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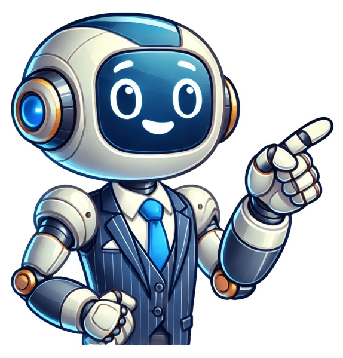

We're getting everything ready for you. The page is loading, and you'll be on your way in just a few moments. Thanks for your patience! Written by J.A Dobado | Last Updated on April 22, 2024What are aromatic heterocycles?A heterocyclic compound is an organic compound in which one or more of the carbon atoms in the backbone of the molecule has been replaced by an atom other than carbon. Typical heteroatoms include nitrogen, oxygen and sulphur. Of this group, those that obey Hückel's rule are called aromatics.Heterocycles with 6 atoms and 6 electrons πAzabenzene (pyridine).Fully unsaturated 6-membered heterocycles can be considered as a benzene molecule in which one or more carbon atoms have been replaced by a heteroatom.Pyridine (or azabenzene) is the simplest of these compounds, with one nitrogen atom in the ring.Like benzene, pyridine is planar, and the only structural difference with benzene is the distortion caused by the shorter distance C—N than that of the C-C bond.It can be represented by a cyclic structure consisting of 5 carbon atoms sp2 to each of which is bonded a hydrogen, and a nitrogen atom sp2.Each of the 6 atoms in the ring has an p orbital orthogonal to the plane of the ring. It has a structure similar to benzene.A complete cycle of p orbitals with 6 electrons, but differs in that it has an unshared pair of electrons from nitrogen in the plane of the ring.Like benzene, pyridine can be represented by two Kekulé resonance structures.The theory of molecular orbitals (TOM) is used to interpret the electronic structure of benzene and pyridine. The atomic orbitals combine to form molecular orbitals.In the Hückel approach, the electrons in the p orbitals are treated independently of those forming the σ bonds in the plane of the ring.The 6 p orbitals combine to give 6 delocalized π molecular orbitals each of which can contain a maximum of 2 electrons.The calculation of the energy of these orbitals leads us to conclude that three of them have lower energy than the isolated p, while the energy of the other three is higher.The three lowest energy orbitals (π bonding orbitals) can accommodate the 6 electrons.The higher energy orbitals (π* anti-bonding) remain empty.Hückel aromaticity rulesHückel defines aromatic molecules as:Planar molecules that present a complete and uninterrupted cycle of p orbitals, stabilizes when they have (4n + 2) πelectrons, for n = 0, 1, 2, 3, 4, … etc.Benzene, pyridine, and other analogs with 6 π electrons obey the Hückel rule when n = 1, so they are classified as aromatic molecules.When we plot the π orbitals of benzene and pyridine, it is observed that the size of the circles roughly indicates the relative coefficients of the orbitals, and the red and blue circles indicate the opposite phases of the wave functions.fig-01 (OM benceno y piridina)The orbitals of pyridine are similar to benzene but there are two notable differences:The π orbitals of pyridine are of lower energy than those of benzene, a consequence of the higher electronegativity of nitrogen relative to carbon.The higher energy (HOMO) occupied OM molecular orbitals of benzene are degenerate (of equal energy), π2 and π3. The HOMO of pyridine have different energy (the π2 has lower energy than the π3). The π2 orbital of pyridine is the HOMO. In addition, the π2 has a large coefficient in nitrogen.The relationship between the structure of benzene and that of pyridine also applies to other six-membered conjugated ring systems with more than one nitrogen atom.The HOMO energy decreases as the number of nitrogens increases. Similarly, so does the LUMO, so the HOMO–LUMO difference is constant.In the pyridine and related heterocycles there is lower electron density π on the carbon atoms of the ring compared to the benzene. This is especially noticeable at the ortho and para positions.For this reason these heterocycles are called π-deficient heterocyclic compounds.Other heterobenzenesThe only atom other than nitrogen in the first row of the periodic table that can replace the CH group of benzene in an uncharged aromatic heterocycle is boron.Borabenzenes, despite their very simple structure and the strength of the B—C bond, have not been isolated in the free state (without a donor ligand on the boron atom) because they are powerful Lewis acids.Some of its complexes have been prepared and 1H-boratobenzene, which is similar to benzene but charged, has been isolated as a lithium salt.On the other hand, uncharged aromatic heterocycles can also incorporate atoms such as silicon, phosphorus, arsenic, and of the second or subsequent row in groups 14 and 15.In addition, other group 16 heterocycles, including oxygen, sulfur, selenium and tellurium, can be included in the positively charged species.Heterocycles with 5 atoms and 6 electrons πUnsaturated planar heterocycles containing 5 atoms can be considered aromatic if they contain 6 electrons.There is no analogous carbocycle other than the cyclopentadienyl anion.This molecule has a symmetrical pentagon structure with 5 carbon atoms with sp2 hybridization and a cyclic set of 5 porbitals with 6 electrons.If we consider pyrrole, it can be an example of a 5-membered aromatic heterocycle. Pyrrole is a planar molecule, which indicates that the nitrogen atom has sp2 hybridization. Furthermore, the 3 σ bonds of nitrogen are located in the molecular plane, and the p orbital, oriented orthogonally to the molecular plane, contains the unshared electron pair.The p orbitals give rise to π clouds above and below the plane of the ring. They are formed by the p orbitals of the carbons and that of nitrogen. It is a cloud derived from 5 p orbitals, but containing 6 σ orbitals (nitrogen with 2). It therefore satisfies Hückel's rule of 4n + 2, when n = 1.The electron pair of nitrogen is involved in the formation of the π-electron cloud. Therefore, this leads to a lower basicityof pyrrole compared to pyridine. The molecular orbitals of pyrrole could be represented as follows:fig-01 (OM pirrol)It manifests itself in the splitting of the π2 and π3 orbitals, with π2, which is located on nitrogen, being the lowest energy orbital.The calculated p electron distribution in pyrrole shows that the ring system is electron rich (6 electrons in 5 atoms). In addition, it is observed that carbon atoms have a higher electron density in π than in benzene. Although this density is higher in nitrogen. Therefore, due to their higher electron density π in carbon, compared to benzene, they are called π-excedent heterocyclic compounds.The 5-membered aromatic heterocycle group is much larger than the 6-membered group because one of the atoms in the ring may be divalent and thus other heteroatoms, such as oxygen or sulfur (e.g., furan or thiophene), may be present.Furthermore, for these derivatives it is possible to construct neutral aromatic heterocycles by replacing one CH with a nitrogen.However, those containing additional nitrogen atoms to the carbons become increasingly deficient in π electrons as the number of nitrogens increases.Benzofused systemsCompounds with structures in which a benzene ring is fused to another aromatic ring retain their aromatic properties although somewhat modified.In naphthalene, the C1—C2 bond is shorter than C2—C3.The hexagonal symmetry of benzene is lost.However, naphthalenes retain the characteristic properties of aromatic compounds.Similarly, when a heterocycle is fused to a benzene ring, the system is classified as aromatic. Thus, we find the 6-membered nitrogen-fused compounds, such as azanaphthalenes:These compounds, such as naphthalene, show an alternation of bond lengths that is consistent with Kekulé structures.Another series of benzofused compounds would be formed by fused 5-membered heterocycles.They also have a high degree of aromaticity. In contrast, those in which the heterocycle binds to benzenethrough the C3—C4 bond, which is the longest of the C—C bonds, have a much lower degree of aromaticity, such as the heterocycles in the figure.There is, as detailed below, a great variety of heterocycles fused to structures other than benzene. Thus, some of them are very relevant as for example the case of purine.Purine.Aromaticity criteria in heterocyclesThermodynamic criteriaAntiaromatic systems are defined as conjugated cyclic systems that are thermodynamically less stable than the corresponding cyclic analogs.Aromatic when the delocalization energy of the cyclic system is greater than that of the acyclic system. (4n+2 Hückel).Non-aromatic when the delocalization energy of the cyclic system is equal to that of the acyclic system. (independientes).Antiaromatic when the delocalization energy of the cyclic system is less than that of the acyclic system. (4n Hückel).ExamplesAnti-aromatic heterocycles (anti-Hückel 4n).Cyclooctatetraene. a) planar antiaromatic (anti-Hückel 4n) structure. b) non-planar "non-aromatic" structure.Both the cation and anion of cyclooctatetraene are planar and are aromatic because they have 6e- and 10e- (Hückel's rule 4n+2), respectively.Bond lengthAromatic compounds, in general, show a bond distance intermediate between the standard double C=C and single C—Cbond values. In benzene, the carbon-carbon distance is 1.395 Å ≅ 1.4 Å, intermediate between the values of the C=Cdouble bond which is equal to 1.33 Å and that of the C—C single bond equal to 1.53 Å.For 6-membered heterocycles, this intermediate value is close to the relational values, always considering the perturbation caused by the heteroatom.Intermediate values between double and single bond for the 6-membered ones, and as a consequence there is a cyclic delocalization of the π electrons in those compounds.For the 5-membered rings there is a considerable degree of alternation which implies a localization of structures. Oxygen has the highest degree of localization.Fused heterocycles have a higher degree of localization.Different structural indices of aromaticity have been proposed as a function of bond distances that can quantify aromaticity in molecules. In the figure, data for different heterocycles are summarized.Percentage (%) aromaticity of different heterocycles (4n+2=6 Hückel π-electrons) compared to benzene.NMR spectroscopy on heterocyclesThe low-field displacement of aromatic protons relative to vinyl protons is justified, due to an induced circular diamagnetic current opposing the external field, inside the ring (ring diamagnetic current).This does not occur in antiaromatic compounds, and therefore the aromaticity of a carbocycle can be measured by its NMR data.In heterocycles there is no rule, since it is not easy to find antiaromatic heterocyclic compounds for comparison.Chemical shifts are influenced by factors other than the induced diamagnetic current, including distortion of the electron distribution π and the solvent effect.A summary of the values of the chemical shifts (δH) of the heterocycles is presented in the following figure. The effect of the diamagnetic current, as can be seen is more qualitative than quantitative. A decreasing current is observed in the following order: benzene pyridine > thiophene > pyrrole > furan.The delocalization energy in pyridine and other benzenoid rings is the same as that of benzene, if the perturbation caused by the exchange of CH for nitrogen is not considered. Thus, they are progressively lower for other heterocycles: quinoline, pyrimidine, pyrrole and thiophene.Aromatic character and other types of unsaturated heterocyclesMonocyclic systems obeying Hückel's ruleMany heterocycles obeying Hückel's rule have been synthesized in unsaturated monocyclic systems. Thus, the heterocycle, usually nitrogenous, can form part of a double bond, as in pyridine, or donate a pair of electrons to the πsystem, as in pyrrole.For heterocycles of the type:we would be in the limiting case, but there is no evidence that a planar cyclic structure having 6 π electrons is favored in such compounds.Ozone, for example, is not cyclic and some triaziridine that has been isolated reverts rapidly to the open form. The results of OM calculations indicate pyramidal nitrogen and cyclic structures with higher energies than for the linear forms.In 4-membered systems of the type:only the dithiete has been isolated:and there is no certainty that the ring is aromatic.On the other hand, different heterocycles with 10 π electrons of different types have been synthesized. Thus, heterocycles with cis double bonds have been obtained, incorporating a pyrrole nitrogen in a 9-membered ring, or two nitrogens in an 8-membered ring, as shown in the figures.Despite the strain, both compounds appear to be flat enough to support an annular current unless the substituents (-R) are strongly electron withdrawing.In this case, the structures will not be planar, due to a higher localization, of the electron pairs, on the heteroatoms, when -R is electron-withdrawing.A third type of structure is one containing two transoidal double bonds joined by a methylene bridge. The system is shown in figure.They can be considered aromatic, according to bond length criteria and their 1H NMR spectra.However, there are still some larger aza-anulenes containing 14 π or 18 π electrons. Their aromaticity has been revealed by their 1H NMR spectra.There are also some fused heterocycles other than benzofused ones that show signs of cyclic delocalization. Indolizine, for example, shows considerable resonance energy,In addition, the heterocycle pyrroloindolizine (pyrrolo[2,1,5,cd]indolizine) also shows electron delocalization on the 3 rings.Tautomerism of heteroaromatic compoundsMany heteroaromatic compounds can exist in two or more tautomeric forms. The most typical example is the pyridines which have a hydroxyl or amine substituent at the α position. Then, the hydroxyl or one of the amine protons can be located either on the heteroatom or on the heterocycle.Equilibria are usually established in solution, by rapid proton transfer.These equilibria are of particular importance in pyrimidine and purine derivatives, because they are part of nucleic acids.If a tautomer is predominant in solution, its structure is usually represented as such, and this is detected by comparison of its spectroscopic data with its alkylated derivatives.Examples:The spectroscopic data of 2-pyridone are very close to those of N-methyl-2-pyridone.Chemical shifts of nitrogens in (15N-RMN) are often used to assign the preferred structure of a tautomeric equilibrium.In another example, pyrazine-2-thione, exists (according to 15N-RMN shift data) as shown in the figure, 97 % as 2-thione.Polar solvents can shift equilibria, as the tautomers are solvated differently.Tautomers generally differ in polarity and in their ability to form hydrogen bonds with the solvent. However, it should be clarified that chemical reactions do not necessarily take place on the predominant structure of a mixture of tautomers. Particularly if proton transfer occurs rapidly.There are other types of tautomerism (e.g., the first 3-hydroxy-pyrimidine ↔ pyrimidinium oxide equilibrium) in aromatic heterocycles collected in the following scheme: Share — copy and redistribute the material in any medium or format for any purpose, even commercially. Adapt — remix, transform, and build upon the material for any purpose, even commercially. The licensor cannot revoke these freedoms as long as you follow the license terms. Attribution — You must give appropriate credit , provide a link to the license, and indicate if changes were made . You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use. ShareAlike — If you remix, transform, or build upon the material, you must distribute your contributions under the same license as the original. No additional restrictions — You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits. You do not have to comply with the license for elements of the material in the public domain or where your use is permitted by an applicable exception or limitation . No warranties are given. The license may not give you all of the permissions necessary for your intended use. For example, other rights such as publicity, privacy, or moral rights may limit how you use the material. Many unsaturated cyclic compounds have exceptional properties that we now consider characteristic of "aromatic" systems. The following cases are illustrative: Compound Structural Formula Reaction with Br2 Thermodynamic Stabilization 1,3-Cyclopentadiene Addition (0 ºC) Slight 1,3,5-Cycloheptatriene Addition (0 ºC) Slight 1,3,5,7-Cyclooctatetraene Addition (0 ºC) Slight Benzene Substitution Large Pyridine Substitution Large Furan Substitution (0 ºC) Moderate Pyrrole Substitution Moderate Benzene is the archetypical aromatic compound. It is planar, bond angles=120º, all carbon atoms in the ring are sp2 hybridized, and the pi-orbitals are occupied by 6 electrons. The aromatic heterocycle pyridine is similar to benzene, and is often used as a weak base for scavenging protons. Furan and pyrrole have heterocyclic five-membered rings, in which the heteroatom has at least one pair of non-bonding valence shell electrons. By hybridizing this heteroatom to a sp2 state, a p-orbital occupied by a pair of electrons and oriented parallel to the carbon p-orbitals is created. The resulting planar ring meets the first requirement for aromaticity, and the π-system is occupied by 6 electrons, 4 from the two double bonds and 2 from the heteroatom, thus satisfying the Hückel Rule. Four illustrative examples of aromatic compounds are shown above. The sp2 hybridized ring atoms are connected by brown bonds, the π-electron pairs and bonds that constitute the aromatic ring are colored blue. Electron pairs that are not part of the aromatic π-electron system are black. The first example is azulene, a blue-colored 10 π-electron aromatic hydrocarbon isomeric with naphthalene. The second and third compounds are heterocycles having aromatic properties. Pyridine has a benzene-like six-membered ring incorporating one nitrogen atom. The non-bonding electron pair on the nitrogen is not part of the aromatic π-electron sextet, and may bond to a proton or other electrophile without disrupting the aromatic system. In the case of thiophene, a sulfur analog of furan, one of the sulfur electron pairs (colored blue) participates in the aromatic ring π-electron conjugation. The last compound is imidazole, a heterocycle having two nitrogen atoms. Note that only one of the nitrogen non-bonding electron pairs is used for the aromatic π-electron sextet. The other electron pair (colored black) behaves similarly to the electron pair in pyridine. Heterocycles – cyclic structures in which the ring atoms may include oxygen or nitrogen – can also be aromatic. Pyridine, for example, is an aromatic heterocycle. In the bonding picture for pyridine, the nitrogen is sp2-hybridized, with two of the three sp2 orbitals forming sigma overlaps with the sp2 orbitals of neighboring carbon atoms, and the third nitrogen sp2 orbital containing the lone pair. The unhybridized p orbital contains a single electron, which is part of the 6 pi-electron system delocalized around the ring. another image of orbitals in pyridine Why do we not assume that the nitrogen in pyrrole is sp3-hybridized, like a normal secondary amine? The answer is simple: if it were, then pyrrole could not be aromatic, and thus it would not have the stability associated with aromaticity. In general, if a molecule or group can be aromatic, it will be, just as water will always flow downhill if there is a downhill pathway available. Imidazole is another important example of an aromatic heterocycle found in biomolecules – the side chain of the amino acid histidine contains an imidazole ring. In imidazole, one nitrogen is 'pyrrole-like' (the lone pair contributes to the aromatic sextet) and one is 'pyridine-like' (the lone pair is located in an sp2 orbital, and is not part of the aromatic sextet). 1. Draw the orbitals of thiophene to show that is aromatic. 2. The following ring is called a thiazolium ring. Describe how it is aromatic. Contributors Heterocyclic compounds contain at least one heteroatom (atom other than carbon) in the cyclic ring structure. The three most frequent heteroatoms are nitrogen (N), oxygen (O), and sulfur (S). Heterocyclic compounds are commonly found in plants and animal products, and they are a key element of over half of all known natural organic compounds. Some examples of natural heterocyclic compounds include alkaloids, natural colors, medicines, proteins, enzymes, and so on. Saturated heterocyclic molecules act similarly to acyclic derivatives but with different steric properties. The usual amines and ethers in this category are piperidine and tetrahydrofuran. However, because of their unstrained nature, unsaturated heterocyclic compounds with 5- and 6-member rings have received a great deal of attention. Pyridine, Thiophene, Pyrrole, Furan, and it's benzo fused derivatives are examples of unstrained unsaturated heterocyclic compounds. Many of these heterocyclic aromatic chemicals are components of key biological molecules, such as DNA and RNA bases and pharmaceuticals. The Hantzch-Widmann nomenclature system is the most important system approved by IUPAC for the nomenclature of heterocyclic compounds. The nature, position, ring size, number, and type of heteroatoms present in each heterocyclic compound are all specified by this naming system. Name: Prefix + Stem + Suffix The following are significant considerations for the systematic nomenclature of heterocyclic compounds. 1. In this nomenclature, the nomenclature of heterocyclic compounds is assigned by combining the 'prefix' (which indicates the presence of a heteroatom) with the stem (which indicates the ring size as well as the saturation and unsaturation in the ring) and the suffixes. When the prefix is followed by a vowel, the final 'a' is dropped. 2. the nomenclature of heterocyclic compounds begins with the heteroatom. If a heterocyclic compound contains more than two separate heteroatoms, the prefixes are stated in the order. 3. When two or more hetero atoms of the same kind are present in a heterocyclic compound, they are denoted by di-, tri-, and so on. 4. The position of the saturated atom is denoted numerically by the prefix 'H-' as part of the ring system's name. It should be noted that where there is a choice of numbering, the indicated place is given the lowest possible number. 5. The stem indicates the size of a monocyclic ring (three to ten membered rings). Prefix for heteroatom in preferential order S.NHeteroatomSymbolPrefix1.OxygenOOxa2.SulfurSThia3.SeleniumSeSelena4.NitrogenNAza5.PhosphorousPPhospha6.ArsenicAsArsa7.AntimonySbStiba Prefix for Heteroatoms in preferential order. S.NRing sizeUnsaturated RingSaturated Ring1.3irenIrane2.4eteEtane3.5OleOlane4.6ineInane5.7epineEpane Some examples of heterocyclic compounds Based on the structure the compound is classified into five different types they are: Three-Membered Heterocyclic Compounds Four-Membered Heterocyclic Compounds Five-Membered Heterocyclic Compounds Six-Membered Heterocyclic Compounds Condensed or Fused Heterocyclic Compounds Aziridine, oxirane (or ethylene oxide), and thiirane are three-membered ring heterocycles containing single atoms of nitrogen, oxygen, and sulfur, respectively. The Gabriel ring closure: The aziridine was first produced in 1888 by heating ß-bromomethylamine in the presence of KOH. The most prevalent three-membered heterocycles are oxiranes (epoxides). Epoxides are easily synthesized by reacting alkenes with peracids, and they typically have high stereospecificity. One of the most common ways of epoxidation is the addition of an oxygen atom to an alkene with peroxycarboxylic acids. Epoxides are more reactive than unstrained ethers due to the high-angle strain of the three-membered ring. The most general reaction class is addition reactions that proceed via electrophilic or nucleophilic ring opening. The oxirane ring can also be opened via hydrolysis, which is the breaking of a bond followed by the addition of water components (H and OH). This reaction produces ethylene glycol (HOCH2CH2OH), which is used as an antifreeze in cooling and heating systems, brake fluid, and as a solvent in the paint and plastics industries. Alkenes react with electrophilic sulfur reagents to generate α-halo-β-sulfur intermediates, which can subsequently be induced to cyclize to thiiranes. Thiirane-ringed molecules are more bactericidal than oxirane-ringed molecules, and some thiirane derivatives have been used as tuberculostats (drugs that inhibit the growth of tuberculosis-causing bacteria), whereas thiirane 1 oxides are insecticides, molluscicides, or herbicides. These heterocyclic compounds have four atoms that can be either saturated or unsaturated. Azetidine, oxetane, and thietane are four-membered rings that each contain one nitrogen, oxygen, or sulfur atom. Azetidines can be prepared by cyclization by nucleophilic substitution of amine nucleophiles. (2+ 2) cycloaddition of alkene to the carbonyl compounds produces oxetane. 1,3 dibromo propane reacts with Na2S to produce thietane. There are five atoms in these heterocyclic rings. This family's parent aromatic chemicals are pyrrole, furan, and thiophene. A pyrrole is formed via the condensation of a 1,4-dicarbonyl molecule with an excess of a primary amine or ammonia. Pyrrole rings can be found in the amino acids proline and hydroxyproline, which are found in many proteins and are especially abundant in collagen, the structural protein of bones, tendons, and skin. The acid-catalyzed cyclization of 1,4-dicarbonyl compounds produces furan. It is known as the Paal-Knorr synthesis. Many sugars exist in molecular forms known as furanoses, which have the tetrahydrofuran ring structure. Maleic anhydride and phthalic anhydride are industrially important furan derivatives that are components of resins and polymers. Gewald developed this approach in 1966. Gewald synthesis is the most common method for producing 2- aminothiophenes. It is made up of the base-catalyzed condensation of a ketone with a CH2 group and a ß-ketonitrile to create an olefin, followed by cyclization with elemental sulfur. These heterocyclic compounds are created by substituting one of the carbon atoms with a hetero atom containing a single pair of electrons. Pyridine is a common example of six-membered heterocyclic compounds. Pyridine, as well as picolines, lutidines, and collidines, can be found in coal tar and bone oil. Pyridine derivatives are extremely important in biology. For example, nicotinic acid is more widely known as niacin, a B-complex vitamin. The Bohlmann-Rahtz Pyridine Synthesis produces substituted pyridines in two stages. Condensation of enamines with ethynyl ketones produces an amino diene intermediate, which undergoes cyclodehydration after heat-induced E/Z isomerization to produce 2,3,6-trisubstituted pyridine. Agrochemicals and pharmaceuticals both use heterocyclic compounds. Heterocyclic compounds are utilized as starting materials in organic chemical synthesis. In corrosion inhibitors, sanitizers, anti-ordinates, and developers, heterocyclic chemicals are utilized. Pesticides, dyes, and plastics all contain heterocyclic compounds. They serve as industrial solvents, intermediates in the manufacture of other compounds, and corrosion inhibitors. Epoxides are also utilized to make polymers, adhesives, and sealants. Pyrrole and its derivatives are frequently employed as intermediates in the manufacture of pharmaceuticals, pharmaceuticals, agrochemicals, dyes, photographic chemicals, fragrances, and other organic compounds. They are utilized as polymerization catalysts, preservatives, and solvents for resin and terpenes. They serve as the gold standard for chromatographic analysis. They are essential raw ingredients in the chemical industry. They are utilized in dental care products as an antimicrobial. They are employed as a solvent suited for dehalogenation. They are employed as a disinfectant. They are utilized as a ligand in coordination chemistry. About Author Molecule with one or more rings composed of different elements For other uses of "ring structure", see Ring structure. For the journal, see Heterocycles (journal). Structures and names of common heterocyclic compounds Pyridine, a heterocyclic compound A heterocyclic compound or ring structure is a cyclic compound that has atoms of at least two different elements as members of its ring(s).[1] Heterocyclic organic chemistry is the branch of organic chemistry dealing with the synthesis, properties, and applications of organic heterocycles.[2] Examples of heterocyclic compounds include all of the nucleic acids, the majority of drugs, most biomass (cellulose and related materials), and many natural and synthetic dyes. More than half of known compounds are heterocycles.[3] 59% of US FDA-approved drugs contain nitrogen heterocycles.[4] The study of organic heterocyclic chemistry focuses especially on organic unsaturated derivatives, and the preponderance of work and applications involves unstrained organic 5- and 6-membered rings. Included are pyridine, thiophene, pyrrole, and furan. Another large class of organic heterocycles refers to those fused to benzene rings. For example, the fused benzene derivatives of pyridine, thiophene, pyrrole, and furan are quinoline, benzothiophene, indole, and benzofuran, respectively. The fusion of two benzene rings gives rise to a third large family of organic compounds. Analogs of the previously mentioned heterocycles for this third family of compounds are acridine, dibenzothiophene, carbazole, and dibenzofuran, respectively. Heterocyclic organic compounds can be usefully classified based on their electronic structure. The saturated organic heterocycles behave like the acyclic derivatives. Thus, piperidine and tetrahydrofuran are conventional amines and ethers, with modified steric profiles. Therefore, the study of organic heterocyclic chemistry focuses on organic unsaturated rings. Some heterocycles contain no carbon. Examples are borazine (B3N3 ring), phosphazene (P3N3 ring), and tetrasulfur tetranitride (S4N4 ring). In comparison with organic heterocycles, which have numerous commercial applications, inorganic ring systems are mainly of theoretical interest. IUPAC recommends the Hantzsch-Widman nomenclature for naming heterocyclic compounds.[5] "Heteroatoms" are atoms in the ring other than carbon atoms. Names in italics are retained by IUPAC and do not follow the Hantzsch-Widman nomenclature Some of the names refer to classes of compounds rather than individual compounds. Also no attempt is made to list isomers. Although subject to ring strain, 3-membered heterocyclic rings are well characterized.[6] Three-membered rings with one heteroatom Heteroatom Saturated Unsaturated Boron Borirane Borirene Nitrogen Aziridine Azirine Oxygen Oxirane(ethylene oxide, epoxides) Oxirene Phosphorus Phosphirane Phosphirene Sulfur Thiirane(ethylene sulfide, episulfides) Thiirene Three-membered rings with two heteroatoms Heteroatoms Saturated Unsaturated 2 × Nitrogen Diaziridine Diazirine Nitrogen + Oxygen Oxaziridine Oxazirine Nitrogen + Sulfur Thiaziridine Thiazirine 2 × Oxygen Dioxirane (highly unstable) 2 × Sulfur Dithiirane (highly unstable) Four-membered rings with one heteroatom Heteroatom Saturated Unsaturated Boron Boretane Borete Nitrogen Azetidine Azete Oxygen Oxetane Oxete Phosphorus Phosphetane Phosphete Sulfur Thietane Thiete Four-membered rings with two heteroatoms Heteroatoms Saturated Unsaturated 2 × Nitrogen Diazetidine Diazete 2 × Oxygen Dioxetane Dioxete 2 × Sulfur Dithietane Dithiete The 5-membered ring compounds containing two heteroatoms, at least one of which is nitrogen, are collectively called the azoles. Thiazoles and isothiazoles contain a sulfur and a nitrogen atom in the ring. Dithioles have two sulfur atoms. A large group of 5-membered ring compounds with three or more heteroatoms also exists. One example is the class of dithiazoles, which contain two sulfur atoms and one nitrogen atom. Five-membered rings with one heteroatom Heteroatom Saturated Unsaturated Antimony Stibolane Stibole Arsenic Arsolane Arsole Bismuth Bismolane Bismole Boron Borolane Borole Germanium Germolane Germole Nitrogen Pyrrolidine(Azolidine not used) Pyrrole(Azole not used)Pyrroline (partially unsaturated) Oxygen Oxolane Furan(Oxole not used) Phosphorus Phospholane Phosphole Selenium Selenolane Selenophene Silicon Silolane Silole Sulfur Thiolane Thiophene(Thiole not used) Tellurium Tellurolane Tellurophene Tin Stannolane Stannole Five-membered rings with two heteroatoms Heteroatoms Saturated Unsaturated (and partially unsaturated) 2 × Nitrogen Pyrazolidine Imidazolidine Pyrazole (Pyrazoline)Imidazole (Imidazoline) Nitrogen + Oxygen OxazolidineIsoxazolidine Oxazole (Oxazoline)Isoxazole (Isoxazoline) Nitrogen + Sulfur ThiazolidineIsothiazolidine Thiazole (Thiazoline)Isothiazole (Isothiazoline) Oxygen + Sulfur OxathiolaneIsoxathiolane OxathioleIsoxathiole 2 × Oxygen Dioxolane Dioxole 2 × Sulfur Dithiolane Dithiole Five-membered rings with three heteroatoms Heteroatoms Saturated Unsaturated 3 × Nitrogen Triazole 2 Nitrogen + Oxygen Oxadiazole 2 Nitrogen + Sulfur Thiadiazole Nitrogen + 2 Oxygen Dioxazole Nitrogen + 2 Sulfur Dithiazole Five-membered rings with four heteroatoms Heteroatoms Saturated Unsaturated 4 × Nitrogen Tetrazole 3 Nitrogen + Oxygen Oxatriazole 3 Nitrogen + Sulfur Thiatriazole Five-membered rings with five heteroatoms Heteroatoms Saturated Unsaturated 5 × Nitrogen Pentazole 4 Nitrogen + Oxygen Oxatetrazole 4 Nitrogen + Sulfur Thiatetrazole The 6-membered ring compounds containing two heteroatoms, at least one of which is nitrogen, are collectively called the azines. Thiazines contain a sulfur and a nitrogen atom in the ring. Dithiines have two sulfur atoms. Six-membered rings with one heteroatom Heteroatom Saturated Unsaturated Ions Antimony Stibinane Stibinine Stibatabenzene cation Arsenic Arsinane Arsinine Arsatabenzene cation Bismuth Bisminane Bismine Bismatabenzene cation Boron Borinane Borinine Boratabenzene anion Germanium Germinane Germine Nitrogen Piperidine(Azinane not used) Pyridine(Azine not used) Pyridinium cation Oxygen Oxane Pyran(Oxine not used) Pyrylium cation Phosphorus Phosphinane Phosphinine Phosphininium cation[7] Selenium Selenane Selenopyran Selenopyrylium cation Silicon Silinane Siline Sulfur Thiane Thiopyran(Thiine not used) Thiopyrylium cation Tellurium Tellurane Telluropyran Telluropyrylium cation Tin Stanninane Stannine Six-membered rings with two heteroatoms Heteroatoms Saturated Unsaturated 2 × Nitrogen Piperazine PyrazinePyrimidinePyridazine Nitrogen + Oxygen Morpholine Oxazine Nitrogen + Sulfur Thiomorpholine Thiazine Oxygen + Sulfur Oxathiane Oxathiin 2 × Oxygen Dioxane Dioxin 2 × Sulfur Dithiane Dithiin Six-membered rings with three heteroatoms Heteroatoms Saturated Unsaturated 3 × Nitrogen Triazinane Triazine 3 × Oxygen Trioxane Trioxin 3 × Sulfur Trithiane Trithiin Six-membered rings with four heteroatoms Heteroatoms Saturated Unsaturated 4 × Nitrogen Tetrazine 2 Nitrogen + 2 Boron Carborazine Six-membered rings with five heteroatomsThe hypothetical chemical compound with five nitrogen heteroatoms would be pentazine. Six-membered rings with six heteroatomsThe hypothetical chemical compound with six nitrogen heteroatoms would be hexazine. Borazine is a six-membered ring with three nitrogen heteroatoms and three boron heteroatoms. In a 7-membered ring, the heteroatom must be able to provide an empty π-orbital (e.g. boron) for "normal" aromatic stabilization to be available; otherwise, homoaromaticity may be possible. Seven-membered rings with one heteroatom Heteroatom Saturated Unsaturated Boron Borepane Borepine Nitrogen Azepane Azepine Oxygen Oxepane Oxepine Phosphorus Phosphepane Phosphepine Sulfur Thiepane Thiepine Seven-membered rings with two heteroatoms Heteroatoms Saturated Unsaturated 2 × Nitrogen Diazepane Diazepine Nitrogen + Oxygen Oxazepane Oxazepine Nitrogen + Sulfur Thiazepane Thiazepine Heteroatom Saturated Unsaturated Nitrogen Azocane Azocine Oxygen Oxocane Oxocine Sulfur Thiocane Thiocine Borazocine is an eight-membered ring with four nitrogen heteroatoms and four boron heteroatoms. Heteroatom Saturated Unsaturated Nitrogen Azonane Azonine Oxygen Oxonane Oxonine Sulfur Thionane Thionine Saturated Unsaturated Heteroatom Nitrogen Oxygen Sulfur Nitrogen Oxygen Sulfur 3-atom ring Aziridine Oxirane Thiirane Azirine Oxirene Thiirene 4-atom ring Azetidine Oxetane Thietane Azete Oxete Thiete 5-atom ring Pyrrolidine Oxolane Thiolane Pyrrole Furan Thiophene 6-atom ring Piperidine Oxane Thiane Pyridine Pyran Thiopyran 7-atom ring Azepane Oxepane Thiepane Azepine Oxepine Thiepine 8-atom ring Azocane Oxocane Thiocane Azocine Oxocine Thiocine 9-atom ring Azonane Oxonane Thionane Azonine Oxonine Thionine Heterocyclic rings systems that are formally derived by fusion with other rings, either carbocyclic or heterocyclic, have a variety of common and systematic names. For example, with the benzo-fused unsaturated nitrogen heterocycles, pyrrole provides indole or isoindole depending on the orientation. The pyridine derivative is quinoline or isoquinoline, and the class of analogues with two nitrogen atoms is known as the benzodiazines. For the azepine derivative, benzazepine is the preferred name. Likewise, the compounds with two benzene rings fused to the central heterocycle are carbazole, acridine, and dibenzoazepine. Heptazine is a tricyclic nitrogen-containing heterocyclic system derived by fusion of three triazine rings, and analog of the carbocycle phenalene. The history of heterocyclic chemistry began in the 1800s, in step with the development of organic chemistry. Some noteworthy developments:[8] 1818: Brugnatelli makes alloxan from uric acid 1832: Dobereiner produces furfural (a furan) by treating starch with sulfuric acid 1834: Runge obtains pyrrole ("fiery oil") by dry distillation of bones 1906: Friedlander synthesizes indigo dye, allowing synthetic chemistry to displace a large agricultural industry 1936: Treibs isolates chlorophyll derivatives from crude oil, explaining the biological origin of petroleum. 1951: Chargaff's rules are described, highlighting the role of heterocyclic compounds (purines and pyrimidines) in the genetic code. Heterocyclic compounds are pervasive in many areas of life sciences and technology.[2] Many drugs are heterocyclic compounds.[9] Spiroketals ^ IUPAC Gold Book heterocyclic compounds ^ a b Thomas L. Gilchrist "Heterocyclic Chemistry" 3rd ed. Addison Wesley: Essex, England, 1997. 414 pp. ISBN 0-582-27843-0. ^ Rees, Charles W. (1992). "Polysulfur-Nitrogen Heterocyclic Chemistry". 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"One-step methylation of aromatic phosphorus heterocycles: synthesis and crystallographic characterization of a 1-methyl-phosphininium salt". Chemical Communications (2021, 57). Royal Society of Chemistry: 9522–9525. doi:10.1039/D1CC03892C. Retrieved 7 March 2025. ^ Campaigne, E. (1986). "Adrien Albert and the rationalization of heterocyclic chemistry". Journal of Chemical Education. 63 (10): 860. Bibcode:1986JChEd..63..860C. doi:10.1021/ed063p860. ^ "IPEXL.com Multilingual Patent Search, Patent Ranking". www.ipexl.com. Archived from the original on 24 September 2015. Retrieved 8 September 2010. Wikimedia Commons has media related to heterocyclic compounds. Wikiquote has quotations related to Heterocyclic compound. Hantzsch-Widman nomenclature, IUPAC Heterocyclic amines in cooked meat, US CDC List of known and probable carcinogens, American Cancer Society Archived 13 December 2003 at the Wayback Machine List of known carcinogens by the State of California, Proposition 65 (more comprehensive) Retrieved from " We come across many helpful organic compounds in our daily lives whose generic names we all recognise, but we are not familiar with their chemical make-ups or chemical nomenclature. The important genetic components DNA and RNA, which are found in human bodies, are made up of heterocyclic substances. All of the dyes used to color clothing, including jeans, include heterocyclic compounds. Vitamins we intake are heterocyclic compounds. Although heterocyclic chemistry is difficult to explain, it is important to realize that the chemicals produced can be employed for a variety of useful and advantageous purposes in applications ranging from pharmaceuticals to TV displays. They are mostly used as veterinary goods, agrochemicals, and medications. Additionally, they are used as sanitisers, developers, antioxidants, corrosion inhibitors, copolymers, and dye ingredients. They serve as the means by which other organic compounds are synthesized. The majority of medications, pesticides, dyes, and polymers are made of heterocyclic compounds. So let's get into more depth about them and learn more about a special category of heterocyclic compounds known as heterocyclic aromatic compounds. TABLE OF CONTENT Heterocyclic Compounds -Introduction Heterocyclic Aromatic Compounds Six-Membered Heteroaromatic Systems Five-Membered Heteroaromatic Systems Bicyclic Heteroaromatic Compounds Practice Problems Frequently Asked Questions - FAQs Heterocyclic Compounds - Introduction Heterocyclic compounds are cyclic compounds having an extra element, such as oxygen, nitrogen, phosphorus, or sulfur, attached to the carbon ring. A heterocyclic compound has at least two different components in its ring. Unstrained 5- and 6-membered rings are the major ones. Most research and applications in the field of heterocyclic chemistry are focused on in this section, which places a focus on unsaturated derivatives in a particular area. Among them are pyridine, thiophene, pyrrole, and furan. A substantial subclass of heterocycles is those fused to benzene rings. For instance, the fused benzene derivatives of pyridine, thiophene, pyrrole, and furan are quinoline, benzothiophene, indole, and benzofuran, respectively. A sizable third class of compounds when two benzene rings are combined. This third class of chemicals includes the molecules dibenzothiophene, acridine, carbazole, and dibenzofuran respectively as equivalents to the previously listed heterocycles. Heterocyclic Aromatic Compounds: As their title indicates, aromatic heterocyclic compounds are cyclic aromatic compounds. Huckel's Rule states that a compound must abide by the following conditions in order to have an aromatic nature: It must be planar in form. The system shouldn't contain any sp3 hybridized atoms. There must be a total of (4n+2) electrons in it. We can remove the second criterion if only one lone pair of sp3 hybridized atoms take part in the conjugation. Heterocyclic aromatic compounds include Furan, Indole, Pyrrole, Thiophene, Pyridazine, Oxazole, Pyrazole, Imidazole, Pyridine, Pyridazine, Purine, Quinoline, Isoquinoline, Carbazole, and others. Six-Membered Heteroaromatic Systems: Structure of Pyridine: By substituting N for CH, pyridine's structure is completely similar to that of benzene. The three main differences are The heteroatom's presence causes the hexagonal geometry to deviate from being perfectly regular, particularly because of the shorter carbon-nitrogen bonds; An unshared electron pair is used to substitute the hydrogen in the ring's plane. This unshared electron pair is positioned in a sp2 hybrid orbital and is not at all connected to the aromatic π electron sextet. A strong permanent dipole, traceable to the greater electronegativity of nitrogen compared with carbon. Here new aromatic heterocycles, pyridazine, pyrimidine, and pyrazine, would be discovered if we continued the procedure of replacing further CH groups with nitrogen atoms on paper. Oxygen-containing six-membered heterocyclic aromatic compound: Although the six-membered aromatic heterocyclic pyridine is by far the most significant, there are oxygen heterocycles called pyrones that resemble pyridones. Although the -Pyrone is somewhat unstable, the pyrones are aromatic. The stable aromatic cations known as pyrylium salts are metal complexes that give various floral colors. Five-Membered Heteroaromatic Systems Structure of Pyrrole: Since pyrrole is similarly aromatic, it undergoes the typical aromatic substitution processes (Friedel-Crafts, nitration, and halogenation) rather than addition reactions, making it more electrophilic reactive than benzene or pyridine. It is crucial to understand that the pyrrole's nitrogen lone pair is a component of the aromatic six-π electron system. Structures of Thiophene and Furan: With the exception of the NH being substituted by S and O, respectively, the structures of thiophene and furan are quite similar to those covered in detail for pyrrole above. As a result, each heteroatom has two lone pairs—one of which is part of the aromatic sextet, like in pyrrole, and the other of which is not—both of which are positioned in sp2 hybrid orbitals in the plane of the ring. Bicyclic Heteroaromatic Compounds: It is simple to extrapolate to those systems that combine two (or more) of these types once the concepts of the structures of benzene, naphthalene, pyridine, and pyrrole have been internalized. For example, quinoline is similar to naphthalene but only has one pyridine ring, and indole is similar to pyrrole but with a benzene ring attached. These are considered as bicyclic Heteroaromatic Compounds. In Indole, if you'd rather think of it that way, it has 10 π electrons and is an aromatic system with eight coming from double bonds, four from single bonds, and one from the nitrogen atom. Practice Problems: Q1. Which of the following compounds is not a heterocyclic aromatic compound? Answer: (D) Solution: As their name suggests, aromatic heterocyclic compounds are cyclic aromatic compounds. It must be planar and have a total of (4n+2) electrons according to Huckel's Rule. It shouldn't contain any sp3 hybridized atoms. We can remove this requirement if only one lone pair of sp3 hybridized atoms participate in the conjugation. In option (A), Its structure is planar and devoid of sp3 hybridized atoms. It has two distinct C and N atoms. Due to the presence of 6e-, lone pairs of nitrogens will not participate in the conjugation. As a result, the compound satisfies all of the aforementioned requirements. It is an aromatic heterocyclic chemical. In option (B), It has a planar structure and the atoms C, O, and N are all different types. Nitrogens won't participate in the conjugation, but one lone pair of sp3 hybridized atoms from the element O will, resulting in the formation of the compound 6e-. As a result, it is an aromatic heterocyclic compound. In option (C), It is planar in shape and has two separate types of atoms, C and N. The conjugation of one lone pair of the sp3 hybridized atom N results in the presence of 6e-. As a result, it is an aromatic heterocyclic compound. In option (D), the sp3 hybridized carbon atom has a non-planar structure and will not take part in the conjugation. As a result, it is not an aromatic heterocycle. Hence, the correct answer is an option (D). Q2. Which statement is correct regarding thiophene and furan? Thiophene has more aromatic character than furan Furan has more aromatic character than thiophene Thiophene and Furan have the same aromatic character. Both Thiophene and Furan are anti-aromatic in nature Answer: A Solution: Relative aromaticity is determined by heteroatom electronegativity. Higher electronegativity atoms cling to their lone electron pair more strongly, which makes delocalization more difficult. Since oxygen is the more electronegative heteroatom among S and O, furan aromaticity declines relative to thiophene. Q3. Which among the following is considered as bicyclic Heteroaromatic Compounds? Indole Quinoline A and B None of the above Answer: C Solution: For example, quinoline is similar to naphthalene but only has one pyridine ring, and indole is similar to pyrrole but with a benzene ring attached. These are considered as bicyclic Heteroaromatic Compounds. Q4. Which of the following compounds is a heterocyclic aromatic compound? Answer: B Solution: The cyclic aromatic compounds known as aromatic heterocyclic compounds must be planar, devoid of sp3 hybridized atoms, and contain a total of (4n+2) electrons. The second condition can be removed if only one lone pair of sp3 hybridized atoms participates in the conjugation (no sp3 hybridized atoms). Option (A) comprises two distinct atoms, C and O, and has a planar structure. The conjugation of the single pair of sp3 hybridized atoms O will result in the presence of 4e-. As a result, it is not an aromatic heterocycle. In option (B), It has a planar structure, no atoms that have undergone sp3 hybridization, and two distinct atoms, C and N. Since nitrogens won't participate in the conjugation, 10e- is the result. As a result, it is an aromatic heterocyclic compound. The non-planar structure in options (C) and (D) contains sp3 hybridized atoms that will not take part in the conjugation. As a result, it is not an aromatic heterocycle. Frequently Asked Questions – FAQs: 1. What do you understand about the term "azole"? Solution: The systematic suffix "-ole" designates a five-membered heterocyclic ring. The term "the azoles" is sometimes used to refer to all five-membered aromatic heterocycles having nitrogen in the ring. The oxygen and sulfur counterparts of imidazole are called oxazole and thiazole, respectively. 2. What is the most common use of the heterocyclic aromatic compound "Pyrimidine"? Solution: The medicinally advantageous framework pyrimidine is used in both bioactive natural items and manufactured medicines. Three functionalized pyrimidines, such as uracil, are present in both DNA and RNA structures. Many antiviral medications, particularly those used to treat HIV, are also made of modified DNA and contain pyrimidines. 3. Is Pyridine considered as a drug or not? Solution: Drugs containing pyridine and dihydropyridine are typically employed as antibacterial, antiviral, anticancer, antioxidant, antihypertensive, antidiabetic, antimalarial, and anti-inflammatory agents, as well as psychopharmacological antagonists and antiamebic compounds. 4. What are the bases present in DNA and RNA? Are they heterocyclic in nature? Solution: There are five types of heterocyclic bases present in DNA and RNA. Five different bases, two sugars, and the phosphate group make up a nucleic acid. All of the bases are aromatic and either monocyclic pyrimidines or bicyclic purines. Nucleic acids only include the two purine bases adenine (A), which we have already encountered, and guanine (G) Chapter 4: Aromatic Compounds A cyclic compound that includes elements other than carbon is called a heterocyclic compound. The most commonly involved heteroatoms are nitrogen, oxygen, and sulfur. Some heterocyclic compounds are also aromatic and show special stability. Examples of heterocyclic aromatic compounds are given here. Fig. 4.4a Heterocyclic aromatic compound examples (electrons in the aromatic system are shown in red color) Among the above examples, pyrrole, furan, and thiophene share similar structure features. All hetero elements, N, O, and S respectively, are in sp2 hybridization. The unhybridized 2p orbital of N, O, and S holds one pair of lone-pair electrons, and the 2p orbital overlaps with the other four 2p orbitals of carbons (also in sp2 hybridization) and forms the conjugated system. The total number of π electrons (shown in red color in Fig. 4.4a) for the conjugated system therefore is 6, that is 2+4, which matches Huckel's number and explains the aromaticity of the compounds. The difference in the structure between pyrrole, furan, and thiophene is how the sp2 hybrid orbitals are used for. For pyrrole, all three sp2 hybrid orbitals are involved in bonding (N in pyrrole has three single bonds), while for furan and thiophene only two of the sp2 hybrid orbitals used for sing bonds and the other sp2 orbital carry one lone-pair electron (shown in black color in Fig. 4.4a). The black color electron pair is not part of the aromatic system. The structure differences between the three heterocyclic aromatic compounds are highlighted in Fig. 4.4b. Fig. 4.4b Structure difference between pyrrole, furan, and thiophene Pyridine is a six-membered ring that is similar to a benzene ring, but with a nitrogen atom. All the elements in pyridine are sp2 hybridized, and the unhybridized 2p orbital for each element has one single electron that makes the total number of π electrons 6, the Huckel's number for aromatic (shown in red color in Fig. 4.4a). Another structural difference between pyridine and benzene is that one of the sp2 orbitals of nitrogen holds one lone pair electron, while all the sp2 orbitals (for carbons) are used for bonding in benzene. Both pyrrole and pyridine are heterocyclic aromatic compounds with a nitrogen atom, and both nitrogen atoms have one pair of lone-pair electrons in the structure formula. Generally speaking, the nitrogen with lone pair electron should show basicity. It turns out that, however, pyridine is basic but pyrrole is not. How do you explain the difference in basicity between the two compounds? Fig. 4.4c Structure and basicity difference between pyrrole and pyridine Such differences can be interpreted by taking a closer look at the structure of each (Fig. 4.4c). In pyridine, the lone pair electron (black color) is in the sp2 orbital of nitrogen and is not part of the aromatic system, therefore it can be used as a base. In pyrrole, the lone pair electron on nitrogen (red color) is in the unhybridized 2p orbital and is part of the aromatic system. Being part of the aromatic system prevents the electron pair from being used as a base, or not available for reacting with a proton. Thus pyrrole is not appreciably basic. Imidazole has two nitrogens, only one is basic. Predict and explain which nitrogen atom is basic. Answer: The nitrogen atom in the #3 position is more basic, with the same reason for the basicity of pyrrole that the lone pair electron of that N is not part of the π system.