THE HÜCKEL-MÖBIUS APPROACH TO PERICYCLIC CHEMISTRY

B.Sc. Chemistry (Hons) Semester VI (Under CBCS)

Examination, 2025

Paper: DSE-B4 (Dissertation)

CU Roll no. **:223114-21-0010**

CU Reg no. **:114-1111-0221-22**

College: **St. Paul's Cathedral Mission College**

St. Paul's Cathedral Mission College
33/1 Raja Rammohan Roy Sarani, Kolkata-700 009
NAAC ACCREDITED
AISHE ID C-11869
Estd. 1865

CERTIFICATE

This is to certify that the dissertation entitled "**THE HÜCKEL-MÖBIUS APPROACH TO PERICYCLIC CHEMISTRY**", submitted to the Department of Chemistry, St. Paul's C. M. College, Kolkata in partial fulfilment for the award of the degree of SEM-VI, DSE-B4 (under CBCS) in the B.Sc. SEM-VI CEMA Examination, 2025, CU, is a record of bona fide work carried out by Rajarshi Biswas, CU Roll no. :223114-21-0010. (CU Reg no. :114-1111-0221-22), under my supervision and guidance.

This is a review work and hasn't been submitted to receive any other degree. All help received by him from various sources have been duly acknowledged.

(Dr. Kaushik Basu).
Assistant Professor
Department of Chemistry
St. Paul's C. M. College

(Dr. Kalyan Kumar Mondal)
Associate Professor
Department of Chemistry
St. Paul's C. M. College

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my teachers, **Dr. Kaushik Basu Sir** and **Dr. Kalyan Kumar Mandal Sir** for their unwavering support and guidance throughout the project on **"THE HÜCKEL-MÖBIUS APPROACH TO PERICYCLIC CHEMISTRY"** and also helping me to find out different type of research paper from the different resources which help me a lot during my project work. I am also grateful to my friends, who provided valuable insights and feedback that helped to shape this work. I am deeply indebted to my family and friends, who offered emotional support and encouragement when it was most needed. Thank you all for their contributions to this project.

CONTENTS

THE HÜCKEL-MÖBIUS APPROACH TO PERICYCLIC CHEMISTRY

INTRODUCTION TO PERICYCLIC REACTIONS.

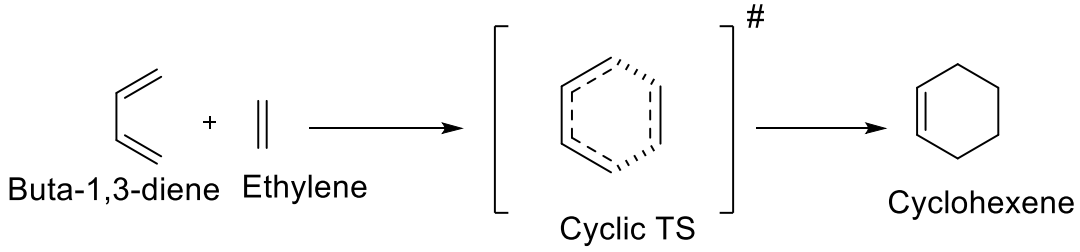
An elegant approach in classifying organic reactions is based on mechanism. Broadly there are three mechanistic classes: ionic, radical and pericyclic. As such pericyclic reactions [1-7] constitute a separate and distinct mechanistic class of organic reactions.

A pericyclic mechanism is characterized by concerted bond-breaking and bond-forming process with cyclic movement of electrons through the formation of a single transition state (TS) [8-10].

Cyclic movement of electrons signifies a cyclic overlap of orbitals (cf. cyclic orbital overlap in an aromatic / antiaromatic system).

A single TS indicates that no intermediate is involved. The electrons move around in a cycle or ring, the word pericyclic (peri meaning around and cyclic meaning circle or ring) was introduced by Woodward and Hoffman in 1969 [11] to christen this class of reactions.

The Diels-Alder reaction provides a classic example of pericyclic reaction between buta-1,3-diene and ethylene to produce cyclohexane, which involves the breaking of three π bonds and formation of two σ bonds and one π bond.



CHARACTERISTICS OF PERICYCLIC REACTIONS.

1) In pericyclic reactions among the reactants and products usually one molecule is unsaturated[12].

2) The reactions involve the formation or cleavage of σ bonds and consumption or formation of π bonds[6].

3) Pericyclic reactions are insensitive to solvent polarity[8].

4) The electronic re-organisation occurs in some sort of cyclic array of participating atomic centres[12].

5) No any reactive intermediate formed (carbocation, carbanion, free radical, carbene etc) in Pericyclic reactions[12].

6) Pericyclic reactions activated by heat (thermal) or light (photochemical)[4].

7) Pericyclic reactions are stereospecific in nature[8].

CLASSIFICATION OF PERICYCLIC REACTIONS.

Pericyclic reactions are mainly classified into the three most common types[6] of reactions.

(1) Electrocyclic reactions.

(2) cycloaddition reactions.

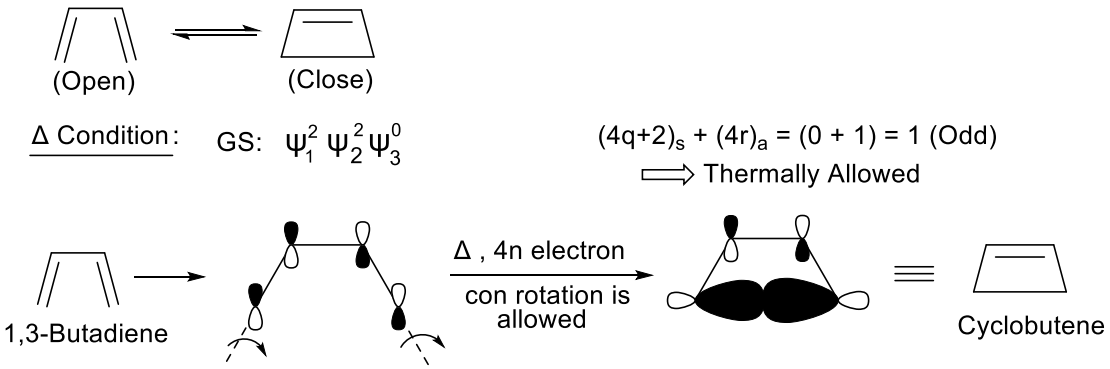
(3) Sigmatropic reactions.

ELECTROCYCLIC REACTIONS.

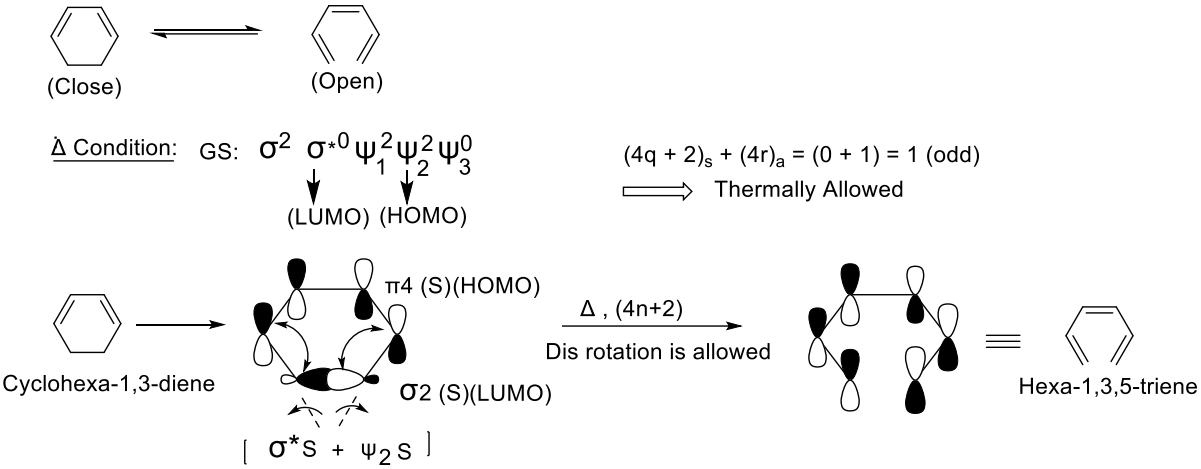
An electrocyclic reaction [3] denotes a ring closing process in which a new σ bond is formed across the termini of a conjugated π system to give a cyclic system with shorter conjugation, or the reverse ring opening process when a σ bond of a cyclic system is broken to give a longer conjugated π system.

Both electrocyclic ring closing (cyclization) and ring opening reactions are unimolecular and are characterized by $\Delta\sigma = 1$.

Electrocyclic Ring Closing for 4n electron system:



Electrocyclic Ring Opening for (4n+2) electron system:

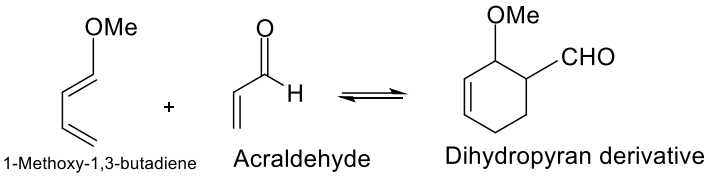


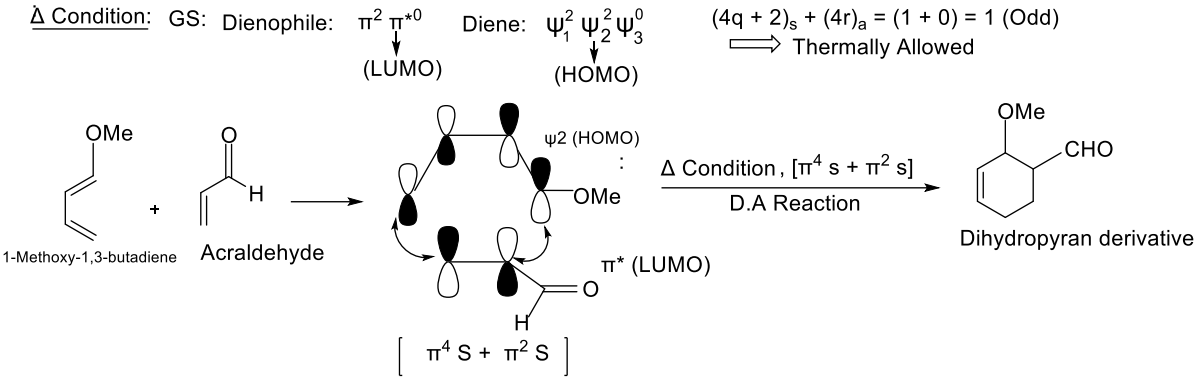
CYCLOADDITION REACTIONS.

A cycloaddition reaction [(1)] indicates the addition of two π reactants to form a cyclic compound with the formation of σ bonds at the ends of the π components and concomitant reduction in π length in each component. Cycloadditions are bimolecular, in the Diels Alder reaction in which two π systems interact to form a cyclic adduct with two σ bonds and a new π bond.

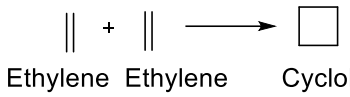
[4 + 2] Cycloaddition Reaction:

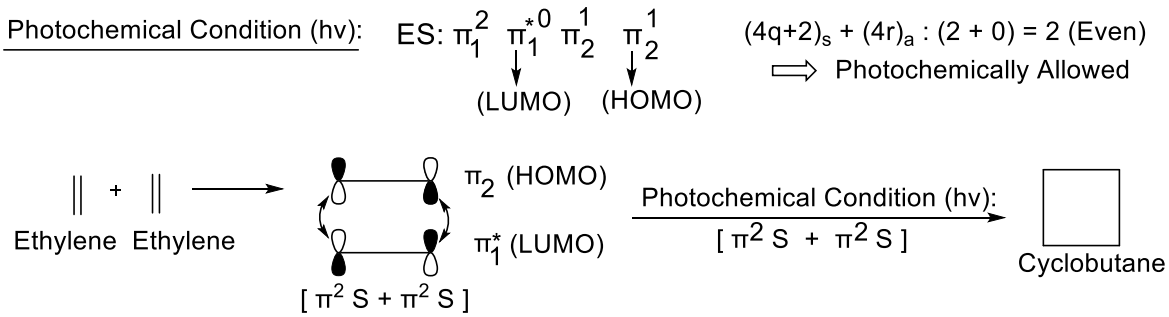
Diels-Alder Reaction:





[2 + 2] Cycloaddition Reaction:



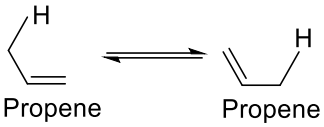


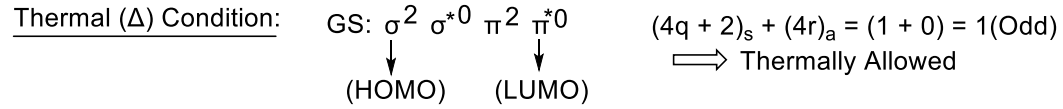
SIGMATROPIC REARRANGEMENT.

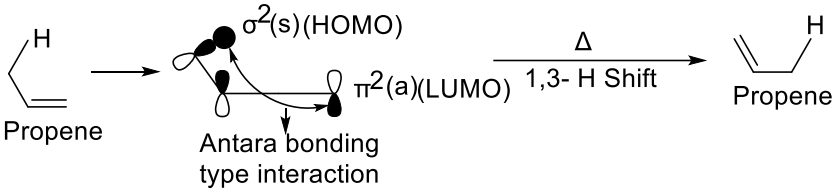
A sigmatropic rearrangement [(1)] indicates the migration of a σ bond (adjacent to one or two π components) from one position to another in a molecule with concomitant reorganization of the π system(s). In this process, an old σ bond is broken and a new σ bond is formed. The reaction is therefore inherently reversible; the direction in which the rearrangement is favoured is determined by thermodynamics. A

sigmatropic rearrangement is evidently unimolecular, and is characterized by $\Delta\sigma = 0$.

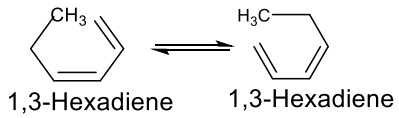
1,3-H Shift:

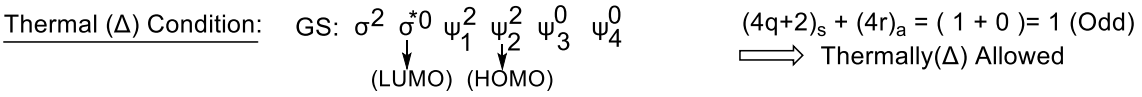


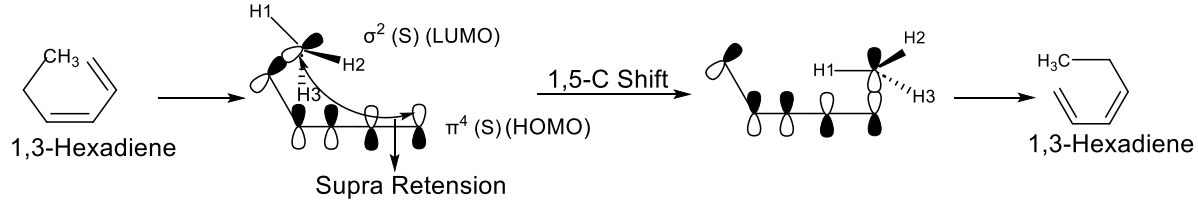




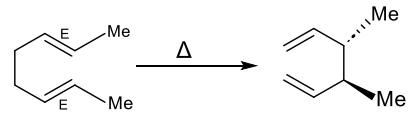
1,5-C Shift:



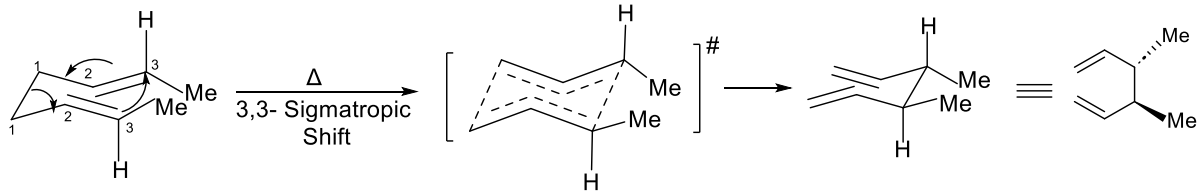




3,3 – Sigmatropic Shift:



It is an example of Cope rearrangement



THE HÜCKEL-MÖBIUS METHOD.

The TS aromaticity [(1)] approach, developed independently by Dewar and Zimmerman, is based on the aromaticity/antiaromaticity of pericyclic TS. Cyclic TSs can be classified as aromatic or antiaromatic, just like the cyclic conjugated polyenes are. Dewar used the perturbational molecular orbital (PMO) theory for aromaticity and antiaromaticity in cyclic conjugated Hückel or Möbius (anti-Hückel) system, and his approach applied to the cyclic TS in concerted reaction is also called the PMO approach [(13)]. Zimmerman put forward the idea of Hückel or Möbius TS in concerted process using the Hückel molecular orbital method [(14)].

The TS aromaticity approach provides two simple rules, one for thermal reaction and the other for photochemical reaction, which are stated as follows.

1. A thermal pericyclic reaction proceeds via an aromatic TS.

2. A photochemical pericyclic reaction proceeds via an antiaromatic TS.

Now the question is: which TS is aromatic and which is antiaromatic? This can be easily decided in a practical manner using the following step-by-step procedure.

Step 1. Draw a cyclic orbital array in the TS using basis set orbitals (set of atomic orbitals) for each component for the pericyclic mode to be analysed.

Step 2. Classify the topology of the orbital array as the Hückel or Möbius system depending on the number of sign inversions in the cyclic array.

Number of sign inversion	**Topology of orbital array**
Zero or even	Hückel
Odd	Möbius

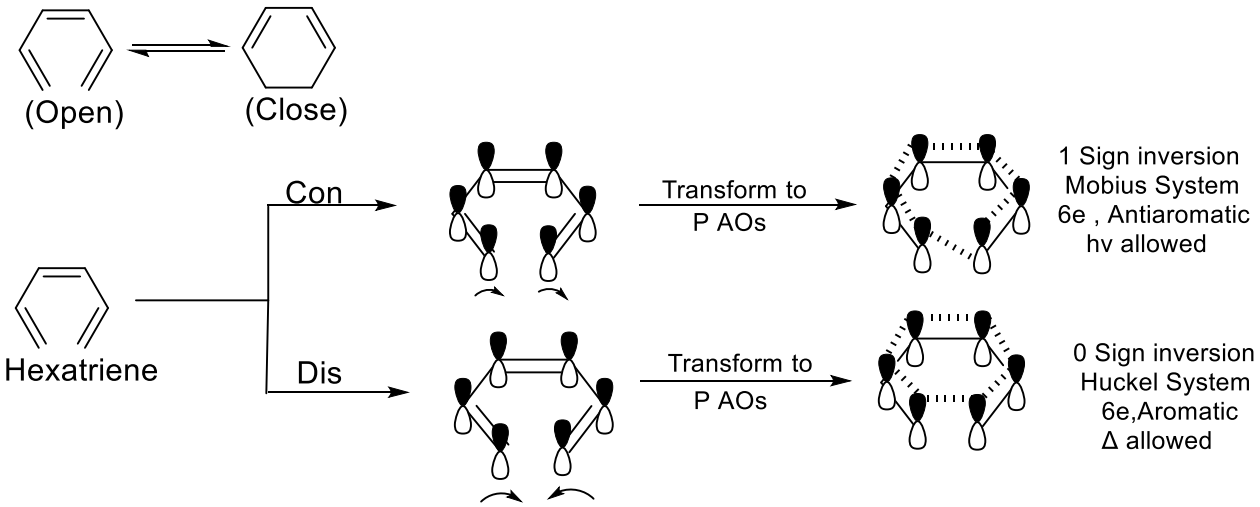
(It should be kept in mind that a sign inversion does not indicate an antibonding overlap with respect to bond formation; the counting of the number of sign inversions is simply a device to determine the Hückel / Möbius topology.)

Step 3. Determine the TS as aromatic or antiaromatic based on the total number of electrons involved.

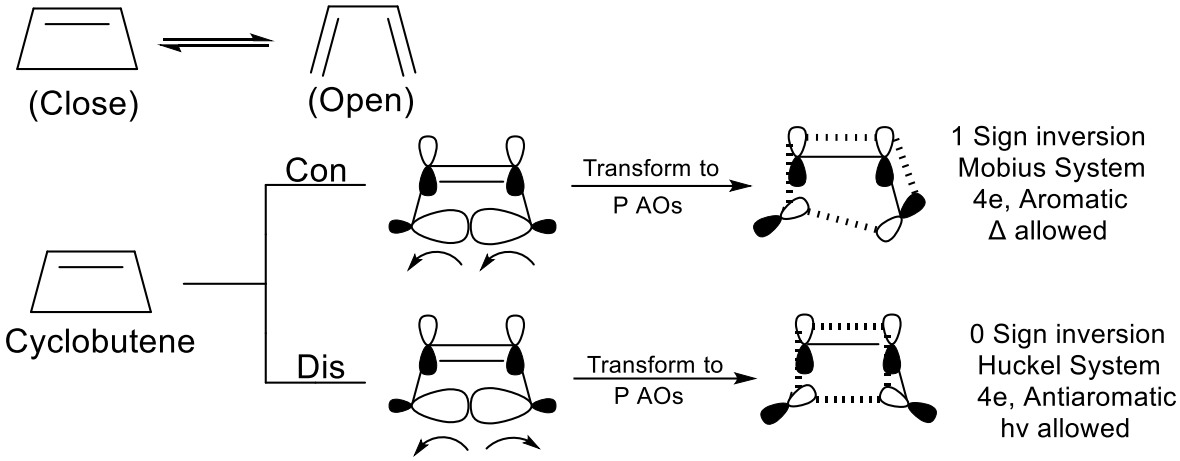
Number of electrons	Hückel System	Möbius System
4n + 2	Aromatic	Antiaromatic
4n	Antiaromatic	Aromatic

Implementation of Hückel-Möbius Concepts in Electrocyclic Reaction:

Ring Closing for (4n + 2) π Electron System:

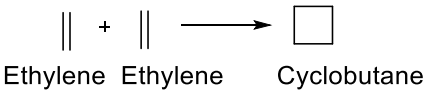


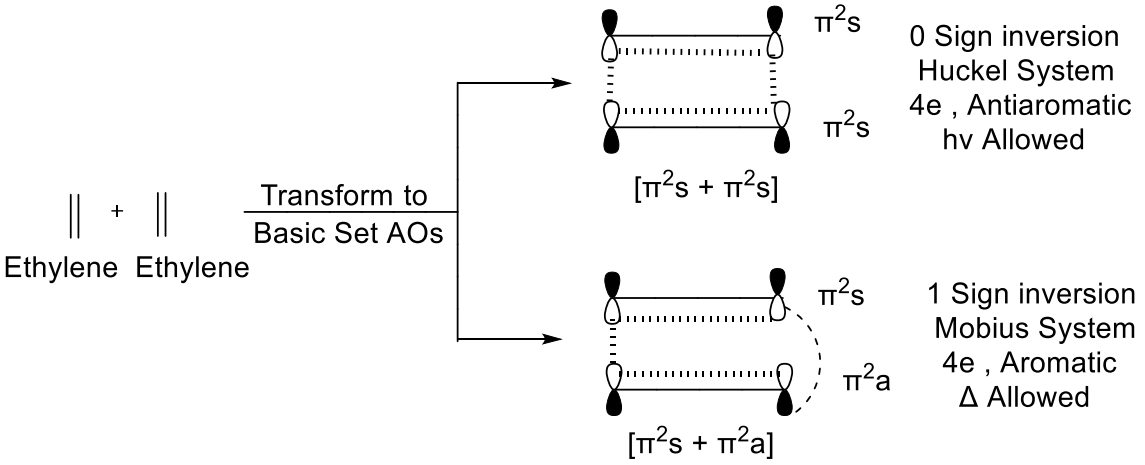
Ring Opening for 4nπ Electron System:



Implementation of Hückel-Möbius Concepts in Cycloaddition Reaction:

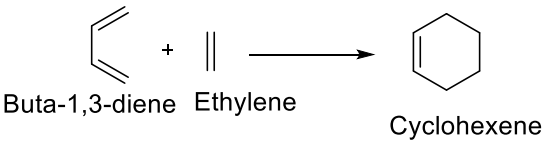
(2 + 2) Cycloaddition Reaction:

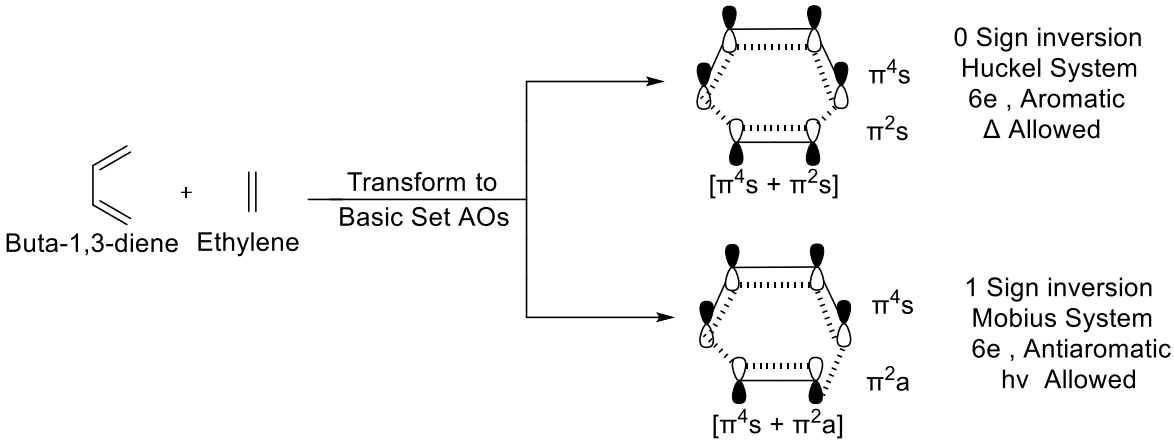




[4 + 2] Cycloaddition Reaction:

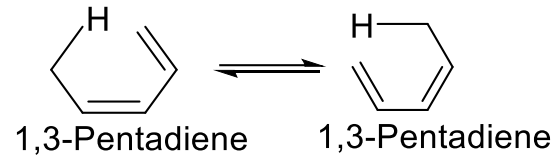
Diels-Alder Reaction:

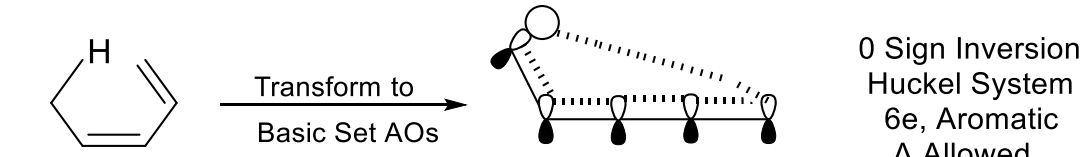


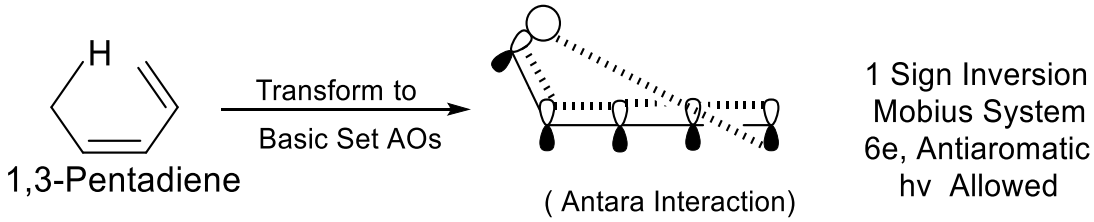


Implementation of Hückel-Möbius Concept in Sigmatropic Rearrangement

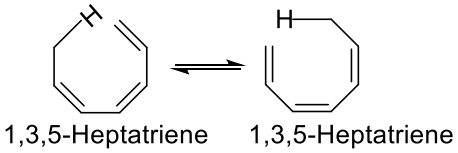
1,5-H Shift:

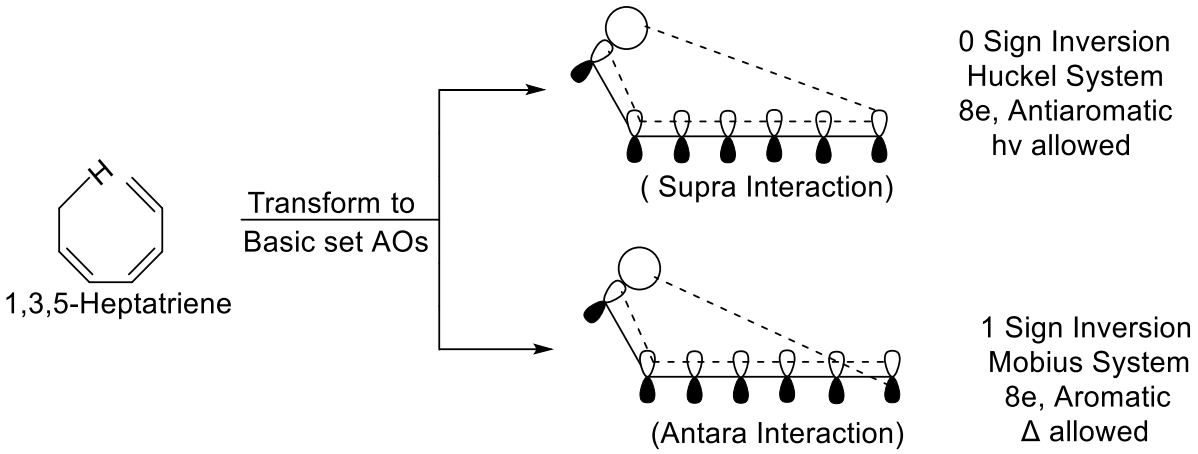




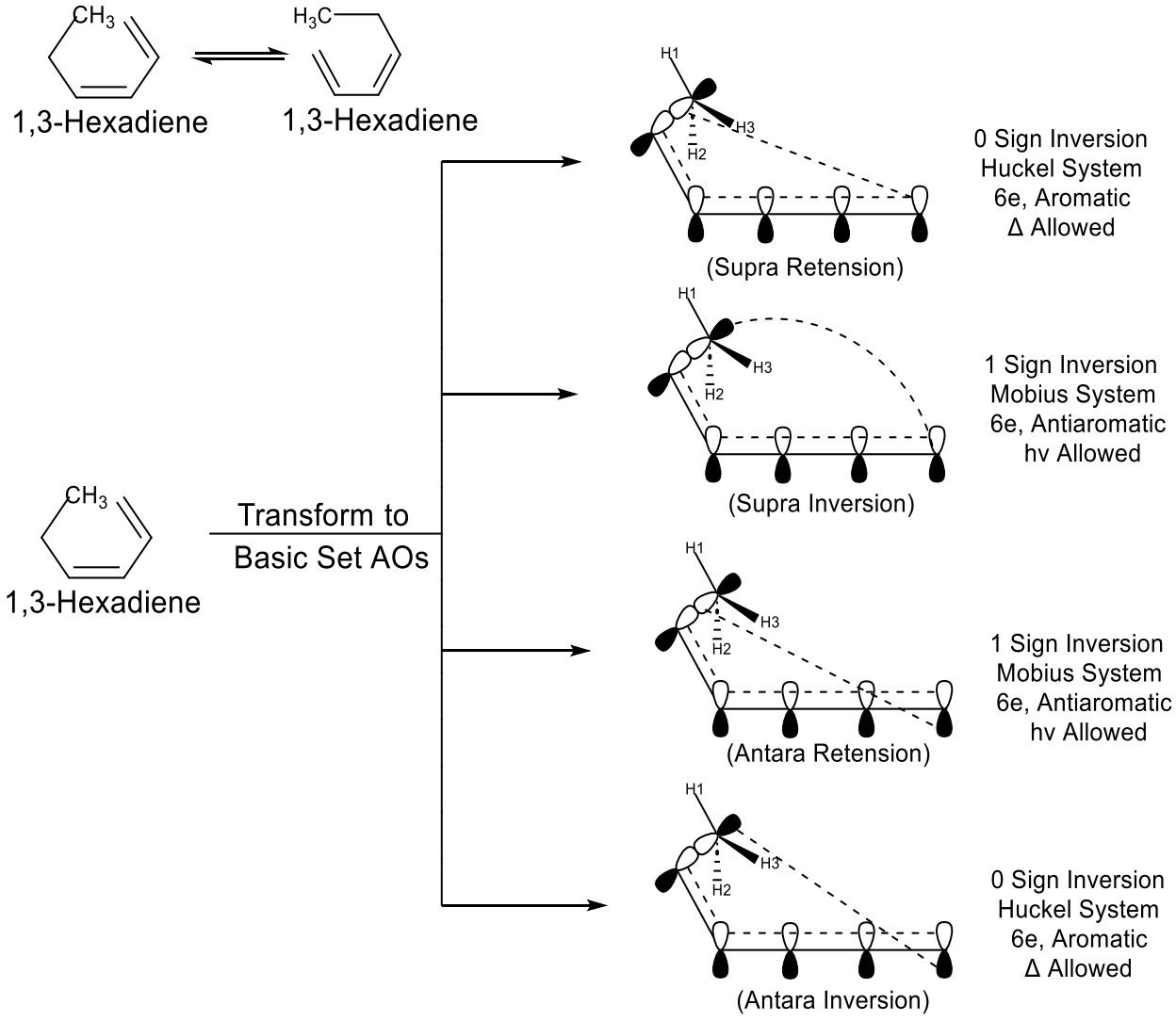


1,7-H Shift:




1,3,5-Heptatriene
Transform to
Basic set AOs
(Supra Interaction)
0 Sign Inversion
Huckel System
8e, Antiaromatic
hv allowed
(Antara Interaction)
1 Sign Inversion
Mobius System
8e, Aromatic
Δ allowed

1,5-C Shift:


1,3-Hexadiene
1,3-Hexadiene
1,3-Hexadiene
Transform to
Basic Set AOs
(Supra Retension)
0 Sign Inversion
Huckel System
6e, Aromatic
Δ Allowed
(Supra Inversion)
1 Sign Inversion
Mobius System
6e, Antiaromatic
hv Allowed
(Antara Retension)
1 Sign Inversion
Mobius System
6e, Antiaromatic
hv Allowed
(Antara Inversion)
0 Sign Inversion
Huckel System
6e, Aromatic
Δ Allowed

ADVANTAGES OF HÜCKEL-MÖBIUS APPROACH.

1. Predicts Reaction Feasibility:

It helps to determine whether a pericyclic reaction is thermally allowed or photochemically allowed based on orbital symmetry [14].

2. Simplifies Orbital Analysis:

Uses the aromaticity (Hückel) or antiaromaticity (Möbius) of transition states to classify reactions [1].

3. Supports Woodward-Hoffmann Rules:

Provides a conceptual basis for the orbital symmetry rules derived by Woodward-Hoffmann [3].

4. Facilitates Stereochemical Predictions:

Helps to predict stereochemistry (conrotatory vs. disrotatory ,suprafacial vs antarafacial) in pericyclic processes [3].

5. Explains Thermal vs Photochemical Pathways:

Clarifies why certain reactions are allowed thermally and others photochemically based on electron count and topology [3].

6. Unifies Reaction Types:

Offers a unified framework for different pericyclic reactions (e.g. electrocyclic, sigmatropic, cycloaditions) [9].

7. Connects to Aromaticity Concepts:

Bridges classical aromaticity (Hückel's 4n+2 rule) with pericyclic transition states [2].

8. Visual Tool for Transition States:

Hückel and Möbius models offer intuitive pictures of electronic arrangements in transition states [14].

LIMITATIONS OF HÜCKEL-MÖBIUS CONCEPTS:

1. Simplistic Assumption:

Assumes idealized geometries and ignores steric/electronic effect [3].

2. Qualitative, Not Quantitative:

Offers only qualitative predictions; cannot calculate activation energies [4].

3. Limited to Cyclic Transition States:

Only applicable when a cyclic, concerted transition state exists [12].

4. Fails for Complex Systems:

Less effective for large or highly substituted molecules [9].

5. Neglects Solvent Effects:

Doesn't consider solvent or environmental influences on reactions [8].

6. Requires Accurate Orbital Assignment:

Incorrect orbital symmetry assignment leads to wrong predictions [12,6].

7. Not Mechanistic:

Doesn't provide step-by-step reaction pathways or intermediates [4].

CONCLUSION:

The Hückel–Möbius approach provides a powerful and elegant framework for understanding pericyclic reactions through the lens of aromaticity and orbital topology [15]. By distinguishing transition states as either Hückel (aromatic) or Möbius (antiaromatic), it offers clear predictions about reaction feasibility under thermal or photochemical conditions [1]. While it simplifies complex orbital interactions and aligns with the Woodward–Hoffmann rules [3], its limitations—such as

idealized assumptions and qualitative nature must be acknowledged [3] . Overall, the Hückel–Möbius concept deepens our conceptual grasp of pericyclic mechanisms and remains a valuable tool in modern organic chemistry.

REFERENCES:

1. Pericyclic Chemistry: Orbital Mechanisms and Stereochemistry , Dipak k. Mondal, Formerly of presidency college/university, Kolkata, India, John Fedor, 2018, ISBN: 978-0-12-814958-4.
2. Lecture notes of Dr K K Mandal, St Paul's Cathedral Mission College, Kolkata.
3. Woodward, R. B.; Hoffmann, R. The Conservation of Orbital Symmetry; Verlag Chemie: Weinheim, 1971. Academic Press: New York, 1970.
4. Gilchrist, L.; Storr, R. C. Organic Reactions and Orbital Symmetry, 2nd ed.; Cambridge University Press: Cambridge, 1979.
5. Marchand, A. P.; Lehr, R. E., Eds. Pericyclic Reactions, Vols. 1 and 2; Academic Press: New York, 1977.
6. Fleming, I. Pericyclic Reactions, 2nd ed.; Oxford University Press: Oxford, 2015.
7. Sankararaman, S. Pericyclic Reactions—A Textbook: Reactions, Applications and Theory; Wiley-VCH: Weinheim, 2005.
8. Carey, F. A.; Sundberg, R. J. Advanced Organic Chemistry, Part A, 5th ed.; Springer: New York, 2007 (chapter 10).
9. Fleming, I. Molecular Orbitals and Organic Chemical Reactions, Student Edition; Wiley: Chichester, 2009. Reference Edition, 2010 (chapters 6 and 8).
10. Houk, K. N.; Gonzalez, J.; Li, Y. Acc. Chem. Res. 1995, 28, 81.
11. Rzepa, H. S. J. Chem. Educ. 2007, 84, 1535.
12. Woodward, R. B.; Hoffmann, R. Angew. Chem. Int. Ed. Engl. 1969, 8, 781.
13. Dewar, M. J. S.; Dougherty, R. C. The PMO Theory of Organic Chemistry. Plenum: New York, 1975.
14. Zimmerman, H. E. Acc. Chem. Res. 1972, 5, 393.
15. Zimmerman, H. E. Acc. Chem. Res. 1971, 4, 272.

ROLE OF BIOCATALYSIS IN ORGANIC TRANSFORMATION

B.Sc. Chemistry (Hons) Semester VI (Under CBCS)

Examination, 2025

Paper: DSE-B4(Dissertation)

CU Roll no. :**223114-21-0004**

CU Reg no. :**114-1111-0209-22**

College: **St. Paul's Cathedral Mission College**

St. Paul's Cathedral Mission College
33/1 Raja Rammohan Roy Sarani, Kolkata-700 009
NAAC ACCREDITED
AISHE ID C-11869
Estd. 1865

CERTIFICATE

This is to certify that the dissertation entitled "**ROLE OF BIOCATALYSIS IN ORGANIC-TRANSFORMATION**", submitted to the Department of Chemistry, St. Paul's C. M. College, Kolkata in partial fulfilment for the award of the degree of SEM-VI, DSE-B4 (under CBCS) in the B.Sc. SEM-VI CEMA Examination, 2025, CU, is a record of bona fide work carried out by Sarthak Biswas, CU Roll no. :223114-21-0004. (CU Reg no. :114-1111-0209-22), under my supervision and guidance.

This is a review work and hasn't been submitted to receive any other degree. All help received by him from various sources have been duly acknowledged.

(Dr. Kaushik Basu)
Assistant Professor
Department of Chemistry
St. Paul's C. M. College

(Dr. Kalyan Kumar Mandal)
Associate Professor
Department of Chemistry
St. Paul's C. M. College

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my teachers, **Dr. Kaushik Basu Sir** and **Dr. Kalyan Kumar Mandal Sir** for their unwavering support and guidance throughout the project on "**ROLE OF BIOCATALYSIS IN ORGANIC TRANSFORMATION"** and also helping me to find out different type of research paper from the different resources which help me a lot during my project work. I am also grateful to my friends, who provided valuable insights and feedback that helped to shape this work. I am deeply indebted to my family and friends, who offered emotional support and encouragement when it was most needed. Thank you all for their contributions to this project.

CONTENTS

ROLE OF BIOCATALYSIS IN ORGANIC TRANSFORMATION

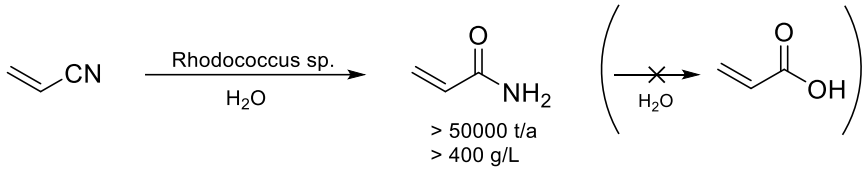
1. ABSTRACT:

Biocatalysis, using defined enzymes for organic transformations, has become a common tool in organic synthesis, which is also frequently applied in industry. The generally high activity and outstanding stereo-, regio- and chemo-selectivity observed in bio-transformations are the result of a precise control of the reaction in the active site of the biocatalyst. This control is achieved by exact positioning of the reagents relative to each other in a fined-turned 3D environment, by specific activating interactions between reagents and the protein, and by subtle movements of the catalyst. Enzyme engineering enables one to adapt the catalyst to the desired reaction and process. A well-filled biocatalytic toolbox is ready to be used for various reactions. Providing nonnatural reagents and conditions and evolving biocatalysts enables one to play with the myriad of options for creating novel transformations and thereby opening new, short pathways to desired target molecules. Combining several biocatalysts in one pot to perform several reactions concurrently increases the efficiency of biocatalysis even further.

2. INTRODUCTION:

Our environmental, economical concerns are highly depend on the organic molecules and it's synthesis from very past time. Although it was not known to the people at the early phase but then chemists were made their interest in it. After that many organic molecules were synthesized via organic synthesis. But there is many problems with normal chemical process in organic synthesis. The major problem is the formation of side product i.e waste, decrease the yield of the target product and it has also many side effect in the environment. To avoid this this green chemistry give us a better way of organic synthesis which is biocatalysis. Biocatalysis refers to the use of living systems or their parts to speed up a chemical reaction.

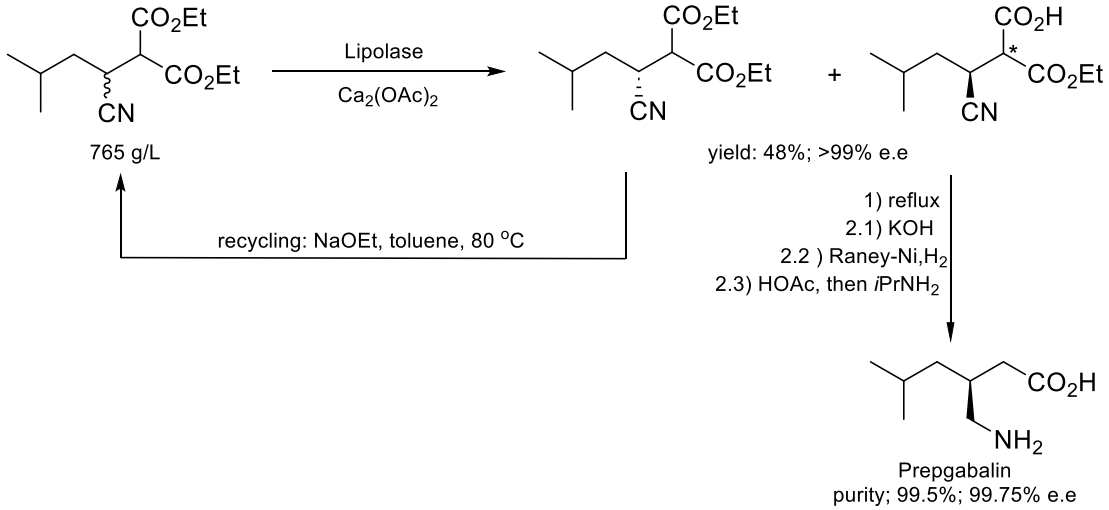
Monohydration of acylonitrilie



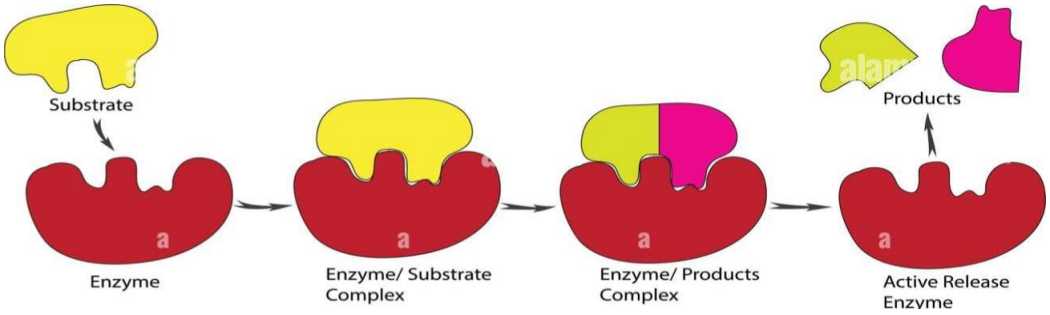
This is an example of formation of acrylamide. The advantage of this reaction is its high chemo-selectivity, exclusively giving the amide, as well as the easier separation of the catalyst from the product compared with metal catalysts **[1]**.

3. ENZYMES AS THE TOOLBOX OF CATALYST:

Humans have used the enzymes for fermentation process, for example to ferment sugars into alcohol in the pre-20th century **[2]**. These processes were the first to demonstrate enzymes catalytic power in transforming organic molecules. However, in between the 1900-1950s the chemists, moreover the scientists started to isolated enzymes from these applications. In 1926, James B. Sumner, crystallized the first enzyme as a protein and this protein is urease **[3]**. During this time, enzymatic reactions were mostly limited to biochemical studies, not yet in synthetic organic chemistry. By 1949, a huge number of enzyme classes had been discovered and characterized extensively. At this time the pathways of enzymatic reactions were not known. In 1984, Emil Fischer proposed the famous 'lock-and-key' model through which an enzyme work in a reaction. According to this model, the active site of an enzyme is structured to fit a specifically shaped substrate. Once the substrate binds to the active site, the enzyme will facilitate the reaction and release products of the reaction **[4]**. In 1990, enzyme gained more traction with the development of green chemistry due to its biocatalyst activity. Due to its stereoselective role it reduces the yield of the side product and increases the yield of target product. So, enzymes are preferred as catalysts for organic transformation.



This is the chemoenzymatic process to produce pregabalin, applying the lipase from Lipolase in a kinetic resolution **[5]**.



Lock and Key Model

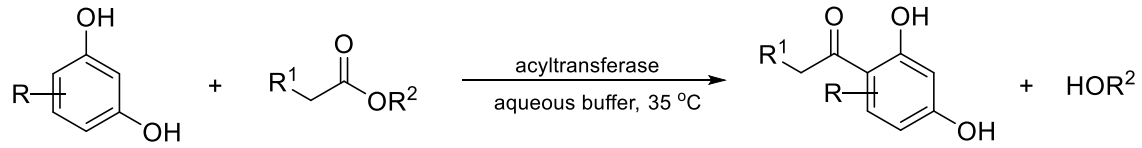
4. FEATURES OF BIOCATALYST:

At the initiative period, it was believed that the acceleration of reaction rate achieved by enzymes is due to the stabilization of transition-state. But now there is many catalyst requires more than just transition-state stabilization. It is notified that in the enzymatic catalytic cycle, each step is controlled by several interactions between substrate and enzymes. These following steps are:

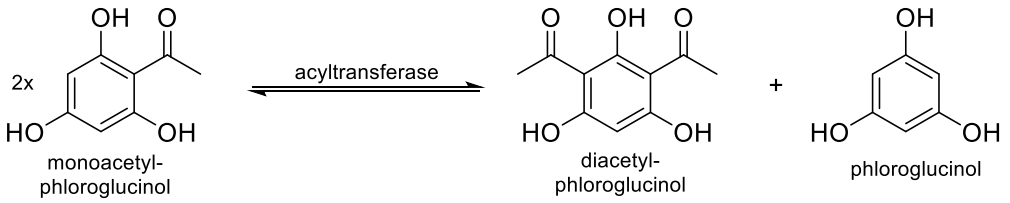
SL NO.	STEP	CHEMISTRY	PURPOSE
I	Binding of substrate	Binding may be covalent but always relies on several weak interactions: hydrogen bonding, π-π interactions Enzyme backbone may adapt to a substrate structure	Precise positioning of substrate and, if required, cofactor in a productive pose to each other in 3D. The more interactions, the tighter the binding. Too tight binding has to be avoided because it may lead to substrate inhibition
Ii	Activation of substrate	Activation may be achieved by acid-base catalysis, metals, cofactors etc. Enzyme backbone may move during catalysis	Initiating the reaction
Iii	Stabilization of transition state	Various residues in the active site may provide an appropriate environment	Lowering energy for transition state
Iv	Product release	Lower binding affinity than for the substrate	To expel the product quickly after the reaction is important to minimize product inhibition. This is easier the more the substrate and the product differ from each other

The biocatalyst combines both the organo-catalysts and heterogeneous catalysts, the formation and flexibility, which are considered important for substrate binding and catalytic turnover **[6]**.

(a) Biocatalytic C-acylation of resorcinol



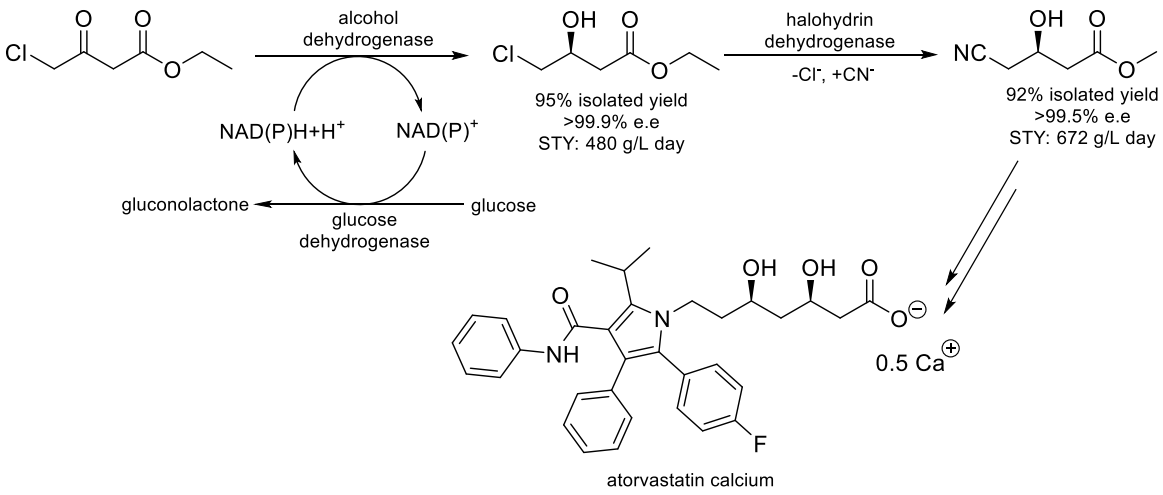
(b) Natural reaction: Disproportionation



In reaction '**4a**', C-acylation of resorcinol, a new C-C bond is formed due to the enzyme acyltransferase **[7]**. But reaction '**4b**' is the natural reaction of acyltransferase that is a disproportionation reaction **[8]**. To ensure this chemo-selectivity, precise binding is required. The important site where the reaction occurs is the active site. This accommodates the catalytically active residues, whereas one residue may bind the substrate through covalent bonding and the other contribute to substrate activation and its correct positioning in the active site. The outer most layer of the enzyme is responsible for the connection with the medium or enabling the formation of dimers or oligomers of the catalyst. This gives the complexity of enzyme structure as catalysts and this features make each enzyme as unique catalyst.

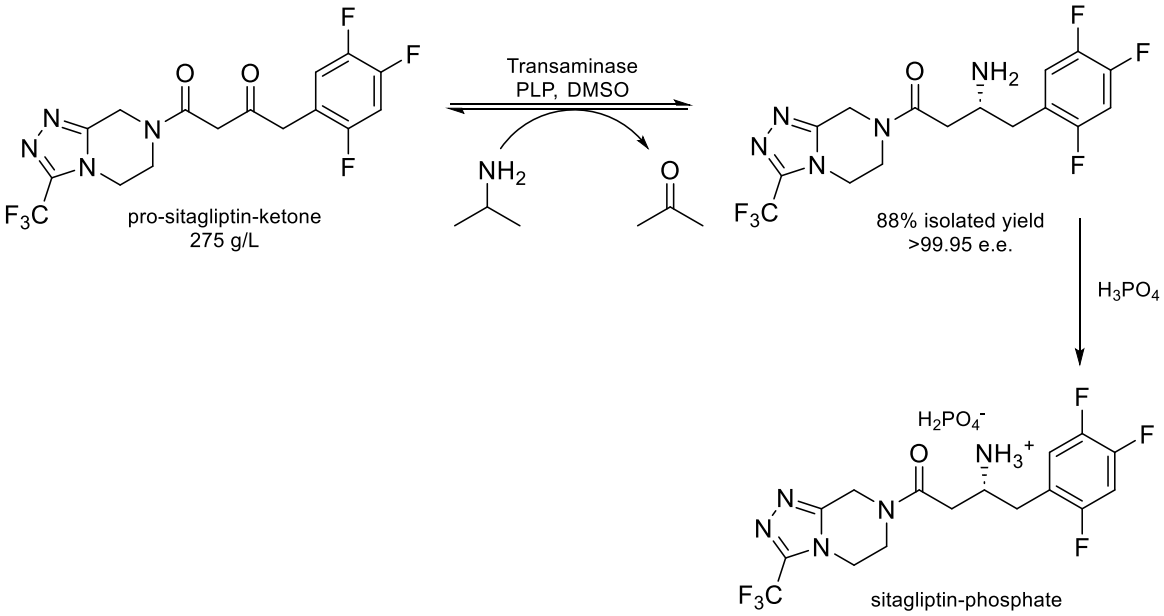
5. SPECIFIC BIOCATALYST FOR A SPECIFIC REACTION AND ONE-STEP BIOTRANSFORMATIONS:

(a) Biocatalysis with Alcohol Dehydrogenase



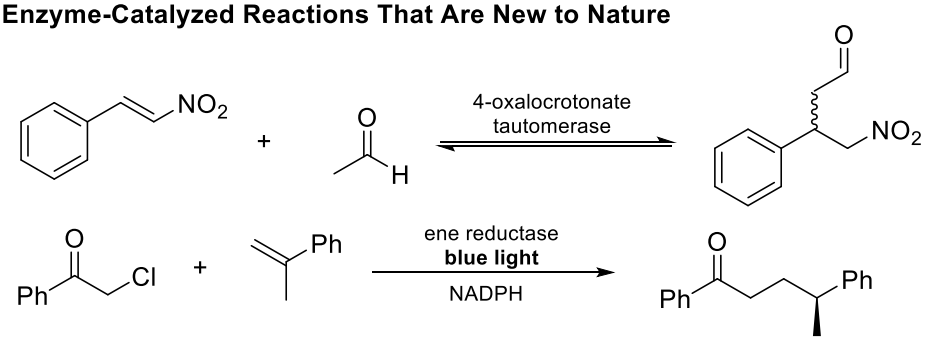
Reaction **'5a'** is a multienzyme process for the production of (R)-4-cyano-3-hydroxybutyrate via the asymmetric reduction of ethyl-4-chloro-3-oxobutanoate with an alcohol dehydrogenase in combination with a GDH recycling system, followed by a halohydrin dehalogenase-catalyzed exchange of the chlorine for a cyano group **[9].**

(b) Biocatalytic Formation of Amines



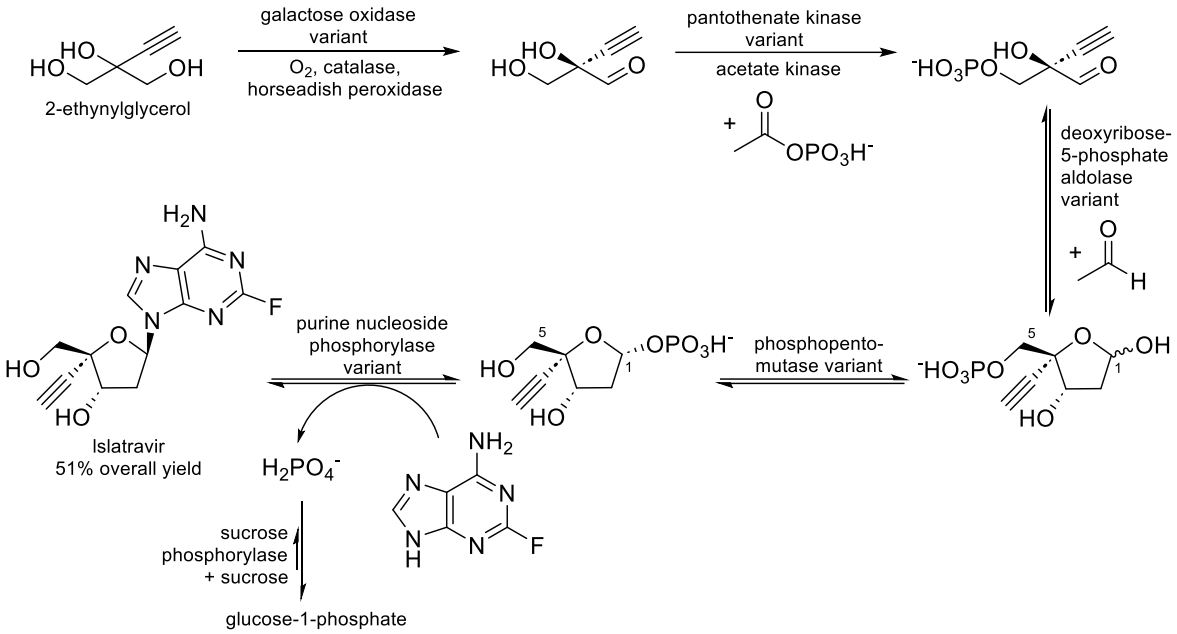
Reaction **'5b'** is the biocatalytic production of sitagliptin using a transaminase, **"PLP= pyridoxal 5'-phosphate".**

(c) Enzyme-Catalyzed Reactions That Are New to Nature



First reaction is the example of 4-Oxalocrotonate tautomerase-catalyzed conjugate addition and second is the Photobiocatalytic intermolecular C-C bond formation by an ene-reductase **[10]**.

(d) Multienzyme Cascade Reactions



This the process for the production of islatravir in a multienzyme cascade sequence.

6 NEW REACTIONS, CATALYZED BY ENZYME:

This reactions are known as novel biochemical transformations developed in the lab that are not known to occur naturally, but are accelerated by enzyme. This process is developed to spread the synthetic capability of enzyme in organic, moreover industrial, pharmaceutical field. This concept gets importance under the areas like: Biocatalysis, Enzyme engineering, Direct evolution, Artificial enzymes **[11]**. This should not be surprising that an enzyme is also just a chemical catalyst and the substrate depending on the amino acid residues present and the substrate and the reaction conditions provided. An example in the broad reactivity exhibited for 4-oxalocrotonate tautomerase, which is a rather short peptide and possesses an N-terminal proline that can be exploited by analogy to proline-based organo-catalysts **[12]**. Although its native reaction is the name-giving tautomerization of 4-oxalocrotonate to its enol, it also catalyses conjugate additions, aldol reactions and asymmetric epoxidations with high enantiomeric excess. There are many wild-type enzymes that often exhibit low activities for reactions other than their natural transformations. These reactions are catalysed by enzyme variants, based on an enzyme structure or by random mutagenesis. One of the enzyme classes demonstrating broad reaction promiscuity is the cytochrome P450 family. These biocatalysts are well-known for regioselective C-H oxidation leading to hydroxylation,

but they also catalyse a variety of other reactions including decarboxylation, epoxidation, reductive dehalogenation, amine/oxygen dealkylation and sulfoxidation **[13]**. In this context, Frances Arnold was awarded Nobel Prize in 2018 in Chemistry **"**for the directed evolution of enzymes**" [14]**. This technique was used to engineer variant cytochrome P450 enzymes (and also known as heme-dependent enzymes) to catalyse carbene-transfer reactions, forming cyclopropanes using diazo-esters as carbene precursors with high diastereo-selectivity and enantioselectivity. We can use protein backbone also as a carrier for abiotic catalysts. Enzymes can be considered as huge chiral ligands for any catalytically active molecule in the active site. Biohybrid catalysts have-been developed whereby the protein backbone binds a chemical catalysts within chiral environment, enabling new-to-nature reactions with protein-based stereo-control **[15]**.

7 FUTURE MOTIVE:

Although biocatalysis make a huge field in today's science, it still a relatively young in all over field. Hene, it is fair to admit that there are still many challenges that need to be addressed. On this basis, it is the time to think on the future motive of biocatalysis. This motive centers on making chemical processes greener, more efficient and more selective-especially in the context of sustainability, pharmaceutical production, and novel reactivity **[16]**. The challenges of biocatalysts are the cost and time required for developing a suitable catalyst in the lab, which need to be reduced to allow the fast implementation of enzyme-catalysed processes in chemical industry. Another important aspect is that biocatalysis needs to be incorporated as part of chemistry at universities to train the chemists of tomorrow in its application and to give them a broader methodological horizon. Future synthetic chemists should be made aware that biocatalysts can be used in one-step transformations or in cascades comprising several biocatalysts or, if suitable, can be incorporated in methodological pathways of living organisms. In the future, a biodegradable biocatalyst may be developed for any specific synthesis desired and thereby shortcut organic synthetic routes to produce the target molecule in a minimum number of steps ideally requiring only environmentally effective reagents.

8 CONCLUSION:

The applications of biocatalysis are very broad, as many reactions can be performed with enzymes and the speed to discover new enzymes will dramatically increase in the future due to efficient tools such as bio-informatics, protein engineering etc. Due to the possibility of using enzymatic cascades, the production of compounds can be but

accelerated. If many chemical reactions can be achieved by biocatalysis, traditional cross-coupling reactions.

9 REFERENCES:

1) Yamada, H.; Kobayashi, M. Nitrile Hydratase and Its Application to Industrial Production of Acrylamide. Biosci., Biotechnol., Biochem.1996, 60, 1391−1400.
2) P. E. McGovern, J. Zhang, J. Tang, Z. Zhang, G. R. Hall, R. A. Moreau, A. Nuñez, E. D. Butrym, M. P. Richards, C. S. Wang, G. Cheng, Z. Zhao, C. Wang, Proc. Natl. Acad. Sci. USA 2004, 101, 17593-17598.
3) Sumner, J.B., The isolation and crystallization of the enzyme urease, Journal of Biological Chemist, 69(2), 435-441.
4) E. Fischer, Einfluss der Configuration auf die Wirkung der Enzyme, Berichte der Deutschen Chemischen Gesellschaft, 27(3),2985-2993.
5) Debarge, S.; McDaid, P.; O'Neill, P.; Frahill, J.; Wong, J. W.; Carr, D.; Burrell, A.; Davies, S.; Karmilowicz, M.; Steflik, J. Evaluation of Several Routes to Advanced Pregabalin Intermediates: Synthesis and Enantioselective Enzymatic Reduction Using Ene-Reductases. Org. Process Res. Dev. 2014, 18, 109−121.
6) Undaresan, V.; Abrol, R. Towards a General Model for Protein-Substrate Stereoselectivity. Protein Sci. 2002, 11, 1330−1339.
7) Schmidt, N. G.; Kroutil, W. Acyl Donors and Additives for the Biocatalytic Friedel-Crafts Acylation. Eur. J. Org. Chem. 2017, 2017,5865−5871.
8) Yang, F.; Cao, Y. Biosynthesis of Phloroglucinol Compounds in Microorganisms–Review. Appl. Microbiol. Biotechnol. 2012, 93, 487−495.
9) Ma, S. K.; Gruber, J.; Davis, C.; Newman, L.; Gray, D.; Wang, A.; Grate, J.; Huisman, G. W.; Sheldon, R. A. A Green-by-Design Biocatalytic Process for Atorvastatin Intermediate. Green Chem. 2010,12, 81−86.
10) Huang, X.; Wang, B.; Wang, Y.; Jiang, G.; Feng, J.; Zhao, H. Photo-enzymatic Enantioselective Intermolecular Radical Hydro-alkylation. Nature 2020, 584, 69−74.
11) Singh P. P., Novel applications of photobiocatalysts in chemical transformations, RSC Advances, 14, 2590-2601.
12) MacMillan, D. W. The Advent and Development of Organocatalysis. Nature 2008, 455, 304−308.
13) Hammerer, L.; Winkler, C. K.; Kroutil, W. Regioselective Biocatalytic Hydroxylation of Fatty Acids by Cytochrome P450s. Catal.Lett. 2018, 148, 787−812.
14) Arnold, F. H. Directed Evolution: Bringing New Chemistry to Life. Angew. Chem., Int. Ed. 2018, 57, 4143−414.
15) Nödling, A. R.; Santi, N.; Williams, T. L.; Tsai, Y.-H.; Luk, L. Y.P. Enabling Protein-Hosted Organocatalytic Transformations. RSC Adv. 2020, 10, 16147−16161.

16) Woodley, J. M. Accelerating the Implementation of Biocatalysisin Industry. Appl. Microbiol. Biotechnol. 2019, 103, 4733−4739

Microwave-assisted synthesis of nitrogen-containing heterocycles

B.Sc. Chemistry (Hons.) Semester VI (CBCS)

Examination, 2025

Paper: DSE-B4 (Dissertation)

CU Roll no: **223114-11-0005**

CU Reg no: **114-1211-0212-22**

College: **St. Paul's Cathedral Mission College**

St. Paul's Cathedral Mission College
33/1 Raja Rammohan Roy Sarani, Kolkata-700 009
NAAC ACCREDITED
AISHE ID C-11869
Estd. 1865

CERTIFICATE

The research work embodied in the present Thesis entitled **MICROWAVE ASSISTED SYNTHESIS OF NITROGEN CONTAINING HETEROCYCLES** has been submitted to the Department of Chemistry, St. Paul's Cathedral Mission College, Kolkata in partial fulfilment for the award of the degree of SEM-VI, DSE-B4 (Under CBCS) in the B.Sc. SEM-VI CEMA Examination, 2025, CU is a record Bonafide work carried out by **Ritwa Jana**, under my Supervision and Guidance.

This is a review work and hasn't been submitted to receive any degree. All help received by him from various sources have been duly acknowledged.

(Dr. Kaushik Basu).
Assistant Professor
Department of Chemistry
St. Paul's C.M. College

(Dr. Kalyan Kumar Mondal)
Associate Professor
Department of Chemistry
St. Paul's C.M. College

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my teachers, **Dr. Kaushik Basu** Sir and **Dr. Kalyan Kumar Mandal** Sir for their unwavering support and guidance throughout the project on "**Microwave-assisted synthesis of nitrogen-containing heterocycles**" and also helping me to find out different type of research paper from the different resources which help me a lot during my project work. I am also grateful to my friends, who provided valuable insights and feedback that helped to shape this work. I am deeply indebted to my family and friends, who offered emotional support and encouragement when it was most needed. Thank you all for their contributions to this project.

CONTENTS

Microwave-assisted synthesis of Nitrogen-containing heterocycles

INTRODUCTION

Heterocycles form by far the largest of the classical divisions of organic chemistry. It is one of the most preliminary and building block, which used in pharmaceutical, more than 90% of pharmaceuticals contain at least one heterocyclic fragment. **[1]**

They also have wide variety of application in the industries such as cosmetics, reprography, plastic, solvents, antioxidants, and vulcanization accelerators and many more. N-based heterocycles are most lime lighted one as it has been found in many bioactive natural products as their structural component, e.g.- vitamins, hormones, antibiotics, alkaloids, Glycosides. It has been found in many natural drugs such as papaverine, emetine, atropine, Morphin, codeine and reserpine etc. thus it considered as "privileged" structures for the synthesis and development of further new drugs.

SIGNIFICANCE OF THE TOPIC

Traditional methods are too time consuming to satisfy the demands of these heterocyclic Compounds. Thus, the and the driving force are easily undefendable for the development of the technique for the synthesis of these complex Heterocycles, and to drive the research field of synthetic Organic chemistry. Green / sustainable chemistry **[2]** has now become a subject of intensive research with High facilities. This concept of "sustainable chemistry "emerged in the late 20^{th} century and now in 21^{st} century it is widely acceptable and a matter of appreciation to being maintain the rate of development of research field of sustainable development in mind.

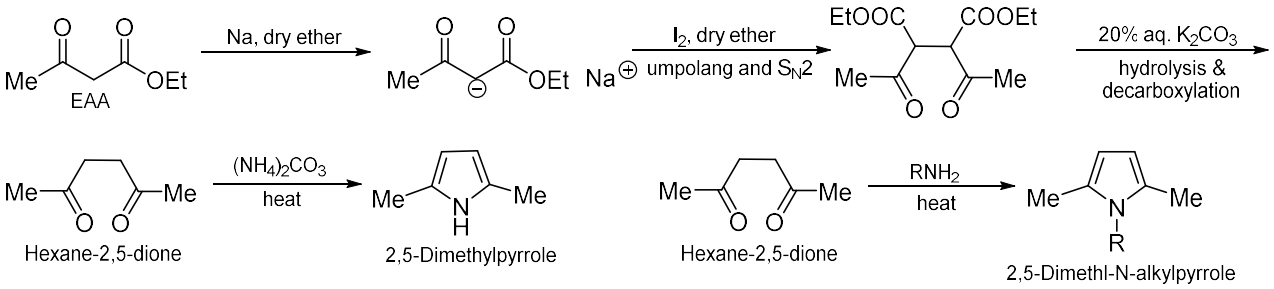
SIGNIFICANCE OF THE METHOD FROM THE VIEW POINT OF GREEN CHEMISTRY

Microwave is one of the potential green Chemistry/sustainable chemistry in 20th century **[3].** The ability of microwave assisted organic synthesis is mostly benefited by its rapid rate of synthesis of organic compounds. This review Outline the use of microwave highlights the importance of a number of N-containing heterocycles and summarizes some advances in their synthesis under MW irradiation through recent selected examples.

SYNTHESIS OF THE COMPOUNDS

PYRROLES:

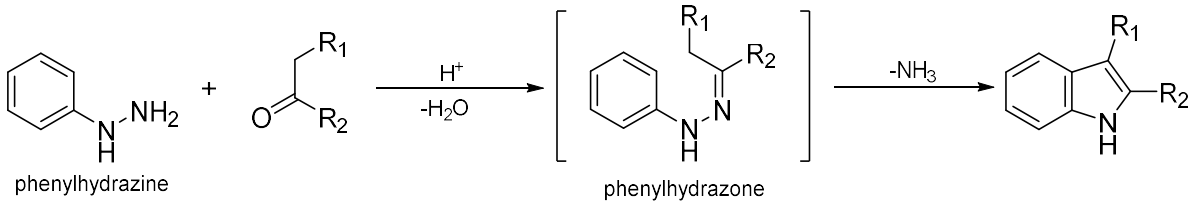
Pyrroles are heterocycles of great importance because pyrrole is a basic substructure of numerous biologically active alkaloids and pharmaceutical products **[4,5].** Classically, pyrroles were synthesized by various methods viz. Knorr pyrrole synthesis **[6],** Paal–Knorr synthesis **[7]**, Hantzsch pyrrole synthesis **[8],** etc.



Scheme 1: Outline for Pyrrole Synthesis.

INDOLES:

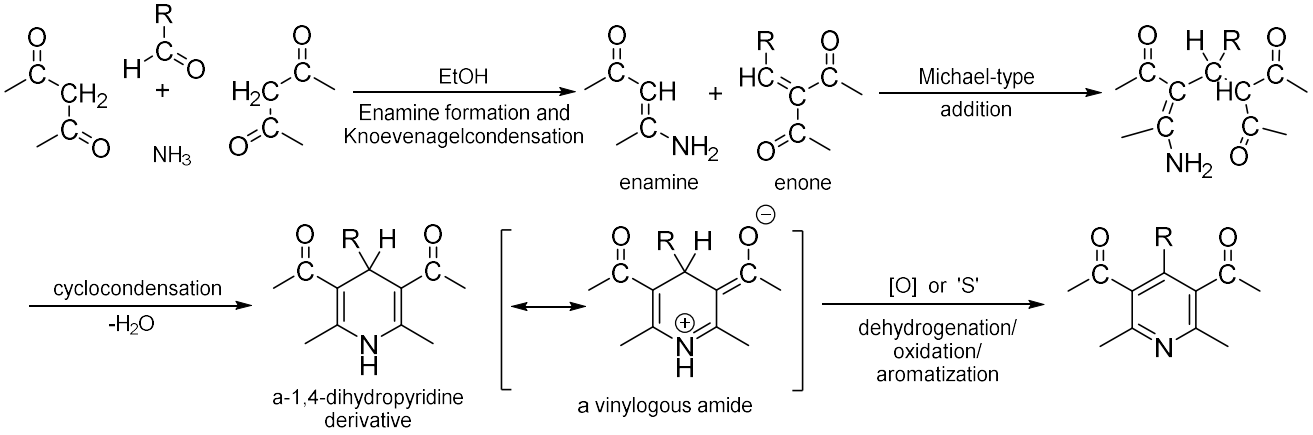
Indole nuclei are broadly found in a large amount of synthetic and natural products. Indole is a popular component of fragrances and the precursor to many pharmaceuticals **[9].** Classically, indoles have been synthesized by various methods **[10,11].** The use of more environmentally friendly protocols for the synthesis of indole derivatives has been reported which are mentioned below.



Scheme 2 : Synthesis of Indoles , Fischer Indole Synthesis

PYRIDINE:

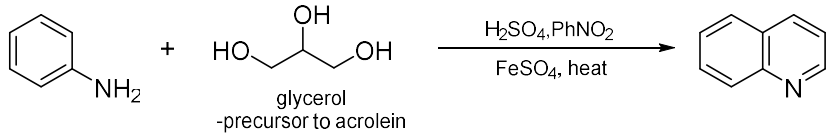
Pyridines have a wide range of applications in medicinal chemistry. Pyridine derivatives have been used as herbicides and for enrichment of cereals. Some bifunctional pyridines are used as nonlinear optical materials, electrical materials, chelating agents
in metal–ligand chemistry, and as fluorescent liquid crystals **[12]**. Despite the numerous synthetic methodologies available in the literature **[12]**, novel methods for pyridines synthesis are still in demand.



Scheme: 3 Mechanism of Hantzsch pyridine synthesis.

QUINOLINE:

Quinoline derivatives occur in various natural products, especially in alkaloids and are often used for the design of many synthetic compounds with diverse pharmacological properties **[13].** A number of methods of quinoline synthesis viz. Skraup, Doebner-von Miller, Friedlander, Pfitzinger, Conrad-Limpach, Combes have been known since the late 1800s.

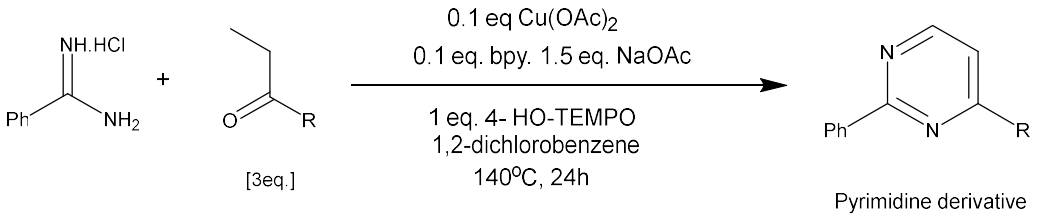


Scheme 4 : Outline of Skraup synthesis for Quinoline

PYRIMIDINE:

Pyrimidine derivatives serve both as biomimetic and reactive pharmacophores due to their diverse medicinal properties. The importance of partially hydrogenated pyrimidine derivatives in medicinal chemistry is widely known **[14].** Most popular method for pyrimidine synthesis is Biginelli reaction **[15].** In order to improve the

yields obtained in the described classic conditions for the synthesis of pyrimidines, much effort has been made.

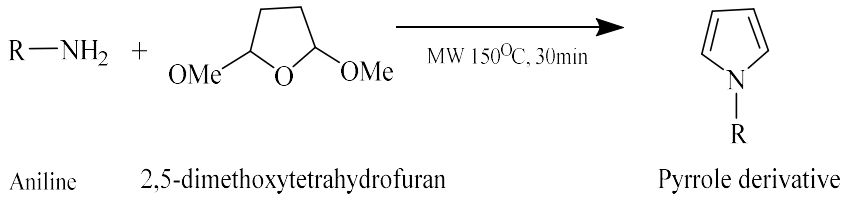


Scheme 5: Outline for the Synthesis of Pyrimidine

REACTIONS ON THE FOLLOWING COMPOUNDS

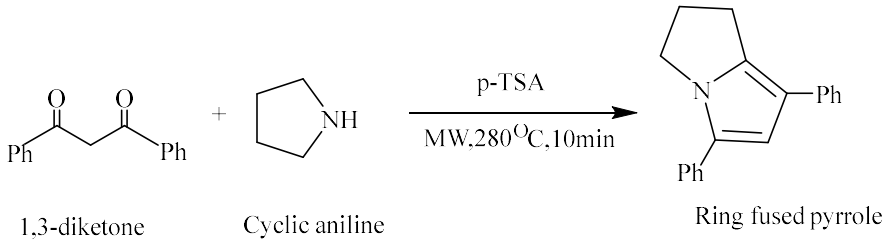
Pyrroles:

Heating an aniline with 2,5-dimethoxytetrahydrofuran in water (0.64M) in a MW reactor at 150°C for 30min resulted in the formation of the corresponding pyrroles in water in 81 – 99% yield. Wilson et. al **[16]** reported this simplified approach to the uncatalyzed Paal-Knorr condensation.



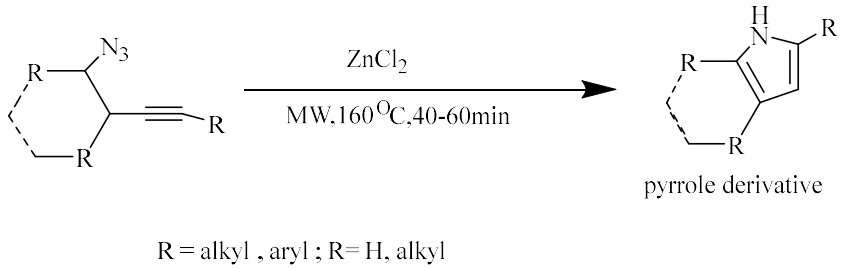
Scheme 6 : Microwave (MW)- induced uncatalysed reaction of 2,5-dimethoxytetrahydrofuran with various amines in water

Synthesis of ring-fused pyrrole in a single operation by the reaction of 1,3-diketone and cyclic aniline under MW irradiation at 280°c in the presence of 0.5 equivalent of *p*-toluenesulfoic acid (*p*-TSA) with 53% yield in 10min **[17].**



Scheme 7 : Synthesis of ring-fused pyrrole under MW irradiation.

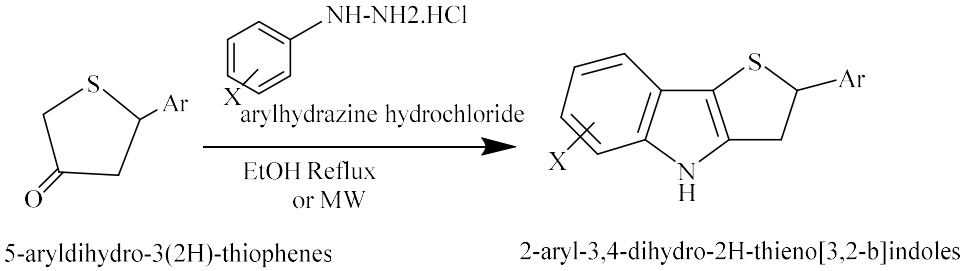
Ligand – free 5-*endo-dig* cyclisation of homopropargyl azide in the presence of 20 mol% $ZnCl_2$ (1.0 M in ether) in CH_2Cl_2 at 105°C provided pyrroles in high to moderate yield **[18].**



Scheme 8: Synthesis of pyrroles by 5-endo-dig cyclization of homopropargyl azide.

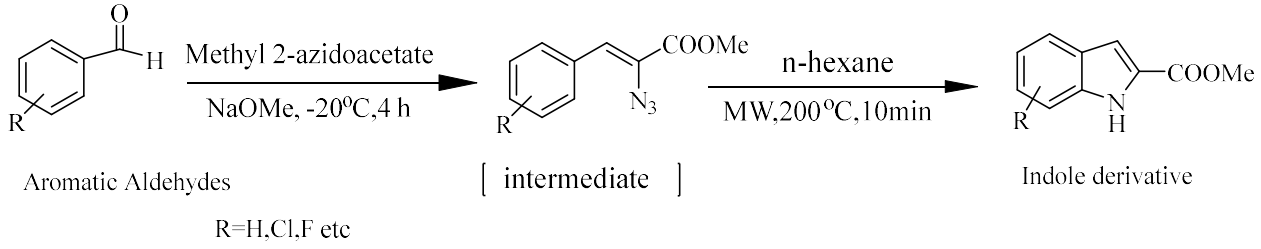
Indole and its derivative:

A series of novel 2-aryl-3,4-dihydro-2*H*-thieno[3,2-b] indoles have been synthesized by Karthikeyan and his co-workers **[19]** regioselectively in excellent yields (85-90%) under MW irradiation at 90ºC in 3-6min. Product were also obtained under condition in refluxing ethanol but completed in 30-70 min.



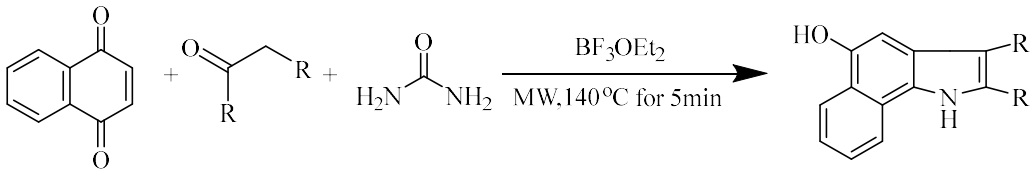
Scheme 9: Reaction of 5-aryldihydro-3(2H)-thiophenes and arylhydrazine hydrochloride.

The synthesis of indoles which begins with the intermediates prepared from the corresponding commercially available aldehydes was accomplished by Lehmann et al **[20].** Formation of indoles took place with 99.9% yield at 200 W, 200ºC and 15min irradiation time. The existing methods for the synthesis of these compounds afford only relatively low to modest yields (53 -79%) in several hours.



Scheme 10: Synthesis of indoles under MW irradiation.

Borthakur et al. recently described this formation of various 5-hydroxybenzo[g]indole at 140ºC for 5min in 80% yield.



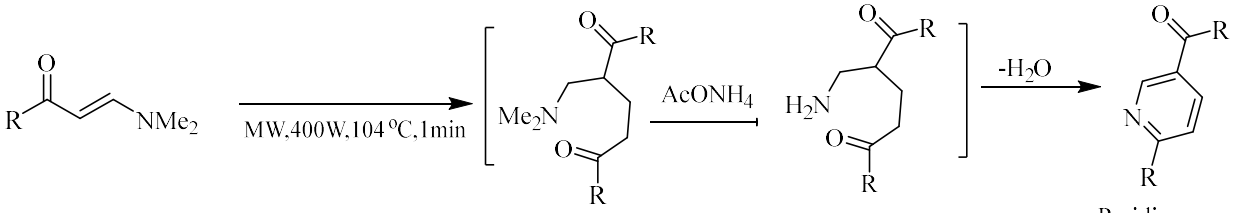
R= morpholine,pyrrolidine,piperidine, R'= aryl groups

2-(*P*-tolyl)-3-morpholine-5-hydroxybenzo[g]indoles

Scheme 11: synthesis of 2-(*P*-tolyl)-3-morpholine-5-hydroxybenzo[g]indoles.

Pyridine:

Heating enantiomers with excess of ammonium acetate (as an ionic liquid), at 110°C for 20min or irradiating under MW for 1min at 105°c (400W), yielded the pyridines. This work was reported by Khadijah et al. Yield obtained following MW procedure is higher (65-77%) than heating method (50-62%).



enaminone

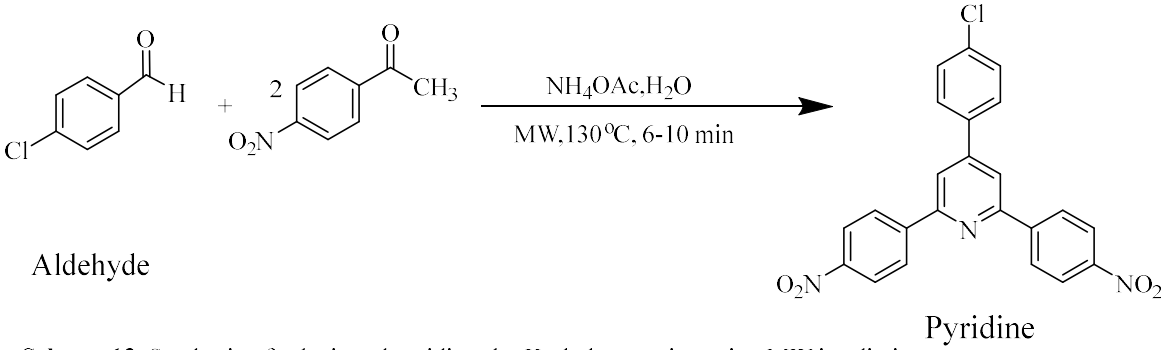
intermediate

Pyridine derivative

R=Methyl, phenyl, 2-furyl, 2-thienyl, 2-pyridyl, p-Me-Ph, 2-pyrrolyl, p-NO_2-Ph, p-Cl-Ph

Scheme 12: Synthesis of 2-aryl (or heteroaryl)-5-aroyl (or heteroaryl)-pyridines

A one-pot effective Krohnke condensation reaction was carried out by Tu et al **[21]** in an aqueous medium using MW irradiation (6-10min) and ammonium acetate for the synthesis of substituted pyridines at 130°C with 90-96% yield. Heating in oil bath requires much more time (2.5-4h) with 76-84% yield.



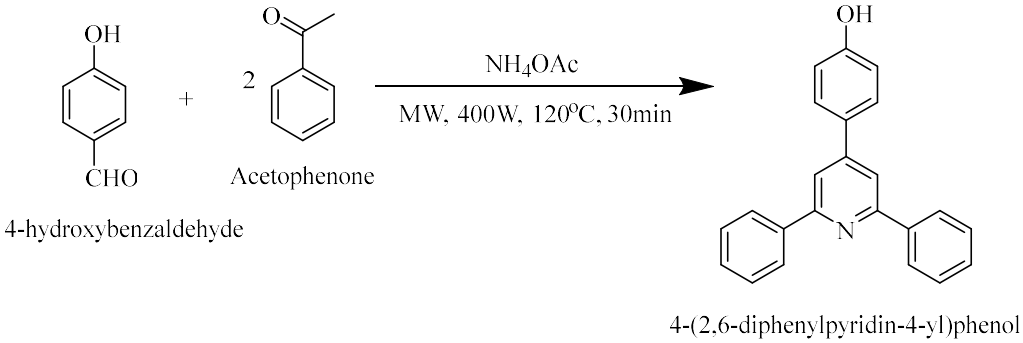
Aldehyde

Pyridine

Scheme 13: Synthesis of substituted pyridines by Krohnke reaction using MW irradiation.

A facile solvent – and catalyst free method for the synthesis of a series of new hydroxylated 2,4,6-trisubstituted pyridines was obtained in high yield (83%) under

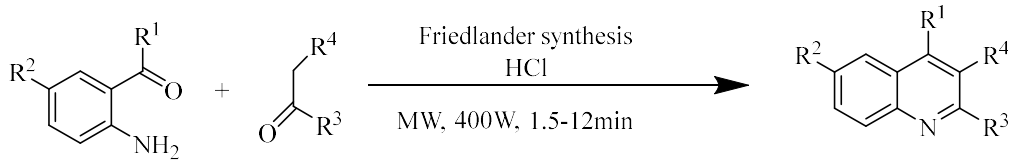
MW irradiation (400W) at 120°C for 30min via a three-component condensation of 4-hydroxybenzaldehyde acetophenone and NH_4OAc **[22].**



Scheme 14: MW - assisted synthesis of 4-(2,6-diphenylpyridin-4-yl)phenol under solvent and catalyst free conditions.

Quinoline:

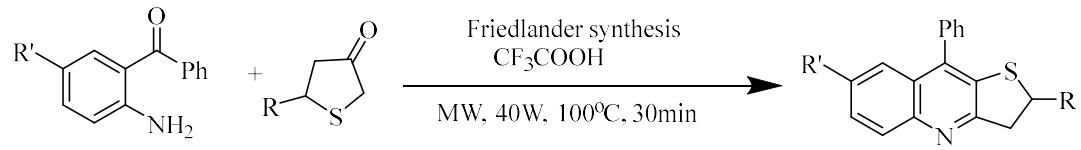
Muscia et al **[23]** synthesized a series of substituted quinolines in good yields (50-90%) via the Friedlander reaction by the reaction of 2-aminoacetophenone or benzophenones with a variety of ketones and keto esters and a catalytic amount of hydrochloric acid within a time period of 1.5-12 min following the MW procedure. Conventional synthesis requires prolong heating at 100 °C.



R= CH_3 ,Ph, R^2=H,NO_2,Cl, R^3,R^4= Me, COOEt, CH_2Cl etc

Scheme 15 : Synthesis of substituted quinolines via the Friedlander reaction catalysed by hydrochloric acid.

Balamurugan et al. **[24]** also have reported regioselective 2,9-diaryl-2,3-dihydrothieno[3,2-b] quinolines via the Friedlander reaction. A mixture of aryldihydro-3(2H)-thiophenone 163, 2-aminoaryl ketone and trifluoroacetic acid was irradiated in an MW oven at 100 °C (40 W) for 30 min. This reaction proceeded more rapidly and afforded better yields (60–98%) than the thermal reaction at 100 °C (60–85% yields in 2–3 h).

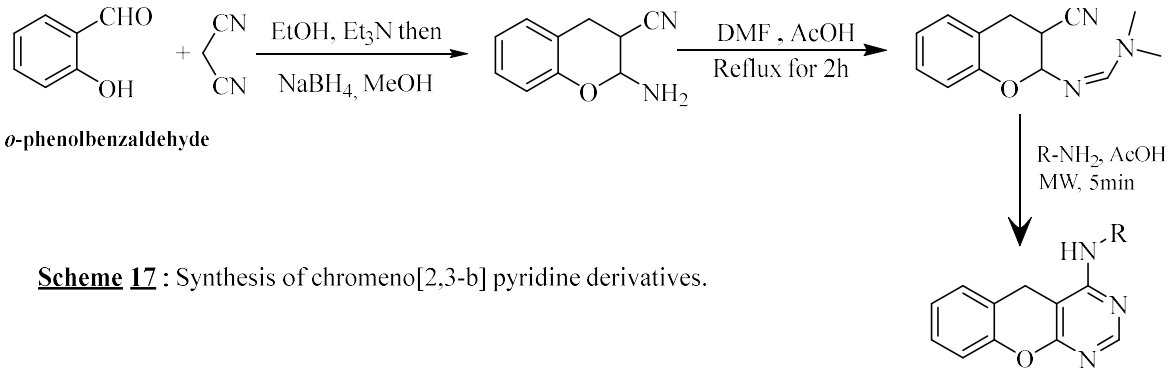


R= Ph, p-MePh, p-ClPh etc, R'=h,Cl

Scheme 16 : Synthesis of substituted quinolines by Friedlander reaction catalysed by trifluoroacetic acid.

Pyrimidine:

Novel chromeno[2,3-b] pyrimidine derivatives were obtained by Rai et al. **[25].** MW irradiation of intermediate with different amines in acetic acid gave within 5 min in reasonably good yields (64–75%). All these compounds were screened for their antimicrobial activity.

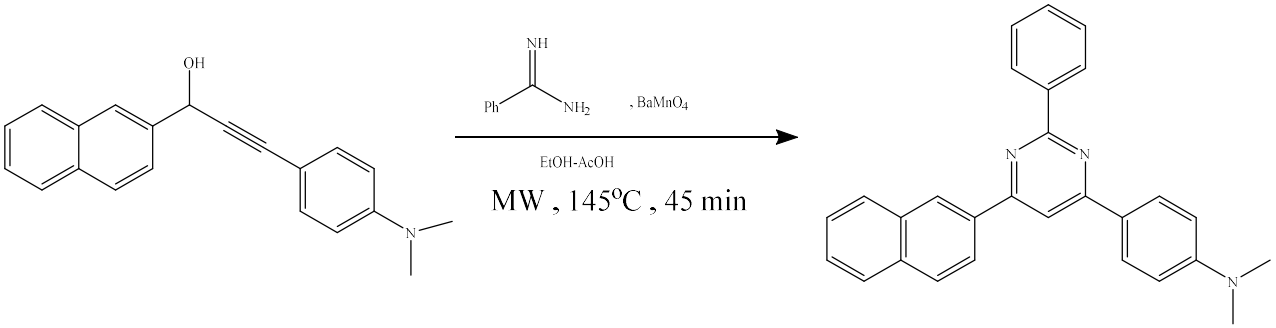


***o*-phenolbenzaldehyde**

chromeno[2,3-b] pyridine derivative

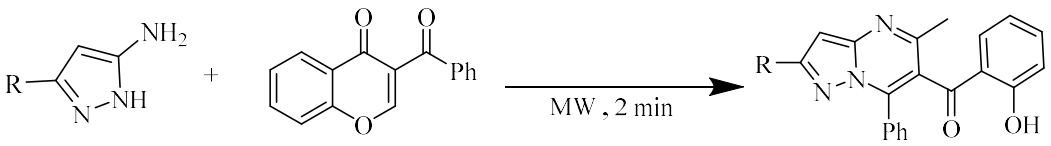
Scheme 17 : Synthesis of chromeno[2,3-b] pyridine derivatives.

2,4,6-Triarylpyrimidines were synthesized by Bagley et al. **[26]** by MW-assisted tandem oxidation/ heterocyclocondensation using $BaMnO_4$ at 145 °C in 45 min. In contrast, traditional method under conductive heating by cyclocondensation at reflux in EtOH in the presence of NaOH, moisture, and air for 10 h produces in 0-40% yield.



Scheme 18 : MW- assisted of 2,4,6- triarylpyrimidines.

6-(2-Hydroxybenzoyl)-5-methyl-7-phenylpyrazolo [1,5-a] pyrimidines have been synthesized directly by the solvent-free reaction between 5-amino-1H-pyrazoles and 3-benzoyl-2-methyl-4H-chromen-4-one using MW-assisted route in 2 min in 88–93% yield. This work was reported by Quiroga et al. **[27]** Conventional heating at 180 °C for 20 min gives the product in 70–76% yield.



R= Me, t-Bu, Ph, 4-CH_3-Ph, 4-OMe-Ph, 4-O_2N-Ph, 4-Cl-Ph , 4-Br-Ph

Scheme 19: Solvent free synthesis of 6-(2-hydroxybenzoyl)-5-methyl-7-phenylpyrazolo[1,5-a]pyrimidines.

CONCLUSION:

The renovation of environment friendly methodologies is certainly one of the current topics. Synthetic organic reactions performed by MW irradiation are growing very rapidly as it provides simple, clean, time saving, efficient and eco-friendly for the synthesis of a large number of organic compounds including N-containing heterocycles. This methodology does not support to use any hazardous chemicals and perform the reaction in very harsh condition. Still, it completes the reaction in lesser time span with higher yields.

REFERENCES:

1. **Bacolini G. Topics Heterocycl. Syst. Synth. React. Prop. 1996; 1:103.**
2. **Santagada V, Frecentese F, Perissutti E, Fiorino F, Severino B, Caliendo G. The application of microwave irradiation as new convenient synthetic procedure in drug discovery. Mini Rev. Med. Chem. 2009; 9:340–358.**
3. **Das¸tan A, Kulkarnia A, To¨ ro¨ k B. Environmentally benign synthesis of heterocyclic compounds by combined microwave-assisted heterogeneous catalytic approaches. Green Chem. 2012; 14:17–37.**
4. **Aydogan F, Basarir M, Yolacan C, Demir AS. New and clean synthesis of N-substituted pyrroles under microwave irradiation. Tetrahedron. 2007; 63:9746–9750.**
5. **Wilson MA, Filzen G, Welmaker GS. A microwave assisted, green procedure for the synthesis of N-aryl sulfonyl and N-aryl pyrroles. Tetrahedron Lett. 2009; 50:4807–4809.**
6. **Knorr L. Synthese von pyrrolderivaten. Ber. Dtsch. Chem. Ges. 1884; 17:1635–1642.**
7. **Paal C. Synthese von thiophen-und pyrrolderivaten (synthesis of thiophene and pyrrole). Ber. Dtsch. Chem. Ges. 1885; 18:367–371.**

8. **Hantzsch A. Neue Bildungsweise von Pyrrolderivaten. Ber. Dtsch. Chem. Ges. 1890; 23:1474–1476.**
9. **Oskooie HA, Heravi MM, Behbahani FK. A facile, mild and efficient one-pot synthesis of 2-substituted indole derivatives catalyzed by Pd (PPh3)2Cl2. Molecules. 2007; 12:1438–1446.**
10. **Karthikeyan SV, Perumal S, Shetty KA, Yogeeswari P, Sriram D. A microwave-assisted facile regioselective Fischer indole synthesis and antitubercular evaluation of novel 2-aryl-3,4-dihydro-2H-thieno [3,2-b] indoles. Bioorg. Med. Chem. Lett. 2009;19: 3006–3009.**
11. **Lehmann F, Holm M, Laufer S. Rapid and easy access to indoles via microwave-assisted Hemetsberger–Knittel synthesis. Tetrahedron Lett. 2009; 50:1708–1709.**
12. **Gupta R, Jain A, Jain M, Joshi R. 'One Pot' synthesis of 2-Amino-3-cyano-4,6-diarylpyridines under ultrasonic irradiation and grindstone technology. Bull. Kor. Chem. Soc. 2010; 30:3180–3182.**
13. **Duvelleroy D, Perrio C, Parisel O, Lasne M-C. Rapid synthesis of quinoline-4-carboxylic acis derivatives from arylimines and 2-substituted acrylates or acrylamides inder indium (III) chloride and microwave activations. Scope and limitations of the reaction. Org. Biomol. Chem. 2005; 3:3794–3804.**
14. **Adib M, Mahmoodi N, Mahdavi M, Bijanzadeh HR. Microwave-assisted simple, one-pot, four-component synthesis of 2,4,6-triarylpyrimidines under solvent free conditions. Tetrahedron Lett. 2006; 47:9365–9368.**
15. **Biginelli P. Aldehyde-urea derivatives of aceto- and oxaloacetic acids. Gazz. Chim. Ital. 1893; 23:360–413.**
16. **Wilson MA, Filzen G, Welmaker GS. A microwave assisted, green procedure for the synthesis of N-aryl sulfonyl and N-aryl pyrroles. Tetrahedron Lett. 2009; 50:4807–4809.**
17. **Deb I, Seidel D. Retro-Claisen condensation versus pyrrole formation in reactions of amines and 1,3-diketones. Tetrahedron Lett. 2010; 51:2945–2947.**
18. **Wyr (bek P, Sniady A, Bewick N, Li Y, Mikus A, Wheeler KA, Dembinski R. Microwave-assisted zinc chloride-catalyzed synthesis of substituted pyrroles from homopropargyl azides. Tetrahedron. 2009; 65:1268–1275.**
19. **Fischer indole synthesis and antitubercular evaluation of Karthikeyan SV, Perumal S, Shetty KA, Yogeeswari P, Sriram D. A microwave-assisted facile regioselective novel 2-aryl-3,4-dihydro-2H-thieno [3,2-b] indoles. Bioorg. Med. Chem. Lett. 2009;19: 3006–3009.**
20. **Lehmann F, Holm M, Laufer S. Rapid andeasy access to indoles via microwave-assisted Hemetsberger–Knittel synthesis. Tetrahedron Lett. 2009; 50:1708–1709.**
21. **Tu S, Jia R, Jiang B, Zhang J, Zhang Y, Yao C, Ji, S. Krohnke reaction in aqueous media: one-pot clean synthesis of 4´-aryl-2,2´:6´,2´´-terpyridines. Tetrahedron. 2007; 63:381–388.**

22. **Yin G, Liu Q, Maa J, She N. Solvent- and catalyst free synthesis of new hydroxylated trisubstituted pyridines under microwave irradiation. Green Chem. 2012; 14:1796–1798.**
23. **Muscia GC, Bollini M, Carnevale JP, Bruno AM, Ası´s SE. Microwave-assisted Friedla¨ nder synthesis of quinolines derivatives as potential antiparasitic agents. Tetrahedron Lett. 2006; 47:8811–8815.**
24. **Balamurugan K, Jeyachandran V, Perumal S, Manja Shetty TH, Yogeeswari P, Sriram D. A microwave assisted, facile, regioselective Friedla¨ nder synthesis and antitubercular evaluation of 2,9-diaryl-2,3-dihydrothieno-[3,2b] quinolines. Eur. J. Med. Chem. 2010; 45:682–688.**
25. **Rai US, Isloor AM, Shetty P, Vijesh AM, Prabhu N, Isloor S, Thiageeswaran M, Fun H-K. Novel chromeno [2,3-b]-pyrimidine derivatives as potential antimicrobial agents. Eur. J. Med. Chem. 2010; 45:2695–2699.**
26. **Bagley MC, Lin Z, Pope SJA. Barium manganate in microwave-assisted oxidation reactions: synthesis of solvatochromic 2,4,6-triarylpyrimidines. Tetrahedron Lett. 2009; 50:6818–6822**
27. **Quiroga J, Portilla J, Abonı´a R, Insuasty B, Nogueras M, Cobo J. Regioselective synthesis of novel substituted pyrazolo[1,5-a] pyrimidines under solvent free conditions. Tetrahedron Lett. 2008; 49:6254–6256.**

There are also many references on the basis of examples.

CONTROVERSY ABOUT pK_a OF WATER

B.Sc. Chemistry (Hons) Semester VI (Under CBCS)

Examination, 2025

Paper: DSE-B4(Dissertation)

CU Roll no. :223114-11-0008

CU Reg no. :114-1211-0219-22

College: St. Paul's Cathedral Mission College

St. Paul's Cathedral Mission College
33/1 Raja Rammohan Roy Sarani, Kolkata-700 009
NAAC ACCREDITED
AISHE ID C-11869
Estd. 1865

CERTIFICATE

This is to certify that the dissertation entitled **"CONTROVERSY ABOUT pK_a OF WATER"**, submitted to the Department of Chemistry, St. Paul's C. M. College, Kolkata in partial fulfilment for the award of the degree of SEM-VI, DSE-B4 (under CBCS) in the B.Sc. SEM-VI CEMA Examination, 2025, CU, is a record of bona fide work carried out by Pritha Mukherjee, CU Roll no. :223114-11-0008. (CU Reg no. :114-1211-0219-22), under my supervision and guidance. This is a review work and hasn't been submitted to receive any other degree. All help received by him from various sources have been duly acknowledged.

(Dr. Kaushik Basu).
Assistant Professor
Department of Chemistry
St. Paul's C. M. College

(Dr. Kalyan Kumar Mandal)
Associate Professor
Department of Chemistry
St. Paul's C. M. College

CONTENTS

CONTROVERSY ABOUT $\boldsymbol{pK_a}$ OF WATER

ABSTRACT

Although the pK_a of water has been shown to be 14.0 at 25 ℃ both experimentally and theoretically[1], a subset of organic chemists has listed the pK_a of the aqueous proton (H^+ or H_3O^+) as -1.7 since at least the early 1930s and at around 1960s, they began appearing in organic chemistry textbooks. Here we trace this error back to Brønsted's early contributions in the 1920s to the Brønsted-Lowry Theory of acids and bases[2,3]. The two different pK_a values was first raised in 1986 by Starkey et al.[4] , Ballinger and Long generally defend the use of these values by citing measurements of equilibrium constant for the water + methoxide acid-base reaction that suggested that methanol (pK_a = 15.54) is stronger acid than water, from this they concluded that pK_a of water must be 15.74 rather than 14.00[5]. Over the next two decades, many researcher to this Journal [6–10] opposed Starkey et al, arguing that the rational values are in fact thermodynamically untenable. Meister et al. published a comprehensive paper in 2014 presenting this point of view from several different perspectives[11].

Here we discuss the problems that invalidate this conclusion, the most important being that it is based on the use of the pure liquid standard state (mole fraction = 1) that is quite different from the standard state for acidities determined in dilute solution (molality = 1). Using the latter standard state the equilibrium constant for the water /

methoxide reaction ranges from 4 to 70, showing water to be stronger acid than methanol, and justifying the use of the thermodynamically correct value, pK_a (H_2O) = 14.00

INTRODUCTION

Acid-base equilibrium are foundational topics in chemistry education. Central to this discussion is the pK_a , which quantifies acid strength. While water's self-ionization is a textbook example, its pK_a value has been inconsistently reported. Organic chemistry sources often cite 15.74, based on historical interpretations, whereas general chemistry texts report 14.00, aligning with thermodynamic conventions. This discrepancy originates from historical misunderstandings of standard states and the interpretation of experimental results, particularly from the works of Bronsted (1920s) and Ballinger and Long (1960)

DEFINITION OF $\boldsymbol{pK_a}$

The pK_a is the negative logarithm (base 10) of the acid dissociation constant (K_a) of a compound. It measures the strength of an acid in solution.

The lower the pK_a, the stronger the acid, as it indicates a greater tendency to donate a proton (H^+).

To calculate the pK_a of an acid, we need it's acid dissociation constant (K_a), which measures the extent of dissociation in solution.

Mathematically, $pK_a = -\log_{10}(K_a)$

HA $\rightleftharpoons$ $H^+ + A^-$

$K_a = \frac{[H^+]\,[A^-]}{[HA]}$, where $[H^+]$ represents concentration of H^+, $[A^-]$ represents concentration of A^- and [HA] represents the concentration of HA.

TEXTBOOKS AND REPORTED pK_a VALUES

Below is a list of chemistry textbooks and the pK_a values for water they report, based on the provided search results and general knowledge of chemistry literature. Note that not all textbooks explicitly state the pK_a of water, and some may avoid listing it due to the controversy. Where specific editions or values are not directly cited in the search results, I've included examples of well-known textbooks that align with the reported trends (e.g., organic chemistry texts using 15.7, general chemistry using 14.0). I also indicate where the information is inferred based on the patterns described in the sources.

1. Chemistry of Organic Compounds, 3rd Edition (1965) by Carl Robert Noller

pK_a Value: 15.74

Details: This textbook is suggested as a possible source of the incorrect pK_a value of 15.74 for water in organic chemistry textbooks. The value likely stems from the influence of a 1960 paper by Ballinger and Long, which propagated the use of the "rational" pK_a value. This book is cited as a historical contributor to the widespread use of 15.74 in organic chemistry education, particularly in Brazil and other regions.

2. March's Advanced Organic Chemistry, 8th Edition (2020) by Michael B. Smith

pK_a Value: 14.0 (correct value), with 15.74 given in brackets

Details: This influential organic chemistry textbook has updated its pK_a value for water to the thermodynamically correct 14.0 in its 8th edition, acknowledging the error in earlier editions and the broader organic chemistry community. The inclusion of 15.74 in brackets reflects an effort to address the historical use of the incorrect value while emphasizing the correct one.

3. Physical Chemistry (1937) by Johannes Brønsted

pK_a Value: 14.0 (conventional) and 15.74 (rational)

Details: Brønsted's early work in the 1920s introduced both the "conventional" (14.0) and "rational" (15.74) pK_a values for water. In his 1937 textbook, he prioritized the conventional value (14.0), defining the autoprotolysis constant of water as equivalent to K_W, thus supporting pK_a = 14.0. However, his earlier mention of the rational value contributed to its adoption in organic chemistry.

4. Organic Chemistry (Various Editions) by John E. McMurry

pK_a Value: 15.7

Details: McMurry's textbook is a widely used organic chemistry resource, and older editions (pre-2020) typically report the pK_a of water as 15.7, following the convention in organic chemistry. While specific editions are not cited in the search results, this aligns with the trend noted in sources that organic chemistry textbooks commonly use 15.7 or 15.74 due to the inclusion of water's molar concentration in the Ka calculation.

5. Chemistry: The Central Science (Various Editions) by Theodore L. Brown, H. Eugene LeMay, et al.

pK_a Value: 14.0

Details: This general chemistry textbook is known for using the thermodynamically correct pK_a value of 14.0 for water, consistent with the autoionization constant $K_w = 10^{-14}$. General chemistry texts, as noted in the sources, typically avoid the erroneous 15.7 value and focus on the standard thermodynamic approach.

6. Atkins' Physical Chemistry (Various Editions) by Peter Atkins and Julio de Paula

pK_a Value: 14.0

Details: This physical chemistry textbook emphasizes fundamental thermodynamic principles, leading to the correct pK_a of water as 14.0. While it may not explicitly list the pK_a of water, it provides the theoretical framework (e.g., Raoult's law, activity coefficients) that supports pK_a = pK_W = 14.0 . The sources note that physical chemistry texts generally align with this value.

7. Riedel/Janiak Inorganic Chemistry (Various Editions)

pK_a Value: 15.74

Details: This inorganic chemistry textbook, particularly noted in German-language contexts, is an exception among inorganic chemistry texts for using the incorrect pK_a value of 15.74 for water. This aligns with the organic chemistry convention rather than the standard thermodynamic value of 14.0 used in most inorganic and general chemistry texts.

8. The Proton in Chemistry (1973) by R. P. Bell

pK_a Value: 15.74

Details: This monograph is cited as listing the incorrect pK_a value of 15.74 for water, reflecting the influence of organic chemistry

conventions at the time. It is noted as a significant source that perpetuated the use of the erroneous value in some chemistry subfields.

Background on pK_a of Water

pK_a = 14.0: This is considered the thermodynamically correct value for water in water at 25°C[1]. It is derived from the autoionization constant of water, $K_w = [H^+][OH^-] = 10^{-14}$, where the pK_a of water equals the pK_w (14.0). This value is used in most general and analytical chemistry textbooks, as it aligns with standard thermodynamic principles where the activity of pure water is taken as 1.

pK_a = 15.7 (or 15.74): This value is often found in organic chemistry textbooks. It originates from including the molar concentration of water (55.3 M) in the equilibrium expression, leading to $K_a = \frac{K_w}{[H_2O]} = \frac{10^{-14}}{55.3} \approx 1.81 \times 10^{-16}$ and thus $pK_a \approx 15.74$. This approach, historically traced to Brønsted's "rational" acidity constant[2,3], is considered thermodynamically incorrect for aqueous solutions but persists in some organic chemistry contexts due to historical precedent and comparisons with other weak acids like methanol.

EXPERIMENTAL CONFUSIONS

Brønsted-Lowry: Brønsted explained the "rational" and "conventional" values[2,3] on the basis of the autoionization of water or autoprotolysis:

$H_2O\ (l) \rightleftharpoons H^+\ (aq) + OH^-\ (aq)$ (1)

The "conventional" (and generally accepted) value comes from solution equilibrium thermodynamics, in which the reactant water

species in the denominator of the equilibrium constant expression has an activity of 1:

$$k_w = \frac{a_{H^+} \cdot a_{OH^-}}{a_{H_2O}} = a_{H^+} \cdot a_{OH^-} \cong \frac{[H^+]}{C^0} \cdot \frac{[OH^-]}{C^0}$$

$$= (1.00 \times 10^{-7})^2 = (1.00 \times 10^{-14}) \qquad (2)$$

Here, e_i refers to the activity of solution component i, and c° = 1 M, the standard concentration. We know that the activity of a pure compound in its standard state is 1, and solute activity is related to the more common concentration terms like molarity, molality, mole fraction through an activity coefficient. The value of the activity coefficient is unity for ideal solutions. For most of the reactions in aqueous solution, it is assumed that concentrations are sufficiently dilute that molarity is a reasonable proxy for molality, and activity coefficients are close to 1, making the activity-based K_{eq} approximately equal to the concentration based ratio.

$$K_w' = \frac{a_{H^+} \cdot a_{OH^-}}{a^*_{H_2O}} \approx \frac{[H^+]\,[OH^-]}{[H_2O]} = \frac{1.00 \times 10^{-14}}{55.33}$$

$$= 1.81 \times 10^{-16} \qquad (3)$$

The "rational" $K_w' = 1.81 \times 10^{-16}$ then leads to pK_a' (H_2O) = 15.74. (In this paper we will distinguish the "conventional" and "rational" values by priming the "rational" symbol, e.g., pK_a'). It is important to point out that common thermodynamic practice for an activity-based equilibrium constant expression approximates the activity of the solvent water as ≈ 1, or essentially pure; this approximation is included in eq.2. On the other hand, eq.4 approximates the activity of solvent water ($a^*_{H_2O}$) as ≈ 55 M. Hence, eq.3 is thermodynamically incorrect, which raises the question of why Brønsted felt justified in presenting the "rational" K_w' and pK_a' of water as acceptable values.

Acid Ionization Equilibrium

Brønsted depicted the autoionization[2] of water in term of two water molecules in his theory, one behaving as acid and the other as base.

H_2O (1) + H_2O (1) $\rightleftharpoons$ OH^- (aq) + H_3O^+ (aq) (4)

(acid) (base)

Brønsted treated two water molecules differently: one as an acid with a molar concentration of 55.33 M (or $K_a' \approx 55.33$ and pK_a' = -1.74) and the other as a base with an activity of ≈ 1.

$$K_w' \equiv \frac{a_{OH^-}.a_{H_3O^+}}{a_{H_2O\ (acid)}.a_{H_2O\ (base\ or\ solvent)}}$$

$$= \frac{a_{OH^-}.a_{H_3O^+}}{a_{H_2O\ (acid)} \times 1}$$

$$\approx \frac{[OH^-][H^+]}{55.33 \times 1} = 1.81 \times 10^{-16}$$

The thermodynamically acceptable approximation of the activity of water as ≈ 1 leads to the activity-based "conventional" value of K_w = 1.00×10^{-14}), and the "conventional" pK_a's of 14 and 0 for water and H^+ (aq). The concentration-based "rational" value of K_w' = 1.81×10^{-16} stems from assigning water its thermodynamically unacceptable molar concentration of 55M, leading to the "rational" pK_a'values of 15.74 and −1.74 for water and H^+ (aq). In other words, "conventional" and "rational" values are based on different conventions for the concentration of solvent water[11].

Ballinger and Long: Ballinger and Long measured the acidities of alcohols, including methanol, in aqueous solution using conductance measurements. Their experiment focused on the acid-base equilibrium between alcohols (ROH) and hydroxide ions (OH^-), represented by the general reaction[5]:

$$\text{ROH}\ (aq) + OH^-(aq) \rightleftharpoons RO^-(aq) + H_2O(aq)$$

Specifically, for methanol (CH_3OH), they studied the reverse reaction involving the methoxide ion (CH_3O^-):

$$H_2O\ (aq) + CH_3O^-(aq) \rightleftharpoons\ OH^-(aq) + CH_3OH(aq)$$

They determined the equilibrium constant for this reaction, $K_b(CH_3O^-)$ defined as:

$$K_b(CH_3O^-) = \frac{a_{OH^-}.a_{CH_3OH}}{a_{CH_3O^-}.a_{H_2O}}$$

$$\approx \frac{[OH^-][CH_3OH]}{[CH_3O^-]}$$

Here, they approximated the activity of water ($a_{H_2O} \approx 1$) and assumed activity coefficients for solutes in dilute solution are nearly 1. Their measurements yielded,

$K_b(CH_3O^-) = 34.6 \pm 2.7$, indicating that the forward reaction in (2) is favoured, meaning water is a stronger acid than methanol.

To calculate methanol's acid dissociation constant ($K_a(CH_3OH)$), they used the conventional autoionization constant of water ($K_w = 1.00 \times 10^{-14}$ at 25°C) and the relationship:

$$K_a(CH_3OH) = \frac{k_w}{k_b(CH_3O^-)} = \frac{1.00\times10^{-14}}{34.6} = 2.89\times 10^{-16}$$

Taking the negative logarithm, they obtained:

$$pK_a(CH_3OH) = -\log(2.89\times 10^{-16}) = 15.54$$

However, Ballinger and Long made an error when comparing methanol's acidity to water's. They used the "rational" pK_a of water (15.74), derived from a concentration-based K_w':

$$K_w' = \frac{[H^+]\,[OH^-]}{[H_2O]} = \frac{1.00 \times 10^{-14}}{55.33}$$

$$= 1.81 \times 10^{-16}$$

$$pK_a'(H_2O) = -\log(1.81 \times 10^{-16}) = 15.74$$

Comparing methanol's pK_a (15.54) to water's "rational" pK_a (15.74), they concluded methanol is 1.5 times more acidic ($10^{15.74-15.54} = 10^{0.2} \approx 1.58$). This was incorrect because methanol's pKa was calculated using the conventional K_w, so it should have been compared to water's conventional pK_a of 14.00, derived from:

$$K_w = [H^+]\,[OH^-] = 1.00 \times 10^{-14}$$

$$pK_a(H_2O) = -\log(1.00 \times 10^{-14}) = 14.00$$

This comparison shows water is significantly more acidic than methanol ($10^{15.54-14.00} = 10^{1.54} \approx 34.7$), consistent with $K_b(CH_3O^-)$ = 34.6. Additionally, they calculated a mole-fraction-based constant, K' = 0.96, using a pure methanol standard state:

$$K' = 0.0277 \times K_b(CH_3O^-) = 0.0277 \times 34.6 = 0$$

This suggested methanol and water have similar acidities, but K' is inappropriate for pK_a comparisons, which use a 1 M standard state. Thus, their experimental data correctly indicate water is ≈ 35 times more acidic than methanol, but their use of the "rational" pK_a for water led to an erroneous conclusion.

CONCLUSION

There are some reasons why it is important to get this value right[12]. The obvious problem is the correct "conventional" pK_a of water = 14.00 shows water to be a 55-fold stronger acid than the incorrect "rational" value of 15.74. Similarly, the correct "conventional" pK_a of H^+(aq) = 0.00 shows H^+ (aq) to be a 55-fold weaker acid than the incorrect "rational" value of −1.74.

And the other reason is students like us get confused when we see $pK_a(H_2O)$ = 14.00 in our first year chemistry text books[13] and $pK_a(H_2O)$ = 15.74 in our some of organic chemistry texts.

So we encourage our organic chemistry textbook authors to remove (some of them already has removed) the non thermodynamic "rational" pK_a values from their pK_a tables, and replace them with the thermodynamic "conventional" pK_a values of water i.e. $pK_a(H_2O)$ = 14.00 at 25 °C.

REFERENCES

(1) Atkins' Physical Chemistry (Various Editions) by Peter Atkins and Julio de Paula

(2) Brønsted, J. Acid and Basic Catalysis. Chem. Rev. 1928, 5 (3), 231−338.

(3) Kauffman, G. B. The Brønsted-Lowry acid base concept. J. Chem. Educ. 1988, 65 (1), 28.

(4) Starkey, R.; Norman, J.; Hintze, M. Who knows the K_a values of water and the hydronium ion? J. Chem. Educ. 1986, 63 (6), 473−474.

(5) Ballinger, P.; Long, F. Acid Ionization Constants of Alcohols. II. Acidities of Some Substituted Methanols and Related Compounds. J. Am. Chem. Soc. 1960, 82 (4), 795−798.

(6) Baldwin, W. G.; Burchill, C. E. Equilibrium constants for water and hydronium ion. J. Chem. Educ. 1987, 64 (12), 1067−1068.

(7) Baldwin, W. G.; Burchill, C. E. The acid equilibrium constant is unity! J. Chem. Educ. 1992, 69 (6), 514−515.
(8) Tapparo, A. The extent of acid-base reactions. J. Chem. Educ. 1992, 69 (6), 515−516.

(9) Keeports, D. Equilibrium constants and water activity. J. Chem. Educ. 2005, 82 (7), 999−999.

(10) Keeports, D. Equilibrium constants and water activity revisited. J. Chem. Educ. 2006, 83 (9), 1290−1290.

(11) Meister, E. C.; Willeke, M.; Angst, W.; Togni, A.; Walde, P. Confusing Quantitative Descriptions of Brønsted-Lowry Acid-Base Equilibria in Chemistry Textbooks−A Critical Review and Clarifications for Chemical Educators. Helv. Chim. Acta 2014, 97 (1), 1−31.

(12) Todd P. Silverstein, and Stephen T. Heller, pK_a Values in the Undergraduate Curriculum: What Is the Real pK_a of Water?

(13) Abrash, H. I. The Relative Acidities of Water and Methanol. J. Chem. Educ. 2001, 78 (11), 1496−1498.

APPLICATION OF TRANSITION METAL ORGANOMETALLIC COMPLEXES AND VARIOUS CATALYTIC PROCESS FOR CO_2 CONVERSION INTO VALUE ADDED CHEMICALS

B.Sc. Chemistry (Hons.) semester VI (Under CBCS)

Examination, 2025

Paper: DSE-B4 (Dissertation)

PRESENTED BY **Sagnik Halder**

CU Roll no: **223114-21-0007**

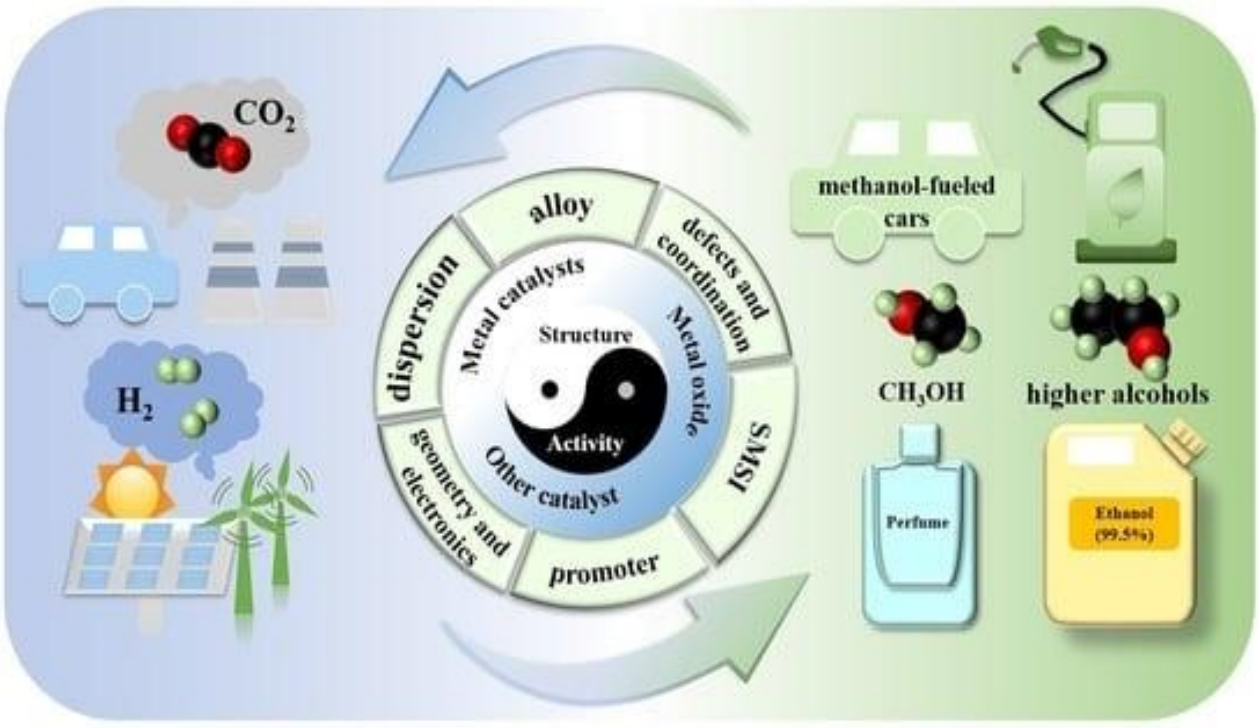
CU REG no: **114-1111-0213-22**

College: **St. Paul's Cathedral Mission College**

CONTENTS

1. Abstract:

The imperative to address rising CO_2 emissions has accelerated research into carbon capture and utilization (CCU) technologies. Hetero generous thermal catalytic CO_2 hydrogenation to alcohols using renewable energy is a highly attractive approach for recycling greenhouse gas into high – value chemicals and fuels thereby decreasing the dependent on fossil fuels , while simultaneously mitigating the CO_2 and environmental problems. Here we discuss the thermodynamic and kinetic analysis of CO_2 hydrogenation reaction. Transition metal organometallic complexes are at the forefront of this effort, offering controlled activation of CO_2 and selective conversion into valuable chemicals—such as methanol, formic acid, cyclic carbonates, and hydrocarbons. This dissertation examines (1) the structural design of catalysts, (2) mechanistic pathways, and (3) catalytic applications across diverse metals (e.g., Ru, Fe, Co, Mn, Cu), emphasizing their reactivity, selectivity, and potential integration with renewable energy processes. To conclude, the current challenges and potential strategies in catalyst design, structural characterization and reaction mechanism are presented for CO_2 converted to valuable compounds.



2. Introduction:

Anthropogenic CO_2 emissions, largely from fossil fuel combustion, are driving global climate challenges like warming and ocean acidification. A sustainable response lies in **CO_2 capture and conversion**, utilizing CO_2 as a renewable, non-toxic carbon feedstock to produce valuable chemicals.

Recent advances in **carbon capture, utilization, and storage (CCUS)** have enabled catalytic routes to transform CO_2 into a wide range of products. These include **formic acid**, **formates**, **methanol**, **ethanol**, **higher alcohols**, **carbon monoxide (CO)**, **methane**, **olefins**, **urea**, and **aromatics**. Among these, **formic acid and formates** serve as hydrogen storage media and intermediates in pharmaceuticals, while **methanol** and **ethanol** are key fuels and chemical building blocks.

Thermochemical hydrogenation of CO_2, especially with green hydrogen from water electrolysis, has emerged as a practical route. However, due to CO_2's thermodynamic stability, conversion requires high temperature and pressure, and precise catalytic control. Challenges include competing side reactions (e.g., methanation, RWGS) and achieving selectivity toward specific products.

Catalyst design is crucial, involving **noble (e.g., Pt, Pd) and non-noble metals (e.g., Cu, Fe)** supported on oxides (e.g., ZnO, ZrO_2) with promoters (e.g., K, Na). Research is increasingly focused on **mechanistic insights**, **in situ characterization**, and **structure–activity relationships** to enhance efficiency and product specificity.

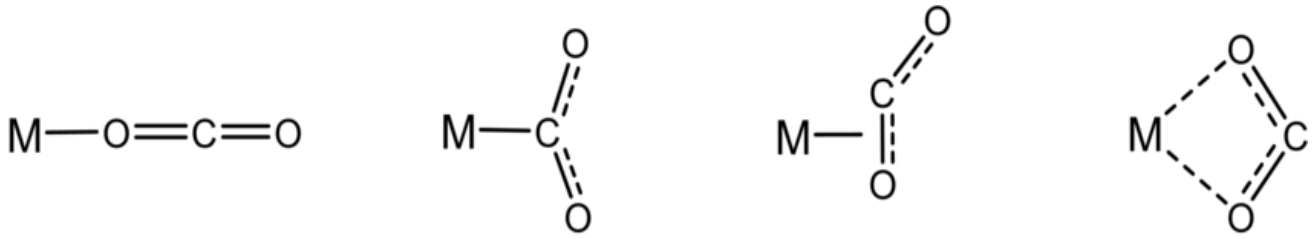
Ultimately, CO_2 conversion to formic acid, alcohols, and other high-value chemicals represents a critical pathway to mitigate emissions and support a circular carbon economy

3. ACTIVATION OF CO_2 :

Carbon dioxide (CO_2) is a **linear molecule (O=C=O)** with a highly **oxidized central carbon (C^{4+})** and no permanent dipole moment. This configuration contributes to its remarkable **thermodynamic and kinetic stability**, making its activation inherently difficult.

- **Bonding:** The C=O bonds are double bonds (with π-bonding character), and the molecule is non-polar due to symmetry.
- **Implication:** Breaking or transforming these strong bonds requires either:
  - Strong nucleophiles (e.g., hydrides)
  - Reducing metal centers

Activation is most often achieved by electron-rich transition metal complexes that can facilitate the formation of **CO_2 adducts**, or insert CO_2 into metal–ligand or metal–hydride bonds. CO_2 can be activated by catalyst in many pathways - 1) Nucleophilic incretion 2) Hydride transfer 3) Lewis acid –base adduct



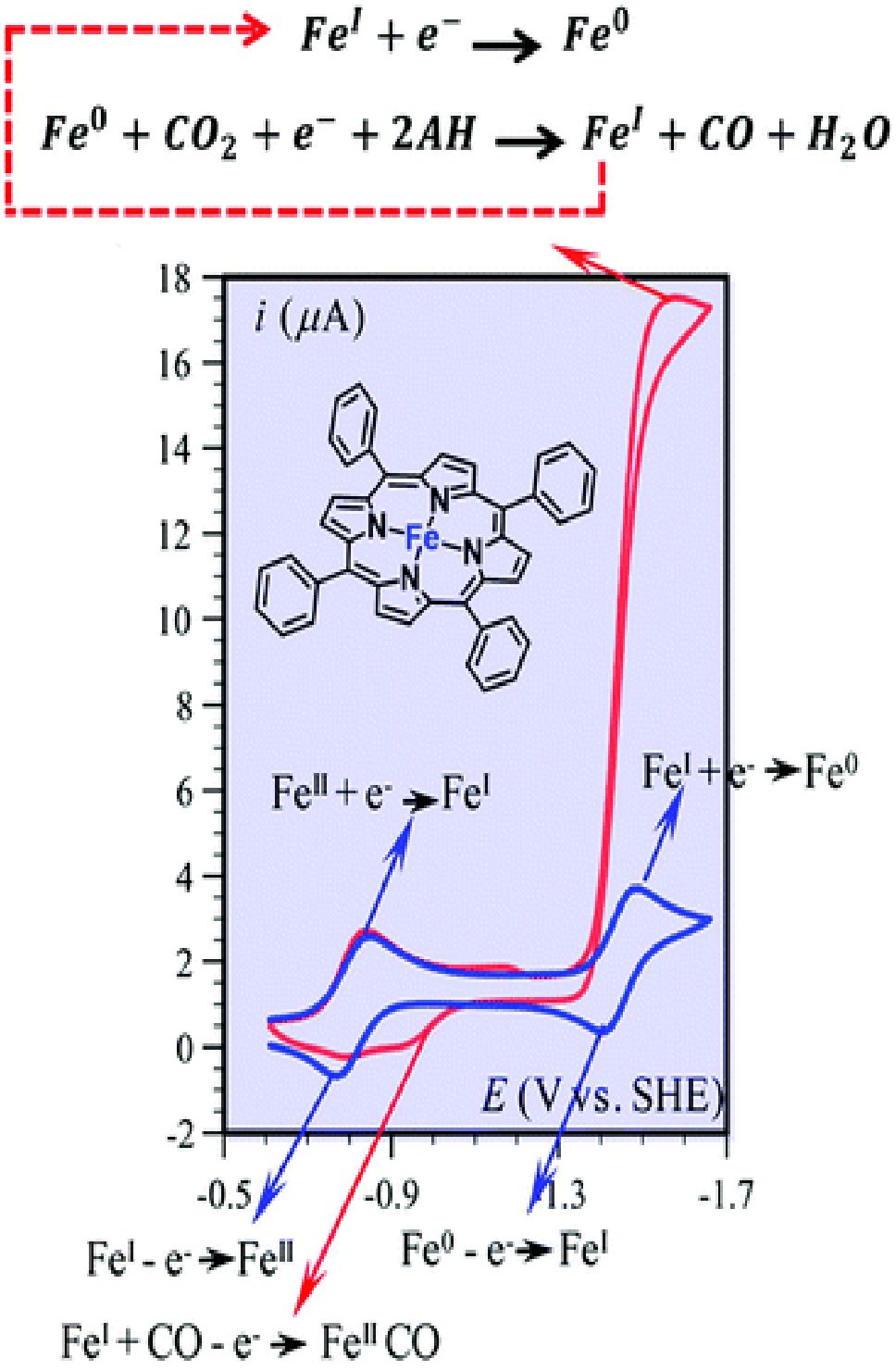
η^1-OCO *end-on* | η^1-CO_2 | η^2-C,O *side on* | η^2-O,O

.

Different modes of coordination of CO_2

4. Homogeneous Molecular Catalysis :

Over the past three decades, **iron(0) porphyrins** have been extensively studied as **homogeneous molecular catalysts** for the electrochemical reduction of CO_2 (CO_2RR). One of the most well-investigated systems is **[Fe(TPP)]Cl (FeTPP)**, where TPP = tetraphenylporphyrin. Early studies in DMF electrolyte identified the **$[Fe(TPP)]^{2-}$** species as catalytically active for converting CO_2 into CO. Though often referred to as Fe^0, more recent **spectroscopic and computational analyses** suggest a more accurate electronic description as **$[Fe(II)(TPP^{\bullet\bullet})]^{2-}$**, highlighting significant electron delocalization onto the porphyrin ring.

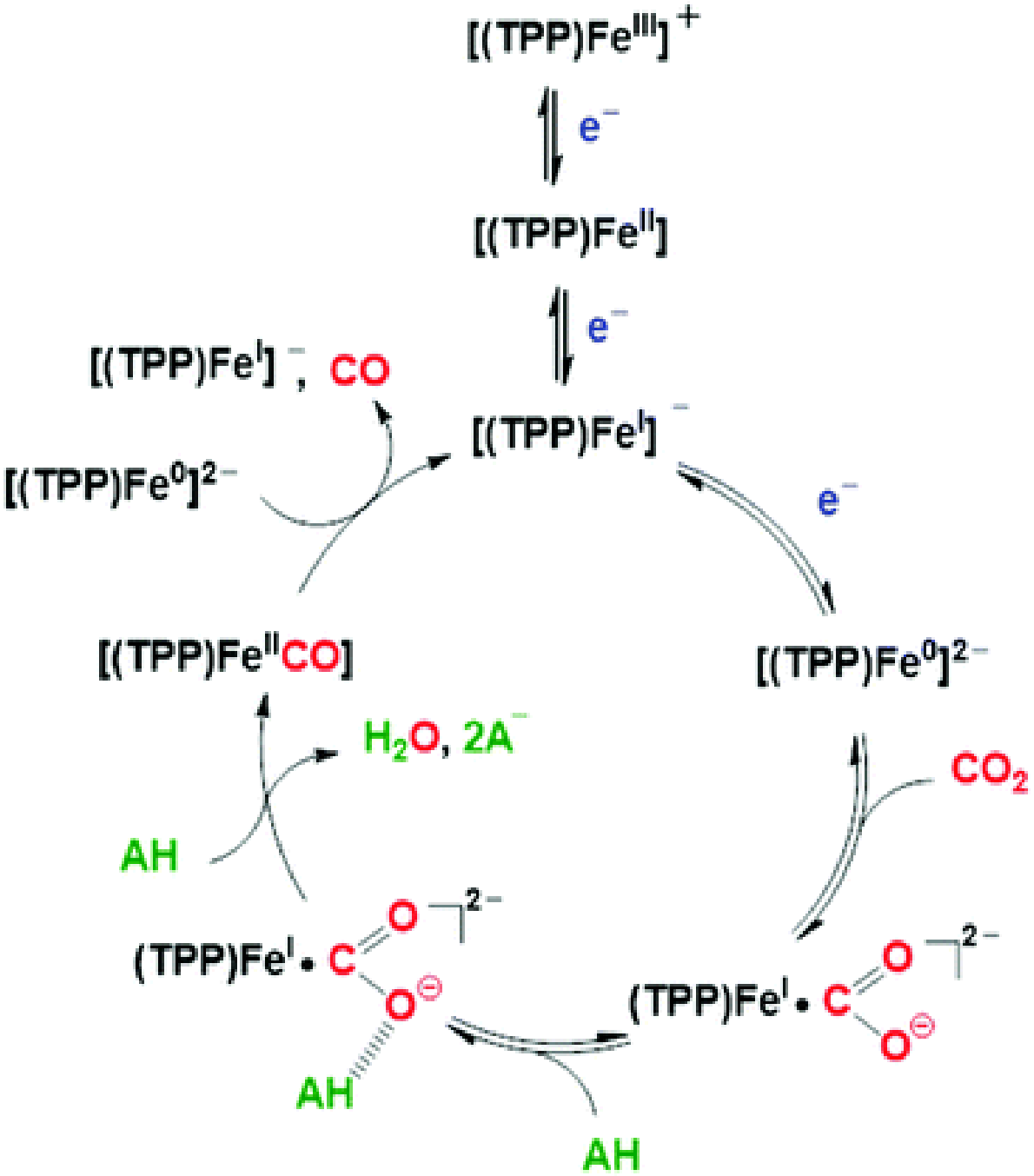


❑ Mechanism: Push–Pull Catalysis:

The **mechanism** is best described as a **two-electron "push–pull" process**:

1. The nucleophilic $[Fe(TPP)]^{2-}$ reacts with CO_2 to form an adduct like **$[Fe(CO_2)(TPP)]^{2-}$**.
2. Electron density is pushed from Fe to CO_2; acid additives stabilize the intermediate through **H-bonding or ion-pair interactions**, pulling electron density further and **promoting C–O bond cleavage**.
3. **Spectroscopy at cryogenic temperatures** has verified intermediates such as $[Fe(II)CO_2]^{2-}$ and $[Fe(II)CO_2H]^{-}$.

Kinetic studies using "foot-of-the-wave" analysis reveal that the **rate-determining step** involves **proton-coupled intramolecular electron transfer** along with **C–O bond cleavage**. The process regenerates the active Fe^0 species after CO release.



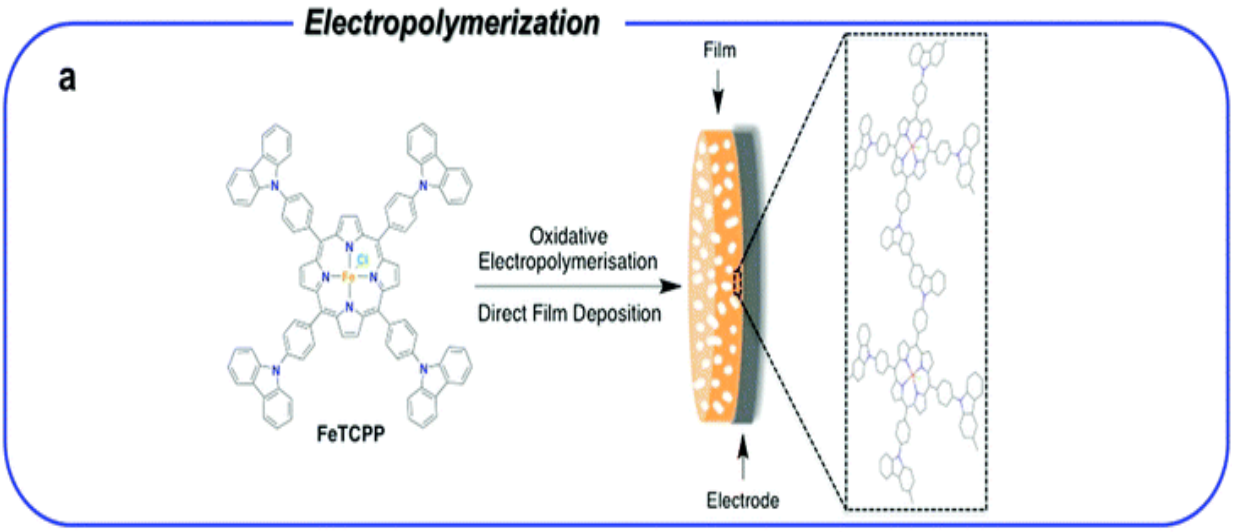
5. Heterogenized Molecular Catalysis :

Immobilization Strategies on Solid Supports

Various strategies have been employed to immobilize iron porphyrin catalysts onto solid electrodes for CO_2 reduction in aqueous media. These include:

❑ Electropolymerization method :

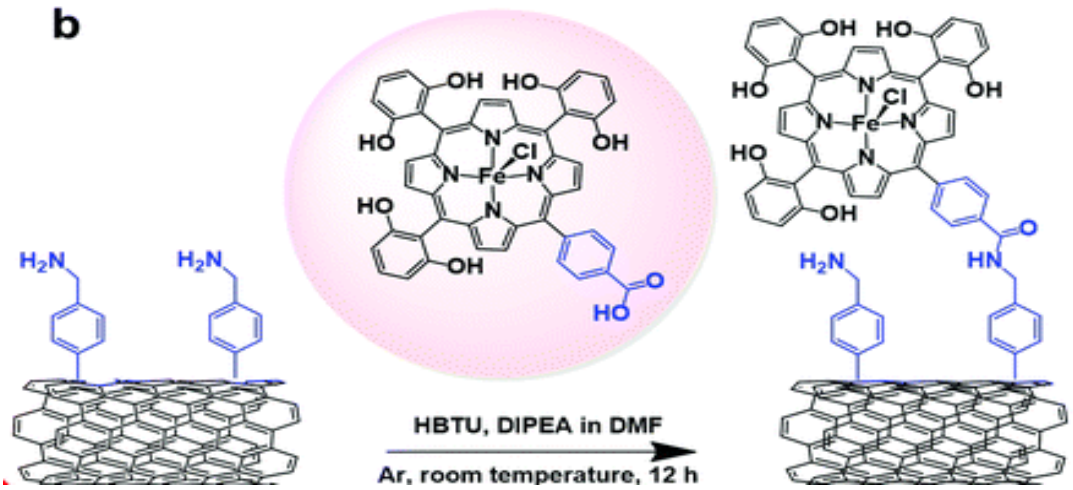
A simple method called electropolymerization was used to carefully coat a glassy carbon (GC) surface with a thin, sponge-like layer made from a special porphyrin molecule that includes a carbazole group. This process allowed the material to form a uniform and porous film on the electrode, which is useful for catalytic applications like CO_2 reduction.



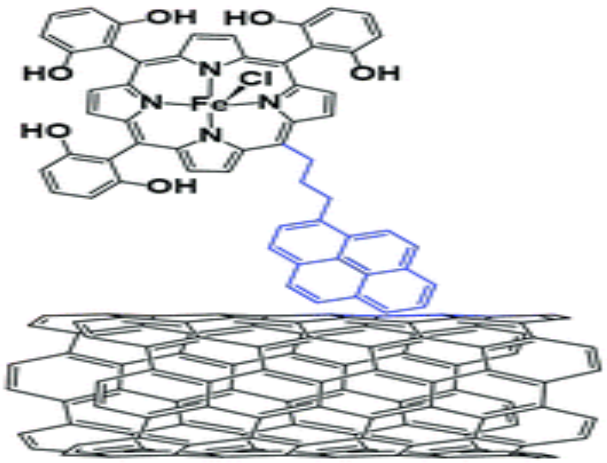
❑ Via multi-walled carbon nanotubes (MWCNTs) :

A modified iron porphyrin with OH groups was attached to multi-walled carbon nanotubes (MWCNTs) using two different methods: **non-covalent** and **covalent** bonding.

- In non-**covalent method**, a pyrene group on the porphyrin helped it stick to the nanotube surface through π–π stacking (a type of weak attraction between flat molecules). This method kept the catalyst's properties intact and led to efficient and selective CO production in water-based solutions with long-lasting performance.



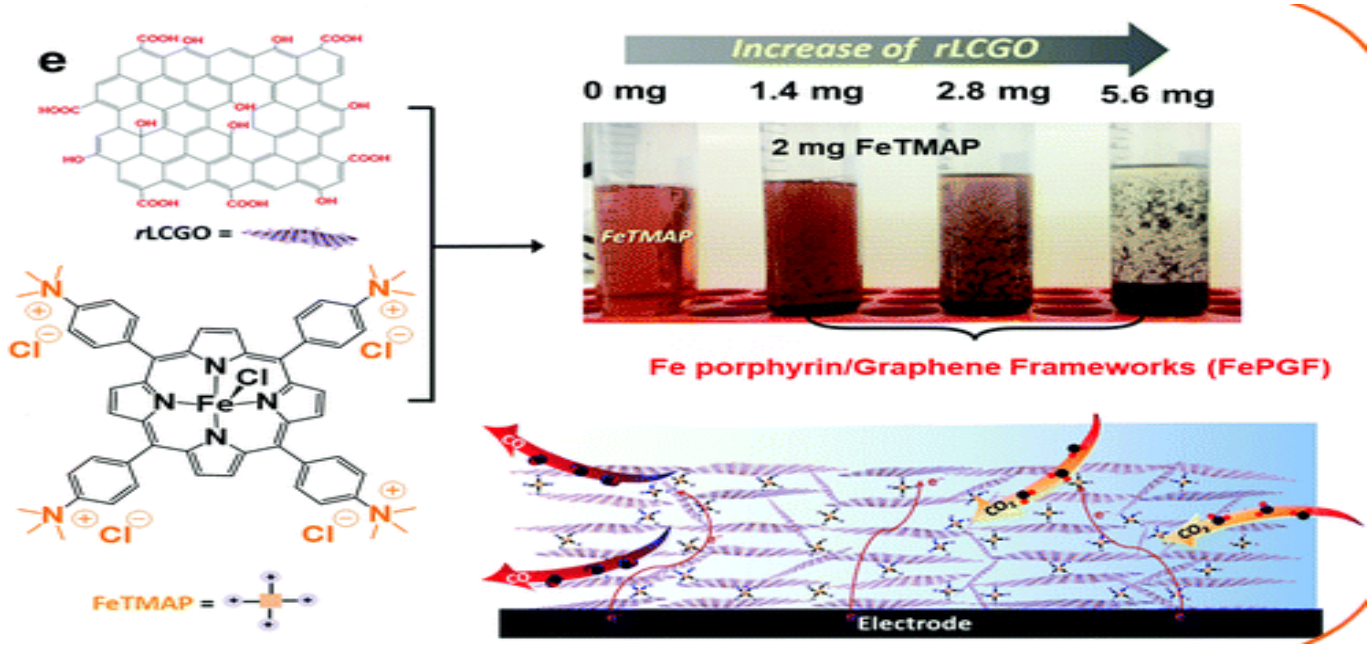
- In **covalent method**, the porphyrin had a carboxylic acid (–COOH) group that chemically bonded with amine (–NH_2) groups on the MWCNT surface, forming a strong amide bond. This also resulted in good catalytic activity for converting CO_2 into CO.



Both methods successfully attached the catalyst to the carbon nanotubes, but in different ways—non-covalently through physical attraction and covalently through chemical bonding.

❑ Via Fe porphyrin / Graphene Framework (Fe PGF) :

Some iron porphyrin molecules can strongly attach to electrode surfaces without needing chemical changes to their structure. For example, Fe–TMAP (Iron–Tetramidomacrocyclic Porphyrin) was successfully anchored to a carbon support using a simple drop-casting method with Nafion binder and carbon powder. This setup was used in a custom-made device to split CO_2 and water into CO and O_2, showing high selectivity (90%) and stable performance over 30 hours. To enhance performance, this compound was combined with reduced liquid crystalline graphene oxide (rLCGO) to form a porous 3D material called FePGF. Due to π–π stacking and electrostatic interactions between the positively charged porphyrin and negatively charged rLCGO, this material improved electron flow and stability, achieving 99% CO selectivity for 10 hours with minimal hydrogen production.

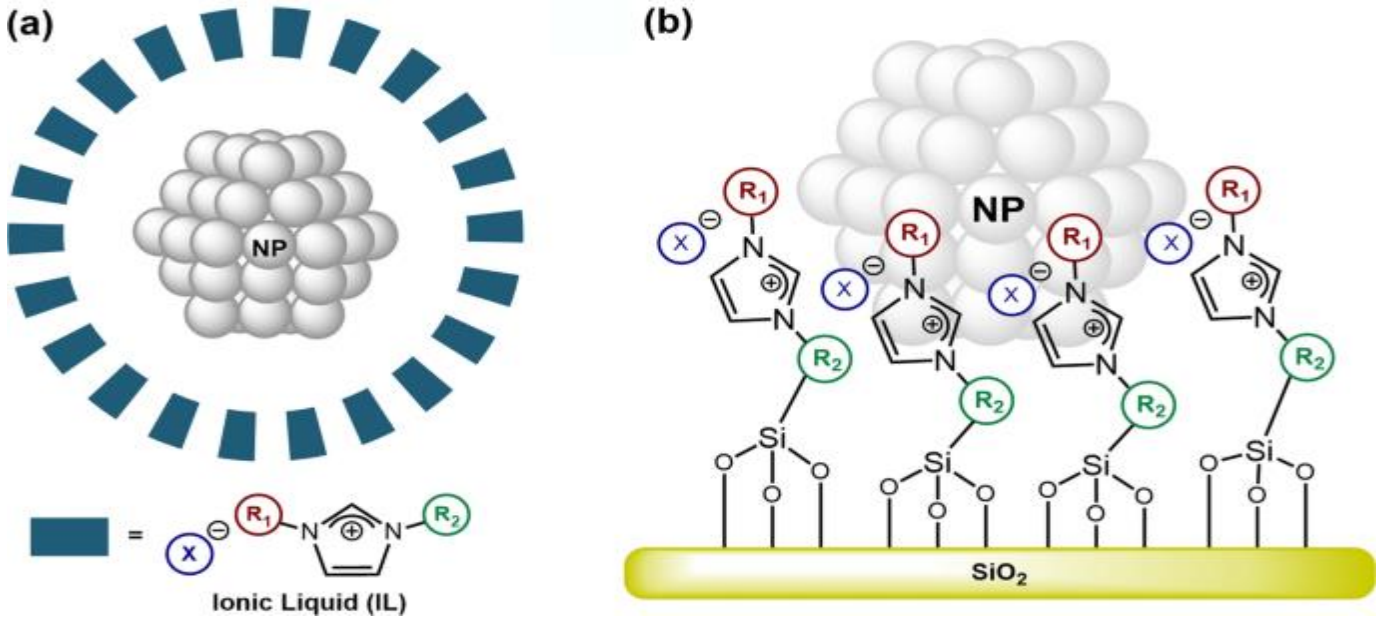


7. CO_2 reduction to Formic acid by using Ru nanoparticles :

Ionic liquids (ILs) are special salts that stay liquid at low temperatures and can act as eco-friendly solvents. They help stabilize metal nanoparticles (NPs) in two ways: by forming protective cages or by attaching them to supports (called SILPs). This control improves catalyst performance and makes separation easier.

Jenani and team made ruthenium (Ru) nanoparticles on different IL supports to study how the ILs affect their size and activity. They found the Ru particles were very small (0.8–2.9 nm) and well spread out. Some IL types made even smaller particles, and the catalysts remained metallic (Ru^0), which is good for reactions.

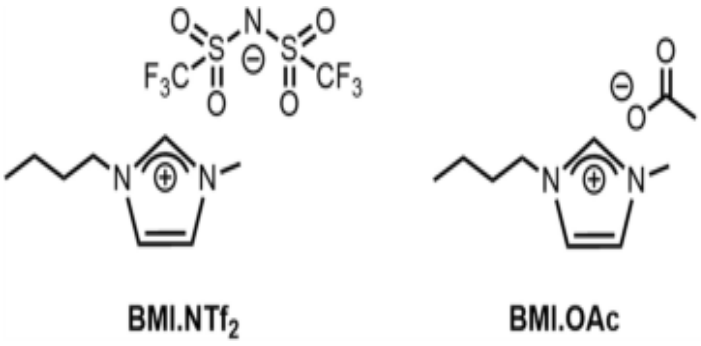
Ionic liquids (ILs)



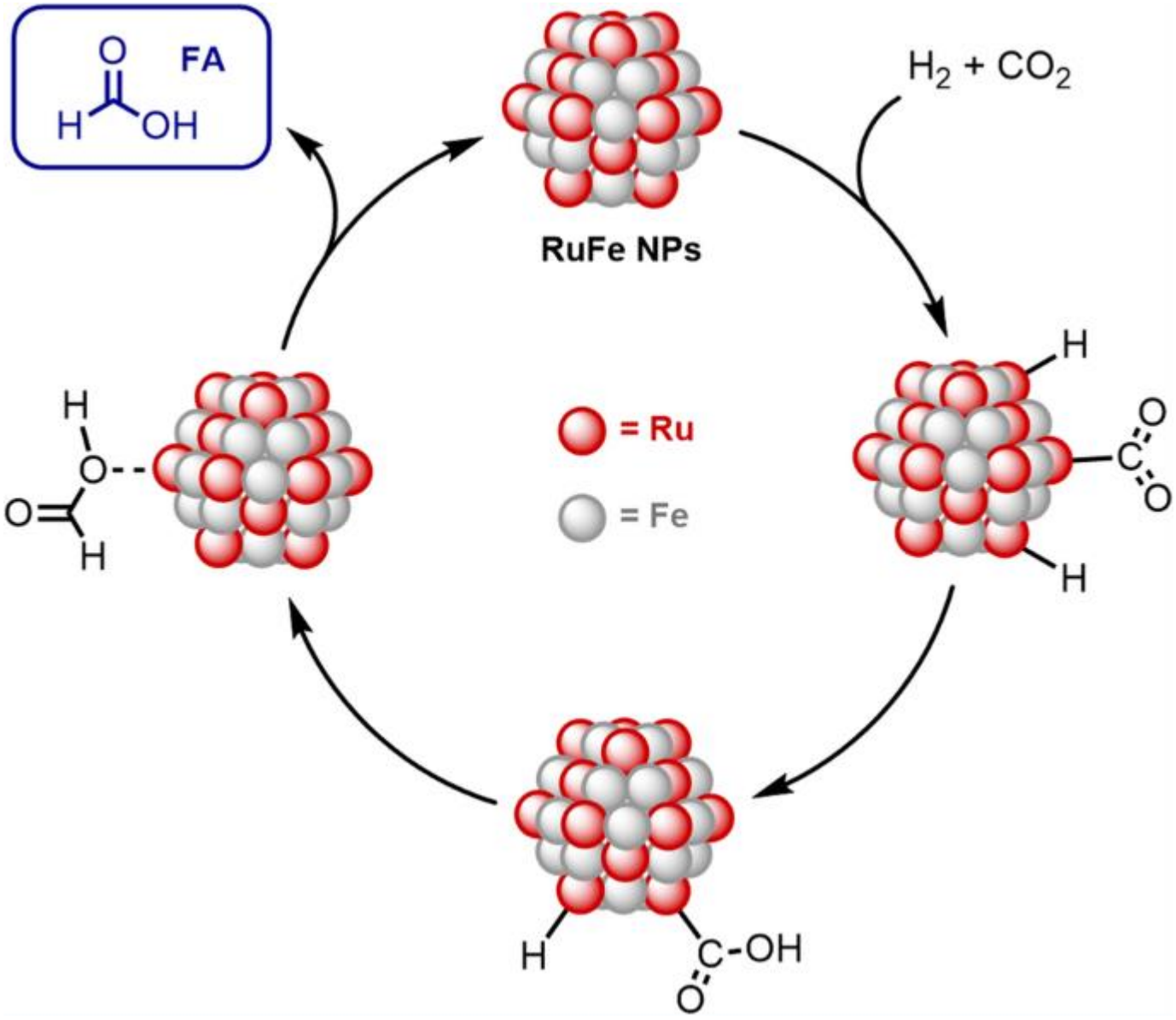
A new catalyst made of tiny particles (nanoparticles) of ruthenium and iron (RuFe NPs), covered with special liquids called ionic liquids (ILs). They used two types of ILs: **BMI.OAc** (water-loving) and **$BMI.NTf_2$** (water-repelling). These ILs affected the product of the CO_2 hydrogenation reaction.

- When **BMI.OAc** was used, the catalyst mainly produced **formic acid (FA)**.
- When **$BMI.NTf_2$** was used, it produced **hydrocarbons** instead.

The best result came from using RuFe NPs with **BMI.OAc** in a mixture of D_2O and DMSO, under high pressure (60 bar) and moderate temperature (333 K). This setup gave good efficiency, producing a decent amount of formic acid (TON = 400, TOF = 23.5 h^{-1}). The DMSO and ILs helped stabilize formic acid by forming hydrogen bonds.

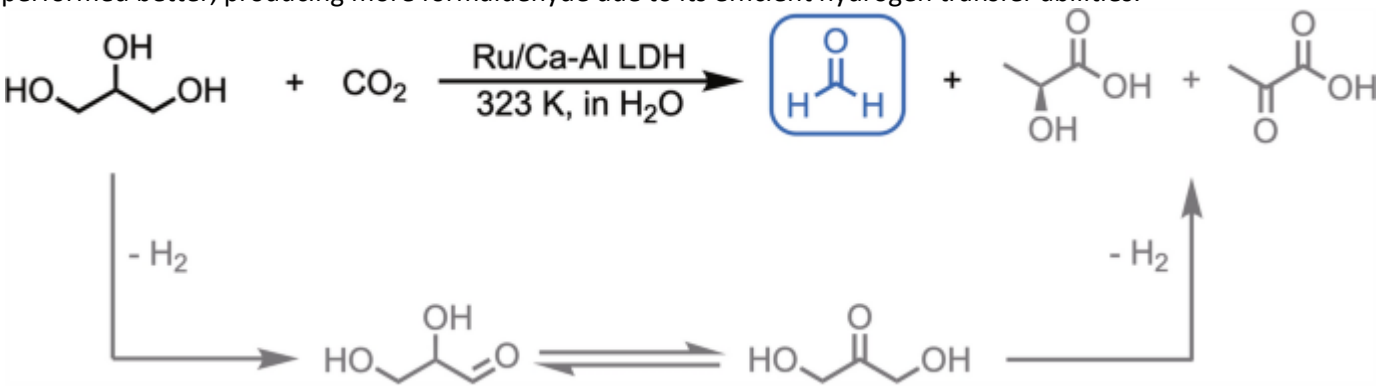


To understand how the catalyst works, they used a technique called high-pressure NMR. They found that **bicarbonate (HCO_3^-)** forms on the catalyst's surface during the reaction. This supports their proposed mechanism: CO_2 and H_2 react on the catalyst, forming HCO_3^-, which is then turned into **formic acid**.

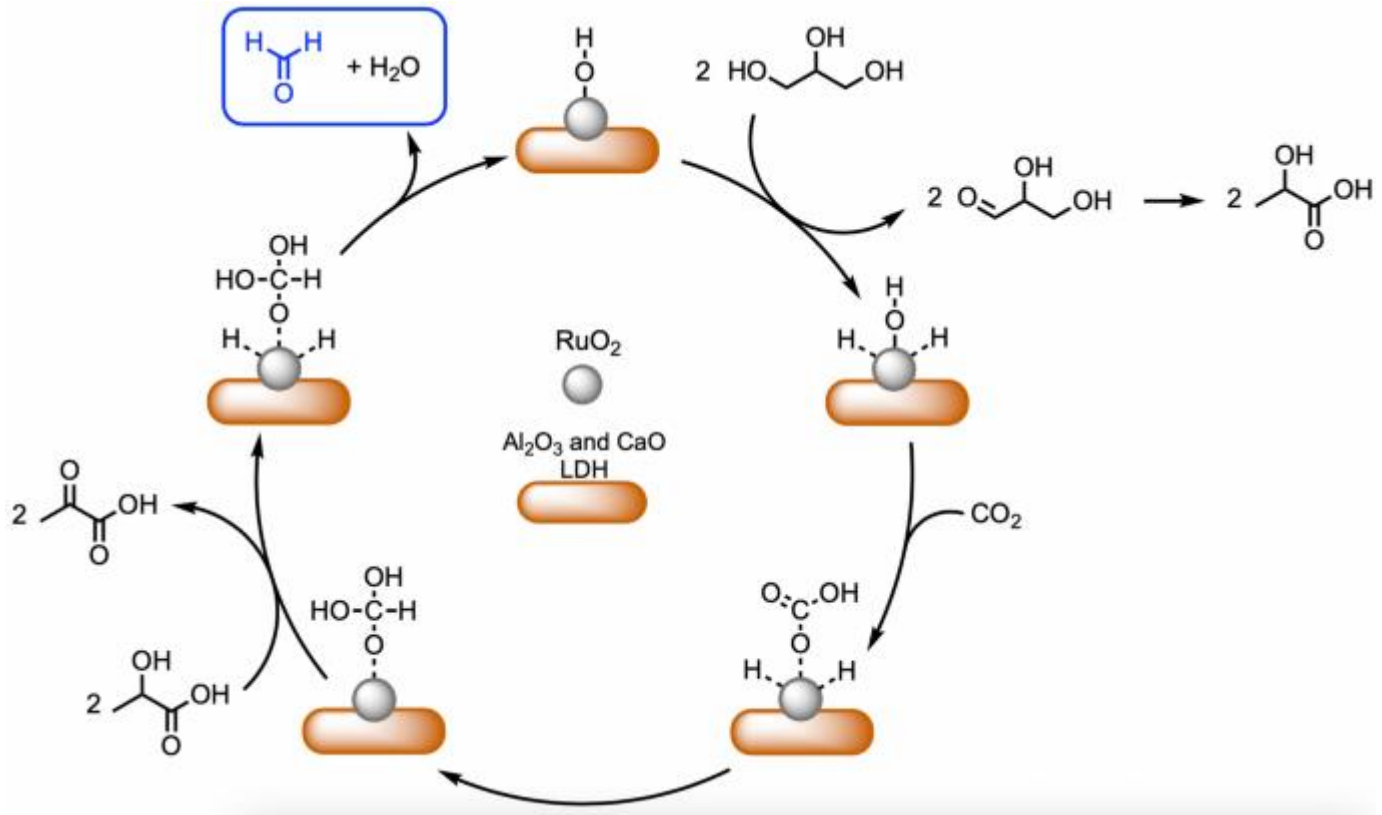


8. Ru @LDH catalysts for CO_2 hydrogenation to Formaldehyde :

Researchers developed catalysts by supporting **ruthenium (Ru) nanoparticles on layered double hydroxides (LDHs)** to convert **carbon dioxide (CO_2) into formaldehyde (HCHO)**. These catalysts, called **Ru@LDH**, were tested using two hydrogen sources: regular **hydrogen gas (H_2)** and a more sustainable option, **glycerol**. Interestingly, glycerol performed better, producing more formaldehyde due to its efficient hydrogen transfer abilities.



The reaction happens in steps: glycerol breaks down on the Ru surface, releasing hydrogen, which then helps reduce CO_2 into formaldehyde. A key part of the reaction involves **bicarbonate and carbonate intermediates**, with **carbonate ions (CO_3^{2-})** proving more effective. High **pH levels (above 10)** and **moderate temperatures** are important to avoid unwanted side reactions like glycerol oxidation, which can lower formaldehyde yield.



The structure of the Ru catalyst also matters. Well-dispersed and properly reduced Ru particles (not oxidized) gave the **highest turnover number (TON)** and selectivity for formaldehyde. However, using too much Ru led to the production of **formic acid instead**, showing that **optimal loading is crucial**.

9. CO_2 hydrogenation to methanol:

Methanol (CH_3OH) is a very important chemical used to make many products and also as a **clean fuel**. It burns cleaner than regular fossil fuels and can also store and carry energy, especially from **renewable sources**.
One exciting way to make methanol is by **converting carbon dioxide (CO_2)** using **hydrogen (H_2)**. This method helps **recycle CO_2** and fight **climate change**. This idea is central to the **"Methanol Economy"**, a vision for a future where methanol is the main energy source.
However, making methanol from CO_2 is hard because CO_2 is a very stable gas. It needs **high temperatures and active catalysts**. But high temperature also causes another reaction (RWGS) that reduces the amount of methanol made. Scientists found that **increasing pressure and the H_2/CO_2 ratio** helps a lot. For example, using more hydrogen (H_2/CO_2 ratio of 10) and working at high pressure (442 bar) greatly improves **CO_2 conversion (up to 95%)** and **methanol selectivity (up to 98%)**, especially using **$Cu/ZnO/Al_2O_3$ catalysts**.

$$CO_2 + 3\,H_2 \xrightleftharpoons{Cu\text{-}Zn/Al_2O_3} CH_3OH + H_2O \quad \Delta H_r^\circ = -49.5\ kJ\ mol^{-1}$$

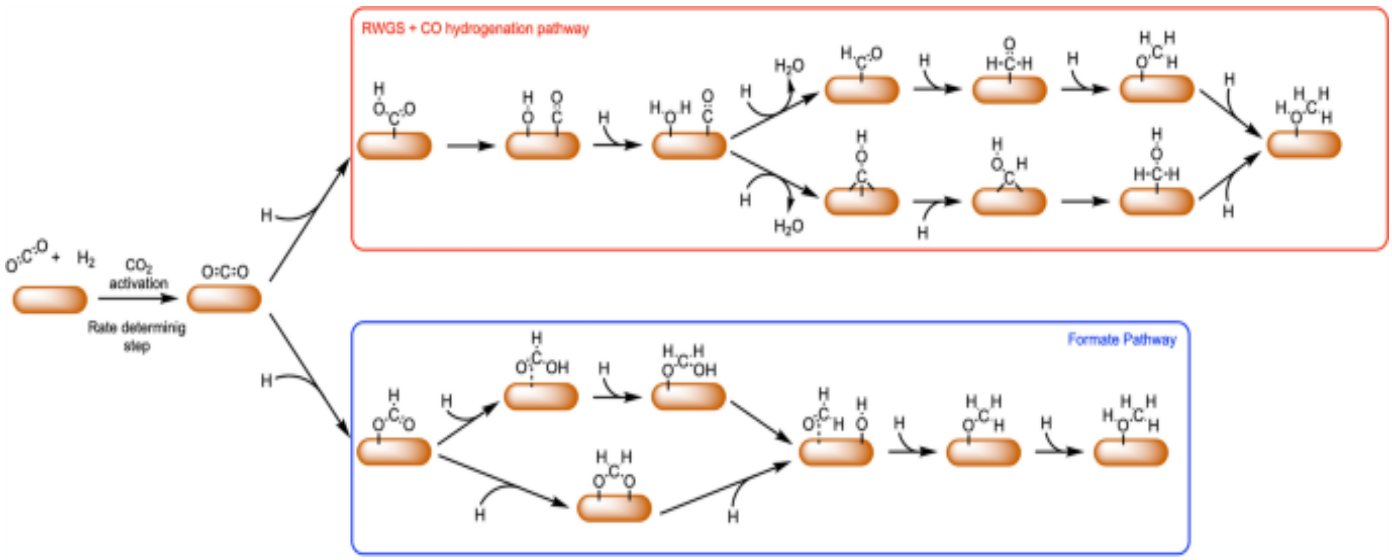
$$CO_2 + H_2 \xrightleftharpoons{Cu\text{-}Zn/Al_2O_3} CO + H_2O \quad \Delta H_r^\circ = 41.2\ kJ\ mol^{-1}$$

Using **more hydrogen (H_2)** and **higher pressure** makes the conversion of **CO_2 to methanol** much more efficient. For example, Bansode et al. showed that increasing the **H_2/CO_2 ratio from 3 to 10** boosted CO_2 conversion from **37% to 95%** and improved **methanol selectivity from 72% to 98%**, using a common **$Cu/ZnO/Al_2O_3$ catalyst**.

Similarly, Gaikwad et al. showed that at **very high pressure (442 bar)** and a 3:1 H_2/CO_2 ratio, about **90% CO_2 conversion** and **over 95% methanol selectivity** were achieved. At high pressure and more hydrogen, side reactions (like making CO instead of methanol) were reduced, and the reaction worked better.

There are **two main pathways** for turning CO_2 into methanol:

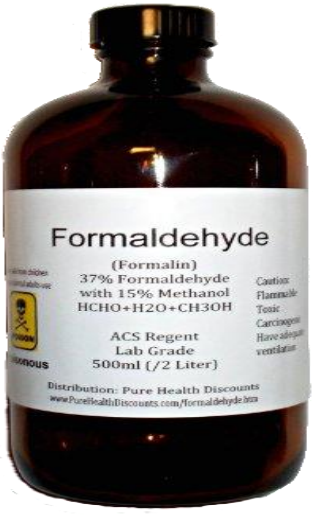
- **Formate pathway** – Most favored. CO_2 first turns into a *formate* intermediate and then into *formaldehyde*, which eventually becomes *methanol*. This happens in steps using atomic hydrogen and catalyst surfaces.
- **RWGS + CO hydrogenation pathway** – CO_2 first becomes *CO*, and then CO turns into *methanol*. This often results in **more CO** byproduct, so it's less preferred



10. Use of CO_2 reduced products :

By reduction of CO_2 we get many value added chemical , Formaldehyde , methanol , formic acid , CO etc.

❑ Use of formaldehyde :

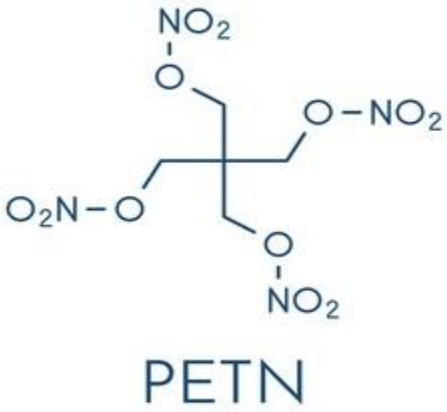


1. Production of Resins and Polymers

- Used to make **urea-formaldehyde**, **phenol-formaldehyde**, and **melamine-formaldehyde** resins.
- Applications: **Plywood, particle board, MDF**, laminates, adhesives, and insulation materials.

2. Chemical Intermediate

- Used in synthesis of various chemicals like:
  - **Pentaerythritol** (for explosives and paints)
  - **Hexamethylenetetramine (hexamine)** (solid fuel tablets, pharmaceuticals)

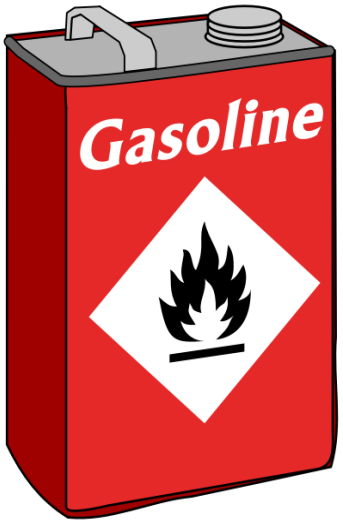


PETN

3. Preservative and Disinfectant

- **Formalin** (37% formaldehyde solution) is widely used:
  - To preserve biological specimens and tissues in laboratories and hospitals.
  - As a **disinfectant** in healthcare and animal housing.

❑ Use of Methanol :



1. Fuel and Energy

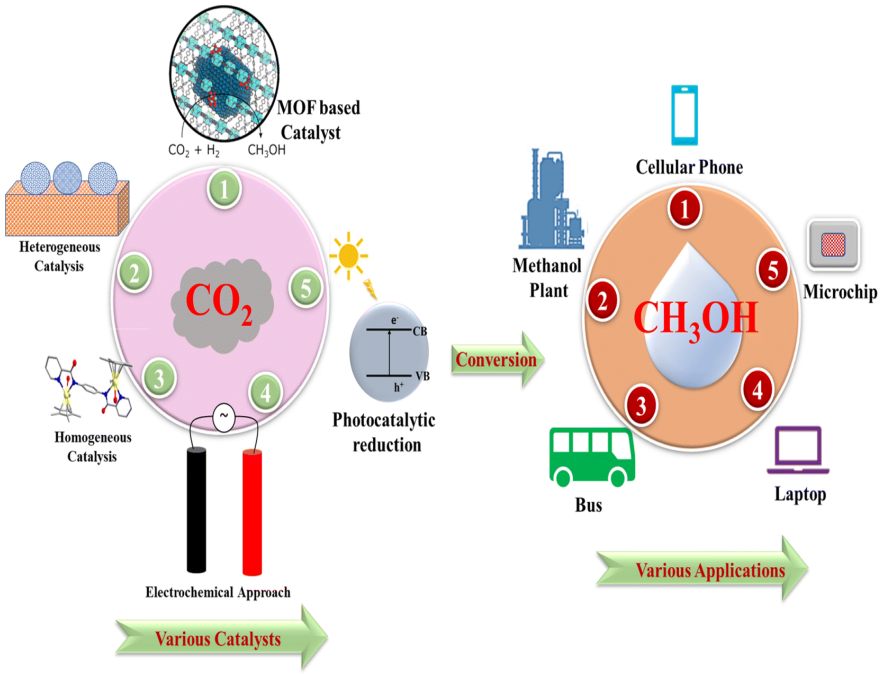
- **Alternative Fuel**: Used as a clean-burning fuel or blended with gasoline (e.g., M85 fuel – 85% methanol).
- **Biodiesel Production**: Acts as a reactant in the **transesterification** of fats/oils to produce biodiesel.
- **Fuel Cells**: Powers **Direct Methanol Fuel Cells (DMFCs)** for portable and off-grid energy systems.

2. Solvent and Antifreeze

- **Solvent**: For inks, resins, adhesives, and dyes due to its polarity and volatility.
- **Antifreeze Agent**: In windshield washer fluids, fuel line antifreeze, and de-icing solutions.

3. Emerging Green Chemistry Uses

- **CO_2 Utilization**: Methanol can be synthesized from $CO_2 + H_2$ — a key part of **carbon recycling** strategies.
- **Methanol Economy**: Proposed as a future energy carrier, replacing fossil fuels in energy storage and transportation



.

10. Future trends :

- **Smarter Catalyst Design**

Scientists will focus on designing better transition metal organometallic complexes with customized ligands to improve CO_2 activation and product selectivity, especially using metals like Ru, Fe, and Rh.

- **Dual-Function and Hybrid Catalysis**

Future catalysts may perform multiple steps (like CO_2 reduction and hydrogenation) in one system. Combining heat, light, or electricity (photo/electro/thermal catalysis) will become more common.

- **Mild and Green Reaction Conditions**

There's a push to make CO_2 conversion happen at lower temperatures and pressures, using eco-friendly solvents like water or ionic liquids and renewable hydrogen.

- **Heterogenized and Single-Atom Catalysts**

Organometallic complexes will be supported on solid materials (like graphene or MOFs) to make them easier to reuse, more stable, and efficient—possibly even as single atoms.

- **AI-Guided Catalyst Discovery**

Machine learning will help discover new catalysts faster by predicting which metal-ligand combinations work best for specific CO_2-based products like methanol or formic acid.

- **Integration into Clean Energy Devices**

Catalysts will be used in solar or electric-powered systems to turn captured CO_2 into useful chemicals, helping reduce carbon emissions and support green energy goals.

11. Conclusion :

The application of **transition metal organometallic complexes** in CO_2 conversion has emerged as a promising approach to address both **climate change** and the growing demand for sustainable chemical feedstocks. These complexes play a vital role in **activating the inert CO_2 molecule** and guiding its transformation into **value-added chemicals** such as **methanol, formic acid, formaldehyde, urea, and carbonates**. Through various **homogeneous and heterogeneous catalytic processes**—including **hydrogenation, electrochemical reduction, photocatalysis**, and **carbonylation**—organometallic catalysts offer high efficiency, selectivity, and tunability.

11. Reference :

1. Koytsoumpa, E.I.; Bergins, C.; Kakaras, E. The CO_2 economy: Review of CO_2 capture and reuse technologies. *J. Supercrit. Fluids* **2018**, *132*, 3–16. [Google Scholar] [CrossRef]
2. Divins, N.J.; Kordus, D.; Timoshenko, J.; Sinev, I.; Zegkinoglou, I.; Bergmann, A.; Chee, S.W.; Widrinna, S.; Karslioglu, O.; Mistry, H.; et al. Operando high-pressure investigation of size-controlled CuZn catalysts for the methanol synthesis reaction. *Nat. Commun.* **2021**, *12*, 1435. [Google Scholar] [CrossRef] [PubMed]
3. Zhang, J.; Guo, C.; Fang, S.; Zhao, X.; Li, L.; Jiang, H.; Liu, Z.; Fan, Z.; Xu, W.; Xiao, J.; et al. Accelerating electrochemical CO_2 reduction to multi-carbon products via asymmetric intermediate binding at confined nanointerfaces. *Nat. Commun.* **2023**, *14*, 1298. [Google Scholar] [CrossRef] [PubMed]
4. Yuan, L.; Hung, S.-F.; Tang, Z.-R.; Chen, H.M.; Xiong, Y.; Xu, Y.-J. Dynamic Evolution of Atomically Dispersed Cu Species for CO_2 Photoreduction to Solar Fuels. *ACS Catal.* **2019**, *9*, 4824–4833. [Google Scholar] [CrossRef]
5. Das, S.; Perez-Ramirez, J.; Gong, J.; Dewangan, N.; Hidajat, K.; Gates, B.C.; Kawi, S. Core-shell structured catalysts for thermocatalytic, photocatalytic, and electrocatalytic conversion of CO_2. *Chem. Soc. Rev.* **2020**, *49*, 2937–3004. [Google Scholar] [CrossRef] [PubMed]
6. Li, Y.; Zheng, S.; Liu, H.; Xiong, Q.; Yi, H.; Yang, H.; Mei, Z.; Zhao, Q.; Yin, Z.-W.; Huang, M.; et al. Sequential co-reduction of nitrate and carbon dioxide enables selective urea electrosynthesis. *Nat. Commun.* **2024**, *15*, 176. [Google Scholar] [CrossRef] [PubMed]
7. Li, Z.; Wu, W.; Wang, M.; Wang, Y.; Ma, X.; Luo, L.; Chen, Y.; Fan, K.; Pan, Y.; Li, H.; et al. Ambient-pressure hydrogenation of CO_2 into long-chain olefins. *Nat. Commun.* **2022**, *13*, 2396. [Google Scholar] [CrossRef] [PubMed]
8. Hung, S.F.; Xu, A.; Wang, X.; Li, F.; Hsu, S.H.; Li, Y.; Wicks, J.; Cervantes, E.G.; Rasouli, A.S.; Li, Y.C.; et al. A metal-supported single-atom catalytic site enables carbon dioxide hydrogenation. *Nat. Commun.* **2022**, *13*, 819. [Google Scholar] [CrossRef] [PubMed]
9. Liu, C.; Kang, J.; Huang, Z.Q.; Song, Y.H.; Xiao, Y.S.; Song, J.; He, J.X.; Chang, C.R.; Ge, H.Q.; Wang, Y.; et al. Gallium nitride catalyzed the direct hydrogenation of carbon dioxide to dimethyl ether as

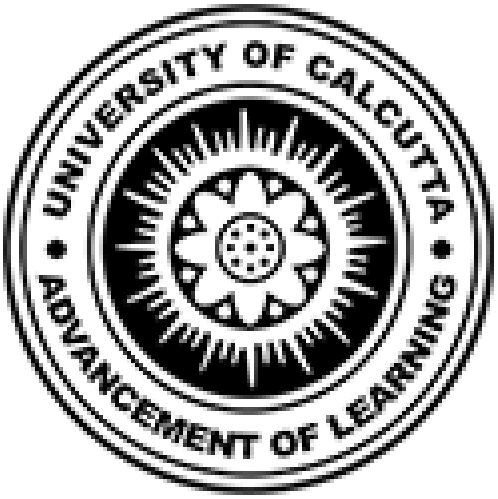
primary product. *Nat. Commun.* **2021**, *12*, 2305. [Google Scholar] [CrossRef]
10. Wang, K.; Zhu, Y.; Gu, M.; Hu, Z.; Chang, Y.-C.; Pao, C.-W.; Xu, Y.; Huang, X. A Derivative of $ZnIn_2S_4$ Nanosheet Supported Pd Boosts Selective CO_2 Hydrogenation. *Adv. Funct. Mater.* **2023**, *33*, 2215148. [Google Scholar] [CrossRef]
11. Melaet, G.; Ralston, W.T.; Li, C.-S.; Alayoglu, S.; An, K.; Musselwhite, N.; Kalkan, B.; Somorjai, G.A. Evidence of Highly Active Cobalt Oxide Catalyst for the Fischer–Tropsch Synthesis and CO_2 Hydrogenation. *J. Am. Chem. Soc.* **2014**, *136*, 2260–2263. [Google Scholar] [CrossRef] [PubMed]
12. Pastor-Perez, L.; Shah, M.; le Sache, E.; Reina, T.R. Improving Fe/Al_2O_3 Catalysts for the Reverse Water-Gas Shift Reaction: On the Effect of Cs as Activity/Selectivity Promoter. *Catalysts* **2018**, *8*, 608. [Google Scholar] [CrossRef]
13. Yang, H.; Zhang, C.; Gao, P.; Wang, H.; Li, X.; Zhong, L.; Wei, W.; Sun, Y. A review of the catalytic hydrogenation of carbon dioxide into value-added hydrocarbons. *Catal. Sci. Technol.* **2017**, *7*, 4580–4598. [Google Scholar] [CrossRef]
14. Liu, S.; Bian, K.; Yang, H.; Sun, M.; Nie, X.; Zhang, X.; Hou, S.; Zhang, G.; Song, C.; Guo, X. Methane transformation into light olefins using methanol as co-reactant over Mo/HZSM-5. *Chem. Eng. Sci.* **2024**, *283*, 119431. [Google Scholar] [CrossRef]
15. Wang, X.; Gao, X.; Song, F.; Wang, X.; Cao, G.; Zhang, J.; Han, Y.; Zhang, Q. Direct Oxidation of Methanol to Polyoxymethylene Dimethyl Ethers over FeMo@HZSM-5 Core–Shell Catalyst. *ACS Catal.* **2024**, *14*, 1093–1097. [Google Scholar] [CrossRef]
16. Ye, Y.; Abou-Hamad, E.; Gong, X.; Shoinkhorova, T.B.; Dokania, A.; Gascon, J.; Chowdhury, A.D. Mapping the Methanol-to-Gasoline Process Over Zeolite Beta. *Angew. Chem. Int. Edit.* **2023**, *62*, e202303124. [Google Scholar] [CrossRef] [PubMed]
17. Xu, D.; Wang, Y.; Ding, M.; Hong, X.; Liu, G.; Tsang, S.C.E. Advances in higher alcohol synthesis from CO_2 hydrogenation. *Chem* **2021**, *7*, 849–881. [Google Scholar] [CrossRef]
18. De, S.; Dokania, A.; Ramirez, A.; Gascon, J. Advances in the Design of Heterogeneous Catalysts and Thermocatalytic Processes for CO_2 Utilization. *ACS Catal.* **2020**, *10*, 14147–14185. [Google Scholar] [CrossRef]

19. Sancho-Sanz, I.; Korili, S.A.; Gil, A. Catalytic valorization of CO_2 by hydrogenation: Current status and future trends. *Catal. Rev. Sci. Eng.* **2021**, *65*, 698–772. [Google Scholar] [CrossRef]
20. Hussain, I.; Jalil, A.A.; Izan, S.M.; Azami, M.S.; Kidam, K.; Ainirazali, N.; Ripin, A. Thermodynamic and experimental explorations of CO_2 methanation over highly active metal-free fibrous silica-beta zeolite (FS@SiO2-BEA) of innovative morphology. *Chem. Eng. Sci.* **2021**, *229*, 116015. [Google Scholar

ACKNOWLEDGEMENT:

I hereby express my deep sense of gratitude to all personalities involved directly and indirectly in my dissertation project work. I would like to express my sincere thanks to all my respected professors for giving me this privilege of working under their guidance and completing this study. Last but not the least; I would like to express my earnest gratitude to all the faculty members of St. Paul's cathedral Mission College who have always been a source of guidance, inspiration and motivation.

UNIVERSITY OF CALCUTTA



INORGANIC NANOPARTICLES

B.Sc.

Chemistry (Honours) Semester - VI (Under CBCS) Examination, 2025

Course: CEMA DSE-B4 (Dissertation)

CU ROLL NO. _____

CU REGISTRATION NO. _____

_____

Signature of the Student

CONTENT: -

INORGANIC NANOPARTICLES

WHAT ARE NANOPARTICLES?

- Nanoparticles are tiny particles, typically between 1 and 100 nanometres in size, where a nanometre is one billionth of a meter. They are invisible to the naked eye and exhibit unique properties due to their small size and large surface area compared to bulk materials. These properties can include changes in colour, melting point, and chemical reactivity.

WHAT IS DIFFRENCE BETWEEN NANOPARTICLES AND MICROPARTICLES?

Nanoparticles and microparticles differ primarily in their size and properties.

- 1. *Size:* - Nanoparticles are typically defined as particles with a size range of 1 to 100 nanometres (nm).

  Microparticles, on the other hand, range from 1 micron (µm) to 1000 microns (1 mm).

- 2. *Surface Area:* - Due to their small size, nanoparticles have a much larger surface area to volume ratio compared to microparticles. This property can enhance their reactivity and interaction with biological systems.

- 3. Physical and Chemical Properties: - Nanoparticles often exhibit unique optical, electrical, and magnetic properties that differ from their bulk counterparts, which can be attributed to quantum effects.

  Microparticles generally retain the properties of the bulk material and do not exhibit the same level of unique behaviour as nanoparticles.

- 4. Applications: - Nanoparticles are widely used in fields such as medicine (drug delivery, imaging), electronics, and materials science due to their unique properties.

  Microparticles are commonly used in applications like drug formulation, cosmetics, and as carriers in various industrial processes.

***ABOUT GOLD AND TiO_2 NANOPARTICLES*: -**

A. GOLD: -

Gold nanoparticles (AuNPs) are tiny particles of gold ranging from 1 to 100 nanometres in size. Due to their unique physical, chemical, and optical properties, they have been widely studied and applied in fields such as medicine, electronics, and catalysis. Here's an overview:

Key Properties of Gold Nanoparticles:

- **Size-dependent colour:** AuNPs appear red, purple, or blue depending on their size and aggregation due to surface plasmon resonance.
- **Surface plasmon resonance (SPR):** Collective oscillation of electrons at the nanoparticle surface when excited by light, leading to strong absorption and scattering.
- **High surface area-to-volume ratio:** Enhances reactivity and interaction with biomolecules.
- **Biocompatibility:** Especially when properly functionalized, making them ideal for medical applications.

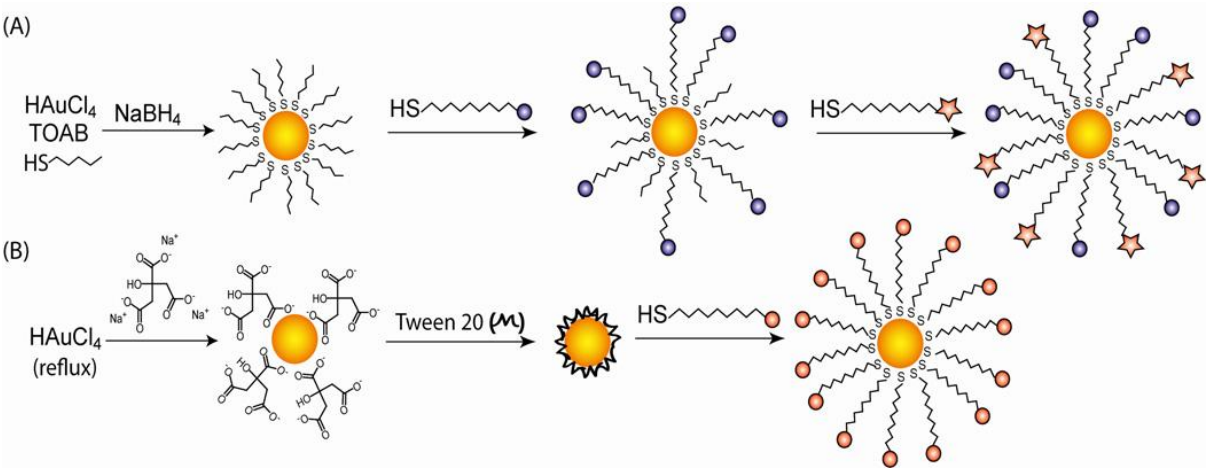
B. **TiO**: -
Titanium dioxide nanoparticles are extremely small particles (1–100 nm) of TiO_2, a white, inorganic compound widely used for its UV-blocking, photocatalytic, and pigment properties.

Key Properties of TiO_2

- **Size:** Typically, 5–100 nm
- **Crystal Forms:** Anatase (most active), Rutile, Brookite
- **Colour:** Bright white pigment

***SYNTHESIS OF GOLD NANOPARTICLES*: -**

Over recent decades, various solution-based methods have been developed to control the size, shape, and surface properties of gold nanoparticles (AuNPs). The Turkevich-Frens method (1951) uses citric acid to reduce and stabilize AuNPs in water, producing spherical particles (10–100 nm). Though widely used, these nanoparticles tend to aggregate during functionalization. To address this, surfactants or two-step modification strategies are used, but high dilution limits large-scale production. In 1994, the Brust-Schiffrin method introduced a biphasic system using TOAB and $NaBH_4$ to produce stable, organic-soluble AuNPs (1.5–5 nm) with low dispersity. These alkanethiol-stabilized particles are highly stable, can be redispersed without aggregation, and are ideal for further surface modification.



(A) Two-phase synthesis of AuNPs by reduction of $HAuCl_4$ in presence of alkanethiols as the stabilizing ligands and $NaBH_4$ as reducing agent. Place-exchange reaction for alkanethiol-protected AuNPs can then be performed with functionalized thiols.

(B) Citrate-stabilized AuNPs were prepared with $HAuCl_4$ solution under reflux conditions where citrate acts as both the stabilizing ligand and reducing agent. The ligand exchange of functionalized thiols for citrate-stabilized AuNPs was achieved by using Tween 20 as an intermediate.

***SYNTHESIS OF TiO_2 NANOPARTICLES*: -**

A. Hydrothermal Synthesis of TiO_2 Nanoparticles

🔬 **Materials Required:**

- Titanium (IV) isopropoxide (TTIP)
- Deionized water (DI water)
- Ethanol (or isopropanol)
- Hydrochloric acid (HCl) or nitric acid (HNO_3)
- Teflon-lined autoclave
- Magnetic stirrer & hot plate
- Centrifuge
- Beakers, pipettes, etc.

🧪 **Step-by-Step Procedure:**

Step 1: Prepare Precursor Solution

- In a beaker, **mix ethanol and DI water** in a 3:1 ratio.
- Under constant stirring, **slowly add TTIP** dropwise to the solution.
    - Example: Add **5 mL TTIP** to **75 mL ethanol + 25 mL DI water**.

Step 2: Adjust pH

- Add **a few drops of HCl (1M)** to lower the pH (around 1–2) to promote hydrolysis and control the particle size.

Step 3: Stir the Mixture

- Stir the mixture continuously for **30–60 minutes** to allow hydrolysis and partial condensation.

Step 4: Transfer to Autoclave

- Pour the homogeneous solution into a **Teflon-lined stainless-steel autoclave**.
- Seal the autoclave tightly.

Step 5: Heat Treatment

- Place the autoclave in an oven at **180 °C** for **12–24 hours**.
- This promotes crystal growth and nanoparticle formation.

Step 6: Cooling

- After the reaction, allow the autoclave to cool **naturally to room temperature**.

Step 7: Collect the Product

- Open the autoclave and transfer the contents to a beaker.
- Use a **centrifuge** to separate the solid TiO_2 particles from the liquid.
- Wash the precipitate several times with **DI water and ethanol**.

Step 8: Drying

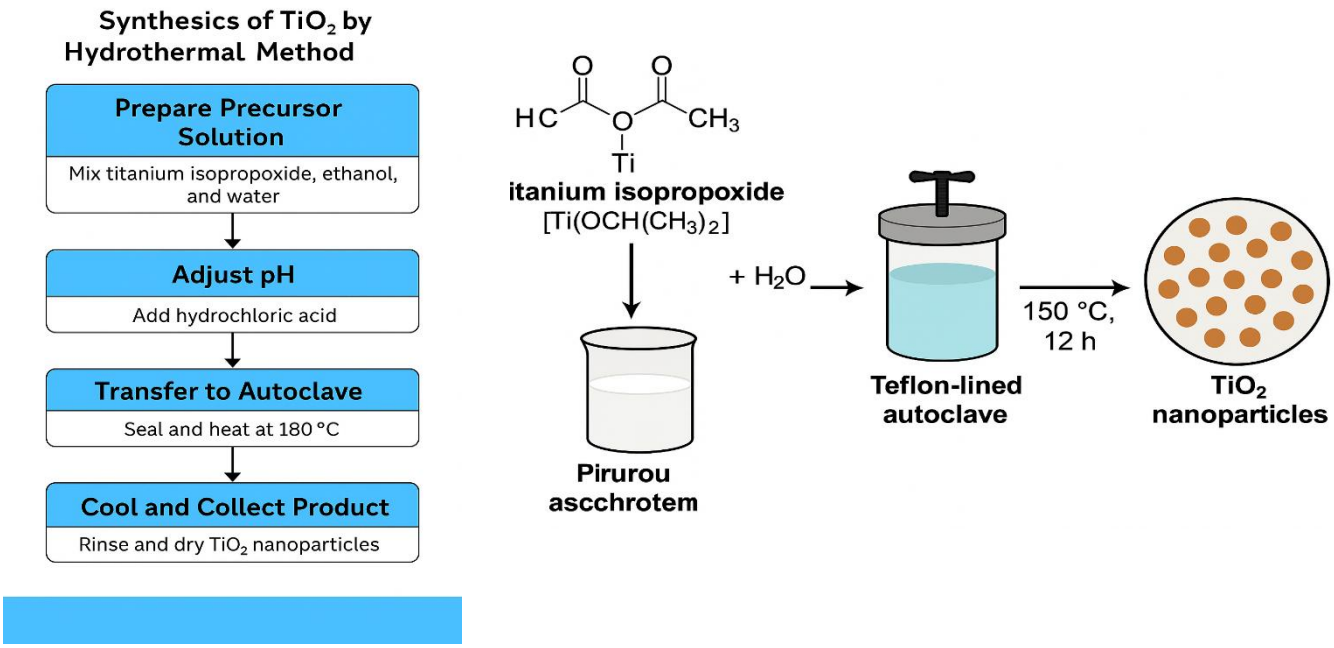
- Dry the washed TiO_2 particles in an oven at **60–80 °C** for 6–12 hours.

Step 9: (Optional) Calcination

- To improve crystallinity, calcine the dried powder in a muffle furnace at **450–600 °C for 2–4 hours**.

✅ **Final Product:**

- Fine, crystalline **TiO_2 nanoparticles**, usually in the **anatase phase**, suitable for photocatalytic or solar applications.



B. Green synthesis of TiO_2 nanoparticles using jasmine flower extract

Green synthesis is an eco-friendly and sustainable method that uses plant extracts as reducing and stabilizing agents to produce nanoparticles. Jasmine (Jasminum spp.) flowers are rich in bioactive compounds like flavonoids, alkaloids, terpenoids, and phenolics, which can reduce titanium precursors to form TiO_2 nanoparticles.

🧪 **Materials Required:**

- Fresh jasmine flowers
- Deionized (DI) water
- Titanium precursor (e.g., Titanium tetraisopropoxide – TTIP or Titanium dioxide – TiO_2 precursor)
- Beakers, magnetic stirrer
- Centrifuge
- Oven/furnace

Step-by-Step Synthesis Process:

1. Preparation of Jasmine Flower Extract:

- Collect **fresh jasmine flowers**, wash thoroughly with water.

- Boil **10–20 g of petals** in **100 mL of DI water** for 15–20 minutes.
- Cool the solution and filter through muslin cloth or Whatman filter paper.
- This extract contains the phytochemicals necessary for nanoparticle synthesis.

2. Preparation of Titanium Precursor Solution:

- Dilute **TTIP** in ethanol or isopropanol with constant stirring.
- Slowly add the **jasmine extract** to the TTIP solution dropwise while stirring.

3. Reaction and Formation of TiO_2 Nanoparticles:

- Stir the mixture for 2–4 hours at room temperature.
- A colour change or precipitation may indicate nanoparticle formation.
- The mixture may also be aged overnight for better yield.

4. Separation and Washing:

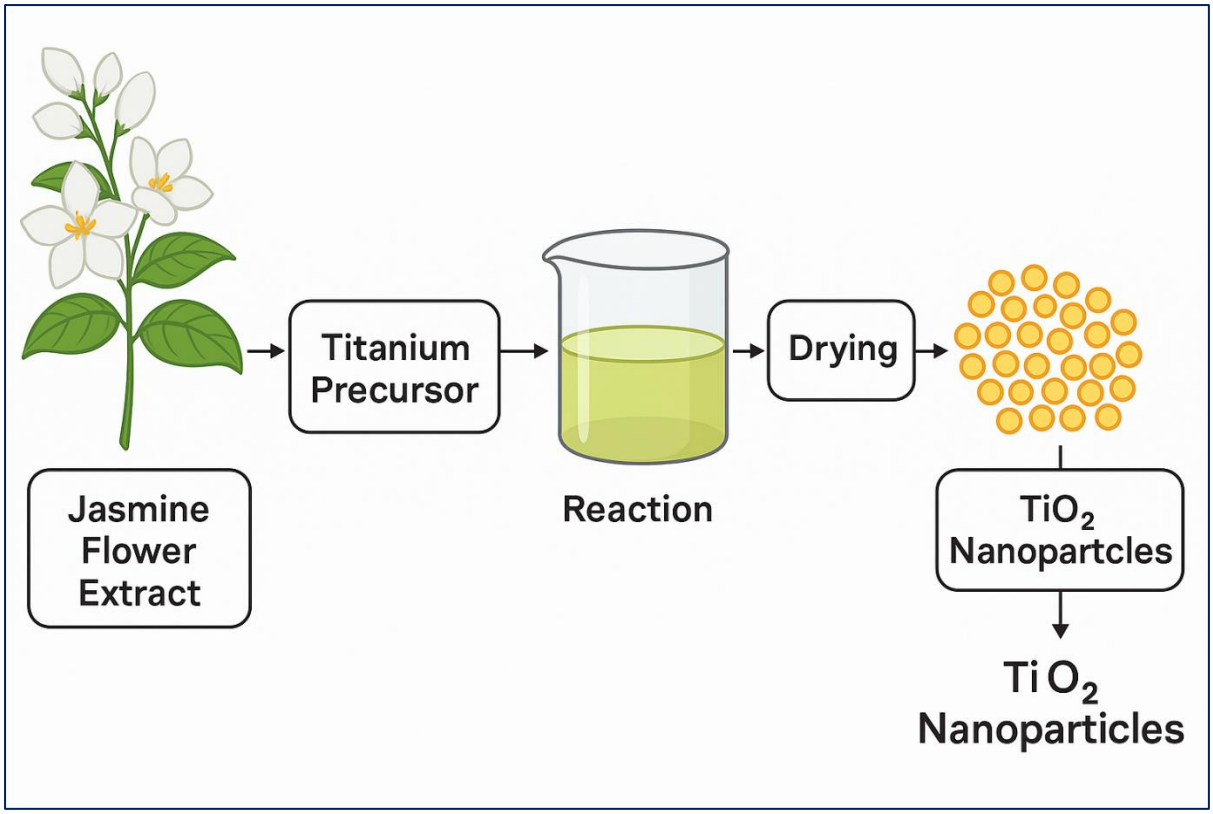
- Centrifuge the solution to collect the precipitated TiO_2 nanoparticles.
- Wash the precipitate 2–3 times with water and ethanol to remove impurities.

5. Drying and Calcination:

- Dry the product at **60–80 °C** for several hours.
- Optionally, **calcine** at **400–500 °C** to improve crystallinity and remove organic residues.

✅ **Final Product:**

TiO_2 nanoparticles stabilized by biomolecules from jasmine extract.



Applications of Gold Nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) are widely used due to their unique optical, chemical, and physical properties. Here are their key applications:

🔬 1. Biomedical Applications

- **Drug Delivery**: Targeted delivery of anticancer or antiviral drugs using AuNPs as carriers.
- **Diagnostics**: Used in rapid tests (e.g., lateral flow assays like COVID-19 test kits).
- **Imaging**: Serve as contrast agents in **CT scans**, **photoacoustic imaging**, and **electron microscopy**.
- **Cancer Therapy**:
    - **Photothermal therapy (PTT)**: Converts light to heat to kill cancer cells.
    - **Radiotherapy Enhancement**: Improves radiation absorption in tumors.

🧪 2. Sensing and Detection

- **Colorimetric sensors**: AuNPs change colour upon binding with specific molecules—used in toxin, DNA, or metal ion detection.
- **Surface-enhanced Raman scattering (SERS)**: Enhances signal sensitivity for trace analysis.

⚙️ 3. Catalysis

- AuNPs act as effective **catalysts** in:
    - CO oxidation
    - Hydrogenation reactions
    - Green chemical transformations

💊 4. Antimicrobial Agents

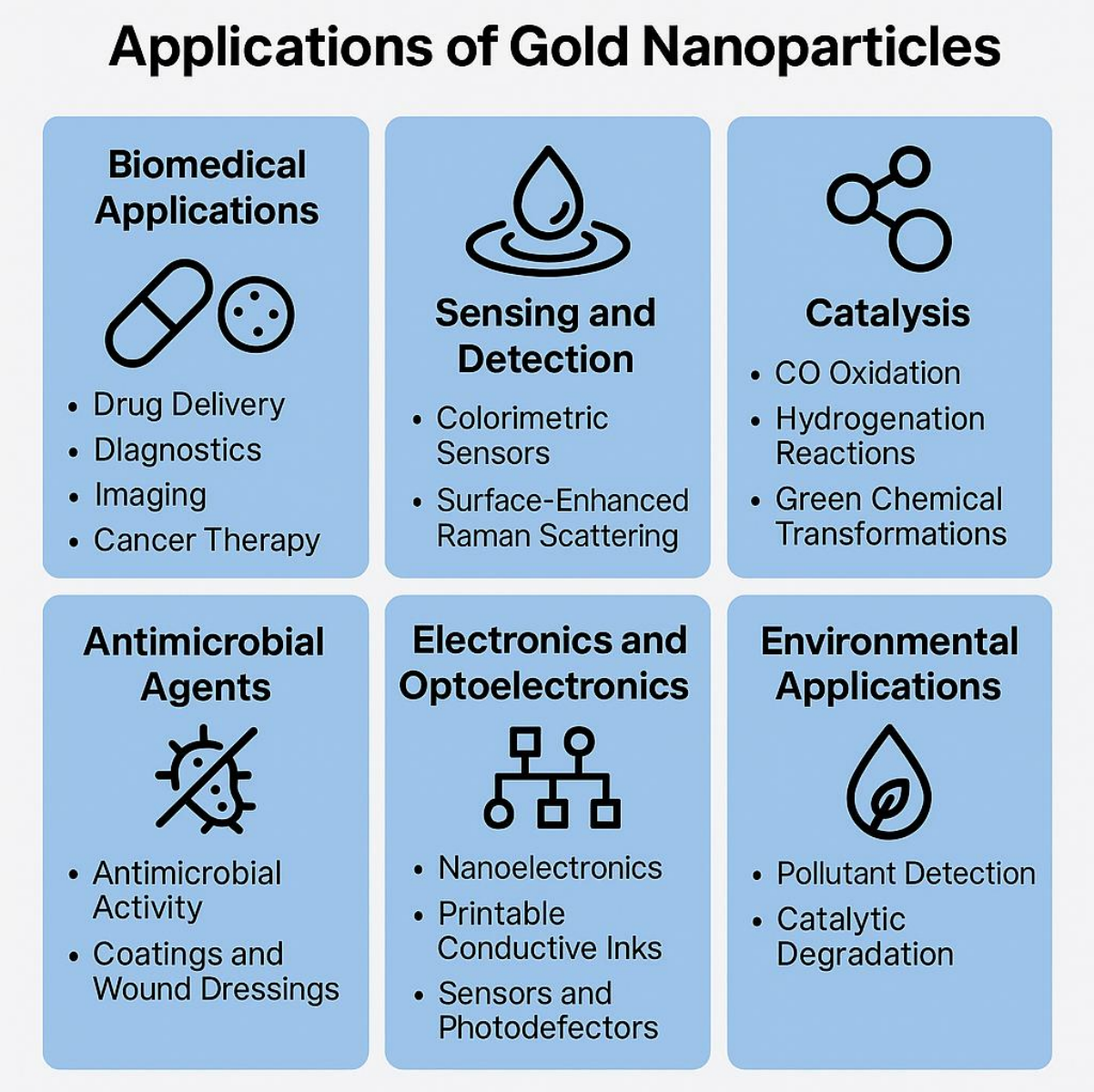
- Functionalized AuNPs show antimicrobial activity against bacteria and fungi.
- Incorporated into coatings or wound dressings.

💡 5. Electronics and Optoelectronics

- Used in:
    - Nanoelectronics
    - Printable conductive inks
    - Sensors and photodetectors
    - Transparent conductive films

📦 6. Environmental Applications

- Used for **pollutant detection** (e.g., heavy metals, pesticides).
- **Catalytic degradation** of organic contaminants in water treatment.



Applications of Titanium Dioxide (TiO_2) Nanoparticles

TiO_2 nanoparticles are widely used due to their **high photocatalytic activity, chemical stability**, and **non-toxicity**. Here are their key applications:

🌞 1. Photocatalysis

- **Water purification**: Degradation of organic pollutants, dyes, and bacteria in wastewater.
- **Air purification**: Breakdown of volatile organic compounds (VOCs) and NOx gases under UV light.
- **Self-cleaning surfaces**: Used in glass, tiles, and paints that degrade grime when exposed to sunlight.

🧪 2. Solar Energy

- **Dye-sensitized solar cells (DSSCs)**: TiO_2 acts as a semiconductor for electron transport in low-cost solar panels.

🧴 3. Cosmetics & Sunscreens

- Acts as a **UV blocker** due to strong UV absorption, protecting skin from harmful rays.
- Preferred for **non-toxic**, **non-irritating** sunscreen formulations.

🧬 4. Biomedical Applications

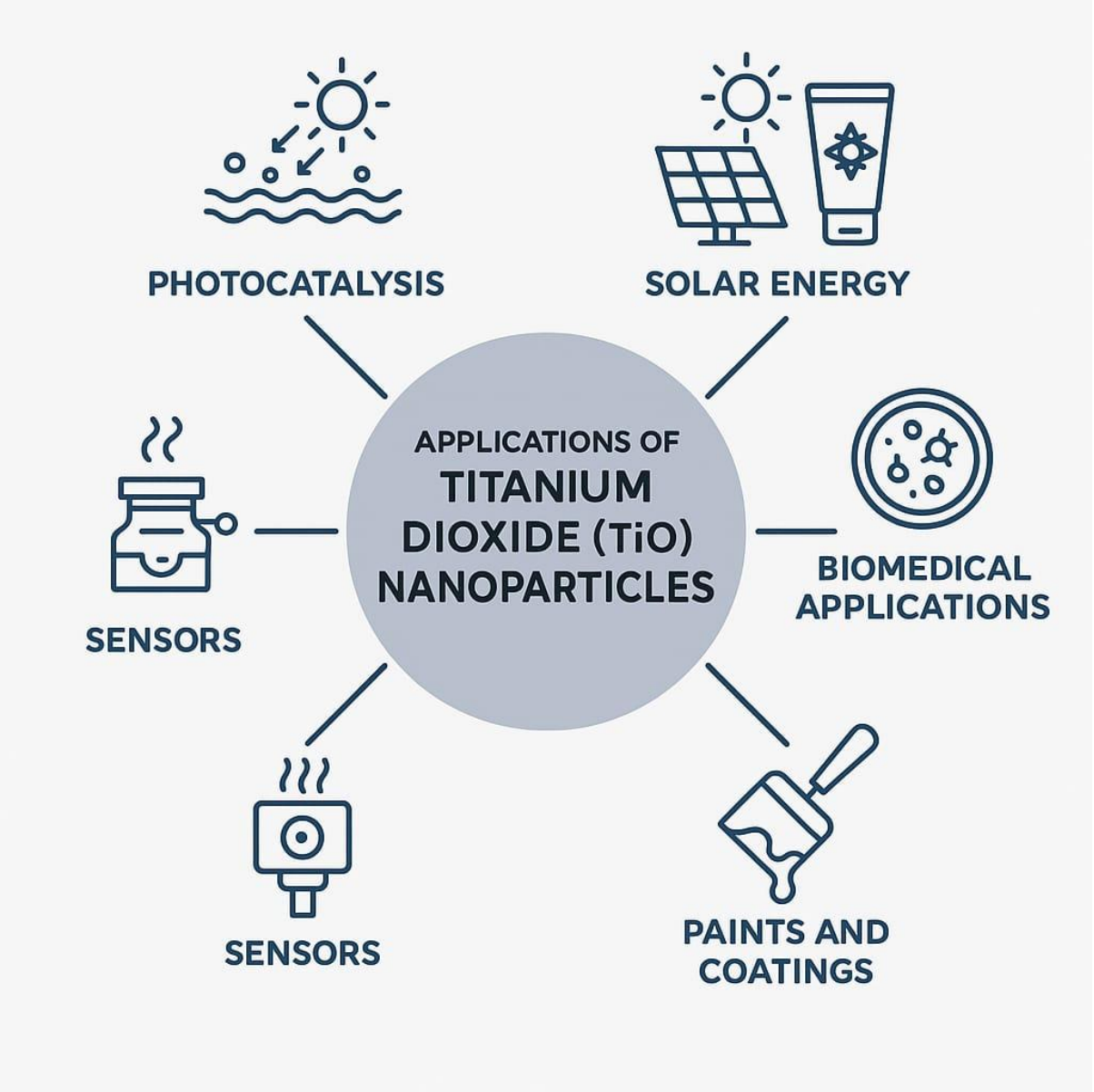
- **Drug delivery**: Used as carriers due to biocompatibility.
- **Antibacterial coatings**: Especially effective under UV light.
- **Biosensors**: Functionalized TiO_2 NPs detect specific biomolecules.

🧱 5. Paints and Coatings

- Enhances **whiteness**, **opacity**, and **UV resistance** in paints and coatings.
- Helps prevent degradation of materials caused by sunlight.

⚙️ 6. Sensors

- Used in **gas sensors** (e.g., for detecting CO, H_2, NO_2) due to high surface area and sensitivity.


PHOTOCATALYSIS
SOLAR ENERGY
APPLICATIONS OF
TITANIUM
DIOXIDE (TiO)
NANOPARTICLES
SENSORS
BIOMEDICAL
APPLICATIONS
SENSORS
PAINTS AND
COATINGS

Abstract

This dissertation explores the synthesis, properties, and applications of inorganic nanoparticles, with a primary focus on gold (AuNPs) and titanium dioxide (TiO_2) nanoparticles. Nanoparticles, defined as particles between 1–100 nm in size, exhibit distinct chemical and physical properties compared to their bulk counterparts due to their high surface area and quantum effects. The work begins by differentiating nanoparticles from microparticles in terms of size, surface area, and reactivity.

Two main types of nanoparticles are discussed:

Gold nanoparticles (AuNPs): Synthesized via Turkevich-Frens and Brust-Schiffrin methods, AuNPs are known for their surface plasmon resonance, biocompatibility, and catalytic abilities.

TiO_2 nanoparticles: Synthesized through hydrothermal and green synthesis (using jasmine flower extract), they are notable for photocatalytic activity and environmental stability.

The applications of both nanoparticles are reviewed extensively. Gold nanoparticles are used in biomedical imaging, drug delivery, cancer therapy, sensing, catalysis, and environmental remediation. TiO_2 nanoparticles find utility in water and air purification, solar energy devices, cosmetics, paints, and biosensing technologies.

This study emphasizes the interdisciplinary importance of nanotechnology in fields such as medicine, materials science, and environmental sustainability, offering insight into future innovations using inorganic nanoparticles.

Reference

- Gold nanoparticles. (n.d.). *Wikipedia*. Retrieved June 25, 2025, from https://en.wikipedia.org/wiki/Gold_nanoparticle

- Titanium dioxide. (n.d.). *Wikipedia*. Retrieved June 25, 2025, from https://en.wikipedia.org/wiki/Titanium_dioxide

- Turkevich method. (n.d.). *Wikipedia*. Retrieved June 25, 2025, from https://en.wikipedia.org/wiki/Turkevich_method

- Brust–Schiffrin method. (n.d.). *Wikipedia*. Retrieved June 25, 2025, from https://en.wikipedia.org/wiki/Brust%E2%80%93Schiffrin_method

- Khan, I., Saeed, K., & Khan, I. (2019). Nanoparticles: Properties, applications and toxicities. *Arabian Journal of Chemistry*, *12*(7), 908–931. https://doi.org/10.1016/j.arabjc.2017.05.011

- Ahmed, S., Saifullah, Ahmad, M., Swami, B. L., & Ikram, S. (2016). Green synthesis of silver nanoparticles using *Azadirachta indica* aqueous leaf extract. *Journal of Radiation Research and Applied Sciences*, *9*(1), 1–7. https://doi.org/10.1016/j.jrras.2015.06.006

- Wang, Z. L. (2000). Transmission electron microscopy of shape-controlled nanocrystals and their assemblies. *Journal of Physical Chemistry B, 104*(6), 1153–1175. https://doi.org/10.1021/jp993409c

Acknowledgment

This dissertation is more than just pages of research—it is a reflection of the many people who stood beside me, encouraged me, and shaped my academic journey.

- To **Dr. Jishnunil Chakraborty (Professor (Assistant) at St. Paul's Cathedral Mission College, Kolkata, India)**, thank you for being a steady compass. Your critical insights and patience helped turn scattered thoughts into focused work. I've learned more than just science under your mentorship—I've learned perseverance and precision.

To my **department**, thank you for fostering an environment where ideas were welcomed, questioned, and refined. The long discussions in hallways and late hours in the lab are memories I will carry forward.

To my **family**, no words will ever be enough. Thank you for believing in me, especially when I doubted myself. Your silent sacrifices and loud encouragement were the invisible threads holding everything together.

And to the quiet moments of doubt, discovery, and resilience—thank you too. They taught me the most.

This work is not mine alone. It belongs to everyone who walked with me, even if only for a while.

Signature of Mentor