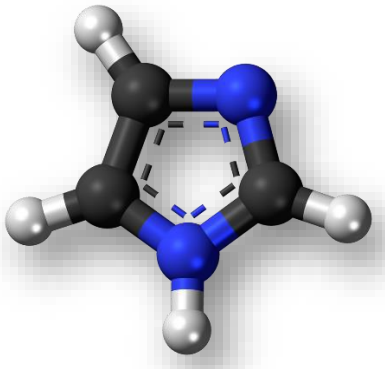
An essay on

Imidazole



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Acknowledgement

I would like to express my special thanks of gratitude to my professor Dr. Gehad Ebrahim, who gave me the golden opportunity to do this wonderful project.

Who also helped me in completing my project. I came to know about so many new things and I'm thankful to her.

Contents

Introduction:

In heterocyclic chemistry, imidazole containing moiety occupied a unique position. It is a five-membered nitrogenous heterocyclic moiety that possesses three carbon, two nitrogen, four hydrogen atoms, and two double bonds having general molecular formula is $C_3H_4N_2$. The nitrogen atoms present at the first and third positions (non–adjacent position) of the ring, position four and five are equivalent. It is also known as 1,3-diazole.[1]

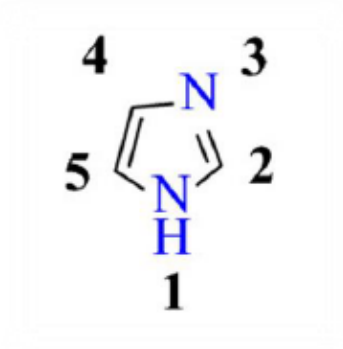


Figure 1:Imidazole

Chemical Properties:

- **Aromaticity:** The imidazole ring exhibits aromaticity due to the presence of a delocalized sextet of π-electrons formed by the nitrogen lone pairs and the p orbitals of the carbon atoms. This aromaticity influences its reactivity and stability.
- **Amphoteric Character:** Imidazole acts as a weak acid due to the ability of the NH group to donate a proton (pKa ~ 14.5). It can also function as a weak base by accepting a proton at the unprotonated nitrogen atom (pKb ~ 7).
- **Nucleophilic Properties:** The unprotonated nitrogen atoms in the imidazole ring possess lone electron pairs. These lone pairs can act as electron donors, making imidazole a nucleophile. This nucleophilicity is weaker compared to some other common nucleophiles like amines.
- **Electrophilic Properties:** The carbon atom between the two nitrogen atoms in the imidazole ring can act as an electrophile under certain conditions. This is because the electron-withdrawing nature of the nearby nitrogen atoms creates a slightly positive charge on the carbon, making it susceptible to attack by nucleophiles. However, the electrophilic character of imidazole is also relatively weak.
- **Metal Chelation:** Imidazole forms stable complexes with metal ions due to the ability of its nitrogen atoms to coordinate with metals. This property makes it a valuable ligand in coordination chemistry.[2]

Physical Properties:

- **Appearance:** Imidazole is a colorless liquid or solid at room temperature, depending on the grade.
- **Melting Point:** High melting point (256 °C) compared to other five-membered heterocycles due to intermolecular hydrogen bonding and a linear molecular association.
- **Boiling Point:** High boiling point (470 °C) due to the presence of the aromatic ring and intermolecular hydrogen bonding.

- **Solubility:** Highly soluble in water and other polar solvents due to the presence of the polar N-H groups and the ability to form hydrogen bonds with water molecules.
- **Density:** Around 1.1 g/cm³
- **Dipole Moment:** Moderate dipole moment (around 3.6 D) due to the electronegativity difference between carbon and nitrogen atoms. [2]

Resonance:

Resonance describes the **delocalization** of electrons within a molecule, resulting in a hybrid structure that is more stable than any single contributing Lewis structure , by shifting an electron within the molecule.

Imidazole exhibits resonance due to the delocalization of pi electrons from the double bonds and the lone pair on one of the nitrogen atoms. This delocalization contributes to its aromatic character and stability.

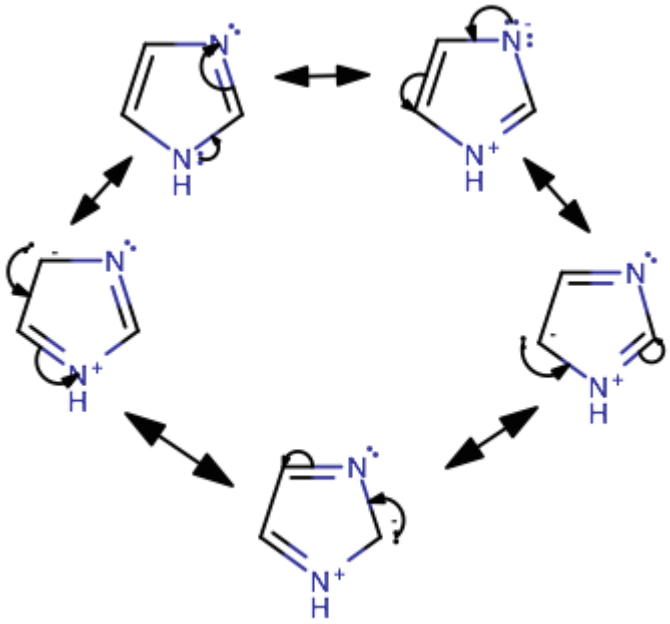


Figure 2: resonance structure of imidazole

Tautomerism:

Imidazole exists in two equivalent tautomeric forms due to the migration of a proton between the two nitrogen atoms in the ring. These tautomers differ in the location of the proton (H+) and the lone pair of electrons on the nitrogen atoms.

- **N1-H Tautomer:** The proton is attached to the nitrogen atom at position 1 (N1) in the ring, while the other nitrogen atom (N3) possesses a lone pair.
- **N3-H Tautomer:** The proton is attached to the nitrogen atom at position 3 (N3), and the lone pair resides on the N1 nitrogen.

Both tautomers are constantly interconverting through a rapid proton transfer process. This process is facilitated by the aromaticity of the imidazole ring. The delocalized π-electron system spreads across the entire ring, making the energy difference between the two tautomers minimal. [3]

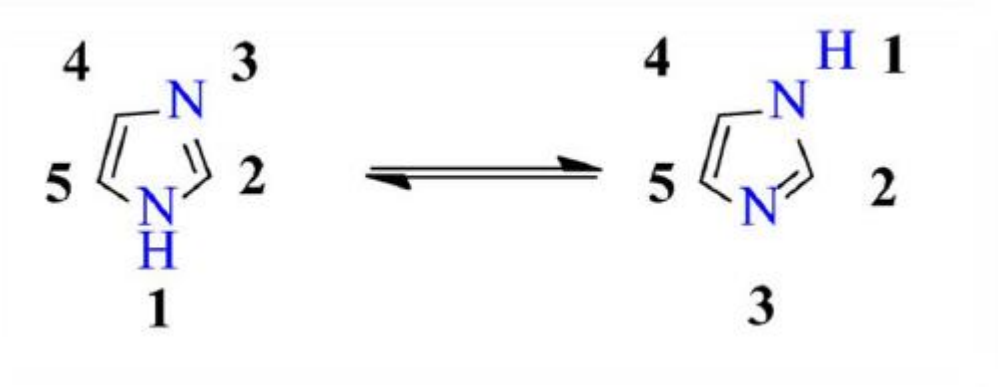


Figure 3: Tautomeric forms of imidazole

- The presence of tautomers can influence the reactivity of imidazole. Depending on the reaction conditions, one tautomer might be slightly more favorable, leading to a preference for specific reaction pathways.
- The NH group in each tautomer can participate in hydrogen bonding with other molecules, impacting solubility and interactions with biomolecules.

Feature	Resonance	Tautomerism
Nature of the phenomenon	Delocalization of electrons	Reversible interconversion of isomers
Change in structure	No bond breaking or formation	Breaking and formation of a proton-transfer bond
Energy relationship	Hybrid structure is more stable than individual Lewis structures	Tautomers have comparable energies

Synthesis of imidazole compounds:

Imidazole was first named glyoxaline because the first synthesis has been made by glyoxal and ammonia. There is a different kind of synthetic route from which we can synthesize 1,3-diazloes, and its derivatives. The most common methods are **Debus-Radiszewski** synthesis, **Wallach** synthesis, from **dehydrogenation** of imidazolines, from alpha halo-ketones, **Marckwald** synthesis, and **amino nitrile**.

1- Glyoxal and ammonia

The synthesis process of imidazole follows the reaction between formaldehyde in ammonia and glyoxal. This process gives low yield of imidazole, but it is still used to form imidazole with C-substitution[4].

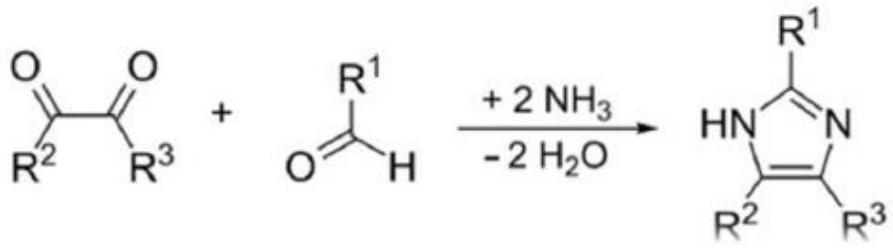


Figure 4: first synthesis of imidazole

2- Dehydrogenation of Imidazoline

In the presence of sulfur, it was reported that, for converting imidazole from imidazoline, a milder reagent, barium managanate was used. Imidazolines are derived from 1, 2 ethane diamine and alkyl nitriels after reacting with BaMnO4 yield 2-substituted imidazole.[5]

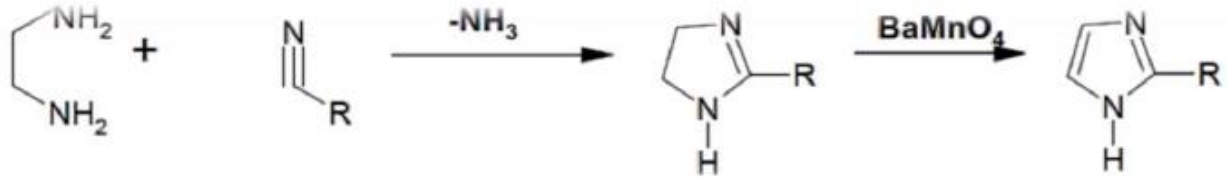


Figure 5: dehydrogenation of imidazoline

3-MarkWald Synthesis

The common process of synthesizing 2- mercapto imidazole from a- aldehyde or amino ketones and alkyl is othiocyanates or potassium thiocyanate. In order to obtain the desirable imidazole, various oxidative methods can be used to remove the sulfur. A- amino aldehyde or ketone are not always prevalent which makes the Markwald synthesis more limited.[6]

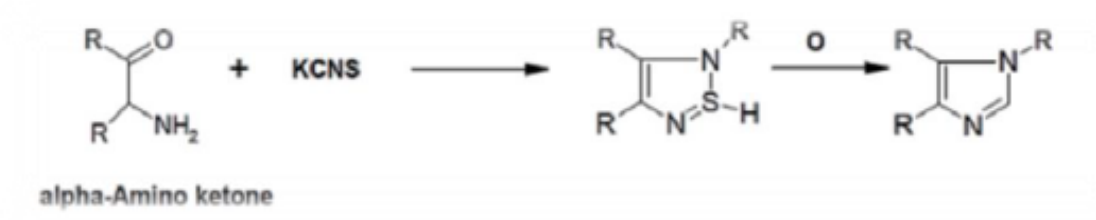


Figure 6 :Mark Wald synthesis

4- Wallach Synthesis

A compound containing chlorine is derived when N, N′ -dimethyl oxamide is treated with phosphorus pentachloride which decreases with hydroiodic acid and provides N- methyl imidazole. N, N′ -diethyl oxamide is converted to a chlorine compound under the same condition, which on decrease yields 1-ethyl –2- methyl imidazole. 5- chloral imidazole is the chlorine compound.[7]

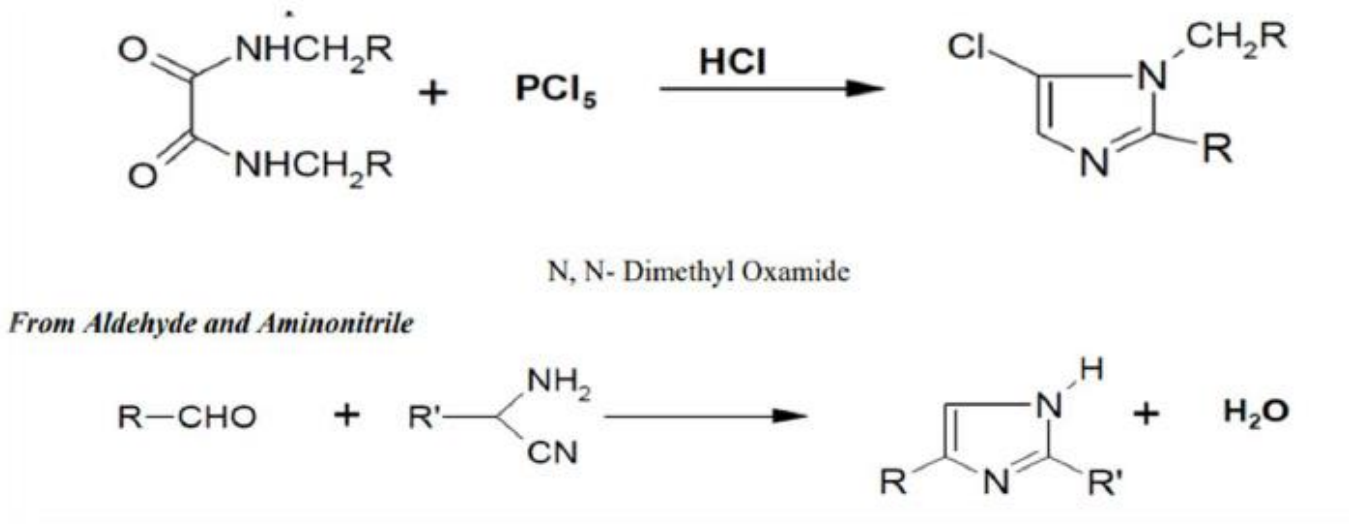


Figure 7: Wallach synthesis

5- Action of Ammonia

The mixture of ammonia and tartaric acid dinitrate and formaldehyde can prepare imidazole upon heating the dicarboxylic acid in quinoline in presence of copper.[8]

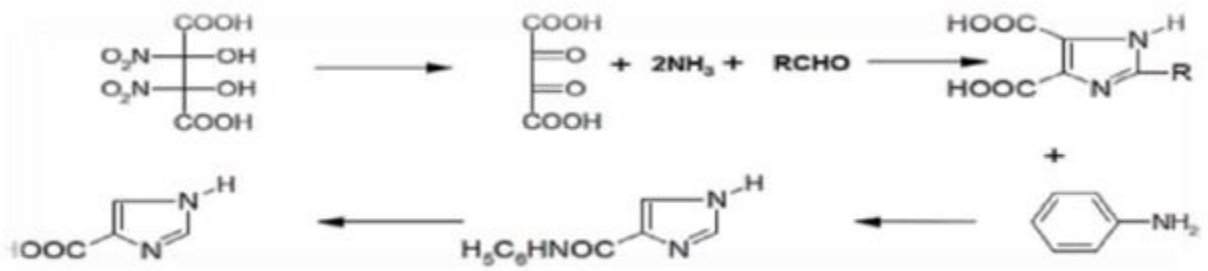


Figure 8 :action of ammonia

6- Debus–Radziszewski

is a multi-component reaction used for the synthesis of imidazoles from a 1,2-dicarbonyl, an aldehyde, and ammonia or a primary amine. The method is used commercially to produce several imidazoles.[9]

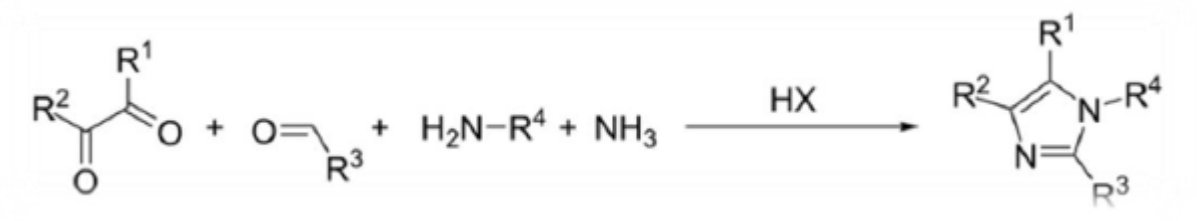


Figure 9: Debus Radziszewski

7- From a- haloketon

This reaction involves an interaction between an imidine and alpha halo ketones. This method has been applied successfully for the synthesis of 2, 4- or 2, 5- biphenyl imidazole phenacyl bromide and benzimidine according to this method afford 2,4-diphenyl imidazole. Similarly, amidine reacts with acyloin or alpha halo ketones to yield imidazoles.[10]

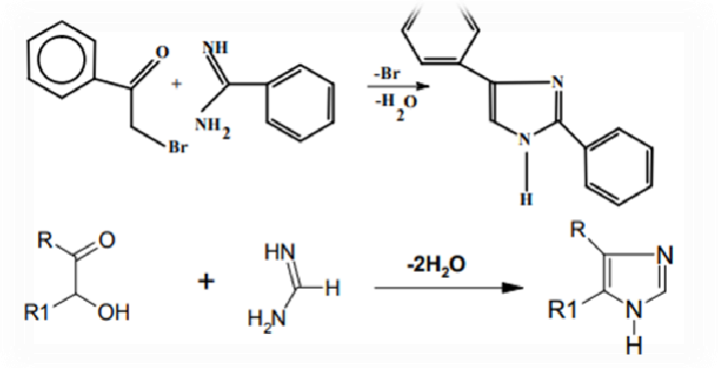


Figure 10

general scheme of imidazole synthesis:

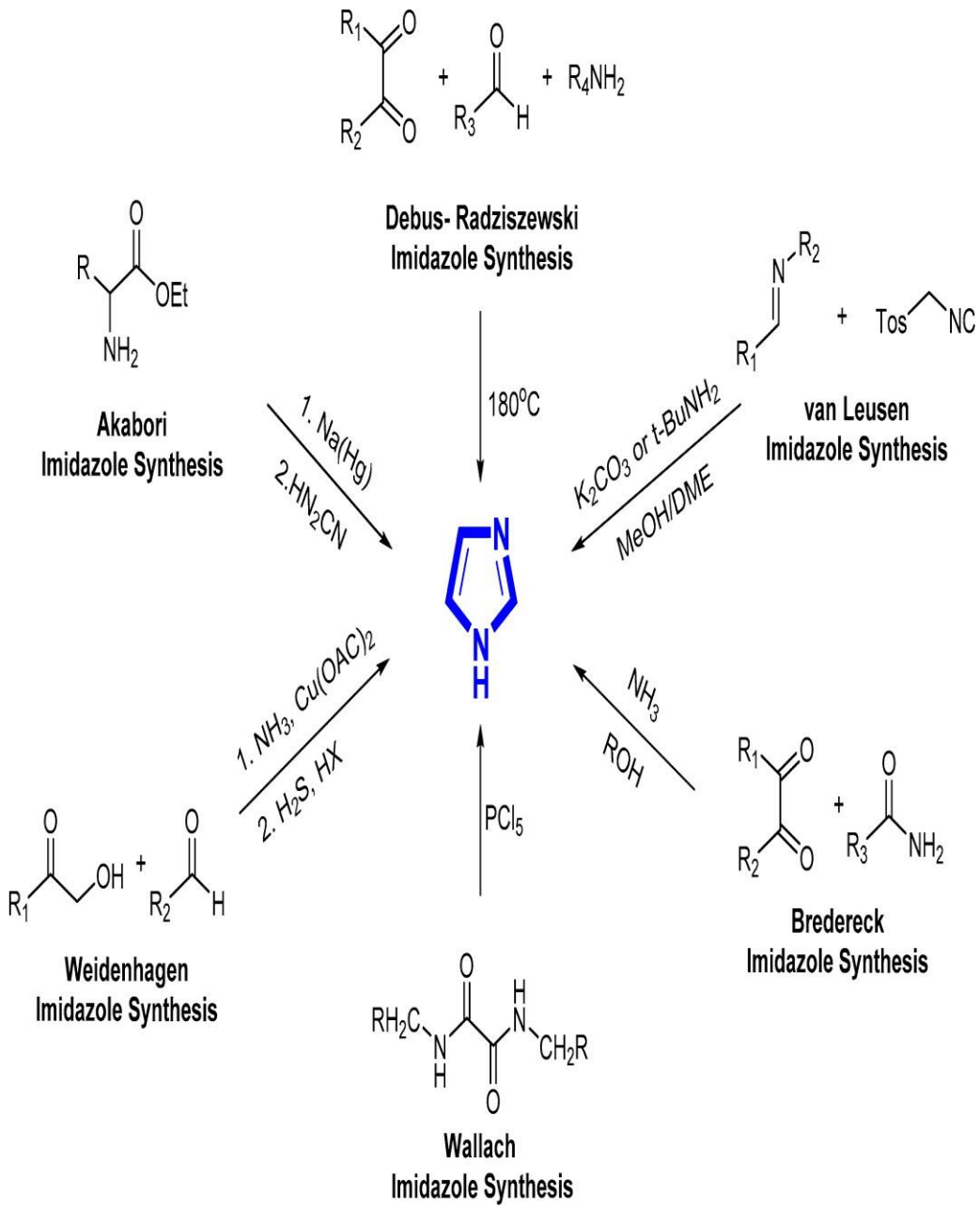


Figure 11

Chemical reaction of imidazole compounds:

1. Reaction with acids and base

Imidazole is a monoacidic base .The protonation of N3-atoms in imidazole produces stable crystalline salt with strong acids. It also possesses weakly acidic properties.

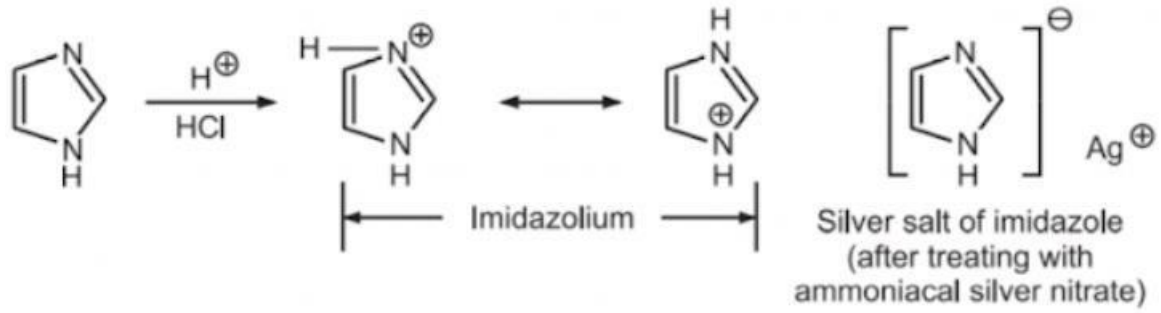


Figure 12

The proton on the N1 atom of imidazole can be removed by a strong base, but it acts as an acid .there are therefore two properties of the compound: acidic and basic. Pyrole is acidic , while pyridine is basic.[11]

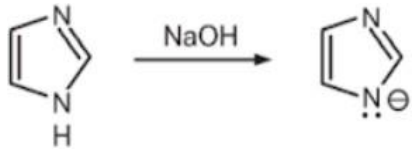


Figure 13

2. Reaction with reducing and oxidizing agent

Imidazole itself is stable to **auto oxidation** (It doesn't readily react with oxygen in the presence of light or heat), and to the action of the weak **oxidizing agent** such as chromic acid **H2CrO4** , but is attacked by potassium permanganate **$KMnO_4$,benzoic acid** and **hydrogen peroxide** and undergoes a ring-opening reaction and the product formed is oxamide, a simple dicarboxamide molecule. Also it don't react with weak reducing agent such as Zn/HCl, but reacts with strong reducing agent such as $LiBH_4$ and give amidazoline. [12]

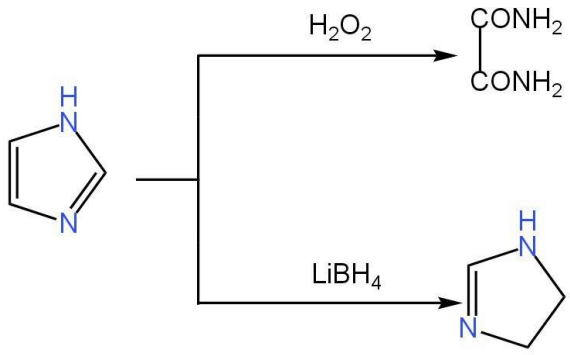


Figure 14

3. Electrophrophilic substitution

Imidazoles do indeed exhibit increased reactivity towards electrophillic aromatic substitution compared to pyrazole, thiazole, furan, and thiophene.

Enhanced Reactivity of Imidazole:

- **Aromatic Character:** The imidazole ring possesses a delocalized π-electron system, granting it aromatic character. This aromatic stability makes it more receptive to electrophilic attack compared to fully saturated rings or those with localized double bonds.
- **Electron-Donating Nitrogen Atoms:** Both nitrogen atoms in the imidazole ring contribute lone pairs of electrons to the aromatic system. These lone pairs increase the electron density in the ring, making it more attractive to electron-deficient electrophiles.

Regioselectivity of Electrophilic Attack:

The resonance structures of the intermediate ion formed during electrophilic attack help us understand the preferred positions for substitution in the imidazole ring:

- **Attack at C4 and C5:** These positions lead to resonance structures where the positive charge is distributed between two nitrogen atoms, resulting in a more stable intermediate.
- **Attack at C2:** This position results in a resonance structure with a highly unfavored positive charge on the nitrogen (N3) atom in the ring. This form is less stable due to the reduced ability of nitrogen to accommodate a positive charge compared to a carbon atom (C4 or C5).

Therefore, electrophilic attack predominantly occurs at C4 and C5 of the imidazole ring due to the formation of more stable resonance structures.[13]

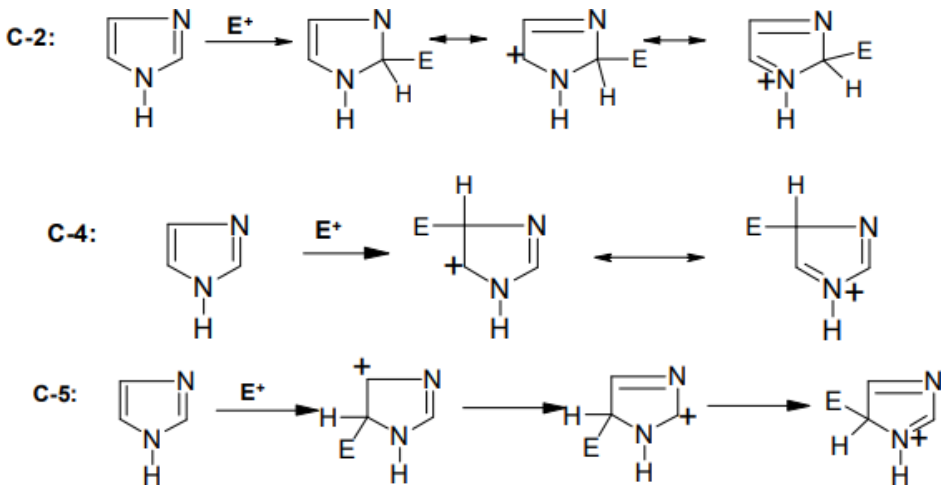


Figure 15

3.1 N-alkilation and N-acylation

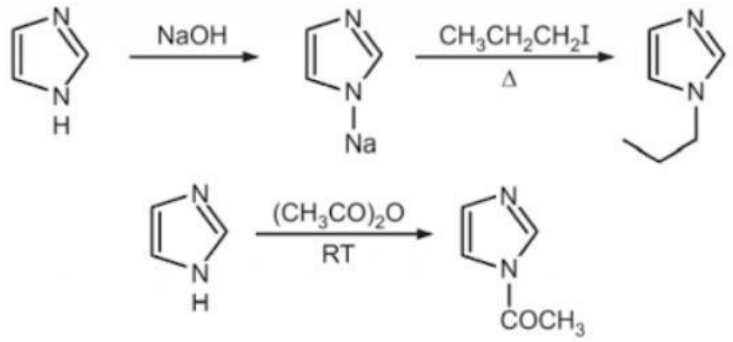


Figure 16

3.2 Halogination

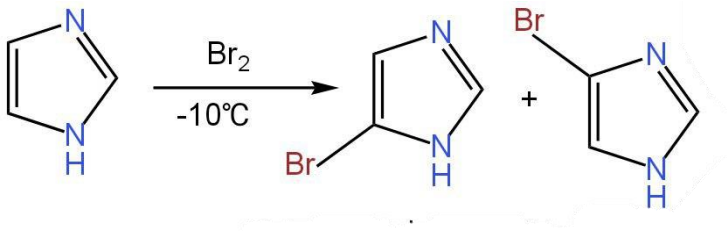


Figure 17

3.3 Nitration

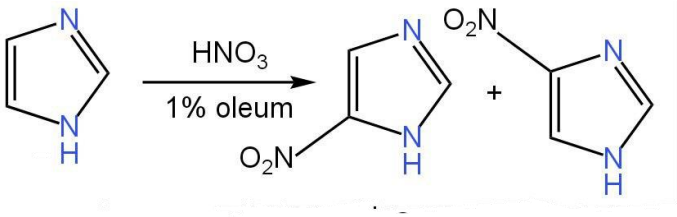


Figure 18

3.4 sulfonation

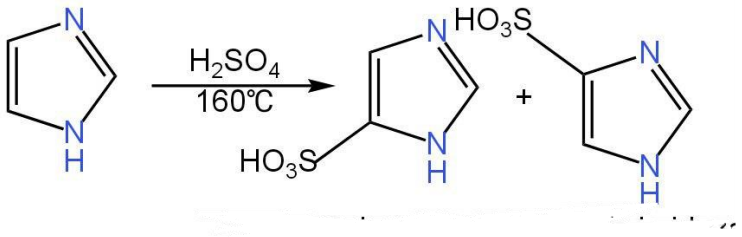


Figure 19

4. Nucleophilic substitution

Imidazole can undergo nucleophilic substitution under certain conditions, but the ease and preferred site of attack depend on several factors. Here's a breakdown:

General Reactivity:

- Imidazole itself exhibits **limited reactivity** towards direct nucleophilic substitution on the ring. This is because the aromatic imidazole ring is relatively stable and less susceptible to nucleophilic attack compared to systems with more reactive double bonds.

Influence of Electron-Withdrawing Groups:

- Introducing **electron-withdrawing groups (EWGs)** like chlorine or nitro groups at specific positions on the imidazole ring can **enhance its reactivity** towards nucleophiles.
- EWGs pull electron density away from the ring, making it more susceptible to nucleophilic attack.

Preferred Site of Attack (C2):

- When electron-withdrawing groups are present, the **C2 position** of the imidazole ring becomes the **favored site** for nucleophilic attack.
- This is because the EWG can stabilize the positive charge that develops on the C2 carbon during the reaction intermediate. The resulting intermediate with the positive charge on C2 benefits from resonance with the EWG, making it more stable and favoring this attack pathway.[14]

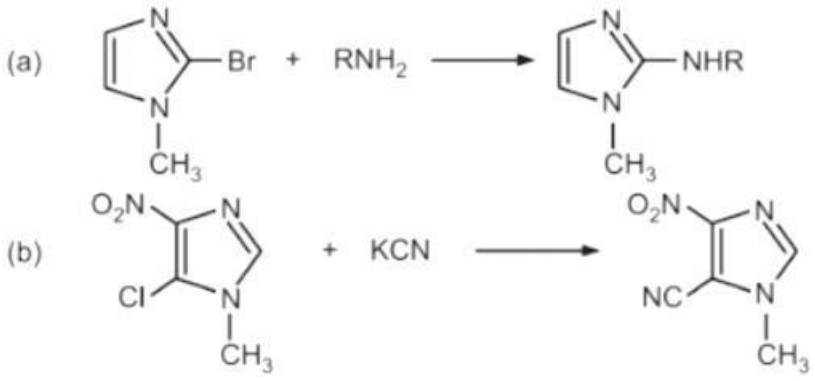


Figure 20

Pharmacological activities of imidazoles

Imidazoles have long held a special place in heterocyclic chemistry, and their derivatives have piqued interest in recent years due to their diverse chemistry and pharmacology features. Imidazole is a biologically and pharmaceutically important heterocyclic ring. As a result, researchers have been interested in imidazole molecules. For a century and a half, **purine**, **histamine**, and other natural compounds all contained the imidazole ring. A number of imidazole drugs have been prepared and marketed for the treatment of various diseases. In view of this, we herein report a detailed account of synthetic procedures for various imidazole drugs.

➢ Anti-cancer effect

Imidazoles are a promising class of molecules with potential applications in cancer treatment. While they aren't directly used as anti-cancer drugs themselves, researchers are exploring their ability to target cancer cells through various mechanisms.[15]

Mechanisms of Action:

Imidazole derivatives can potentially target cancer cells in several ways:

- **Cell Cycle Arrest:** These molecules may interfere with the normal cell division process, preventing cancer cells from multiplying uncontrollably.
- **Induction of Apoptosis:** They might trigger programmed cell death (apoptosis) in cancer cells, leading to their elimination.
- **Anti-Angiogenesis:** Imidazole derivatives could disrupt the formation of new blood vessels that nourish tumors, starving them of essential nutrients and oxygen.
- **Kinase Inhibition:** Some derivatives may target specific enzymes (kinases) that play a crucial role in cancer cell signaling pathways, disrupting their growth and survival.
- **DNA Damage:** Imidazole derivatives might interact with DNA, causing damage that hinders cancer cell replication.

Advantages:

- **Structural Versatility:** The imidazole ring can be modified with various functional groups, allowing for the design of derivatives with specific anti-cancer properties.
- **Targeted Therapy:** These derivatives can potentially target specific pathways in cancer cells, minimizing side effects on healthy tissues.
- **Combination Therapy:** Imidazole derivatives can be combined with other anti-cancer drugs to enhance treatment efficacy.

Examples:

- **Mercaptopurine:** This drug, used in leukemia treatment, incorporates an imidazole ring and disrupts DNA function in cancer cells.[16]
- **Losartan:** This angiotensin II receptor blocker, used for hypertension, contains an imidazole moiety and might have additional anti-cancer benefits[17]

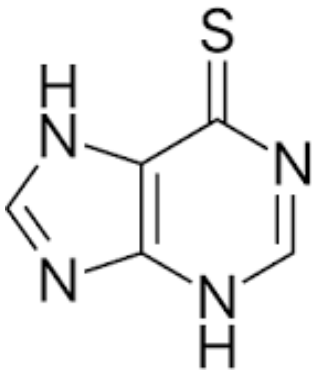


Figure 21: Mercaptopurine

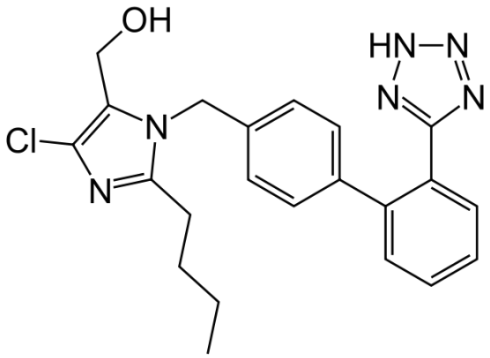


Figure 22: lostram

➢ antidepressant activity

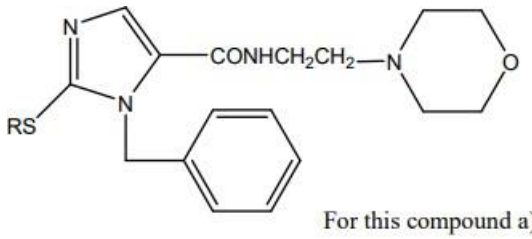
While imidazole itself doesn't directly exhibit strong antidepressant activity, some imidazole derivatives possess properties that can influence mood and potentially contribute to antidepressant effects.

Indirect Mechanisms:

- **Modulating Neurotransmitters:** Some imidazole derivatives might influence the levels or activity of neurotransmitters like serotonin or norepinephrine in the brain. These neurotransmitters play a crucial role in mood regulation, and imbalances can contribute to depression. Imidazole derivatives could potentially act as reuptake inhibitors, preventing the reabsorption of these neurotransmitters by neurons, leading to increased availability for signaling and potentially improved mood. However, more research is needed to understand the specific mechanisms involved.
- **Inhibiting Enzymes:** Certain imidazole derivatives might inhibit enzymes involved in the breakdown of these neurotransmitters, allowing them to last longer and exert a more prolonged effect.
- **Nitric Oxide (NO) Pathway:** Some studies suggest that imidazole derivatives might interact with the nitric oxide (NO) pathway, which is implicated in depression. However, the exact role of NO in this context and how imidazole derivatives might influence it require further investigation.

Examples:

- **Moclobemide:** This is a monoamine oxidase inhibitor (MAOI) antidepressant with an imidazole moiety in its structure. However, its antidepressant effect is primarily attributed to its ability to inhibit the enzyme monoamine oxidase A (MAO-A), not solely due to the imidazole ring itself.[18]



For this compound a)R=CH_3,

b)R=C_2H_5

c)R=$CH_2C_6H_5$

Figure 23: Moclobemide

➢ Anti-fungal activity

Imidazoles are a powerful weapon in the fight against fungal.

Mechanisms of Action:

1. **Target a Crucial Enzyme**

   Imidazoles target a vital enzyme in fungi called **lanosterol 14α-demethylase (LDM)**. This enzyme plays a starring role in the production of **ergosterol**, a molecule essential for building strong fungal cell walls.

2. **Disrupting the Building Blocks**

   By inhibiting **LDM**, imidazoles throw a wrench in the ergosterol production line. Without enough ergosterol, fungal cell walls become weak and leaky.

3. **Fungal Fallout**

   This weakened state makes it difficult for the fungus to survive. Essential nutrients leak out, and the fungus becomes vulnerable to the harsh environment. Ultimately, the fungus struggles to grow and reproduce, leading to its demise.

Examples of Imidazole Antifungals:

- Clotrimazole (used for athlete's foot, jock itch, ringworm).[19]
- Miconazole (used for yeast infections, athlete's foot).[20]
- Ketoconazole (used for dandruff, oral thrush).[21]

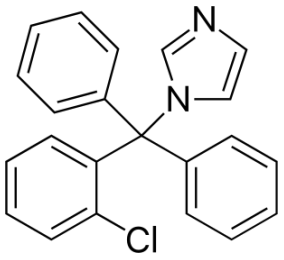


Figure 24: Clotrimazole

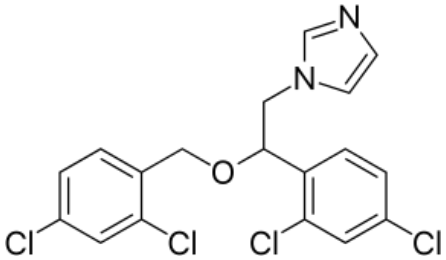


Figure 25:Miconazole

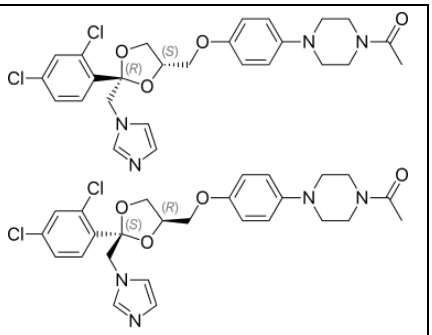


Figure 26:Ketoconazole

➢ Anti-bacterial activity

The antibacterial activity of imidazoles is a bit less clear-cut compared to their well-established antifungal effects. they are generally:

- **Less potent:** Imidazoles tend to be more effective against fungi than bacteria.
- **Narrower spectrum:** They may only target specific types of bacteria, often Gram-positive bacteria.

Possible Mechanisms of Action:

- **Disrupting bacterial cell membranes:** Imidazoles might interact with the bacterial cell membrane, making it more permeable and leaky. This can disrupt essential functions and lead to bacterial cell death.
- **Inhibiting bacterial enzymes:** Some imidazoles might target and inhibit enzymes crucial for bacterial growth and survival.
- **Interfering with bacterial DNA replication:** Imidazoles might interfere with the process of bacterial DNA replication, hindering their ability to reproduce.

Examples :

- **Metronidazole:** This medication has a broader spectrum of activity and is primarily used against parasitic infections and certain types of bacteria like H. pylori (associated with peptic ulcers).[22]

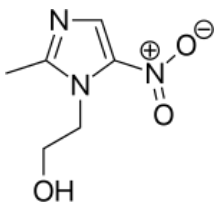


Figure 27:Metronidazole

➢ Anti-inflammatory activity

Imidazoles show potential for anti-inflammatory activity, but the mechanisms are still under investigation.[23]

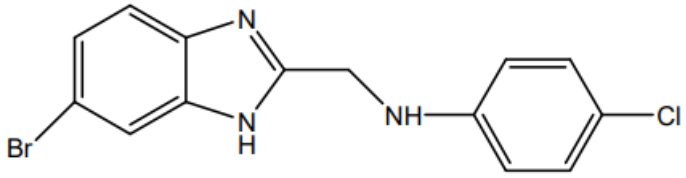
Indirect Effects:

Unlike some anti-inflammatory drugs that directly target inflammation pathways, imidazoles seem to work more indirectly. Here are some potential mechanisms:

- **Inhibition of Enzymes:** Certain imidazoles might inhibit enzymes involved in the inflammatory response, such as cyclooxygenase (COX) enzymes. COX enzymes produce inflammatory mediators like prostaglandins. By inhibiting these enzymes, imidazoles could potentially reduce inflammation.
- **Neutrophil Activity:** Some imidazoles might influence the activity of neutrophils, a type of white blood cell involved in inflammation. They might decrease neutrophil migration to inflammation sites or reduce the release of harmful substances from neutrophils.
- **Reactive Oxygen Species (ROS):** Imidazoles might have antioxidant properties, helping to reduce the production of reactive oxygen species (ROS) that contribute to inflammation.

Examples :

- The use of imidazole derivatives as anti-inflammatory drugs remains an area of ongoing research, but in general imidazole derivatives with anti-inflammatory properties are **N-substituted imidazoles** such as:[24]



N-((6-bromo-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-chlorobenzenamine

Figure 28

➢ Antileishmanial activity

Imidazoles, while not directly superstar Leishmania slayers, show some potential in the fight against Leishmaniasis.

Indirect Effects on Leishmania:

- imidazole derivatives can influence the environment or processes within the host (human or animal) that indirectly affect Leishmania survival.

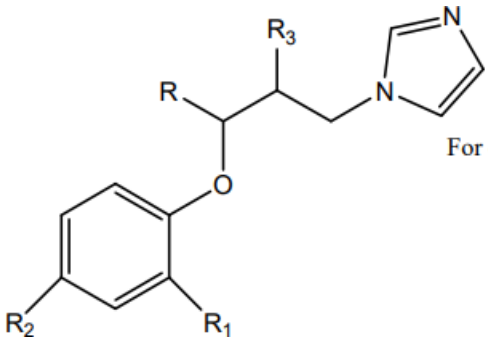
Potential Mechanisms:

- **Boosting Immune Response:** Certain imidazole derivatives might modulate the immune system, potentially enhancing the host's ability to fight off Leishmania infection. This could involve stimulating immune cells or increasing the production of substances that target the parasite.

- **Interfering with Leishmania Growth:** Some imidazole derivatives might disrupt essential processes for Leishmania growth and survival within the host cells. This could involve hindering their ability to acquire nutrients or replicate.
- **Synergy with Other Drugs:** Imidazole derivatives might be explored in combination with existing Leishmaniasis drugs to achieve a synergistic effect, meaning the combined effect is greater than the sum of their individual effects. This could potentially improve treatment outcomes.

Examples :

Kalpana bhandari et al synthesized a series of substituted **aryloxy alkyl and aryloxy aryl alkyl imidazole** and evaluated in vitro as antileishmanial against Leshmania donovani. Among all compounds exhibited 94–100% inhibition.[25]



For compound R, R_1, R_2, R_3
A =Ph, H, CF_3, H
B =CH_3,H, CF_3, H
C =CH_3,H, NO_2, H
D =CF_3, F, NO_2, H
E =CH_3,NO_2,H, H
F =CH_3,CH_3,NO_2,H

Figure 29

➢ Anti-tubercular activity

Imidazoles show promise as anti-tubercular agents, but it's important to understand how they work and the current state of their use:

The Rise of Imidazole-Containing Anti-tuberculars:

- Drug-resistant tuberculosis (TB) is a growing concern, and researchers are actively seeking new treatment options.
- Imidazole derivatives have emerged as a promising class of anti-tubercular agents due to their ability to target Mycobacterium tuberculosis (Mtb), the bacteria that causes TB.

Targeting Mtb:

- The exact mechanism by which imidazole derivatives fight Mtb is still being investigated, but some potential modes of action include:
    - **Inhibiting Enzymes:** Imidazole derivatives might target specific enzymes crucial for Mtb growth and survival. Examples include enzymes involved in cell wall synthesis or fatty acid metabolism.
    - **Disrupting Membrane Function:** Some imidazoles might interact with the Mtb cell membrane, making it more permeable and leaky. This can disrupt essential functions and hinder bacterial growth.

- **Interfering with Nucleic Acid Synthesis:** Imidazole derivatives might interfere with the process of Mtb replicating its genetic material (DNA), hindering its ability to reproduce.[26]

Example

- **Delamanid** is an FDA-approved medication for the treatment of multidrug-resistant TB (MDR-TB). It is an imidazole derivative that works by inhibiting a specific enzyme involved in Mtb's fatty acid metabolism.[27]

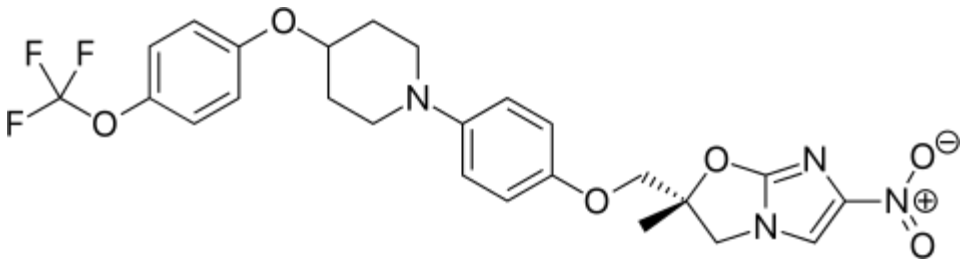


Figure 30

➢ Antiviral activity

The antiviral potential of imidazoles is a fascinating area of research, though not as extensively established as their antifungal properties.

Promising, But Not Direct Acting:

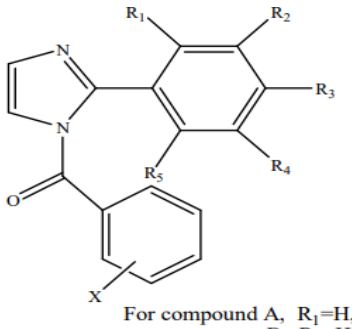
- Unlike their clear-cut role in targeting fungal enzymes, imidazoles don't directly inactivate viruses themselves. However, some imidazole derivatives exhibit antiviral activity by interfering with various stages of the viral lifecycle.

Potential Mechanisms:

- **Viral Attachment and Entry:** Certain imidazoles might hinder the ability of viruses to attach to and enter host cells, thereby preventing initial infection.
- **Viral Replication:** Some imidazole derivatives might interfere with the process by which viruses replicate their genetic material inside infected cells. This disrupts viral multiplication and spread.
- **Viral Assembly and Release:** Imidazole derivatives might disrupt the process of viral particle assembly or release from infected cells, limiting the production of new infectious viruses.

Examples :

imidazole derivatives and the antiviral screening of **substituted phenyl**:[28]



For compound A, R_1=H,R_2=H,R_3=Cl,R_4=H,R_5=H,X=4-NO_2
B, R_1=H,R_2=H,R_3=NO_2,R_4=H,R_5=H,X=4-NO_2

Figure 31

Applications of imidazole

Protein Purification:

Imidazole isn't directly used for protein purification itself, but it plays a crucial role in a specific protein purification technique called **Immobilized Metal Affinity Chromatography (IMAC)**. Here's how it works:

The Power of Tags:

- Scientists often engineer proteins with specific tags, short peptide sequences attached to the protein of interest. These tags allow for easier purification and manipulation of the protein.

His-tag and Nickel:

- A common tag used in IMAC is a **His-tag**, a sequence of several histidine amino acids (histidine contains an imidazole ring in its side chain).
- The chromatography column used in IMAC contains a solid matrix with nickel ions (Ni^{2+}) attached.

The Role of Imidazole:

1. **Binding:** The histidine residues in the His-tag have a high affinity for nickel ions. When a mixture containing the His-tagged protein is passed through the column, the His-tag binds to the nickel ions, immobilizing the protein on the column.
2. **Elution:** This is where imidazole comes in. After unwanted proteins are washed away, a solution containing **increasing concentrations of imidazole** is introduced.
3. **Competition:** Imidazole competes with the His-tags for binding to the nickel ions. As the imidazole concentration increases, it gradually displaces the His-tagged protein from the nickel.
4. **Collection:** The eluted protein, free from contaminants, is then collected in fractions. The appropriate imidazole concentration for elution depends on the specific protein and needs to be carefully optimized.[30]

Buffering and Chelation:

Buffering:

- Imidazole can function as a **buffer** solution, helping to maintain a stable pH within a specific range (typically around 6.2-7.8) in biological experiments.
- This stability is crucial for many enzymes and other cellular processes to function correctly. Enzymes often have an optimal pH range for activity, and deviations from this range can significantly reduce their effectiveness or even render them inactive.

How Imidazole Buffers Work:

- Imidazole exists in two forms in water: an unprotonated form (neutral) and a protonated form (positively charged). The ratio of these forms depends on the solution's pH.

- When the pH needs to be adjusted slightly higher (more alkaline), imidazole can accept a proton from water molecules, becoming protonated and consuming the excess H+ ions.
- Conversely, if the pH needs to be lowered slightly (more acidic), the protonated form of imidazole can donate its proton back to the solution, releasing H+ ions and buffering against a decrease in ph.

Chelation:

- Imidazole also acts as a **chelating agent**, meaning it can form complexes with certain metal ions. This ability is particularly useful in protein purification techniques.[31]

Drug Discovery and Pharmaceuticals:

- The imidazole ring structure is a valuable tool in **drug discovery**. Many existing medications, including **antifungals** (clotrimazole, miconazole), **antihypertensives** (clonidine, moxonidine), and even theophylline (a stimulant found in coffee and tea), contain imidazole derivatives.
- Imidazole derivatives are also used to treat **denture stomatitis**.

Industrial Applications:

- **Corrosion Inhibitor:** Imidazole acts as a corrosion inhibitor for some transition metals, particularly copper. This is important because corrosion can significantly decrease a metal's conductivity. By forming a protective layer on the metal surface, imidazole helps prevent this degradation.
- **Fire Retardants:** Several industrially important chemicals incorporate imidazole derivatives. One prominent example is polybenzimidazole (PBI). This fire-resistant material combines an imidazole ring fused to a benzene ring, making it highly effective in fire retardant applications.
- **Components in Photography and Electronics:** Imidazole derivatives can be found in various compounds used within the photography and electronics industries. The exact nature of these applications might involve specific functionalities of the derivatives, but the details are not as readily available.[32]

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