

Aromatic Heterocyclics

Aromaticity		Cyclic structure. Planar structure that allows an uninterrupted delocalized π electron system. Number of π electrons = $4n+2$.			
Types		6-membered	5-membered		
		Pyridine	Thiophene	Pyrrole	Furan
Structure		6-membered N containing aromatic heterocyclic. All atoms are sp^2 . Lone pair on N is localized.	5-membered S containing aromatic heterocyclic. All atoms are sp^2 hybridized. One of the lone pairs on S is delocalized.	5-membered N containing aromatic heterocyclic. All atoms are sp^2 hybridized. The lone pair on N is delocalized.	5-membered O containing aromatic heterocyclic. All atoms are sp^2 hybridized. One of the lone pairs on O is delocalized.
Properties	Boiling Point	Higher boiling point than benzene due to pd-pd interactions.	Similar to benzene due to mainly intermolecular id-id interactions. Electronegativity of S is similar to C and electron cloud size of thiophene is similar to benzene.	Higher than benzene and pyridine due to intermolecular pd-pd and id-id interactions. H-bonding not possible due to delocalization of lone pairs on N into the ring.	Lowest due to mainly id-id interactions since its dipole moment is reduced by the partial donation of the lone pair on O into the ring.
	Solubility	Soluble in water due to ability to H-bond with water.	Not soluble in water.	Poor solubility in water due to slight polarity and inability to form H-bonds with water.	Poor solubility in water due to slight polarity and inability to form H-bonds with water.
	Basicity	Basic since lone pair of electrons on N are in the sp^2 orbital in the plane to the ring and are localized. Weaker base than NH_3 and alkyl amines since electrons in sp^2 orbitals are closer to and more strongly attracted to the nucleus and less available for protonation.	-	Very weak base since the lone pair on N are delocalized into the π system and not available for protonation.	-
	Aromaticity	-	The extent of delocalization varies inversely with the electronegativity of the heteroatom (i.e. furan < pyrrole < thiophene) since a more electronegative heteroatom holds on to its electron density more greatly and the resonance structures with a positive charge on the heteroatom make less of a contribution to the resonance hybrid.		
Reactions	Acid-Base	Mild tertiary amine base to neutralize acids formed.	-	Protonated under very strong acidic conditions. Aromaticity lost in the process.	-
	Electrophilic Substitution	Susceptibility	Thiophene, pyrrole and furan are all more reactive than benzene towards electrophilic substitution since: a. The lone pair of electrons on the heteroatom is donated to the ring, making it more electron rich. b. The aromatic sextet is delocalized over 5 atoms instead of 6 and hence they are more highly activated. Hence, milder reagents and conditions or the presence of deactivating groups are often necessary to control the reactions. Electron withdrawing substituents make further substitution on the heterocycle more difficult, adding chemical stability to the ring and enabling reactions to be performed in Lewis acids.		
			Thiophene has the lowest reactivity since it is a Period 3 element and its 3p orbitals overlap less efficiently with the 2p orbitals of the carbocation. Hence, charge dispersal by resonance is limited, forming a less stable carbocation intermediate.	Pyrrole is more reactive than furan since N is less electronegative than O and its lone pair of electrons is more readily delocalized over the carbocation intermediate, stabilizing its positive charge. Both pyrrole and furan are more reactive than thiophene and hence are unstable in the presence of mineral acids.	
		Directing Effects	Electrophilic substitution can take place at C3 where electron density is highest. Attack at C2 and C4 results in a positive charge on the electronegative N atom, making the intermediate unstable. Pyridines with electron donating substituents can activate it towards electrophilic substitution. Such substituents are 2,4-directing.		
		Conditions	Vigorous reaction conditions. No Friedel Crafts Alkylation.	Nitrated using acetyl nitrate (HNO_3 in acetic anhydride). Acylated with acyl chlorides or acid anhydrides with $AlCl_3$ or $SnCl_4$ as the Lewis acid catalyst.	Nitrated using acetyl nitrate since it is unstable to mineral acids. Acylated at $0^\circ C$ with acid anhydride and BF_3 as the Lewis acid catalyst since it is unstable to strong Lewis acids. Monobrominated by Br_2 in dioxane at $0^\circ C$. Brominated by Br_2 in methanol.
	Nucleophilic Aromatic Substitution	Remarks	Pyridine can be oxidized to pyridine N-oxide using H_2O_2 in acetic acid. The electrons on O are delocalized into the pyridine ring, enhancing the electron density an activating it. Electrophilic substitution occurs at C2 and C4 due to a higher electron density, but primarily at C4 due to repulsion between the electrophile and the positively charged N. The oxide can be removed using trivalent P compounds (PCl_3).	-	- Nitration of furan involves the electrophilic addition of NO_2^+ followed by the nucleophilic addition of CH_3COO^- on C4, resulting in 1,4 addition and forming a stable addition product. When pyridine is added to remove a proton, the nitro-substituted product is obtained. Furan can undergo acid hydrolysis to give butane dialdehyde.
		Susceptibility	2-,4-substituted halopyridines are more susceptible towards nucleophilic aromatic substitution compared to unsubstituted pyridines since the halide is a better leaving group than a hydride.	-	-
		Directing Effects	Nucleophilic aromatic substitution can take place at C2 or C4 due to the decreased π electron density at these positions and the formation of the most stable intermediate anion where the negative charge is on the most electronegative N atom.	-	-
	Nucleophilic Aromatic Substitution	Conditions	$NaNH_2$, $140^\circ C$ to give 2-aminopyridine. $R-NH_2$ to give amine. $R-O^-$ to give ether.	-	-