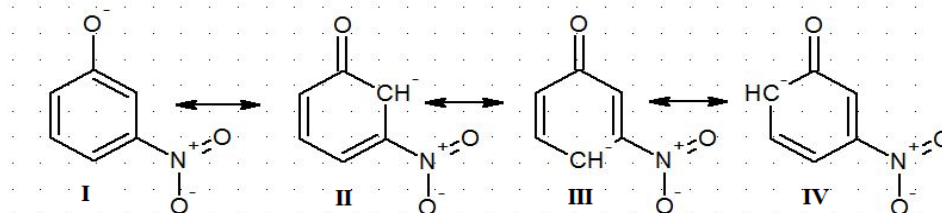
▪ **Resonance forms of 2,4,6-trinitrophenol or picric acid**

- Resonance around the nitro groups (NO_2), around the ring, and you can also have one with the hydroxyl group (OH) making giving it a + charge.

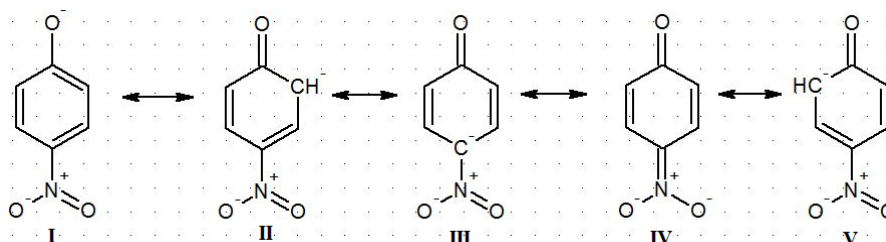


▪ **Why is meta-nitrophenol less acidic than para-nitrophenol?**

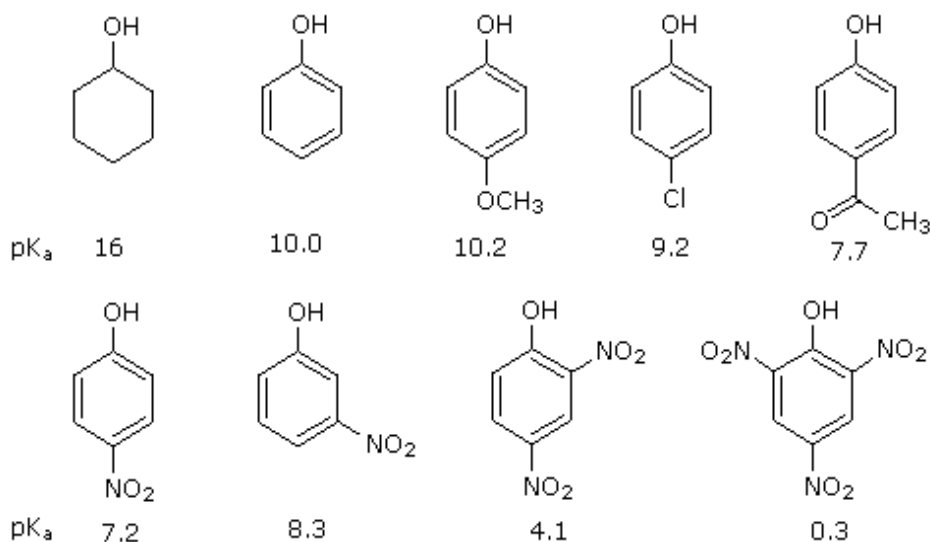
- The acidity of nitrophenols (or any acid for that matter) is determined by the stability of the conjugate base. In the case of *m*-nitrophenol and *p*-nitrophenol, the relative stability can be determined by looking at the resonance structures.
- Whereas *p*-nitrophenol has an additional resonance structure where the negative charge is delocalised onto the oxygen's of the nitro group, which is highly electronegative and therefore stabilise the charge effectively. This stabilisation is not possible in the case of *m*-nitrophenol because there is no opportunity via resonance for delocalisation onto the nitro group.
- Resonance forms of *m*-nitrophenol



- Resonance forms of *p*-nitrophenol



▪ ***pK_a* values of various phenol derivatives**



▪ **Why is picric acid more acidic than benzoic acid?**

- Picric acid is more acidic than benzoic acid because picric acid contains three **NO₂ groups** which is electron withdrawing group. Presence of electron withdrawing group on ring increases acidic character on the other hand presence of electron donating group on ring decreases the acidic character.

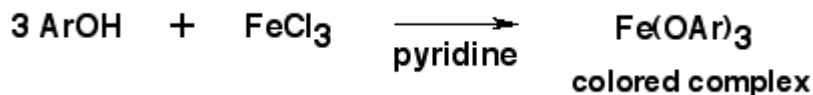
❖ Qualitative tests for Phenol

▪ *Identification of Phenols – Ferric Chloride Test*

- Compounds with a phenol group will form a blue, violet, purple, green, or red-brown color upon addition of aqueous ferric chloride. This reaction can be used as a test for phenol groups.

(a) Iron (III) Chloride Test for Water-Soluble Phenols

- **Reaction:**



- **Procedure:** The iron (III) chloride test for phenols is not completely reliable for acidic phenols, but can be administered by dissolving 15 mg of the unknown compound in 0.5 mL of water or water-alcohol mixture and add 1 to 2 drops of 1% aqueous iron (III) chloride solution.
- **Observation:** A red, blue, green, or purple color observed.

(b) Iron(III) Chloride - Pyridine Test for Water-Insoluble Phenols

- **Procedure** (for water-insoluble phenols or less reactive phenols): A more sensitive test for phenols consists of dissolving or suspending 15 mg of the unknown in 0.5 mL of methylene chloride and adding 3-5 drops of a 1% solution ferric chloride in methylene chloride. Add a drop of pyridine and stir.
- **Observation:** Addition of pyridine and stirring will produce a color if phenols or enols are present.

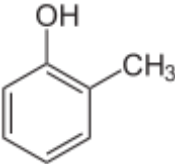
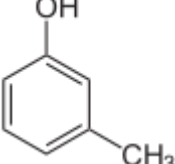
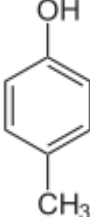
❖ Uses of Phenol

- Approximately two-third of the total phenol produced worldwide is used to prepare reagents used in plastic manufacturing industries.
- The polymerization reaction of phenol with formaldehyde is used to commercially prepare phenolic resins.
- Phenol is also used in the study and extraction of bio-molecules. Molecular biology finds application of phenol in the extraction of nucleic acids from tissue samples for further investigations.
- Phenol is also used in cosmetic industry in the manufacturing of sunscreens, skin lightening creams and hair coloring solutions.
- Phenol is also a versatile precursor to a large collection of drugs, most notably aspirin but also many herbicides and pharmaceutical drugs.

"Diamonds are a girl's best friend" is a well-known saying. Diamonds are created from carbon under extreme pressurize and over time, so carbon will eventually become "a girl's best friend" - hence her "future best friend."

CRESOLS

- **Cresols** (also hydroxytoluene) are organic compounds which are methylphenols. They are a widely occurring natural and manufactured group of aromatic organic compounds, which are categorized as phenols (sometimes called phenolics).
- Cresols have a disinfectant and corrosive effect due to the degradation of proteins.

Isomers of Cresol			
Structural formula			
General			
Common name	o-cresol	m-cresol	p-cresol
Systematic name	2-methylphenol	3-methylphenol	4-methylphenol
Other names	<i>ortho</i> -cresol	<i>meta</i> -cresol	<i>para</i> -cresol
Molecular formula	C ₇ H ₈ O		
Molar mass	108.14 g/mol		
Appearance at room temperature and pressure	colorless crystals	thicker liquid	greasy-looking solid
Properties			
Density and phase	1.05 g/cm ³ , solid	1.03 g/cm ³ , liquid	1.02 g/cm ³ , liquid
Solubility in water at 20–25 °C	2.5 g/100 ml	2.4 g/100 ml	1.9 g/100 ml
Soluble in strongly alkaline water			
Melting point	29.8 °C	11.8 °C	35.5 °C
Boiling point	191.0 °C (464.2 K)	202.0 °C (475.2 K)	201.9 °C (475.1 K)
Acidity (pK _a)	10.28	10.09	10.26
Toxicity (LD ₅₀ in Rats)	1.35 g/kg, oral	2.02 g/kg, oral	1.8 g/kg, oral

❖ Uses of Cresols

- Mixed cresols are used as disinfectants, preservatives, and wood preservatives.
- **o-Cresol** is used as a solvent, disinfectant, and chemical intermediate.
- **m-Cresol** is used to produce certain herbicides, as a precursor to the **pyrethroid insecticides**, to produce antioxidants and to manufacture the explosive, 2,4,6-nitro-m-cresol.
- **p-Cresol** is used largely in the formulation of antioxidants and in the fragrance and dye industries.
- **Uses for various Drugs Synthesis:**
 - *o*-Cresol used for synthesis of Carvacrol.
 - *m*-Cresol used for synthesis of Toliprolol, Tolamolol etc.
 - *p*-Cresol is consumed mainly in the production of antioxidants, e.g., **Butylated HydroxyToluene (BHT)**

Note By: *Pyrethroid insecticides* are a special chemical class of active ingredients found in many of the modern insecticides found on store shelves and used by pest management professionals. The name **pyrethroid** means “**pyrethrum-like**” and refers to the origin of this class of pesticides.

❖ **Health Hazard Information**

▪ **Acute Effects:**

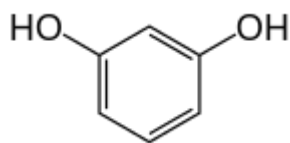
- Acute inhalation exposure by humans to mixed cresols results in respiratory tract irritation, with symptoms such as dryness, nasal constriction, and throat irritation. Mixed cresols are also strong dermal irritants.

▪ **Chronic Effects (Noncancerous):**

- No information is available on the chronic effects of mixed cresols in humans.
- Animal studies have reported effects on the blood, liver, kidney, and CNS, as well as reduced body weight, from oral and inhalation exposure to mixed cresols.

RESORCINOL

- **Resorcinol** (or resorcin) is a benzenediol (*m*-dihydroxybenzene).



Preferred IUPAC name	Benzene-1,3-diol
Other names	Resorcinol; Resorcin, <i>m</i> -Dihydroxybenzene, 1,3-Benzenediol, 1,3-Dihydroxybenzene, 3-Hydroxyphenol, <i>m</i> -Hydroquinone, <i>m</i> -Benzenediol
Chemical formula	C ₆ H ₆ O ₂
Molar mass	110.1 g/mol
Appearance	White solid, turns pink on exposure to air, light, and iron
Odor	Faint
Density	1.28 g/cm ³ , solid
Melting point	110 °C (230 °F; 383 K)
Boiling point	277 °C (531 °F; 550 K)
Solubility in water	110 g/100 mL at 20 °C
Acidity (pK_a)	9.15

❖ Uses of Cresols

▪ Medicinal Uses

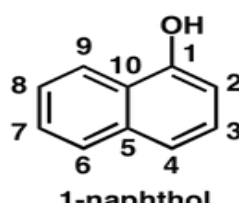
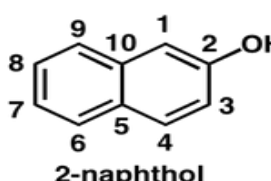
- It is an antiseptic and disinfectant, and is used 5 to 10% in ointments in the treatment of chronic skin diseases such as psoriasis, hidradenitis suppurativa, and eczema.
- It has also been employed in the treatment of gastric ulcers in doses of 125 to 250 mg in pills, and is said to be analgesic and hemostatic (stops bleeding) in its action.
- A 2% solution used to treat external vaginal itching and irritation.
- **Resorcinol** is a skin protectant and topical analgesic.

▪ Chemical Uses

- It is used in the production of diazo dyes and plasticizers and as a UV absorber in resins.
- Resorcinol is an analytical reagent for the qualitative determination of ketoses (Seliwanoff's test).
- Resorcinol reacts with formaldehyde to form a thermoset resin which can form the basis of an **aerogel** (frozen smoke).

Naphthol

- Naphthol is a fluorescent colorless (or occasionally yellow) crystalline solid with the formula $C_{10}H_7OH$. It has two isomer of 1-naphthol and 2-naphthol, differing by the location of the hydroxyl group on the naphthalene ring. The naphthols are naphthalene homologues of phenol, but more reactive.

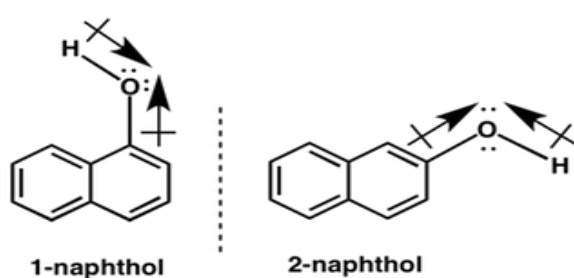
Isomers of Naphthol		
Structural formula	 <p style="text-align: center;">1-naphthol</p>	 <p style="text-align: center;">2-naphthol</p>
IUPAC name	Naphthalen-1-ol	Naphthalen-2-ol
Other names	1-Hydroxynaphthalene; 1-Naphthalenol; alpha-Naphthol	2-Hydroxynaphthalene; 2-Naphthalenol; beta-Naphthol; Naphth-2-ol
Molecular formula	$C_{10}H_8O$	$C_{10}H_8O$
Molar mass	144.17 g/mol	144.17 g/mol
Appearance at room temperature and pressure	Colorless or white solid; commercial material is often strongly colored	Colorless crystalline solid
Density	1.10 g/cm ³	1.280 g/cm ³
Solubility	Both isomers are soluble in simple alcohols, ethers, and chloroform.	
Melting point	95 to 96 °C	121 to 123 °C

✓ Polarity of naphthols

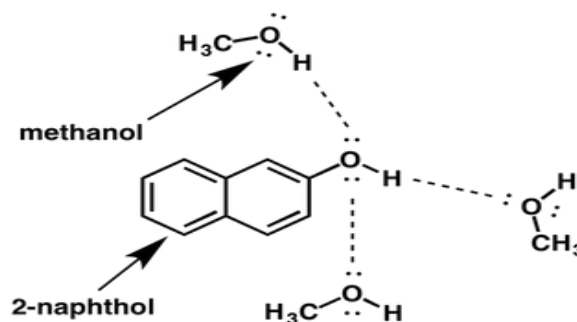
- Since naphthols contain a hydroxyl group, it's a highly polar molecule, with the oxygen atom attracting electron density through the bonds toward itself. For a molecule to be polar, there has to be a difference in electronegativity (the ability of an atom to attract electrons to itself) between one or more atoms, and in the case of naphthol, oxygen is more electronegative than both carbon and hydrogen.
- For this reason, it can 'hog' more of the electron density in the form of the bonds, making it polar.

✓ Solubility

- In terms of the solvents that naphthol is soluble in (things it will form solutions with), it's very versatile. Because of the presence of the hydroxyl group, it can hydrogen bond with other alcohol-based (polar) solvents like ethanol, methanol, and isopropanol. The ability to form these hydrogen bonds makes it readily soluble in these kinds of solvents. For example, consider the case of 2-naphthol forming hydrogen bonds with methanol molecules



Polarity of naphthol



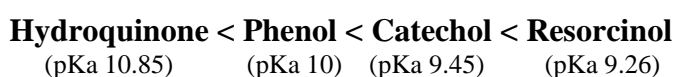
Naphthol forming hydrogen bonds with methanol molecules

❖ Uses of Naphthols

- Naphthols (both 1 and 2 isomers) are used as biomarkers for livestock and humans exposed to polycyclic aromatic hydrocarbons
- 1-Naphthol is a precursor to a variety of insecticides including carbaryl and pharmaceuticals including nadolol. It undergoes azo coupling to give various azo dyes, but these are generally less useful than those derived from 2-naphthol.
- In **Molisch's test**, 1-naphthol dissolved in ethanol, known as Molisch's reagent, is used as reagent for detecting the presence of carbohydrates.
- The **Sakaguchi test** uses 1-naphthol with sodium hypobromite to detect the presence of arginine in proteins.
- The **Voges-Proskauer Test** uses 1-naphthol in potassium hydroxide (KOH) solution to detect the breakdown of glucose into acetoin which is used by bacteria for external energy storage. A positive test will be indicated by the appearance of a red color of the original yellow solution.

❖ What is the order of acidic strength among phenol, catechol, resorcinol and hydroquinone?

- Resorcinol is more acidic than catechol, followed by phenol. Because
 - **Hydroquinone**: strong +M effect and weak -I effect
 - **Phenol**: the normal resonance in all phenols
 - **Resorcinol**: -I effect
 - **Catechol**: +M effect, stronger -I effect and hydrogen bonding
- Taking these factors into account, it is easy to see why hydroquinone is least acidic. Hydrogen bonding and the vicinity of the -OH to the anion (for the stronger -I effect) make catechol more acidic than the phenol despite its +M contribution. Resorcinol has only -I effect and no counteracting electron-donating effects, which makes it the most acidic.



Organic Chemistry has become a vast rubbish heap of puzzling and bewildering compounds.