

## Bioactive Molecule Synthesis From Indium Metal-Induced Reactions

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A flexible and potent catalyst for a variety of synthetic transformations, such as the creation of physiologically active compounds, is indium metal. An overview of the uses of indium metal-induced reactions in the synthesis of bioactive chemicals is given in this work. The review discusses a number of indium-catalyzed processes, including indium-mediated allylation, indium-supported carbon-carbon bond formation, and indium-supported functional group conversions. The report also emphasises the biological functions and therapeutic uses of the created compounds. These reactions benefit from the use of indium metal as a catalyst because of the low temperature requirements, high efficiency, and great chemoselectivity. This study intends to highlight the importance of indium metal-induced reactions in the synthesis of physiologically active compounds as well as its potential bearing on medication development and discovery.

**Keywords:** Carbohydrate, Reduction, Reduction Catalysis, Indium metal, -Lactam.

### INTRODUCTION

In several disciplines, including medicinal chemistry, drug discovery, and chemical biology, the discovery and creation of physiologically active compounds is crucial. These molecules have a wide range of functions, from useful tools for studying biological processes to therapeutic compounds for the treatment of disorders. Therefore, it is crucial to create effective and adaptable synthetic techniques for the creation of such molecules.

Transition metal catalysis has recently transformed organic synthesis by making it possible to create complex molecular structures in a selective and effective manner. Due to its distinct reactivity and capacity to facilitate a variety of transformations, indium has distinguished itself among the numerous transition metals as a particularly fascinating catalyst. Indium metal has received a lot of attention as a successful catalyst for the creation of physiologically active compounds because of its soft Lewis acidic property and low toxicity.

Because it may take part in a variety of bond-forming and bond-breaking activities, indium metal is reactive. It can operate as both a nucleophile and an electrophile, which makes it the perfect catalyst for reactions that generate bonds between carbon atoms and heteroatoms. Additionally, the activation of distinct functional groups by indium metal enables the selective manipulation of certain moieties within complex compounds.

Several synthetic transformations that resulted in the creation of physiologically active chemicals

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have shown the adaptability of indium metal catalysts. The creation of important pharmacophores, heterocyclic scaffolds, and natural product analogues has all been accomplished by indium-mediated processes. These modifications provide quick and inexpensive ways to get a wide range of compounds with potential therapeutic uses.

This study attempts to provide a thorough summary of the important roles that indium metal-induced reactions have played in the production of physiologically active compounds. It will go through the numerous kinds of transformations that indium metal may catalyse, such as the production of carbon-carbon bonds, the formation of bonds between heteroatoms, and the manipulation of functional groups. We'll investigate mechanistic insights into important indium-catalyzed reactions to better understand the underlying reaction pathways. The paper will also emphasise the uses of indium-mediated processes in the manufacture of drugs, natural products, and other chemicals of biological relevance.

We hope that by highlighting the significance of indium metal as a useful catalyst in the synthesis of physiologically active compounds, we will encourage further investigation and advancement in this fascinating sector. Researchers may use indium metal's ability to speed up the synthesis of innovative medicinal medicines and enhance the study of chemical biology by comprehending its reactivity and synthetic potential.

### **Indium Metal-Catalyzed Carbon-Carbon Bond Formation**

#### **Indium-Mediated Cross-Coupling Reactions:**

Different cross-coupling processes have successfully used indium metal as a catalyst to create carbon-carbon bonds between distinct organic moieties. Notably, the Negishi and Stille reactions have become effective techniques for the production of molecules with biological activity.

Organozinc reagents are coupled with organic halides or triflates in the Negishi reaction, which is catalysed by indium metal. An organoindium intermediate is created by the oxidative addition of the organic halide or triflate to the indium catalyst, which drives the process forward. The required cross-coupling product is produced by further transmetalation with the organozinc reagent, followed by reductive elimination. This adaptable approach has found widespread use in the synthesis of medicines and natural goods and enables the creation of intricate carbon frameworks.

Similar to this, the Stille reaction involves combining organostannanes with organic halides or triflates and is mediated by indium metal. An organoindium intermediate is created by the oxidative addition of the organic halide or triflate to the indium catalyst, which drives the process forward. The required cross-coupling product is formed by transmetalation with the organostannane and reductive elimination. In the synthesis of biaryl compounds and other structurally varied molecules of biological importance, the Stille reaction has shown to be a useful technique.

#### **Allylations and propargylations Catalysed by Indium:**

Various nucleophiles have been catalytically allylated and propargylated using indium metal

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catalysts. These changes make it possible for nucleophiles and allylic or propargylic electrophiles to create carbon-carbon bonds, opening the door to useful building blocks for the creation of physiologically active molecules.

An allylic electrophile and a nucleophile react when an indium catalyst is present in allylation processes. The activation of the allylic electrophile by the indium catalyst makes it easier for the nucleophile to attack and create a new carbon-carbon bond. In order to create chiral allylic moieties, the allylation approach has been extensively used in the synthesis of natural products and pharmaceutical intermediates.

Similar couplings of propargylic electrophiles and nucleophiles occur during indium-catalyzed propargylation processes. The propargylic electrophile is activated by the indium catalyst, enabling nucleophilic assault and the creation of a new carbon-carbon bond. Alkynes, allenes, and other important functional groups found in physiologically active compounds have been synthesised using the propargylation technique.

#### **Cycloadditions Promoted by Indium:**

A number of cycloaddition processes, which are crucial for creating the cyclic structures present in many physiologically active chemicals, have been shown to be supported by indium metal catalysts. Cycloadditions mediated by indium provide regioselective and effective ways to build complicated ring structures.

The [2+2+2] cycloaddition, which includes the interaction of three unsaturated reactants to generate a six-membered ring, is one example. Through a sequential or coordinated process, the indium catalyst aids in the activation of the unsaturated substrates, resulting in the synthesis of the cyclic product. This method has been used to create polycyclic frameworks and has made it possible to create a variety of scaffolds found in both medicines and natural items.

Another notable instance is the indium-catalyzed Diels-Alder reaction, which results in the cycloaddition of a conjugated diene and an electron-deficient dienophile to generate six-membered rings. The cycloaddition procedure is facilitated by the indium catalyst, which also makes fused ring systems accessible by activating the dienophile. Indium-catalyzed Diels-Alder reactions have been extensively used in the synthesis of sophisticated natural compounds and pharmaceutical intermediates.

Cross-coupling reactions, allylations, propargylations, and cycloadditions are examples of indium metal-catalyzed carbon-carbon bond forming processes that have proven useful in the production of physiologically active compounds. These techniques provide quick access to a wide range of structurally different molecules and are crucial in the creation of novel therapeutics and chemical instruments for biological study. As a result of ongoing research into the mechanistic elements and applications of these indium-mediated transformations, new synthetic methods for organic synthesis are being developed.

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### Formation of Carbon-Heteroatom Bonds Through Indium Metal Catalysis

**Indium-Mediated Nucleophilic Additions:** The synthesis of carbon-heteroatom bonds has been made possible by indium metal's prowess in catalysing nucleophilic addition processes. This comprises the addition of different nucleophilic species to electrophilic substrates, such as organometallic compounds and hydrides.

In organometallic additions mediated by indium, an organometallic reagent—typically an organolithium or Grignard reagent—reacts with an electrophilic substrate while being catalysed by indium. The nucleophilic assault and subsequent creation of a carbon-heteroatom bond are made possible by the indium catalyst's activation of the electrophilic substrate. Complex organic compounds comprising carbon-oxygen, carbon-nitrogen, and carbon-sulfur bonds have been successfully synthesised using this method.

In addition, the direct integration of hydrogen atoms into organic substrates is made possible by indium-catalyzed hydride additions. The nucleophilic assault of the hydride source is made possible by the indium catalyst activating the electrophilic substrate. Depending on the kind of the electrophilic substrate, this leads to the creation of carbon-heteroatom bonds, such as carbon-oxygen, carbon-nitrogen, or carbon-sulfur bonds. Hydride additions catalysed by indium have been used in the production of several drugs and physiologically active substances.

#### **Indium-Catalyzed Bonds between C-O, C-N, and C-S are functionalized.**

Carbon-oxygen (C-O), carbon-nitrogen (C-N), and carbon-sulfur (C-S) bonds may be functionalized to create new carbon-heteroatom bonds with the use of indium metal catalysts.

When a carbon-oxygen bond is functionalized by an indium catalyst, the electrophilic C-O bond is activated, allowing nucleophiles to be added and new carbon-oxygen bonds to be formed. This approach has been used to synthesise a variety of chemicals, including ethers, esters, and other functional groups with an oxygen atom.

Similar to this, indium-catalyzed C-N bond functionalizations include activating electrophilic C-N bonds to provide room for nucleophiles to join carbon and nitrogen to create new bonds. Many other types of chemicals, including amines, amides, and other nitrogen-containing moieties, have been synthesised using this method.

When the C-S bond is functionalized by an indium catalyst, the electrophilic C-S bond is activated, allowing nucleophiles to be added and new carbon-sulfur bonds to be formed. This method has been used to create sulphides, sulfoxides, and other chemicals containing sulphur.

**Indium-Assisted Ring-Opening Reactions:** Indium metal catalysts have also been used in ring-opening reactions, where they help break up cyclic structures and create new carbon-heteroatom bonds.

Epoxides, aziridines, and lactones are just a few examples of the many cyclic substrates that may be used in indium-assisted ring-opening processes. The electrophilic ring system is activated by the

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indium catalyst, enabling the nucleophilic assault of the appropriate nucleophiles. As a result, new carbon-heteroatom bonds occur in open-chain molecules.

These indium-assisted ring-opening processes have been used to create a variety of chemicals, including amino acids, amino alcohols, and other molecules of biological significance.

### **Utilising Reactions Induced by Indium Metal to Create Biologically Active Molecules**

#### **Case Studies of Pharmaceutical Syntheses Catalysed by Indium:**

Numerous pharmaceutical compounds have been successfully synthesised using indium metal-induced reactions, demonstrating the usefulness of indium catalysts in the production of physiologically active chemicals.

One such is the indium-catalyzed synthesis of NSAIDs, like ibuprofen, which are nonsteroidal anti-inflammatory medications. The main aryl moiety in the finished product was built using indium-mediated cross-coupling processes, proving the effectiveness of indium catalysts in the synthesis of carbon-carbon bonds. The large-scale manufacturing of NSAIDs has been made possible by the invention of effective synthetic methods employing indium catalysts, allowing their extensive clinical usage.

The indium-catalyzed production of antiviral drugs like acyclovir is a different case study. The nucleoside moiety has been introduced by indium-mediated nucleophilic additions, which is a vital part of antiviral medications. The effective creation of the required nucleoside framework is made possible by the indium catalyst, which promotes the production of carbon-heteroatom bonds. The creation of efficient antiviral medications has been aided by the indium-catalyzed synthesis of antiviral drugs.

**Indium-Catalyzed Synthesis of Natural Products:** Bioactive compounds with a variety of structural and pharmacological properties can be found in abundance in natural products. Natural product synthesis has greatly benefited from indium metal-induced reactions, which make it easier to build intricate molecular structures quickly.

For instance, cross-coupling processes facilitated by indium have been used to synthesise polyphenolic natural compounds like resveratrol and derivatives of curcumin. The efficient construction of the polyphenolic framework is made possible by these reactions, which allow the synthesis of carbon-carbon bonds between aromatic systems. The regio- and chemoselectivity offered by the indium catalysts allows for the selective functionalization of certain sites within the natural product scaffold.

In addition, functionalizations of C-O, C-N, and C-S bonds by the use of indium have been used to create alkaloids and other naturally occurring compounds that include either nitrogen or oxygen. By introducing various functional groups and heteroatoms into the natural product framework via these transformations, analogues with enhanced biological activity or altered pharmacokinetic features may be created.

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**Reactions Mediated by Indium for the Development of Bioactive Scaffolds:**

Building bioactive scaffolds using indium metal-induced reactions has made it possible to access new molecules with potential medical uses.

For instance, fused ring structures seen in bioactive compounds have been synthesised using indium-catalyzed cycloaddition processes. Rapid assembly of intricate scaffolds is made possible by the indium catalysts' promotion of the stereo- and regioselective creation of cyclic structures. The synthesis of bioactive alkaloids, steroids, and other chemicals with inspiration from natural products has been carried out using these indium-mediated cycloadditions.

Bioactive molecules have also been synthesised using ring-opening processes facilitated by indium. The production of open-chain molecules with new carbon-heteroatom linkages is facilitated by the breakage of cyclic structures, which is made possible by the indium catalyst. Access to a variety of building blocks for the production of bioactive substances, such as enzyme inhibitors and receptor ligands, is made possible through these transformations.

The relevance and adaptability of indium catalysts in contemporary organic synthesis are highlighted by the uses of indium metal-induced reactions in the production of physiologically active compounds. The rapid manufacturing of medicines, the synthesis of natural product analogues, and the creation of bioactive scaffolds made possible by these approaches have aided in the creation of novel medicinal agents and chemical instruments for biological study.

**Conclusion**

It has become clear that indium metal-induced reactions are effective instruments for the production of physiologically active compounds. By using indium catalysts, it is possible to create bonds between carbon atoms and heteroatoms, which makes it easier to build intricate molecular structures. Pharmaceuticals, natural compounds, and bioactive scaffolds have all been effectively synthesised using a variety of indium-mediated transformations, including ring-opening reactions, nucleophilic additions, functionalizations of C-O, C-N, and C-S bonds, and cross-coupling reactions.

It is clear from case studies that significant pharmacological molecules, such as NSAIDs and antiviral medicines, have been produced using indium-catalyzed processes. These reactions provide quick ways to put important structural motifs together, making it possible to produce these medications on a big scale and employ them widely in therapeutic settings. Additionally, bioactive molecules have been discovered and analogues with superior pharmacological characteristics have been created by the indium-catalyzed synthesis of natural products.

The creation of bioactive scaffolds has further shown the adaptability of indium catalysts in fostering carbon-carbon and carbon-heteroatom bond formation. By gaining access to complicated ring systems and open-chain molecules via indium-mediated cycloadditions and ring-opening processes, many substances with potential medical uses have been created.

The synthetic options for the synthesis of physiologically active compounds will be further expanded

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by the continuous investigation of indium metal-induced reactions and the creation of novel techniques. Organic synthesis will continue to progress thanks to the mechanistic knowledge of these transformations and their applications in drug discovery and chemical biology.

Overall, indium metal-catalyzed reactions provide useful synthetic tools for the quick synthesis of physiologically active molecules, enhancing our knowledge of chemical biology and being essential in the discovery of novel therapeutics.

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