STEREOSELECTIVE SYNTHESIS OF AXIALLY CHIRAL (HETERO)BIARYLS, BRIDGED ISOCHROMANS AND AMINO INDANONES

BHUVNESH SINGH

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY DELHI
APRIL 2025

Stereoselective Synthesis of Axially Chiral (Hetero)Biaryls, Bridged Isochromans and Amino Indanones

By

Bhuvnesh Singh

Department of Chemistry

Submitted

In fulfillment of requirements of degree of Doctor of Philosophy to the

Indian Institute of Technology, Delhi

April 2025

This Ph.D. thesis is dedicated to my

Mom & Dad

Special gratitude to my parents for their

unconditional love, being my best friends and

inspiration.

CERTIFICATE

This is to certify that the thesis entitled, **"Stereoselective Synthesis of Axially Chiral (Hetero)Biaryls, Bridged Isochromans and Amino Indanones"**, being submitted by **Mr. Bhuvnesh Singh** to the ***Indian Institute of Technology Delhi*** for the award of the degree of **Doctor of Philosophy** in Chemistry is a record of bonafide research work carried out by him. **Mr. Bhuvnesh Singh** worked under my guidance and supervision and has fulfilled the requirements for the submission of a Ph.D. thesis, which to my knowledge has reached the requisite standard.

The results illustrated and incorporated in this dissertation have not been submitted in part or full to any other University or Institute for the award of any degree or diploma.

Prof. Ravi P. Singh

Research Supervisor,

Department of Chemistry

Indian Institute of Technology Delhi

Hauz Khas, New Delhi-110016, India.

Acknowledgments

I extend my heartfelt gratitude to all those who have contributed to the completion of this doctoral dissertation. First and foremost, I want to thank my supervisor ***Prof. Ravi P. Singh*** *without his enthusiasm, encouragement, support, and continuous optimism, this thesis would hardly have been completed. I am also very grateful to him for his scientific advice and knowledge and many insightful discussions and suggestions. He showed me different dimensions to approach a research problem and the need to be persistent to accomplish any goal. His advice on both research as well as on my career has been invaluable. I also must thank the members of my SRC committee,* ***Prof. A. J. Elias****,* ***Prof. V. Haridas****, and* ***Prof. Anurag S. Rathore*** *for their valuable suggestions and advice in general. I also thank all the past and the present Head of the Department of Chemistry, for the academic support and the facilities provided to carry out my research work. I would also like to thank* ***Prof. A. J. Elias*** *(Chairman, DRC) for streamlining curricular formalities. I would like to express my special gratitude towards* ***Prof. V. Haridas****, for his timely encouragement, valuable suggestions and support. I gratefully acknowledge all the faculty members and staff for providing the necessary facilities to pursue my research activities. I would also like to thank* ***Prof. Neetu Singh****, for her kind and generous nature, constant support, and encouragement. I would also like to thank MHRD-India, India, for providing the research fellowship that allowed me to undertake this research program. I would also like to greatly acknowledge* ***Prof. S. Nagendran****, coordinator of the X-ray facility, for providing me an opportunity to learn and operate the single crystal X-ray diffractometer. I would like to thank Dr. Pritam, Dr. Soumyadip, Dr. Vivek, and Dr. Prakash for helping me to learn and solve the X-ray Crystal data. I would like to extend my sincere thanks to all the teachers of the chemistry department for their support whenever it was required.*

A supportive and healthy environment is crucial for staying and surviving in a working place. The foundation stone of this group was laid down by my senior lab mates Dr. Amjad Ali, Dr. Krishna Kumar, Dr. Soumyadeep Hore and Dr Sanjay Singh. I would like to thank them for not only creating a cordial working environment in the lab but also for timely guidance and enduring support in continuing and completing my research projects. I feel very lucky to have such seniors in my life and I express my special gratitude to them. I would like to thank Dr. Md. Belal, Dr. Abhijeet Srivastava, Dr. Krishna Kumar, Dr. Vijay Gupta, Dr. Krishna Nand Tripathi, Dr. Manish Kumar Jaiswal, Dr. Soumyadip Hore, Dr. Diksha Gambhir, Dr. Amjad Ali, Dr.

Sanjay Singh, Dr. Dewal Deshmuk and Dr. Shashank Singh for the support, and guidance at various times. I also thank Mr. Keshav, Mr. Manoj, Mrs. Poornima, and Mr. Narugopal for helping me in recording NMR, and HRMS. I also thank Mr. Virender Sharma, in-charge III of central glass blowing facility for his timely help. I am thankful to all the members of this department who helped me in one way or the other to carry out my work successfully.

I am forever thankful to my colleagues in the lab for their friendship and support. Their presence was very important in a process that is often felt as tremendously solitaire. They formed the core of my research time and we have been there for one another throughout this journey. I would like to thank all my colleagues (present and past) Ravneet, Manju, Shashank, Harish, Ravi Saini, Abhijeet, Arindam, Kalyan, Chandan, Shreya, Najmuddin, Saurabh, Mubarik, Aarti, Satish, Priyankar, Rajesh, Sunil, Akash, Neha, Gyanshree, Surjeet, Anjum, Dhyanesh, Payal, Rajnish, Lalit, Avika , Gayatri and Imran. It is a pleasure to thank my friends Mr. Digya Pratap, and Mr. Shivam Agarwal, and my teacher Mr. Sachin for creating my interest in chemistry and inspiring me to complete my Ph.D. dissertation. Words cannot express how grateful I am to my family: my parents, Sh. Kehar Singh and Mrs. Rajwati Chauhan and my brother Mr. Shubham Chauhan, my loving sister Mrs. Ruby Singh Chauhan for always supporting and encouraging me the best possible way, for unconditional support, blessings, constant love and encouragement to pursue my interests. A special credit goes to my nephew Vinayak who has been the light of my life, brings smile to my face and gives me extra strength and motivation to get things done.

Finally, I extend a heartfelt appreciation to my dearest friend, Ms. Shreya, for consistently standing by me, helping me during the lab work and motivating me through the ups and downs of my life, always reminding me of my true self.

In closing, I wish to thank Lord Krishna, whose benevolent blessings have showered upon me, infusing me with unwavering strength and boundless courage to fearlessly confront the formidable challenges that have graced my path.

Bhuvnesh Singh

ABSTRACT

The thesis entitled "***Stereoselective Synthesis of Axially Chiral (Hetero)Biaryls, Bridged Isochromans and Amino Indanones***" is divided into five chapters which are mainly focused on the development of both transition metal catalysed and organocatalytic stereoselective C-C bond formation. In chapter two, the concept of asymmetric cooperative catalysis has been demonstrated to achieve axially chiral heterobiaryls. While in chapter three, the concept of organocatalyst has been utilized to achieve axially chiral heterobiaryls. Chapter four realizes the concept of stereoselective domino/cascade addition and cycloaddition reaction. Finally, in chapter five, stereoselective synthesis of kinetically favoured 3-amino indanones has been described.

Chapter 1: This chapter discloses a brief description of general organic chemistry, chirality, and its role in day-to-day life, asymmetric catalysis where special emphasis has been made on organocatalysis, and various activation modes of organocatalysis. Finally, the concept of cooperative catalysis, atropoisomerism has been elaborated with the main focus on the activation of alkynes by silver metal as catalyst.

Chapter 2: Herein, we unraveled a chiral silver phosphate catalysed direct 5-*endo-dig* nucleophilic cyclization of alkynyl naphthalene substituted hydrazones under mild conditions, affording various C−C axially chiral pyrazoles in excellent yields and enantioselectivities. Control experiments suggested that a combination of silver(I) and chiral phosphoric ligand is detrimental for facilitating the reaction. Silver salt was found to expedite the desired chemical transformation, while the chiral phosphoric acid was responsible for inducting the enantioselectivity of the reaction. Furthermore, synthetic applications and the product's thermal stability have also been investigated.

Chapter 3: In this work, we have successfully demonstrated a tandem 6 π electrocyclization of alkynyl imines facilitated by NBS, resulting in the enantioselective synthesis of axially chiral 3-haloquinolines. The reaction proceeded efficiently under mild conditions, showcasing excellent functional group tolerance and high overall efficiency. Notably, this protocol represents the first reported method for the direct synthesis of 3-halogenated axially chiral biaryl quinolines *via* vinylidene ortho quinone methide (VQM) intermediate. This current

methodology presents a robust pathway for the generation of diverse classes of highly functionalized axially chiral quinolines.

Chapter 4: A stereoselective silver catalysed one pot vinylogous aldol addition followed by a cascade [4+2] cycloaddition reaction of α-arylidene pyrazolinones with *in situ* generated isobenzopyrylium ions has been developed under mild reaction conditions, which provides an unpreceded bridged bicyclo [2.2.2] [3.3.1] pentacyclic [5-6-6-6-6] isochromans consisting of a chroman, isochroman and a diazole unit in one molecule, with good to high yields as a single diastereomer.

Chapter 5: We disclosed a unique intermolecular approach for stereoselective synthesis of 3-amino indanones bearing quaternary carbon from 2-alkynyl acetophenones and anilines. A catalytic system comprised of silver salt and phosphoric acid effectively transformed a range of 2-alkynyl acetophenones and anilines to corresponding amino indanones in moderate to good yields. Moreover, an enantioselective route to access substituted 3-amino indanones was also achieved using silver salt and chiral phosphoric acid to afford corresponding indanones up to 99% ee. Furthermore, several transformations of 3-amino indanones were carried out which demonstrate the synthetic utility of the developed protocol.

सार

"अक्षीय रूप से काइअरल (हेटेरो) बायरिल्स, ब्रिज्ड आइसोक्रोमैन्स और एमिनो इंडेनोन्स का स्टीरियोसिलेक्टिव संश्लेषण" शीर्षक वाली थीसिस को पाँच अध्यायों में विभाजित किया गया है, जो मुख्य रूप से संक्रमण धातु उत्प्रेरित और ऑर्गेनोकैटेलिटिक स्टीरियोसिलेक्टिव सी-सी बॉन्ड गठन दोनों के विकास पर केंद्रित हैं। अध्याय दो में, अक्षीय रूप से चिरल हेटेरोबायरिल्स को प्राप्त करने के लिए असममित सहकारी उत्प्रेरण की अवधारणा का प्रदर्शन किया गया है। जबकि अध्याय तीन में, अक्षीय रूप से काइअरल हेटेरोबायरिल्स को प्राप्त करने के लिए ऑर्गेनोकैटेलिस्ट की अवधारणा का उपयोग किया गया है। अध्याय चार में स्टीरियोसिलेक्टिव डोमिनो/कैस्केड एडिशन और साइक्लोडिशन प्रतिक्रिया की अवधारणा को साकार किया गया है। अंत में, अध्याय पाँच में, गतिज रूप से पसंदीदा **3**-एमिनो इंडेनोन्स के स्टीरियोसिलेक्टिव संश्लेषण का वर्णन किया गया है।

अध्याय **1:** यह अध्याय सामान्य कार्बनिक रसायन विज्ञान, चिरैलिटी और दिन-प्रतिदिन के जीवन में इसकी भूमिका, असममित कटैलिसीस का संक्षिप्त विवरण प्रकट करता है जहां ऑर्गेनोकैटेलिसिस पर विशेष जोर दिया गया है, और ऑर्गेनोकैटेलिसिस के विभिन्न सक्रियण मोड। अंत में, सहकारी कटैलिसीस की अवधारणा, एट्रोपोइसोमेरिज्म को उत्प्रेरक के रूप में चांदी धातु द्वारा एल्काइन्स के सक्रियण पर मुख्य ध्यान देने के साथ विस्तृत किया गया है।

अध्याय **2:** इसमें, हमने हल्के परिस्थितियों में एल्काइनिल नेफ़थलीन प्रतिस्थापित हाइड्राज़ोन के एक काइअरल सिल्वर फॉस्फेट उत्प्रेरित प्रत्यक्ष **5**-एंडो-डिग न्यूक्लियोफिलिक चक्रण को उजागर किया, जो उत्कृष्ट पैदावार और एनेंटियोसेलेक्टिविटी में विभिन्न सी–सी अक्षीय चिरल पाइराज़ोल प्रदान करता है। नियंत्रण प्रयोगों ने सुझाव दिया कि सिल्वर(**I**) सिल्वर साल्ट वांछित रासायनिक परिवर्तन को तेज करने के लिए पाया गया, जबकि चिरल फॉस्फोरिक एसिड प्रतिक्रिया की एनेंटियोसेलेक्टिविटी को प्रेरित करने के लिए जिम्मेदार था। इसके अलावा, सिंथेटिक अनुप्रयोगों और उत्पाद की थर्मल स्थिरता की भी जांच की गई है।

अध्याय **3:** इस कार्य में, हमने एनबीएस द्वारा सुगम किए गए एल्काइनिल इमाइन के एक टेंडेम 6π इलेक्ट्रोसाइक्लाइज़ेशन को सफलतापूर्वक प्रदर्शित किया है, जिसके परिणामस्वरूप अक्षीय रूप से चिरल **3**-हेलोक्विनोलिन का एनेंटियोसेलेक्टिव संश्लेषण हुआ है। प्रतिक्रिया हल्की परिस्थितियों में कुशलता से आगे बढ़ी, जिसमें उत्कृष्ट कार्यात्मक समूह सहिष्णुता और उच्च

समग्र दक्षता दिखाई गई। उल्लेखनीय रूप से, यह प्रोटोकॉल विनाइलिडीन ऑर्थो क्विनोन मेथाइड (**VQM**) मध्यवर्ती के माध्यम से **3**-हैलोजेनेटेड अक्षीय रूप से चिरल बायरिल क्विनोलिन के प्रत्यक्ष संश्लेषण के लिए पहली रिपोर्ट की गई विधि का प्रतिनिधित्व करता है। यह वर्तमान पद्धति अत्यधिक कार्यात्मक अक्षीय रूप से चिरल क्विनोलिन के विविध वर्गों की पीढ़ी के लिए एक मजबूत मार्ग प्रस्तुत करती है।

अध्याय **4:** एक स्टीरियोसिलेक्टिव सिल्वर उत्प्रेरित एक पॉट विनाइलोगस एल्डोल एडिशन के बाद इन सीटू उत्पन्न आइसोबेंजोपाइरीलियम आयनों के साथ α-एरिलिडीन पाइराज़ोलिनोन्स की एक कैस्केड **[4+2]** साइक्लोडिशन प्रतिक्रिया को हल्के प्रतिक्रिया स्थितियों के तहत विकसित किया गया है, जो एक अणु में एक क्रोमैन, आइसोक्रोमैन और डायज़ोल इकाई से युक्त एक अभूतपूर्व ब्रिज्ड बाइसाइक्लो **[2.2.2]** **[3.3.1]** पेंटासाइक्लिक **[5-6-6-6-6]** आइसोक्रोमैन प्रदान करता है, जिसमें एकल डायस्टेरियोमर के रूप में अच्छी से उच्च पैदावार होती है।

अध्याय **5:** हमने **2**-एल्काइनिल एसिटोफेनोन और एनिलिन से चतुर्धातुक कार्बन वाले **3**-एमिनो इंदानोन के स्टीरियोसिलेक्टिव संश्लेषण के लिए एक अद्वितीय अंतर-आणविक दृष्टिकोण का खुलासा किया। सिल्वर सॉल्ट और फॉस्फोरिक एसिड से युक्त एक उत्प्रेरक प्रणाली ने **2**-एल्काइनिल एसिटोफेनोन और एनिलिन की एक श्रृंखला को मध्यम से अच्छी पैदावार में संबंधित एमिनो इंडेनोन में प्रभावी रूप से परिवर्तित किया। इसके अलावा, प्रतिस्थापित **3**-एमिनो इंडेनोन तक पहुँचने के लिए एक एनेंटियोसेलेक्टिव मार्ग भी सिल्वर सॉल्ट और चिरल फॉस्फोरिक एसिड का उपयोग करके प्राप्त किया गया था ताकि संबंधित इंडेनोन को **99% ee** तक पहुँचाया जा सके। इसके अलावा, **3**-एमिनो इंडेनोन के कई रूपांतरण किए गए जो विकसित प्रोटोकॉल की सिंथेटिक उपयोगिता को प्रदर्शित करते हैं।

TABLE OF CONTENTS

			Page
Certificate			I
Acknowledgments			II
Abstract			IV
Table of Contents			VIII
List of Figures			XII
List of Schemes			XIV
List of Tables			XVII
Abbreviations			XVIII
Chapter	**1**	**Introduction**	
	1.1	General Information	02
	1.2	Chirality	02
	1.2.1	Stereoisomers	03
	1.3.	Significance of Chirality	04
	1.3.1	Influence of chirality in taste	04
	1.3.2	Influence of chirality in odour	05
	1.3.3	Influence of chirality pharmacology	06
	1.4	Chirality Induction	07
	1.4.1	Chiral Pool	07
	1.4.2	Chiral Auxiliary	08
	1.4.3	Asymmetric Catalysis	08
	1.5.	Organocatalysis	09
	1.5.1	Background	09
	1.5.2	Types of Organocatalysis	11
	1.5.2.1	Covalent Organocatalysis	11
	1.5.2.2	Non-Covalent Organocatalysis	12
	1.5.2.2.1	Brønsted Acid Catalysis	12
	1.5.2.2.2	Brønsted Base Catalysis	13
	1.5.2.2.3	Ion Pair Catalysis	14
	1.6	Principle of Vinylogy	15

	1.7	Silver and its activation	16
	1.7.1	Activation of 2-alkynyl benzaldehyde by silver	17
	1.8	Cooperative Catalysis	17
	1.9	Atropisomerism	20
	2.0	Thesis Overview	21
	2.0.1	Silver and chiral phosphoric acid catalysed enantioselective synthesis of axially chiral pyrazoles	22
	2.0.2	A chiral Brønsted base catalysed atroposelective synthesis of axially chiral aryl quinolines	22
	2.0.3	A Silver catalysed domino/cascade vinylogous annulation of 3-alkylidene pyrazolone and alkynyl Aldehydes: access to bridged polyketide oligomers	23
	2.0.4	A diastereoselective and enantioselective approach for the synthesis of cyclic β-Amino Indanones	23
	2.1	References	25
Chapter	**2**	**Silver and Chiral Phosphoric Acid Catalysed Enantioselective Synthesis of Axially Chiral Pyrazoles**	
	2.1	Introduction	28
	2.2	Our Strategy	33
	2.3	Results and Discussion	34
	2.4	Conclusion	40
	2.5	Experimental section	42
	2.5.1	General Information	42
	2.5.2	General procedure for the preparation of starting material	42
	2.5.3	General procedure for the preparation of	

		axially chiral pyrazoles	43
	2.5.4	General procedure for the reparation of racemic pyrazoles	43
	2.5.5	Characterization of starting materials and products	44
	2.5.6	Representative HPLC Chromatograms	78
	2.5.7	Representative ^{1}H, and ^{13}C Spectra	95
	2.5.17	Crystal data and ORTEP diagram for **73s**	128
	2.6	References	129
Chapter	**3**	**A Chiral Brønsted Base Catalysed Atroposelective Synthesis of Axially Chiral Aryl Quinolines**	
	3.1	Introduction	133
	3.2	Objective	138
	3.3	Results and Discussion	138
	3.4	Conclusion	143
	3.5	Experimental Section	144
	3.5.1	General Information	144
	3.5.2	Preparation of substrates	144
	3.5.3	General procedure for the synthesis of Chiral 4-aryl quinolines adduct	145
	3.5.4.	General procedure for the synthesis of racemic 4-aryl quinolines adduct	145
	3.5.5	Characterization of Axially chiral 3-bromo 4-aryl quinolines	146
	3.5.6	Representative HPLC Chromatograms	153
	3.5.7	Representative ^{1}H and ^{13}C Spectra	168
	3.5.8	Single Crystal X-ray Data of compound **100a**	183
	3.6	References	184
Chapter	**4**	**Bioinspired Synthesis of Bridged Isochromane Fused Pyrazoles by a Silver Catalyzed Cascade Reaction and Its Application for Antibacterial Activity**	
	4.1	Introduction	188
	4.2	Objective	195
	4.3	Results and discussion	196
	4.4	Conclusion	206
	4.5	Experimental Section	208
	4.5.1	General Information	208
	4.5.2	Methodology	208

4.5.2.1	*In-vitro* assay	208
4.5.3	starting material and their synthesis	211
4.5.4	Synthesis of alkynyl aldehydes	211
4.5.5	3-alkylidene pyrazolone used in this protocol	212
4.5.6	General procedure for the synthesis of α-arylidene pyrazolinones	213
4.5.7	General procedure for the synthesis of Bridged [2.2.2] polycyclic adduct	213
4.5.8	Prodecure for Product derivatization	213
4.5.9	Procedure for Control experiment	214
4.5.10	Procedure for gram scale synthesis	214
4.5.11	characterization of starting and products	214
4.5.12	Representative ^{1}H, and ^{13}C, and ^{19}F NMR spectra	234
4.5.13	Single crystal XRD data **131a**	263
4.5.14	Single crystal XRD data **134**	264
4.6	References	266

Chapter 5 A Diastereoselective Approach for the Synthesis of Cyclic β-Amino Indanones

5.1	Introduction	270
5.2	Objective	274
5.3	Results and Discussion	275
5.4	Conclusion	282
5.5	Experimental Section	283
5.5.1	General Information	283
5.5.2	starting materials and their synthesis	284
5.5.3	General procedure for 2-ethynyl acetophenones	285
5.5.4	General procedure for the synthesis of 3-amino indanones	286
5.5.6	Optimization studies of diastereoselective 3-amino indanones	287
5.5.8	Characterization of products	288
5.5.9	HPLC chromatograms of 160a, 160s-t	303
5.5.10	Representative ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra	309
5.5.11	Single crystal X-ray data of **160h**	321
5.5.6	References	323
	Bio-Data	326

List of Figures

Figure No.	Figure Caption	Page
1.1	Non-superimposable mirror image of the hand	03
1.2	Representative example of enantiomers	03
1.3	Role of chirality in taste	05
1.4	Role of chirality in odor	06
1.5	Role of chirality in pharmacology	07
1.6	Representative examples of amino and NHC catalysts.	12
1.7	Chiral phosphoric acid activation mode	13
1.8	Representative examples of chiral Brønsted acid.	13
1.9	Chiral Brønsted base activation mode	14
1.10	Representative examples of chiral Brønsted base catalysts	14
1.11	Representative examples of chiral ion pair catalysts	15
1.12	Representative examples of vinylogous nucleophiles.	16
1.13	Multifaceted properties and applications of silver	17
1.14	Activation of alkyne of 2-qlkynyl benzaldehyde by silver	17
1.15	Different pathways for the interaction in AOMC.	18
1.16	Energy profile of cooperative catalysis	20
1.17	Schematic diagram for atroposelective synthesis	21
1.18	6,6-biaryls, 5-6 biaryls and challenging 5,6-biaryls	21
2.1.1	Axially chiral pyrazoles with biological activity	28
2.2.1	Reaction design	34
2.3.1	Racemization studies of **73a**	39
2.3.2	Plausible mechanism	40
2.5.1	ORTEP drawing of **73s**	129
3.1.1	Biologically active compounds containing 4-aryls Quinolines and axially chiral quinolines	133
3.2.1	Reaction design	138
3.3.1	Plausible mechanism	142
3.5.1	ORTEP drawing of **100a**	184
4.4.1	Antibiotic targets and mechanism of resistance	188
4.1.2	Biologically active methylene bridged pyrano[2,3-b]pyran fused natural products	189
4.2.1	Reaction design	196
4.3.1	Scale up synthesis, control experiment and	

	product derivatization	201
4.3.2	DFT calculation study	203
4.3.3	Cellular activity in mammalian cells	204
4.3.4	Cellular activity in bacterial cells	205
4.5.1	ORTEP diagram for compound **130a.**	263
4.5.2	ORTEP diagram for compound **134.**	264
5.1.1	Bioactive compounds with indanone and indane scaffolds	270
5.2.1	Reaction design	275
5.3.1	Control experiment and synthetic transformations	282
5.3.2	Plausible mechanism	283
5.5.1	Crystal structure of **160h**	330

List of Schemes

Scheme No.	Scheme Caption	Page
1.1	The procedure for the RAMP-/SAMP-hydrazone methodology	08
1.2.	Hydrocynation of aldehydes through cinchona alkaloids catalysis	10
1.3	First L-proline catalyzed asymmetric aldol reaction through HOMO raising strategy	10
1.4	First organocatalytic aldol reaction through LUMO lowering strategy	11
1.5	Chiral phosphoric acid(CPA)/palladium catalysed enantioselective cascade annulation via counter-anion exchange	19
1.6	Ag(I)/CPA catalysed atroposelective synthesis of axially chiral pyrazole	22
1.7	Chiral Brønsted base catalysed atroposelective synthesis of axially chiral 4-aryls quinolines	23
1.8	Silver catalysed stereoselective synthesis of methylene bridged polycyclic pyrano[2,3-b]pyran fused adducts.	23
1.9	Silver catalysed stereoselective synthesis of β-amino indanones	24
2.1.1	Silver and CPA catalysed enantioselective synthesis of axially chiral C2-substituted indoles	29
2.1.2	Gold and silver catalysed enantioselective synthesis of axially chiral C2-substituted indoles	29
2.1.3	Cobalt catalysed enantioselective synthesis of axially chiral C2-naphthol substituted 3-haloindoles	30
2.1.4	Organocatalysed catalysed enantioselective synthesis of axially chiral C2-naphthol substituted indoles	30
2.1.5	Organocatalysed atroposelective synthesis of double axially chiral C2-naphthol substituted 3-haloindoles	31
2.1.6	Palladium and Quinox ligand catalysed enantioselective synthesis of axially chiral C2- aryl substituted indoles.	31
2.1.7	Organocatalysed enantioselective synthesis of axially	

	chiral 4-naphthalene substituted pyrazoles.	32
2.1.8	Atroposelective C-H arylation for the synthesis of axially chiral C5-naphthalene substituted triazoles and pyrazoles.	32
2.1.9	Organocatalysed atroposelective synthesis of C5-naphthol substituted pyrazoles	33
2.1.10	Palladium and Antiphos ligand catalysed atroposelective synthesis of chiral C5-substituted triazoles and pyrazoles.	33
2.3.1	Scope of alkynyl hydrazones	36
2.3.2	Scope of alkynyl hydrazones	38
2.3.3	control experiment	39
3.1.1	Copper catalysed synthesis of 3-bromo quinolines *via* 6π-electrophilic cyclization	134
3.1.2	TBAB mediated synthesis of 3-bromo quinolines via 6-endotrig radical cyclization.	134
3.1.3	CPA catalysed atroposelective synthesis of axially chiral 4-aryl quinolines	135
3.1.4	CPA catalysed enantioselective synthesis of axially chiral 4-aryl quinolines	135
3.1.5	Proline derivative catalysed atroposelective synthesis of axially chiral 4-aryl 3-formyl quinolines	136
3.1.6	Proline derivative catalysed atroposelective synthesis of axially chiral 4-naphthalene 3-formyl quinolines	136
3.1.7	CPA catalysed atroposelective synthesis of both centrally chiral hydroquinolines and axially chiral quinolines.	137
3.1.8	CPA catalysed atroposelective synthesis chiral 4-naphthol substituted quinolines.	137
3.3.1	substrate Scope	141
4.1.1	Platinum catalysed [4+2] annulation of alkynyl aldehydes	

	and allylic alcohols.	191
4.1.2	Palladium catalysed [4+2] cycloaddition of alkynyl aldehydes and silyloxy acrylates	191
4.1.3	DPP catalysed stereoselective [4+2] annulation of 1[H]-isochromene acetal and vinyl boronic acids	192
4.1.4	A Brønsted acid catalysed stereoselective synthesis of benzobicyclo[3.3.1] oxocines and benzobicyclo-[3.2.2] oxepines	192
4.1.5	A gold and scadium catalysed asymmetric synthesis of tetracyclic isochromans	193
4.1.6	A stereoselective vinylogous aldol addition of 3-alkylidene oxindoles and alkynyl aldehydes	193
4.1.7	Asymmetric [3+3] annulation of α,β-unsaturated aldehydes and α-arylidene pyrazolinones.	194
4.1.8.	Asymmetric mannich reaction N-Boc ketimine and 3-alkylidene pyrazolones	194
4.1.9	Asymmetric aldol addition of α-arylidene pyrazolinones. and trifluromethyl ketones	195
4.1.10	Asymmetric rhodium catalysed [3+2] annulation of α-arylidene pyrazolinones and unsymmetrical alkynes	195
4.3.1	Substrate scope of alkynyl aldehydes	199
4.3.2	Substrate scope of α-arylidene pyrazolinones	200
5.1.1	Copper catalysed synthesis of indanones fused pyrolidines	271
5.1.2	Copper-catalysed synthesis of 3-hydroxy indanones from 2-ethynyl benzaldehydes.	272
5.1.3	A diastereoselective synthesis of 1-indanones *via* 1,4-oxa migration/cyclization process	272
5.1.4	Cesium carbonate catalysed synthesis of β -amino	

	indenones from N-tert-butyl-2-(1-alkynyl) benzaldimines.	273
5.1.5	KOH mediated synthesis of β-amino indenones from 2-alkynyl benzaldehydes and primary amines	273
5.1.6	TFA mediated intramolecular mannich reaction for the synthesis of cyclic β -amino indanones	273
5.1.7	A metal free approach for the synthesis of 1,3-diaminesubstituted indenes and β-amino indanones.	274
5.3.1	Scope of anilines	277
5.3.2	scope of 2-alkynyl acetophenones	278

List of Tables

Table No.	Table Caption	Page
2.3.1	Optimization of reaction condition	35
3.3.1	Optimization Studies	139
4.3.1	Optimization Studies	197
5.3.1	Optimization studies	276
5.3.2	Optimization studies	279

List of Abbreviations

Abbreviation	Full form
Ac	Acetate
MeCN/CH_3CN/ACN	Acetonitrile
Ar	Aryl
AI	Artificial Intelligence
Ag	Silver
AgOAc	Silver acetate
AgOTf	Silver Triflate
Ag_2CO_3	Silver Carbonate
$BF_3.OEt_2$	Boron trifluoride etherate
^{t}Bu	*tert*-Butyl
$CDCl_3$	Deuterated chloroform
CH_2Cl_2 /DCM	Dichloromethane
CPA	Chiral Phosphoric Acid
CF_3Ph	Trifluoro toluene
CuI	Copper iodide
cm-1	Wavenumbers
°C	Degrees Celsius
dr	Diastereomeric ratio
DPP	Diphenyl phosphate
d	Doublet
dd	Doublet of doublets
DMSO-d_6	Deuterated dimethyl sulfoxide
δ	Chemical shift
er	Enantiomeric ratio
ee	Enantiomeric excess
ESI-TOF	Electrospray ionization - Time-of-flight
EtOAc	Ethyl acetate
Et_2O	Diethyl ether
H_2O	Water

hr	Hour
HOMO	Highest occupied molecular orbital
HPLC	High-performance liquid chromatography
HRMS	High resolution mass spectroscopy
J	Coupling constant
λ	Wavelength
LUMO	Lowest unoccupied molecular orbital
min	Minute
MTBE	Methyl *tert*-butyl ether
m	Multiplet
MHz	Megahertz
mL	Millilitre
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-*2H*-tetrazolium bromide
μL	Microlitre
NHC	N-Heterocyclic carbenes
Na_2SO_4	Sodium Sulphate
NBS	N-Bromosuccinimide
$NaHCO_3$	Sodium bicarbonate
NaCl	Sodium chloride
NMR	Nuclear Magnetic Resonance
N_2	Nitrogen gas
o	Ortho
p-TsOH	*para*-Toluenesulfonic acid
PTC	Phase Transfer Catalyst
$PdCl_2(PPh_3)_2$	dichlorobis(triphenylphosphine)palladium(II)
PhCl	Chlorobenzene
PCC	Pyridinium chloro chromate
^{i}Pr	Isopropyl
p	para
rt	room temperature
ROS	Reactive oxygen species
s	Singlet

SOMO	Singly unoccupied molecular orbital
TLC	Thin Layer Chromatography
TFA	Trifluoroacetic acid
TfOH	Triflic acid
THF	Tetrahydrofuran
TMS	Tetramethylsilane
TBAB	Tetra-*N*-butylammonium bromide
UV	Ultraviolet
VQM	Vinylidene quinone methide
ZOI	Zone of inhibition
MCL-1	Myeloid cell leukemia one
PRMT5	