

**DEVELOPMENT OF NOVEL METAL AND NON-METAL
CATALYSTS FOR THE SUSTAINABLE SYNTHESIS OF
BIS(INDOLYL)METHANES, C-3 ALKYLATED OXINDOLES,
AND BENZOIC ACIDS**

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**Development of novel metal and non-metal catalysts
for the sustainable synthesis of bis(indolyl)methanes,
C-3 alkylated oxindoles, and benzoic acids**

by

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Department of Chemistry

Submitted

In fulfilment of the requirements of the degree of Doctor of

Philosophy



Indian Institute of Technology Delhi

February 2024

Dedicated

to

My Parents and Teachers

CERTIFICATE

This is to certify that the thesis entitled “*Development of novel metal and non-metal catalysts for the sustainable synthesis of bisindolyl methanes, C-3 alkylated oxindoles, and benzoic acids*” being submitted by Ms. **Parul Saini** to *Indian Institute of Technology Delhi*, for the award of the degree of **Doctor of Philosophy**, is a record of bonafide research work carried out by her. Ms. **Parul Saini** has worked under my supervision and guidance and has fulfilled all the requirements for the submission of a Ph.D. thesis, which to my knowledge has reached the requisite standard and is worthy of consideration for the award of Ph.D. degree.

The work embodied in this thesis has not been submitted, in part or full, to other university or institute for the award of any degree or diploma.

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ABSTRACT

The thesis entitled "*Development of novel metal and non-metal catalysts for the sustainable synthesis of bisindolyl methanes, C-3 alkylated oxindoles, and benzoic acids*" presents the results obtained from the research work carried out on the development, characterization and application of novel metal and non-metal catalysts as catalysts for the oxidation and oxidative coupling reactions to synthesis value-added chemicals. The accompanied research work has been divided into seven chapters.

Chapter 1 This chapter provides the introduction to the work described in this thesis which centers around the recent trend in catalysis, and focuses on finding alternatives to traditional catalysts based on precious metals and toxic elements especially by adopting greener methodologies. The recent research aims to utilize more earth-abundant catalysts based on first-row transition metals and p-block elements to promote sustainability. This is followed by the current research on using water as a green and sustainable solvent for oxidation and oxidative coupling reactions. A brief discussion of the literature about earth-abundant transition metal catalysts for sustainable catalysis follows this.

The chapter ends with the scope of the present of work carried out and reported in the thesis.

Chapter 2 describes the general experimental procedures adopted in the synthesis of new compounds and details of characterization techniques utilized. Specific synthetic details of the starting materials described in the thesis are also presented.

Chapter 3 describes the oxidative coupling of benzylamines with indole to synthesis bis(indolyl)methanes (BIMs) in the aqueous medium. A water-soluble, inexpensive

cobalt complex was used as the catalyst. Cobalt being an earth-abundant metal and atmospheric air being the most affordable and safest oxidant, this method has considerable scope in the synthesis of BIMs.

Chapter 4 describes the development of a new air-stable phosphine-free 8-AQ (8-aminoquinoline) based Mn(I) carbonyl complex as the catalyst for the C(α)-alkylation of oxindoles with alcohols. The Mn complex [(8-AQ)Mn(CO)₃Br] works effectively as a catalyst for the α -alkylation of oxindoles by both secondary as well as primary alcohols. A diverse array of aryl, cyclic and acyclic aliphatic secondary alcohols and primary alcohols are tolerant to this new catalyst for the C(α)-alkylation of oxindoles.

Chapter 5 describes an efficient and metal-free method for synthesizing derivatives of 3,3-bis(indolyl)propanoates and bis(indolyl)propanones in a water medium. This protocol offers an excellent way to utilize water as an inexpensive and green solvent. In this study, molecular iodine has been used as a metal-free catalyst. In addition to substrates scope, detailed mechanistic studies have also been carried out to find out the possible reaction pathway.

Chapter 6 deals with the an efficient and metal-free methodology for the oxidation of benzyl halides to benzoic acids. This method involves using an inexpensive green oxidant (TBHP) in an aqueous basic medium. This protocol offers an excellent way to avoid added catalysts and involves the use of an in situ generated halide ion as the catalyst. It is also the first report on the oxidation of benzyl iodides to benzoic acids. The substrate scope showed the applicability of this metal free, sustainable and economical oxidation method.

Chapter 7 gives the overall conclusions of the entire work carried out in the present study.

सारांश

शोध प्रबंध जिसका शीर्षक है "*बिसिंदोलाइल मेथेन, सी-3 अल्किलेटेड ऑक्सिंडोल्स, और बेंजोइक एसिड के सतत सिंथेसिस के लिए नई धातु और गैर-धातु उत्प्रेरक का विकास*" के शीर्षक के अंतर्गत प्रस्तुत किया जाता है, जिसमें नए धातु और गैर-धातु उत्प्रेरक के विकास, विशेषतः ऑक्सीकरण और ऑक्सीडेटिव युग्मन अभिक्रियाओं के लिए उत्प्रेरक के रूप में, मूल्य-जोड़ित रासायनिक पदार्थों की संश्लेषण के लिए प्राप्त परिणामों का प्रस्तुतीकरण और उपयोग प्रस्तुत किया गया है। साथ ही, इस शोध कार्य को सात अध्यायों में विभाजित किया गया है।

अध्याय 1 यह अध्याय इस शोध प्रबंध में वर्णित कार्य का परिचय प्रदान करता है जो उत्प्रेरण में हालिया प्रवृत्ति पर केंद्रित है, और विशेष रूप से हरित पद्धतियों को अपनाकर कीमती धातुओं और विषाक्त तत्वों पर आधारित पारंपरिक उत्प्रेरक के विकल्प खोजने पर केंद्रित है। यह शोध पहली पंक्ति के परिवर्तन धातुओं और पी-ब्लॉक तत्वों पर आधारित ज़मीन-संशोधकों का और अधिक उपयोग करने का उद्देश्य रखता है, जो सततता को प्रोत्साहित करने के लिए हैं। इसके बाद, जल का हरित और सतत द्रावक के रूप में ऑक्सीकरण और ऑक्सीडेटिव युग्मन अभिक्रियाओं के लिए उपयोग करने के बारे में वर्तमान शोध का विवरण है। हरित प्रारंभिक पंक्ति के संशोधन के बारे में साहित्यिक चर्चा की संक्षेप रूप में चर्चा की गई है, जो सतत प्रायोगिकता के लिए धरती के संपूर्ण तात्वों पर आधारित है।

इस अध्याय का अंत शोध प्रबंध में किए गए और रिपोर्ट किए गए वर्तमान के कार्य की व्यापकता के साथ समाप्त होता है।

अध्याय 2 में नए यौगिकों के संशोधन में अपनाई गई सामान्य प्रयोगिक प्रक्रियाओं का वर्णन और उपयोग की गई विशेष विशेषज्ञता तकनीकों के विवरण किए गए हैं। शोध प्रबंध में वर्णित प्रारंभिक सामग्रियों के विशेष संशोधन विवरण भी प्रस्तुत हैं।

अध्याय 3 में पानी माध्यम में बेंजीलएमीनों के ऑक्सिडेटिव युग्मन का विवरण किया गया है, जिससे बिस(इंडोलील)मेथेन (BIMs) का संशोधन किया गया। एक पानी-विलिन और सस्ता कोबाल्ट संयोजक को उत्प्रेरक के रूप में उपयोग किया गया। कोबाल्ट एक धरती-प्रचुर मेटल होता है और वायुमंडलीय हवा सबसे सस्ता और सबसे सुरक्षित ऑक्सीकरणकर्ता होता है, इस तरीके से BIMs के संशोधन में विचार्य सीमा होती है।

अध्याय 4 में 8-AQ (8-आमिनोकिनोलिन) पर आधारित एक नई हवा-स्थिर फॉस्फाइन-मुक्त Mn(II) कार्बोनिल संयोजक के विकास का वर्णन किया गया है, जो उत्प्रेरक के रूप में उपयोग होता है, जिसका उपयोग एल्कोहल के साथ ऑक्सिडोल्स के C(α)-अल्किलेशन के लिए किया गया है। Mn संयोजक [(8-AQ)Mn(CO)₃Br] ऑक्सिडोल्स के α-अल्किलेशन के लिए उत्प्रेरक के रूप में प्रभावी रूप से काम करता है, सेकेंडरी और प्राइमरी एल्कोहल दोनों द्वारा ऑक्सिडोल्स के C(α)-अल्किलेशन के लिए। इस नए उत्प्रेरक के लिए आरिल, साइक्लिक, और असाइक्लिक या लिफ्रैटिक सेकेंडरी एल्कोहल और प्राइमरी एल्कोहल के विभिन्न विविध सरणी को इस्तेमाल किया जा सकता है।

अध्याय 5 में पानी माध्यम में 3,3-बिस(इंडोलिल)प्रोपैनोएट्स और बिस(इंडोलिल)प्रोपैनोंस के परिवर्तनों की शोध प्रबंध के लिए एक प्रभावी और धातु-मुक्त तरीका का वर्णन किया गया है। इस प्रोटोकॉल में पानी को एक सस्ता और हरित द्रावक के रूप में उपयोग करने का एक उत्कृष्ट तरीका प्रस्तुत किया गया है। इस अध्ययन में, धातु-मुक्त कैटलिस्ट के रूप में आयोडीन का उपयोग किया गया है। सबसे सामग्री की व्यापकता के अलावा, संभावित प्रतिक्रिया मार्ग की खोज के लिए विस्तार से यांत्रिक अध्ययन भी किए गए हैं।

अध्याय 6 में बेंजील हैलाइड को बेंजोयक अम्लों में ऑक्सीकरण के लिए एक प्रभावी और धातु-मुक्त विधि को विवेचित किया गया है। इस तरीके में पानी के बेसिक माध्यम में सस्ते हरित ऑक्सीकरणकर्ता (TBHP) का उपयोग करने की शामिल है। इस प्रोटोकॉल में सहायक कैटलिस्ट का उपयोग और किया गया है और कैटलिस्ट के रूप में उत्पन्न होने वाले हैलाइड आयन का उपयोग करता है। यह बेंजील आयोडाइड्स को

बेंजोयक अम्लों में ऑक्सीकरण करने की पहली रिपोर्ट भी है। सबसे सामग्री की व्यापकता ने इस धातु-मुक्त, हरित, और आर्थिक ऑक्सीकरण विधि के लागू होने की साबित की।

अध्याय 7 प्रस्तुत अध्ययन में किए गए पूरे काम की समग्र निष्कर्षण प्रस्तुत करता है।

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List of Abbreviations Used

Anal.	Analysis
<i>i</i> Pr	Isopropyl
Calcd.	Calculated
Cb	Cyclobutadiene
Me	Methyl
Et	Ethyl
Ph	Phenyl
Mp	Melting point
RT	Room Temperature
h	Hour(s)
min	Minutes
THF	Tetrahydrofuran
UV	Ultraviolet Spectroscopy
TLC	Thin Layer Chromatography
NMR	Nuclear Magnetic Resonance Spectroscopy
HRMS	High Resolution Mass Spectroscopy
PyO	Pyridine- <i>N</i> -oxide
NOESY	Nuclear Overhauser effect spectroscopy
BHT	Butylated hydroxytoluene
TEMPO	(2, 2, 6, 6-tetramethylpiperidin-1-yl)oxyl
TMEDA	Tetramethylethylenediamine
TDG	Transient directing group

DMSO	Dimethyl sulfoxide
SCXRD	Single crystal X-ray diffraction
DCM	Dichloromethane
DMF	<i>N, N</i> -dimethyl formamide
Aq.	Aqueous
DCE	1, 2-dichloroethane
TBHP	<i>tert</i> -Butyl hydroperoxide
TBPB	<i>tert</i> -Butyl peroxybenzoate
GC-MS	Gas Chromatography Mass Spectrometry