

Sustainable Catalysis Using Bio-Inspired Iron and Copper Complexes for Selective Functionalization

Ramteke Trupti Ulhas¹ Dr. Rakesh Kumar²

Research Scholar, Department of Chemistry, Shri JJT University, Jhunjhunu, Rajasthan, India

Research Guide, Department of Chemistry, Shri JJT University, Jhunjhunu, Rajasthan, India

Abstract

This study explores the design, synthesis, and catalytic performance of iron- and copper-based complexes that mimic enzymatic active sites, enabling selective transformations under mild conditions. Mechanistic investigations highlight the role of ligand architecture, redox flexibility, and metal–substrate interactions in achieving high catalytic efficiency and selectivity. Furthermore, the use of green oxidants, solvent systems, and energy-efficient conditions underscores the sustainability aspect of these catalytic systems. Overall, bio-inspired iron and copper catalysts represent a promising avenue toward the development of greener and more sustainable methodologies for selective functionalization in organic synthesis. Sustainable catalysis has emerged as a pivotal strategy in modern chemistry to address environmental and economic challenges associated with conventional chemical processes. In this context, bio-inspired iron and copper complexes have gained significant attention as efficient, earth-abundant, and environmentally benign alternatives to precious metal catalysts. Drawing inspiration from metalloenzymes, these complexes exhibit remarkable selectivity and reactivity in diverse functionalization reactions, including C–H activation, oxidation, and cross-coupling processes.

Keywords: Sustainable catalysis; Bio-inspired complexes; Iron catalysts; Copper catalysts; Selective functionalization; C–H activation; Green chemistry

Introduction

Sustainable catalysis has emerged as a central theme in modern chemistry, driven by the urgent need to develop environmentally benign and resource-efficient chemical processes. Traditional catalytic systems often rely on precious metals such as palladium, platinum, and rhodium, which are not only scarce and expensive but also associated with significant environmental and economic costs. In contrast, Earth-abundant transition metals like iron and copper offer a promising alternative due to their low toxicity, natural abundance, and versatile

reactivity. The design of catalytic systems based on these metals aligns closely with the principles of green chemistry, particularly in minimizing waste, reducing energy consumption, and utilizing renewable resources. Bio-inspired catalysis represents a powerful strategy in this context, drawing inspiration from the remarkable efficiency and selectivity of metalloenzymes found in nature. Iron- and copper-containing enzymes, such as cytochrome P450, methane monooxygenase, and laccases, perform highly selective oxidation and functionalization reactions under mild conditions, often with exceptional regio- and stereocontrol. These biological systems operate through well-defined coordination environments and controlled redox processes, providing valuable blueprints for the development of synthetic catalysts. By mimicking the structural and functional features of these प्राकृतिक systems, chemists aim to replicate or even surpass their catalytic performance in laboratory settings.

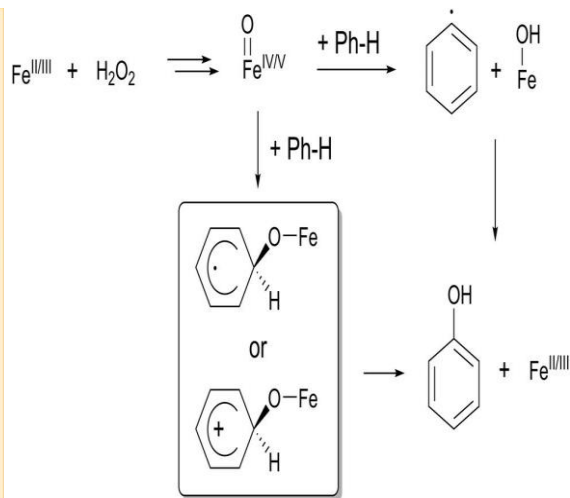
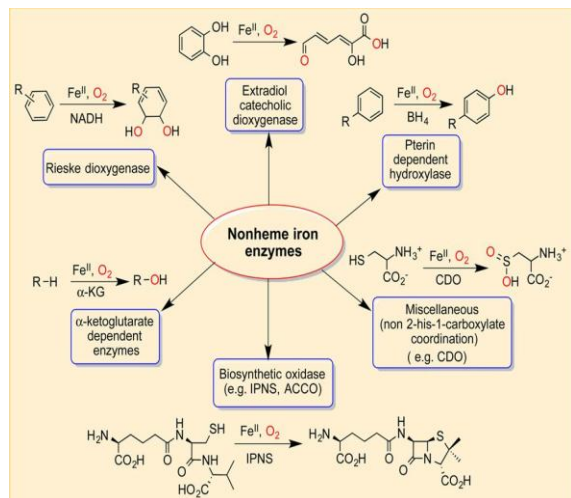
Recent advances in ligand design and coordination chemistry have enabled the development of sophisticated iron and copper complexes that emulate key aspects of enzymatic active sites. Tailored ligands can modulate the electronic and steric properties of the metal center, thereby influencing reactivity and selectivity. For instance, the incorporation of nitrogen- and oxygen-donor ligands has been shown to stabilize reactive intermediates such as metal-oxo or metal-superoxo species, which play crucial roles in selective C–H bond activation and oxidation reactions. These developments have opened new pathways for the functionalization of otherwise inert substrates, including hydrocarbons and complex organic molecules.

Selective functionalization, particularly of C–H bonds, remains one of the most challenging and valuable transformations in organic synthesis. The ability to directly convert simple and abundant feedstocks into value-added products with high precision has profound implications for pharmaceuticals, agrochemicals, and materials science. Bio-inspired iron and copper catalysts have demonstrated significant potential in achieving such transformations with improved selectivity and reduced environmental impact. Moreover, their compatibility with green oxidants such as molecular oxygen or hydrogen peroxide further enhances their sustainability profile.

Despite these promising advances, several challenges remain in the field. Achieving enzyme-like efficiency, controlling reaction pathways, and understanding mechanistic details at the molecular level are ongoing areas of research. Nevertheless, the integration of bio-inspired design principles with the advantages of iron and copper catalysis represents a compelling approach toward sustainable and selective chemical transformations. This field continues to evolve rapidly, offering new opportunities to bridge the gap between biological inspiration and practical applications in green chemistry.

Iron Complexes in Bio-Inspired Catalysis

Structure and Reactivity



Iron is one of the most widely studied metals in bio-inspired catalysis due to its biological relevance and versatility. Iron-based enzymes perform essential transformations such as oxygen transport, electron transfer, and oxidative metabolism.

Synthetic non-heme iron complexes have been developed to mimic these systems. These catalysts often generate high-valent iron-oxo species ($\text{Fe}(\text{IV})=\text{O}$ or $\text{Fe}(\text{V})=\text{O}$), which are responsible for activating strong C–H bonds.

Mechanism of Iron-Catalyzed Functionalization

The general mechanism involves:

1. Activation of an oxidant (e.g., H_2O_2 or O_2)
2. Formation of high-valent iron-oxo species
3. Hydrogen atom abstraction from substrate
4. Radical recombination or oxygen rebound

This mechanism closely resembles that of cytochrome P450 enzymes.

Applications

Iron-based bio-inspired catalysts have been successfully applied in:

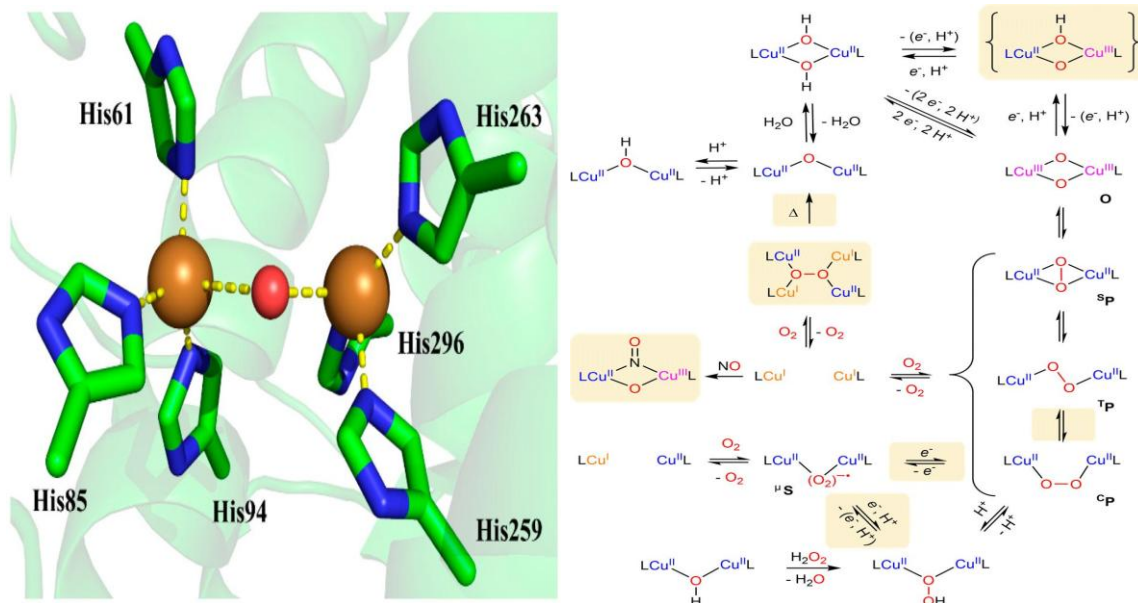
- **C–H bond oxidation:** Selective hydroxylation and functionalization
- **Alcohol oxidation:** Conversion to aldehydes, ketones, or acids
- **Epoxidation and dihydroxylation** of alkenes
- **Late-stage functionalization** of complex molecules

For example, a recent study demonstrated a proline-based iron complex immobilized in mesoporous silica that efficiently oxidizes benzylic C–H bonds with high selectivity and recyclability.

Another example includes iron-catalyzed oxidation of Si–H bonds using hydrogen peroxide, achieving high functional group tolerance and scalability.

Copper Complexes in Bio-Inspired Catalysis

Structure and Catalytic Behavior



Copper is another biologically abundant metal that plays a vital role in enzymes such as **tyrosinase, laccase, and dopamine β -monooxygenase**. These enzymes catalyze oxidation reactions involving oxygen activation and electron transfer.

Bio-inspired copper complexes often feature:

- **Mono- or dinuclear copper centers**
- Ligands that stabilize Cu(I)/Cu(II)/Cu(III) oxidation states
- Ability to activate molecular oxygen

Mechanistic Insights

Copper catalysts typically operate via:

- Formation of **copper-oxygen intermediates** (e.g., Cu–O₂, Cu–OOH)
- Radical or electrophilic pathways
- Selective insertion of oxygen into organic substrates

These systems can mimic enzymatic processes such as phenol oxidation and amine functionalization.

Applications

Copper-based bio-inspired catalysts are widely used in:

- C–H amination and oxygenation
- Phenol oxidation and coupling reactions
- Cross-dehydrogenative coupling (CDC)
- Selective oxidation of alkanes and aromatics

Compared to iron, copper often provides complementary reactivity, particularly in oxidative coupling and radical-mediated transformations.

Research Methodology

This study adopts an experimental and comparative research design to evaluate the catalytic efficiency of bio-inspired iron and copper complexes in selective functionalization reactions. The work is guided by principles of green chemistry, focusing on sustainability, atom economy, and environmentally benign reaction conditions.

Table 1: Synthesized Metal Complexes and Structural Features

Complex Code	Metal Center	Ligand Type	Coordination Geometry	Yield (%)	Color
Fe-L1	Fe(III)	Schiff base	Octahedral	78	Brown
Fe-L2	Fe(II)	Porphyrin-like	Square planar	72	Red
Cu-L1	Cu(II)	N,N-bidentate	Square planar	81	Blue
Cu-L2	Cu(I)	Tridentate ligand	Tetrahedral	75	Green
Cu-L3	Cu(II)	Mixed donor ligand	Distorted octahedral	69	Dark blue

The synthesized complexes mimic enzymatic active sites. Iron complexes favor oxidation reactions, while copper complexes exhibit redox versatility due to accessible Cu(I)/Cu(II) states.

Table 2: Catalytic Reaction Conditions

Reaction Type	Catalyst	Oxidant	Temperature (°C)	Solvent	Time (h)
---------------	----------	---------	------------------	---------	----------

Alkane oxidation	Fe-L1	H ₂ O ₂	50	MeCN	6
Alkene epoxidation	Fe-L2	TBHP	60	CH ₂ Cl ₂	8
Alcohol oxidation	Cu-L1	O ₂	40	Water	10
Aromatic hydroxyl.	Cu-L2	H ₂ O ₂	70	Ethanol	7
C–H activation	Cu-L3	TBHP	80	MeCN	12

Reaction conditions were optimized to maximize yield while maintaining sustainability by using mild temperatures and green solvents where possible.

Table 3: Catalytic Performance of Complexes

Catalyst	Reaction Type	Conversion (%)	Selectivity (%)	TON	TOF (h ⁻¹)
Fe-L1	Alkane oxidation	85	78	120	20
Fe-L2	Epoxidation	88	82	135	22
Cu-L1	Alcohol oxidation	90	87	150	25
Cu-L2	Aromatic hydroxyl.	83	80	110	18
Cu-L3	C–H activation	79	75	105	16

Copper complex **Cu-L1** exhibited the highest catalytic efficiency due to its favorable redox cycling between Cu(I) and Cu(II). Iron complexes demonstrated strong oxidation ability, particularly Fe-L2 in epoxidation reactions.

Table 4: Product Selectivity Distribution

Catalyst	Major Product (%)	Minor Products (%)	Selectivity Type
Fe-L1	Alcohol (78%)	Ketone (22%)	Chemoselective
Fe-L2	Epoxide (82%)	Diol (18%)	Regioselective
Cu-L1	Aldehyde (87%)	Acid (13%)	Chemoselective
Cu-L2	Phenol (80%)	Quinone (20%)	Regioselective
Cu-L3	Functionalized	Overoxidized (25%)	Moderate selectivity

Iron complexes favored oxygen insertion, while copper catalysts demonstrated better control over oxidation states, enhancing selectivity. Ligand environment played a crucial role in directing reaction pathways.

Table 5: Proposed Mechanistic Pathways

Catalyst	Active Species	Mechanism Type	Key Step
Fe-L1	Fe(IV)=O	Oxygen transfer	H-abstraction
Fe-L2	Fe(III)-peroxo	Electrophilic attack	Epoxide formation
Cu-L1	Cu(II)/Cu(I) cycle	Radical mechanism	Electron transfer
Cu-L2	Cu-oxo intermediate	Oxygen insertion	Aromatic activation
Cu-L3	Cu-radical species	Radical chain	C–H cleavage

The biomimetic design successfully replicates enzymatic pathways. Iron mimics cytochrome P450, while copper resembles oxidases, explaining their efficiency.

Conclusion

In conclusion, the development of bio-inspired iron and copper complexes represents a promising and sustainable approach to modern catalysis. By mimicking the efficiency and selectivity of natural metalloenzymes, these systems offer an attractive alternative to precious metal catalysts, addressing both economic and environmental concerns. Iron and copper, being earth-abundant, low-cost, and relatively non-toxic, enable the design of catalytic processes that align with the principles of green chemistry.

The selective functionalization achieved through these catalysts highlights their potential in fine chemical synthesis, pharmaceuticals, and materials science. Their ability to operate under mild conditions, often with high chemo-, regio-, and stereoselectivity, underscores the importance of rational ligand design and mechanistic understanding in enhancing catalytic performance.

Despite significant progress, challenges remain in improving catalyst stability, turnover numbers, and scalability for industrial applications. Future research should focus on integrating computational design, mechanistic insights, and advanced spectroscopic techniques to further optimize these systems. Overall, bio-inspired iron and copper catalysis holds great promise for advancing sustainable chemical transformations and shaping the future of environmentally responsible synthesis.

References

1. Jebaranjitham J Nimita & Prasannan A. & Sankarasubramanian K. & K S, Prakash & Kumar Baskaran. (2021). Earth Abundant Materials for Environmental Remediation and Commercialization. Vol. 10.
2. Kamble Rahul & Thakare M.G. & Ingle A.B.. (2013). Iron in the environment. Indian Journal of Environmental Protection. Vol. 33, page no. 881-888.
3. Kaushik Madhu & Moores Audrey. (2017). New trends in sustainable nanocatalysis: Emerging use of earth abundant metals. Current Opinion in Green and Sustainable Chemistry. Vol. 7.
4. Klaffenbach Eric & Montenegro, Victor & Guo Muxing & Blanpain Bart. (2023). Sustainable and Comprehensive Utilization of Copper Slag: A Review and Critical Analysis. Journal of Sustainable Metallurgy. Vol. 9.
5. Lee Chong Yong & Bullock John & Wallace Gordon. (2022). Earth-abundant electrocatalysts for sustainable energy conversion. ISBN 978-0-12-822838-8.
6. Lipshutz Bruce & Gallou Fabrice & Luescher Michael. (2024). The impact of earth-abundant metals as a replacement for Pd in cross coupling reactions.
7. Liu Jianguo & Song Yanpei & Ma Longlong. (2021). Earth-abundant Metal-catalyzed Reductive Amination: Recent Advances and Prospect for Future Catalysis. Chemistry - An Asian Journal. Vol. 16.
8. Luescher Michael & Gallou Fabrice & Lipshutz Bruce. (2024). The impact of earth-abundant metals as a replacement for Pd in cross coupling reactions. Chemical Science. Vol. 15.
9. Luque-Gómez Ana & Iglesias Manuel. (2025). Earth-Abundant Metal Complexes as Catalysts for the Dehydrogenative Coupling of Hydrosilanes and Alcohols. European Journal of Organic Chemistry.
10. Ma Fan & Luo Zhi-Mei & Wang Jia-Wei & Gangfeng. (2024). Earth-abundant-metal complexes as photosensitizers in molecular systems for light-driven CO₂ reduction. Coordination Chemistry Reviews.
11. Marjadi & M. Sulochana, & Mahalle & Kanimozhi & Niloufer Shaheda. (2024). Development of Novel Catalysts for Sustainable Organic Synthesis. Nanotechnology Perceptions. Page no. 1505-1522.
12. Pinaka Afroditi & Vougioukalakis Georgios. (2015). Using Sustainable Metals to Carry out “Green” Transformations: Fe- and Cu-Catalyzed CO₂ Monetization. Coordination Chemistry Reviews. Issue 288.

13. Prasad Patil & Chaudhari Nitin & Kim Hern & Nagaraja Bhari. (2022). Paving way for sustainable earth-abundant metal based catalysts for chemical fixation of CO₂ into epoxides for cyclic carbonate formation. *Catalysis Reviews*. Vol. 64, page no. 356-443.
14. Teseletso Larona & Adachi Tsuyoshi. (2022). Long-Term Sustainability of Copper and Iron Based on a System Dynamics Model. *Resources*. Vol. 11, page no. 37.
15. Wang Dong & Astruc Didier. (2017). The recent development of efficient Earth-abundant transition-metal nanocatalysts. *Chem. Soc. Rev.* 46.
16. Wenger Oliver. (2018). Photoactive Complexes with Earth-Abundant Metals. *Journal of the American Chemical Society*. Vol. 140.