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“Distinguish Between Conventional And Nonconventional Method Of Synthesis Of Schiff Base”

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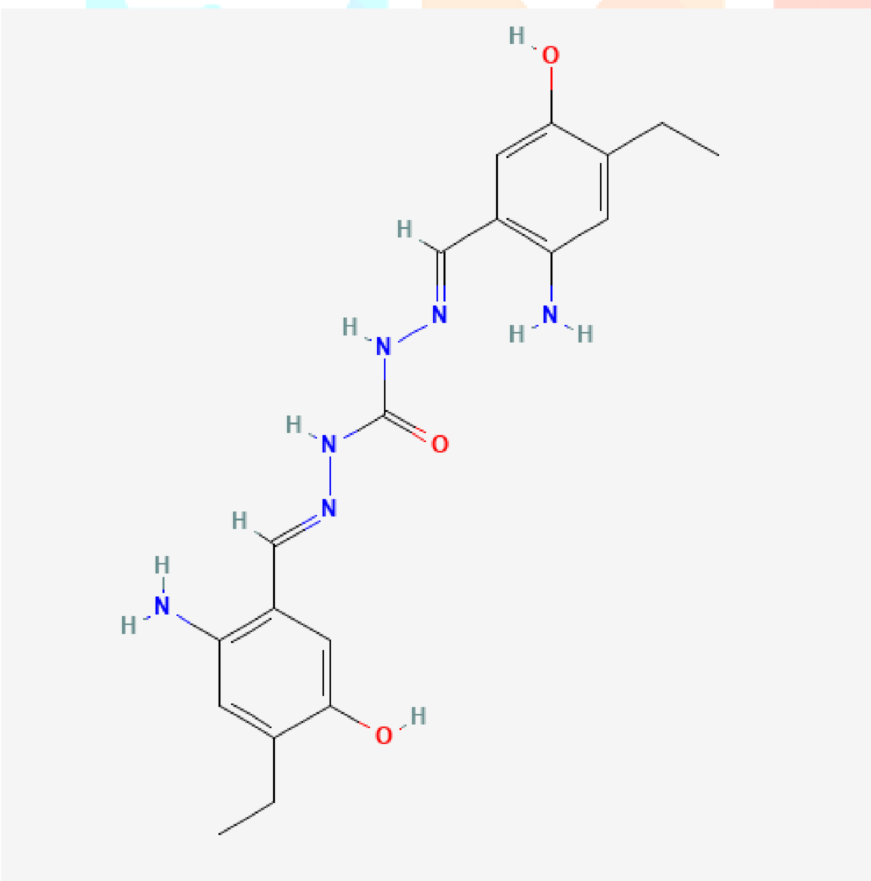
ABSTRACT



SCHIFF BASE

The goal of current research is to develop environmentally friendly methods for synthesizing Schiff bases. Excellent yields (95–98%) for the synthesis have been described using very easy and efficient procedures. Schiff base is typically synthesized by refluxing a mixture of amine and aldehyde (or ketone) in an organic medium, either with or without acid catalysis. The current synthesis adheres to the green chemistry idea. As part of ongoing research, we report effective practical methods such as UV light, the simple mortal-pastel approach (mechanochemistry), and sonication (sonochemistry).

TLC was used to track the reaction's overall progress, and IR and NMR were used to describe it. These techniques are more practical than traditional procedures, because they allow for higher yield reactions under milder circumstances with faster reaction times, no pollution, and safer analysis. Among the benefits of these methods are their low cost, ease of use, and high efficiency.

These techniques are more practical than traditional procedures, because they allow for higher yield reactions under milder circumstances with faster reaction times, no pollution, and safer analysis. These characteristics allow for the correlation of current methods for the safer and more effective synthesis of additional compounds.

Keywords: mechanochemistry, green synthesis, Schiff bases, sonication, ultra-violet radiation, and mortar pastel synthesis.

INTRODUCTION

Schiff bases contain a wide range of biological actions and are well-known in the pharmaceutical business. Because of these importance, several synthetic approaches have been devised to create Schiff base; nevertheless, despite these advancements, the synthesis of these chemicals is still not optimal. Therefore, the creation of high-yielding, clean, and ecologically benign (Green Chemistry) methods for the synthesis of Schiff base continues to be a top priority in organic synthesis.

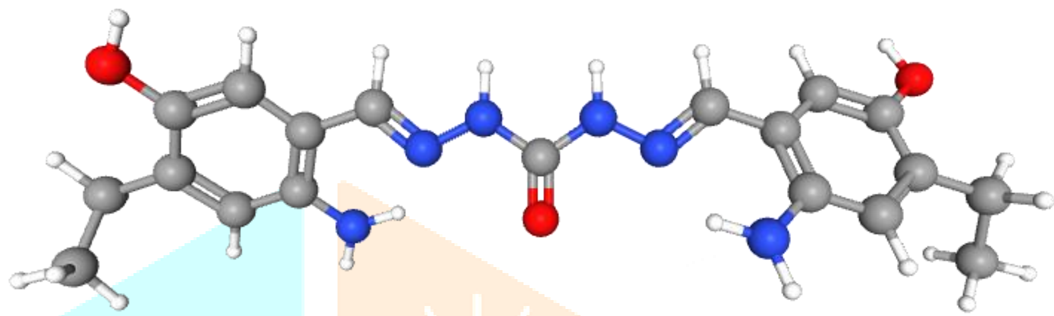
Schiff bases are extremely intriguing chemicals for biochemistry, medicine, and pharmacy because of their widespread distribution in nature6–8. They are created in living things as byproducts of a variety of natural processes. Schiff base, for instance, is found in the rods of the retina, where it forms between opsin and 11-cis-retinal as the initial stage of a series of changes that enable shape perception even at dusk9–10. A few Schiff bases are able to attach to DNA11. Schiff bases may be a desirable substitute for DNA polymerase in cases when it is not feasible to repair damaged DNA. It might stop diseases including diabetes, cancer, and neurological conditions from developing12.

However, certain imine systems are capable of more than just DNA repair. Their second undeniable benefit is that, like cis-platin, they can attach to tumor cell DNA to stop them from proliferating.13. Schiff bases based on hydrazone, thiosemicarbazone, or benzazepine are being studied clinically for the treatment of several cancer types.

The quest for more ecologically friendly methods of synthesizing Schiff bases reflects their growing significance in a variety of fields, particularly in the fields of medicine and pharmacy. Eco-friendly synthetic methods are employed by researchers to improve the efficiency of the reactions that affect the economics of technological processes or to decrease post-reaction wastes39–40. Achieving a substrate conversion rate near 100% and avoiding the need to employ surplus substrates are optimal conditions for chemical synthesis.

Using readily available and reasonably priced raw materials is also crucial, as is incorporating hazardous wastes into the process of removing them from the environment if at all possible. This study describes several traditional and environmentally friendly Schiff base synthesis techniques, paying special emphasis to their efficacy.

3D Conformer Of Schiff Base | Interactive Chemical Structure Model



LITERATURE REVIEW :-

Classical organic chemistry reactions serve as the basis for conventional procedures, which call for very simple arrangement. They usually entail a primary amine reacting with a carbonyl molecule under specific circumstances, usually with the aid of a base, acid, or solvent catalyst.

- CONVENTIONAL METHOD : This is the most used technique, which involves condensing a primary amine with an aldehyde or ketone in an appropriate solvent (such as methanol or ethanol). The reaction is conducted under reflux, frequently for a number of hours.

  Benefits: Easy to understand and execute. Basic laboratory supplies are needed.

  Limitations include lengthy reaction durations (up to several hours), the potential for byproduct production, and energy consumption from prolonged heating. [1]

Solvent-Free Method Description: The reaction takes place at room temperature or with mild heat without the use of a solvent. From an environmental standpoint, this method is beneficial since it does away with the requirement for organic solvents.

Reaction Mechanism: In the absence of a solvent, the amine condenses with the carbonyl group, typically requiring just gentle heating or mechanical mixing, much like the reflux approach.

Benefits include cost effectiveness, environmental friendliness, and the avoidance of solvent waste.

Limitations: To prevent adverse reactions, exact control over temperature and reaction time is necessary. [2],Polish journal of Chemistry

- NONCONVENTIONAL METHOD for the Synthesis of Schiff Bases

Non-conventional methods are contemporary approaches that use cutting-edge technology like microwave radiation, ultrasound, and more environmentally friendly chemical processes, departing from standard heating and solvent-based treatments.

Microwave-Assisted Synthesis: The reaction mixture is heated by microwave radiation. Rapid and consistent heating is provided by this technique, which frequently leads to quicker reactions and larger yields.

Reaction Mechanism: Localized heating and increased reactivity are the results of polar molecules (such amines and carbonyl compounds) absorbing energy from the microwave.

Benefits:

Decreased Reaction Time: Unlike traditional procedures, which might take several hours, reactions can be finished in minutes to hours.

Higher Yields: Less byproducts and adverse effects.

Energy Efficiency: Uses less energy than traditional heating methods.

Limitations: May not be available in all laboratories due to the requirement for specific microwave equipment. [1]

- Synthesis Aided by Ultrasound (Sonochemistry)

When the reaction mixture is exposed to high-frequency ultrasonic waves, microbubbles (cavitation) quickly develop and collapse, resulting in localized heating and increased reactivity.

Mechanism of Reaction: Ultrasound-induced cavitation generates hot spots in the reaction mixture, raising the temperature and pressure there and speeding up the process.

Benefits:

Enhanced Reaction Rate: By hastening the production of Schiff bases, ultrasound shortens reaction times.

Cleaner effects: Improved selectivity and less adverse effects.

Solvent-Free: A lot of reactions can be conducted without the use of solvents, which makes the process more environmentally friendly.

Limitations: Needs an ultrasonic probe or bath, which can be expensive and needs to be adjusted for various systems.

- Green Chemistry Methods
  Green chemistry focuses on conducting the Schiff base synthesis in mild settings utilizing environmentally friendly solvents (such as water, ethanol, or ionic liquids) or no solvents at all. [3]

  Reaction Mechanism: The reaction is carried out by catalyzed or traditional means, but the use of harmful and toxic solvents and reagents is minimized.

  Benefits:

  Eco-friendly: Less of an impact on the environment through the use of green solvents or none at all.

  Energy-efficient: Conditions are often softer and reactions are frequently faster.

  Limitations: High yields with various starting materials may require tuning, and green solvents might be costly.

- The solid-phase synthesis process involves attaching one of the reactants, usually the amine, to a solid support like silica or resin. The Schiff base is then created by adding the carbonyl compound to the solid-supported amine.

  Reaction Mechanism: The solid support's surface is where the reaction takes place, which frequently contributes to the Schiff base's higher yield and purity.

  Benefits

  Simple Product Isolation: Simple purification is required to separate products from the solid phase.

  Recyclability: It is frequently possible to reuse the sturdy support.

  Limitations: Special setup and solid-phase reagents are needed.

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- Description of Enzyme-Catalyzed Synthesis: In mild conditions, enzymes (like transaminases) can catalyze the synthesis of Schiff bases, resulting in increased selectivity and specificity.

  Reaction Mechanism: By supplying a highly selective active site and reducing the activation energy, the enzyme promotes the condensation reaction.

  Benefits:

  Mild Reaction Conditions: Strong acids or bases or high temperatures are not required.

  High Selectivity: By producing fewer byproducts, enzymes offer superior selectivity.

  Eco-friendly: Makes use of natural catalysts, which frequently eliminates the need for dangerous chemicals.

Limitations: Not all Schiff bases can be prepared using enzymes, and it can be expensive.

Industry	**Demand**	**Market Growth Trend**	**Key Applications**
Pharmaceuticals	High demand for drug development and bioactivity	Strong growth due to cancer, infection, and neurodegenerative diseases	Drug development, antimicrobial agents, anticancer drugs
Chemicals	Stable demand in coordination chemistry and catalysis	Growth in sustainable chemistry and high-performance materials	Catalysts, polymers, dyes, photoactive compounds
Agriculture	Moderate demand for eco-friendly pesticides	Growth in green chemistry and sustainable farming practices	Pesticides, herbicides, bioactive agents
Textiles	Steady demand for colorants and textiles	Niche growth in eco-friendly and sustainable textiles	Dyes, pigments, textile finishing
Nanotechnology	Growing demand for functionalized nanomaterials	Rapid growth in nanotechnology and smart materials	Nanoparticle synthesis, sensors, catalysis
Environmental Sensors	Growing demand for eco-friendly sensors	Increasing demand due to environmental and health monitoring	Biosensors, pollutant detection, medical diagnostics

MARKET COMPARISON

EXISTING MEDICATION :-

- Schiff Base of 4-(Dimethylamino) Pyridine: This derivative of the Schiff base is being investigated for potential medical uses due to its antibacterial and anticancer properties.
- Bis-Schiff Base-Cobalt(II) Complex: This cobalt-based Schiff base complex has anti-inflammatory and antioxidant properties in addition to possible cancer treatment uses.
- 2-Hydroxy-1-naphthaldehyde Schiff Base: Researched for its antibacterial and anticancer properties, with possible use in drug formulations.
- Salicylaldimine: An antibacterial and anticancer derivative of Schiff base.
- Metal-complexes of Schiff bases, especially those containing copper and zinc, have antibacterial and anticancer properties. These are known as chloro-Schiff base complexes.
- 2-Hydroxybenzaldehyde and aniline Schiff Base: This Schiff base has been examined for its antibacterial, anticancer, and antioxidant properties.
- Schiff Base 2,6-Di-tert-butylphenol is well-known for its antioxidant and anti-inflammatory properties, as well as its potential for drug administration.

MEDICATION SIDE EFFECTS

Rare –

• Severe stomach or abdominal discomfort and cramping

• Tenderness in the abdomen.

Blood in the urine.

• severe, watery diarrhoea that can also be bloody.

• A significant change in the quantity or frequency of urine production.

• A rise in thirst.

• Pain in the lower back.

• alterations in mood or thought.

1. Conventional Methods

- **Process and Conditions:**

Aldehydes and ketones are usually refluxed or stirred with primary amines in organic solvents (such ethanol or methanol) at high temperatures in conventional synthesis. Glacial acetic acid and other acid catalysts are frequently employed to speed up the reaction and remove water, which is important because water can prevent the production of Schiff bases. [1]

- **Drawbacks:**

• Requires many hours of reaction time.

• Involves using organic solvents, which raises environmental issues.

• Extra procedures might be required for the purification of the product and the elimination of water.

• Slower reactions and lesser yields when compared to green techniques

2. Non-Conventional (Green) Methods

- **Process and Innovations:**

Non-traditional techniques include a variety of green chemical strategies, such as:

• Microwave-Assisted Synthesis: Higher yields in minutes are possible due to the reaction's rapid acceleration caused by rapid heating.

• Ultrasound Irradiation: In milder environments, it increases yields and response rates.

• Solvent-Free (Grinding) Methods: These methods reduce reaction durations by combining and grinding reactants, frequently at room temperature, without the use of solvents.

• Aqueous Media: Water, occasionally at room temperature, is utilized as a solvent to create a safe environment and make product isolation easier.

• Stirring at Room Temperature: Some syntheses work well without heating and with only basic magnetic stirring. [3]

- **Advantages:**

• Reaction times were significantly shortened from minutes to hours. [3]

• Yields that are higher or on par with traditional techniques.

• Less waste and little to no usage of dangerous solvents.

• Easy work-up, usually involving only drying and filtering; • Economical and environmentally beneficial.

- **Comparative Findings from Recent Literature**

• Offer and Efficiency: When compared to conventional reflux-based processes, microwave and grinding techniques routinely offer higher yields and faster responses.

• Effect on the Environment:

Green techniques adhere to the principles of sustainable chemistry by avoiding or using organic solvents and toxic chemicals as little as possible.

• Practicality: Aqueous and solvent-free syntheses are simple, need minimal energy and equipment, and can be scaled for industrial use.

- Obstacles:

  Conventional techniques are often less preferred because of efficiency and environmental considerations, although they can still be helpful for specific substrates or in situations where specialist equipment is not available.

METHODOLOGY

-The traditional Schiff base synthesis method
Schiff Base Synthesis Employing Organic Solvents

Reactants include benzaldehyde (C_6H_5CHO), an aromatic aldehyde, and aniline ($C_6H_5NH_2$), a primary amine.

GENERAL REACTION

$C_6H_5NH_2 + C_6H_5CHO \rightarrow C_6H_5CH{=}N–C_6H_5 + H_2O$

- Methodology for the Ethanol Experiment / [Conventional method]

1. Materials:
   18.6 ml of aniline

   18.6 ml of benzaldehyde
   10 to 15 milliliters of ethanol (as solvent)

2. Procedure:

   o Dissolve aniline in ethanol in a round-bottom flask.
   o Add benzaldehyde gently while stirring.
   o For one to three hours, heat the reaction mixture under reflux (70 to 80°C).

o Use Thin Layer Chromatography (TLC) to track the development.
o After completion, chill the mixture to room temperature.

3. Product Isolation:

o N-Benzylideneaniline, a yellow crystalline compound, starts to precipitate as it cools.

To purify, filter the solid and rinse it with cold ethanol.

o Use a desiccator or oven to dry the product.

- Yield: Typically 70–85%

- Description

~52–55°C is the melting point.

• IR Spectrum:
C=N stretch at around 1610–1640 cm^{-1}

• ^{1}H NMR:
o Singlet for proton about 8.5–8.6 ppm for –CH=N
o Aromatic region: multipleplets, 7.0–7.8 ppm

Advantages and Disadvantages

Aspect	Organic Solvent Method
Advantages	Familiar setup, good solubility, easy to monitor
Disadvantages	Longer reaction time, energy use (reflux), solvent waste
Yield	Moderate to high (70–85%)
Environmental Impact	Higher than green methods

Summary

Parameter	Description
Method Type	Conventional (organic solvent)
Solvent Used	Ethanol or methanol
Temperature	70–80°C (reflux)
Time	1–3 hours
Product	N-Benzylideneaniline

Purification	Filtration and recrystallization
Yield	~70–85%

- Non conventional method of Schiff base synthesis

Non-Conventional Schiff Base Synthesis Techniques:

1. Microwave-Assisted Synthesis: Shortens reaction times from hours to minutes by accelerating processes.
2. Ultrasound-Assisted Synthesis: Uses cavitation to increase reaction speeds.
3. Water as a Solvent: An economical, non-toxic, and environmentally beneficial solvent.

N-Benzylideneaniline in Water

Reactants:

- Aniline ($C_6H_5NH_2$) – a primary aromatic amine
- Benzaldehyde (C_6H_5CHO) – an aromatic aldehyde

Product:

- N-Benzylideneaniline ($C_6H_5CH=N–C_6H_5$) – a Schiff base

Byproduct:

- Water (H_2O)

GENERAL REACTION :-

$C_6H_5NH_2 + C_6H_5CHO \rightarrow C_6H_5CH=N–C_6H_5 + H_2O$

Materials:

- 18.6 ml Aniline
- 18.6 ml Benzaldehyde
- 5 mL distilled water

TOTAL YEILD –

TOTAL YEILD – 85-90 %

Procedure:

• Put benzaldehyde and aniline straight into a beaker with five milliliters of distilled water.
• Stir the mixture for 30 to 60 minutes at room temperature or over low heat (around 40 to 50°C).
• Use Thin Layer Chromatography (TLC) to track the reaction's development.

• As the reaction continues, a yellow precipitate of N-Benzylideneaniline is formed.

Isolation:

The precipitate should be filtered.
• To get rid of contaminants, wash with cold water.
• Use a desiccator or a vacuum to dry the product.

Yield: Under ideal circumstances, it is usually 85–90%.

Benefits of Water-Based Synthesis

• Eco-friendly: Water is a solvent that is safe for the environment and non-flammable.
• Easy work-up: Purification is made simple by the product precipitating out.

• Economical: No costly catalysts or solvents are required.
• Mild conditions: The reaction works best at room temperature or a little higher.

Features of N-Benzylideneaniline

A yellow crystalline solid with a melting point of around 52 to 55°C

• Imine (C=N) stretch in the infrared spectrum: approximately 1610–1640 cm^{-1}
• ^{1}H NMR:
Proton of imine (-CH=N-): singlet at 8.5–8.6 ppm
o Multiplets of aromatic protons: 7.0–7.8 ppm

Component	**Detail**
Reaction Type	Schiff base formation
Solvent	Water
Reaction Time	30–60 minutes
Product Yield	~85–90%
Environmental Impact	Very low (green chemistry)

DISCUSSION

In terms of yield, environmental friendliness, safety, and efficiency, the unconventional approaches perform noticeably better than the standard ones. In addition to being useful, their incorporation into academic and industrial contexts is essential for sustainable chemistry. Future research can investigate automation and hybrid approaches (such as ultrasound plus green catalysts) for even greater improvement.

METHOD	REACTION TIME	YIELD (%)	SOLVENT USED	ENVIRONMENTAL IMPACT
CONVENTIONAL (REFLUX)	6–12 hours	65–80%	Ethanol/Methanol	High
MICROWAVE-ASSISTED	2–10 minutes	80–95%	Minimal or none	Low
ULTRASOUND-ASSISTED	10–30 minutes	85–90%	Minimal or water	Low
SOLVENT-FREE GRINDING	5–15 minutes	75–85%	None	Very Low
NATURAL ACID CATALYSIS	20–40 minutes	70–88%	Water/Natural Juice	Very Low

CONCLUSION

Schiff bases are chemical compounds with a wide range of structures and uses that are of great interest to the medical and pharmaceutical industries. Throughout the 20th century, they were mostly acquired using traditional methods. Alternative methods for synthesizing these chemicals are required because certain current Schiff base syntheses involve hazardous solvents (benzene, toluene). Furthermore, the scientific community started looking for "green" substitutes for the well-known syntheses of numerous chemical substances with significant, in-depth uses around the end of the 1990s. These investigations have led to the development of a set of environmentally friendly techniques for producing organic chemicals, such as Schiff bases, which have enhanced research.

Fruit juice synthesis is the newest of the green methods for creating aromatic imines. There is a good deal of information about making Schiff bases with lemon juice in the literature. The first presentation of the Schiff bases synthesis results in lemon or apple juice from the Jonagold apple type took place in 2020. The authors have demonstrated the connection between the structure of the aldehyde used to create Schiff base and the pH of fruit juice.

Traditional Schiff base synthesis generally involves heating a combination of an amine and either an aldehyde or ketone under reflux conditions while utilizing organic solvents. This method usually takes several hours to finish and requires a considerable amount of energy. Although it is commonly employed and relatively simple, it is not as efficient or environmentally friendly due to prolonged reaction durations, the use of solvents, and lower overall yields.

On the other hand, alternative methods such as microwave-assisted or ultrasonic synthesis provide quicker and more efficient options. These techniques can reduce reaction times to just minutes, often eliminating or significantly decreasing the need for solvents, and leading to increased product yields. Furthermore, they are regarded as greener and more sustainable, aligning with contemporary objectives in green chemistry.

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