CYCLIZATION/CYCLOADDITION REACTIONS OF NITRILES, ALLENES AND ACTIVE METHYLENE COMPOUNDS

A THESIS
SUBMITTED FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

By

A. KALYANI

SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD
HYDERABAD - 500 046, INDIA

MARCH 2022

I DEDICATE THIS THESIS TO

My Family,
Teachers
and God

CONTENTS

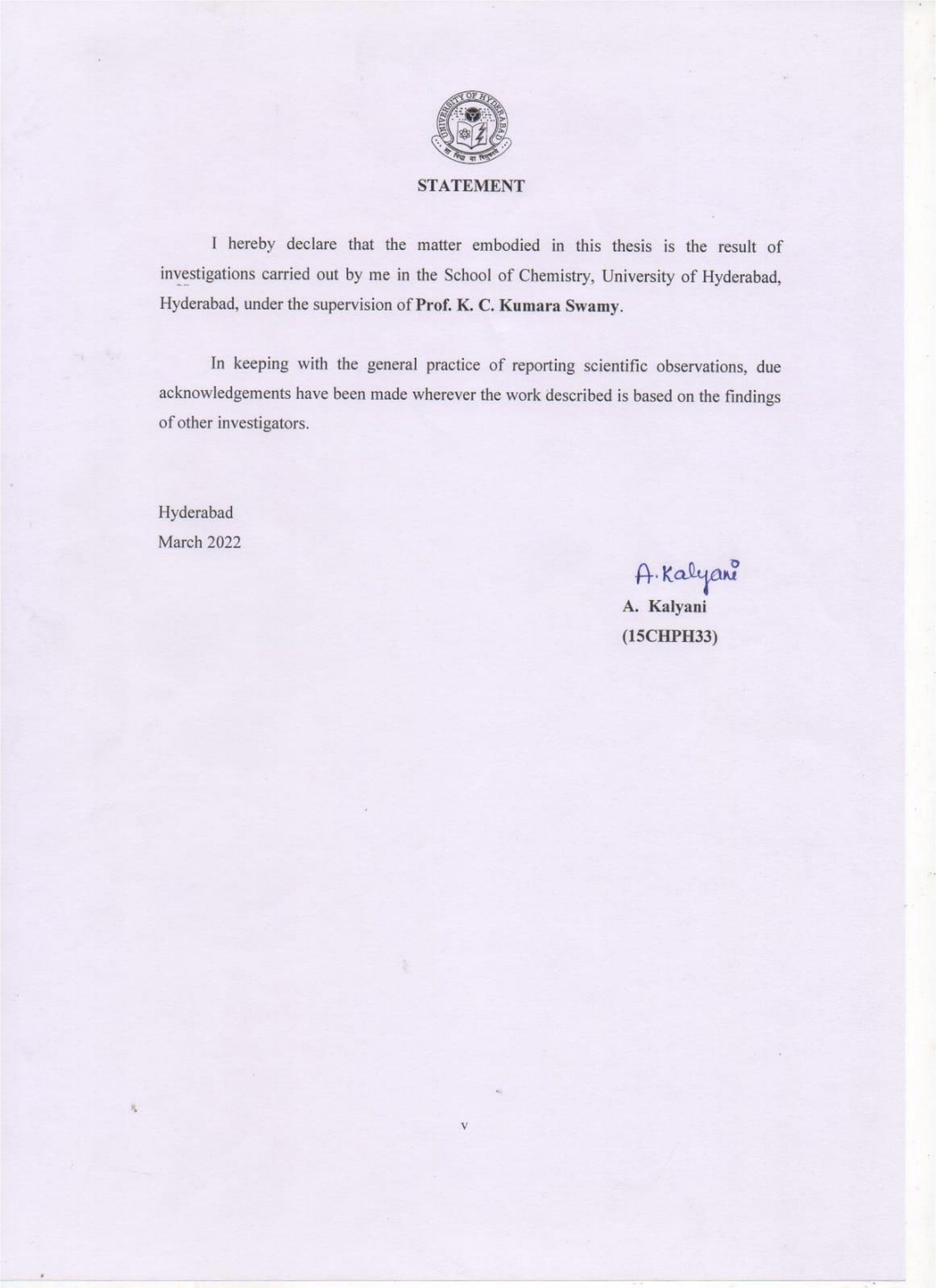
PART A

CYCLIZATION/ CYCLOADDITION REACTIONS OF NITRILES AND ALLENES

PART B

CYCLIZATION REACTIONS OF ACTIVE METHYLENE COMPOUNDS

APPENDIX



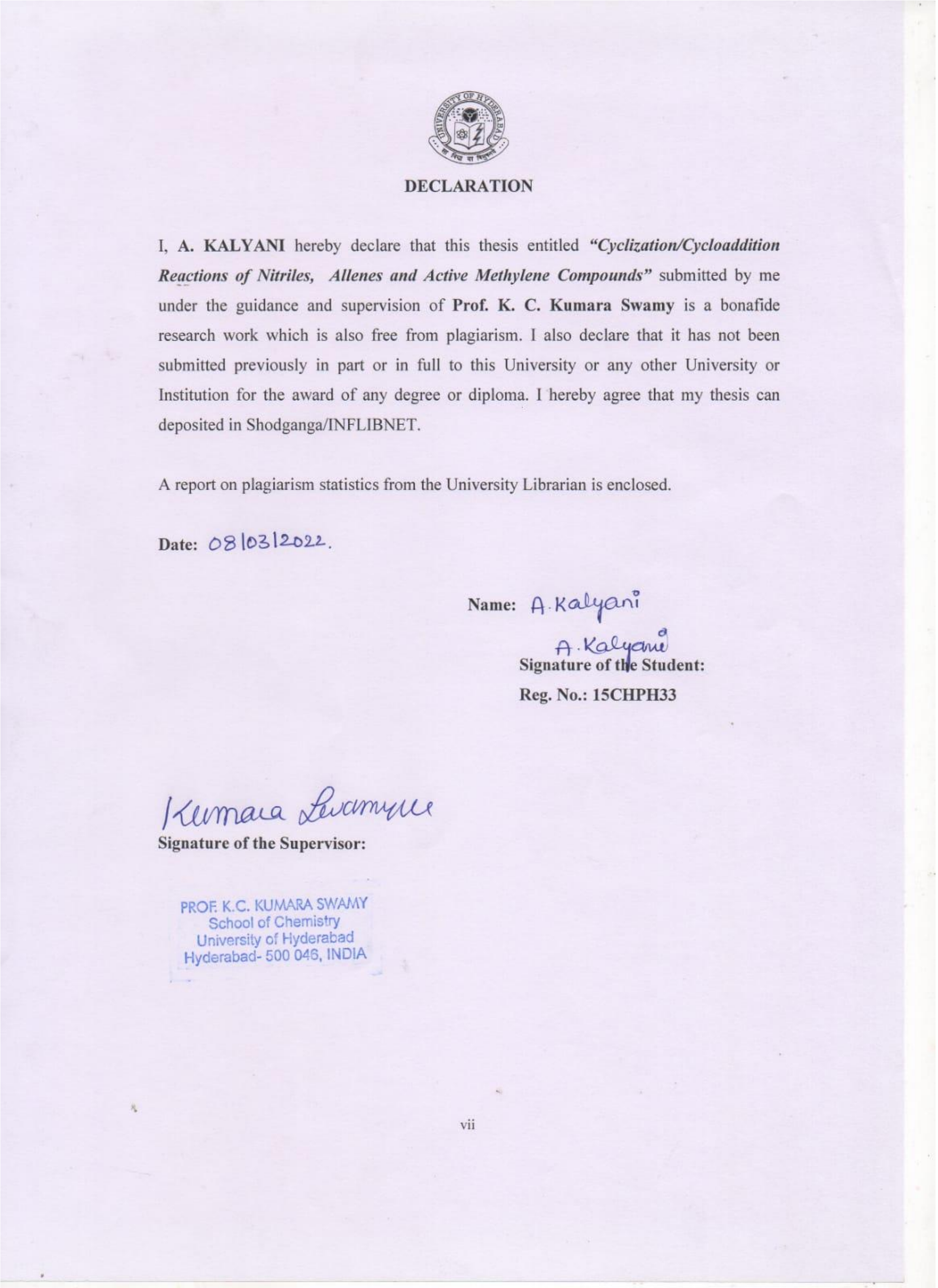
STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of **Prof. K. C. Kumara Swamy**.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

Hyderabad
March 2022

A. Kalyani
A. Kalyani
(15CHPH33)



DECLARATION

I, **A. KALYANI** hereby declare that this thesis entitled ***"Cyclization/Cycloaddition Reactions of Nitriles, Allenes and Active Methylene Compounds"*** submitted by me under the guidance and supervision of **Prof. K. C. Kumara Swamy** is a bonafide research work which is also free from plagiarism. I also declare that it has not been submitted previously in part or in full to this University or any other University or Institution for the award of any degree or diploma. I hereby agree that my thesis can deposited in Shodganga/INFLIBNET.

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A. Kalyani

Signature of the Student:

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Kumara Swamy

Signature of the Supervisor:

PROF. K.C. KUMARA SWAMY
School of Chemistry
University of Hyderabad
Hyderabad- 500 046, INDIA

CERTIFICATE

This is to certify that the thesis entitled ***“Cyclization /Cycloaddition Reactions of Nitriles, Allenes and Active Methylene Compounds”*** has been carried out by Ms. **A. Kalyani**, bearing registration number **15CHPH33** in partial fulfillment of the requirements for award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by her under my supervision and guidance.

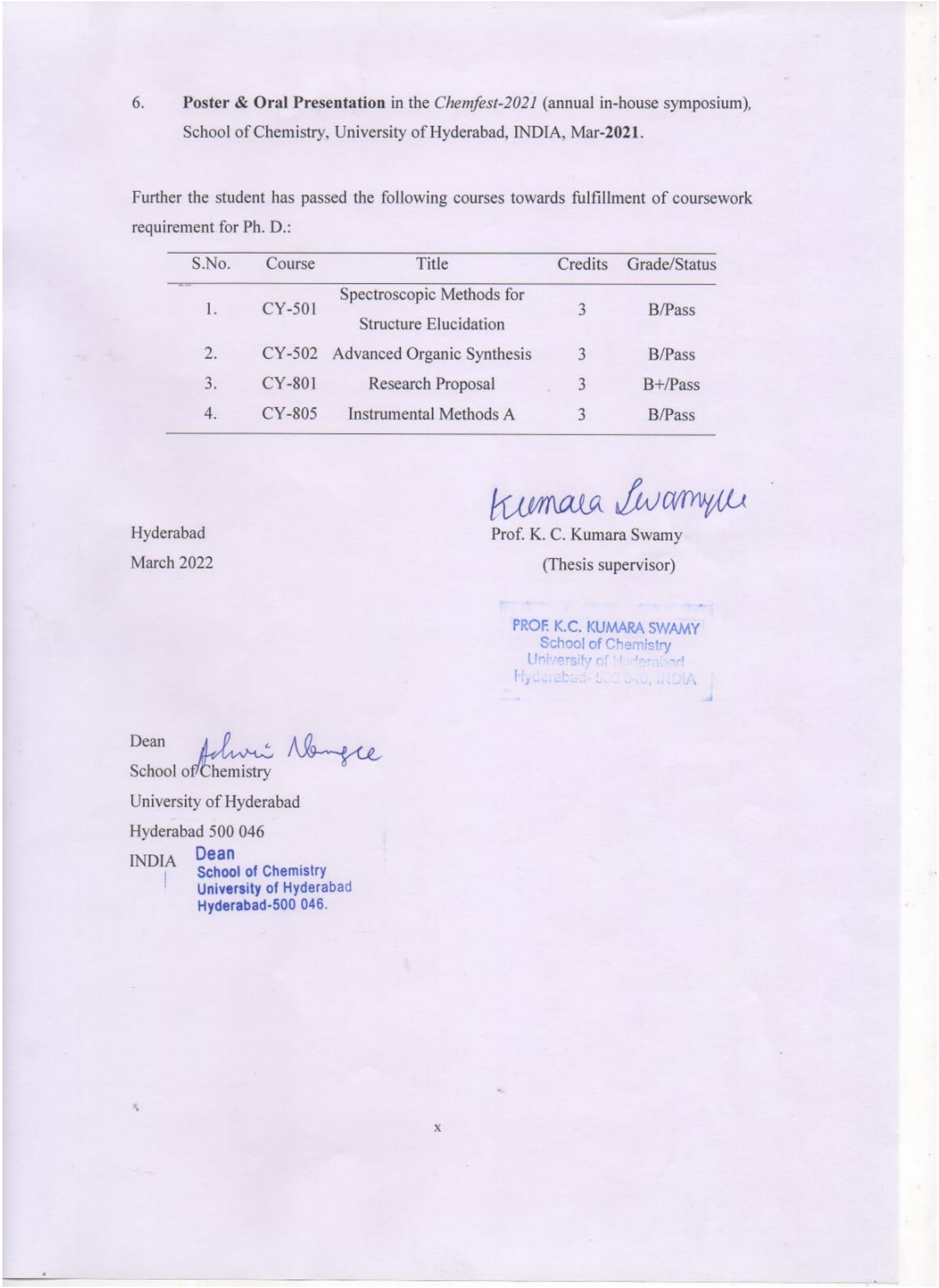
This thesis is free from plagiarism and has not been submitted previously in part or in full to this or any other University or Institution for award of any degree or diploma. Further the student has four publications before the submission of her thesis.

Parts of this thesis have been published in the following two publications:

1. **Adula Kalyani**, R. N. Prasad Tulichala, Sachin Chauhan and K. C. Kumara Swamy*
   Tetrahedron Lett. **2022**, *89*, 153600. https://doi.org/10.1016/j.tetlet.2021.153600.
2. Rajnikanth Sunke, **Adula Kalyani**, K C Kumara Swamy*
   J. Org. Chem. **2020**, *85,* 1073.

She has also made presentations in the following conferences:

1. Poster presentation in the *National Meeting of Synthetic and Theoretical Chemists-2017*, School of Chemistry, University of Hyderabad, Hyderabad, INDIA, **Oct-2017**
2. Poster presentation in the Inspire Fellowship Review Meeting, K L University, Guntur, INDIA, **June- 2019**
3. Poster presentation in the 26th CRSI- National Symposium in Chemistry, VIT-Vellore, Feb- **2020**.
4. Poster presentation in the *Chemfest-2020* (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Feb-**2020**.
5. Poster presentation in the *XVIth J-NOST Conference for Research Scholars*, IISc-Bangalore, INDIA, Oct-**2020**.



6. **Poster & Oral Presentation** in the *Chemfest-2021* (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Mar-**2021**.

Further the student has passed the following courses towards fulfillment of coursework requirement for Ph. D.:

S.No.	Course	Title	Credits	Grade/Status
1.	CY-501	Spectroscopic Methods for Structure Elucidation	3	B/Pass
2.	CY-502	Advanced Organic Synthesis	3	B/Pass
3.	CY-801	Research Proposal	3	B+/Pass
4.	CY-805	Instrumental Methods A	3	B/Pass

Kumara Swamy

Hyderabad
March 2022

Prof. K. C. Kumara Swamy
(Thesis supervisor)

PROF. K.C. KUMARA SWAMY
School of Chemistry
University of Hyderabad
Hyderabad- 500 046, INDIA

Dean
School of Chemistry
University of Hyderabad
Hyderabad 500 046
INDIA

Dean
School of Chemistry
University of Hyderabad
Hyderabad-500 046.

ACKNOWLEDGEMENTS

With high regards and profound respect, I wish to express my deep sense of gratitude to **Prof. K. C. Kumara Swamy** for his guidance, freedom and valuable suggestions throughout my research work. It has been a great privilege for me to work with him throughout the course of my stay. He has been quite helpful in improving my confidence, patience and communication skills.

I thank the present and former Deans, School of Chemistry, for providing me the facilities needed for my research. I extend my sincere thanks to all the faculty members for their cooperation on various aspects.

I am deeply indebted to all my teachers right from my school to University for the support and training I received in my academic career.

I am also thankful to my former lab-mates Dr. Rajnikanth, Dr. A. Leela Siva Kumari, Dr. A. Siva Reddy, Dr. M. Anitha, Dr. K. Selvaraj, Dr. R. N. Prasad, Dr. Anasuya, Dr. Mahendhar, Dr. Sanjeeva and Mr. Ravi for their co-operation in the lab. I am especially thankful to junior lab-mates **Mr. Sachin** and **Mr. Asif** for their enormous help. I acknowledge help from my present lab-mates: Mr. Shankar, Mr. Sandeep, Mr. Shubham, Mr. Suraj and Mr. Shabbir.

I thank all the non-teaching staff of the School of Chemistry for their help. It is my privilege to acknowledge persons-in-charge of NMR, IR and single crystal XRD. I also thank ACRHEM-University of Hyderabad for allowing me to get some HRMS spectra.

I thank INSPIRE (New Delhi) for financial support. I also thank Department of Science and Technology (New Delhi; under FIST and PURSE) and UGC (New Delhi; under UPE and CAS) for setting up many equipment facilities at the University of Hyderabad.

I would like to express my heartfelt thanks to my beloved parents Late **A. Rajashekar** and Late **Vijaya** for their enormous love, kindness and faith on me. I am extremely thankful to my beloved would be husband **Ayyappa** for his enormous love, support and affection. I also express my heartfelt thanks to my beloved sister **Raghaveni**, brother **Raghavendra**, brother-in-law **Mahesh** and nephew **Srivastal** for their love, affection, encouragement and support throughout this journey.

I also thank my relatives **Jagadheesh** (Late), Buchamma, Usha rani, Shobha rani, Vasanth Kumar, Raju, Sonu, Sravani, Manjunath, Akshay, Venkata Shivudu and Samba Shivudu for their support.

I would like to express my sincere gratitude to my friends Latha, Chandrareddy, Mihika, Venkat, Kalyan, Laxmikanth, Kirthi, Sowmya, Ramya, Shanthi, Jhansi, Vani, Khambham Sai Kumar and Sahaja for their affection, encouragement and support throughout this journey.

A. Kalyani...

LIST OF PUBLICATIONS

(A) Published papers:

1. Palladium Catalyzed Nitrile Insertion and Cyanation of Biindoles: Synthesis of Indole Fused *α*- Carboline Scaffolds *via* Double C-H Activation
Adula Kalyani, R. N. Prasad Tulichala, Sachin Chauhan and K. C. Kumara Swamy*
Tetrahedron Lett. **2022**, *89*, 153600. https://doi.org/10.1016/j.tetlet.2021.153600.

2. Cu(I)-Catalyzed Ligand- Free Tandem One-Pot or Sequential Annulation *via* Knoevenagel Intermediated: An Entry into Multifunctional Naphthalenes, Phenanthrenes, Quinolines, and Benzo[b] carbazoles.
Rajnikanth Sunke, **Adula Kalyani**, K C Kumara Swamy*
J. Org. Chem. **2020**, *85*, 1073.

(B) The following papers are in the pipeline (write up stage)

3. [Pd]-Catalyzed Cyclization Reactions of Phosphorus Based Allenes and Thermal induced Cycloaddition Reactions of Phosphorus/ Sulphur based Allenes or Allenoates with 3,6-diphenyl-1,2,4,5-tetrazine (*to be communicated*).
Mallepalli Shankar,[a] **Adula Kalyani**,[a] Mandala Anitha, K. C. Kumara Swamy (to be communicated) (**M.S.** and **A.K.** with equal contribution).

4. Phosphine Catalyzed [4+2] Cycloaddition of α-Methyl Allenoates and Enynones: An Approach for the Synthesis of Furan Fused cycloheptene carboxylates by [Au]-Catalysis.
Adula Kalyani, Sachin Chauhan, A. Leela Siva Kumari, K C Kumara Swamy* (*to be communicated*).

Other Publications

5. Advances in chemoselective and /or stereoselective semihydrogenation of alkynes
K. C. Kumara Swamy*, Alla Siva Reddy, K. Sandeep, **A. Kalyani**
*Tetrahedron Lett***. 2018,** *59*, 419**.**

6. New reactions of allenes, alkynes, ynamides, enynones and isothiocyanates
K. C. Kumara Swamy*, G. Gangadhararao, Mandala Anitha, A. Leela Siva Kumari, Alla Siva Reddy, **Adula Kalyani,** Srinivasarao Allu
J. Chem. Sci. **2018,** *7,* 99**.**

Participation in Conferences/ Symposia

1. Palladium Catalyzed Nitrile Insertion via Double C-H Activation: An Approach to Indole Fused α-Carbolines

   Adula Kalyani, T. R. N. Prasad and K. C. Kumara Swamy*

   National Meeting of Synthetic and Theoretical Chemists-2017, School of Chemistry, University of Hyderabad, Hyderabad, INDIA, Oct-**2017** (**Poster Presentation**).

2. Organic transformations of allenes, nitriles and active methylene esters

   Adula Kalyani and K. C. Kumara Swamy*

   Inspire Fellowship Review Meeting, K L University, Guntur, INDIA, June- 2019 (**Poster Presentation**).

3. Cu(I)-Catalyzed Ligand-free Tandem One Pot or Sequential Annulation via Knoevenagel Intermediate: An Entry into Multifunctional Naphthalenes, Phenanthrenes and Quinolines

   Adula Kalyani, Rajnikanth Sunke, and K. C. Kumara Swamy*

   26th CRSI- National Symposium in Chemistry, VIT- Vellore, Feb-**2020** (**Poster Presentation**)

4. Cu(I)-Catalyzed Tandem One Pot Annulation : An Entry into Multifunctional Naphthalenes, Phenanthrenes, Quinolines and Benzo(*b*)carbazoles

   Adula Kalyani, Rajnikanth Sunke, and K. C. Kumara Swamy*

   Chemfest-2020 (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Feb-**2020** (**Poster Presentation**)

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   Adula Kalyani, Rajnikanth Sunke, and K. C. Kumara Swamy*

   XVIth J-NOST Conference for Research Scholars, IISc-Bangalore, INDIA, Oct-**2020** (**PosterPresentation**).

6. Transition Metal Catalyzed Cycloadditions/ Cyclizations of Allenes

   Adula Kalyani and K. C. Kumara Swamy*

   Chemfest-2021 (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Mar-**2021** (**Poster & Oral Presentation**).

7. New Catalytic Organic Transformations Involving Allenes/Alkynes, Nitriles, Ynamides or Enynones

   K. C. Kumara Swamy,* Alla Siva Reddy, **Adula Kalyani**, and Srinivasarao Allu

   XVIIth Modern Trends in Inorganic Chemistry-2017 (MTIC-XVII), Organized by CSIR-NCL, Pune, India, Dec-2017.

8. Catalytic Transformations Involving Allenes/Alkynes and Ynamides- Identification of Some Intermediates

   K. C. Kumara Swamy,* K. Sandeep, Mallepalli Shankar, **Adula Kalyani** and Mandala Anitha

   20th International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis, Heidelberg, Germany, and July-2019.

9. Reactivity of Phosphonate and Sulfonate Based Systems: Some New Findings

   K. C. Kumara Swamy,* **A. Kalyani**, Suraj, M. Shankar, A. Srinivasarao.

   International Conference on Main-group Molecules to Materials-II, NISER-Bhubaneswar, Dec-2021.

Synopsis

This thesis is divided into two parts: **Part-A** and **Part-B**. **Part-A** deals with the following topics: (i) Palladium catalyzed nitrile insertion followed by cyclization into 2,3′-biindole to yield indole fused α-carboline scaffolds and cyanation of biindoles, (ii) Cyclization and cycloaddition reactions of phosphorus based allenes in the presence of [Pd]-catalyst to yield Pd-incorporated metal complexes and P-containing naphthalenes respectively, and (iii) Phosphine catalyzed cycloaddition of allenes with enynones followed by gold catalyzed intramolecular cyclization to yield furan fused polycycles. Overall, this part deals with the chemistry of compounds involving an *sp*-hybridized carbon (e.g., nitrile, allene, enynone). **Part-B** deals with Cu(I)-catalyzed ligand-free tandem one pot or sequential annulation *via* Knoevenagel intermediate that affords multifunctional naphthalenes, phenanthrenes, quinolines and benzo[*b*]carbazoles.

Each part is subdivided into three chapters: (a) Introduction (literature survey), (b) Results and Discussion, and (c) Experimental Section. The prepared compounds in the present study are, characterized by MP, IR and NMR (^{1}H, ^{13}C and ^{31}P) techniques followed by HRMS. X-ray structure determination is undertaken wherever required. Summary as well as references are given at the end of each part.

PART A

In Chapter 1, a review of literature on aspects relevant to this part is presented. In Chapter 2, the results obtained on these aspects are discussed while in Chapter 3, the experimental details are described. The precursors used in the present study are shown in Chart 1 [*Note*: The numbering of compounds given here is different from that in the main part of the thesis]. Compounds other than **1a-l** are prepared by methodologies available (with modifications where necessary) in the literature.

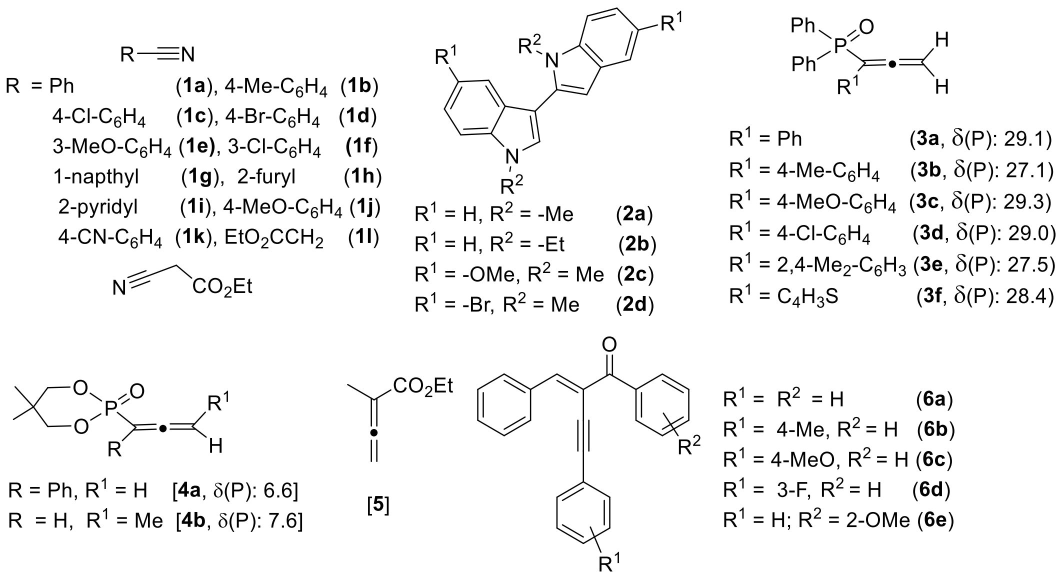
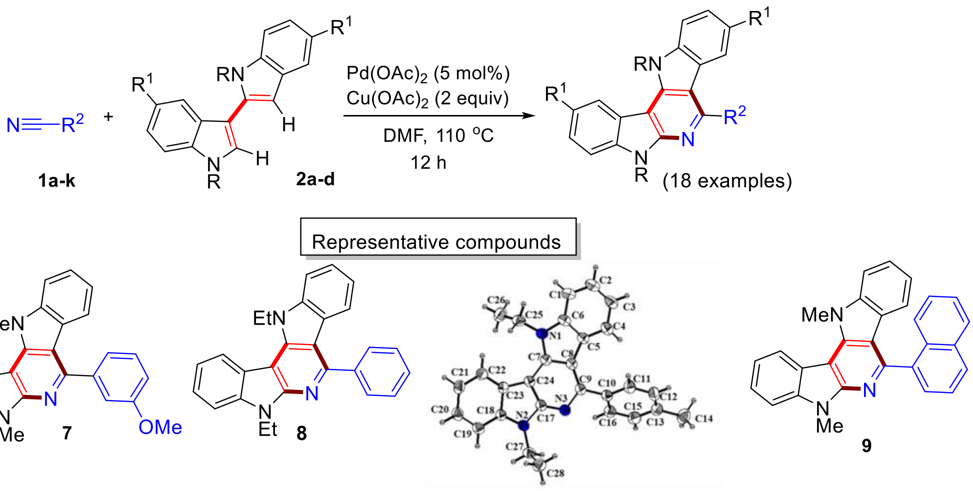


Chart 1: Precursors used in this study (part A).

(i)(a) [Pd]-catalyzed insertion of nitriles in to 2,3′-biindoles followed by cyclization to yield indole fused α-carbolines (pyridodiindoles)

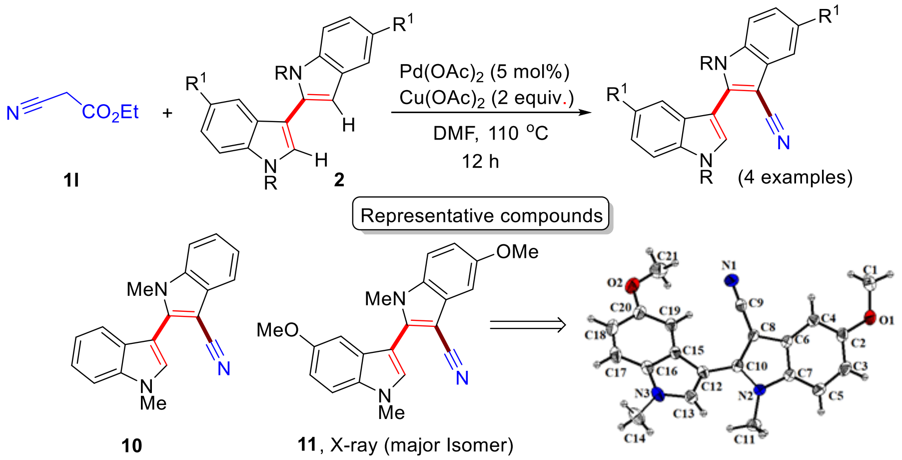
We treated biindoles aromatic nitriles **1a-k** with **2a-d** in the presence of $Pd(OAc)_2$ (5 mol%), and $Cu(OAc)_2$ (equiv) in DMF at 110 °C for 12 h (Scheme 1). We obtained indole fused α-carbolines (e.g., **7-9**), which are likely to be formed by double C-H activation and cyclization of 2,3′-biindoles with nitriles *via* C-C and C-N bond formation in a single step.



Scheme 1: Synthesis of indole fused α-carbolines (pyridodiindoles) from nitriles and 2,3′-biindoles

(i)(b) $Pd(OAc)_2$ catalyzed C-3 cyanation of 2,3′-biindoles using ethyl cyanoacetate

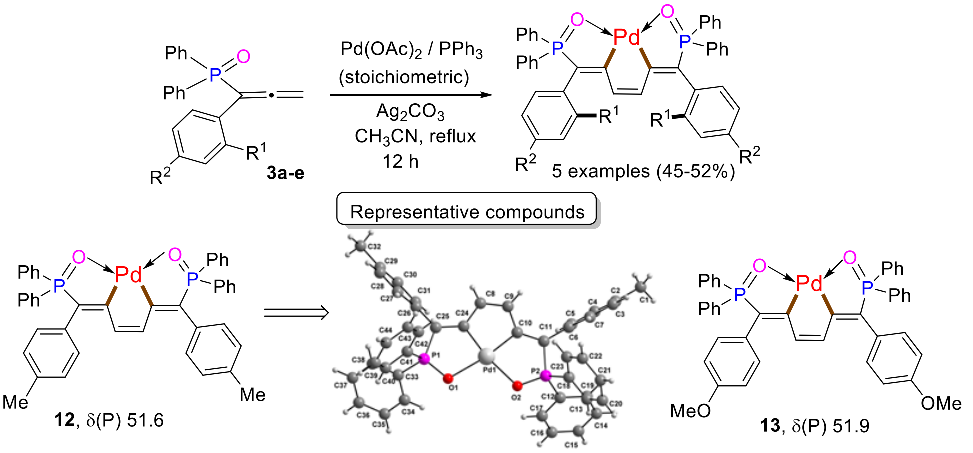
We treated ethyl cyanoacetate **1l** with biindole **2a-d** using Pd(OAc)$_2$ (5 mol%) and Cu(OAc)$_2$ (equiv) in DMF at 110 °C for 12 h (Scheme 2). Interestingly, this reaction led to C-3 cyano-biindoles (e.g., **10-11**) *via* a *retro*-Mannich pathway with the elimination of ethyl acetate; in some cases, there is a possibility of formation of isomeric mixture.



Scheme 2: Pd(OAc)$_2$ catalyzed C-3 cyanation of 2,3′-biindoles using ethyl cyanoacetate.

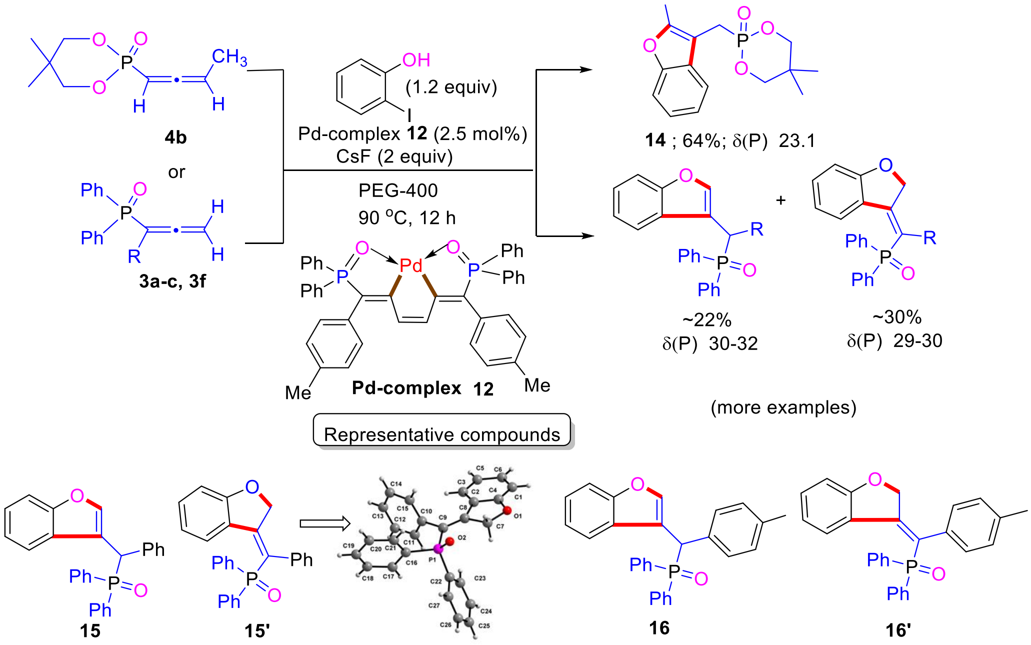
(ii)(a) [Pd]-mediated synthesis of P-containing complexes from allenylphosphine oxides and their utility

Allenylphosphine oxides of type **3** react with 0.5 mole equiv of Pd(OAc)$_2$ in the presence of Ag$_2$CO$_3$ (1 equiv) and PPh$_3$ (1 equiv) in CH$_3$CN solvent at reflux for 12 h afford P-containing [Pd]-complexes (e.g., **12-13**; Scheme 3). This reaction may proceed through [Pd]-mediated intramolecular cyclization. The 1:2 [Pd: allene] reaction mixture indicated the formation of at least a couple of more [Pd]-complexes. So far, we have been successful in isolating only the major [Pd]-allene complex in each case.



Scheme 3: Synthesis of Pd-incorporated complexes from allenylphosphine oxides

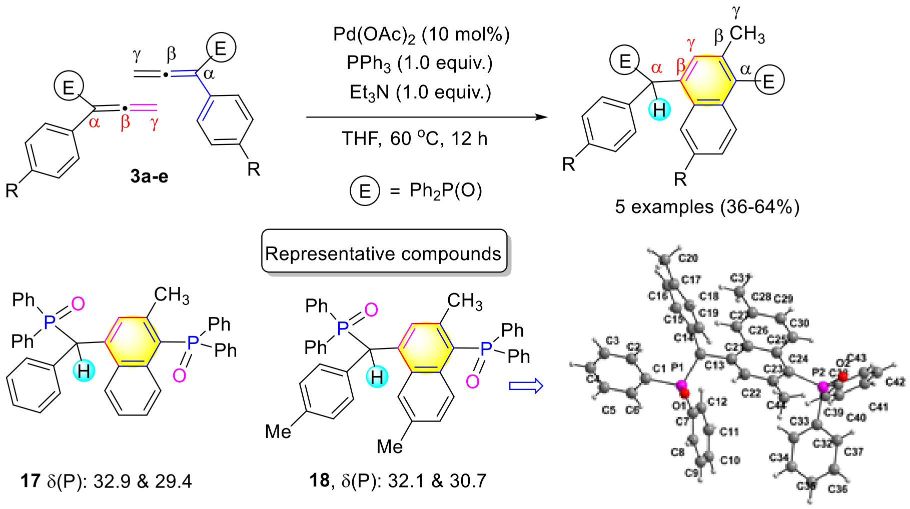
In order to check any possible catalytic activity of [Pd]-allene complexes prepared as above, we treated allenylphosphonate **4b** with 2-iodophenol (1.2 equiv) in the presence of [Pd]-complex **12** (2.5 mol%) and CsF (base) in PEG-400 solvent at 90 °C for 12h (Scheme 4). Satisfyingly, we obtained phosphano-benzofuran **14** in moderate yields. When we repeated the same reaction by using allenylphosphine oxides **3a-b**, we were able to isolate phosphano-benzofurans **15-16** (minor) and **15′-16’** (major). Some more compounds have also been synthesized.



Scheme 4: Synthesis benzofurans and dihydro-benzofurans from P-allenes using complex **12** as the catalyst

(ii)(b) Pd(OAc)$_2$-catalyzed transformations of allenylphosphine oxides leading to P-containing naphthalenes

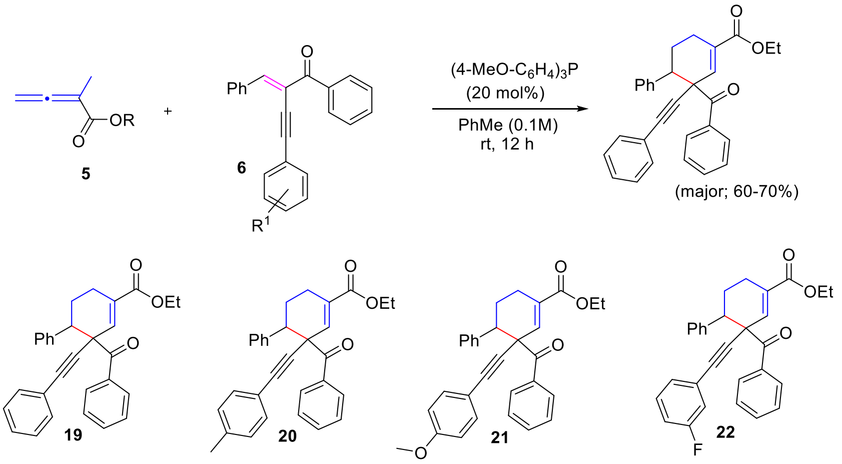
When we treated allenylphosphine oxides **3** with Pd(OAc)$_2$ (10 mol%), Ph$_3$P (1 equiv) and Et$_3$N (1 equiv) in THF solvent at 60 °C in 12 h, we observed the formation of compounds of type **17-18** (Scheme 5). The ^{31}P{^{1}H} NMR spectra of **17-18** showed two peaks of equal intensity indicating that two molecules of allenylphosphine oxide are involved in the reaction. Based on the NMR data, we surmised that the formed product was an unsymmetrical dimer in which (*β*,*γ*)-double bond of one allene and (*α*,*β*)-double bond of another allene moiety are involved, which means intramolecular [4+2] cycloaddition of two allenylphosphine oxides has taken place to yield a new six-membered ring to afford P-containing naphthalene derivatives as shown in scheme 5. The structure of compound **18** was proven by single crystal X-ray crystallography.



Scheme 5: Synthesis of P-containing naphthalenes from allenylphosphine oxides

(iii)(a) Phosphine catalyzed cycloaddition reaction of allenoates with enynones to yield cyclohexene carboxylates

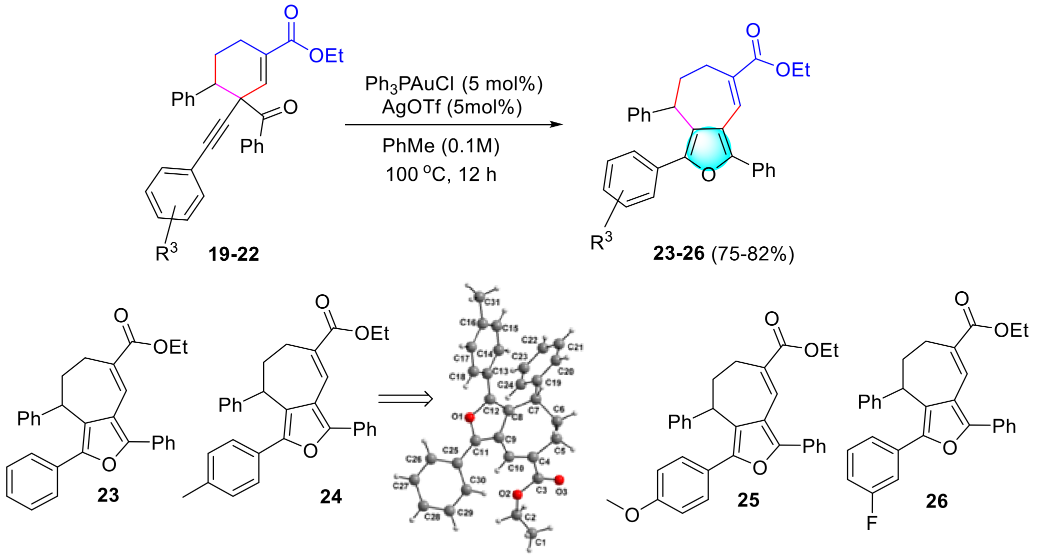
Multifunctional cyclohexene carboxylates (e.g., **19-22**) were obtained by treating alkyl-2-methyl-2,3-butadienoate **5** with enynones **6** in the presence of tris(4-methoxyphenyl phosphine) as catalyst with toluene as the solvent at rt (25 °C) (Scheme 6). This reaction involves phosphine catalyzed intermolecular [4+2] cycloaddition pathway. The purity was only ~90% in these cases, probably because of the stereo- as well as regio-isomers. These details also are discussed in the thesis.



Scheme 6: Phosphine catalyzed synthesis of cyclohexene carboxylate

(iii)(b) [Au]-catalyzed reactions of cyclohexene carboxylates to yield furan fused cycloheptene carboxylates

Treatment of cyclohexene carboxylates **19-22** with the gold catalyst, Ph_3PAuCl (5 mol%) and AgOTf (5 mol%) in toluene solvent at 100 °C for 12 h afforded furan fused cycloheptene-carboxylates **23-26** (Scheme 7). The mechanistic pathway probably involves intramolecular cyclization and ring opening/ expansion followed by aromatization.



19-22

23-26 (75-82%)

23

24

25

26

Scheme 7: Synthesis of furan fused cycloheptene-carboxylates through [Au]-catalysis

PART-B

In this part, reactions utilizing active methylene compounds are explored. Chapter 4 deals with a review of literature on transition metal catalyzed cyclizations/transformations by using active methylene compounds. Chapter 5 delves upon the results obtained on these aspects. Chapter 6 is the experimental section for this part. The main precursors used are shown in Chart 2. Important results of this part are discussed below.

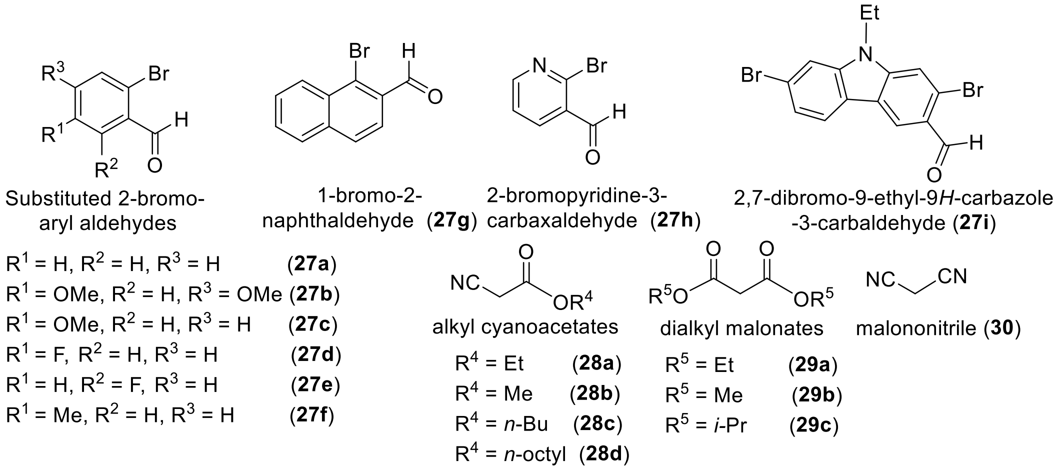
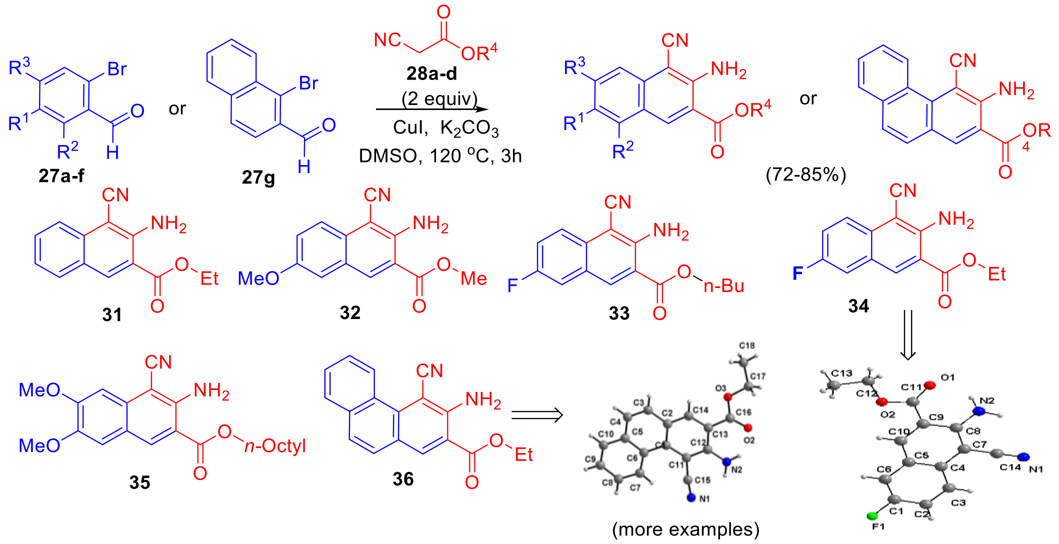


Chart 2: Precursors used in this work (part B)

(iv)(a) [Cu]-catalyzed ligand-free synthesis of multifunctional naphthalenes, phenanthrenes, quinolines, benzo[*b*]carbazoles by using 2-bromo aryl aldehydes and active methylene compounds

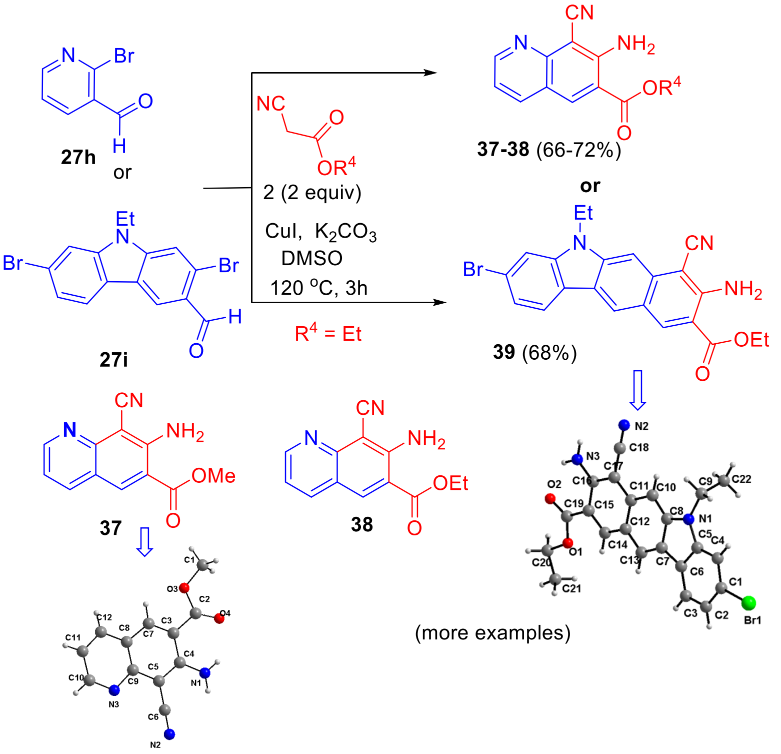
Here, the reactions of 2-bromobenzaldehyde **27a-f** with alkyl 2-cyanoacetate **28a-d** in the presence of CuI (10 mol%) and K_2CO_3 (3 equiv) in DMSO at 120 °C for 3 h afforded the multisubstituted naphthalenes (e.g., **31-35**). We extended our methodology for the synthesis of phenanthrene **36** from 1-bromo-2-naphthaldehyde **27g** as the precursor (Scheme 8). The mechanism of this conversion involves Knoevenagel condensation, C-arylation, and decarboxylation followed by aromatization.



Scheme 8: Synthesis of multifunctional naphthalenes/ phenanthrenes

(iv)(b) Cu(I)-Catalyzed tandem synthesis of multifunctional quinolines and benzo[*b*]carbazoles

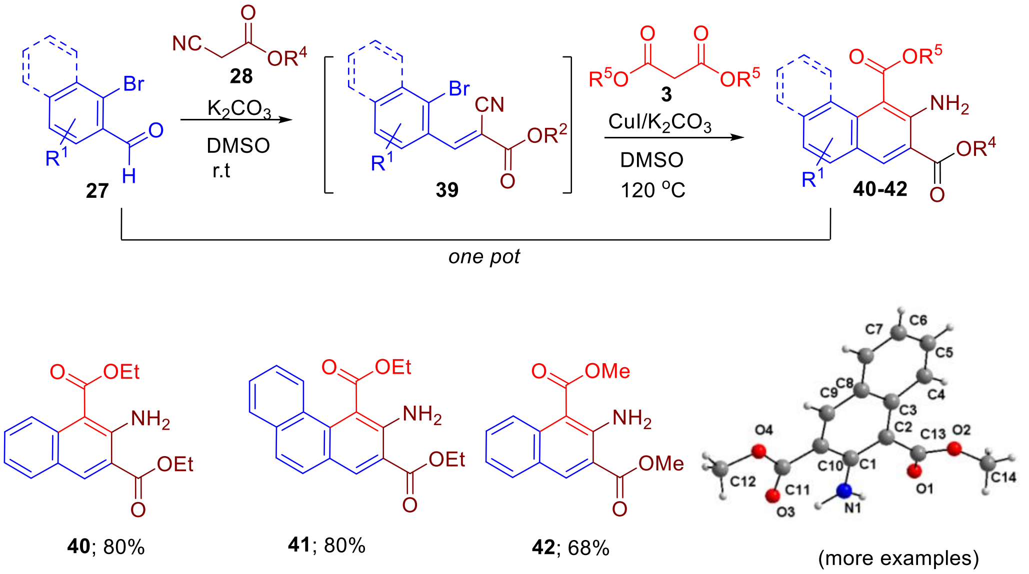
Continuing our above studies, we examined the reaction of 2-bromo-3-pyridinecarboxaldehyde **27h** with alkyl cyanoacetates **28** in presence of above optimized conditions. Satisfyingly, the reaction led to the desired products (e.g., **37-38**) in moderate to good yields 72-52%. We have successfully extended this chemistry to the synthesis of alkyl 7-amino-8-cyano-5-ethyl-5*H*-benzo[*b*]carbazole-9-carboxylate **39** (Scheme 9).



Scheme 9: Synthesis of multifunctional quinolines and benzo[*b*]carbazoles

(iv)(c) Cu(I)-catalyzed one-pot sequential synthesis of dialkyl-2-aminonaphthalene from (*E*)-alkyl 3-(2-bromophenyl)-2-cyanoacrylate I

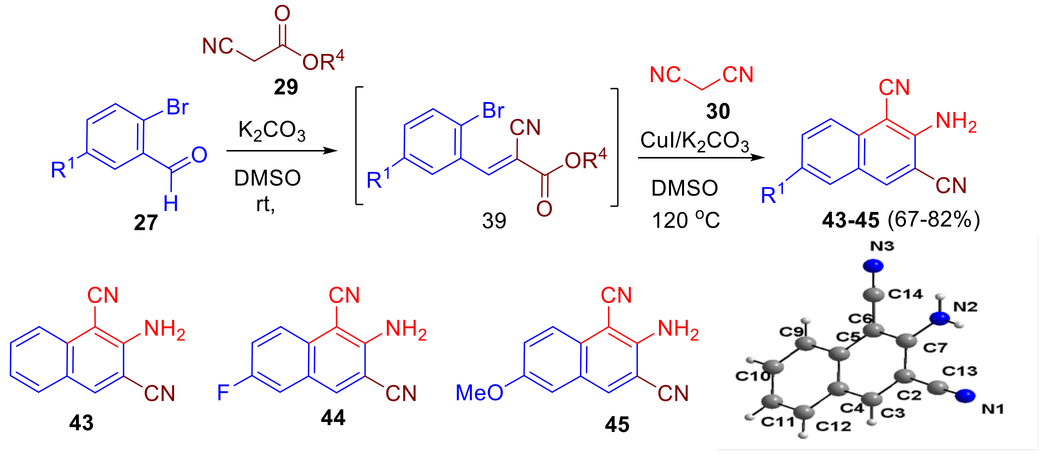
To extend our concept by expanding the scope of substrates, we treated 2-bromobenzaldehyde **27a** (1.0 mmol) with alkyl cyanoacetate **28a-b** (1.0 mmol**)** and K_2CO_3 (1.0 mmol) in DMSO at rt for 1 h to generate intermediates **39a-b**; then CuI (10 mol%), K_2CO_3 (2.0 mmol) and diethylmalonate (**29a**, 1.0 mmol) were added and the contents heated at 120 °C for 2 h. The overall reaction proceeded smoothly to afford diethyl 2-aminonaphthalene-1,3-dicarboxylate **40-41** in 68% yield (Scheme 10). This new one-pot sequence also allowed for the synthesis of polysubstituted phenanthrene **42** in 80% yield from 1-bromo-2-naphthaldehyde **27g** (Scheme 10).



Scheme 10: Cu(I)-catalyzed one-pot sequential synthesis of amino-naphthalene/phenanthrene-dicarboxylates

(iv)(d) Cu(I)-catalyzed one-pot sequential synthesis of 2-aminonaphthalene-1,3-dicarbonitriles

In order to explore the above one-pot sequential method further, malononitrile (**30**; 1 mmol) was used to replace dialkyl malonates **29**. Very interestingly, this reaction afforded 2-aminonaphthalene-1,3-dicarbonitriles **43-45** in 67-82% yield (Scheme 11).

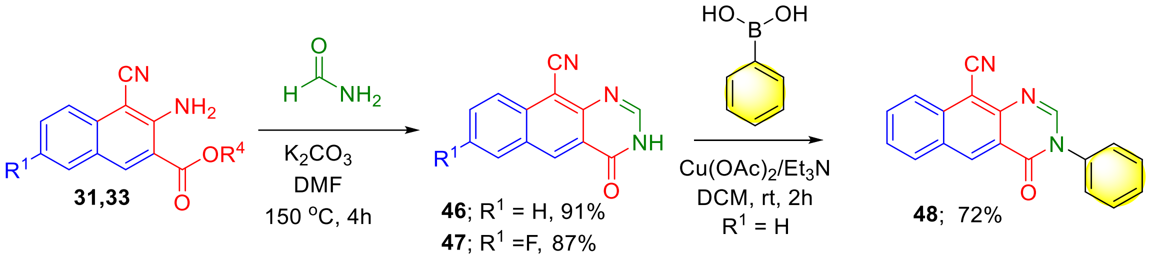


Scheme 11: Cu(I)-catalyzed one-pot synthesis of 2-aminonaphthalene-1,3-dicarbonitrile

(iv)(e) Utilization of the multifunctional naphthalenes

To demonstrate the utility of the present protocol, further structural elaboration of compounds **31** and **33** was performed *via* the reaction with formamide in the presence of

K_2CO_3 to give the corresponding benzo[*g*]quinazoline **46-47**. Later, compound **46** was converted to 4-oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile **48** by using [Cu]-mediated C-N bond forming reaction (Scheme 12).



Scheme 12: Synthesis of 4-oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile from prepared multifunctional naphthalenes

PART A

CYCLIZATION/CYCLOADDITION REACTIONS OF NITRILES AND ALLENES

INTRODUCTION

1.1 General Introduction

Organic substrates with an *sp*-hybridized carbon such as alkynes, nitriles and allenes (**1.1-1.6**) are valuable precursors for numerous synthetic transformations.[1] Although many nitriles are normally used as solvents, they do possess an *sp*-hybrid carbon and hence may be utilized for addition/insertion into acyclic compounds *via* transition metal catalyzed C-H activation.[2] Thus transformations of nitriles into versatile N-heterocycles has been of some utility in organic synthesis.[3-5] Allenes, due to the presence of cumulative double bonds with a central *sp*-hybridized carbon, are quite reactive and are versatile synthons in organic reactions in the synthesis of highly functionalized complex molecules, natural products and active metal complexes.[6] They are also useful substrates in C-C bond formation, C-H functionalization, cyclization, cycloaddition, dimerization and addition reactions.[7-9] Allenylphosphonates, allenylphosphine oxides and allenoates can be synthesized easily using low cost materials; hence these also have proven to be valuable precursors for privileged transformations.[10] Structural representation for all of these is shown in Chart 1.1. Numerous heterocycles like pyrazolines,[11a] pyrrolo-indoles,[11b] chromenes,[11c] quinolines,[11d] sultams,[11e] furans,[11f] naphthalenes,[11g] indoles,[11h] benzofurans, benzopyrans and isocoumarins[11i] can be synthesized *via* allenes.

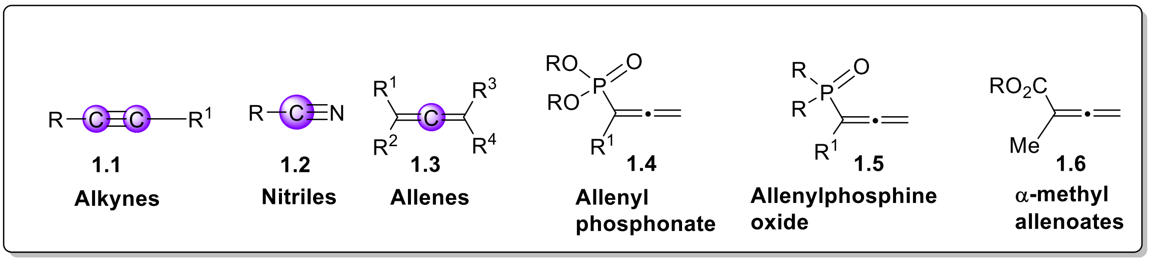
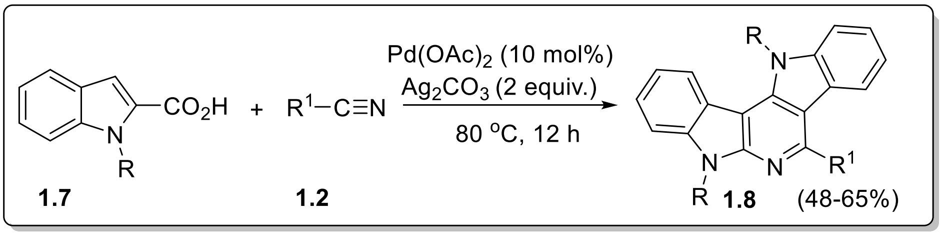


Chart 1.1: Basic structures of *sp*-hybridized precursors discussed in this chapter

In this chapter, literature relevant to (i) transition metal catalyzed addition/insertion of nitriles to yield heterocycles, (ii) transition metal catalyzed/mediated intramolecular cycloaddition/ cyclization reactions of allenes, (iii) intermolecular cycloaddition /annulation reactions of allenoates, (iv) cycloaddition and/ or cyclization reactions of enynones/enynols, where enynone/enynol acts as a 2C synthon, and (v) synthesis of substituted furan fused polycyclic compounds from [Au]/[Ag] catalysis and will be covered.

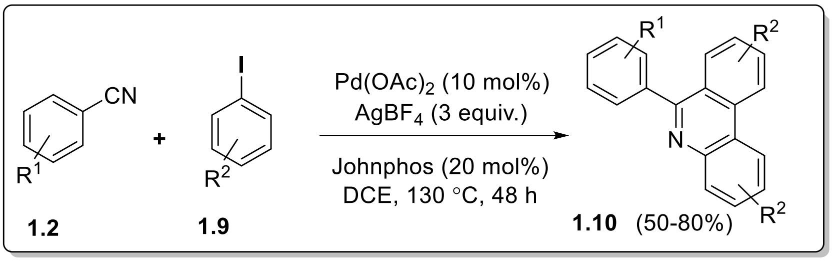
1.2 Transition- metal catalyzed insertion of nitriles followed by cyclization to yield heterocycles

In the year 2015, our group reported the Pd(OAc)$_2$-catalyzed generation of indolocarbolines **1.8** in moderate yields from indole-2-carboxylic acids *via* decarboxylative dual C-H activation of indole-2-carboxylic acids **1.7** followed by nitrile insertion **1.2** (Scheme 1.1).[12] This conversion involved (i) coordination of Pd-with carboxylic acid group (ii) carbopalladation at C3- position of indole (iii) decarboxylation, (iv) transmetalation, (v) reductive elimination [Pd]-catalyst followed by nitrile insertion, intramolecular C-H activation and subsequent cyclization.



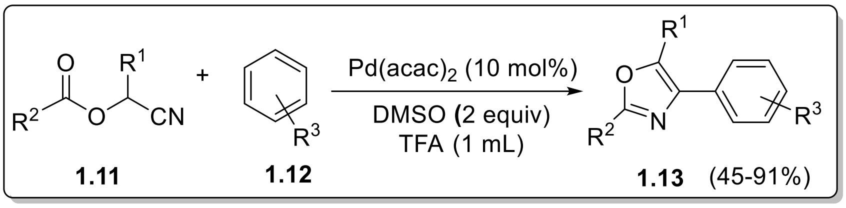
Scheme 1.1: [Pd]-catalyzed insertion of nitriles to indole substrates

In the year 2018, Kumar's group reported the synthesis of multisubstituted phenanthrenes **1.10** by using aryl iodides **1.9** and alkyl or aryl nitriles **1.2** *via* [Pd]-catalysis (Scheme 1.2).[2] This conversion involves [Pd]-catalyzed nucleophilic addition of aryl iodides to nitriles, formation of C-C and C-N bonds followed by imine directed double C-H activation.



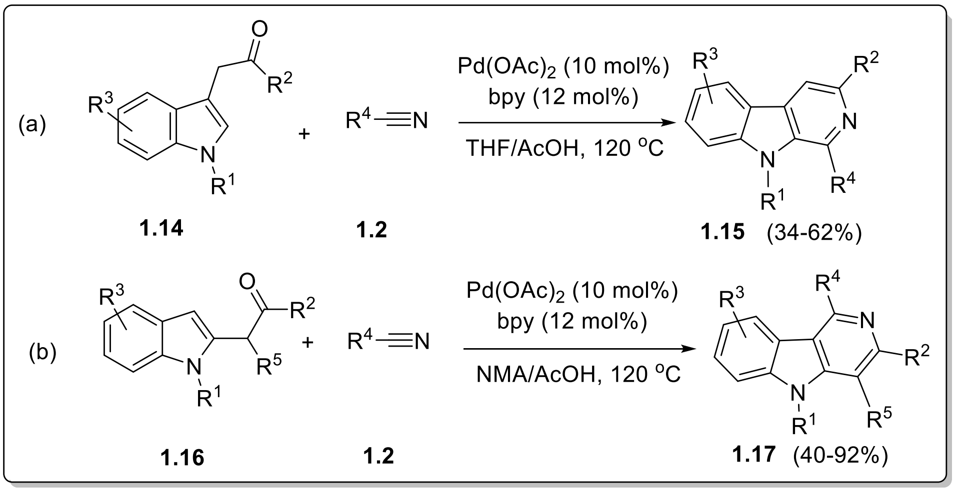
Scheme 1.2: [Pd]-catalyzed reaction of nitriles with aryl iodides

Very recently, Chen's group developed a protocol for the synthesis of functionalized oxazoles **1.13** by using arenes **1.12** and functionalized nitriles (cyanomethyl carboxylates) **1.11** *via* Pd-catalysis (Scheme 1.3).[13] This reaction involved [Pd]-catalyzed C-H activation, carbopalladation of arene group followed by coordination with nitrile moiety then protonation of *in situ* formed imine species to give products after regenerating the catalyst.



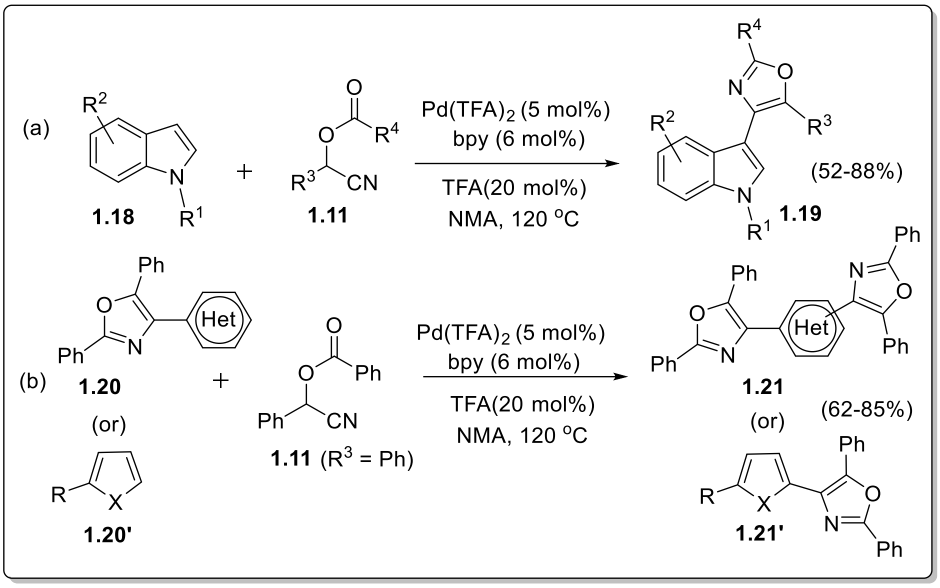
Scheme 1.3: [Pd]-catalyzed insertion of cyanomethyl carboxylates into arenes

Liao *et al* demonstrated [Pd]-catalyzed synthesis of β-carbolines **1.15** and γ-carbolines **1.17** through C-H addition of C-3 substituted and C-2 substituted indole moieties **1.14** and **1.16** (respectively) to the nitrile **1.2** followed by cyclization (Scheme 1.4).[14] This conversion from indoles to carbolines proceeded through direct palladation, coordination to nitrile followed by C-H addition with indole moieties and protonolysis, and finally aromatization followed by regeneration of catalyst obtained desired products.



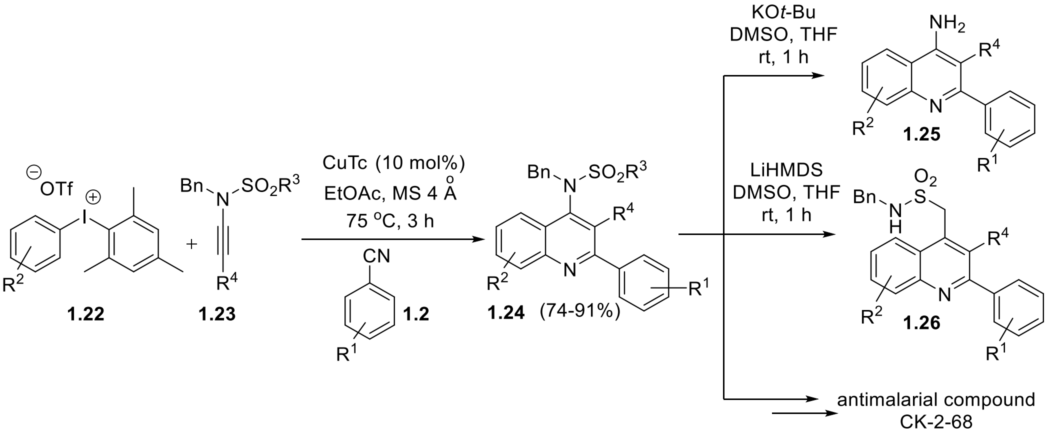
Scheme 1.4: [Pd]-catalyzed insertion of nitriles into indole substrates leading to carbolines

The same group of Liao in 2019 reported the synthesis of multifunctional trisubstituted oxazoles **1.19** and **1.21/21′** from [Pd]-catalyzed C-H addition of polysubstituted heteroarenes **1.18** or **1.20/1.20′** to the cyano moiety of cyanohydrins **1.11** (Scheme 1.5).[15] Initial reaction between heteroarene with [(bpy)Pd(TFA)$_2$] generates a palladium complex, which undergoes coordination with cyano group of cyanohydrins followed by addition with heteroarene and subsequent intramolecular cyclization, protonolysis, elimination and aromatization to form the oxazoles.



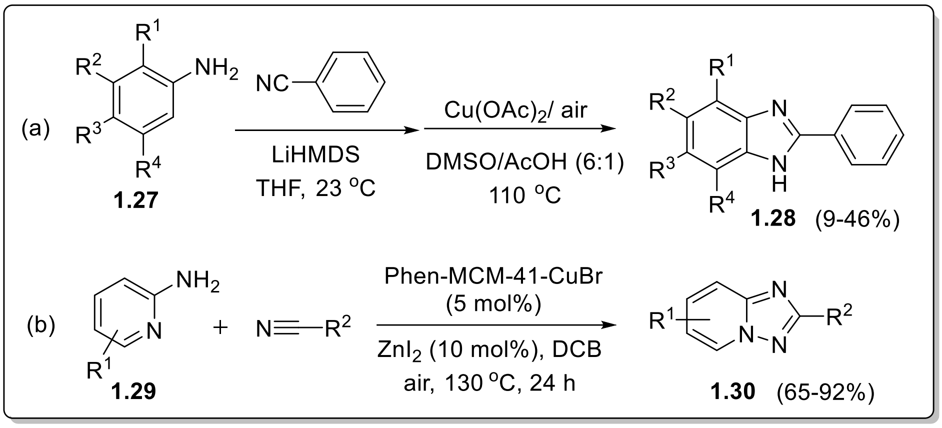
Scheme 1.5: [Pd]-catalyzed insertion of cyanohydrins to form oxazoles

Park's group reported a regio-controlled synthesis of substituted 4-aminoquinolines **1.25-1.26** by [Cu]-catalyzed three component reaction of diaryliodoniums **1.22**, ynamides **1.23** and nitriles **1.2**. Here, [1,3] N to C shift to quinolin-4-ylmethanesulfonamide followed by deprotection of benzyl group, sulfonamide moiety are involved. This approach was also extended to synthesize the antimalarial compound CK-2-68 (Scheme 1.6).[16]



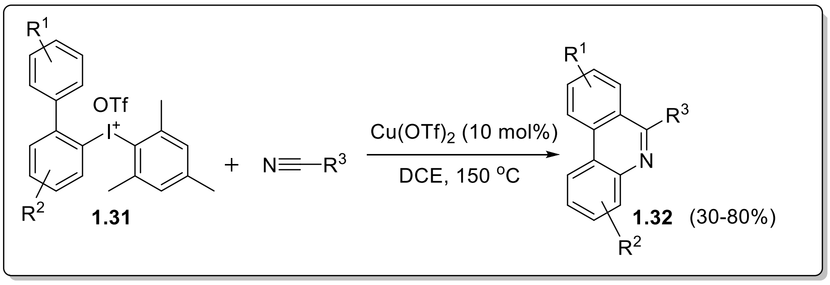
Scheme 1.6: [Cu]-catalyzed insertion of nitriles to form aminoquinolines

Schmitt and colleagues employed anilines **1.27** and benzonitrile to obtain benzimidazoles **1.28** *via* amidine formation followed by oxidative cyclization of anilines using [Cu]-catalysis (Scheme 1.7a).[17] This concept was also extendable to the synthesis of azabenzimidazoles and purines. Earlier in 2019, Cai *et al* reported [Cu]-catalyzed synthesis of 1,2,4-triazoles **1.30** by using 2-amino pyridines **1.29** upon reaction with nitriles *via* heterogeneous addition-oxidative cyclization (Scheme 1.7b).[18] Nucleophilic attack of pyridine moiety on nitrile promoted by copper catalyst with the formed intermediate undergoing proton-transfer followed by [Cu]-catalyzed intramolecular oxidative cyclization affords products **1.35**. Formation of 1,2,4-triazoles from amidines follows a similar pathway.



Scheme 1.7: [Cu]-catalyzed insertion of nitriles to form benzimidazoles and 1,2,4-triazoles

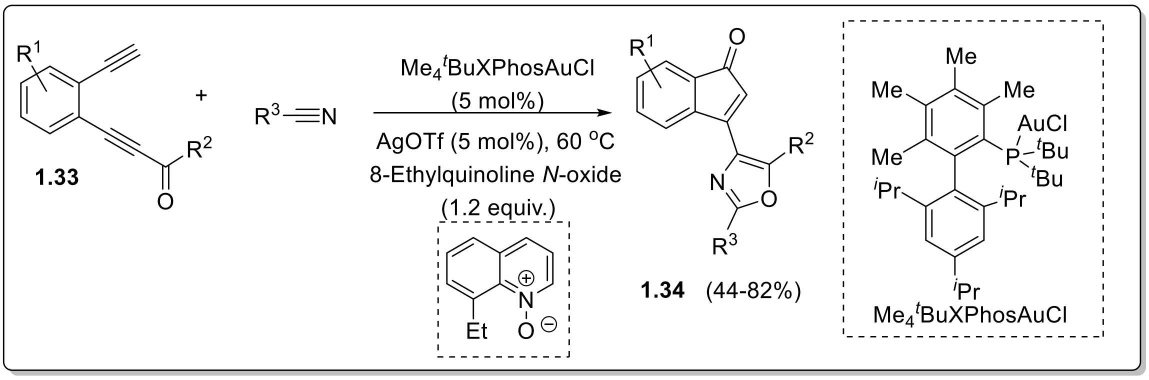
Phenanthridines **1.32** can be obtained by reacting diaryl-iodonium salts **1.31** with nitriles *via* a copper catalysis as shown by Li *et al.* (Scheme 1.8).[19] This conversion involves oxidative addition of [Cu]-catalyst to diaryliodonium salt, addition of nitrile to the formed complex followed by electrophilic annulation.



Scheme 1.8: [Cu]-catalyzed insertion of nitriles to form phenanthridines

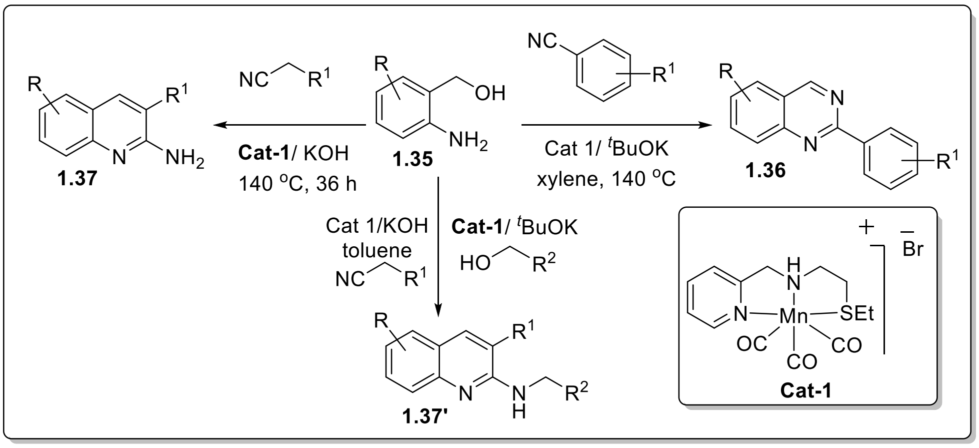
Wang, Hashmi and colleagues demonstrated a gold catalyzed synthesis of substituted oxazoles **1.34** by using diyne **1.33** and nitriles through 1,6-carbene transfer (Scheme 1.9).[20] This conversion involves π-activation of terminal alkyne in the presence of [Au]-

catalyst to generate α-oxo gold carbene through oxidation of alkynes by *N*-oxides. The formed gold carbene undergoes intramolecular cyclopropenation followed by ring opening to form vinyl carbene which subsequently gives the desired product by the reaction with nitriles.



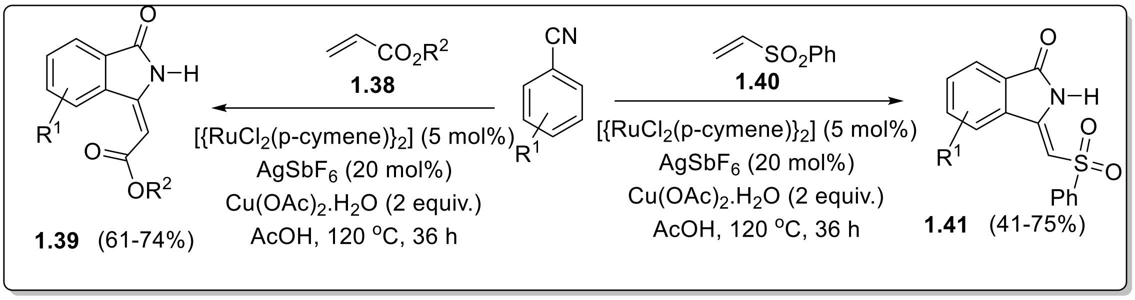
Scheme 1.9: [Au]-catalyzed insertion of nitriles to diynes to form substituted oxazoles

In the year 2019, Srimani *et al* reported Mn-pincer complex (**Cat-1**) catalyzed synthesis of quinazolines **1.36** and 2-aminoquinolines **1.37** through dehydrogenative cyclization by using 2-aminobenzyl alcohol **1.35** upon reaction with nitriles (Scheme 1.10).[21] The synthesis of quinazolines took place *via* dehydrogenation and formation of C-C and C-N bonds whereas formation of 2-(alkylamino)quinolines **1.37′** proceeded through sequential dehydrogenative annulation followed by *N*-alkylation with the alcohols.



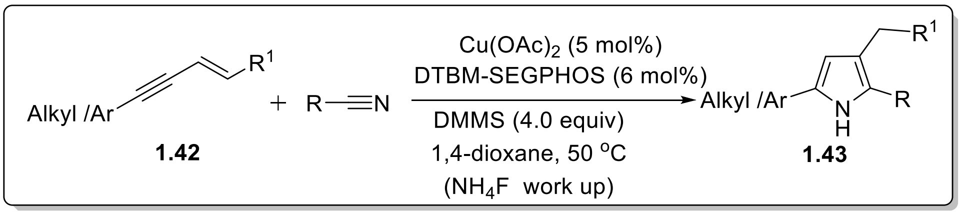
Scheme 1.10: [Mn]-catalyzed insertion of nitriles to aminobenzyl alcohol

Jeganmohan *et al* synthesized 3-methyleneisoindolinones **1.39** and **1.41** with *Z*-selectivity by using activated alkenes **1.38** and **1.39** (alkyl acrylates or phenyl vinyl sulfone) by the reaction with aromatic nitriles *via* [Ru]-catalysis (Scheme 1.11).[22]



Scheme 1.11: [Ru]-catalyzed reaction of nitriles with acrylates

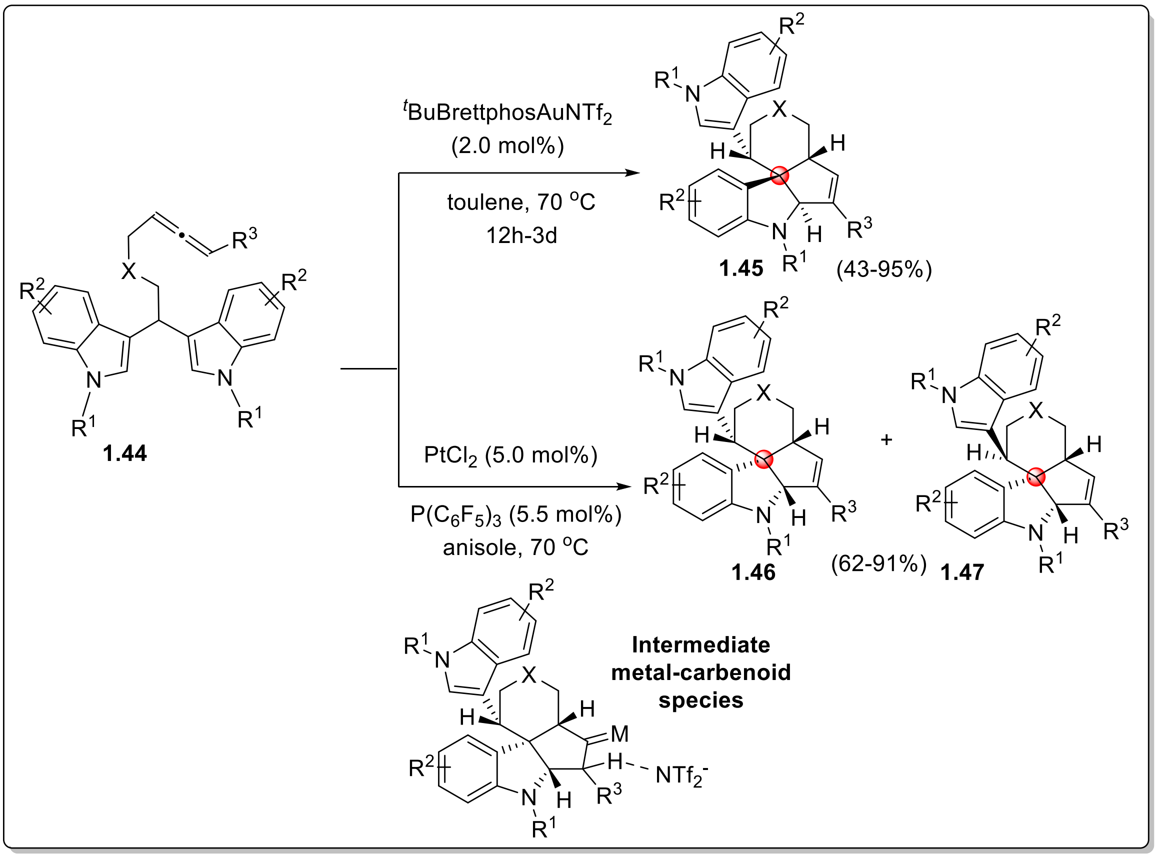
Buchwald *et al* developed [Cu]-catalyzed synthesis of multisubstituted pyrroles **1.43** by using enynes **1.42** and nitriles (Scheme 1.12)[23] which follows reductive coupling followed by intermolecular cyclization.



Scheme 1.12: [Cu]-catalyzed reaction of nitriles with enynes

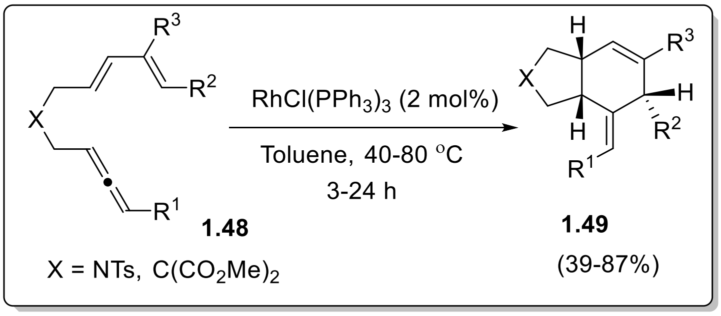
1.3. Transition-metal catalyzed/mediated intramolecular cyclization/ cycloaddition reactions of allenes

Recently, Shi and co-workers reported catalyst controlled cycloaddition reaction of bis-(indol-3-yl)-allenes. This reaction led to different spiroindolines with a spiro-quaternary center (Scheme 1.13).[24] [Au]-catalysis afforded asymmetric desymmetrization product **1.45** with good regioselectivity, whereas [Pt]-catalysis in the presence of $P(C_6F_5)_3$ provided enantiomeric products **1.46-1.47** in good yields. They proposed a mechanism, with assistance from DFT- calculations, in which nucleophilic attack on compound **1.44**, and then reaction with the allene to indole moiety gave cyclized intermediate producing [Pt] or [Au]-carbenoid. This would undergo [1,2]-proton transfer followed by release of catalyst leads to products **1.45** and **1.46-1.47** respectively.



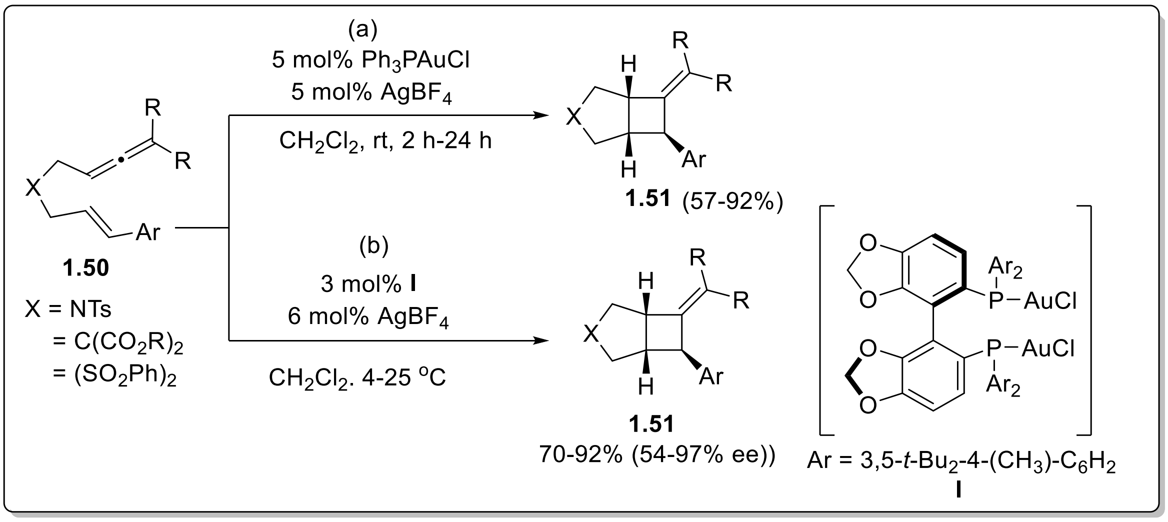
Scheme 1.13: Intramolecular reaction leading to spiroindolines using [Au] or [Pt] catalysis

In the year 2018, Ma *et al* reported [Rh]-catalyzed intramolecular cycloaddition of allene moiety with 1,3-diene group in **1.48** to yield diastereoselective *cis*-5,6-fused bicyclic compounds **1.49** having an exocyclic double bond (Scheme 1.14).^{25} This conversion proceeded through cyclometalation and allylic rearrangement followed by reductive elimination.



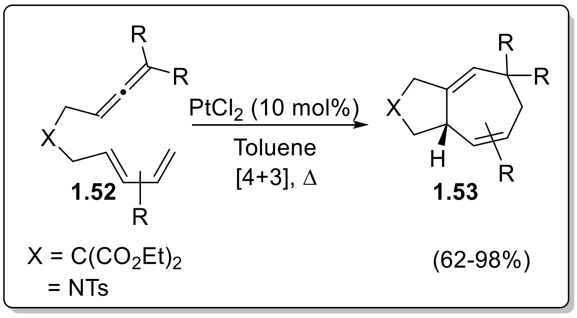
Scheme 1.14: [Rh]-catalyzed intramolecular cycloaddition of allene-dienes

Toste's group has discovered a gold catalyzed [2+2] cycloaddition reaction of allenenes **1.50** to produce substituted cyclobutanes **1.51** (Scheme 1.15).[26] The mechanism of this conversion involves the formation of carbocation *via* nucleophilic attack of alkene moiety to the Au(I)-activated allene, then formed vinyl [Au]-species attacks the benzylic carbocation generating cyclobutane compound **1.51.** The presence of external nucleophile like MeOH opposes the intermediate regioselectivity and generates *trans*-cyclopentane. They also demonstrated enantioselective [2+2] cycloaddition adduct **1.51** in the presence of Au(I)-biaryl complex **I**.



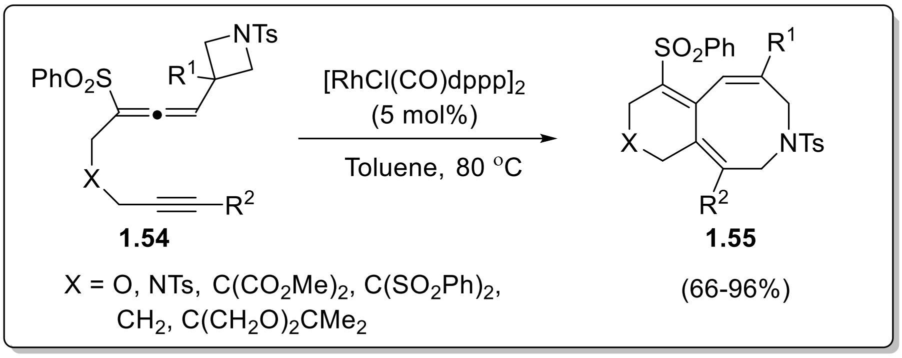
Scheme 1.15: Gold(I)-catalyzed [2 + 2]-cycloaddition of allenenes

In the year 2008, Mascaeñas and his co-workers described platinum [4+3]-cycloaddition of allene-diene **1.52** within the molecule (Scheme 1.16).[27] They constructed bicyclic system **1.53** which has seven membered carbocycle as one of the moieties. In this conversion, allene serves as 3C source and the diene source serves as 4C source.



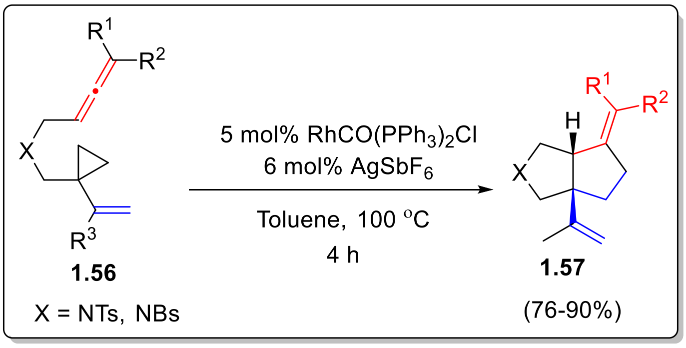
Scheme 1.16: [Pt]-catalyzed [4 + 3]-cycloaddition of allene-dienes

In the year 2016, Mukai's group reported intramolecular hetero-[6+2] cycloaddition of allenylazetidine moiety with alkyne group in **1.54** in the presence of a [Rh]-catalyst. This reaction proceeded *via* metal coordination with allene moiety and alkyne moiety of starting material, C-C bond cleavage of azetidine ring followed by [6+2] type ring closing reaction to yield azabicyclo[6.4.0]dodecatrienes **1.55** (Scheme 1.17).[28]



Scheme 1.17: [Rh]-catalyzed intramolecular [4+3] cycloaddition of allene-ynes

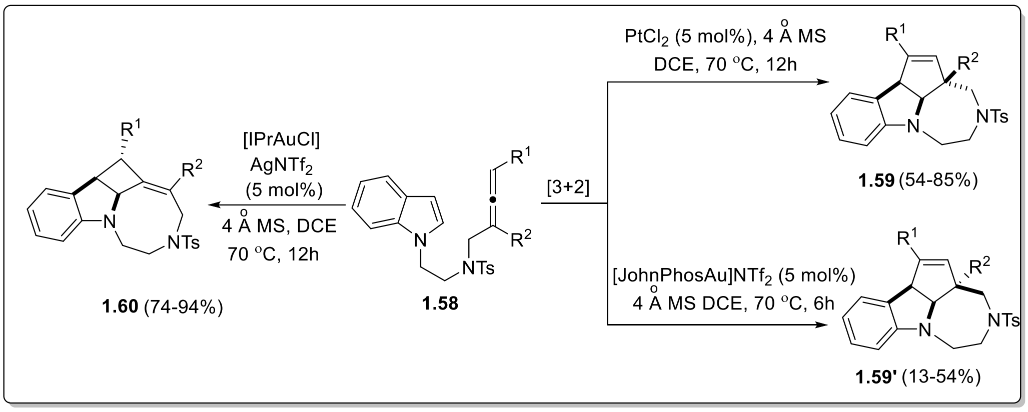
In the year 2018, Yu *et al* reported intramolecular [3+2] cycloaddition reaction of 1-allenyl-vinylcyclopropanes **1.56** to construct 5/5 or 5/6 fused bicycles **1.57** with quaternary stereo-center at bridgehead position as shown in Scheme 1.18.[29] This [3+2] cycloaddition involves the binding of the catalytic rhodium species to alkene group of vinylcyclopropane ring, followed by cleavage of the ring to give reactive intermediate. The inner double bond of allene gets inserted to Rh-C bond, and finally reductive elimination of intermediate may generate fused bicycle **1.57** by regenerating the catalyst.



Scheme 1.18: [Rh]-catalyzed [3 + 2]-cycloaddition of allenyl-vinylcyclopropanes

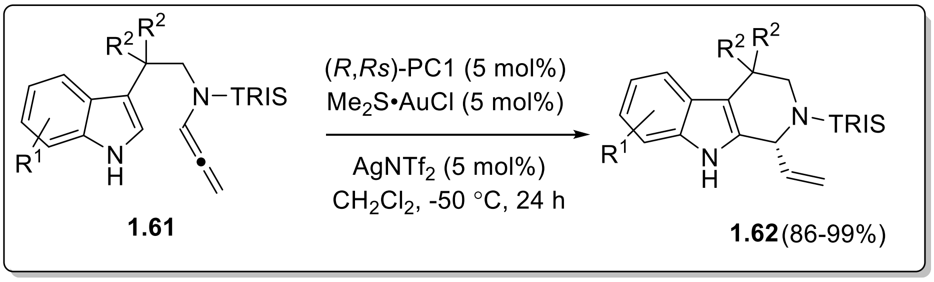
Shi and co-workers demonstrated catalyst dependent stereo-divergent and regioselective synthesis of indole fused heterocyclic compounds **1.59** *via* intramolecular [3+2] cycloaddition pathway using indolylallenes. In the presence of other gold or platinum catalysts, they obtained different diazabenzo[a]cyclopenta[cd]azulenes (**1.59,**

1.59′) as epimers. They obtained **1.60** in the presence of IPrAuCl/ $AgNTf_2$ by highly regioselective [2+2] cycloaddition (Scheme 1.19).[30]



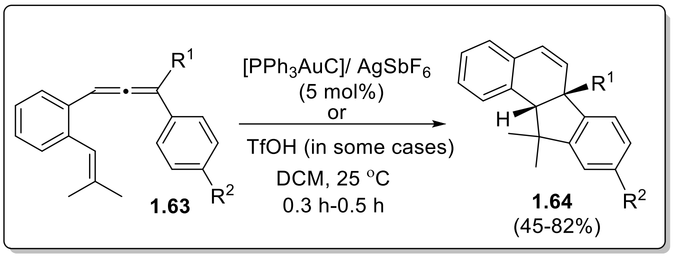
Scheme 1.19: [Au]- or [Pt]-catalyzed [3 + 2] or [2+2] cycloaddition of indolylallenes

In the year 2017, Zhang and co-workers reported intramolecular cyclization of *N*-allenamides **1.61** by using [Au]-catalysis to yield tetrahydrocarbolines **1.62** in the presence of a chiral sulfonamide ligand (Scheme 1.20).[31] The practicality of this reaction was shown by the total synthesis of (*R*)-desbromoarborescidine A and formal synthesis of (*R*)-desbromoarborescidine C.



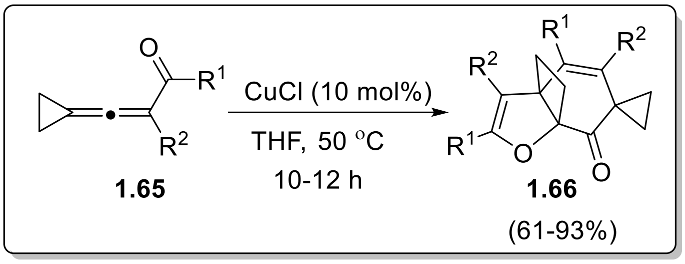
Scheme 1.20: [Au]-catalyzed cyclization of *N*-allenamides

In the year 2009, Liu *et al* reported [3+2] intramolecular cycloaddition reaction of 1-aryl-1-allen-6-enes of type **1.63** in the presence of [PPh_3AuCl]/ $AgSbF_6$ catalyst to generate *cis*-fused dihydrobenzo[a]fluorenes of type **1.64** (Scheme 1.21)[32] *via* 6-*endo-dig* cyclization. This reaction proceeded with the formation of *trans*/*cis* mixtures of substituted naphthalenic cations, which were further converted into desired products.



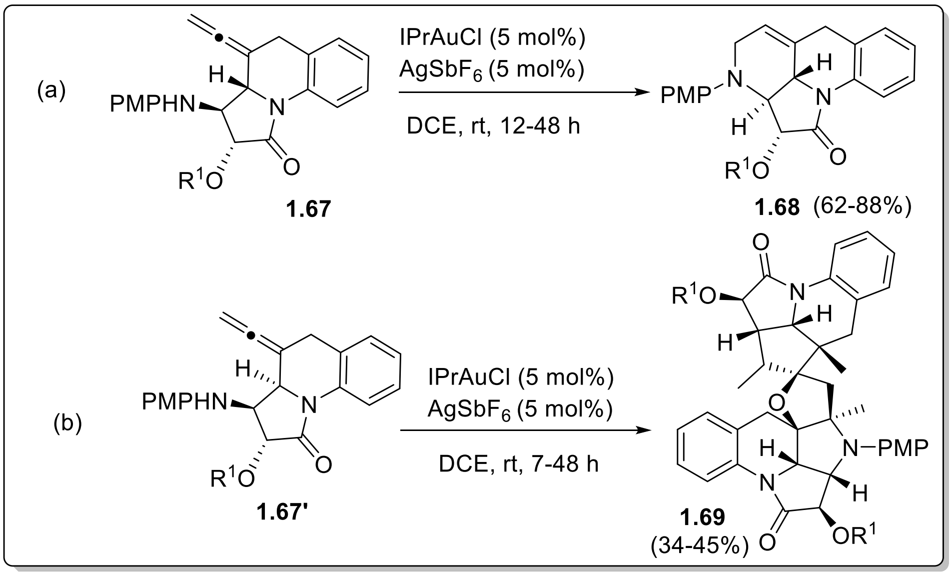
Scheme 1.21: [Au]-catalyzed cyclization of allenenes

In the year 2013, Wu's group developed a methodology of [Cu]-catalyzed intramolecular cyclization and dimerization of 3-cyclopropylideneprop-2-en-1-one **1.65** to synthesize benzofuran-7(3a*H*)-one derivatives **1.66** with a spirocyclopropane ring and a bridged four membered ring (Scheme 1.22).[33] The mechanistic pathway for this conversion involves (i) intramolecular cycloisomerization, (ii) sequential [4+2] cycloaddition (after dimerization) followed by (iii) opening of oxa-bridge, and then the ring.



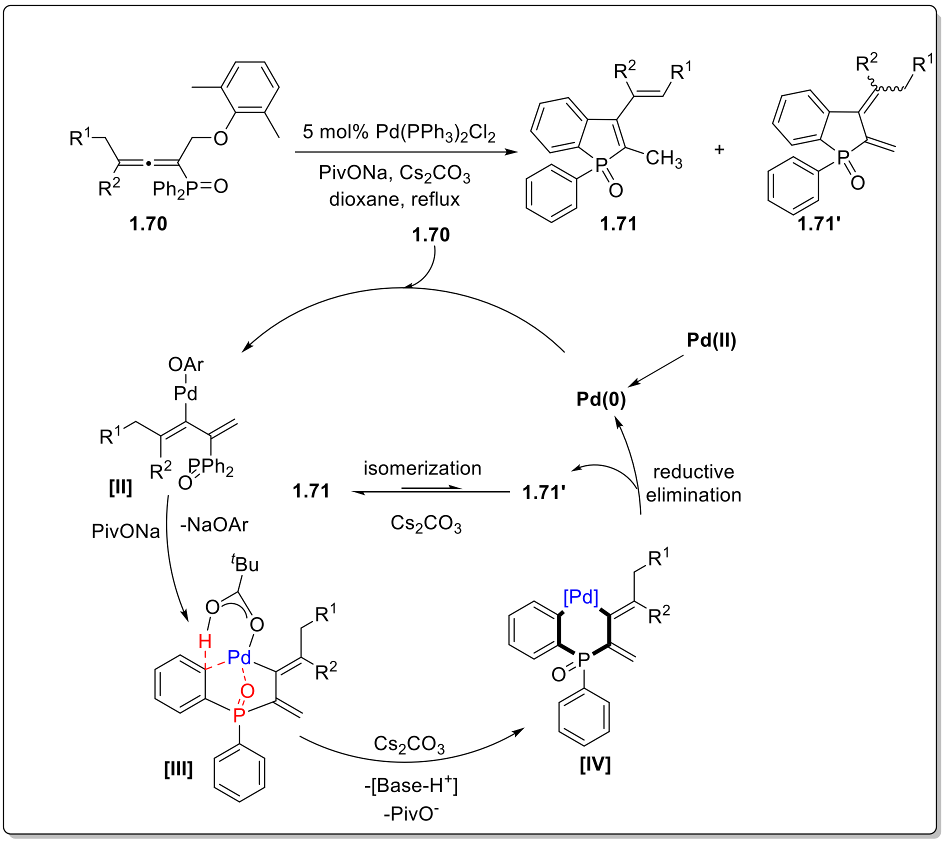
Scheme 1.22: [Cu]-catalyzed cyclization of allenones

In the year 2015, Torres *et al* reported gold catalyzed synthesis of benzo[*b*]pyrrolo-napthridine-1-ones *via* intramolecular cyclization of indolizidinone-tethered *β*-amino allenes. The *syn* isomer **1.67** gave simple cycloisomerization product **1.68** (Scheme 1.23a) whereas *anti*-isomer **1.67′** afforded enantiopure fused spiranic azapolycycles **1.69** *via* dimerization and spirocyclization pathway (Scheme 1.23b).[34]



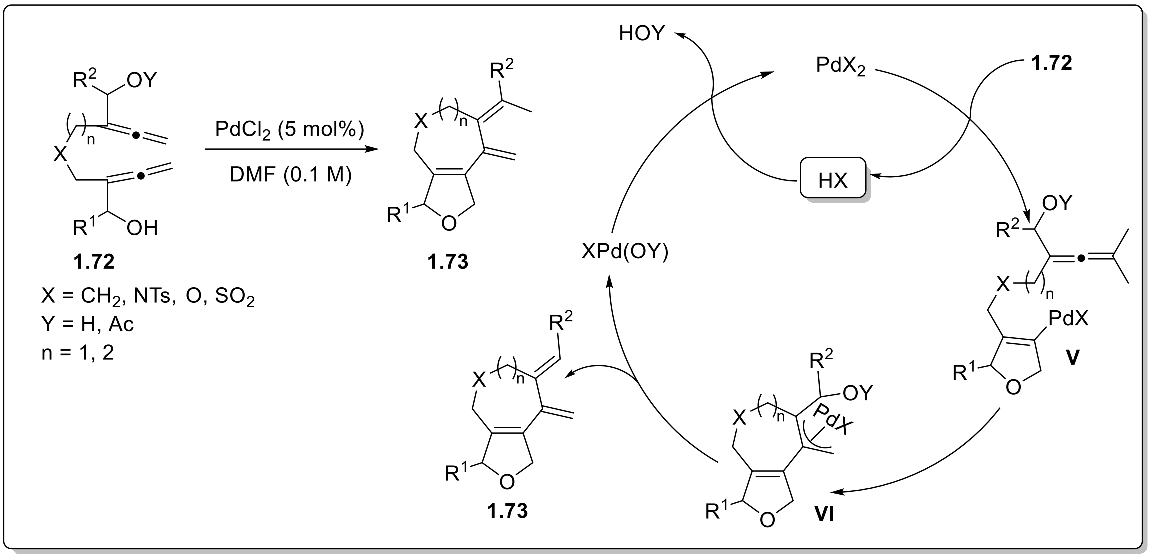
Scheme 1.23: [Au]-catalyzed cyclization of *β*-amino allenes

Wu and co-workers reported palladium catalyzed intramolecular cyclization of P-allenes (allenylphosphine oxides) **1.70** to obtain 3-alkenyl benzo[b]phosphole oxides **1.71** (Scheme 1.24).[35] This conversion involves oxidative addition, immediate cleavage of C-O bond leading to form **II**, followed by C-H activation in the presence of pivalate to generate **III**, which upon eliminating pivalic acid produces six membered palladium complex **IV**. This by reductive elimination gave isomer **1.71′** of product, which in the presence base produced product **1.71** along with regenerated Pd(0) catalyst.



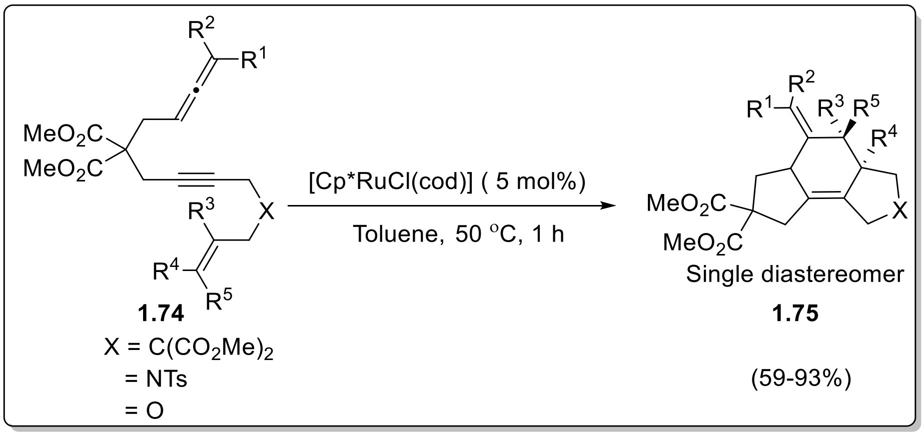
Scheme 1.24: Intramolecular [Pd]-catalyzed cyclization of allenylphosphine oxides

Ma's group demonstrated the synthesis of dihydrofuran fused bicyclic compounds through [Pd]-catalyzed intramolecular cyclization of bisallenols. Between two -OH groups, one was protected with acetate (Scheme 1.25).[36] Mechanism of this conversion involves oxy-palladation of allene **1.72**, generating intermediate **V**. Then intramolecular carbopalladation of another allene moiety in **V** produces P-allylic palladium intermediate **VI**. Further, elimination of acetate group leads to the furan fused bicyclics **1.73**.



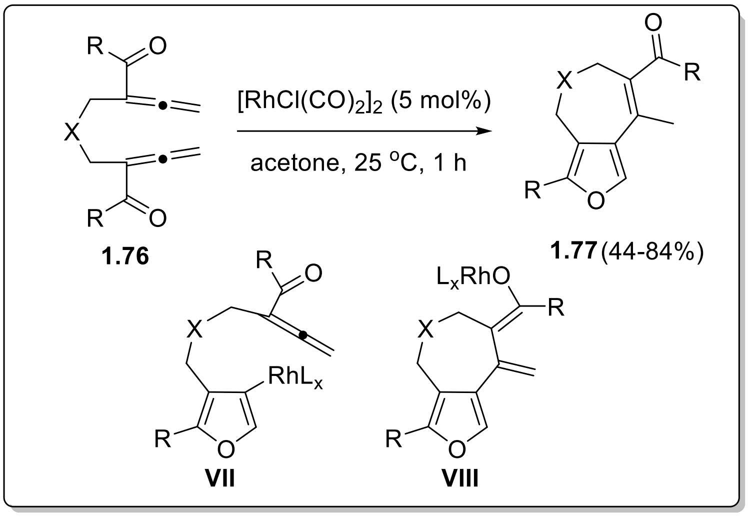
Scheme 1.25: Intramolecular [Pd]-catalyzed cyclization of bis-allenols

In the year 2012, Sato *et al* developed a methodology for intramolecular [2+2+2] cyclization of allene-ene-ynes **1.74** *via* [Ru]-catalysis (Scheme 1.26) through a ruthenacyclopentane intermediate.[37] Initially, allene and alkyne groups of the starting material coordinates with the active site of catalyst to give an intermediate which upon oxidative addition of alkyne with internal double bond of allene affords ruthenacyclopentane species. Further, insertion of alkene generates ruthenacycloheptane, followed by reductive elimination affords tricyclic compounds **1.75**.



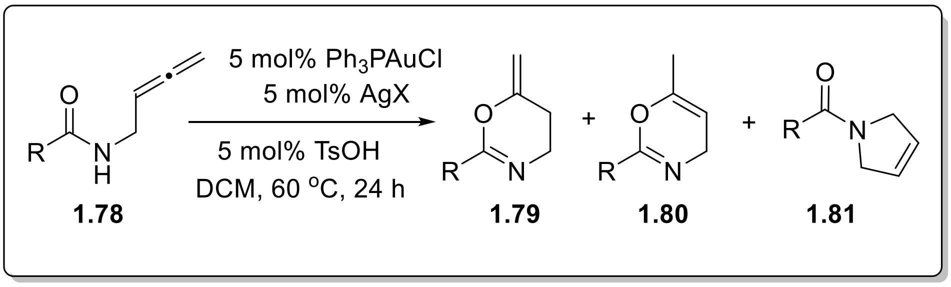
Scheme 1.26: Intramolecular [Rh]-catalyzed cyclization of allenynes

Ma and colleagues reported a rhodium(I)-catalyzed synthesis of 3,4-fused bicyclic furans **1.77** by intramolecular cycloisomerization using 1,5-bis(1,2-allenylketone) **1.76** (Scheme 1.27).[38] The conversion involves cyclic oxymetalation of the starting material **1.76** with rhodium, generating intermediate **VII**. Carbometalation of another unreacted allene unit leads to an intermediate **VIII** with oxygen-bound rhodium dienolate, which upon protonolysis may generate product **1.77**.



Scheme 1.27: Intramolecular [Rh]-catalyzed cyclization of bis-allenes

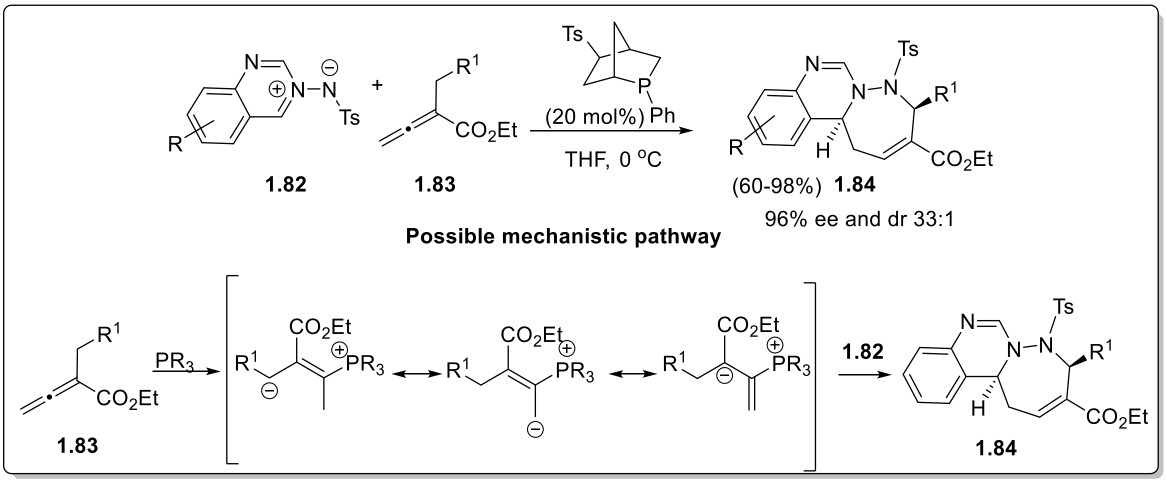
Hashmi *et al* reported gold catalyzed synthesis of 1,3-oxazines **1.79-1.81** by cyclization of allenamides **1.78**; along with oxazines they also obtained dihydropyrroles and *N*-acylpyrrolines **1.81** as minor products (Scheme 1.28).[39] Mechanistic studies by *in situ* ^{31}P NMR spectroscopy suggested only one additional species during the conversion in each case.



Scheme 1.28: Intramolecular [Au]-catalyzed cyclization of allenamides

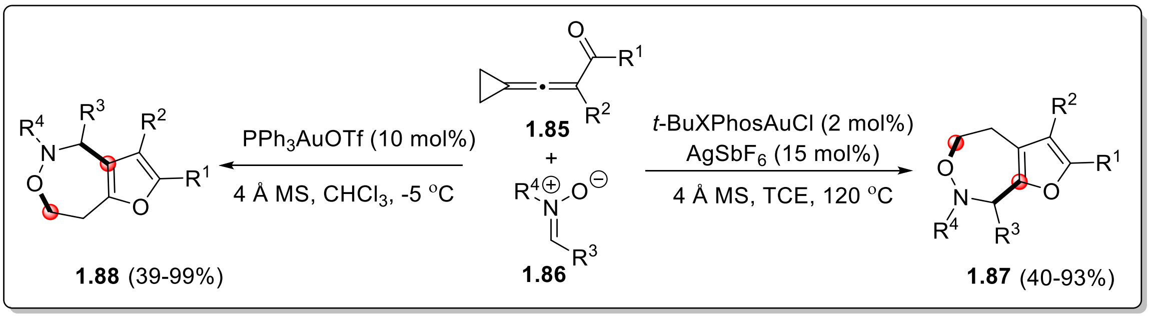
1.4. Intermolecular cycloaddition /annulation reactions of allenoates (with allenoate as 4C-synthon)

In the year 2016, Guo’s group developed a methodology for the synthesis of quinazoline-fused tricyclic heterocycles **1.84** with good enantio- as well as diastereo-selectivity by using allenoates **1.83** *via* [4+3] cycloaddition with cyclic azomethine imines **1.82** through chiral phosphine catalysis (Scheme 1.29).[40] Plausible pathway for this conversion is shown below.



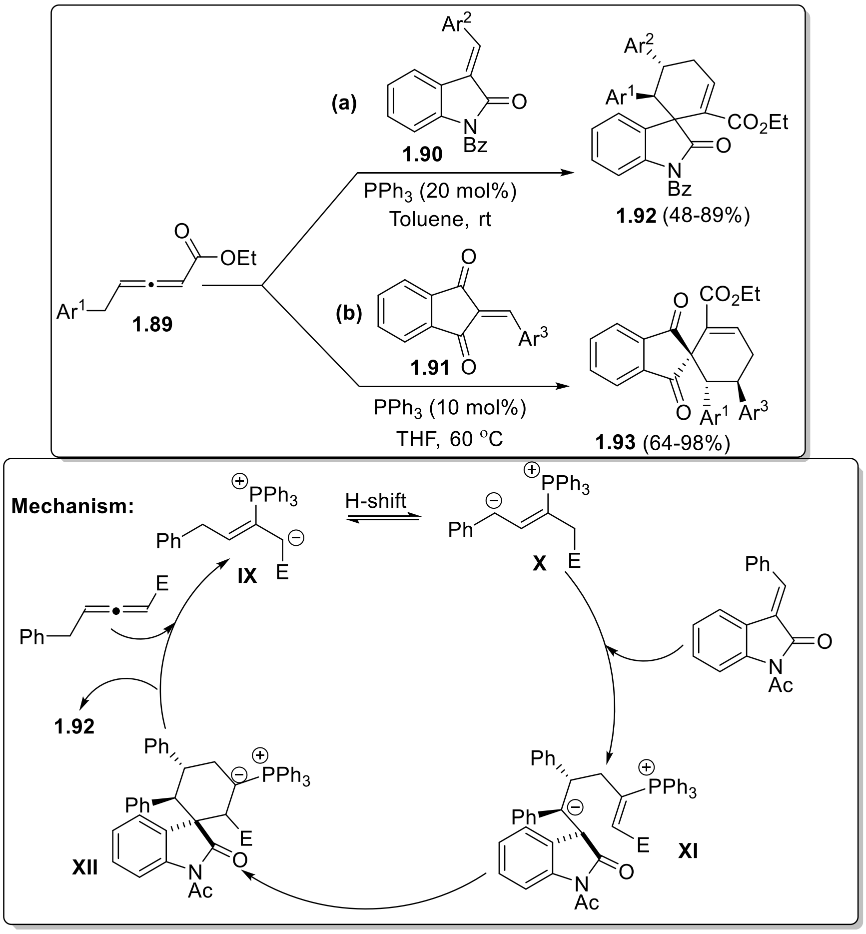
Scheme 1.29: Phosphine-catalyzed cyclization of allenoate with azomethine imines and a possible mechanistic pathway

Recently, Miao, Ren and co-workers reported gold-catalyzed [4+3] cycloaddition reaction of allenyl ketones **1.85** having a cyclopropyl moiety with nitrones **1.86** to produce furan fused heterocycles **1.87-1.88** with good stereo- as well as regio-selectivity (Scheme 1.30).[41] Initially, double bond of allenone moiety induces nucleophilic cyclization leading to a spirocyclic oxonium/carbene. Ring-expansion followed by elimination of metal occurs in the presence catalytic t-BuXPhosAuCl/ $AgSbF_6$; the cationic gold moiety might predominantly react with strained C-C double bond with ring opening, which further could cyclize with nitrone species to give cycloadduct **1.87**. In the presence of PPh_3AuOTf, ring opening followed by intermolecular [4+3] cycloaddition gives product **1.88**.



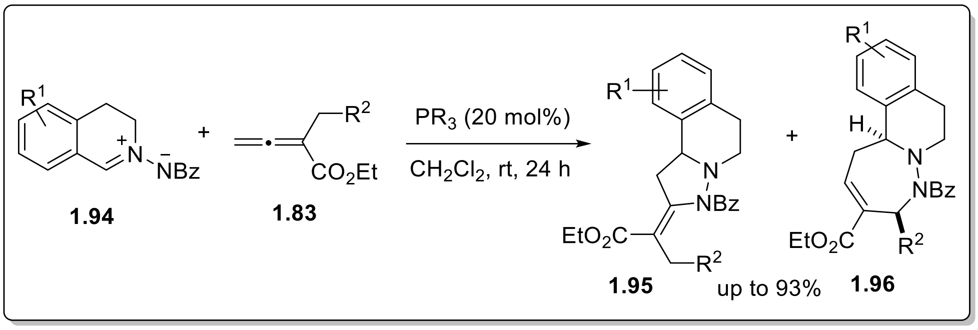
Scheme 1.30: [Au]-catalyzed cyclization of allenyl ketones

Voituriez, Marinetti and co-workers reported Ph_3P mediated synthesis of spirocyclic oxindoles **1.92** by the reaction between substituted δ-aryl penta-2,3-dienoates **1.89** and 3-arylideneoxindoles **1.90** *via* [4+2] annulation. Here, allenoate serves as a 4-C source (Scheme 1.31a).[42a] A plausible pathway for the conversion involves phosphine addition to the β-position of allenoate to produce **IX**; 1,4-H-shift moves negative charge to the δ-position. The phenyl ring present favors this rearrangement to stabilize **X**. Species **X** undergoes addition to olefinic moiety to produce **XI**, which undergoes immediate cyclization to give **XII**; then H-shift and elimination of phosphine gives **1.92**. in a somewhat similar report, Li *et al* reported a methodology for the construction of substituted spiro[4.5]dec-6-enes **1.93** by the reaction between γ-substituted allenoates **1.89** and 2-arylidene-1H-indene-1,3(2H)-diones **1.91** (Scheme 1.31b).[42b] The mechanism for the formation of **1.93** is similar to that for reaction shown in Scheme 1.31a. The allenoates act as 4-carbon synthons in this annulation process.



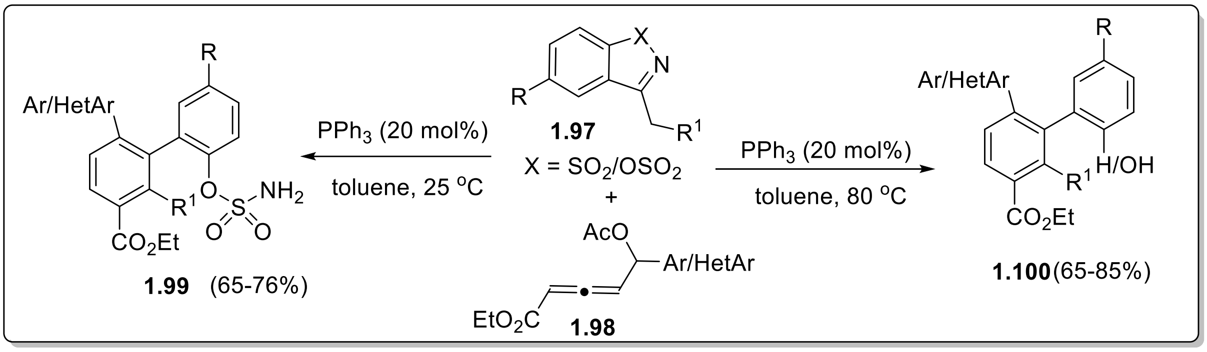
Scheme 1.31: Phosphine-catalyzed spirocyclization of allenoates

Guo *et al* demonstrated a methodology for the synthesis of 1,2,3,5,10b-hexahydropyrazolo[5,1-a]isoquinolines **1.95** and 1,4,5,7,8,12b-hexahydro[1,2]diazepino[7,1-a]isoquinoles **1.96** through [3+2] and [4+3] cycloaddition reactions of cyclic azomethine imines **1.93** with allenoates **1.94** respectively *via* phosphine catalysis (Scheme 1.32).[43] In all these phosphine catalyzed reactions, initially, the phosphine attacks the *sp*-hybridized carbon.



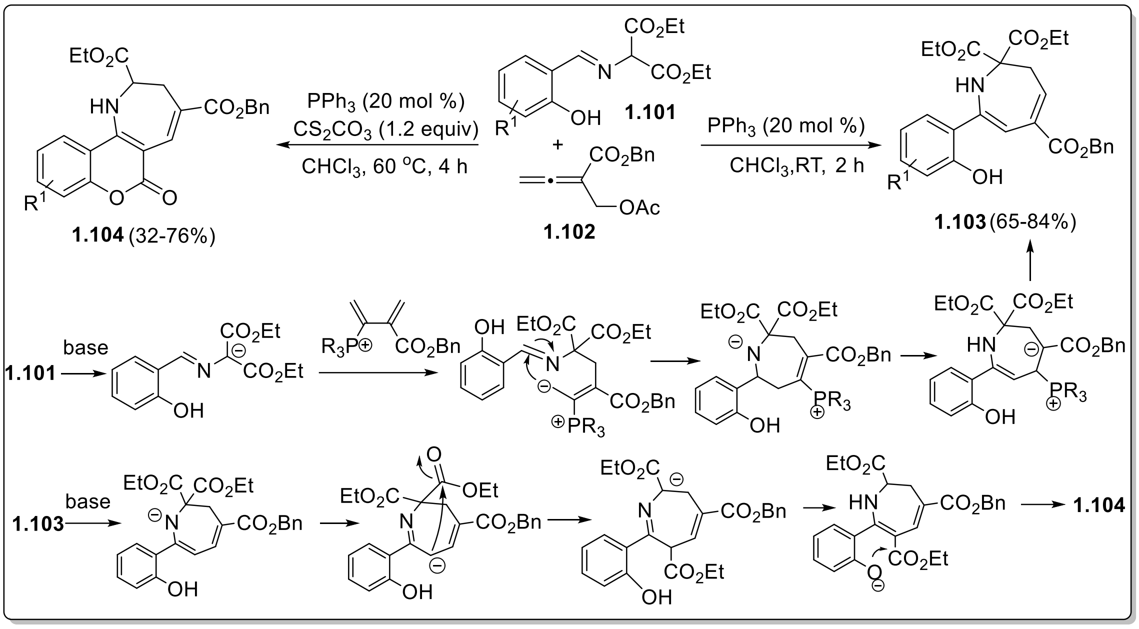
Scheme 1.32: Phosphine-catalyzed cyclization of allenoates with azomethine imines

Our group has reported Lewis base catalyzed [4+2] annulations between cyclic *N*-sulfonyl imines **1.97** and δ-acetoxy allenoates **1.98**. In the presence of phosphine, imines acts as C/C donors and generate terphenyls **1.99-1.100** through S$_N$2’-attack, Michael addition, Mannich coupling and C-N bond cleavage/aromatization (Scheme 1.33).[44]



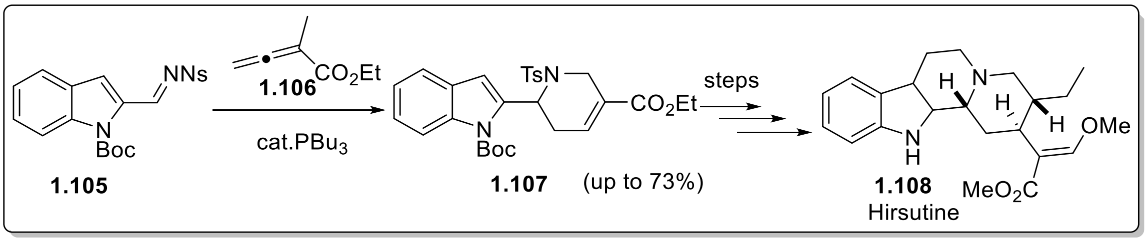
Scheme 1.33: Phosphine-catalyzed cyclization of acetoxy allenoates with sulfonylimines

Recently, Zhou’s group obtained azepine-2,2,4-tricarboxylates **1.103** from aldimine esters **1.101** and β′-acetoxy allenoates **1.102** by using phosphine catalysis. The formation of **1.103** using catalytic PPh_3 or [4+3]/1,5-ethoxycarbonyl migration/lactonization for the formation of chromeno[4,3-b]azepin-6(1H)-ones **1.104** when the reaction was performed in the presence of PPh_3 and Cs_2CO_3 as shown in Scheme 1.34.[45]



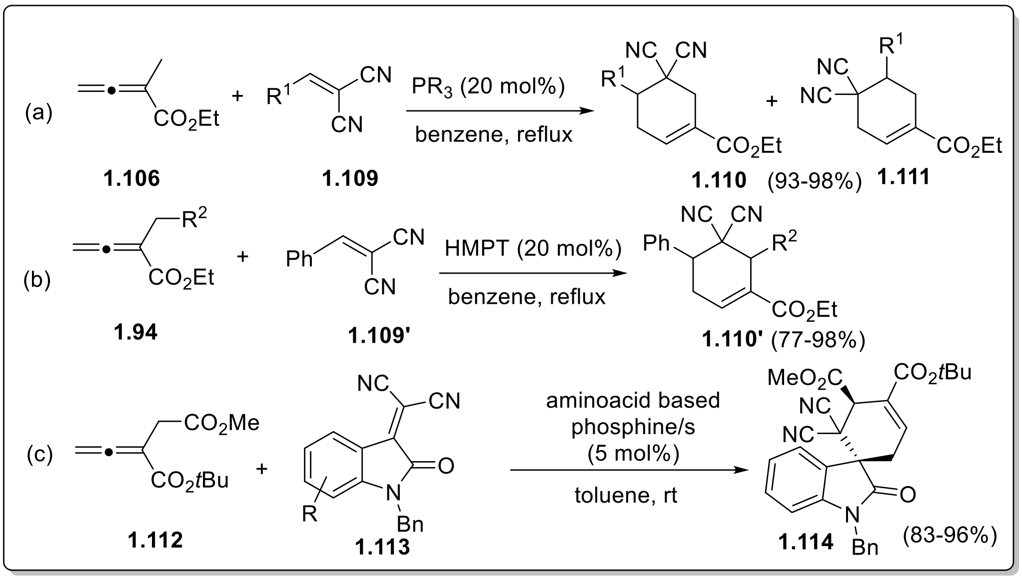
Scheme 1.34: Phosphine-catalyzed cyclization of acetoxy allenoates with aldimine esters

In the year 2012, Kwon's group developed [4+2] annulation of the indolyl imine **1.105** with α-methyl allenoate **1.106**. This application was a key step in the total synthesis of hirsutine **1.108** from **1.107**, which is an indole alkaloid (Scheme 1.35).[46]



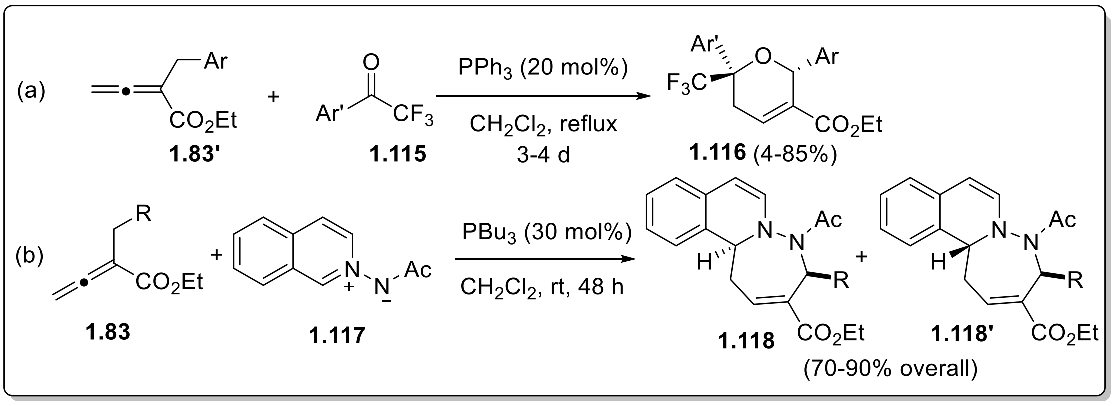
Scheme 1.35: Phosphine-catalyzed cyclization of allenoates with aldimines

In the year 2007, Kwon's group developed a methodology for the synthesis of polysubstituted cyclohexenes (**1.110-1.111**) from allenoates **1.94** by the reaction with benzylidene malononitrile groups (**1.109**, **1.109′**) by means of phosphine catalysis.[47] The reaction proceeded *via* [4+2] annulation (Scheme 1.36a-b). In contrast to this, Lu and co-workers reported a methodology for the synthesis of 3-spirocyclohexene-2-oxindoles **1.114** through amino acid-phosphine catalysis by using allenoates **1.112** and activated alkenes **1.113** (with malononitrile type moiety) *via* [4+2] cycloaddition pathway (Scheme 1.36c).[48]



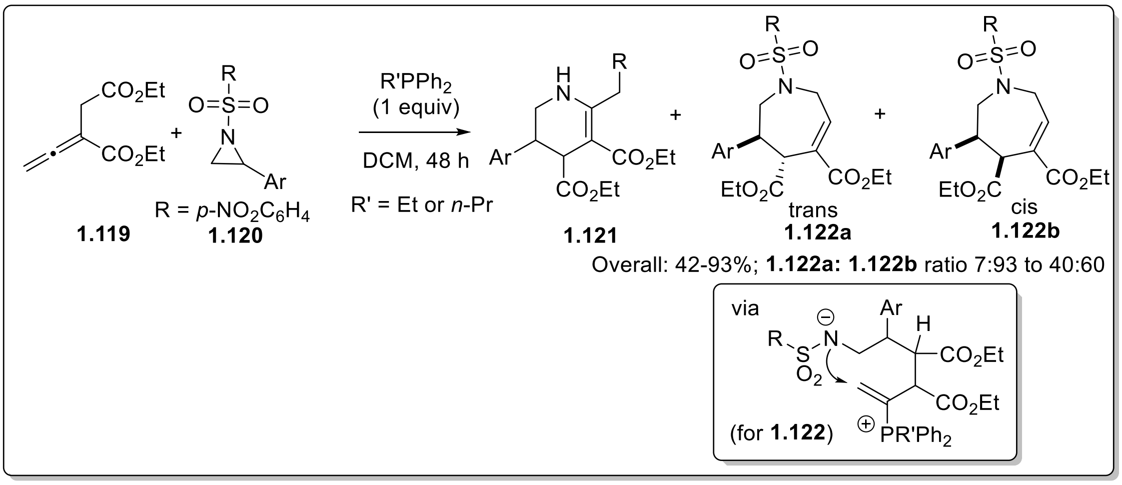
Scheme 1.36: Phosphine/aminophosphine catalyzed cyclization using allenoates and benzylidene or indole based malononitriles

Phosphine catalysis has also been widely used for many other reactions of allenoate chemistry. Ye *et al* reported a methodology for the preparation of 6-trifluoromehyl-5,6-dihydopyrans **1.116** from benzyl allenoates **1.83′** and trifluoromethyl ketones **1.115** by using posphine catalysed [4+2] annulation pathway (Scheme 1.37a).[49] Guo's group reported tributylphosphine catalyzed synthesis of nitrogen fused heterocycles **1.118-1.118′** from allenoates **1.83** by reaction with azomethine imines **1.117** *via* [4+3] cycloaddition (Scheme 1.37b).[50]



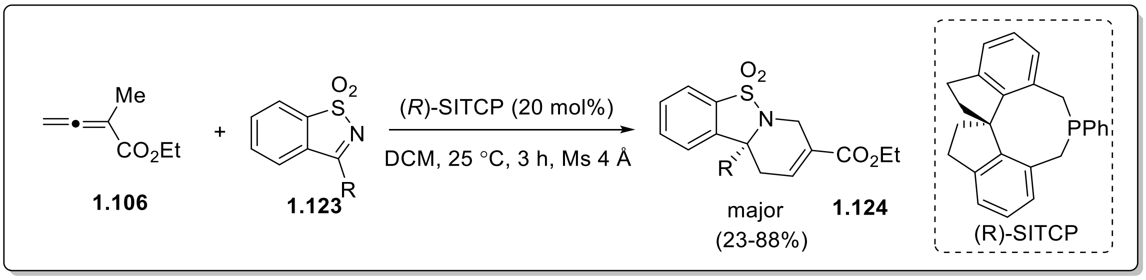
Scheme 1.37: Phosphine catalyzed [4 + 2] and [4 + 3] cyclization/annulation of allenoates

Kwon, Guo and co-workers also reported phosphine mediated [3+3] and [4+3]-annulations of allenoate **1.119** with aziridines **1.120** with for the synthesis of functionalized tetrahydroazepines **1.122** in excellent diastereoselectivity, along with a 6-membered *N*-heterocycles **1.121** (Scheme 1.38).[51] While PPh_3 preferentially led to **1.121** *via* intramolecular desulfonylation, alkyl substituted phosphines R'PPh_2 led to 7-membered ring compounds **1.122**. This methodology is the first phosphine-promoted [4+3]-annulation involving aziridines and allenoates.



Scheme 1.38: Intermolecular cyclization/annulation of allenoates with aziridines

In the year 2014, Sasai and group reported an organocatalytic and enantioselective synthesis of tetrahydropyridines **1.123** from allenoate **1.106** and saccharin derived ketimines **1.124** *via* [4+2] cycloaddition (Scheme 1.39).[52]

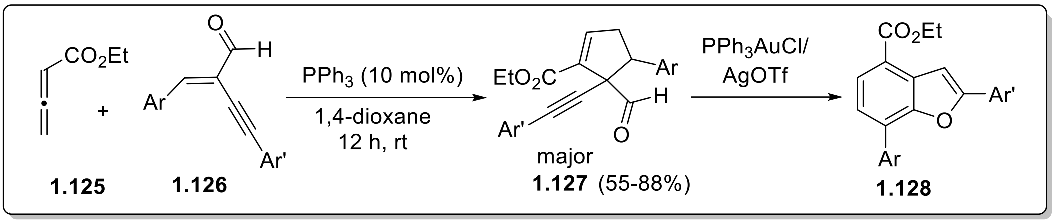


Scheme 1.39: Phosphine catalyzed reaction of allenoate with a ketamine

It is clear from the above examples that allenoates function as good substrates in multitudes of cyclization/annulation reactions, especially under phosphine catalysis. This is an aspect we wanted to explore in the current work.

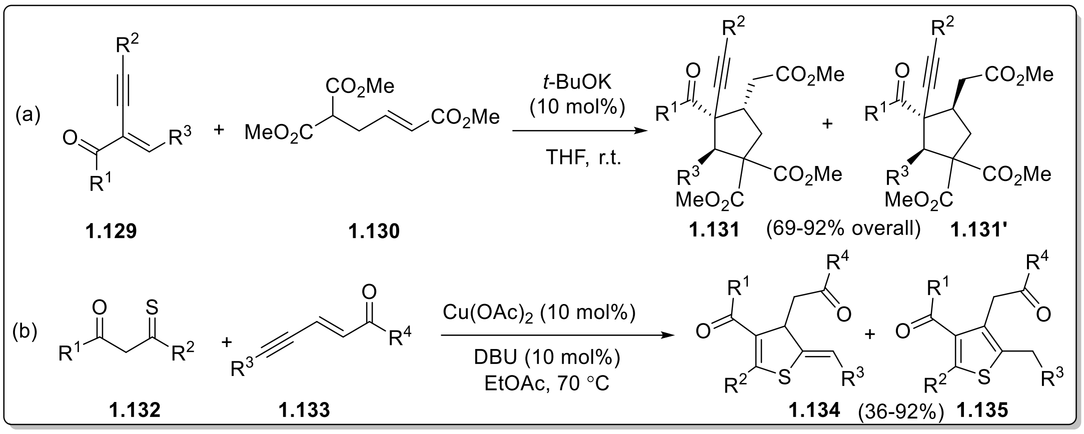
1.5. Cycloaddition and/or cyclization reactions involving enynones/enynals (where enynone/enynal acts as a 2C synthon)

Enynones and enynals consist of three different functional groups and are powerful building blocks for the synthesis of diverse polycyclic compounds.[53] These precursors readily undergo cycloaddition reactions, which subsequently can undergo chemical transformations in the presence of transition metal catalysis.[54] Since our group is working on allenes/allenoates, we were curious to check the reactivity of allenoates with enynones. A few reports on reactions of enynones where enynones/enynals acted as a 2C synthon are given below. We ourselves reported a Ph_3P catalyzed [3+2]-cycloaddition between allenoates **1.125** and enynals **1.126** to obtain functionalized cyclopentenes **1.127** (major), which under [Au]/[Ag] catalysis led to benzofurans **1.128** through 1,2-alkyl migration and aromatization (Scheme 1.40).[55]



Scheme 1.40: Phosphine catalyzed reaction of allenoate **1.125** with enynal **1.126**

In the year 2009, Zhang's group developed a methodology for the synthesis of multifunctional cyclopentanes **1.131-1.131′** by using enynones **1.129** upon reaction with malonate derived α,β-unsaturted substrates **1.130** by using base catalysis (Scheme 1.41a).[56] Later in 2018, Luo, Deng and their coworkers reported a methodology for the synthesis of dihydrothiphenes **1.134** and multifunctionalized fully substituted thiophenes **1.135** *via* [Cu]-catalysis by reacting thioamides **1.132** with enynones **1.133** where enynone acted as a 2C synthon. This conversion proceeded through Michael addition and cyclization followed by protonation (Scheme 1.41b).[57] Although there are several other reports on the reactivity of enynones/enynals,[58] they are not related to the present work and hence are not elaborated here.

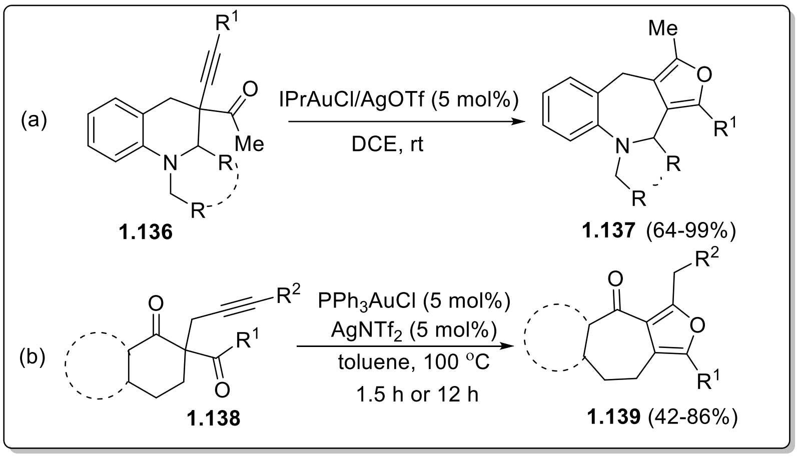


Scheme 1.41: Examples showing reactivity enynones (as 2C-synthons)

1.6 Synthesis of substituted furan fused polycyclic compounds from [Au]/[Ag] catalysis

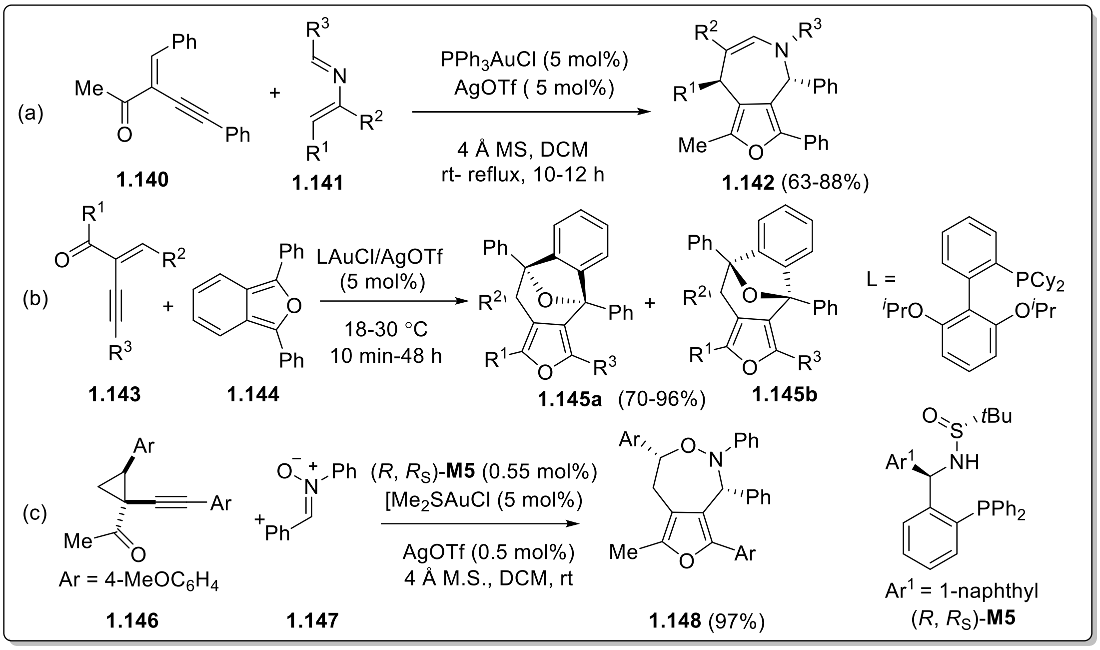
Furan is an important scaffold in many natural products, pharmaceuticals; it is also a fundamental unit in organic molecular electronics.[59] Synthesis of multisubstituted polycyclic furans utilizing gold catalysis by activation and functionalization of alkynes/ alkenes has drawn much attention.[60] Since a part of our work deals with [Au]-catalysis, a few relevant literature reports that feature synthetic methods for polycyclic furan-fused compounds *via* [Au]-catalysis are described below.

In the year 2012, Zhang and co-workers developed a synthetic methodology for furan fused heterocyclic compounds **1.137** from substituted ring-fused tetrahydroquinolines **1.136** using IPrAuCl/ AgOTf catalyst combination (Scheme 1.42a).[61] The precursors underwent C-C bond cleavage and cyclization followed by 1,2'-alkyl migration to yield furan fused tetrahydroazepines **1.137**. In the year 2017, Zhu *et a*l developed synthesis of furan fused polycyclics **1.139** *via* gold and silver catalyzed ring expansion of alkynones **1.138** as shown in Scheme 1.42b.[62] This reaction proceeded through ring fragmentation with [Au]-protodeauration, then aromatization followed by Friedel-Crafts reaction.



Scheme 1.42: [Au]-catalyzed reaction of enynones leading to fused furan scaffolds

Zhang and co-workers reported the synthesis of polysubstituted furan-fused azepines **1.142** in excellent diastereoselectivity from 2-(1-alkynyl)-2-alkene-1-ones **1.140** by reacting with hetero-dienes **1.141** using [Au]/[Ag] catalysis (Scheme 1.43a).[63] The reaction involves (i) cyclization of ketone in the presence of [Au]-catalyst, (ii) addition of imine species to the formed carbocation, (iii) intramolecular 2,7-spirocyclization followed by 1,2-alkyl migration. The same group reported the synthesis of furan-fused polycyclic compounds **1.145a-b** from enynones **1.143** and 1,3-diphenylisobenzofurans **1.144**, by cycloisomerization/[4+3] cycloaddition using gold catalysis (Scheme 1.43b).[64] Zhang *et al* also developed a methodology for the synthesis of furan fused heterocyclic compounds **1.148** by using 1-(1-alknyl)cyclopropyl ketone **1.146** and nitrones **1.147** *via* gold catalyzed [4+3] cycloaddition as shown in Scheme 1.43c.[65]



Scheme 1.43: [Au]-catalyzed reaction of enynones to obtain fused furan scaffolds

The above discussion makes it clear that compounds with an *sp*-hybridized carbon have versatile reactivity with much current interest. Specific topics to be investigated in this work are delineated under the objectives section.

OBJECTIVES OF THE PRESENT WORK - PART A

The main motto of this part of the present work was to study cyclization and or cycloaddition reactions of nitriles, allenes, and allenoates, (all of which possess a *sp*-hybridized carbon) *via* transition metal catalysis. It was planned to study

(i) [Pd]-catalyzed reaction of 2,3′-biindoles by the reaction with **nitriles** to see if a general method can be found to obtain fused α-carbolines (pyridodiindoles) and cyanation of 2,3′-biindoles

(ii) Cyclization and cycloaddition reactions of **allenylphosphine oxides** in presence of [Pd] obtained [Pd] incorporated complexes and phosphorus-containing naphthalenes,

(iii) [4+2]-Cycloaddition reaction between **allenoates** and **enynones** followed by [Au]-catalysis that could afford multifunctional cyclohexenes and cyclohepteno-furan carboxylates.

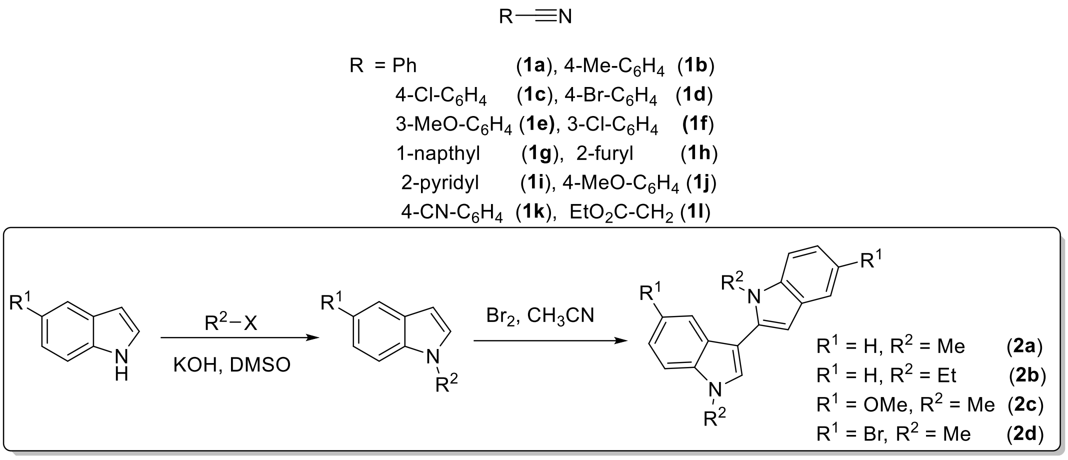
RESULTS AND DISCUSSION

In this part, we shall discuss transition metal catalyzed cyclization/ cycloaddition reactions of nitriles, allenylphosphine oxides, and allenoates. Precursors used along with their synthesis will be presented in section 2.1. In section 2.2, [Pd]-catalyzed nitrile insertion into 2,3′-biindoles with C-H activation and cyclization to obtain indole fused α-carbolines (pyridodiindoles) as well as cyanation of biindoles from ethyl cyanoacetate are presented. In the next section 2.3, unusual behavior of allenylphosphine oxides in the presence of different amounts of $Pd(OAc)_2$ loading will be discussed. This aspect refers to the formation of Pd-incorporated allene complexes in the presence of stoichiometric amount of [Pd]-catalyst. Thus prepared complex could itself be used as a catalyst for nucleophilic addition reactions of phosphorus based allenes. This is followed by intramolecular cycloaddition of allenes in the presence of catalytic $Pd(OAc)_2$ to generate multifunctional P-containing naphthalenes. In the last part of this chapter (section 2.4), phosphine catalyzed cycloaddition reactions of α-methyl allenoate with enynones will be discussed; the products so obtained were utilized in [Au]-catalyzed cyclization/ rearrangement to yield multisubstituted dihydrocyclohepta-furan carboxylates. Characterization of the obtained products has been done by using mp (for solids), IR, NMR, LCMS, and HRMS/CHN analyses along with single crystal X-ray structure determination for illustrative compounds.

2.1 Precursors and their synthesis

2.1.1 Nitriles 1a-l and 2,3′-biindoles 2a-d

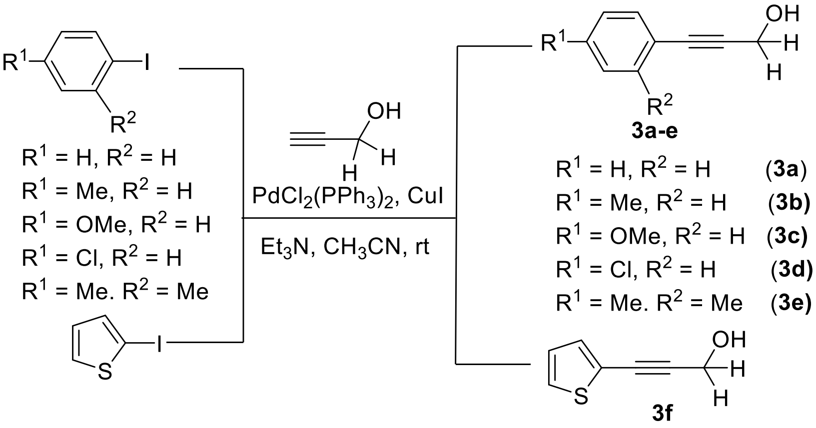
Nitriles **1a-l** are available commercially. 2,3′-Biindoles **2a-d** were prepared by using a known literature procedure (Scheme 1).[66] The yields of 2,3′-biindoles were in the range of 60-70% after purification by column chromatography.



Scheme 1: Nitriles and 2,3′-biindoles used in the present study; also shown is the synthetic route to 2,3’-indoles

2.1.2 Propargylic alcohols 3a-f

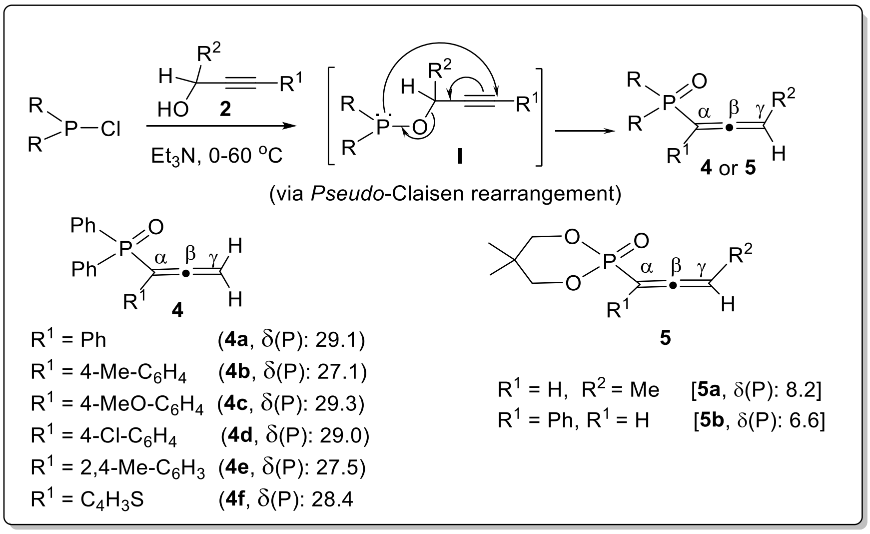
The propargylic alcohols **3a-f**, which were used as starting materials for the synthesis of allenes, have been prepared by Sonogashira cross-coupling between aryl iodides and propargylic alcohol (Scheme 2) by following a literature procedure.[67]



Scheme 2: Synthesis of propargylic alcohols **3a-f**

2.1.3 Allenylphosphine oxides 4a-f and allenylphosphonates 5a-b

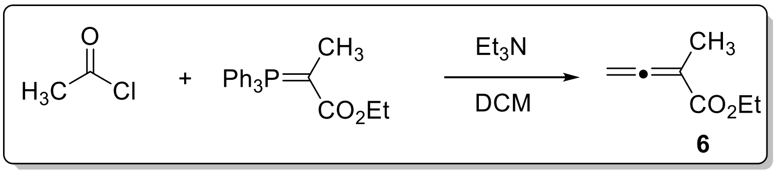
Allenylphosphine oxides **4a-f** and allenylphosphonates **5a-b** were prepared by following a method which was reported from our laboratory (Scheme 3).[68a-c] The synthesis involves the reaction of P^{III}-Cl precursor R_2PCl [R = Ph or R_2 = $(OCH_2CMe_2CH_2O)$] with the propargylic alcohols **3** in the presence of triethylamine. Allenylphosphine oxides or allenylphosphonates are formed *via* a *pseudo*-Claisen rearrangement of the initially formed P^{III} intermediate **I**. The ^{31}P NMR spectra of allenylphosphine oxides **4a-f** and allenylphosphonates **5a-b** exhibit a characteristic peak in the ranges δ 27-30 and δ 6-8, respectively.



Scheme 3: Synthesis of allenylphosphine oxides **4a-f** and allenylphosphonates **5a-b** from propargylic alcohols

2.1.4 α-Methyl allenoate 6

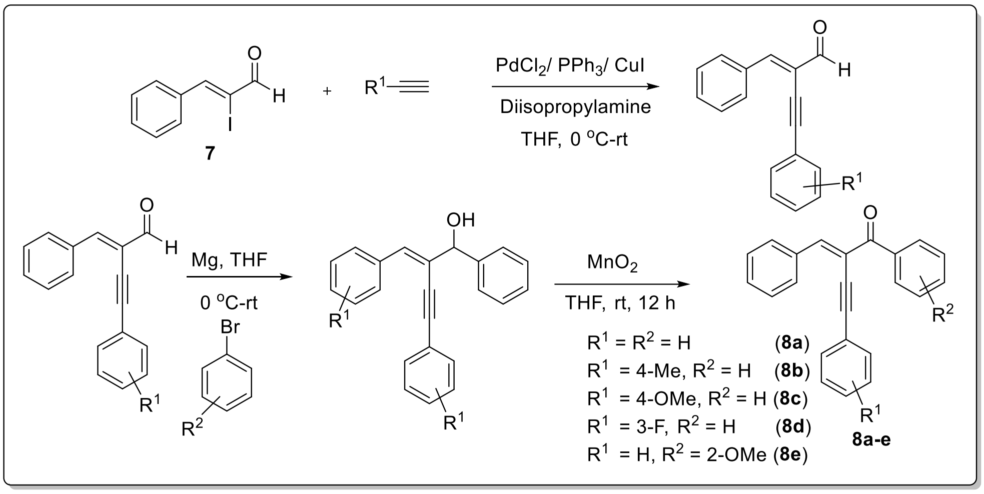
Allene **6** was prepared by controlled addition of acetyl chloride in DCM to a solution of the phosphorus ylide in DCM and Et_3N (Scheme 4).[68d]



Scheme 4: Synthesis of α-methyl allenoate **6**

2.1.5 Functionalized enynones 8a-e

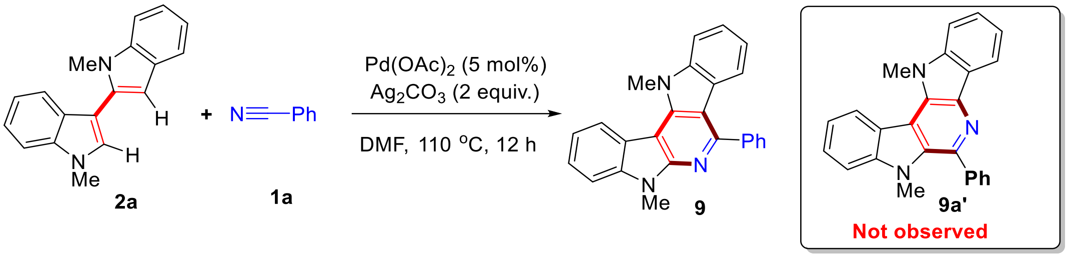
Functionalized enynone substrates **8a-e** were synthesized from the Grignard reaction of corresponding enynals (which were prepared by corresponding 2-iodo-cinnamaldehydes **7** with various phenylacetylenes)[69a-c] with aryl/alkyl halides, followed by oxidation by using MnO_2 (Scheme 5).[69d]



Scheme 5: Synthesis of enynones **8a-e** from 2-iodo-cinnamaldehydes **7**

2.2 [Pd]-Catalyzed reaction of 2,3′-biindoles with nitriles: Synthesis of indole fused α-carbolines (pyridodiindoles and cyanated biindoles

As our research group has been working on transition metal catalyzed reactions of molecules possessing *sp*-hybridized carbon, we became interested to check the reactivity of nitriles towards 2,3′-biindoles in the presence of [Pd]-catalysts. In such an attempt, we treated benzonitrile **1a** with biindole **2a** in the presence of $Pd(OAc)_2$ (5 mol%) and Ag_2CO_3 (2 equiv) in DMF at 110 °C for 12 h (Scheme 6; entry 1 in Table 1). We obtained the desired product **9** in 64% yield along with 15% of unreacted starting material. Next, we examined the reaction with different oxidants such as AgOAc, Ag_2O, $Cu(OTf)_2$ and $CuCl_2$ (entries 2-5). No product was observed by using $CuCl_2$ as the oxidant and only traces of product **9** was formed by using $Cu(OTf)_2$. Use of AgOAc or Ag_2O as an oxidant afforded a lower yield of the α-carboline **9**. Satisfyingly, we observed an yield of 86% when we used $Pd(OAc)_2$ (5 mol%) as the catalyst with $Cu(OAc)_2$ (2 equiv) as the oxidant in DMF solvent at 110 °C for 12 h (entry 6). Use of $PdCl_2$ as catalyst did not enhance the amount of product **9** (entry 7). The reactions by using other Pd-catalysts like $Pd(TFA)_2$ (5 mol% or 2.5 mol%), $PdCl_2(PPh_3)_2$ (5 mol% or 2.5 mol%) or $Pd(dppf)Cl_2$•DCM (5 mol%) did not improve the yield of product (entries 8-10). Changing the solvent from DMF to xylene, acetonitrile, or toluene also did not increase the yield (entries 11-13). There was no product formation when THF and nitromethane were used as solvents (entries 14-15). Also, we did not observe any product formation in the absence of the catalyst (entry 16). Finally, addition of 20 mol% of PPh_3 only slightly increased the yield (Entry 17). Hence, we chose the conditions in entry 6 to study the scope of this reaction. It should be noted that the isomeric β-carboline 9**a’** was not observed in this reaction.



Scheme 6: Synthesis of indole fused α-carbolines (pyridodiindoles) from 2,3′-biindole and nitrile

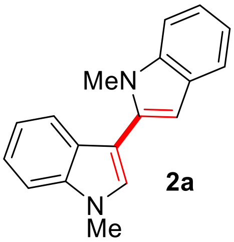
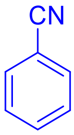
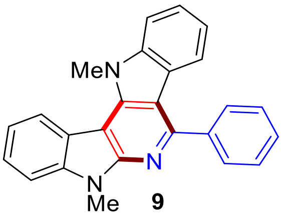
Table 1. Optimization of the reaction conditions for the synthesis of indole fused α-carbolines.[a]

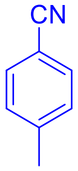
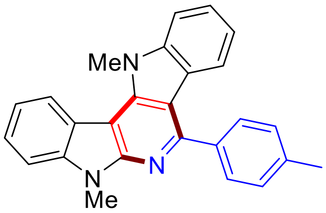
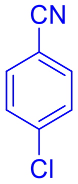
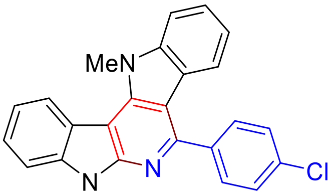
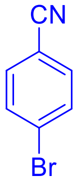
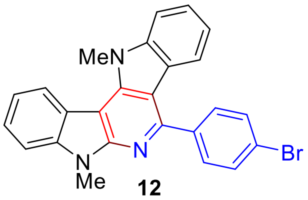
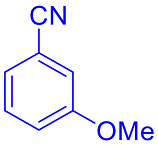
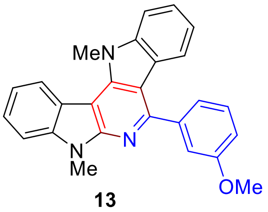
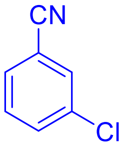
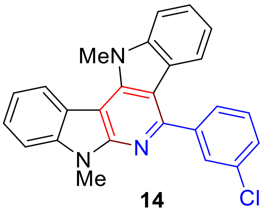
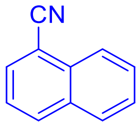
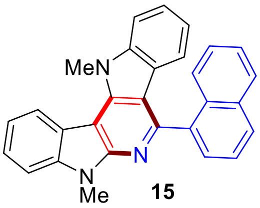
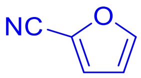
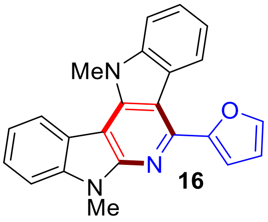
Entry	Pd-catalyst	Oxidant	Solvent	Yield **9** (%)[b]
1	$Pd(OAc)_2$	Ag_2CO_3	DMF	64
2	$Pd(OAc)_2$	AgOAc	DMF	60
3	$Pd(OAc)_2$	Ag_2O	DMF	58
4	$Pd(OAc)_2$	$Cu(OTf)_2$	DMF	70
5	$Pd(OAc)_2$	$CuCl_2$	DMF	nd
6[c]	**$Pd(OAc)_2$**	**$Cu(OAc)_2$**	**DMF**	**86**
7	$PdCl_2$	$Cu(OAc)_2$	DMF	nd
8	$Pd(TFA)_2$	$Cu(OAc)_2$	DMF	79(35[d])
9	$PdCl_2(PPh_3)_2$	$Cu(OAc)_2$	DMF	22(12[d])
10	$Pd(dppf)Cl_2$	$Cu(OAc)_2$	DMF	nd
11	$Pd(OAc)_2$	$Cu(OAc)_2$	Xylene	48
12[e]	$Pd(OAc)_2$	$Cu(OAc)_2$	CH_3CN	25
13	$Pd(OAc)_2$	$Cu(OAc)_2$	Toluene	36
14[e]	$Pd(OAc)_2$	$Cu(OAc)_2$	THF	nd
15[e]	$Pd(OAc)_2$	$Cu(OAc)_2$	CH_3NO_2	nd
16[f]	-	$Cu(OAc)_2$	DMF	nd
17[g]	$Pd(OAc)_2$	$Cu(OAc)_2$	DMF	88

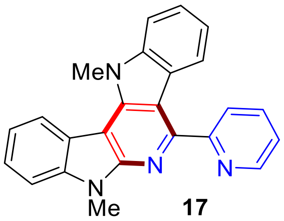
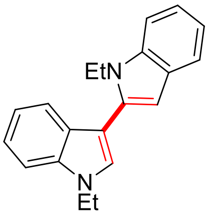
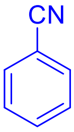
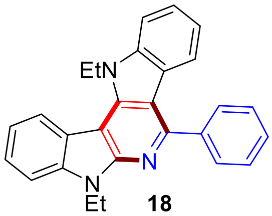
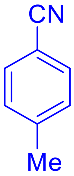
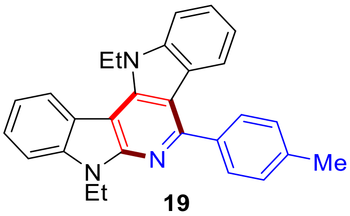
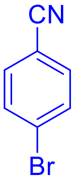
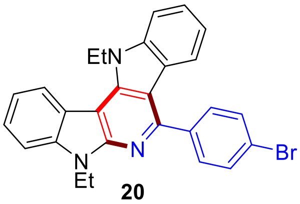
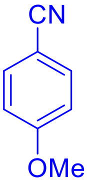
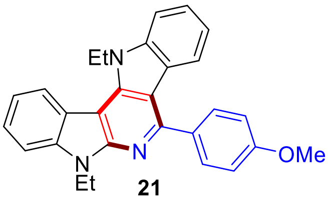
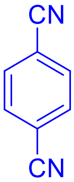
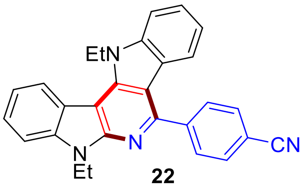
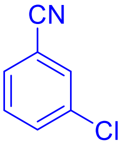
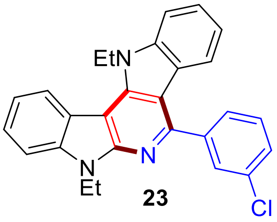
[a]Reagents and conditions: 2,3′-biindoles (0.38 mmol), nitrile (0.38 mmol), Pd(OAc)$_2$ (5 mol%, 0.019 mmol), Cu(OAc)$_2$ (0.76 mmol, 2 equiv), solvent (2 mL), 110 °C (oil bath), 12 h. [b]Isolated yield. [c]The optimized conditions are given in bold. [d]Reaction performed by using 2.5 mol% of catalyst. [e]Reaction performed at reflux. [f]No catalyst was used; nd = not detected. [g]Reaction performed by adding 20 mol% of PPh$_3$.

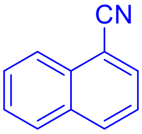
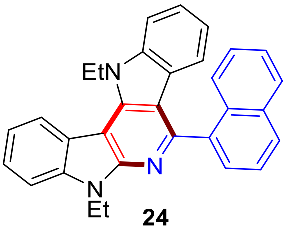
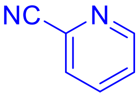
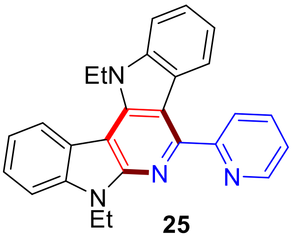
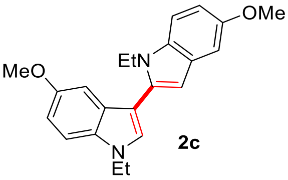
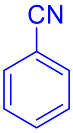
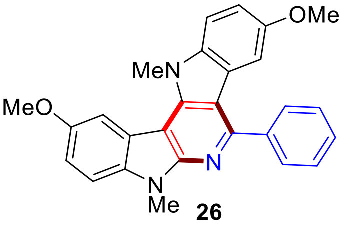
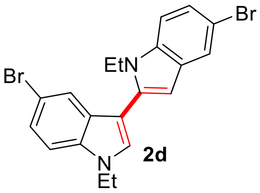
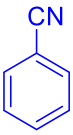
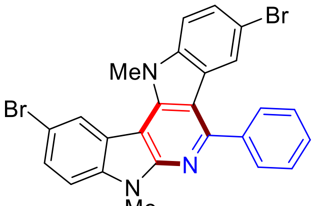
The substrate scope for the palladium-catalyzed reaction is presented in (Table 2). Initially, we examined the reaction of biindole **2a** with various nitriles by changing the substituents on the phenyl ring (H, 4-Cl, 4-Br, 3-Cl, Me, OMe) and obtained good to excellent yields of products **9-14**. 1-Naphthyl derivative **15** could also be obtained in high yield. Even heterocycle-containing nitriles such as 2-furonitrile and 2-cyanopyridine reacted well to give the respective α-carbolines in good yields (**16**-**17**). Similar results were obtained by replacing N-Me with N-Et. Thus *N*-ethyl biindole **2b** reacted with aryl cyanides to afford the respective α-carbolines (1**8-21**, **23-25**) in excellent yields. Interestingly, only one cyano group of 1,4-dicyanobenzene **1k** reacted to give product **22** in high yield. α-Carbolines **26-27** were obtained upon using substituted biindoles **2c-d** and benzonitrile **2a**. However, reactions using aromatic nitriles bearing nitro, amino and aldehyde functional groups were unsuccessful. Unexpectedly, we obtained C-3 cyano biindoles **28-31** *via* a *retro*-Mannich pathway with the elimination of ethyl acetate in the reaction of biindoles **2a-d** with ethyl cyanoacetate **1l** (Scheme 7); details are given in (Table 3).[71] In the case of **30-31**, an isomeric mixture was observed. The structures of compounds **10,** **14**, **19** and **30** were further confirmed by single crystal X-ray analysis (Figures 1-2).

Table 2. Substrate Scope for the synthesis of indole fused α-carbolines from biindoles *via* [Pd] catalysis[a]

Entry	2,3′-biindole	Nitriles	Indole fused a-carbolines	yield (%)[b]
1	 **2a**	 **1a**	 **9**	92

2	**2a**	 **1b**	 **10** **(X-ray)**	81
3	**2a**	 **1c**	 **11**	84
4	**2a**	 **1d**	 **12**	84
5	**2a**	 **1e**	 **13**	81
6	**2a**	 **1f**	 **14** **(X-ray)**	82
7	**6a**	 **1g**	 **15**	81
8	**6a**	 **1h**	 **16**	80

9	**6a**	 **1i**	 **17**	80
10	 **6b**	 **1a**	 **18**	86
11	**6b**	 **1b**	 **19** **(X-ray)**	89
12	**6b**	 **1d**	 **20**	82
13	**6b**	 **1j**	 **21**	88
14	**6b**	 **1k**	 **22**	81
15	**6b**	 **1f**	 **23**	88

16	**6b**	 **1g**	 **24**	80
17	**6b**	 **1i**	 **25**	82
18	 **2c**	 **1a**	 **26**	81
19	 **2d**	 **1a**	 **27**	84

^{a}Reaction conditions: **2** (0.38 mmol), **1** (0.38 mmol), Pd(OAc)$_2$ (5 mol%, 0.019 mmol) and Cu(OAc)$_2$ (2 equiv) in DMF (2 mL) at 110 °C (oil bath) for 12 h. ^{b}Isolated yield.

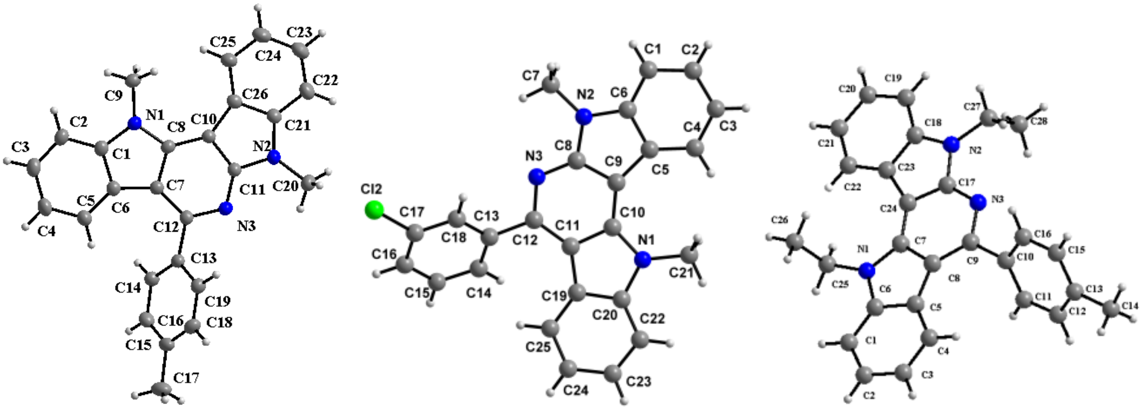
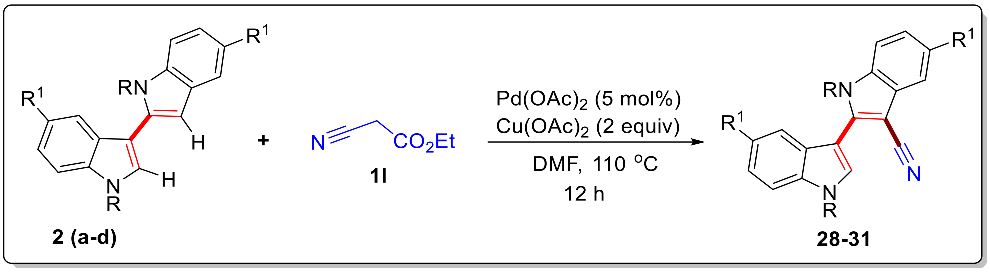


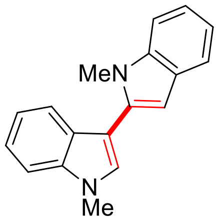
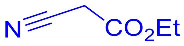
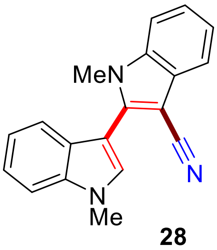
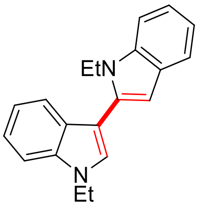
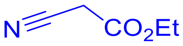
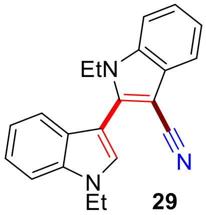
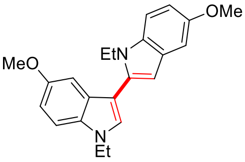
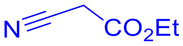
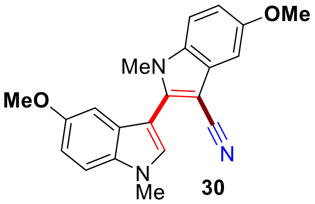
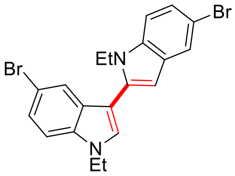
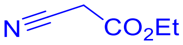
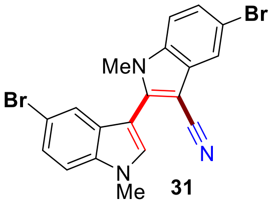
Figure 1: Molecular structures of compounds **10**, **14** and **19**. Selected bond lengths [Å] with esds: Compound **10** C(8)-C(7) 1.423(2), C(7)-C(12) 1409(2), C(12)-N(3) 1.343(2), N(3)-C(11) 1.333(2), C(11)-C(10) 1.406(2), C(10)-C(8) 1.410(2). Compound **14** C(8)-C(9) 1.408(6), C(9)-C(10) 1.402(6), C(10)-C(11) 1.427(5), C(11)-C(12) 1.404(5), C(12)-

N(3) 1.342(5), N(3)-C(8) 1.334(5), C(12)-C(13) 1.488(5). Compound **19** C(8)-C(7) 1.423(2), C(7)-C(24) 1.410(2), C(24)-C(17) 1.412(2), C(17)-N(3) 1.334(2), N(3)-C(9) 1.346(2), C(9)-C(8) 1.404(2), C(8)-C(7) 1.423(2), C(9)-C(10) 1.481(2).



Scheme 7: $Pd(OAc)_2$ catalyzed C-3 cyanation of 2,3′-biindoles using ethyl cyanoacetate.

Table 3. Substrate scope for C-3 cyanation of 2,3′-biindoles *via* [Pd] catalysis[a]

Entry	Biindolyls	Nitriles	C-3-Cyanated 2,3'-biindole	yield (%)[b]
1			 **28**	86
2				89
3			 **(X-ray)**	86
4				81

[a]Reaction conditions: **2** (0.38 mmol), **1l** (0.38 mmol), $Pd(OAc)_2$ (5 mol%, 0.019 mmol) and $Cu(OAc)_2$ (2 equiv) in DMF (2 mL) at 110 °C (oil bath) for 12 h. [b]Isolated yield.

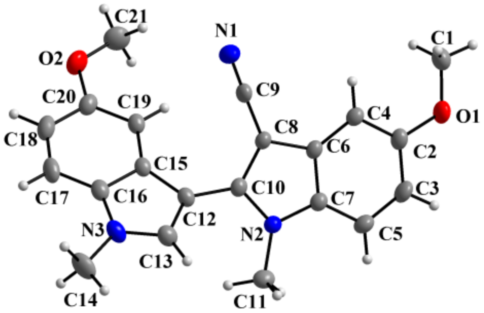
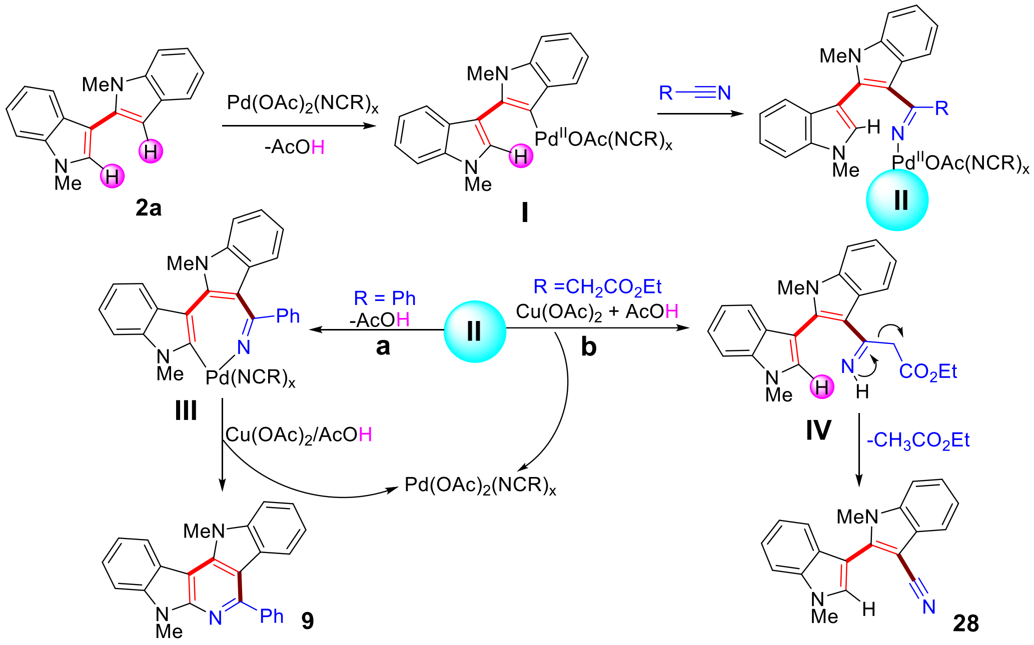


Figure 2: Molecular structure of compound **30**. Selected bond lengths [Å] with esds: N(1)-C(9) 1.149(3), C(9)-C(8) 1.413(3), C(8)-C(10) 1.387(3), C(10)-C(12) 1.456(3), C(12)-C(15) 1.446(3), C(15)-C(19) 1.393(3).

Based on a few literature reports[71-72] we propose that the formation of α-carbolines from 2,3′-biindoles and nitriles proceeds through palladium catalyzed double C-H activation of biindoles followed by nitrile insertion leading to new C-C and C-N formation simultaneously as shown in (Scheme 8; path a). It is likely that the nitriles that we have used are at least weakly coordinated to the palladium [cf. $PdCl_2(PhCN)_2$ is known]. Initially, in the presence of $Pd(OAc)_2$, biindole generates Pd(II) complex **I**, followed by insertion of nitrile group giving species **II**, which upon second C-H activation generates **III**. This upon reductive elimination of [Pd]-catalyst affords α-carboline **9**. In the presence of $Cu(OAc)_2$, the catalyst may be regenerated. In the formation of the cyanated product **28**,[70-71] intermediates of types **I** and **II** (with R being CH_2CO_2Et) may still be involved; species **II**, upon reacting with the previously generated AcOH may lead to species **IV** that could then lead to C3-cyano biindole **28** by the elimination of ethyl acetate *via retro*-Mannich pathway (Scheme 8; path b). The role of copper acetate in this case may just to facilitate exchange of acetate groups.



Scheme 8: Plausible pathways for the formation α-carbolines and 3-cyano-biindoles

Photophysical properties of 18, 21, 20 and 24:

Since α-carbolines as prepared above possess conjugated fused nitrogen heterocyclic motifs, we expected that they will show some fluorescence properties. Hence preliminary UV−visible and fluorescence spectra for compound **18, 21**, **20**, and **24** were recorded. As expected, these compounds are fluorescence active (cf. Figure 3). The absorption peak wavelengths (λ_{abs}), molar extinction coefficient (ε), and emission peak wavelengths (λ_{em}) in solution are summarized in Table 4. We think that with suitable substitution, the products may become useful for further applications.

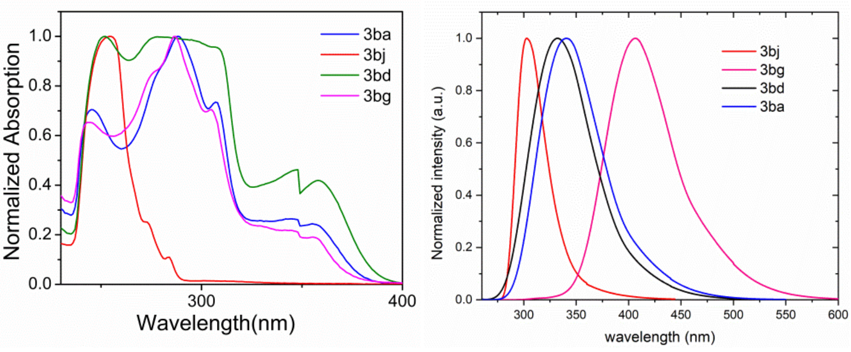


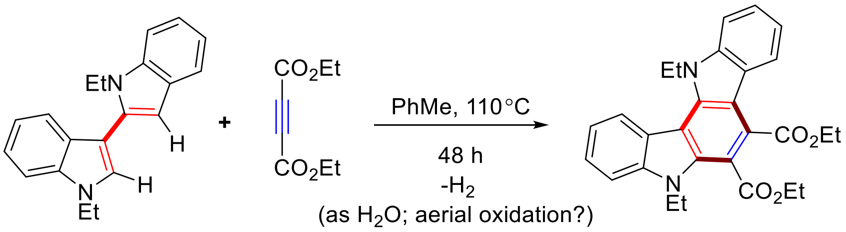
Figure 3: Absorbance and fluorescence emission spectra of **18**, **21**, **20** and **24** in $CHCl_3$ (10^{-5} M) at rt (25 °C). (**3ba**, **3bj**, **3bd** and **3bg** in the figure are compounds **18**, **21**, **20** and **24**).

Table 4: UV−Visible absorption and fluorescence emission data for **18**, **21**, **20** and 24[a]

Compound	λ_{abs}(nm)	ε ($10^4 M^{-1} cm^{-1}$)	λ_{em}(nm)
18	356	4.1	432
21	358	11.3	440
20	305	8.5	447
24	284	27.3	303

[a] Data in solution were collected in $CHCl_3$ (10^{-5} M) 25 °C

To check whether 2,3′-biindoles can act as a dienophile in [4 + 2] cycloaddition or not (and also to check the reactivity of 2 and 3′ positions), we performed the reaction between biindole **2b** and diethyl acetylene dicarboxylate **32** in toluene solvent at 110 °C for 48 h and isolated the carbazole **33** in good yield (Scheme 9). This reaction involves the *sp*-hybridized acetylenic carbons. However, as this type of compound was reported earlier,[72] we did not explore it further.



2b (0.38mmol) **32** (0.38mmol) **33** (75%)

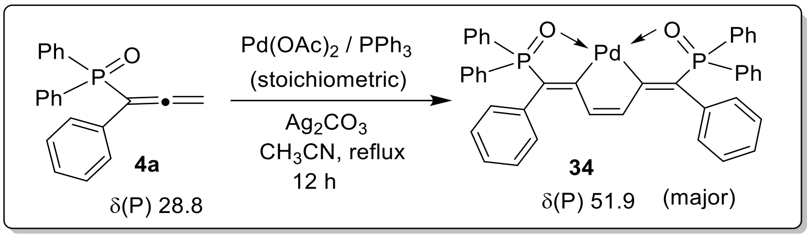
Scheme 9: Synthesis of indolocarbazole from biindole and diethyl acetylene dicarboxylate

2.3 [Pd]-catalyzed/mediated cyclization/ cycloaddition reactions of allenylphosphine oxides to yield Pd-incorporated complexes and P-containing naphthalenes

Cyclization as well as cycloaddition reactions of allenes have drawn much attention in the synthesis of multifunctional organic compounds. By using phosphorus based allenes, our research group has explored several new reactions that have generated diverse homo- and heterocycles *via* transition metal catalysis.[73] However, the intramolecular dimerization-cum-cyclization/ cycloaddition of allenylphosphinates and allenylphosphine oxides are rather rare. In the current work, we serendipitously discovered the formation of Pd-incorporated complexes and P-containing naphthalenes from allenylphosphine oxides by varying the quantities of [Pd]-catalyst (stoichiometric/catalytic) in a single synthetic operation.

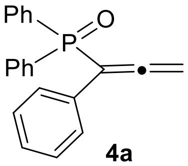
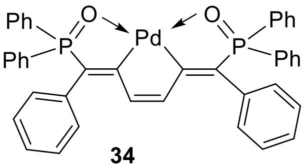
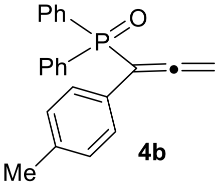
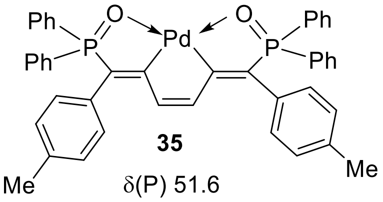
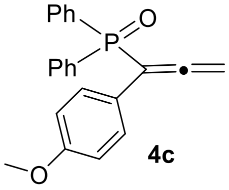
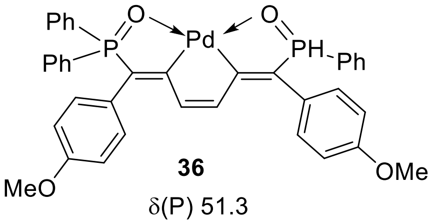
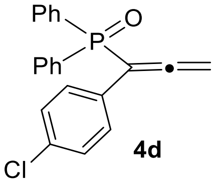
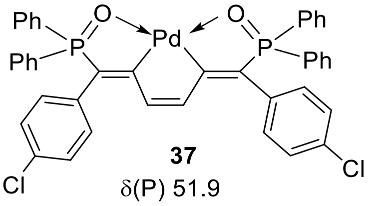
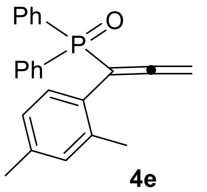
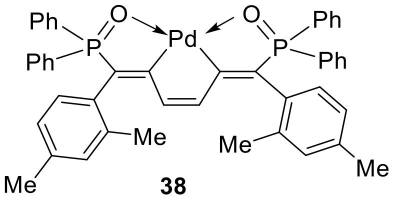
2.3.1 Formation of Pd-incorporated complexes from allenylphosphine oxides and stoichiometric amount of Pd(OAc)$_2$

Initially we were curious to check intramoecular cyclizations and/ or cycloadditions of P-allenes (especially allenylphosphine oxides) in the presence of [Pd]-catalyst. In such an attempt, when we treated allenylphosphine oxide **4a** with a little excess of Pd(OAc)$_2$ (more than 20 mol%) in the presence of K_2CO_3 and PPh_3 in CH_3CN solvent for 48 h, to our delight, upon checking ^{31}P-NMR of reaction mixture, we observed traces of left over P-allene along with peaks which had significant downfield ^{31}P chemical shift compared to P-allene **4a**. This gave us indication of the formation of metal incorporated product. Next, we treated allenylphosphine oxide **4a** with Pd(OAc)$_2$ (0.5 equiv), K_2CO_3 (1 equiv) and PPh_3 (0.5 equiv) in CH_3CN solvent at reflux for 48 h, we could isolate the palladium incorporated complex **34** in 30% yield (Scheme 10). In order to improve the yield, we performed the reaction by using different bases like *t*-BuOK, Cs_2CO_3, Ag_2CO_3, and Na_2CO_3. Among these, Ag_2CO_3 gave good yield (41%) of **34** (major) in 12 h. We were able to synthesize different substituted Pd-incorporated complexes **34-38** in moderate yields by changing the alkyl groups on the α-phenyl ring of allenylphosphine oxide **4**. Details are given in Table 5. The structure of compound **35** was further confirmed by single crystal X-ray analysis (Figure 4). When we performed the reaction with thiophene ring containing P-allene **4f**, we observed the formation of Pd-complexes (through ^{31}P NMR spectra) but could not isolate the required product in a pure state; the corresponding spectra are shown in Figure 5. Interestingly, though, when we performed a similar reaction using allenyl phosphonates **5b**, we did not observe any Pd-complex formation [^{31}P NMR evidence]. This may be due to the lower donating ability from oxygen in the phosphonates relative to phosphine oxides.



Scheme 9: Synthesis of Pd-incorporated complex **34** from allenylphosphine oxide **4a**

Table 5. Synthesis of Pd-incorporated complexes from allenylphosphine oxides and $Pd(OAc)_2$[a]

Entry	Allenylphosphine oxide	P- containing naphthalenes	yield (%)[b]
1	 **4a** δ(P) 29.1	 **34** δ(P) 51.9	41
2	 **4b** δ(P) 27.1	 **35** δ(P) 51.6 (x-ray)	45
3	 **4c** δ(P) 29.3	 **36** δ(P) 51.3	51
4	 **4d** δ(P) 29.0	 **37** δ(P) 51.9	26
5	 **4e** δ(P) 27.5	 **38** δ(P) 51.6	35

[a] Standard conditions: allenylphosphine oxide (0.316 mmol) in dry CH_3CN, $Pd(OAc)_2$ (0.158 mmol), PPh_3 (0.158 mmol) and Ag_2CO_3 (0.316 mmol) at reflux for 12 h. [b] Isolated yields.

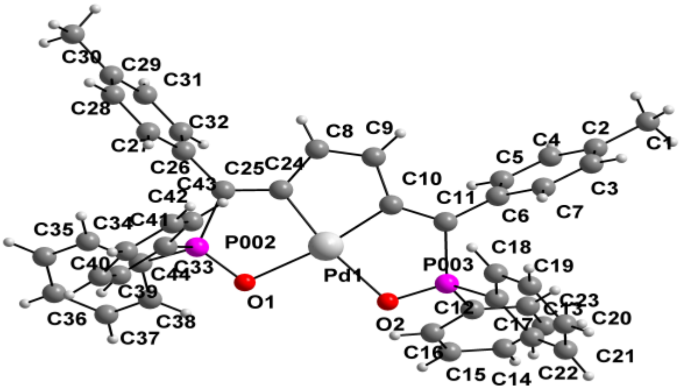


Figure 4: Molecular structure of compound **35**. Selected bond lengths [Å] with esds: P(1)-O(1) 1.5109(19), O(1)-Pd(1) 2.1671(18), Pd(1)-C(24) 1.949(3), C(24)-C(25), C(25)-P(1), C(24)-C(8) 1.465(4), C(8)-C(9) 1.341(4), C(9)-C(10) 1.456(4), C(10)-C(11) 1.356(4), C(11)-P(2) 1.796(3), P(2)-O(2) 1.510(2), O(2)-Pd(1) 2.1630(18).

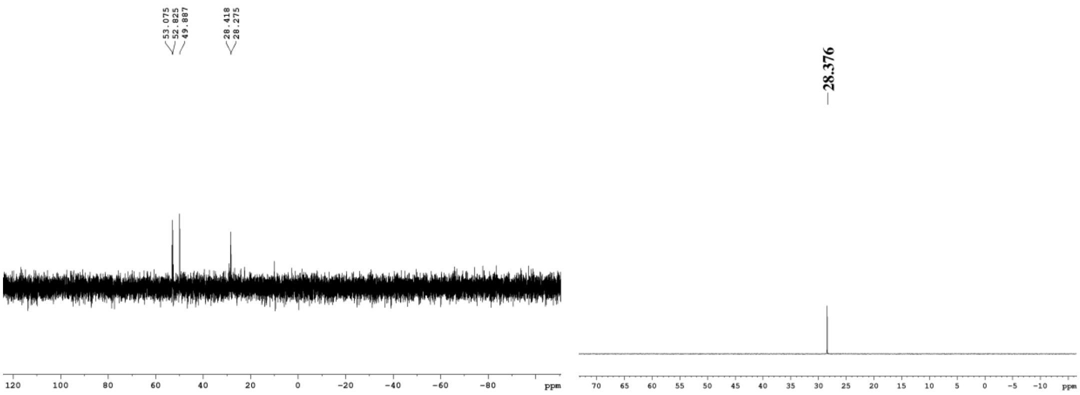


Figure 5: ^{31}P NMR spectra of crude reaction mixture (left) and allene **4f** (right)

Formation of [Pd]-complexes **34-38** takes place by the elimination of two molecules of acetic acid per complex. However, these data do throw up challenges while rationalizing the mechanism of [Pd]-catalyzed reactions of allenylphosphonates/allenylphosphine oxides with aryl iodides or iodophenols.[74] Since the complexes have a stoichiometry of 1:2 [Pd: allene], and in the catalytic reactions we use only 2.5-10 mol% of the palladium catalyst/precatalyst, it appears likely that complexes of type **34-38** may actually take part in the catalysis. Even more challenging is the fact that the 1:2 [Pd: allene] reaction mixture indicates the formation of at least a couple of more [Pd]-complexes (shown in figure 6b). So far we have been successful in isolating only the major [Pd]-allene complexes **34-38**. This aspect perhaps would require more investigation.

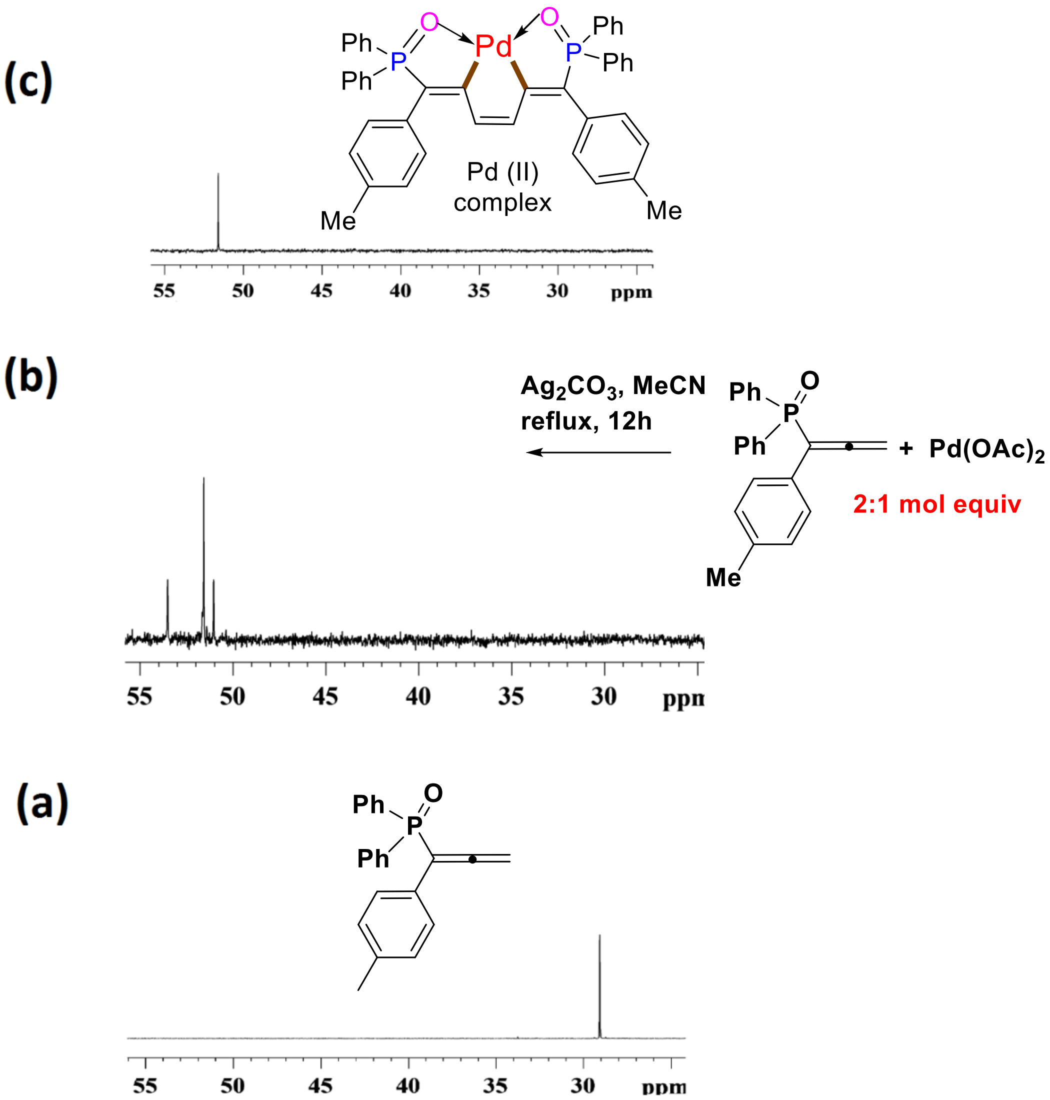
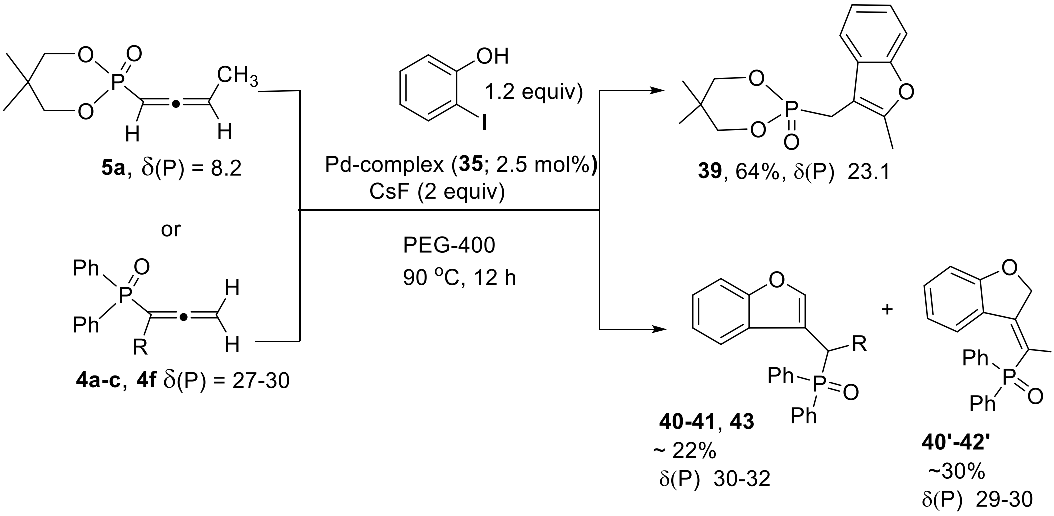


Figure 6: ^{31}P NMR spectrum of the 1:2 [Pd:allene] reaction mixture using **4b** (b); also shown are the ^{31}P NMR spectra of **4b** (a) and **35** (c).

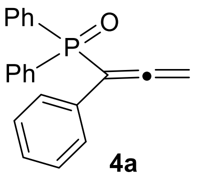
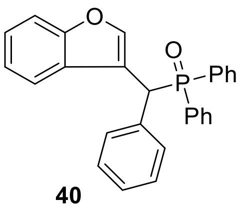
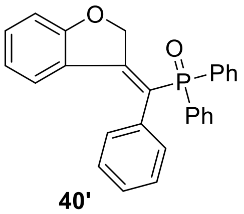
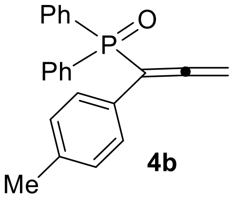
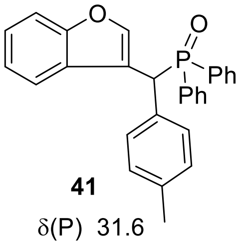
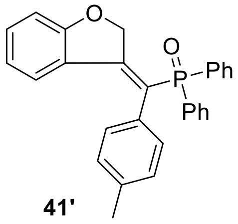
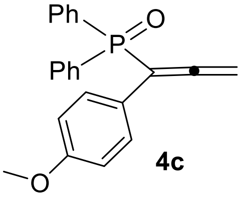
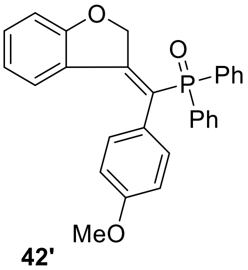
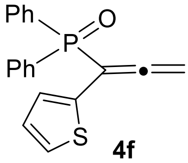
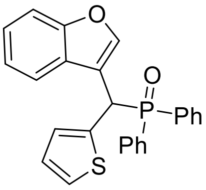
2.3.2 Utility of [Pd] incorporated complex 35 in the reaction of phosphorus based allenes with 2-iodophenol

In order to check any possible catalytic activity for [Pd]-allene complexes prepared as above, we treated allenylphosphonate **5a** with 2-iodophenol in the presence of [Pd]-complex **35** and CsF (base) in PEG-400 solvent at 90 °C for 12h (Scheme 10). This is based on a previous report from our laboratory.[74] Satisfyingly, we obtained phosphano-benzofuran **39** in moderate yields. When we repeated the same reaction by using allenylphosphine oxides **4a-c** and **4f**, to our delight we could able to isolate phosphano benzofurans **40-41** and **43** like above (as minor products) along with one more product in each case that showed the same mass (HRMS), but different H/^{13}C/^{31}P NMR spectra. Notably, in the reaction of **4a** with 2-iodophenol, the second product **40′** showed two doublets at δ 5.78 (2H, ^4J ~ 4.5 Hz) and 5.99 (1H, ^2J = 8.0 Hz) in the ^{1}H NMR; compound **40**, by contrast, exhibited only a doublet at δ 4.93 (1H, ^2J = 9.5 Hz.). In the ^{13}C{^{1}H} NMR spectrum, product **40′** exhibited a doublet at δ 75.3 [^3J (^{13}C-^{31}P= 4.6 Hz] which corresponded to a *C*H$_2$ carbon (DEPT). Product **40** exhibited a doublet at δ 42.7 (^1J = 63.0 Hz). After complete analysis of ^{1}H/^{13}C/^{31}P spectra and single crystal X-ray structure, the compound has been confirmed as dihydro phosphano-benzofuran **40′** (major product; Figure 7). We could also isolate similar products **41′-42′** (Table 6). In a few reactions, we isolated only one of the two isomers due to close *R$_f$* values. Thus it is possible that complexes of type may actually be involved in our reactions reported earlier[75] since these complexes are formed in 1:2 ([Pd]: allene) ratio. i.e., stoichiometrically there was more of allene compared to Pd(OAc)$_2$. Although yields are only moderate, the results show that our [Pd] complexes are catalytically active. When we performed the same reaction of allenyl phosphine oxides by using Pd(OAc)$_2$ as the catalyst, we had to use 10 mol% of Pd(OAc)$_2$ for 24 h to obtain the products in decent yields.



Scheme 10: Synthesis benzofurans and dihydrobenzofurans from phosphorus-based allenes (P-allenes) in the presence of complex **35**

Table 6. Utility of Pd-complex **35** for the synthesis of benzofurans and dihydrobenzofurans from phosphorus-based allenes (P-allenes)

Entry	Allenylphosphine oxide	Benzofuran	Dihydro benzofuran
1	 **4a** δ(P) 28.8	 **40** δ(P) 31.7	 **40'** δ(P) 29.5 (X-ray)
2	 **4b** δ(P) 28.8	 **41** δ(P) 31.6	 **41'** δ(P) 29.5
3	 **4c** δ(P) 27.5	Not isolated	 **42'** δ(P) 29.7
4	 **4f** δ(P) 28.3	 **43** δ(P) 30.6	Not isolated

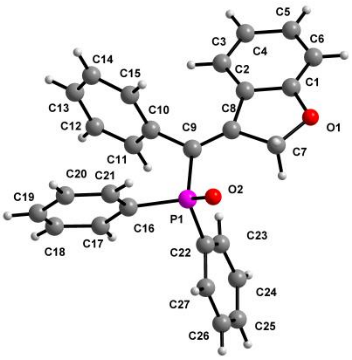
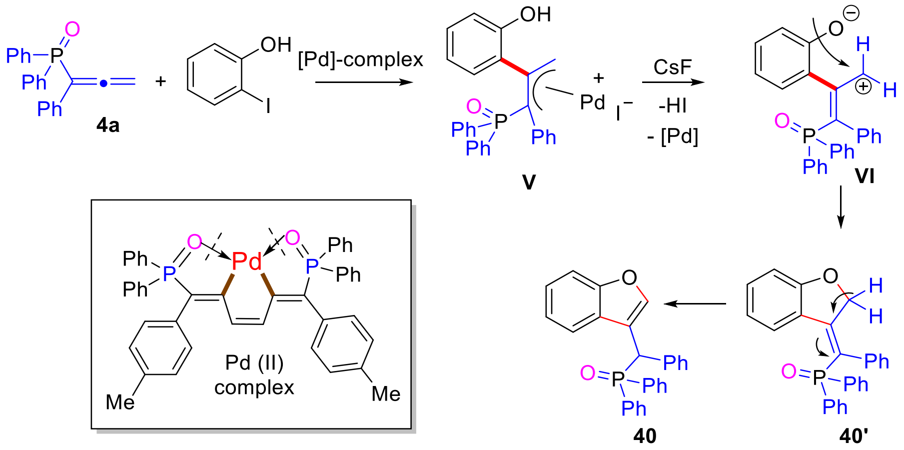


Figure 7: Structure of Compound **40′**. Selected bond lengths [Å] with esds are given in parentheses: O(1)-C(7) 1.426(17), C(7)-C(8) 1.54(2), C(8)-C(9) 1.325(19), C(9)-C(10) 1.50(2), C(9)-P(1) 1.830(15), P(1)-O(2) 1.473(9), P(1)-C(22) 1.790(17), P(1)-C(16) 1.825(17).

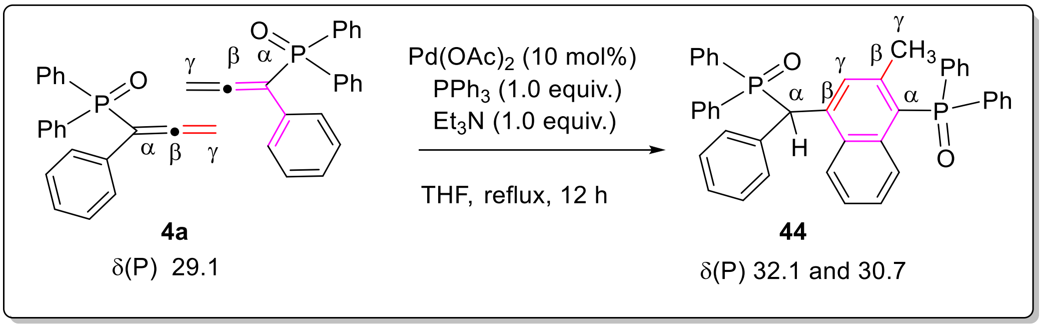
On the basis of literature reports,[75] we propose the formation of intermediate **V** from allenes and iodophenol in the presence of Pd(OAc)$_2$. The formed intermediate **V** in the presence of base, undergo elimination of HI/[Pd] to form **VI**. Attack of the phenolic oxygen at terminal carbon gives dihydrobenzofuran **40′** that may undergo proton shift leading to the formation of benzofuran **40**.



Scheme 11: Plausible pathway for the formation of **40/40′**

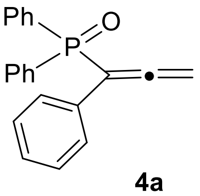
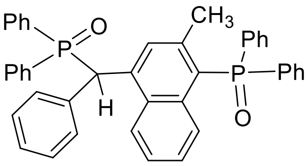
2.3.3 Pd(OAc)$_2$-catalyzed transformations of allenylphosphine oxides leading to P-containing naphthalenes

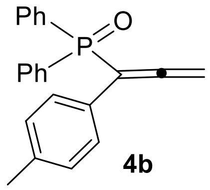
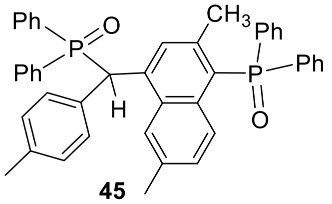
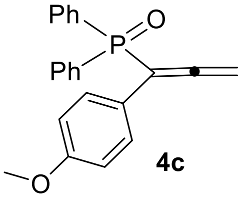
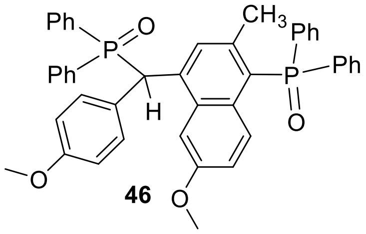
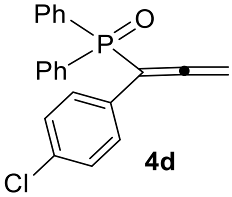
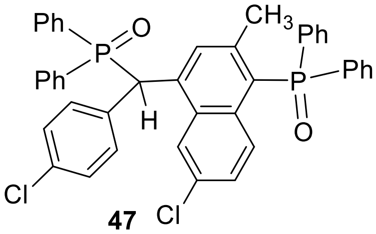
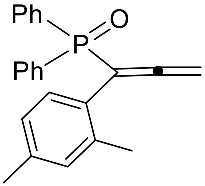
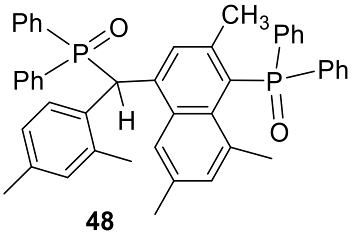
Initially, we performed a reaction using allenylphosphine oxide **4a** and Pd(OAc)$_2$ (catalytic amount)/ Ph$_3$P/Et$_3$N. Serendipitously, this reaction afforded compound **44** (Scheme 12). The ^{31}P{^{1}H} NMR spectrum of **44** showed two peaks of equal intensity at δ 32.2 and 30.6 indicating that two molecules of allenylphosphine oxide are involved in the reaction. Based on these NMR data, we ascertained that the formed product was an unsymmetrical dimer in which (*β*,*γ*)-double bond of one allene and (*α*,*β)*-double bond of another allene were involved. Similar products **44-48** could also be obtained in moderate yields (Table 7). We could obtain single crystal structure of compound **45** (Figure 8) which was crystallized from ethyl acetate/hexane (2:1) mixture. It may be noted that here intramolecular [4+2] cycloaddition of two allenylphosphine oxides has taken place to yield a new six-membered ring as shown in (Scheme 12). This reaction was performed because in an earlier reaction, we had noticed that, in addition to the dimers, the reaction mixture exhibited other peaks in the ^{31}P NMR spectra of the reaction mixtures about which we were curious about. This part of the work was done in conjunction with another colleague in the laboratory wherein several other similar products were also obtained by using allenes of type $(OCH_2CMe_2CH_2O)_2P(O)(C(Ar)=C=CH_2$.[76]



Scheme 12: Synthesis of P-containing naphthalenes from allenylphosphine oxides

Table 7. Synthesis of phosphorus based naphthalenes from allenylphosphine oxides[a]

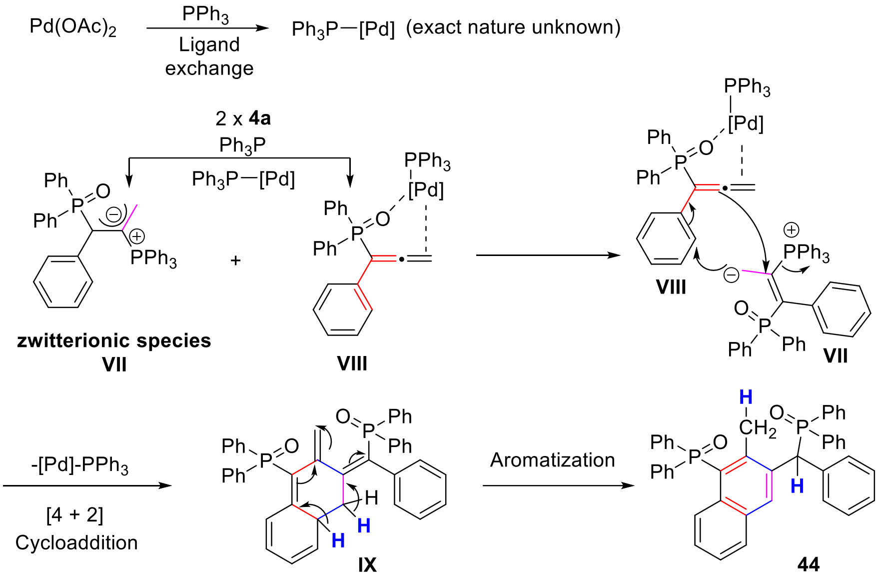
Entry	Allenylphosphine oxide	P- containing naphthalenes	yield (%)[b]
1	 **4a** δ(P) 29.1	 **44** δ(P) 32.1 and 30.7	64

1	 **4b** δ(P) = 28.8	 **45** δ(P) = 32.1 and 30.7 (X-ray)	54
2	 **4c** δ(P) = 27.5	 **46** δ(P) = 32.3 and 31.0	48
3	 **4d** δ(P) = 29.3	 **47** δ(P) = 31.7 and 30.7	44
4	 **4e** δ(P) = 27.5	 **48** δ(P) = 32.9 and 29.4	45

[a]Standard conditions: allenylphosphine oxide (0.316 mmol) in dry THF, $Pd(OAc)_2$ (0.032 mmol), Ph_3P (0.316 mmol) and Et_3N (0.316 mmol) at reflux for 12 h. [b]Isolated yield.

Although phenyl rings in principle can participate in [4+2]-cycloaddition reactions in which the aryl ring contributes a part of the diene component, they are not that common. The role of $Pd(OAc)_2$ and PPh_3 here is perhaps to activate the allenic double bonds leading to species **VII-VIII** since the reaction does not occur (or negligible) in the absence of the [Pd]-catalyst or PPh_3. The formed intermediate upon intramolecular [4+2] cycloaddition gives **IX**. This is followed by aromatization to afford naphthalenes (Scheme

13). Although we have not studied the mechanism in detail, coordination of the allene double bond to [Pd] is known.[74] The phosphoryl bond is itself capable of coordinating (*vide supra*). Also, the *sp*-hybridized central carbon of the allene is quite nucleophilic and hence is susceptible for attack by the phosphine.[77]



Scheme 13. A possible pathway for the formation of the dimer **44** from 4**a**.

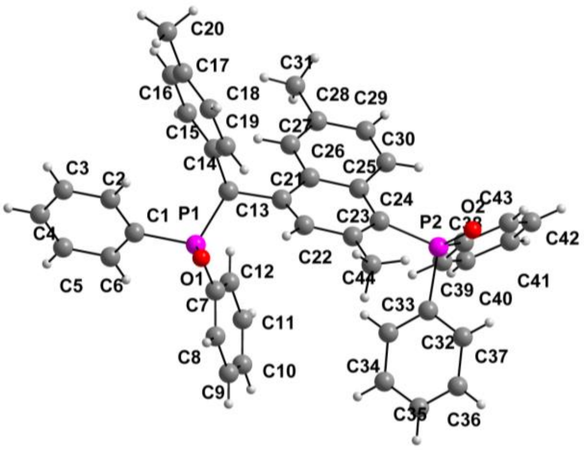


Figure 8: Molecular structure of compound **45**. Selected bond lengths [Å]: C(13)-C(21) 1.526(3), C(21)-C(22) 1.361(3), C(22)-C(23) 1.407(3), C(23)-C(24) 1.397(3), C(24)-C(25) 1.429(3), C(21)-C(26) 1.441(3), C(26)-C(27) 1.410(3), C(27)-C(28) 1.374(4), C(28)-C(31) 1.499(4), C(28)-C(29) 1.404(4), C(29)-C(30) 1.352(4), C(30)-C(25) 1.432(3).

2.4 Phosphine catalyzed [4+2] cycloaddition reactions of α-methyl allenoates with enynones

In this section, we shall discuss [4+2] cycloaddition reactions of allenoates with multisubstituted enynones in the presence of phosphine. Although we had faced difficulties in obtaining analytically pure samples in most cases (due to diastereomers/isomers), the spectroscopic data along with the X-ray structure of the product confirms the novel reactions encountered in this section.

2.4.1 Phosphine catalyzed cycloaddition reaction of allenoates 6 with enynones 8

Initially, when we treated enynone (**8a**, 1.0 equiv) with allenoate (**6**, 0.5 equiv) in the presence of Ph_3P (0.5 equiv) in toluene for 48 h at rt (25 ^{o}C), we isolated the multisubstituted cyclohexene carboxylate **49** in 32% yield based on the enynone (entry 1; Table 8). Since allenoate is less stable than the enynone and could decompose over the reaction time, for the subsequent reaction we used 1.0 equiv of allenoate and obtained **49** in 56% yield (entry 2). To increase the yield further, we marginally increased the stoichiometry of the allenoate to 1.2 equiv; the yield was better (62%, entry 3). We then performed the reaction using the phosphine $P(4\text{-}MeOC_6H_4)_3$ (0.1 equiv) which gave yields (24% and 48%, entries 4-5) in the reaction time from 24 h to 36 h. We performed the reaction using $P(4\text{-}MeOC_6H_4)_3$ (0.2 equiv) for different duration of time (12 h- 36 h; entry 6), and observed 82% yield of compound **49** in 48 h duration (entry 7). We also checked other phosphines/ bases like PPh_3, P(*n*-Bu)$_3$, BINAP, P(*o*-tol)$_3$, and $P(4\text{-}Cl\text{-}C_6H_4)_3$ (entries 8-11), but $P(4\text{-}MeOC_6H_4)_3$ was still the best. No product was observed in the absence of base or by using BINAP (entries 17 and 9). Among the solvents toluene, THF, 1,4-dioxane, MeCN, nitromethane, Me_2CO_3 (entries 12-16) tested, toluene was found to be the solvent of choice. Best conditions (82% yield) for obtaining multisubstituted cyclohexene carboxylate **49** were by treating allenoate (1.2 equiv) and enynone (1 equiv) in the presence of $P(4\text{-}MeOC_6H_4)_3$ (0.2 equiv) in toluene for 48 h at rt (entry 7). There is a possibility of formation of two regio-isomers (**49** and **49′**) for the product; data analysis suggested the possibility of having 4-possible stereo-isomers (Figure 9). Hence purity of the isolated compounds was only up to 90% for the major product **49**.

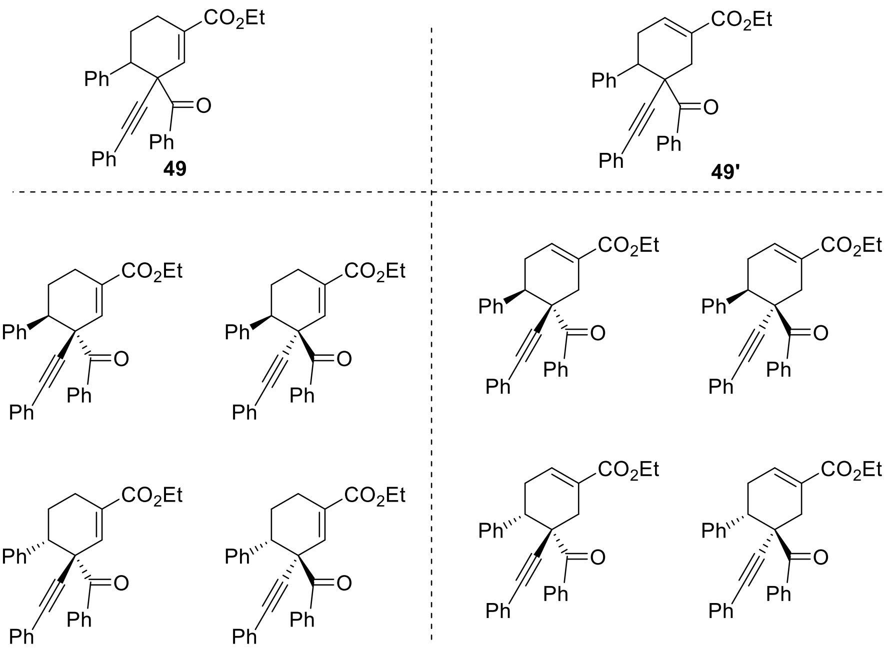
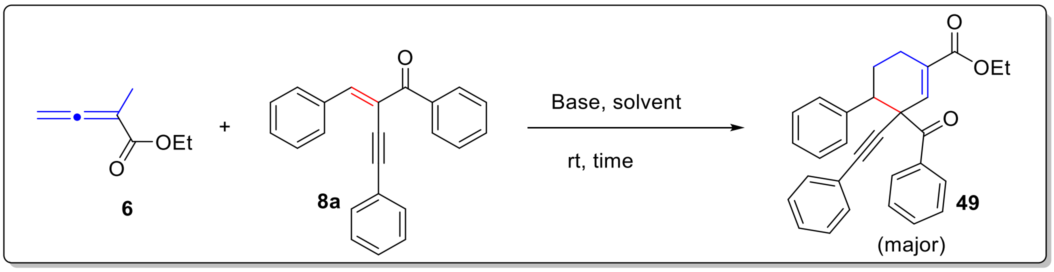


Figure 9: Possible isomers for the cyclohexene carboxylate **49/49′**

Table 8. Optimization of conditions for the synthesis of cyclohexene carboxylate **49**.



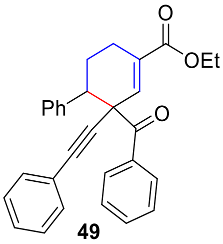
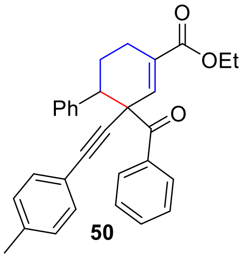
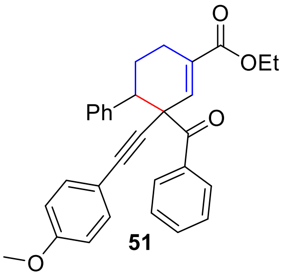
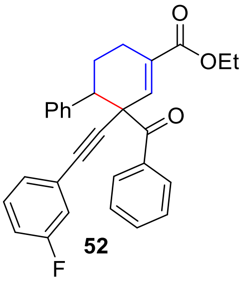
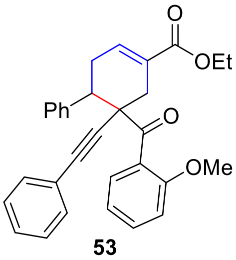
Entry	Phosphine/base (equiv)	Allene (equiv)	Solvent	Time	Yield (%)[b] major isomer
1	PPh_3 (0.5)	0.5	Toluene	48 h	32[a]
2	PPh_3 (0.5)	1.0	Toluene	48 h	56
3	PPh_3 (0.5)	1.2	Toluene	48 h	62
4	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.1)	1.2	Toluene	36h	24
5	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.1)	1.2	Toluene	48 h	48
6	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	Toluene	12 h (or 36 h)	35 or 62
7	**$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2 equiv)**	**1.2**	**Toluene**	**48 h**	**82**

8	PBu_3	1.2	Toluene	12 h or 48 h	Traces (12h) or 28 (48h)
9	BINAP (0.5)	1.2	Toluene	48 h	NR
10	$P(o\text{-tol})_3$ (0.5)	1.2	Toluene	48 h	60
11	$P(C_6H_4\text{-}4\text{-}Cl)_3$ (0.5)	1.2	Toluene	48 h	35
12	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	1,4-dioxane	48 h	64
13	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	THF	48 h	52
14	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	MeCN	48 h	41
15	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	$MeNO_2$	48 h	NR
16	$P(C_6H_4\text{-}4\text{-}OMe)_3$ (0.2)	1.2	Me_2CO_3	48 h	NR
17	-	1.2	Toluene	48 h	NR

[a]Reaction conditions: Enynone (**8a**; 1.0 equiv), allenoate (**6**; 0.5 equiv), phosphine (0.5 equiv), solvent (2 mL) at rt for the stipulated time. [b]Isolated yield of **49**. [c]Optimized conditions: Enynone (**8a**; 1.0 equiv), allenoate (**6**; 1.2 equiv), phosphine (0.2 equiv), and toluene (2 mL) at rt (25 °C) for 48 h. NR = No Reaction.

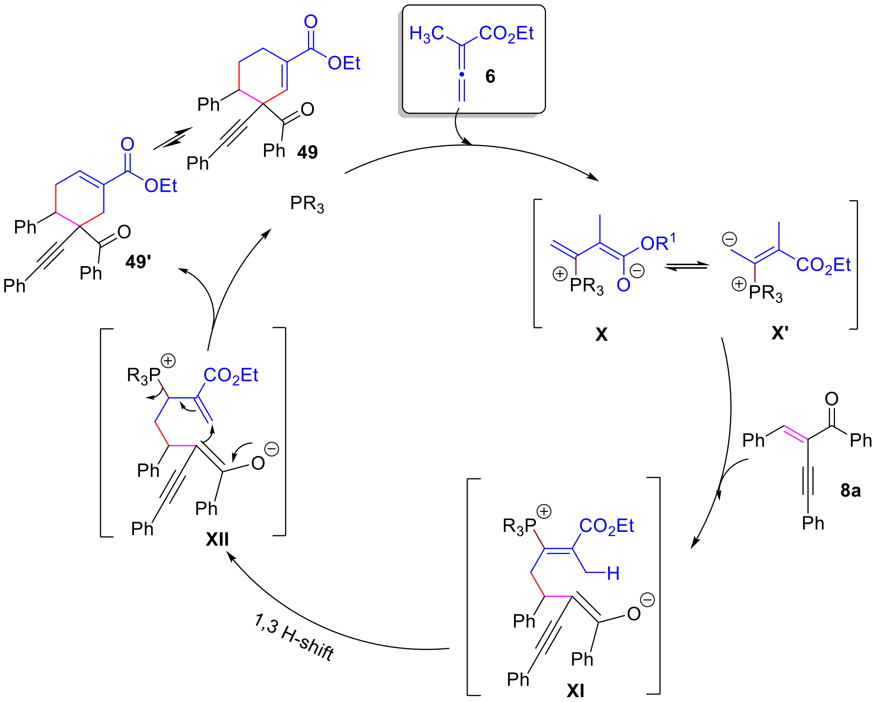
After having optimized conditions in hand, we moved to the substrate scope as shown in Table 2. Enynones having different functional groups (OMe, F, Me) on the phenyl ring successfully gave good yield of cyclohexene carboxylates **50-52** *via* [4+2] annulation in ~78% yields. Although we performed many more reactions, purity of the products has not been satisfactory. Interestingly, though, we were able to isolate another isomer **53** in case of the reaction with **8e**; we could not isolate this isomer as yet in other cases. The X-ray structure of compound **53** is shown in Figure 10. Thus it appears that both isomers are possible in this reaction.

Table 9. Synthesis of cyclohexene carboxylates from allenoates and enynones[a]

S.No	Allenoate	Enynone	Cyclohexene carboxylate	Yield of major isomer (%)[b]
1	**6**	**8a**	 **49**	82
2	**6**	**8b**	 **50**	75
3	**6**	**8c**	 **51**	74
4	**6**	**8d**	 **52**	72
5	**6**	**8e**	 **53** (X-ray)	72

[a]Standard conditions: allenoate (0.389 mmol), enynone (0.324 mmol), phosphine (0.065 mmol) in toluene at rt (25 °C) for 48 h. [b]Isolated yield of the major isomer.

In accordance with the literature reports,[78a] a plausible pathway for the formation of polysubstituted cyclohexene carboxylate is shown in Scheme 14. Initially, allenoate in the presence of phosphine generates zwitterionic form **X** which is in equilibrium with **X'**; this may attack the enynone to generate intermediate **XI**. Proton shift (cf. **XII**), cyclization and elimination of phosphine may generate the required cyclohexene carboxylate **49′**, which further upon isomerization of double bond may give compound **49**.[78b]



Scheme 14: Probable pathway for the formation of cyclohexene carboxylates **49/49′** (and **50-53** from allenoate **6** and enynones **8a-e**.

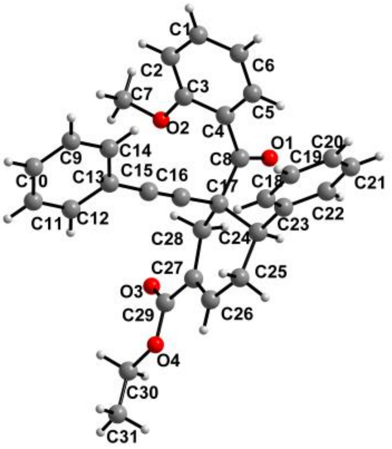


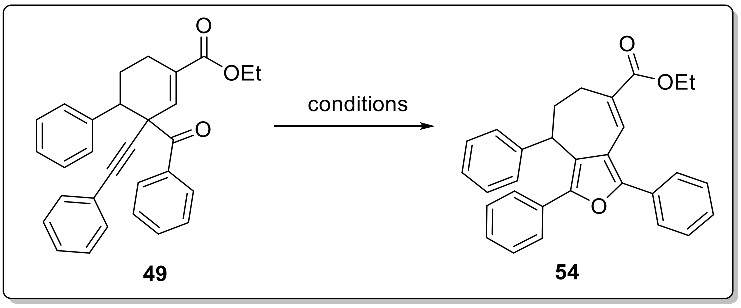
Figure 10: Molecular structure of compound **53**. Selected bond lengths [Å] with esds are given in parentheses. C(17)-C(28) 1.544(2), C(25)-C(24) 1.505(2), C(17)-C(24) 1.570(2),

C(25)-C(26) 1.485(2), C(26)-C(27) 1.323(2), C(27)-C(28) 1.506(2), C(17)-C(8) 1.549(2), C(17)-C(16) 1.474(2), C(24)-C(23) 1.505(2).

2.4.2 Gold-catalyzed transformation of cyclohexene carboxylates to furan fused cycloheptene carboxylates

From the literature, it is expected that if groups like ketone (or aldehyde) and alkyne are present on same atom, they may undergo catalytic self-cyclization to yield heterocycles.[55],[61] Having this in mind, we wanted to explore the reactivity of the above compounds. For this purpose, we treated our cyclohexene carboxylate **49** with Ph_3PAuCl (10 mol%) and $AgSbF_6$ (5 mol%) at rt/100 °C for 24 h. Pleasingly, we obtained 32%/ 48% of furan fused functionalized cycloheptene carboxylate **54** (entries 1-2, Table 10). When we compared the $^{13}C\{^1H\}$ NMR spectra of cyclohexene carboxylate **49** and the obtained product **54**, we observed that the ketone carbonyl peak as well as the alkyne peaks were absent in the product. The IR/NMR and HRMS data were consistent with the ring expanded product as shown in Table 10. In order to increase the yield of the product **54**, we checked THF [80 °C (oil bath); entry 3], toluene [100 °C (oil bath); entry 4] and found that there was no improvement in the yield. However, when we performed the reaction by changing catalyst combination to $Ph_3PAuCl/AgOTf$ in toluene at 100 °C for 24 h, we obtained 82% yield of product **55** (entry 5). There was no product formation in the absence of silver salt (entry 6). Other gold catalysts like AuCl, $AuBr_3$, and IPrAuCl, even in the presence of AgOTf, did not give the expected product (entries 7, 8 and 10). No improvement in the yield of compound **54** was observed using $Ph_3PAuCl/NaOTf$ or by using $Ph_3PAuCl/AgOTf$ in CH_3CN solvent (entries 9 and 10). Fortunately, we observed 80% yield in presence of Ph_3PAuCl (5 mol%)/AgOTf (5 mol%) in toluene at 100 °C in 48 h (entry 11). Since the catalyst loading was less here, we chose this condition for further work.

Table 10: Optimization study for the synthesis of furan fused heterocycle 54*[a]*

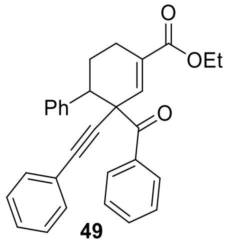
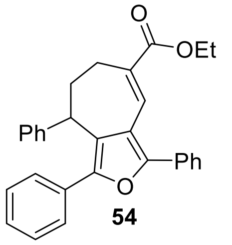


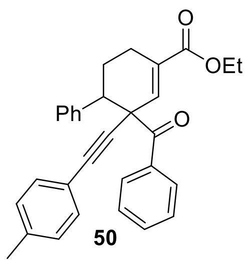
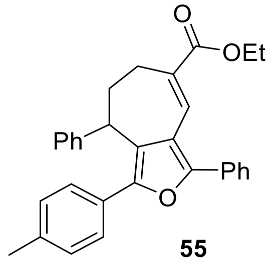
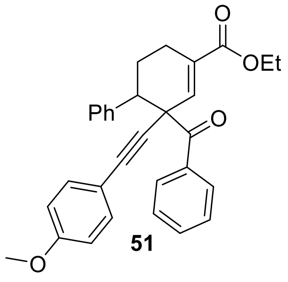
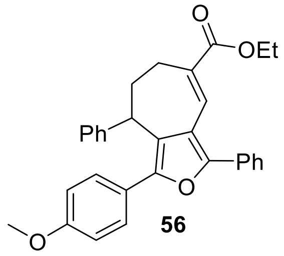
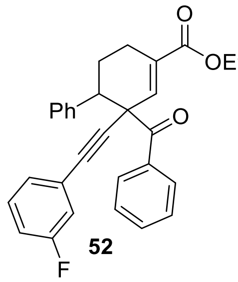
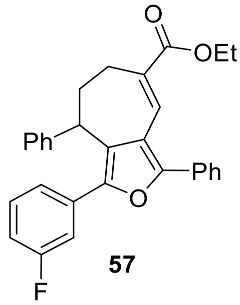
Entry	Catalyst (10 mol%/ 5 mol%)	Solvent	Temp (ºC)	Time (h)	Yield of **54** (%)^b
1	Ph_3PAuCl/ $AgSbF_6$	1,4-dioxane	rt	24	32
2	Ph_3PAuCl/ $AgSbF_6$	1,4-dioxane	100 ºC	24	48
3	Ph_3PAuCl/ $AgSbF_6$	THF	80	24	34
4	Ph_3PAuCl/ $AgSbF_6$	PhMe	100	24	53
5	Ph_3PAuCl/AgOTf	PhMe	100	24	82
6	Ph_3PAuCl	PhMe	100	24 (or 48)	NR
7	AuCl/AgOTf	PhMe	100	72	NR
8	$AuBr_3$/AgOTf	PhMe	100	48	NR
9	Ph_3PAuCl/NaOTf	PhMe	100	48	24
10	IPrAuCl/AgOTf	CH_3CN	reflux	24	30
11	**Ph_3PAuCl/AgOTf (each 5 mol%)**	**PhMe**	**100**	**48**	**80**^{c}

^{a}Reaction conditions: cyclohexene carboxylate (**49**, 1 equiv), Ph_3PAuCl (5 mol%), AgOTf (5 mol%), solvent (2 mL) at specified temperature/time. ^{b}Isolated yield of **54**.

Having these optimal conditions in hand, we explored the substrate scope by using substituted cyclohexene carboxylates to obtain dihydro-*4H*-cyclohepta[*c*]-furan carboxylates **54-57** under the above mentioned optimized conditions. These data are presented in Table 11. X-ray structure of the product **55** is shown in Figure 11.

Table 11: Substrate scope for the synthesis of dihydro-*4H*-cyclohepta[*c*]furan carboxylates

Sl. No	Cyclohexene carboxylates	Dihydro-*4H*-cyclohepta[*c*]-furan carboxylates	Yield (%)^b
1	 **49**	 **54**	82^a

2	 **50**	 **55** (X-ray)	72
3	 **51**	 **56**	79
4	 **52**	 **57**	78

[a]Standard conditions: Cyclohexene carboxylates (0.230 mmol), Ph_3PAuCl (0.012 mmol), AgOTf (0.012 mmol) in toluene at rt (100 °C) for 48 h. [b]Isolated yield of the product.

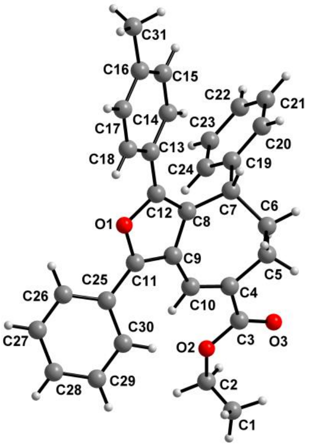
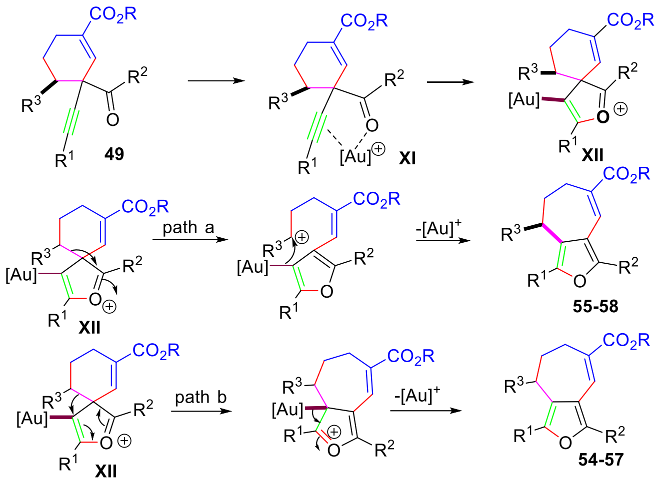


Figure 11: Molecular structure of compound **55**. Selected bond lengths [Å] with esds: O(1)-C(12) 1.387(3), C(12)-C(8) 1.364(3), C(8)-C(9) 1.444(3), C(9)-C(11) 1.377(3), C(11)-O(1) 1.364(3), C(8)-C(7) 1.507(3), C(7)-C(6) 1.540(4), C(6)-C(5) 1.511(3), C(5)-C(4) 1.501(4), C(4)-C(10) 1.343(3), C(10)-C(9) 1.445(3).

Based on the available literature,[55.61] we propose a plausible pathway for the gold catalyzed formation of furan fused functionalized cycloheptene carboxylate **54** from cyclohexene carboxylates in Scheme 15 [*Note:* The best condition for the conversion of **49′** to **49** is still under investigation]. Initially, [Au] coordinates with the alkyne group of compound **49** and also activates carbonyl group to give **XIII** which generates the spirocyclic intermediate **XIV**. Species **XIV** may undergo ring expansion in either of the two pathways a or b, followed by elimination of gold catalyst to generate the furan-fused compounds **54-57**.



Scheme15: Plausible pathways for the formation of tetrahydrocyclohepteno-furan carboxylates *via* [Au] catalysis.

SUMMARY

1. We have demonstrated a simple and high yield methodology for the synthesis of indole fused α-carbolines *via* [Pd] catalysis from 2,3′-biindoles by treating the latter with carbo/heterocyclic nitriles. This reaction involves C-H activation and the formation of new C-C and C-N bonds. Under the same conditions, interestingly, 2,3′-biindoles react with ethyl cyanoacetate to effect cyanation at the 3′-position of one of the indole moieties.

2. [Pd]-Catalyzed cycloaddition reactions and [Pd]-mediated cyclization reactions of allenylphosphine oxides afford P-containing naphthalenes and [Pd]-P complexes, respectively. The [Pd]-P complex so obtained could be used as a catalyst in the reaction of allenylphosphonates/ allenylphosphine oxides with 2-iodophenols.

3. We have developed phosphine-catalyzed synthetic route to multifunctional cyclohexene carboxylates through [4+2] cycloaddition of α-methyl allenoate with enynones. Thus prepared cyclohexene carboxylates produced trisubstituted furan fused cycloheptene carboxylates under [Au]-catalysis.

EXPERIMENTAL SECTION

General information: Chemicals and solvents were purchased from Aldrich and used without further purification.

Melting point: Melting points were determined using a SUPERFIT hot stage apparatus and are uncorrected.

Elemental analyses: Elemental analyses were carried out on a Perkin-Elmer 240C CHN or Thermo Finnigan EA1112 CHNS analyzer.

Infrared spectroscopy: IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer.

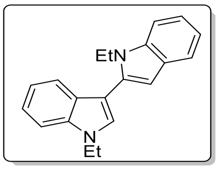
NMR spectroscopy: From sections 3.1-3.14 ^{1}H, ^{13}C NMR spectra were recorded using 5 mm tubes on a Bruker 400 MHz NMR spectrometer (unless specified otherwise) [field strengths: 400 and 100 MHz respectively] in $CDCl_3$ solution (unless specified otherwise) with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C: $\delta = 0$). From sections 3.15-3.20 ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded using 5 mm tubes on a Bruker 500 MHz NMR spectrometer (unless specified otherwise) [field strengths: 500, 125 and 202 MHz respectively] in $CDCl_3$ solution (unless specified otherwise) with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C: $\delta = 0$) and ext. 85% H_3PO_4 (^{31}P: $\delta = 0$) respectively. All *J* values are in Hz.

LC-MS and HRMS: LC-MS equipment was used to record mass spectra for isolated compounds where appropriate. LC-MS data were obtained using electrospray ionization (positive mode) on a C-18 column. Mass spectra were recorded using HRMS (ESI-TOF analyzer) equipment.

UV-Visible and Emission: Absorption spectra were recorded on a Varian model Cary 100 UV-Vis spectrometer. Absorption spectra of solution samples were recorded in transmission mode and solid samples in diffuse reflectance mode and fluorescence emission spectra were recorded on a Jobin-Yvon Spex Fluoromax-4 spectrometer coupled with a Peltier device.

The precursor nitriles **1a-l** are available commercially. 2,3'-Biindoles **2a**-d,[66] aryl substituted propargylic alcohols **3a-f**,[67] allenylphosphine oxides **4a-f**,[68a-c] allenylphosphonates **5a-b**,[68a-c] α-methyl allenoate **6**[68d] and enynones **8a- e**[69a-d] were synthesized by following literature procedures. Aryl iodides, propargylic alcohols, acetyl chloride and 2-iodophenol are commercially available. Compound **2b** is new.

Compound 2b



Yield: 1.92 g (77%).

Mp: 134-138 °C.

IR (neat): 3049, 2974, 2931, 1613, 1589, 1459, 1376, 1337, 1264, 1157, 1013, 781, 733 $cm^{-1.}$

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 1H)), 7.68 (d, *J* = 7.5 Hz, 1H), 7.47 - 7.43 (m, *2*H), 7.39-7.31 (m, 1H), 7.28-7.23 (m, 2H), 7.22-7.19 (m, 1H), 7.18-7.15 (m, 1H), 6.63 (s, 1H), 4.32-4.25 (m, 4H), 1.58 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H).

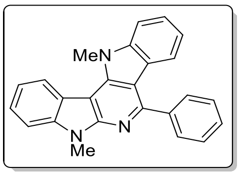
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 136.9, 136.1, 134.4, 128.9, 128.2, 126.5, 122.3, 121.0, 120.5, 120.3, 120.2, 119.6, 109.8, 109.7, 107.6, 102.2, 41.3, 38.8, 15.6.

HRMS (ESI): Calcd. for $C_{20}H_{21}N_2$ (M^+ + H): *m/z* 289.1704. Found: 289.1705.

3.1 General procedure for the synthesis of α-carbolines (9-27):

To a Schlenk tube was added biindole **2** (0.38 mmol), one of the nitriles **1a**-k (0.38 mmol), $Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (0.77 mmol) and DMF (2 mL). The contents were stirred at 110 °C (oil bath temperature) overnight. After completion of the reaction as monitored by TLC, the crude reaction mixture was passed through a pad of celite and washed with ethyl acetate (20 mL) and concentrated in vacuum. The resulting solution was washed with water (3 x 15 mL) followed by brine solution (25 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain the pure desired compound by using hexane-ethyl acetate as the eluent.

Compound 9



Yield: 0.106 g (92%)

Mp: 191-195 °C.

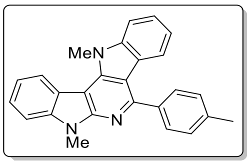
IR (neat): 3050, 2921, 1591, 1462, 1353, 1264, 733, 703 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.0 Hz, 1H), 7.91-7.89 (m, 2H), 7.64-7.56 (m, 5H), 7.54-7.51 (m, 2H), 7.48-7.44 (m, 1H), 7.38-7.34 (m, 1H), 7.13–7.09 (m, 1H), 4.57 (s, 3H), 4.12 (s, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 152.3, 150.5, 143.4, 141.3, 140.9, 139.3, 129.4, 128.6, 128.5, 124.8, 124.6, 123.1, 122.6, 121.4, 120.1, 119.6, 119.1, 111.6, 109.3, 108.7, 97.9, 34.0, 28.4.

HRMS (ESI): Calcd. for $C_{25}H_{20}N_3$ (M^+ + H): *m/z* 362.1657. Found: 362.1659.

Compound 10



Yield: 0.116 g (81%)

Mp: 232-235 °C.

IR (KBr): 3053, 2920, 2851, 1591, 1477, 1323, 1268, 730, 550 cm^{-1}

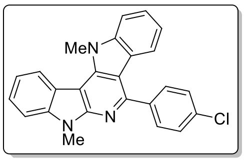
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.58-7.51 (m, 3H), 7.47-7.42 (m, 3H), 7.37-7.34 (m, 1H), 7.14–7.11 (m, 1H), 4.57 (s, 3H), 4.11 (s, 3H), 2.55 (s, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ ^{13}C NMR$\{^1H\}$ (100 MHz, $CDCl_3$) δ 151.5, 149.6, 142.4, 139.9, 138.3, 137.4_3, 137.3_9, 128.3, 128.2, 123.7, 123.6, 122.1, 121.5, 120.4, 119.1, 118.6, 118.2, 110.5, 108.3, 107.7, 96.7, 33.1, 27.4, 20.5

HRMS (ESI): Calcd. for $C_{26}H_{22}N_3$ (M^+ + H): *m/z* 376.1814. Found: 376.1819.

This compound was crystallized from $CHCl_3$-hexane (2:1) mixture at room temperature.

Compound 11



Yield: 0.128 g (84%)

Mp: 180-186 °C.

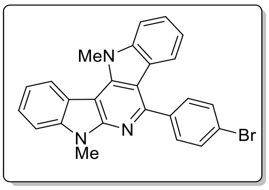
IR (neat): 3063, 2920, 2851, 1619, 1592, 1464, 1322, 1262, 1092, 1023, 798, 733 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.60-7.56 (m, 5H), 7.53-7.51 (m, 1H), 7.49-7.46 (m, 1H), 7.38-7.34 (m, 1H), 7.16–7.13 (m, 1H), 4.54 (s, 3H), 4.09 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 151.0, 150.6, 143.6, 141.1, 139.9, 139.5, 134.8, 131.0, 128.8, 125.1, 124.9, 122.9, 122.7, 121.3, 120.4, 119.8, 119.2, 111.6, 109.5, 108.9, 98.1, 34.2, 28.4.

HRMS (ESI): Calcd. for $C_{25}H_{19}ClN_3$ (M^+ + H) and (M^+ + H + 2): *m/z* 396.1268, 398.1238. Found: 396.1262, 398.1235.

Compound 12



Yield: 0.142 g (84%)

Mp: 180-184 °C

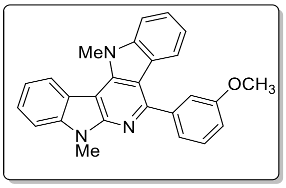
IR (neat): 3050, 2921, 2851, 1589, 1461, 1264, 741, 675 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.5 Hz, 1H), 7.80-7.74 (m, 4*H*), 7.59-7.36 (m, 5H), 7.36-7.35 (m, 1H), 7.16-7.13 (m, 1H), 4.57 (s, 3H), 4.10 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.9, 150.5, 143.5, 141.0, 140.2, 139.4, 131.7, 131.2, 125.0, 124.8, 122.9, 122.8, 122.6, 121.2, 120.3, 119.8, 119.1, 111.4, 109.4, 108.8, 98.1, 34.1, 28.4.

HRMS (ESI): Calcd. for $C_{25}H_{19}BrN_3$ (M^+ + H) and (M^+ + H + 2): *m/z* 440.0762, 442.0742. Found: 440.0761, 442.0742.

Compound 13



Yield: 0.122 g (81%)

Mp: 210-214 °C

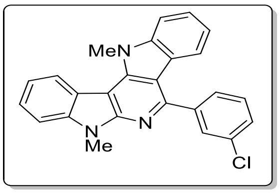
IR (neat): 3003, 2920, 2851, 1590, 1461, 1323, 736, 730 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.59-7.54 (m, 4H), 7.52-7.44 (m, 4H), 7.38-7.35 (m, 1H), 7.15-7.12 (m, 2H), 4.54 (s, 3H), 4.10 (s, 3H), 3.92 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 159.8, 152.1, 150.5, 143.4, 142.6, 140.9, 139.3, 129.6, 124.8, 124.7, 123.0, 122.6, 121.9, 121.5, 120.2, 119.7, 119.1, 114.9, 114.4, 111.5, 109.4, 108.7, 98.0, 55.5, 34.1, 28.4.

HRMS (ESI): Calcd. for $C_{25}H_{19}BrN_3$ ($C_{26}H_{22}N_3O$ (M^+ + H): *m/z* 392.1763. Found: 392.1762.

Compound 14



Yield: 0.124 g (82%)

Mp: 172-174 °C

IR (neat): 3003, 2920, 2851, 1590, 1461, 1323, 736, 730 cm^{-1}.

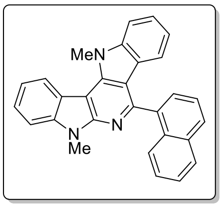
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.58 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 0.5 Hz, 1H), 7.80-7.78 (m, 1H), 7.59-7.53 (m, 6H), 7.50-7.47 (m, 1H), 7.39-7.36 (m, 1H), 7.17-7.14 (m, 1H), 4.59 (s, 3H), 4.13 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 150.5, 150.4, 143.5, 143.0, 141.0, 139.4, 134.5, 129.7, 129.6, 128.7, 127.7, 125.0, 124.9, 122.7, 121.2, 120.3, 119.8, 119.0, 111.5, 109.4, 108.8, 98.2, 34.1, 28.4.

HRMS (ESI): Calcd. for $C_{25}H_{19}ClN_3$ (M^+ + H) and (M^+ + H + 2): *m/z* 396.1268, 398.1238. Found: 396.1269, 398.1240.

This compound was crystallized from $CHCl_3$-hexane (2:1) mixture at room temperature.

Compound 15



Yield: 0.128 g (81%)

Mp: 180-186 °C

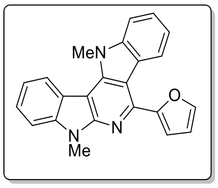
IR (neat): 2922, 2852, 1591, 1255, 1097, 782, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.79-7.78 (m, 1H), 7.74-7.71 (m, 1H), 7.62-7.57 (m, 3H), 7.52-7.48 (m, 2H), 7.41-7.34 (m, 2H), 7.31-7.27 (m, 1H), 6.89-6.85 (m, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 4.61 (s, 3H), 4.11 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 151.1, 150.7, 143.0, 140.9, 139.3, 138.7, 133.9, 131.9, 128.8, 128.2, 127.0, 126.3, 126.1, 126.0, 125.7, 124.8, 124.7, 122.9, 122.6, 121.3, 120.3, 119.7, 119.2, 113.3, 109.4, 108.5, 98.2, 34.1, 28.6.

HRMS (ESI): Calcd. for $C_{29}H_{22}N_3$ (M^+ + H): *m/z* 412.1814. Found: 412.1812.

Compound 16



Yield: 0.108 g (80%)

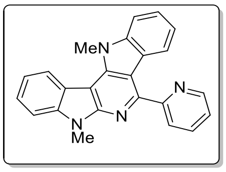
IR (neat): 3050, 2922, 2853, 1579, 1467, 1404, 1358, 1258, 1164, 1013, 798, 743 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81-7.77 (m, 2H), 7.68 (d, *J* = 3.6 Hz, *1*H), 7.57-7.46 (m, *3*H), 7.37-7.33 (m, 4H), 7.29-7.28 (3, 1H), 3.95 (s, 3H), 3.80(s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.6, 146.9, 143.6 , 137.2, 137.1, 130.7, 128.0, 126.6, 123.3, 122.8, 122.1, 121.0, 120.0, 119.2, 117.5, 110.3, 110.1, 103.3, 85.3, 33.3, 32.0.

HRMS (ESI): Calcd. for $C_{23}H_{18}N_3O$ (M^+ + H): *m/z* 352.1450. Found: 352.1449.

Compound 17



Yield: 0.108 g (80%).

Mp: 153-159 ^{o}C.

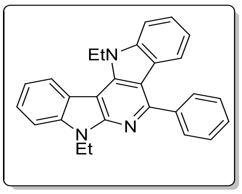
IR (neat): 2958, 2922, 2852, 1461, 1264, 742, 560 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.89(s, 2H,), 8.55 (d, *J* = 8.0 Hz *1*H), 7.84 (d, *J* = 5.0 Hz, 2H),7.59-7.53 (m, 3H), 7.51-7.48 (m, 2H), 7.39-7.35 (m, 1H), 7.17-7.13 (m, 1H), 4.52 (s, 3H), 4.07(s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.4, 150.1, 149.0 , 148.9, 143.5, 141.0, 139.5, 125.3, 125.1, 124.3, 122.8, 122.2, 121.1, 120.4, 119.9, 118.9, 111.3, 109.4, 190.0, 98.5, 34.1, 28.3.

HRMS (ESI): Calcd. for $C_{24}H_{19}N_4$ (M^+ + H): *m/z* 363.1603. Found: 363.1609.

Compound 18



Yield: 0.128 g (86%).

Mp: 158-162 ^{o}C.

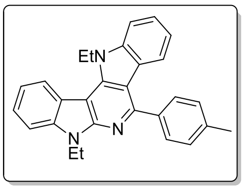
IR (neat): 3051, 2975, 2930, 1614, 1585, 1473, 1326, 1191, 1028, 796, 733 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.38(d, *J* = 8.0 Hz, 1H), 7.89 (dd, *J* =1.5 Hz, 2H), 7.64-7.55 (m, *6H*,), 7.51 (d, *J* = 8.0 Hz, 1H), 7.45-7.38 (m, 1H), 7.12-7.09 (m, 1H), 7.12-7.08 (m, 1H), 5.05 (q, *J*= 7.0 Hz, 2H), 4.75 (q, *J*= 7.0 Hz, 2H), 1.83 (t, *J*= 7.5 Hz, 3H), 1.53 (t, *J*= 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 152.4, 149.9, 142.6, 141.5, 139.8, 138.2, 129.4, 128.5_3, 128.4_5, 124.7, 124.5, 123.2, 122.5, 121.5, 120.1, 119.7, 119.4, 111.5, 109.4, 108.5, 97.5, 40.6, 36.6, 16.2, 14.1.

HRMS (ESI): Calcd. for $C_{27}H_{23}N_3$ (M^+ + H): *m/z* 390.1970. Found: 390.1972.

Compound 19



Yield: 0.147 g (95%).

Mp: 150-156 °C.

IR (KBr): 3051, 2975, 2930, 1614, 1585, 1473, 1326, 1191, 1028, 796, 733 cm^{-1}.

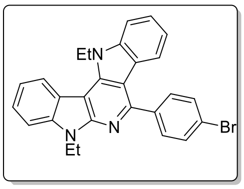
1H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* =8.0 Hz, 2H), 7.63-7.58 (m, 2H), 7.56-7.53 (m,2H), 7.46-7.42 (m, 3H), 7.39-7.36 (m, 1H), 7.13-7.10 (m, 1H), 5.04 (q, *J*= 7.2 Hz, 2H), 4.75 (q, *J*= 7.2 Hz, 2H), 2.55 (s, 3H), 1.82 (t, *J*= 7.2 Hz, 3H), 1.52 (t, *J*= 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.6, 149.9, 142.6, 139.7, 138.6, 138.4, 138.2, 129.3, 129.2, 124.6, 124.4, 123.3, 122.5, 121.5, 120.0, 119.7, 119.4, 111.5, 109.4, 108.5, 97.4, 40.6, 36.6, 21.6, 16.2, 14.1.

HRMS (ESI): Calcd. for $C_{28}H_{26}N_3$ (M^+ + H): *m/z* 404.2125. Found: 404.2121.

This compound was crystallized from $CHCl_3$-hexane (2:1) mixture at room temperature.

Compound 20



Yield: 0.150 g (82%).

Mp: 160-165 °C.

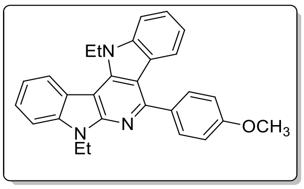
IR (neat): 3063, 2973, 2927, 1613, 1587, 1466, 1347, 1226, 742, 579 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.0 Hz, 1H), 7.80-7.75 (m, 4H), 7.62 (d, *J* = 8.0 Hz, 1*H*), 7.58-7.55 (m, 3H), 7.48-7.45 (m, 1H), 7.40-7.37 (m, 1H), 7.16-7.13 (m, 1H), 5.03 (q, *J* = 7.2 Hz, 2H), 4.73 (q, *J* = 7.2 Hz, 2H), 1.82 (t, *J* = 7.2 Hz, 3H), 1.52 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 149.8, 142.6, 140.4, 139.8, 138.3, 131.7, 131.3, 124.9, 124.7, 122.9, 122.6, 121.3, 120.2, 119.8, 119.3, 111.4, 109.5, 108.7, 97.7, 40.7, 36.7, 16.2, 14.1.

HRMS (ESI): Calcd. for $C_{27}H_{23}BrN_3$ (M^+ + H) and (M^+ + H + 2): *m/z* 468.1075., 470.1058. Found: 468.1073, 470.1056.

Compound 21



Yield: 0.141 g (88%).

Mp: 210-214 °C.

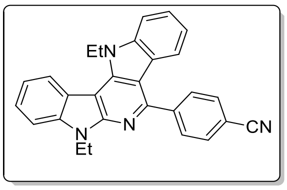
IR (neat): 3053, 2983, 2932, 1584, 1471, 1326, 1264, 1236, 736, 738 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.85-7.83 (m, 2H), 7.64-7.61 (m, 2H), 7.56-7.53 (m, 2H), 7.46-7.43 (m, 1H), 7.39-7.36 (m, 1H), 7.16-7.11 (m, 3H), 5.04 (q, *J* = 7.2 Hz, 2H), 4.75 (q, *J* = 7.2 Hz, 2H), 3.98 (s, 3H), 1.82 (t, *J* = 7.2 Hz, 3H), 1.52 (t, *J* = 7.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 152.2, 149.9, 142.6, 139.7, 138.2, 134.0, 130.8, 124.6, 124.4, 123.4, 122.5, 121.5, 120.0, 119.7, 119.4, 113.9, 111.5, 109.4, 108.5, 97.3, 55.5, 40.6, 36.6, 16.2, 14.1.

HRMS (ESI): Calcd. for $C_{28}H_{25}N_3O$ (M^+ + H): *m/z* 420.2076. Found: 420.2077.

Compound 22



Yield: 0.141 g (88%).

Mp: 180-184 °C.

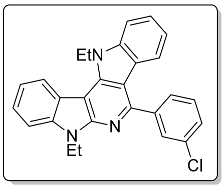
IR (neat): 2921, 2851, 2210, 1963, 1589, 1370, 1217, 816, 686 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.85-7.83 (m, 2H), 7.64-7.61 (m, 2H), 7.56-7.53 (m, 2H), 7.46-7.43 (m, 1H), 7.39-7.36 (m, 1H), 7.16-7.11 (m, 3H), 5.04 (q, *J* = 7.2 Hz, 2H), 4.75 (q, *J* = 7.2 Hz, 2H), 3.98 (s, 3H), 1.82 (t, *J* = 7.2 Hz, 3H), 1.52 (t, *J* = 7.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.59-7.57 (m, 2H), 7.50-7.47 (m, 2H), 7.42-7.38 (m, 1H), 7.16-7.13 (m, 1H), 5.05 (q, *J* = 7.2 Hz, 2H), 4.74 (q, *J*= 7.2 Hz, 2H), 1.83 (t, *J*= 7.2 Hz, 3H), 1.52 (t, *J*= 7.0 Hz, 3H).

HRMS (ESI): Calcd. for $C_{28}H_{23}N_3O$ (M^+ + H): *m/z* 415.1922. Found: 415.1921.

Compound 23



Yield: 0.143 g (88%).

Mp: 200-204 °C.

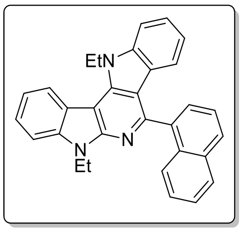
IR (neat): 3063, 2973, 2927, 1613, 1587, 1466, 1347, 1226, 742, 579 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.0 Hz, 1H*), 7.88 (s, 1H)*, 7.79-7.77 (m, 1H*),* 7.64- 7.62 (m, 1H), 7.58-7.52 (m, 4H), 7.48-7.45 (m, 1H), 7.40-7.38 (m, 1H), 7.16-7.13 (m, 1H), 5.04 (q, *J*= 7.2 Hz, 2H), 4.75 (q, *J*= 7.2 Hz, 2H), 1.82 (t, *J*= 7.2 Hz, 3H), 1.53 (t, *J*= 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 150.6, 149.8, 143.2, 142.6, 139.8, 138.3, 134.4, 129.7, 129.6, 128.6, 127.7, 124.9, 124.7, 122.9, 122.6, 121.3, 120.3, 119.8, 119.2, 111.4, 109.5, 108.7, 97.8, 40.6, 36.7, 16.2, 14.1.

HRMS (ESI): Calcd. for $C_{27}H_{23}ClN_3$ (M^+ + H): *m/z* 424.1580, 426.1551. Found: 424.1581, 426.1553.

Compound 24



Yield: 0.134 g (80%).

Mp: 190-195 °C.

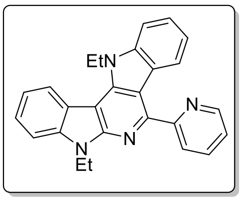
IR (neat): 3063, 2973, 2927, 1613, 1587, 1466, 1347, 1226, 742, 579 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.78-7.71 (m, 2H), 7.67-7.64 (m, 2H), 7.60-7.57 (m, 1H), 7.53-7.50 (m, 2H), 7.44-7.41 (m, 1H), 7.37-7.28 (m, 2H), 6.87 (t, J = 7.5 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 5.07 (q, *J* = 7.0 Hz, 2H), 4.74 (q, *J*= 7.0 Hz, 2H), 1.87 (t, *J* = 7.0 Hz, 3H), 1.51 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 149.9, 142.2, 139.8, 138.8, 138.2, 134.0, 132.0, 128.8, 128.2, 127.1, 126.3, 126.1, 126.0, 125.7, 124.7, 124.6, 123.1, 122.6, 121.4, 120.3, 119.8, 119.4, 113.2, 109.5, 108.4, 97.8, 40.7, 36.8, 16.3, 14.2.

HRMS (ESI): Calcd. for $C_{31}H_{26}N_3$ (M^+ + H): *m/z* 440.2127. Found: 440.2126.

Compound 25



Yield: 0.128 g (81%).

Mp: 180-184 °C.

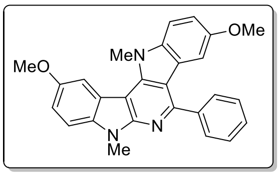
IR (neat): 2921, 2851, 2210, 1963, 1589, 1370, 1217, 816, 686 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.59-7.57 (m, 2H), 7.50-7.47 (m, 2H), 7.42-7.38 (m, 1H), 7.16-7.13 (m, 1H), 5.05 (q, *J* = 7.2 Hz, 2H), 4.74 (q, *J*= 7.2 Hz, 2H), 1.83 (t, *J*= 7.2 Hz, 3H), 1.52 (t, *J*= 7.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.7, 146.1, 142.7, 139.9, 138.4, 132.3, 130.4, 125.2, 125.0, 122.7, 122.5, 121.0, 120.3, 120.0, 119.1, 119.0, 112.2 111.4, 109.5, 108.9, 98.0, 40.7, 36.7, 16,1, 14.0.

HRMS (ESI): Calcd. for $C_{28}H_{23}N_3O$ (M^+ + H): *m/z* 415.1922. Found: 415.1921.

Compound 26



Yield: 0.129 g (81%).

Mp: 155-160 °C.

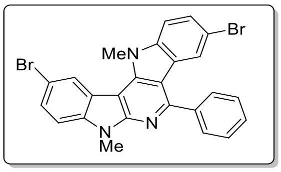
IR (neat): 2925, 2852, 1594, 1547, 1488, 1264, 1147, 1036, 733, 703 $cm^{-1.}$

1H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 2.0 Hz, 1H), 7.88-7.86 (m, 2H), 7.63-7.60 (m, 2H), 7.58-7.56 (m, 1H), 7.45 (d, *J* = 9.0 Hz, 1H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.19 (dd, *J* = 9.0 Hz, 1H), 7.05 (dd, *J* = 9.0 Hz, 1H), 6.95 (d, *J* = 2.5 Hz, 1H), 4.49 (s, 3H), 4.07 (s, 3H), 4.0 (s, 3H), 3.67 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.2, 153.8, 152.5, 150.9, 143.7, 141.1, 135.7, 134.5, 129.5, 128.7, 128.5, 123.7, 119.6, 113.2, 112.2, 111.2, 109.6, 109.3, 107.6, 104.8, 97.8, 56.4, 55.6, 34.2, 28.5.

HRMS (ESI): Calcd. for $C_{27}H_{24}N_3O_2$ (M^+ + H): *m/z* 422.1868. Found: 422.1870.

Compound 27



Yield: 0.165 g (84%).

Mp: 152-156 °C.

IR (neat): 2925, 2852, 1594, 1547, 1488, 1264, 1147, 1036, 733, 703 $cm^{-1.}$

1H NMR (500 MHz, $CDCl_3$): δ 8.58 (d, *J* = 1.5 Hz, 1H), 7.86-7.84 (m, 2H), 7.67-7.60 (m, 5H), 7.53 (dd, *J* = 2.0 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 4.46 (s, 3H), 4.06 (s, 3H).

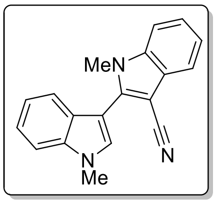
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.3, 150.8, 143.5, 140.4, 139.5, 137.9, 129.2, 128.7, 127.6, 127.5, 125.0, 124.7, 124.0, 120.6, 113.5, 112.6, 110.9, 110.8, 110.2, 97.1, 34.3, 28.5.

HRMS (ESI): Calcd. for $C_{25}H_{18}Br_2N_3$ (M^+ + H) and (M^+ + H + 2): *m/z* 517.9867, 519.9845, 521.9823 Found: 517.9864, 519.9849, 521.9830.

3.2 General procedure for the synthesis of 3-cyano-2,3’-biindoles (28-31)

A procedure similar to that for **9** was used using the same molar quantities of the 2,3'-biindole and ethyl cyanoacetate **1l**; the eluent was ethyl acetate (1:9)

Compound 28



Yield: 0.092 g (86%).

Mp: 140-144 ^{o}C.

IR (neat): 2922, 2851, 2211, 1470, 1370, 1218, 771, 748 cm^{-1}.

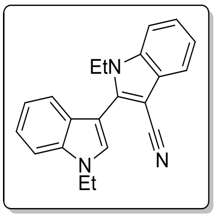
1H NMR (500 MHz, $CDCl_3$): δ 7.69-7.67 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.37-7.33 (m, 3H), 7.28-7.24 (m, 2H), 7.23-7.21 (m, 1H), 7.17-7.14 (m, 1H), 3.81 (s, 3H), 3.67 (s, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 143.6, 137.1_4, 137.1_0, 130.7, 128.0, 126.6, 123.3, 122.8, 122.1_3, 121.1_0, 120.5, 119.2, 117.4, 110.3, 110.1, 103.2, 85.2, 33.3, 32.0.

HRMS (ESI): Calcd. for $C_{19}H_{16}N_3$ (M^+ + H): *m/z* 286.1344. Found: 286.1340.

This compound was crystallized from ethyl acetate-hexane (2:1) mixture at room temperature.

Compound 29



Yield: 0.106 g (89%).

Mp: 141-144 ^{o}C.

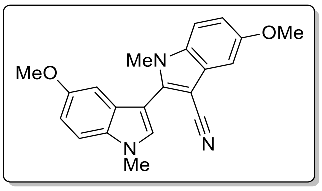
IR (neat): 2923, 2852, 2210, 1571, 1460, 1386, 1227, 1134, 1015, 741, 700 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.51-7.49 (m, 3H), 7.39-7.35 (m, 2H), 7.33-7.32 (m, 1H), 7.28-7.24 (m, 1H), 4.35-4.29 (m, 4H), 1.61 (t, *J* = 7.0 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 142.8, 136.2, 135.8, 128.5, 128.4, 126.8, 123.2, 122.7, 122.0, 120.8, 120.0, 119.4, 117.2, 110.7, 110.1, 103.4, 86.1, 41.5, 39.9, 15.4, 15.2.

HRMS (ESI): Calcd. for $C_{21}H_{20}N_3$ (M^+ + H): *m/z* 314.1657. Found: 314.1650.

Compound 30



Yield: 0.112 g (86%).

Mp: 164-168 °C.

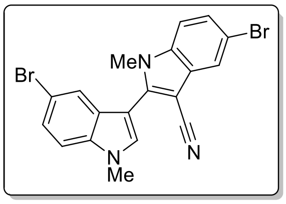
IR (neat): 2922, 2852, 2210, 1620, 1579, 1488, 1367, 1292, 1175, 1033, 832, 798 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): (major isomer) δ 7.41 (s, 1H), 7.34 (dd, *J* = 1.7 Hz, 2H), 7.23 (d, *J* = 2.5 Hz, 1H), 7.02-7.0 (m, 2H), 6.97 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.76 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): (mixture of isomers) δ 156.1, 155.2, 143.6, 132.3, 132.0, 130.8, 128.9, 127.1, 117.6, 113.6, 113.2, 111.2, 110.9, 103.0, 101.7, 100.7, 84.7, 55.9_5, 55.9_1, 33.5, 32.1.

HRMS (ESI): Calcd. for $C_{21}H_{20}N_3O_2$ (M^+ + H): *m/z* 346.1555 . Found: 346.1556. A small amount (< 5%) of a minor isomer was shown in the ^1H NMR spectrum.

Compound 31



Yield: 0.137 g (82%).

Mp: 188-192 °C .

IR (neat): 2982, 2851, 2212, 1599, 1446, 1366, 1122, 1071, 1015, 862, 739 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$): (major isomer) (mixture of isomers ratio) 1:5δ 7.89 (d, *J* = 1.0 Hz, 1H), 7.62 (d, *J* = 1.5 Hz, 1H), 7.48 (s, 1H), 7.46-7.42 (m, 2H), 7.35-7.30 (m, 2H), 3.91 (s, 3H), 3.74 (s, 3H).

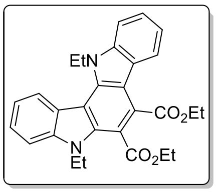
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): (mixture of isomers) δ 143.6, 135.9, 131.9, 130.3, 129.4, 128.1, 127.7, 126.6, 126.0, 123.6, 122.4, 121.9, 116.8, 116.4, 115.8, 114.7, 112.5, 112.2, 111.8$_4$, 111.8$_0$, 102.4, 85.2, 33.6, 32.6, 32.3, 32.2.

HRMS (ESI): Calcd. for $C_{19}H_{14}N_3Br_2$ (M^+ + H) and (M^+ + H + 2): *m/z* 441.9558, 443.9529 . Found: 441.9551, 443.9535.

3.3 General procedure for the synthesis of carbazole 33

To ascertain the reactivity of the 2- and 3'-positions of the 2,3′-biindoles, we examined the reaction between biindole 2**b** and diethyl acetylene dicarboxylate **32** in toluene at 110 °C for 48 h. The [4 + 2] cycloaddition product (after aromatization, removal of hydrogen) carbazole **33** was obtained in good yield.

Compound 33



Yield: 0.131 g (75%).

Mp: 180-184 °C.

IR (neat): 2979, 2934, 1723, 1611, 1573, 1475, 1368, 1273, 1225, 1191, 1055, 1022, 746 cm^{-1}.

1H NMR (500 MHz, $CDCl_3$):δ 8.41 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.59-7.54 (m, 3H), 7.50-7.47 (m, 1H), 738-7.35 (m, 1H), 7.31- 7.26 (m, 1H), 4.97 (q, *J* = 7.0 Hz, 2H), 4.60 (q, *J* = 7.0 Hz, 2H), 4.52- 4.45 (m, 4H), 1.70 (t, *J* = 7.0 Hz, 3H), 1.48 (t, *J* = 7.0 Hz, 6H), 1.43 (t, *J* = 7.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 160.1, 168.6, 141.3, 141.2, 138.4, 136.4, 125.7, 125.4, 125.1, 122.82, 122.77,121.0, 120.8, 120.3, 120.1, 112.9, 109.8, 109.6, 108.9, 62.0, 61.9, 41.3, 40.1, 15.9, 14.2, 14.1, 13.7.

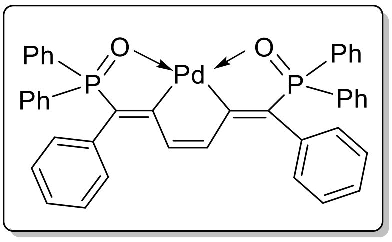
HRMS (ESI): Calcd. for $C_{28}H_{28}N_2O_4$ (M^+ + H): *m/z* 457.2127. Found: 457.2126.

3.4 General procedure for the synthesis of Pd-P complexes 34-38

To an oven dried Schlenk tube, allenylphosphine oxide **4a** (0.316 mmol), $Pd(OAc)_2$ (0.158 mmol), Ag_2CO_3 (0.316 mmol), PPh_3 (0.158 mmol) and dry CH_3CN (2 mL) were added. The contents were sealed under nitrogen atmosphere and stirred at reflux for 12 h.

After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to room temperature, ethyl acetate (20 mL) was added to the mixture, filtered and the filtrate concentrated under vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (7:3) as the eluent to afford Pd-complex **34**. Compounds **35-38** were prepared by following the same procedure and by using the same molar quantities.

Compound 34



Yield: 42 mg (36%, R_f = 0.65 (7:3 hexane + ethyl acetate)).

Mp: 200-204 ^{o}C.

IR (KBr): 3055, 2922, 2851, 2161, 1736, 1520, 1435, 1366, 1264, 1123, 1062, 942, 737, 699, 609 cm^{-1}.

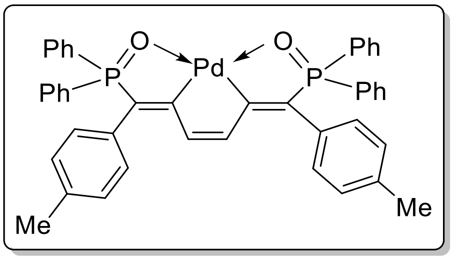
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.77-7.73 (m, 8H), 7.57-7.53 (m, 4H), 7.45-7.41 (m, 8H), 7.20-7.15 (m, 6H); 6.85 (d, *J* = 8.0 Hz, 4H), 6.41 (s, 2H)

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 180.6 (*J* = 12.5 Hz), 147.1 (*J* = 18.7 Hz), 135.6 (*J* = 18.6 Hz), 133.3 (*J* = 117.7 Hz, P-*C*), 132.3 (*J* = 9.6 Hz), 131.9 (*J* = 2.1 Hz), 131.4, 130.1 (*J* = 4.5 Hz), 128.2 (*J* = 11.9 Hz), 128.1. 126.8.

^{31}P NMR(162 MHz, CDCl$_3$) δ 32.7, 29.3.

HRMS (ESI): Calcd for $C_{46}H_{43}O_2P_2$ (M^{+}+H): m/z 689.2738. Found 689.2736.

Compound 35



Yield: 46.8 mg (45%, R_f = 0.58 (7:3 hexane + ethyl acetate)).

Mp: 185-191 ^{o}C.

IR (KBr): 3055, 2922, 2851, 2161, 1736, 1520, 1435, 1366, 1264, 1123, 1062, 942, 737, 699, 609 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.77-7.72 (m, 8H), 7.54-7.52 (m, 4H), 7.45-7.40 (m, 8H), 6.97 (d, *J* = 8.0 Hz, 4H), 6.73 (d, *J* = 8.0 Hz, 4H), 6.40 (s, 2H), 2.29 (s, 6H).

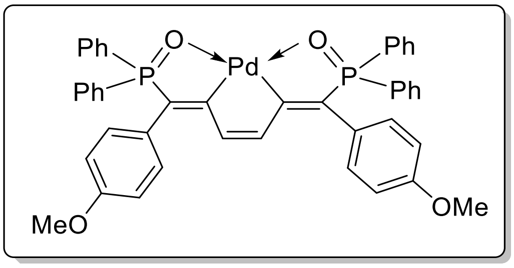
^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 180.5 (*J* = 13.4 Hz), 147.0 (*J* = 19.2 Hz), 136.4 (*J* = 1.5 Hz), 132.2 (*J* = 8.5 Hz), 132.5, 132.3, 132.2, 132.0 (*J* = 99.1 Hz), 131.8 (*J* = 2.1 Hz), 129.9 (*J* = 4.5 Hz), 128.8, 128.2 (*J* = 11.7 Hz), 21.1.

^{31}P NMR (162 MHz, CDCl$_3$) δ 51.6.

HRMS (ESI): Calcd for $C_{44}H_{37}O_2P_2Pd$ (M$^+$+H): m/z 765.1303. Found 765.1302.

This compound was crystallized from ethyl acetate-hexane (2:1) mixture at room temperature.

Compound 36



Yield: 56 mg (51%, R_f = 0.68 (7:3 hexane +ethyl acetate)).

Mp: 210-214 °C.

IR (KBr): 3002, 2923, 2852, 1603, 1570, 1519, 1461, 1436, 1285, 1246, 1177, 1123, 1062, 1029, 948, 922, 749 cm^{-1}.

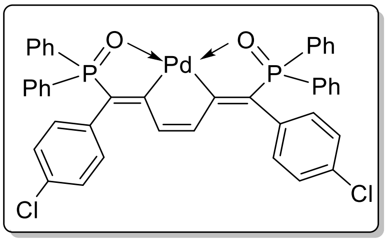
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.77-7.72 (m, 8H), 7.56-7.52 (m, 4H), 7.45-7.41 (m, 8H), 6.78-6.70 (m, 8H), 6.40 (s, 2H), 3.77 (s, 6H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 180.3 (*J* = 13.7 Hz), 158.4, 146.8 (*J* = 18.7 Hz), 132.9 (*J* = 118.4 Hz), 132.3 (*J* = 9.7 Hz), 131.9 (*J* = 2.0 Hz), 131.5, 131.1 (*J* = 4.4 Hz), 128.2

^{31}P NMR (162 MHz, CDCl$_3$) δ51.3.

HRMS (ESI): Calcd for $C_{44}H_{37}O_4P_2Pd$ (M$^+$+H): m/z 797.1202. Found 797.1203.

Compound 37



Yield: 46 mg (41%, R_f = 0.68 (7:3 hexane +ethyl acetate).

Mp: 200-204 °C.

IR (KBr): 3055, 2921, 2851, 1738, 1625, 1589, 1520, 1481, 1435, 1366, 1262, 1216, 1120, 1089, 1063, 1313, 952, 928, 829, 748 cm^{-1}.

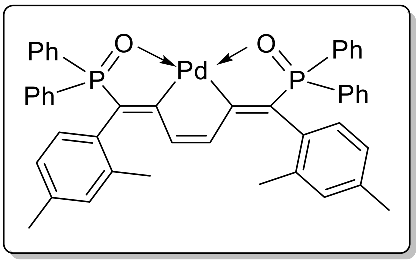
^{1}H NMR (500 MHz, $CDCl_3$):) δ 7.75-7.71 (m, 8H), 7.58-7.55 (m, 4H), 7.47-7.43 (m, 8H), 7.15 (d, *J* = 8.3 Hz, 4H); 6.77-6.75 (m, 4H), 6.37 (s, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 181.1 (*J* = 12.8 Hz), 147.1 (*J* = 18.5 Hz), 134.0 (*J* = 18.9 Hz), 132.8, 132.7, 132.2, 132.1, 131.8, 131.3, 131.2, 131.3 (*J* = 100.0 Hz, P-*C*), 128.5, 128.4.

^{31}P NMR(162 MHz, $CDCl_3$) δ51.9.

HRMS (ESI): Calcd for $C_{42}H_{31}Cl_2O_2P_2Pd$ (M^++H) and (M^++H+2): m/z 805.0211, 807.0215. Found 805.0218, 807.0209.

Compound 38



Yield: 44 mg (40.3 %, R_f = 0.65 (7:3 hexane + ethyl acetate)).

Mp: > 200 °C.

IR (KBr): 3055, 2969, 2922, 2852, 1437, 1367, 1216, 1119, 901, 753 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$):) δ 7.77-7.72 (m, 8H), 7.64-7.61 (m, 2H), 7.55-7.53 (m, 4H), 7.50-7.41 (m, 10H), 6.82 (s, 2H), 6.43 (d, J = 7.0 Hz, 4H), 2.13 (s, 12H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 180.2 (*J* = 13.4 Hz), 147.0 (*J* = 19.0 Hz), 137.3, 135.3 (*J* = 18.5 Hz), 133.9 (*J* = 118.8, P-*C* Hz), 132.9, 132.7, 132.5, 132.4, 132.3, 131.8, 131.7, 128.5, 128.3, 127.9, 126.2, 126.1, 21.2.

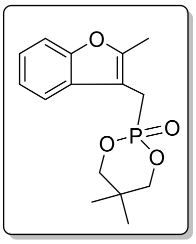
^{31}P NMR(162 MHz, $CDCl_3$) δ51.6.

HRMS (ESI): Calcd for $C_{46}H_{41}O_2P_2Pd$ (M^++H): m/z 793.1616. Found 793.1612.

3.5 General procedure for the synthesis of P-benzofurans and dihydro-phosphano benzofurans (39-41, 43 and 40′-42′)

In an oven dried Schlenk tube, allenylphosphonate **5a** (64 mg, 0.316mmol), 2-iodophenol (0.38 mmol), [Pd]-complex **35** (0.008 mol, 2.5 mol%) and CsF (0.632 mm) were taken in PEG-400 solvent (2 mL) and the contents stirred at 90 °C (oil bath) for 12h. After completion of the reaction as monitored by TLC, the crude mixture was passed through a pad of celite, washed with ethyl acetate (20 mL). The resulting solution was washed with water (3 x 15 mL) followed by brine solution (25 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain phosphano-benzofuran **39**. When we repeated the same reaction by using allenylphosphine oxides **4a-c** and **4f** with same molar quantities, we isolated phosphano benzofurans **40-41** and **43** (as minor products) along with dihydro-phosphano-benzofuran **40′-42′** (major). Compounds **40-41** (higher R_f) moved faster compared to **40′-42′** (lower R_f).

Compound-39



Yield: 38 mg (40 %, R_f = 0.55 (7:3 hexane + ethyl acetate)).

Mp: 141-145 °C.

IR (KBr): 2965, 1631, 1474, 1455, 1405, 1370, 1268, 1126, 1060, 1009, 918, 819 cm^{-1}.

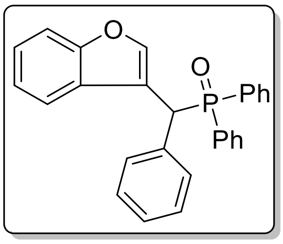
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.52-7.50 (m, 1H), 7.40-7.38 (m, 1H), 7.24-7.22 (m, 2H), 4.20-4.17 (m, 2H), 3.64-3.59 (m, 2H), 3.27 (d, J = 20.5 Hz, 2H), 2.46 (d, *J* = 4.5 Hz, 3H), 0.89 (s, 3H), 0.74 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$):) δ 153.8, 152.9 (*J* = 9.9 Hz), 128.9, 123.5, 122.5, 119.0, 110.6, 104.8 (*J* = 11.4 Hz), 74.9 (*J* = 6.5 Hz), 32.4 (*J* = 5.9 Hz), 21.4 (*J* = 142.0 Hz, P-*C*), 21.3, 21.1, 12.1.

^{31}P NMR (162 MHz, CDCl$_3$) δ 23.1.

HRMS (ESI): Calcd for $C_{15}H_{20}O_4P$ (M^++H): m/z 295.1099 Found 295.1101.

Compound 40



Yield: 32 mg (22 %, R_f = 0.58 (7:3 hexane + ethyl acetate)).

Mp: 138-144 °C .

IR (neat): 2921, 2852, 1453, 1436, 1173, 1099, 719, 697 cm^{-1}.

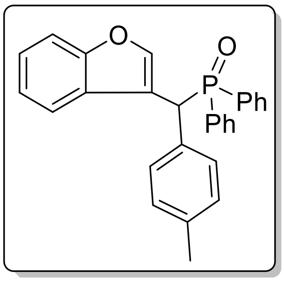
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.26 (s, 1H), 7.86-7.82 (m, 2H), 7.48- 7.44 (m, 3H), 7.42-7.39 (m, 4H), 7.32-7.28 (m, 6H), 7.26-7.23 (m, 1H), 7.17-7.14 (m, 3H), 4.93 (d, *J* = 9.5 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 154.6, 144.4 (*J* = 6.0 Hz), 134.8 (*J* = 5.5 Hz), 132.5 (*J* = 8.8 Hz), 131.8 (*J* = 2.5 Hz), 131.7, 131.5 (*J* = 2.5 Hz),131.2 (*J* = 8.8 Hz), 131.1 (*J* = 8.4 Hz), 129.8 (*J* = 5.3 Hz), 128.6 (*J* = 11.3 Hz), 128.3 (*J* = 1.6 Hz), 128.1 (*J* = 11.8 Hz), 127.5 (*J* = 9.4 Hz), 127.2 (*J* = 2.4 Hz), 124.4, 122.5, 119.1, 116.3 (*J* = 4.4 Hz), 111.5, 43.2 (*J* = 66.0 Hz). The phenyl groups attached to P probably show some inequality.

^{31}P NMR (162 MHz, CDCl$_3$) δ 31.7.

HRMS (ESI): Calcd for $C_{27}H_{22}O_2P$ (M^++H): m/z 409.1357. Found 409.1354.

Compound 41



Yield: 25 mg (20 %, R_f = 0.58 (7:3 hexane + ethyl acetate)).

Mp: 145-152 ^{o}C .

IR (KBr): 3339, 2924, 2832, 1979, 1702, 1589, 1466, 1115, 1020, 904, 747, 696 cm^{-1}.

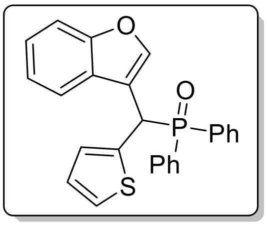
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.84-7.80 (m, 2H), 7.51- 7.36 (m, 8H), 7.33-7.29 (m, 2H), 7.25-7.22 (m, 1H), 7.19-7.13 (m, 3H), 6.96 (d, *J* = 8.0 Hz, 2H), 4.91 (d, *J* = 9.5 Hz, 1H), 2.23 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 154.6, 144.3 (*J* = 6.0 Hz), 136.8, 132.7, 132.6, 131.7 (*J* = 15.0 Hz), 131.5 (*J* = 18.6 Hz), 131.3 (*J* = 8.7 Hz), 131.1 (*J* = 8.4 Hz), 129.7, 129.6, 129.0, 128.6 (*J* = 11.3 Hz), 128.1 (*J* = 11.7 Hz), 127.5 (*J* = 9.2 Hz),124.3, 122.5, 119.1, 116.4 (*J* = 4.5 Hz), 111.5, 42.7 (*J* = 66.4 Hz), 21.0.

^{31}P NMR (162 MHz, $CDCl_3$) δ 31.6.

HRMS (ESI): Calcd for $C_{28}H_{24}O_2P$ (M$^+$+H): m/z 423.1514 Found 423.1515.

Compound 43



Yield: 28 mg (22 %, R_f = 0.58 (7:3 hexane + ethyl acetate)).

Mp: 148-153 ^{o}C .

IR (neat): 2922, 1452, 1367, 1215, 1173, 1100, 745, 718, 695 cm^{-1}.

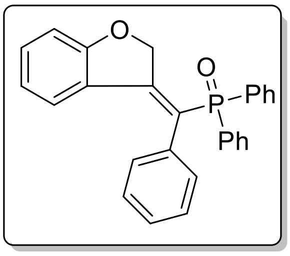
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 1.5 Hz, 1H), 7.79-7.75 (m, 2H), 7.69-7.65 (m, 2H), 7.51-7.47 (m, 2H), 7.44-7.38 (m, 4H), 7.37-7.33 (m, 2H), 7.27-7.24 (m, 1H), 7.20-7.17 (m, 1H), 7.09-7.08 (m,1H), 6.99-6.98 (m, 1H), 6.83-6.81 (m, 1H), 5.28 (d, *J* = 10.0 Hz, 1H).

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 154.6, 144.5 (d, *J* = 5.6 Hz), 137.0 (d, *J* = 5.8 Hz), 132.0 (d, *J* = 10.5 Hz), 131.8 (*t* = 2.6 Hz), 131.4 (d, *J* = 8.8 Hz), 131.2, 131.1 (d, *J* = 8.9 Hz), 128.6 (d, *J* = 11.6 Hz), 128.3 (d, *J* = 11.9 Hz), 127.8 (d, *J* = 6.0 Hz), 127.1 (d, *J* = 7.6 Hz), 126.9 (d, *J* = 2.3 Hz), 125.2 (d, *J* = 2.5 Hz), 124.5, 122.6, 119.3, 116.4 (d, *J* = 4.0 Hz), 111.5, 38.3 (d, *J* =71.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 30.6.

HRMS (ESI): Calcd for $C_{25}H_{20}O_2PS$ (M^{+}+H): m/z 415.0926. Found 415.0926.

Compound 40'



Yield: 39 mg (30 %, R_f = 0.64 (7:3 hexane + ethyl acetate)).

Mp: 185-192 °C .

IR (neat): 3057, 2922, 2852, 1465, 1437, 1184, 1116, 990, 722, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.60 (m, 4H), 7.50-7.48 (m, 2H), 7.40-7.36 (m, 4H), 7.24-7.18 (m, 4H), 6.92-6.88 (m, 3H), 6.54-6.51 (m, 1H), 5.99 (d, *J* = 8.0 Hz, 1H), 5.78 (d, *J* = 4.5 Hz, 2H).

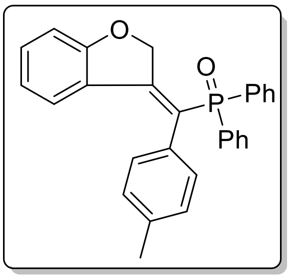
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 165.4, 152.7 (d, *J* = 7.5 Hz), 136.7 (d, *J* = 9.6 Hz), 132.5, 132.1 (d, *J* = 9.8 Hz), 132.0, 131.8 (d, *J* = 2.6 Hz), 131.2, 130.2 (d, *J* = 3.9 Hz), 129.1, 129.0, 128.2 (d, *J* = 11.9 Hz), 127.6 (d, *J* = 1.9 Hz), 125.7, 124.9 (d, *J* = 15.0 Hz), 121.7, 121.0, 120.4, 111.0, 75.3 (d, *J* = 4.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 29.5.

HRMS (ESI): Calcd for $C_{27}H_{22}O_2P$ (M^{+}+H): m/z 409.1357. Found 409.1353.

This compound was crystallized from chloro benzene-hexane (2:1) mixture at room temperature.

Compound 41′



Yield: 38 mg (29 %, R_f = 0.62 (7:3 hexane + ethyl acetate)).

Mp: 178-184 °C.

IR (neat): 2918, 1590, 1465, 1439, 1215, 1100, 904, 749 cm^{-1}.

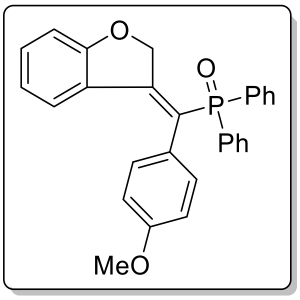
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62-7.58 (m, 4H), 7.51-7.48 (m, 2H), 7.40-7.36 (m, 4H), 7.22-7.19 (m, 1H), 7.0 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 6.5 Hz, 2H), 6.56-6.53 (m, 1H), 6.03 (d, *J* = 8.0 Hz, 1H), 5.77 (d, *J* = 4.5 Hz, 2H), 2.23 (s, 3H)

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 165.4, 152.7 (d, *J* = 8.1 Hz), 137.4 (d, *J* = 2.1 Hz) 133.4 (d, *J* = 9.5 Hz), 132.4, 132.1 (d, *J* = 9.4 Hz), 131.7 (d, *J* = 2.1 Hz), 131.3, 130.0 (d, *J* = 4.1 Hz), 129.7, 128.2 (d, *J* = 11.9 Hz), 125.8, 125.0 (d, *J* = 14.6 Hz), 121.7, 120.3, 111.0, 75.3 (d, *J* = 4.5 Hz), 21.2.

^{31}P NMR (162 MHz, $CDCl_3$) δ 29.5.

HRMS (ESI): Calcd for $C_{28}H_{24}O_2P$ (M^++H): m/z 423.1514 Found 423.1515.

Compound 42'



Yield: 38mg (32 %, R_f = 0.64 (7:3 hexane + ethyl acetate)).

Mp: 169-175 °C.

IR (neat): 3056, 2922, 2852, 1509, 1465, 1437, 1249, 1176, 1116, 991, 903, 748, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.59 (m, 4H), 7.51-7.48 (m, 2H), 7.41-7.38 (m, 4H), 7.22-7.19 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.77-6.73 (m, 4H), 6.57-6.54 (m, 1H), 6.08 (d, *J* = 8.0 Hz, 1H), 5.78 (d, *J* = 4.5 Hz, 2H), 3.79 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.4, 159.0, 153.2 (d, *J* = 8.3 Hz), 132.5, 132.2 (d, *J* = 9.1 Hz), 131.8, 131.4, 131.1, 128.6 (d, *J* = 10.0 Hz), 128.3 (d, *J* = 11.7 Hz), 125.7, 125.0 (d, *J* = 15.1 Hz), 121.3, 120.4, 114.5, 111.0, 75.3 (d, *J* = 4.3 Hz), 55.3.

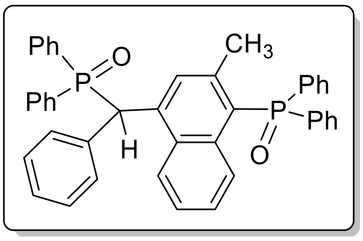
^{31}P NMR (162 MHz, $CDCl_3$) δ 29.7

HRMS (ESI): Calcd for $C_{28}H_{24}O_2P$ (M^++H): m/z 439.1463. Found 439.1466.

3.6 General procedure for $Pd(OAc)_2$-catalyzed transformations of allenylphosphine oxides leading to P-containing naphthalenes (44-48)

To an oven dried Schlenk tube, allenylphosphine oxide **4a** (100 mg, 0.316 mmol), $Pd(OAc)_2$ (7.2 mg, 0.032 mmol), PPh_3 (82.9 mg, 0.316 mmol) and Et_3N (32.0 mg, 0.316 mmol) in dry THF (2 mL) were added. The contents were sealed under a nitrogen atmosphere and stirred at reflux for 12 h. After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to room temperature, ethyl acetate (20 mL) added, filtered and the filtrate concentrated under vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (4:6) as the eluent to afford Naphthalenes (**44**). Compounds **45-48** prepared following the same procedure and by using the same molar quantities.

Compound 44



Yield: 64 mg (64%).

Mp: 140-144 °C.

IR (KBr): 3056, 2929, 2847, 2223, 1591, 1492, 1436, 1414, 1320, 1170, 1115, 1100, 1028, 998, 908, 751, 723, 696, 645, 593 cm^{-1}

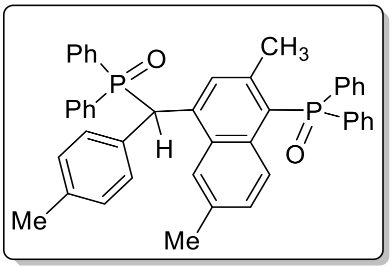
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 2.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.66-7.59 (m, 4H), 7.58-7.46 (m, 7H), 7.43-7.34 (m, 10 H), 7.31-7.29 (m, 2H), 7.22-7.19 (m, 4H), 5.55 (d, *J* = 10.5 Hz, 1H), 2.12 (d, *J* = 0.5 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.1 (*J* = 8.8 Hz), 138.4, 136.3, 135.8, 135.7 (*J* = 8.7 Hz), 135.3, 134.9 (*J* = 5.3 Hz), 133.0, 132.8, 132.7, 132.6, 132.2, 132.1, 132.0, 131.7, 131.5, 131.4, 131.3, 131.1 (*J* = 8.5 Hz), 130.9, 130.8, 130.7, 130.2 (*J* = 5.4 Hz), 128.8, 128.74, 128.67, 128.6, 128.5, 128.4, 128.3, 128.2, 127.3, 125.9 (*J* = 6.7 Hz), 124.9, 123.9, 122.7, 48.1 (*J* = 65.8 Hz), 24.9 (*J* = 5.2 Hz).

^{31}P NMR(162 MHz, $CDCl_3$) δ 32.2, 30.6.

HRMS (ESI): Calcd for $C_{42}H_{35}O_2P_2$ (M^++H): m/z 633.2112. Found 633.2112.

Compound 45



Yield: 54 mg (52%).

Mp: 164-168 °C.

IR (KBr): 3054, 2922, 2854, 1712, 1590, 1510, 1483, 1437, 1380, 1173, 1115, 1101, 1025, 997, 751, 720, 696, 605 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.5 Hz, 1H), 8.29 (s, 1H), 7.74 (s, 1H), 7.63-7.58 (m, 6H), 7.54-7.48 (m, 5H), 7.40-7.39 (m, 7H), 7.28-7.26 (m, 4H), 7.02-7.00 (m, 3H), 5.50 (d, *J* = 10.0 Hz, 1H), 2.38 (s, 3H), 2.27 (s, 3H), 2.10 (s, 3H).

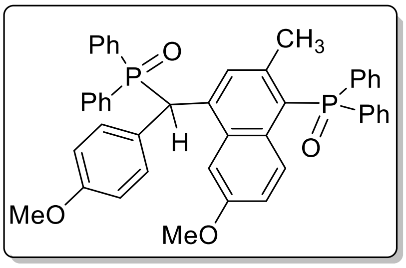
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.1 (*J* = 8.9 Hz), 137.8, 136.9, 136.4, 135.9, 135.3, 134.9, 133.9, 133.8, 133.2, 132.9, 132.7, 132.2, 132.0, 131.9_0, 131.8_5, 131.6, 131.5_2, 131.4_7, 131.4, 131.1 (*J* = 8.3 Hz), 130.1 (*J* = 5.3 Hz), 129.1, 128.7_5, 128.7_0, 128.6_2, 128.5_8, 128.4, 128.3, 128.2, 128.0, 124.4, 123.4, 121.9, 47.7 (*J* = 66.4 Hz), 24.7 (*J* = 4.7 Hz), 21.8, 21.1.

^{31}P NMR(162 MHz, $CDCl_3$) δ 32.1, 30.7.

HRMS (ESI): Calcd for $C_{44}H_{39}O_2P_2$ (M^++H): m/z 661.2425. Found 661.2427.

This compound was crystallized from ethyl acetate-hexane (2:1) mixture at room temperature.

Compound 46



Yield: 50 mg (48%).

Mp: 175-180 ^{o}C.

IR (KBr): 3054, 2928, 2836, 2360, 1673, 1608, 1508, 1461, 1437, 1301, 1250, 1219, 1175, 1071, 1031, 828, 792, 720, 696 cm^{-1}

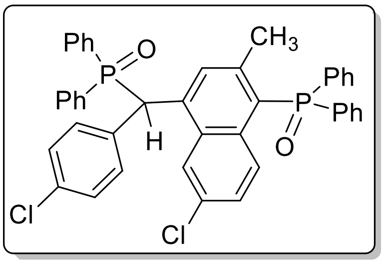
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.62 (d, *J* = 9.5 Hz, 1H), 8.26 (s, 1H), 7.66-7.59 (m, 4H), 7.54-7.49 (m, 7H), 7.43-7.38 (m, 7H), 7.31-7.28 (m, 3H), 7.25-7.23 (m, 2H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 2H), 5.32 (d, *J* = 10.0 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 2.02 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 158.8, 157.0, 140.2 (*J* = 8.8 Hz), 137.4, 136.1, 135.7, 135.3, 134.8, 133.1, 132.8, 132.3$_5$, 132.2$_9$, 132.0, 131.5$_7$, 131.5$_6$, 131.5, 131.4$_3$ (*J* = 1.4 Hz), 131.3$_2$, 131.2$_8$, 131.2, 131.1 (*J* = 8.6 Hz), 130.1 (*J* = 6.0 Hz), 128.7$_3$, 128.6$_7$, 128.6$_4$, 128.5$_8$, 128.4$_5$, 128.3$_6$, 128.3, 128.2, 126.6 (*J* = 5.1 Hz), 124.5, 123.7, 116.7, 113.8, 103.3, 55.1$_9$, 55.1$_7$, 48.0 (*J* = 65.8 Hz), 24.5 (*J* = 5.1 Hz).

^{31}P NMR(162 MHz, CDCl$_3$) δ 32.3, 31.0.

HRMS (ESI): Calcd for $C_{44}H_{38}O_4P_2Na$ (M^++Na): m/z 715.2143. Found 715.2142.

Compound 47



Yield: 89 mg (44%).

Mp: 156-160 ^{o}C.

IR (KBr): 3054, 2928, 2836, 2360, 1673, 1608, 1508, 1461, 1437, 1301, 1250, 1219, 1175, 1071, 1031, 828, 792, 720, 696 cm^{-1}.

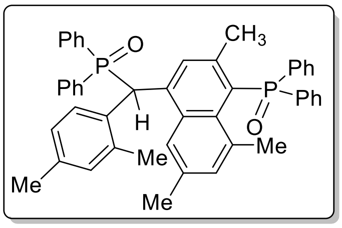
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.73 (d, *J* = 9.5 Hz, 1H), 8.32 (s, 1H), 7.86 (s, 1H), 7.63-7.58 (m, 6H), 7.55-7.49 (m, 5H), 7.45-7.41 (m, 7H), 7.32-7.31 (m, 4H), 7.20-7.19 (m, 2H), 7.17 (s, 1H), 5.38 (d, *J* = 9.5 Hz, 1H), 2.06 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 143.0 (*J* = 8.9 Hz), 137.0, 136.9, 135.7, 135.2, 134.7, 134.2, 134.1, 133.9, 133.8, 133.7, 133.5, 133.3 (*J* = 5.6 Hz), 132.3, 132.2, 132.1, 132.0, 131.8, 131.5, 131.3, 131.0 (*J* = 8.8 Hz), 130.3 (*J* = 5.8 Hz), 128.9, 128.8, 128.6, 128.5, 126.7, 125.5, 124.5, 121.6, 47.5 (*J* = 65.0 Hz), 29.7.

^{31}P NMR (162 MHz, CDCl$_3$) δ 31.7, 30.7.

HRMS (ESI): Calcd for $C_{42}H_{32}Cl_2O_2P_2$ (M^{+}+H): m/z 701.1333. Found 701.1332.

Compound 48



Yield: 91mg (45%).

Mp: 140-144 ^{o}C.

IR (KBr): 3015, 2969, 2924, 2853, 1698, 1437, 1367, 1215, 1116, 953, 753, 702 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.29 (d, *J* = 2.5Hz, 1H), 8.00 (s, 1H), 7.68-7.64 (m, 2H), 7.54-7.50 (m, 9H), 7.48-7.38 (m,7H), 7.37-7.22 (m, 2H), 6.98 (s, 1H), 6.84 (s, 1H), 6.67 (s, 2H), 5.91 (d, *J* = 12.0 Hz, 1H), 2.79 (s, 3H), 2.15 (s, 9H), 2.07 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 143.2 (*J* = 7.9 Hz), 137.6, 137.4, 137.3 (d, *J* = 8.0 Hz), 136.9, 136.3, 136.1, 135.5, 135.1, 135.0, 134.3, 133.9 (*J* = 6.3 Hz), 133.4, 132.6, 132.5, 131.64, 131.56, 131.3, 131.2, 131.1_5, 131.0_6, 130.9, 130.8, 130.3, 128.8, 128.6, 128.5, 128.4, 128.3, 128.14, 128.05, 126.9 (*J* = 7.6 Hz), 50.9 (*J* = 65.8 Hz), 26.7, 24.3 (*J* = 5.1 Hz). 21.4, 21.0.

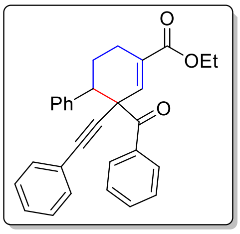
^{31}P NMR(162 MHz, $CDCl_3$) δ 32.7, 29.3.

HRMS (ESI): Calcd for $C_{46}H_{43}O_2P_2$ (M^++H): m/z 689.2738. Found 689.2736.

3.7 General procedure for phosphine-catalyzed cycloadditions of allenoate with enynone leading to cyclohexene carboxylates (49-53)

To an oven dried Schlenk tube, allene **6** (0.389 mmol), phosphine (0.065 mmol) and enynone (0.324 mmol) in dry toluene (2 mL) were added. The contents were sealed under a nitrogen atmosphere and stirred at rt (25 °C) for 48 h. After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to room temperature, ethyl acetate (20 mL) added, filtered and the filtrate concentrated under vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (19:1) as the eluent to afford compound **49**. Compounds **49-53** prepared following the same procedure and by using the same molar quantities.

Compound 49 (semisolid; purity *ca.* 90%; diastereomers may be present along with residual solvent)



Yield: 0.114 g (82%)

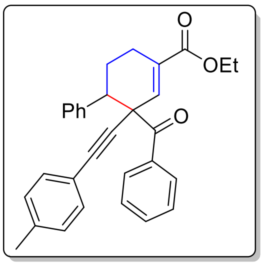
IR (neat): 2983, 1707, 1681, 1598, 1490, 1237, 1087, 762 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71-7.69 (m, 2H), 7.49-7.47 (m, 2H), 7.45-7.41 (m, 1H), 7.32-7.27 (m, 9H), 7.25-7.22 (m, 2H), 4.25 (q, *J* = 7.0 Hz, 3H), 3.66-3.63 (m, 1H), 3.19- 3.16 (m, 1H), 3.01-2.95 (m, 2H), 2.67-2.61 (m, 1H), 1.34 (t, *J* = 7.0 Hz, 3H). Other minor peaks were also present.

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 201.8, 166.6, 140.8, 138.6, 137.7, 131.7, 131.3, 129.1, 128.5, 128.3, 128.2, 123.0, 89.3, 88.9, 60.7, 52.0, 45.5, 37.0, 31.1, 14.3 (a few peaks were merged).

HRMS (ESI): Calcd. for $C_{30}H_{27}O_3$ [M^++H] *m/z* 435.1960, found 435.1959.

Compound 50 (semisolid; purity *ca*. 90%; diastereomers may be present along with residual solvent)



Yield: 0.108 g (75%)

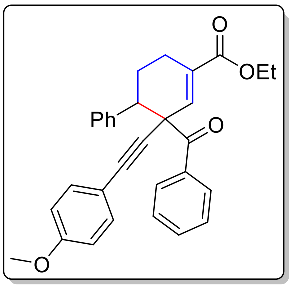
IR (neat): 2981, 1706, 1680, 1597, 1491, 1445, 1378, 1264, 1239, 1179, 1092, 1028, 733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.67 (m, 2H), 7.50-7.49 (m, 2H), 7.46- 7.40 (m, 1H), 7.32- 7.23 (m, 9H), 7.14 (d, *J* = 8.0 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.68-3.64 (m, 1H), 3.21-3.01 (m, 3H), 2.99-2.95 (m, 1H), 2.38 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): (major component) δ 201.9, 166.6, 140.9, 138.6, 138.5, 137.7, 131.7, 131.2, 129.2, 129.1, 128.5, 128.2, 127.5, 127.2, 119.9, 89.0, 88.6, 60.7, 52.1, 45.5, 37.0, 31.1, 21.5; 14.1.

HRMS (ESI): Calcd. for $C_{31}H_{29}O_3$ [M$^+$+H] *m/z* 449.2118, found 449.2118.

Compound 51 (semisolid; purity *ca*. 90%; diastereomers may be present along with residual solvent)



Yield: 0.108 g (74%)

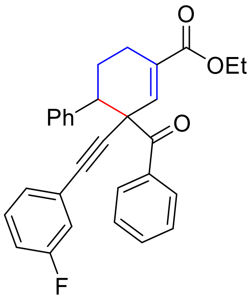
IR (neat): 2924, 1712, 1610, 1512, 1490, 1377, 1248, 1177, 1073, 1025, 759 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72-7.70 (m, 2H), 7.48-7.44 (m, 2H), 7.42-7.41 (m, 1H), 7.31-7.23 (m, 8H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.25 (q, *J* = 7.2, 2H), 3.82 (s, 3H), 3.65-3.61 (m, 1H), 3.18-3.13 (m, 1H), 3.03-2.92 (m, 2H), 2.65-2.59 (m, 1H) 1.33 (t, *J* = 7.2, 3H).

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): (major peaks) δ 201.9, 166.6, 159.6, 140.9, 138.6, 137.7, 132.7, 131.7, 129.1, 128.5, 128.1, 127.2, 115.1, 114.0, 88.7, 87.8, 60.6, 55.3, 52.0, 45.5, 36.9, 31.1, 14.3.

HRMS (ESI): Calcd. for $C_{31}H_{29}O_4$ [M^++H] *m/z* 465.2066, found 465.2067.

Compound 52 (semisolid; purity *ca.* 90%; diastereomers may be present along with residual solvent)



Yield: 0.104 g (72%)

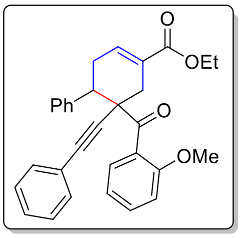
IR (neat): 2926, 1709, 1682, 1613, 1589, 1489, 1446, 1247, 785, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.81 (m, 2H), 7.47-7.44 (m, 1H), 7.37-7.25 (m, 11H), 6.96-6.92 (m, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.72-3.68 (m, 1H), 3.20-3.11 (m, 2H) 2.98-2.90 (m, 1H), 2.68-2.64 (m, 1H), 1.34 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): (major peaks) δ 200.9, 166.4, 162.6 (d, *J* = 243.7 Hz), 143.7, 143.6, 138.3, 137.3, 132.1, 132.0, 129.5 (d, *J* = 8.3 Hz), 128.5, 128.3, 127.8, 125.0 (d, *J* = 2.7 Hz), 122.7, 115.8 (d, *J* = 21.7 Hz), 114.0 (d, *J* = 20.8 Hz), 89.2, 88.9, 60.7, 51.7, 44.7, 37.0, 31.2, 14.3.

HRMS (ESI): Calcd. for $C_{30}H_{26}FO_3$ [M^++H] *m/z* 453.1861, found 453.1862.

Compound 53



Yield: 0.100 g (75%)

M.P: 134-139 °C

IR (neat): 2922, 2852, 1710, 1655, 1598, 1507, 1452, 1263, 1235, 1094, 1027, 817, 699 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.45-7.43 (m, 2H), 7.30- 7.20 (m, 8H), 7.10- 7.07 (m, 2H), 6.80 (d, *J* = 8.5 Hz, 1H), 6.67-6.64 (m, 1H), 5.80 (dd, *J* = 1.5, 7.0 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 3.78 (s, 3H), 3.51-3.47 (m, 1H), 3.25-3.22 (m, 1H), 3.09-3.0 (m, 1H), 3.0-2.93 (m, 1H), 2.62-2.56 (m, 1H), 1.36 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 207.6, 166.8, 156.3, 140.4, 138.5, 131.3, 130.6, 129.6, 128.3, 128.2, 128.1, 127.9, 127.3, 126.0, 123.3, 120.1, 110.0, 89.5, 85.9, 60.5, 55.4, 54.6, 46.6, 37.3, 31.7, 14.3.

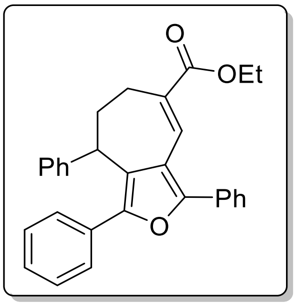
HRMS (ESI): Calcd. for $C_{31}H_{29}O_4$ [M$^+$+H] *m/z* 465.2066, found 465.2063.

This compound was crystallized from ethyl acetate-hexane (2:1) mixture at room temperature.

3.8 General procedure for [Au]-catalyzed cyclizations of cyclohexene carboxylates to yield furan fused cycloheptene carboxylates (54-57)

To an oven dried Schlenk tube, compound **49** (0.230 mmol), Ph$_3$PAuCl (0.012 mmol) and AgOTf (0.012 mmol) in dry toluene (2 mL) were added. The contents were sealed under a nitrogen atmosphere and stirred at rt (oil bath temperature) for 24 h. After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to room temperature, ethyl acetate (20 mL) added, filtered and the solution concentrated under vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (19:1) as the eluent to afford compound **54**. Compounds **55-57** prepared following the same procedure and by using the same molar quantities.

Compound 54 (semisolid; purity *ca.* 90%; stereoisomers may be present)



Yield: 0.82 g (82%).

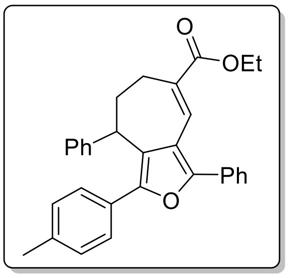
IR (neat): 2923, 2852, 1718, 1664, 1596, 1449, 1260, 1024, 760, 698 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.06 (br, 1H), 7.80 (d, *J* = 6.8 Hz, 2H), 7.56-7.46 (m, 6H), 7.37-7.33 (m, 4H), 7.30-7.23 (m, 3H), 4.66 (d, *J* = 4.0 Hz, 1H), 4.21-4.19 (m, 2H), 2.84-2.80 (m, 1H), 2.39-2.37 (m, 1H), 2.30-2.24 (m, 1H), 2.18-2.14 (m, 1H), 1.30-1.29 (m, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 168.6, 153.9, 148.5, 143.3, 130.4_3, 130.3_6, 130.1, 129.6, 128.7_8, 128.7_7, 128.5, 128.0, 127.9, 127.6, 126.4, 126.2, 124.3, 120.3, 60.7, 41.2, 31.4, 26.1, 14.3.

HRMS (ESI): Calcd. for $C_{30}H_{27}O_3$ [M$^+$+H] *m/z* 435.1955, found 435.1565.

Compound 55



Yield: 0.74 g (72%)

Mp: 146-148 °C

IR (neat): 2924, 1699, 1602, 1506, 1447, 1256, 1218, 1092, 1049, 1018, 819, 735, 697 cm^{-1}.

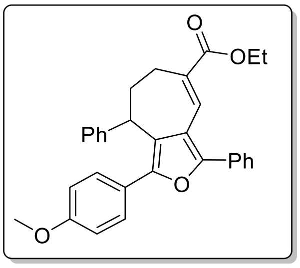
^{1}H NMR (400 MHz, CDCl$_3$): δ 8.05 (m, 1H), 7.79-7.77 (m, 2H), 7.55-7.51 (m, 2H), 7.45-7.41 (m, 1H), 7.37-7.32 (m, 4H), 7.24-7.20 (m, 3H), 7.16-7.14 (m, 2H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.21-4.16 (m, 2H), 2.81 (dd, *J* = 18.8, 3.6 Hz, 1H), 2.40-2.37 (m, 1H), 2.35 (s, 3H), 2.29-2.22 (m, 1H), 2.18- 2.07 (m, 1H), 1.31-1.27 (m, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.7, 153.7, 148.7, 143.4, 137.6, 130.5, 129.9, 129.7, 129.2, 128.8, 128.7, 128.4, 128.0, 127.9, 127.6, 126.3, 126.2, 123.6, 120.2, 60.7, 41.2, 31.4, 26.1, 21.2, 14.3.

HRMS (ESI): Calcd. for $C_{31}H_{29}O_3$ [M$^+$+H] *m/z* 449.2116, found 449.2113.

This compound was crystallized from ethyl acetate-chloroform (2:1) mixture at room temperature.

Compound 56 (semisolid; purity *ca.* 90%; stereoisomers may be present)



Yield: 0.79 g (79%)

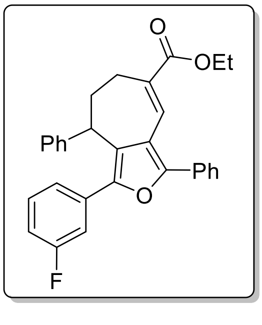
IR (neat): 2927, 1705, 1660, 1597, 1448, 1254, 1170, 1027, 736 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (m, 1H), 7.80-7.78 (m, 2H), 7.55-7.52 (m, 2H), 7.45-7.39 (m, 3H), 7.37-7.33 (m, 2H), 7.29-7.22 (m, 3H), 6.89-6.87 (m, 2H), 4.60 (d, *J* = 4.4 Hz, 1H), 4.21-4.19 (m, 2H), 3.82 (s, 3H), 2.82 (dd, *J* = 18.8, 4.0 1H), 2.39-2.10 (m, 3H), 1.32-1.29 (m, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): (major peaks) δ 168.7, 159.2, 153.4, 148.7, 143.5, 130.5, 129.9, 129.7, 128.7, 128.3, 128.0, 127.9, 127.8, 127.7, 126.3, 123.2, 122.8, 120.2, 114.0, 60.7, 55.3, 41.2, 31.5, 26.0, 14.2.

HRMS (ESI): Calcd. for $C_{31}H_{29}O_4$ [M^++H] *m/z* 465.2066, found 465.2061.

Compound 57 (semisolid; purity *ca.* 90%; stereoisomers may be present)



Yield: 0.78 g (78%)

IR (neat): 2923, 2852, 1711, 1667, 1593, 1448, 1256, 1177, 1094, 788, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 1H), 7.80-7.78 (m, 2H), 7.57-7.53 (m, 2H), 7.47-7.45 (m, 2H), 7.38-7.30 (m, 5H), 7.04-7.02 (m, 1H), 6.99-6.92 (m, 2H), 4.65 (d, *J* = 4.4 Hz, 1H), 4.23-4.18 (m, 2H), 2.84 (dd, *J* = 18.8, 2.8 Hz 1H), 2.41-2.36 (m, 1H), 2.31-2.24 (m, 1H), 2.18-2.09 (m, 1H), 1.32-1.29 (m, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.5, 163.2 (d, *J* = 244.5 Hz), 154.1, 148.7, 146.0_3, 145.9_6, 130.4, 130.3, 130.2, 129.7 (d, *J* = 35.4 Hz), 128.8, 128.6_4, 128.6_1, 127.9 (d, *J* = 12.7 Hz), 126.2, 123.6$_0$, 123.5$_8$, 120.0, 115.0 (d, *J* = 21.4 Hz), 113.4 (d, *J* = 21.1 Hz), 60.8, 41.0, 31.2, 26.1, 14.3.

HRMS (ESI): Calcd. for $C_{31}H_{26}FO_3$ [M^++H] *m/z* 453.1866, found 453.1868.

3.9 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **10, 14, 19**, **30**, **35**, **40′**, and **45, 53** and **55**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer using Mo-K_α radiation (λ = 0.71073 Å) or Cu- K_α (λ = 1.54184 Å). Structures were solved and refined using standard methods.[79] Absorption corrections were done using SADABS program, where applicable. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier and refined isotropically. Crystal data are summarized in Tables 12-14. The quality of data for compound **40’** was not great since the crystal quality was not good; hence an ‘A’ alert is there. However structure solution and refinement could be done satisfactorily.

Table 12: Crystal data for compounds **10**, **14**, **19** and **30** [a]

Compound	**10**	**14**	**19**	**30**
Emp. formula	$C_{26}H_{21}N_3$	$C_{25}H_{18}ClN_3$	$C_{28}H_{25}N_3$	$C_{21}H_{19}N_3O_2$
Formula weight	375.46	395.87	403.51	345.39
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*I2/a*	*P*21/c1	*C12/c1*	*P*21/n
a /Å	18.3117 (7)	12.9840(9)	43.5216(11)	13.631(5)
b /Å	14.1566 (4)	20.7822(14)	6.03172(14)	7.505(2)
c /Å	16.2686 (7)	7.2865(5)	16.5557(4)	17.609(6)
α/deg	90	90	90	90
β/deg	115.467(5)	104.647(7)	98.612(2)	98.672(14)
γ/deg	90	90	90	90
V /Å^3	3807.6 (3)	1092.3(2)	4297.04(18)	1780.8(10)
Z	8	4	8	4
Dcalc /g cm^{-3}]	1.310	1.382	1.247	1.288
μ /mm^{-1}	0.078	0.218	0.074	0.085
F(000)	1584.0	824.0	1712.0	728.0
Data/ restraints/ parameters	3970/0/266	3358/0/265	3777/0/284	3126/0/239
S	1.075	0.922	1.065	0.992
R1 [I>2σ(I)]	0.0633	0.0662	0.0504	0.0705
wR2 [all data]	0.1875	0.2083	0.1560	0.1646
Max./min. residual electron dens. [eÅ^{-3}]	0.902/-0.971	0.415/-0.402	0.158/-0.162	0.385/-0.353

[a] $R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 13: Crystal data for compounds **35**, **40'**, and **45** ^{a}

Compound	**35**	**40'**	**45**
Emp. Formula	$C_{44}H_{36}O_2P_2Pd$	$C_{27}H_{21}O_2P$	$C_{44}H_{39}O_3P_2$
Formula weight	765.07	408.41	677.69
Crystal system	Orthorhombic	Triclinic	Triclinic
Space group	*Pbca*	*P*-1	*P*-1
a /Å	21.918(3)	10.001(7)	11.478(3)
b /Å	15.241(2)	11.138(6)	12.334(3)
c /Å	22.159(4)	11.888(12)	14.871(4)
α/deg	90	102.420(14)	107.993(10)
β/deg	90	105.022(19)	111.95(1)
γ/deg	90	115.73(3)	94.357(10)
V /Å^3	7402.3(19)	1066.9(15)	1812.9(8)
Z	8	2	2
Dcalc /g cm^{-3}]	1.373	1.271	1.382
μ /mm^{-1}	0.624	0.150	0.160
F(000)	3136.0	428.0	714.0
Data/ restraints/ parameters	6489/0/444	3003/0/271	6388/0/453
S	1.092	0.855	1.101
R1 [I>2σ(I)]	0.0309	0.0992	0.0621
wR2 [all data]	0.0900	0.4027	0.1776
Max./min. residual electron dens. [eÅ^{-3}]	0.371/-0.622	0.381/-0.365	0.733/-0.886

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 14: Crystal data for compounds **51, 55**^{a}

Compound	**51**	**55**
Emp. Formula	$C_{31}H_{28}O_3$	$C_{31}H_{28}O_4$
Formula weight	448.53	464.53
Crystal system	Monoclinic	Monoclinic
Space group	*P21/n*	*I2/a*
a /Å	11.6905(5)	19.7177(5)
b /Å	8.2792(4)	7.8743(2)
c /Å	25.1517(8)	32.7285(9)
α/deg	90	90
β/deg	97.733(3)	90.299(2)
γ/deg	90	90
V /Å^3	2412.24(17)	5081.5(2)
Z	4	8
Dcalc /g cm^{-3}]	1.235	1.214
μ /mm^{-1}	0.078	0.079
F(000)	952.0	1968.0
Data/ restraints/ parameters	4234/1/313	4480/0/322
S	1.092	1.080
R1 [I>2σ(I)]	0.0309	0.0419
wR2 [all data]	0.0900	0.1197
Max./min. residual electron dens. [eÅ^{-3}]	0.179/-0.505	0.315/-0.527

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

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PART B

CYCLIZATION REACTIONS OF ACTIVE METHYLENE COMPOUNDS

INTRODUCTION

4.1 General Introduction: Synthesis and utility of multifunctional carbo/heterocycles from active methylene precursors

Multifunctional naphthalenes, phenanthrenes, qunolines and carbazoles have diverse applications in pharmaceutical industry, nanotechnology, electronic materials, and chiral catalysis.[1,2] A few of these are also present as basic scaffolds in natural products as well.[3] Among the methods available for the synthesis of such molecules, transition metal catalysis is an important one.[4] Though a wide number of approaches are present in the literature, Cu(I) catalyzed synthetic routes,[5] especially by using active methylene compounds in a single step, are limited. Active methylene compounds are readily available and amenable to various synthetic transformations.[6] This aspect prompted us to explore these precursors for the synthesis of multifunctional carbocycles (e.g., naphthalenes, phenanthrenes) and heterocycles (e. g., quinolones, benzo(*b*)carbazoles). Selected natural products and bio-relevant molecules possessing naphthalene, quinoline, phenanthrene and benzo(*b*)carbazole skeletons are depicted in Figure 4.1.[7a-d] The compounds from literature are labeled as 4.1, 4.2 etc. in this chapter so as to distinguish them from those prepared in the present study (cf. chapter 5).

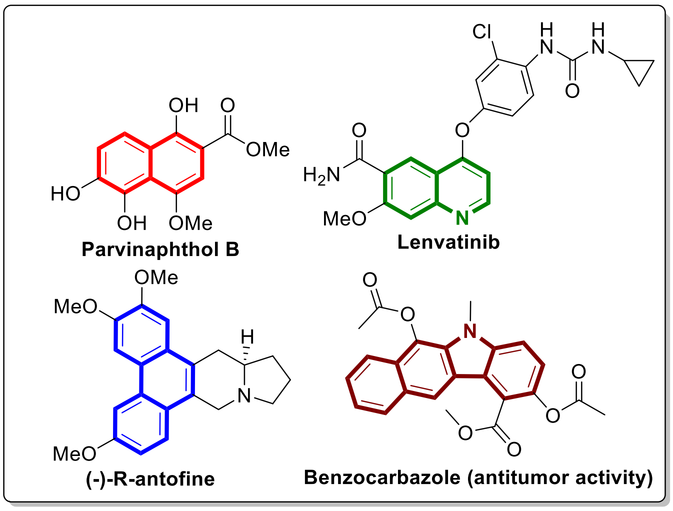


Figure 4.1: Selected natural products/ bio-relevant molecules possessing naphthalene, quinoline, phenanthrene and benzo(*b*)carbazole scaffolds

4.2 Introduction: Active methylene compounds

Active methylene compounds **4.1** are those in which a methylene group present in between two electron withdrawing groups; in most cases the electron withdrawing group is the carbonyl functionality. Representative structural types (**4.2-4.7**) are shown in Figure 4.2. These precursors are widely utilized in numerous synthetic transformations.[8] Examples include the synthesis of functionalized cyclopentenes from enynes,[9a] indenes from *gem*-dibromo olefins,[9b] isoquinolines/ isoindolinones[9d]/ indazolones from aromatic propargyloxy aldehydes,[9e] benzopyrano pyridines from 2-amino-3-formyl chromones,[9f] spirooxindoles from isatins,[9g] furans from *gem*-difluoro alkenes,[9h] and perillyl-4*H*-pyran hybrid molecules from β-diketones.[9i] Illustrative reactions to generate bio-relevant products (cf. Figure 4.3, compounds **4.8-4.10**) like pyrimidine analogues **4.8**),[10a] dihydropyrano indoles (**4.9**),[10b] spiroindoline pyrrolidines (**4.9**),[10c] and pyrano chromenes[10d] are shown in Scheme 4.1. In this chapter, literature on the [Cu]-catalyzed synthesis of carbo- and heterocycles by using active methylene compounds will be covered.

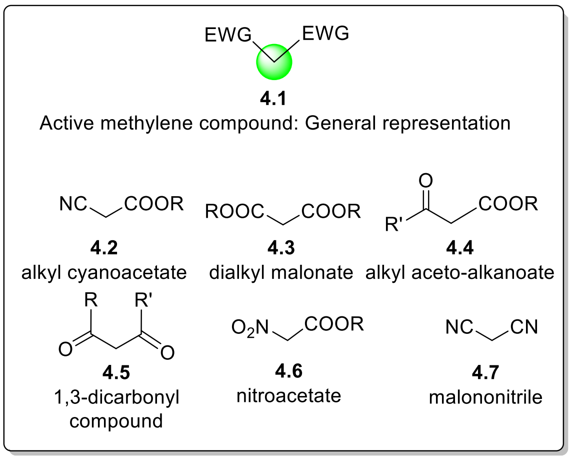


Figure 4.2: Representative structural types for active methylene compounds

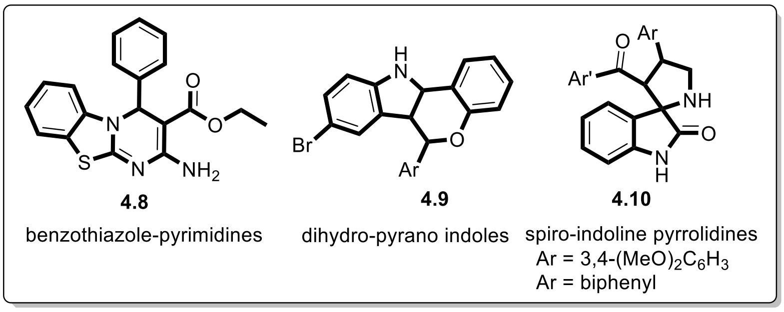
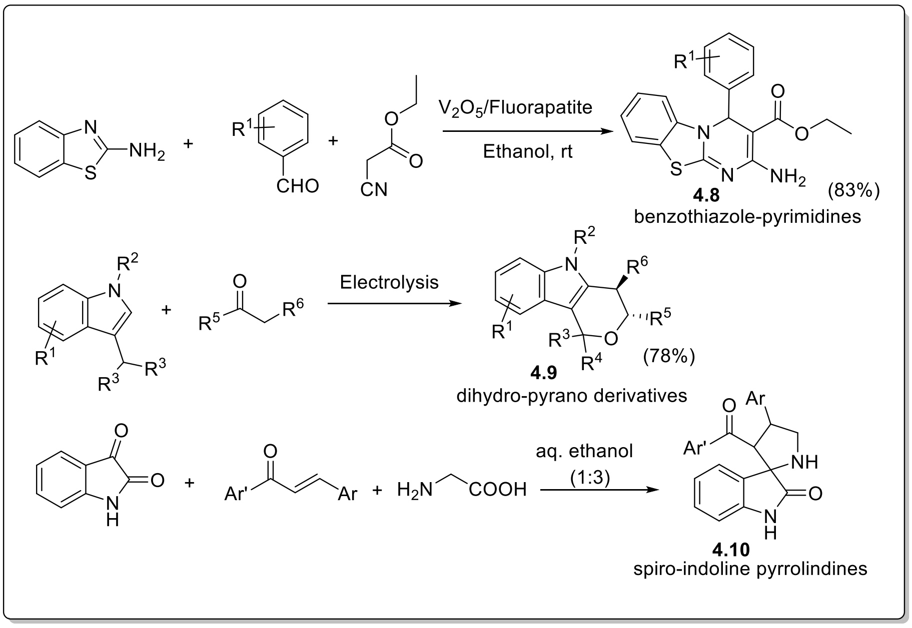


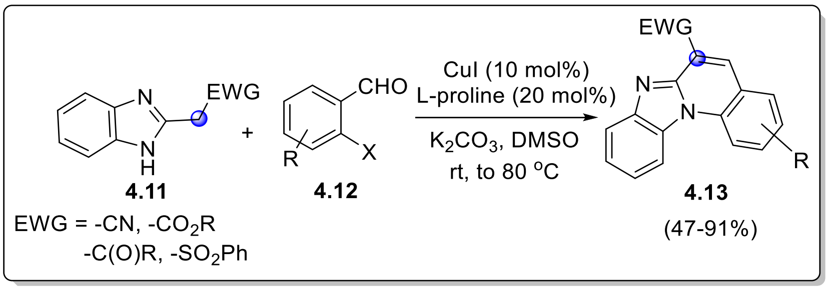
Figure 4.3: Selected compounds (building blocks) synthesized using active methylene compounds



Scheme 4.1: Synthesis of a few biologically relevant products from active methylene compounds

4.3 Cu-catalyzed synthesis of carbocycles and heterocycles by using active methylene compounds

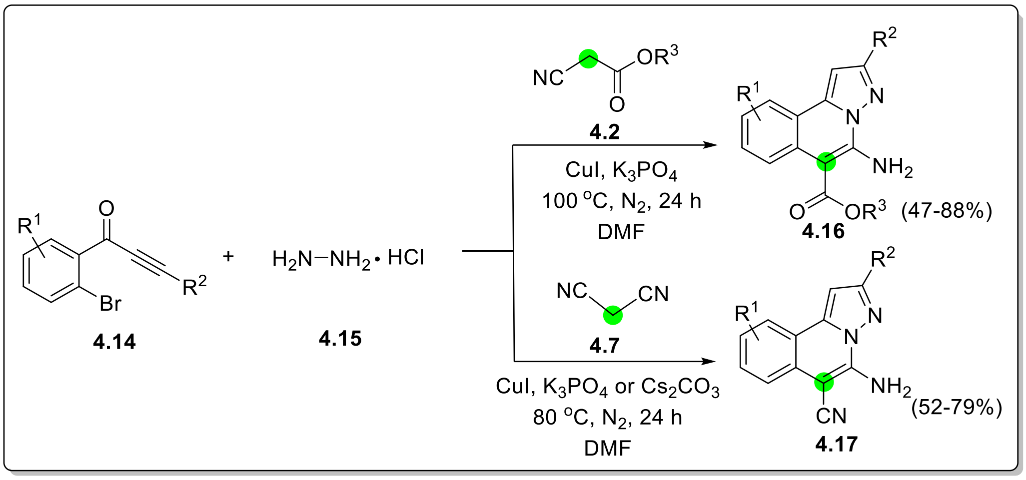
Cai *et al* reported copper catalyzed synthesis of aza-fused polycyclic quinolines **4.13** from *o*-halo-aromatic aldehydes **4.12** from the reaction with active methylene group containing benzimidazole moiety (**4.11**) *via* intermolecular condensation and C-N coupling reaction in the presence of CuI/ L-proline (Scheme 4.2).[11] For this conversion, electron deficient substrates were favored compared to electron rich groups in delivering the corresponding products.



Scheme 4.2: [Cu]-catalyzed synthesis of benzimidazo[1,2-a]-quinolines

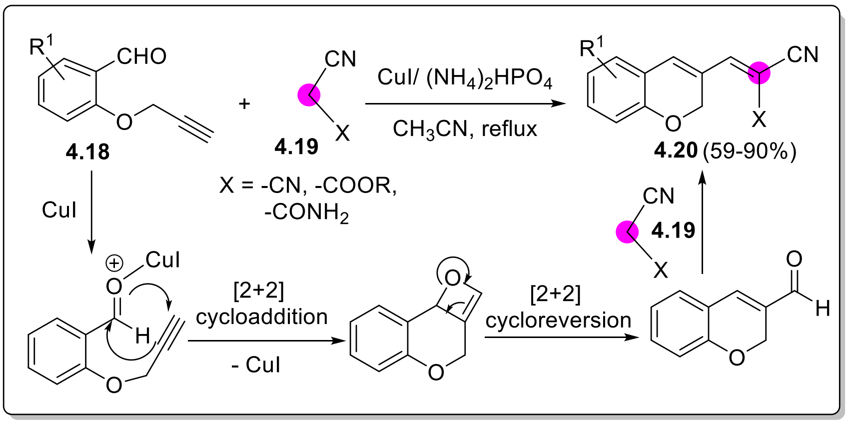
In the year 2012, Fu's group demonstrated one-pot copper catalyzed synthesis of *H*-pyrazolo[5,1-*a*]isoquinolines **4.16** and **4.17** from substituted 1-(2-bromophenyl)-3-phenylprop-2-yn-1-one **4.14**, hydrazine hydrochloride **4.15** and active methylene group possessing compounds **4.2** or **4.7** (alkyl cyanoacetate or malononitrile) (Scheme 4.3).[12]

This conversion involves initial reaction between bromo substituted alkyne moiety and hydrazine in the presence of K_3PO_4 or Cs_2CO_3, then coupling (*C*-arylation) between formed intermediate species and active methylene compound, followed by intramolecular nucleophilic attack of NH (of formed pyrazolo group) to cyano group. Isomerization of the imine to amine gives the desired products.



Scheme 4.3: [Cu]-catalyzed one-pot synthesis of *H*-pyrazolo[5,1-*a*]isoquinolines

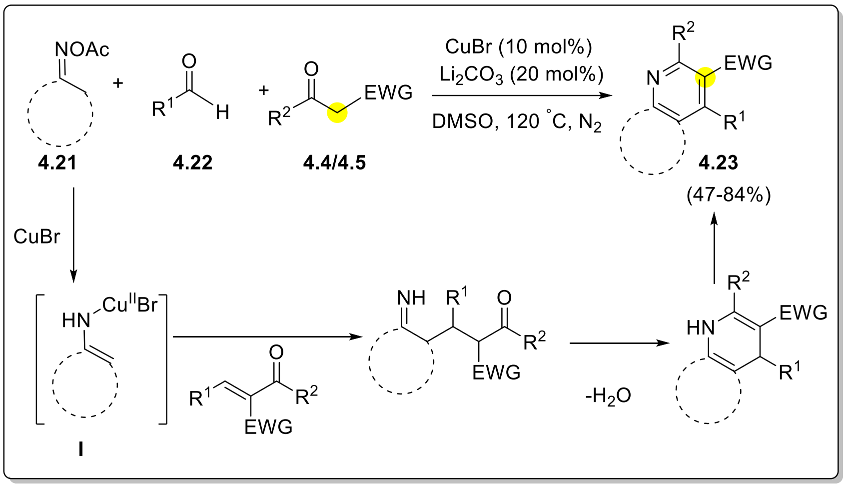
In the year 2013, Singh and co-workers developed a methodology for the synthesis of 2*H*-chromen-3-yl derivatives **4.20** from substituted *o*-propargyl salicylaldehyde **4.18** by reaction with malononitrile, alkyl cyanoacetates or cyanoacetamide (**4.19**) *via* a copper-catalyzed [2+2] cycloaddition and cyclo-reversion followed by condensation (Scheme 4.4).[13]



Scheme 4.4: Synthesis of 2*H*-chromen-3-yl derivatives by using *o*-propargyl salicylaldehyde

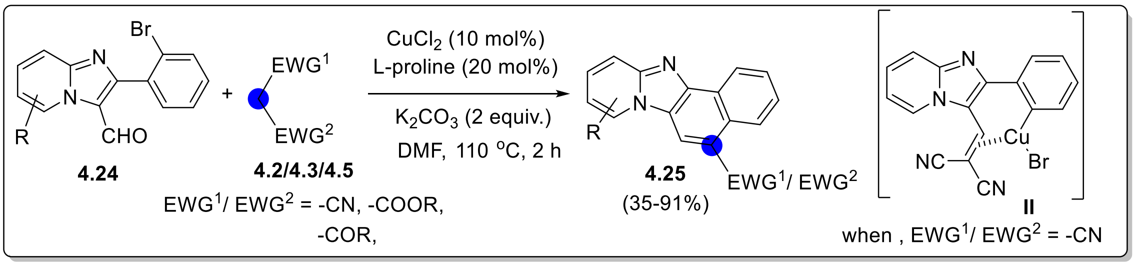
A copper catalyzed three component reaction between various oximes **4.21**, substituted aldehydes **4.22** and 1,3-dicarbonyl compounds/ alkyl aceto-alkanoates **4.4/4.5** for the synthesis of functionalized pyridines **4.23** has been reported by Jiang *et al*

(Scheme 4.5).[14] In the presence of copper salt, cleavage of N-O bond in oxime occurs generating Cu(II) enamide complex **I**; it will react with the imine moiety generated by the reaction between aldehyde and active methylene compound. Then the formed complex will undergo intramolecular tautomerization followed by nucleophilic attack and subsequent aromatization to give the desired products **4.23**.



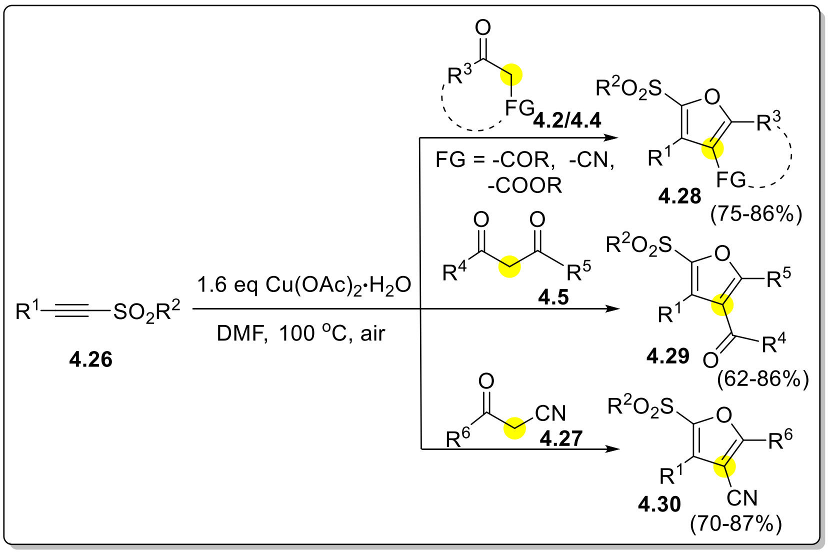
Scheme 4.5: Multi-component Cu-catalyzed synthesis of functional pyridines

In the year 2015, Kumar *et al* synthesized π-extended naphtho-fused imidazo [1,2-*a*]pyridines **4.25** by using 2-(2-bromophenyl)imidazo[1,2-*a*]pyridine-3-carbaldehyde **4.24** and **4.2/4.3/4.5** in the presence of $CuCl_2$ (Scheme 4.6).[15] The mechanism of this conversion may involve Knoevenagel condensation and chemoselective cross-coupling followed by C-C bond cleavage (cf. species **II**). The obtained compounds were fluorescent with high quantum yields.



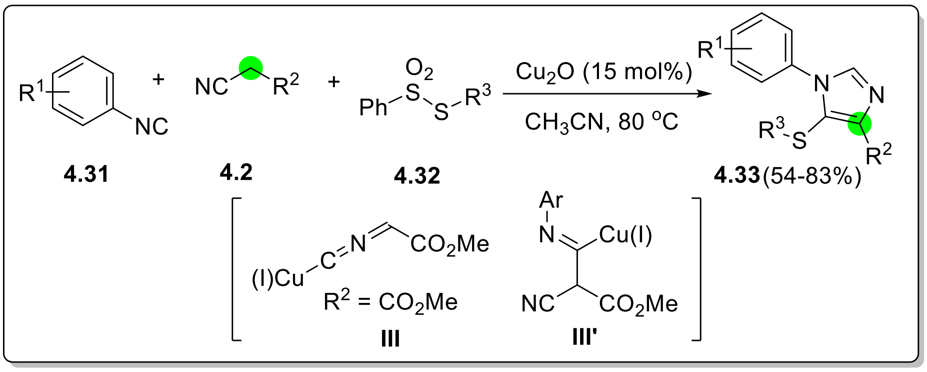
Scheme 4.6: $CuCl_2$-Catalyzed synthesis of naphtho-fused imidazo [1,2-*a*]pyridines

Xie *et al* reported a methodology for the synthesis of multi-functional sulfonyl-substituted furans by using copper catalyzed intermolecular coupling between acetylenic sulfones **4.26** and 1,3-dicarbonyl compounds, alkyl cyanoacetate or *β*-carbonyl ester (**4.2-4.4, 4.5**, **4.27**,) (Scheme 4.7).[16] The mechanism of this conversion involves Michael-type addition, isomerization of Michael-addition adduct, SET of isomerized intermediates followed by intramolecular radical cyclization and oxidation gives the products **4.28-4.30**.



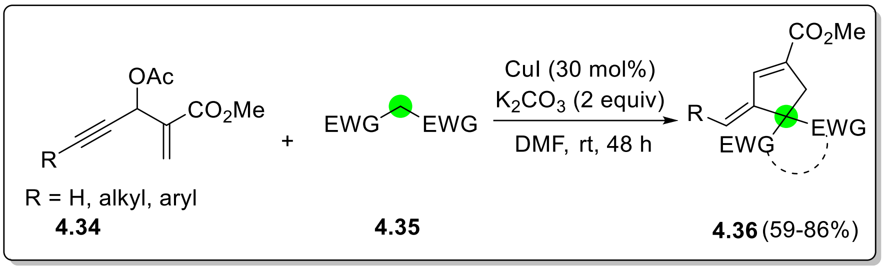
Scheme 4.7: Cu-catalyzed Synthesis of multifunctional sulfonyl-substituted furan compounds

In the year 2019, Wang and co-workers reported a copper-catalyzed synthetic route to trisubstituted imidazoles **4.33** *via* [3+2] cycloaddition by the formation of new C-C, C-N and C-S bonds in a single step (Scheme 4.8).[17] The initial reaction between active methylene compound **4.2** and Cu_2O gives intermediate **III**. Nucleophilic attack of aryl isocyanide **4.31** then gives species **III**$'$; intramolecular addition, followed by reaction of the obtained intermediate with benzene sulfonothioate **4.32** gave the desired product.



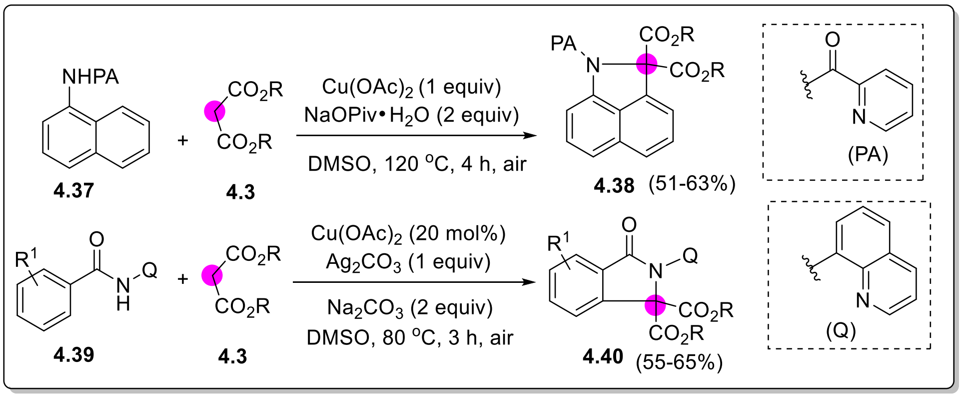
Scheme 4.8: Cu-catalyzed synthesis multisubstituted imidazoles

In the year 2014, Reddy *et al* demonstrated Cu(I)-catalyzed synthesis of substituted alkylidene cyclopentenes **4.36** by using Morita-Baylis-Hillman (MBH) acetates **4.34** with active methylene compounds **4.35** through cascade allylic substitution followed by 5-exo-dig-carbocyclization (Scheme 4.9).[18] The mechanism of this conversion involves initial base mediated monoalkylation of **4.34** in the presence of active methylene compound followed by CuI promoted 5-*exo-dig* carbocyclization, and anti-addition of alkyne.



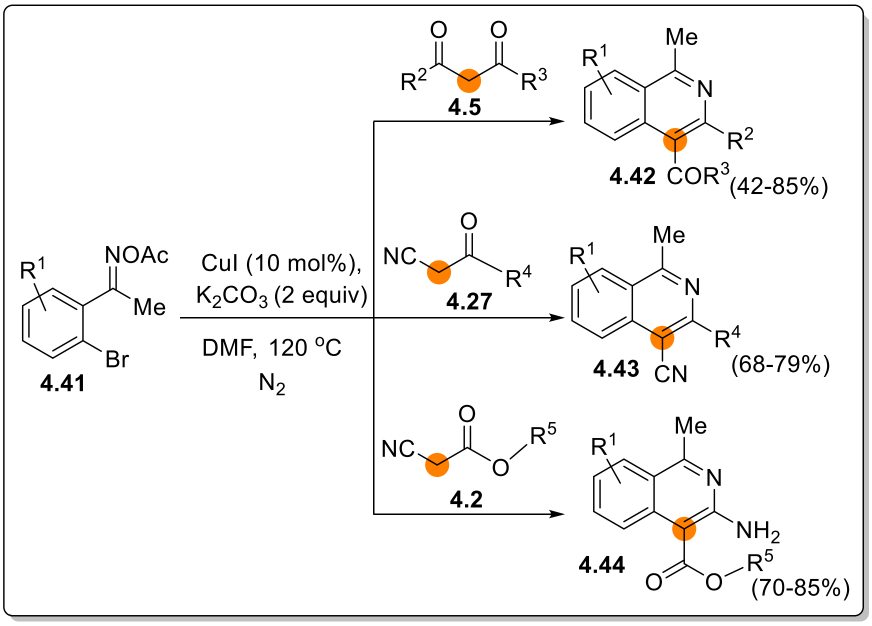
Scheme 4.9: Synthesis of substituted alkylidene cyclopentenes from MBH-acetates

Recently, Punniyamurthy and co-workers reported copper-mediated synthesis of dihydrobenzoindoles **4.38** and isoindolinones **4.40** by using 1-napthylamides **4.37** or 8-aminoquinolinamides **4.39** and malonates (Scheme 4.10).[19] This reaction proceeded through (i) cupration of active methylene compound in the presence of $Cu(OAc)_2$, (ii) ligand exchange with starting material **4.37**/**4.39**, (iii) $Cu(OAc)_2$ mediated oxidation and (iv) reductive elimination followed by intramolecular dehydrogenative coupling.



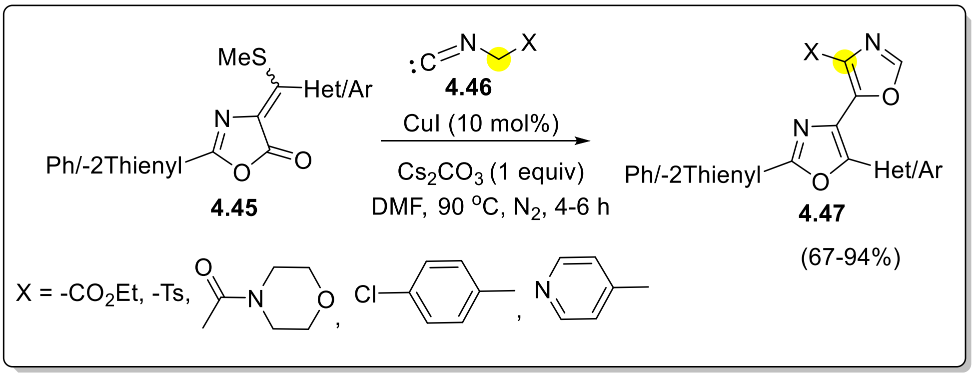
Scheme 4.10: Copper-mediated synthesis of dihydrobenzoindoles and isoindolines

In the year 2016, Jiang *et al* reported copper catalyzed synthesis of multifunctional isoquinolines **4.42-4.44** by using the reaction of 2-haloaryloxime acetates **4.41** with *β*-diketones **4.5**, *β*-ketonitriles **4.27**, or alkylcyano acetates **4.2** (Scheme 4.11).[20] Initially, halo-aryloxime acetate couples with the active methylene compound. This is followed by cleavage of N-O bond in the presence of CuI generating copper enamide. Subsequent intramolecular nucleophilic attack followed by regeneration of copper catalyst leads to multifunctional isoquinolines.



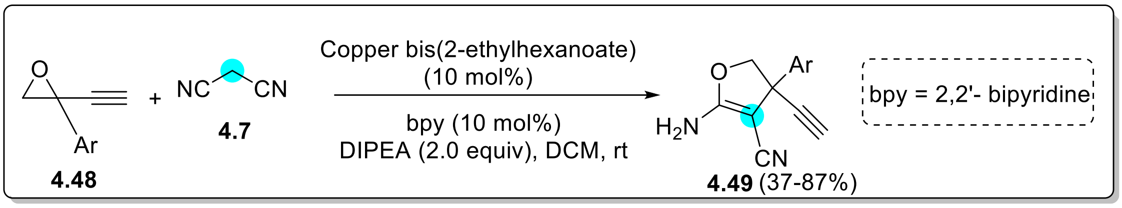
Scheme 4.11: Synthesis of multifunctional isoquinolines by using 2-haloaryloxime acetates

In the year 2013, Ila's group reported the synthesis of multisubstituted bisoxazoles **4.47** by the reaction of 2-(2-thienyl)-4-[(aryl/heteroaryl)-methylene]-5-oxazolones **4.45** with active methylene compounds having isocyanides (**4.46**) in the presence of CuI *via* formation of one C-C and two C-O bonds (Scheme 4.12).[21] The mechanism of this conversion involved (i) coordination between activated methylene isocyanide and CuI, (ii) nucleophilic ring opening of oxazolone **4.45** in the presence of cupriomethylene isocyanide followed by (iii) sequential construction of two oxazole rings to give bisoxazoles **4.47**.



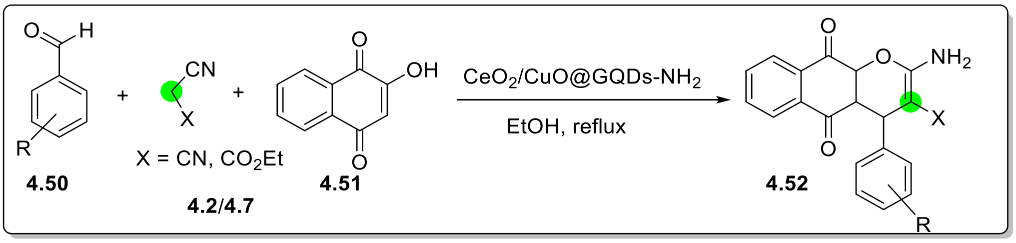
Scheme 4.12: Synthesis of multisubstituted bisoxazoles through [Cu]-catalysis

A copper catalyzed domino method for the synthesis of multifunctionalized dihydrofurans **4.49** from ethynyl epoxides **4.48** and malononitrile *via* [3+2] annulation pathway was developed by Lin's group (Scheme 4.13).[22]



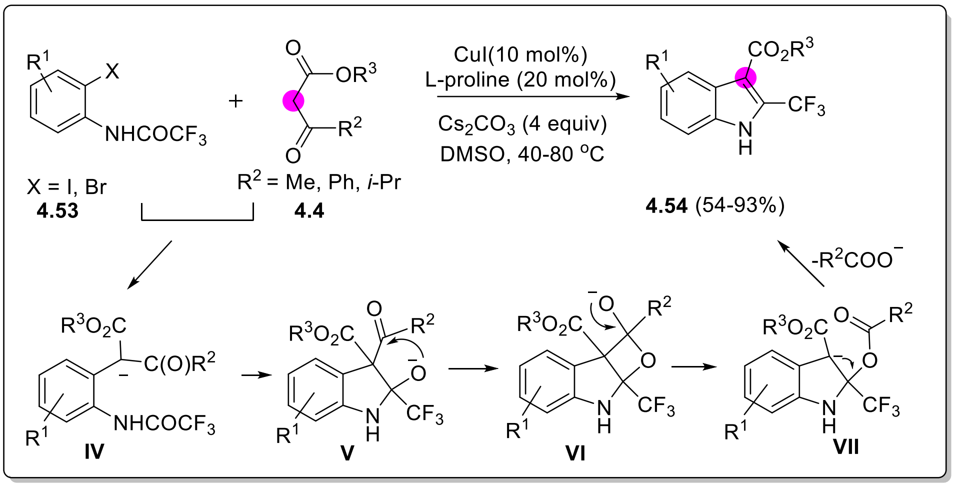
Scheme 4.13: Synthesis of multifunctionalized dihydrofurans from ethynyl epoxides

Recently, Ghomi *et al* developed a methodology for the synthesis of multifunctional benzo[*g*]chromenes **4.52** through a multi component reaction among aromatic aldehydes **4.50**, malononitrile or ethyl cyanoacetate and 2-hydroxy-1,4-naphthaquinone **4.51** by using the heterogeneous catalyst, amino-substituted CeO_2/CuO@graphene quantum dot nanocomposite material. Formation of chromene derivatives involves initial condensation reaction between aldehydes and active methylene compounds to give Knoevenagel intermediate. This will react with naphthoquinone moiety to generate active species, which undergoes imine to amine tautomerization followed by aromatization to form the desired products **4.52** (Scheme 4.14).[23]



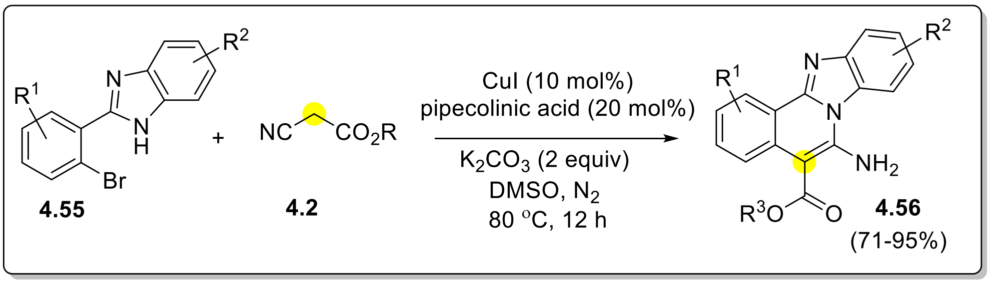
Scheme 4.14: Multi-component reaction for the synthesis of benzo[*g*]chromenes

Multifunctional indoles **4.54** have been prepared by Ma and co-workers *via* a copper catalyzed cascade reaction of 2-halotrifluoroacetanildes **4.53** with active methylene compounds **4.4**. This conversion proceeds through a coupling reaction and condensation followed by deacylation mechanism (Scheme 4.15).[24] A plausible mechanism involving intermediates **IV- VII** is also shown in the scheme.



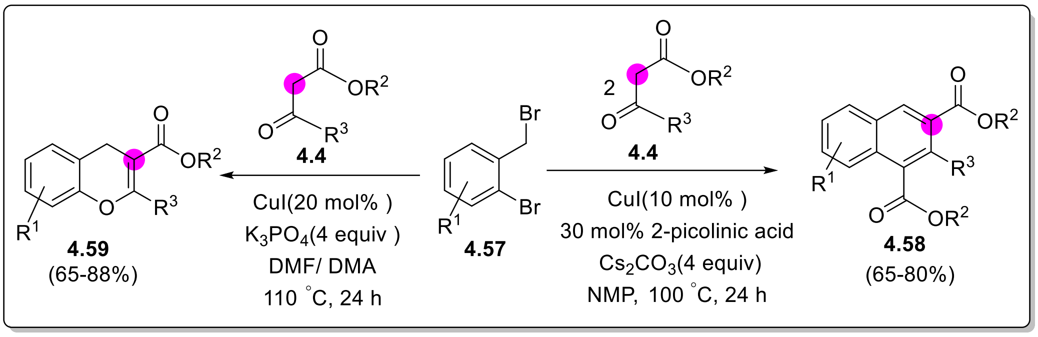
Scheme 4.15: Synthesis of multifunctional indole derivatives *via* [Cu]-catalysis

In the year 2011, Fu *et al* reported a methodology for the synthesis of benzimidazoisoquinolines **4.56** *via* a copper catalyzed cascade reaction of 2-(2-halophenyl)benzoimidazoles **4.55** with alkyl cyanoacetates **4.2** under mild conditions (Scheme 4.16).[25] This methodology provides benzimidazoisoquinolines having amino and carboxylate groups in good to excellent yields. Initially, CuI catalyst reacts with the ligand and generates a complex in the presence of a base. The generated complex reacts with substituted benzoimidazole. Then oxidative addition followed by *C*-arylation with active methylene compound and intramolecular nucleophilic attack of NH of imidazole moiety to alkyl cyanoacetate gives the desired products.



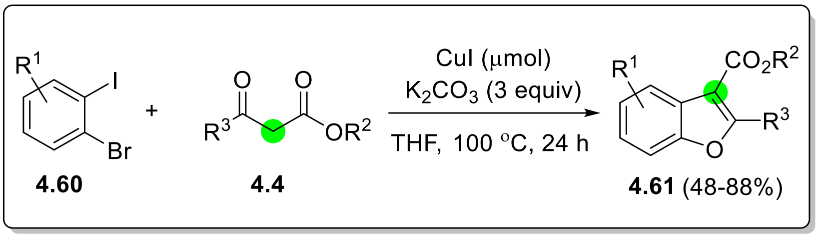
Scheme 4.16: Synthesis of multifunctional benzimidazoisoquinolines *via* [Cu]-catalysis

Beifuss and coworkers developed a copper catalyzed domino method for the synthesis of naphthalene derivatives **4.58** and substituted chromenes **4.59** *via* the reaction of bromo benzylbromide **4.57** upon reaction with active methylene compound **4.4**. This protocol involves β-keto ester and two equivalents of methylene moiety to give naphthalene derivatives **4.58** through intermolecular coupling reaction between two starting materials, intermolecular *C*-arylation, intramolecular 1,2-addition, cleavage of carboxylic acid and aromatization; one equivalent of β-keto ester upon reaction with bromobenzyl bromide through *C*-benzylation followed by *O*-arylation gives 4*H*-chromenes **4.59** (Scheme 4.17).[26]



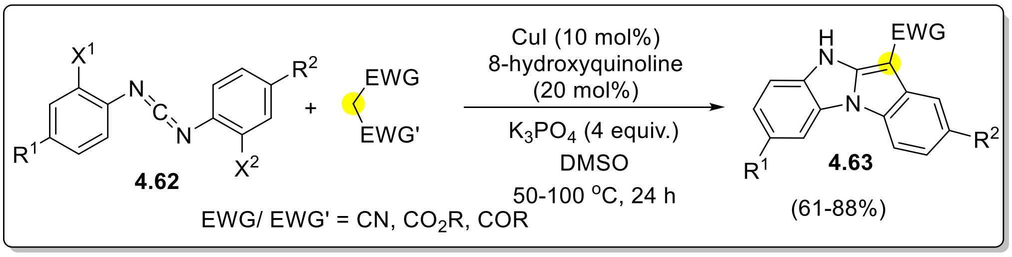
Scheme 4.17: Cu-catalyzed synthesis of multifunctional naphthalenes and chromenes

Ma's group reported the synthesis of 2,3-disubstituted benzofurans **4.61** through copper catalysis by using 1-bromo-2-iodobenzene **4.60** and *β*-keto ester **4.4** *via* intermolecular C-C bond formation (copper catalyzed coupling) followed by intramolecular C-O bond formation (Scheme 4.18).[27]



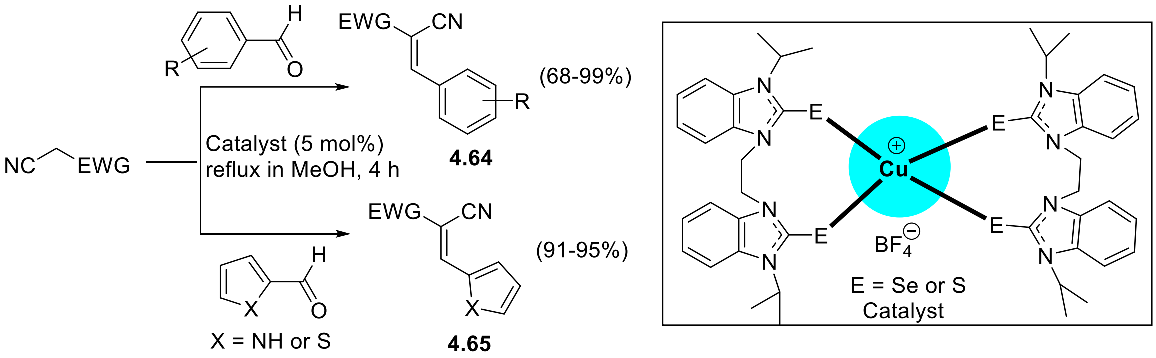
Scheme 4.18: Synthesis of disubstituted benzofurans from 1-bromo-2-iodobenzene

In the year 2014, Lv *et al* developed a copper catalyzed cascade method for the synthesis of poly substituted benzo[4,5]imidazo[1,2-*a*]indoles derivatives **4.63** *via* the reaction of bis-(*o*-haloaryl)carbodiimides **4.62** with active methylene compounds (Scheme 4.19).[28] This conversion involves C-N coupling, C-C coupling followed by decarboxylation and isomerization to obtain the desired products (Scheme 4.19).

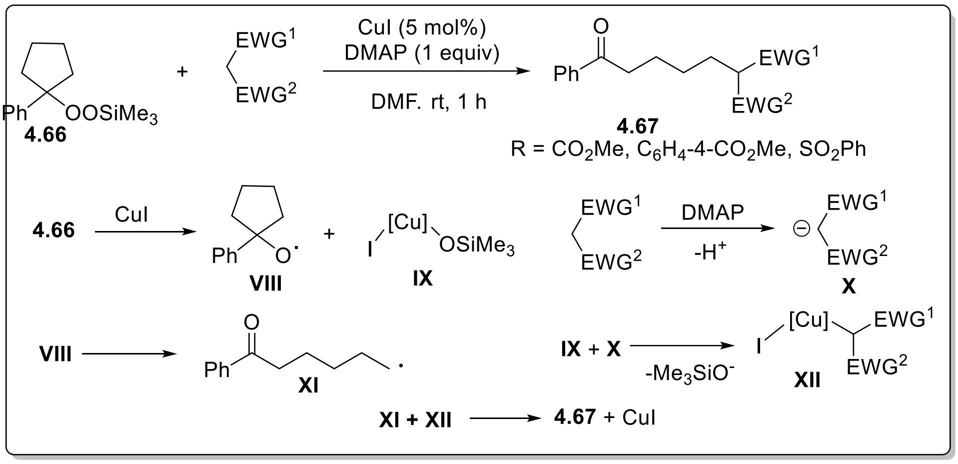


Scheme 4.19: Synthesis of polysubstituted benzo[4,5]imidazo[1,2-*a*]indoles from bis-(*o*-haloaryl)carbodiimides

A few very recent literature reports wherein [Cu]-catalyzed transformations by using active methylene group compounds are available, but these do not involve cyclization. Thus Knoevenagel condensation between different aldehydes and active methylene compounds by using Cu(I) chalcogenones (cf. products **4.64-4.65**; Scheme 4.20) has been reported by Mannarsamy *et al.*[29] This condensation process may involve the coordination of oxygen atom of aldehyde moiety with Cu(I) center. Similar reactions though, are well-precedent. Maruoka *et al.* developed monoalkylation of active methylene compounds by using alkylsilyl peroxides *via* copper catalysis (product **4.67**; Scheme 4.21).[30] Initially, alkylsilyl peroxide in the presence of Cu-catalyst gives alkoxy radical **VIII** along with [Cu]-complex **IX**. Base (DMAP) removes a proton for the active methylene compound to give enolate **X**. Species **VIII** generates **XI** by ring opening. Ligand exchange between **X** and silanoxide **IX** to lead to **XII**, followed by coupling of alkyl radical **XI** with copper complex **XII** affords the desired product **4.67**.



Scheme 4.20: Cu(I)-chalcogenone catalyzed Knoevenagel condensation



Scheme 4.21: Monoalkylation of active methylene compounds with alkylsilyl peroxides

OBJECTIVES OF PRESENT WORK – PART B

The literature survey, as discussed above, is not exhaustive but does suggest room for exploiting the reactivity of active methylene compounds. The motto of the present work was to explore the synthesis of multifunctional and polysubstituted naphthalenes, phenanthrenes, quinolines as well as benzo[*b*]carbazoles by using aromatic *o*-halo aldehydes upon reaction with active methylene group possessing compounds, (alkyl cyanoacetates, dialkyl malonates and malononitrile) *via* [Cu]-catalysis.

RESULTS AND DISCUSSION

In this chapter, we will discuss in detail on the transformation involving 2-bromo-aryl aldehydes and active methylene compounds *via* copper catalysis. Information about the precursors that are used in this chapter is presented in section 5.1. After this, synthesis of multifunctional carbo/heterocycles (naphthalenes, phenanthrenes, quinolines and benzo[*b*]carbazoles) by making use of active methylene group containing compounds (alkyl cyanoacetates, dialkyl malonates and malononitrile) in the presence of CuI as the catalyst is discussed. In the last section, structural elaboration of prepared compounds to yield dihydrobenzo[*g*]quinazolines followed by photophysical properties of prepared phenanthrene derivatives is also delved into.[31] The obtained products were characterized by mp (for solids), NMR, IR and HRMS (or LCMS/CHN). The relative positions of functional groups are assigned in representative cases by single crystal X-ray analysis.

5.1 Precursors used in the present study

The precursors that include substituted 2-bromo-benzaldehydes (**1a-f**), 1-bromo-2-naphthaldyde (**1g**), 2-bromopyridine-3-carboxaldehyde (**1h**), alkyl cyanoacetates (**2a-d**), dialkyl malonates (**3a-c**) and malononitrile (**4**) are available commercially and are purchased from Aldrich (cf. Chart 1). 2,7-Dibromo-9-ethyl-9H-carbazole-3-carbaldehyde **1i** was prepared by using a literature method.[32]

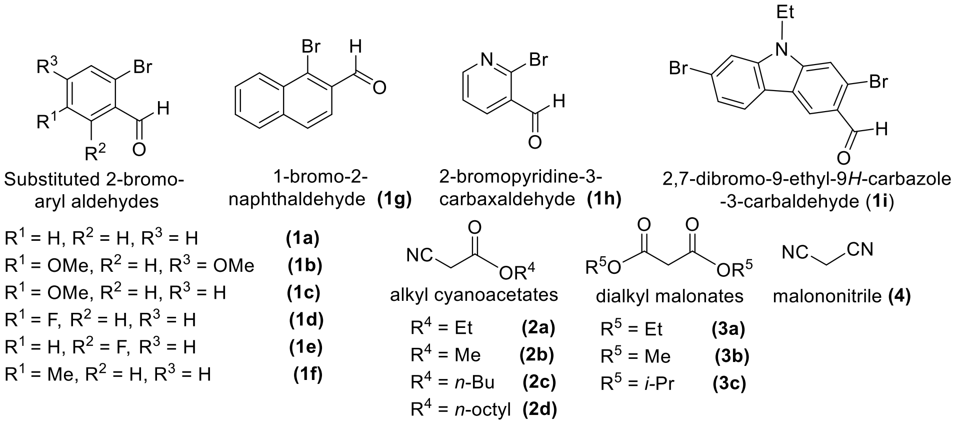


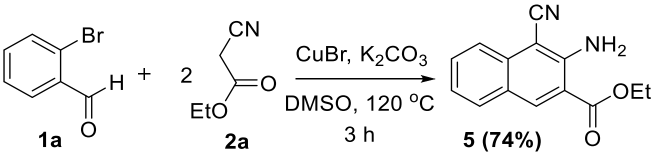
Chart 1: Precursors used in the present work

5.2 Copper-catalyzed transformation of *o*-bromoaryl aldehydes into multifunctional carbo/ heterocycles by using active methylene group containing compounds

Synthesis of various carbo/ heterocycles by using active methylene compounds as one of the precursors is well explored (as shown in the introduction). But, most of the reactions involved usage of complex starting materials, multiple step conversions and used additional ligand along with catalyst. In this section, we report copper catalyzed synthesis of polysubstituted aromatic compounds with multiple functional groups (naphthalenes, phenanthrenes, quinolines and benzo[*b*]carbazoles) by using readily available *o*-bromoaryl aldehydes and active methylene compounds in a single synthetic operation without using any additional ligand.

5.2.1 [Cu]-catalyzed ligand-free synthesis of multifunctional naphthalenes, phenanthrenes, quinolines, benzo[*b*]carbazoles by using 2-bromo aryl aldehydes and active methylene compounds

Initially, 2-bromobenzaldehyde **1a** was treated with ethyl 2-cyanoacetate **2a** in the presence of CuBr (10 mol%) and K_2CO_3 (3.0 equiv) in DMSO at 120 °C for 3 h. TLC analysis showed complete consumption of **1a** gave ethyl 3-amino-4-cyano-2-naphthoate **5** in 74% yield (Scheme 1). We next moved to improve the yield of the product by screening different parameters of reaction. Details are given in Table 1.



Scheme 1: Reaction of 2-bromobenzaldehyde (**1a**) with ethyl 2-cyanoacetate (**2a**)

First, we checked the reaction by using 0.1 equiv of copper catalysts CuBr, CuCl, CuI, $CuCl_2$, $Cu(OAc)_2$ and $Cu(OTf)_2$ in the presence of 3.0 equiv of K_2CO_3 as the base and DMSO as the solvent at 120 °C (Table 1, entries 1-6). Among these, CuI provided the highest yield and the target product **5** was isolated in 81% yield (entry 4). In the absence of copper catalyst, product **5** was not at all observed (entry 7). Lowering of catalyst quantity to 5 mol % decreased the yield (entry 8) whereas increasing the catalyst loading to (20 mol %) did not improve the yield of the reaction (entry 8). Among the bases

K_2CO_3, Cs_2CO_3, Na_2CO_3, K_3PO_4, *t*-BuOK, Et_3N and DBU (entries 4 and 9-14) tested, highest yield was observed using K_2CO_3. Among the solvents DMSO, *N,N*-dimethylacetamide (DMA), 1,4-dioxane, toluene and PEG-400 tested (entries 4, 16-19), DMSO was found to be the solvent of choice, although DMF (entry 15) also gave a comparable yield. Conducting the reaction at 70 ^{o}C/10 h or 150 ^{o}C/ 3 h afforded **5** in nearly the same yield (entry 20). It is also noteworthy that this reaction required neither an inert atmosphere nor any additional ligand to produce alkyl 3-amino-4-cyano-2-naphthoate **5** in good yield (entry 22). So, reaction conditions in entry 4 was determined as optimal condition [**1a** (1.0 mmol), **2a** (2.0 mmol), CuI (10 mol %), and K_2CO_3 (3.0 mmol) in DMSO at 120 °C/ 3 h].

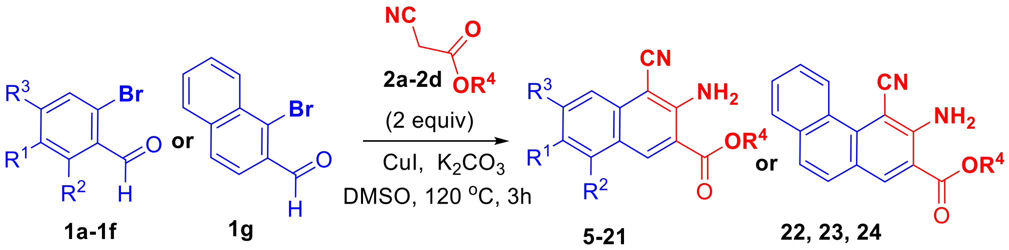
Table 1. Optimization of the Reaction Conditions[a]

Entry	Catalyst	Base	Solvent	yield of **5** (%)[b]
1	CuBr	K_2CO_3	DMSO	74
2	CuCl	K_2CO_3	DMSO	52
3	$CuCl_2$ (anh.)	K_2CO_3	DMSO	47
4	**CuI**	**K_2CO_3**	**DMSO**	**81**[c]
5	$Cu(OAc)_2$(anh.)	K_2CO_3	DMSO	54
6	$Cu(OTf)_2$	K_2CO_3	DMSO	52
7	-	K_2CO_3	DMSO	-[d]
8	CuI	K_2CO_3	DMSO	54 (80)[e]
9	CuI	Cs_2CO_3	DMSO	76
10	CuI	Na_2CO_3	DMSO	71
11	CuI	K_3PO_4	DMSO	60
12	CuI	*t*-BuOK	DMSO	42
13	CuI	Et_3N	DMSO	14
14	CuI	DBU	DMSO	25
15	CuI	K_2CO_3	DMF	75
16	CuI	K_2CO_3	DMA	37
17	CuI	K_2CO_3	Dioxane	10
18	CuI	K_2CO_3	Toluene	11

19	CuI	K_2CO_3	PEG-400	7
20	CuI	K_2CO_3	DMSO	77 (80)[f]
21	CuI	-	DMSO	-[g]
22	CuI	K_2CO_3	DMSO	80(77)[h]

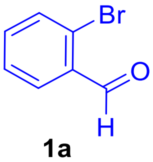
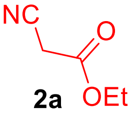
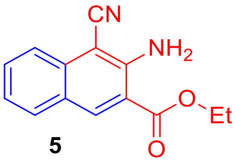
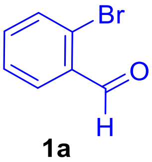
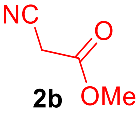
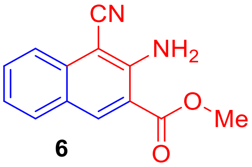
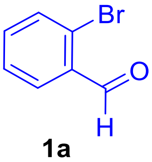
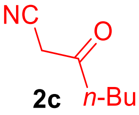
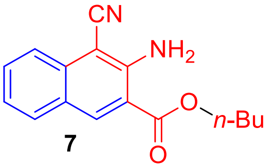
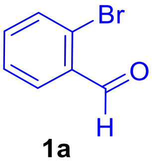
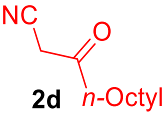
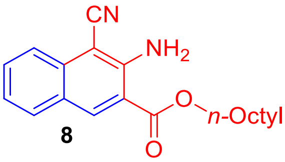
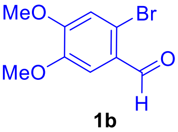
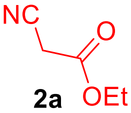
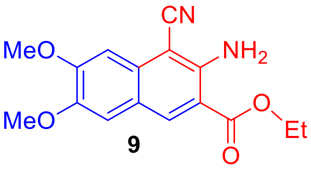
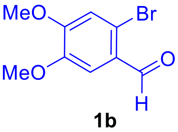
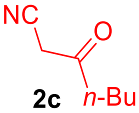
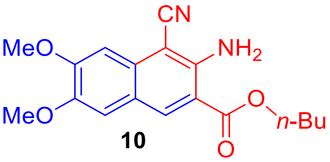
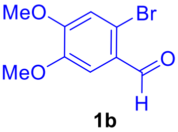
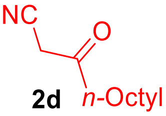
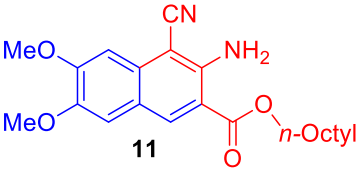
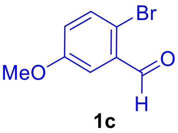
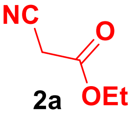
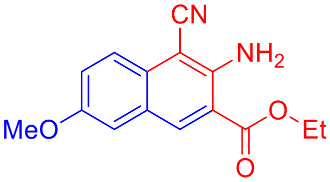
[a]Reaction conditions: **1a** (0.54 mmol), **2a** (1.09 mmol), base (1.62 mmol), catalyst (0.054 mmol), solvent (2 mL), 120 °C (oil bath) for 3 h in a stoppered Schlenk tube in air. [b]Isolated yield of **5**. [c]Reaction performed under nitrogen gave the same yield but under oxygen (balloon) the yield was only 45%. [d]No catalyst was added. [e]5 mol % and 20 mol % of CuI were used. [f]The yields are for the reactions performed at 70 °C/10 h (77%) and 150 °C/ 3 h (80%) respectively. [g]No base was added. [h]10 mol % of L-proline (or 1,10-phenanthroline) as ligands were used.

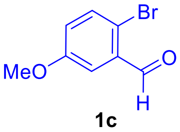
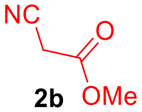
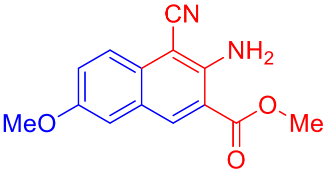
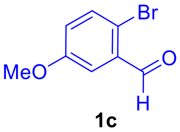
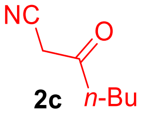
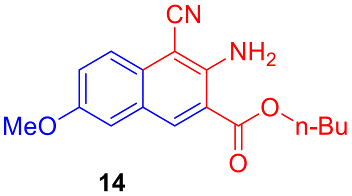
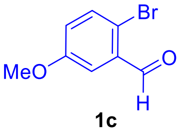
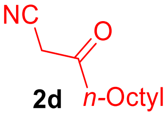
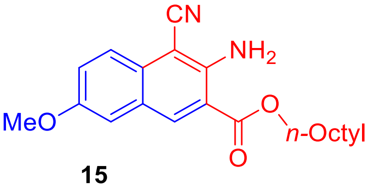
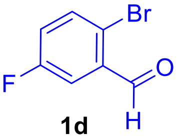
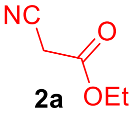
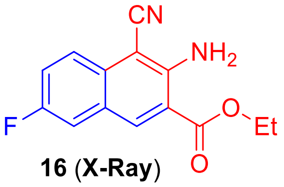
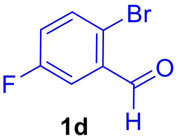
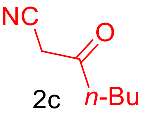
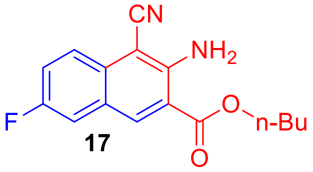
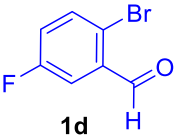
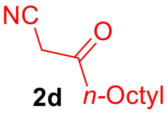
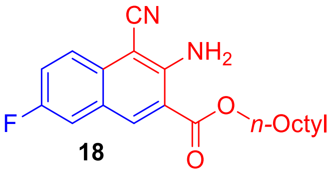
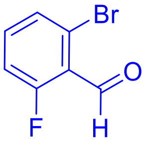
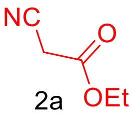
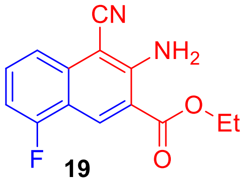
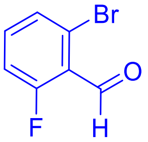
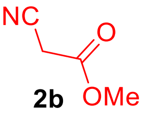
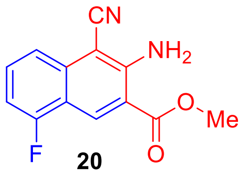
When we moved to substrate scope (Table 2), 2-bromobenzaldehydes **1a-1f** possessing electron-neutral, electron rich or electron-withdrawing substituents and the nitriles **2a-d** containing CO_2R^4 [where, R^4 = Et, Me, *n*-Bu, *n*-octyl] smoothly converted to the corresponding products **5-21** in good yields. X-ray single crystal structure of compound **16** shown in Figure 1 (left). We were pleased to find that the tandem reaction of 1-bromo-2-naphthaldehyde **1g** with different alkyl-2-cyanoacetates (**2a-b** and **2d**) afforded the alkyl 3-amino-4-cyanophenanthrene-2-carboxylates **22** (X-ray structure shown in Figure 1, right), **23** and **24** in good yields.

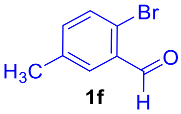
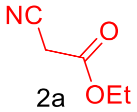
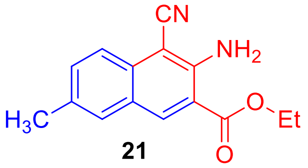
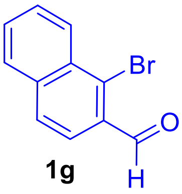
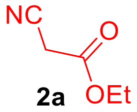
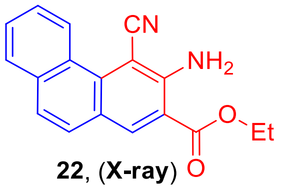
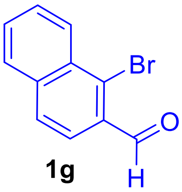
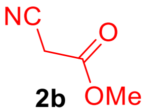
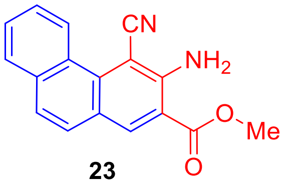
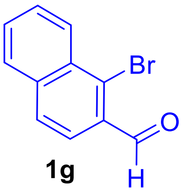
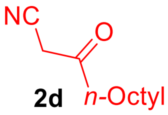
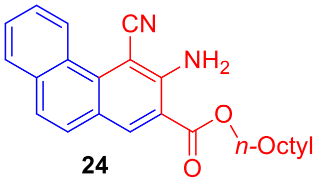


Scheme 2: Substrate scope for the synthesis of multifunctional naphthalenes/ phenanthrenes

Table 2. Substrate Scope for [Cu]-Catalyzed Tandem Synthesis of Multifunctional Naphthalenes and Phenanthrenes 5-24[a]

Entry	2-bromoaryl aldehydes	Alkyl cyanoacetate	Naphthalene/ phenanthrene products	yield (%)[b]
1	 **1a**	 **2a**	 **5**	81
2	 **1a**	 **2b**	 **6**	77
3	 **1a**	 **2c**	 **7**	72
4	 **1a**	 **2d**	 **8**	68
5	 **1b**	 **2a**	 **9**	85
6	 **1b**	 **2c**	 **10**	80
7	 **1b**	 **2d**	 **11**	82
8	 **1c**	 **2a**	 **12**	79

9	 **1c**	 **2b**	 **13**	71
10	 **1c**	 **2c**	 **14**	68
11	 **1c**	 **2d**	 **15**	73
12	 **1d**	 **2a**	 **16** (**X-Ray**)	70
13	 **1d**	 2c	 **17**	67
14	 **1d**	 **2d**	 **18**	65
15	 **1e**	 2a	 **19**	61
16	 **1e**	 **2b**	 **20**	68

17	 **1f**	 2a	 **21**	80
18	 **1g**	 **2a**	 **22**, (**X-ray**)	72
19	 **1g**	 **2b**	 **23**	62
20	 **1g**	 **2d**	 **24**	65

[a]Reaction conditions: **1** (0.5 mmol), **2** (1.0 mmol), K_2CO_3 (1.6 mmol), CuI (0.05 mmol), DMSO (2 mL) in a stoppered Schlenk tube in air at 120 °C (oil bath) for 3h.

[b]Yield of the product **5-24**.

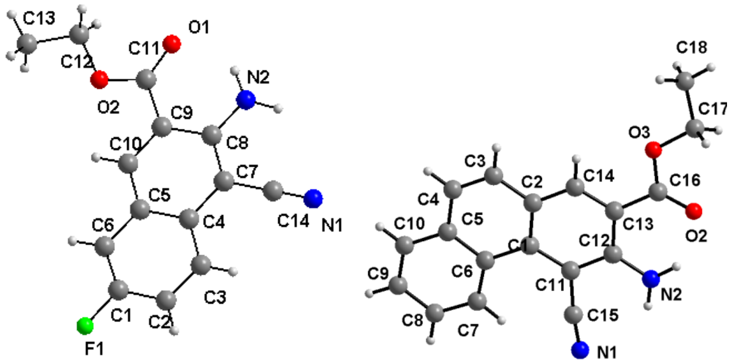
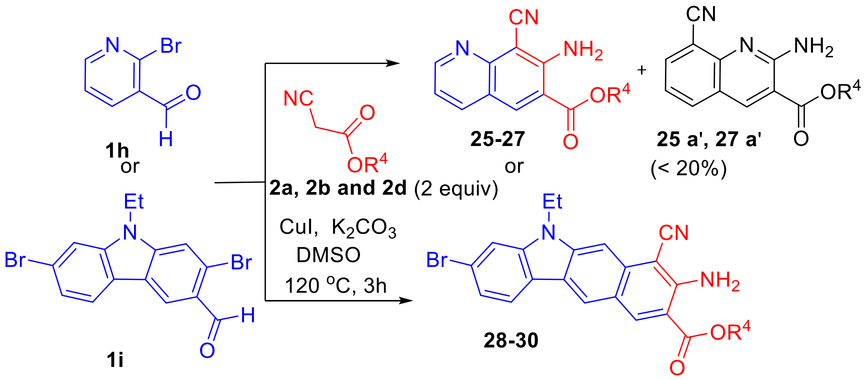


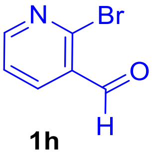
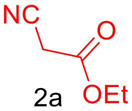
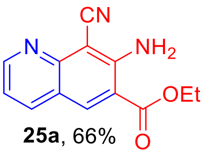
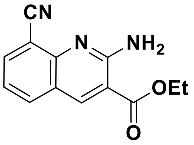
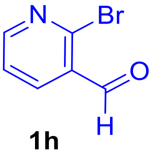
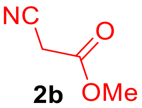
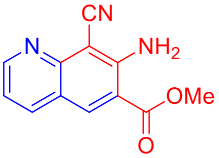
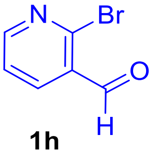
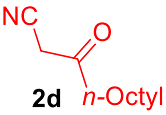
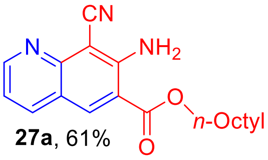
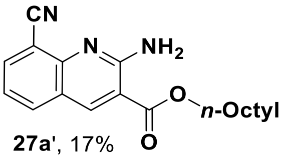
Figure 1. Molecular structures of compouds **16** (left) and **22** (right). Selected bond parameters: Compoud **16** C(4)-C(7) 1.427(3), C(7)-C(8) 1.399(3), C(8)-C(9) 1.437(3), C(9)- C(11) 1.487(3), C(9)-C(10) 1.372(3), C(5)-C(10) 1.408(3), C(8)-N(2) 1.355(3) , C(7)-C(14) 1.416(3) [Å]. Compoud **22** C(1)-C(11) 1.426(2), C(2)-C(14) 1.406(2), C(11)-C(12) 1.414(2), C(12)- C(13) 1.420(2), C(13)-C(14) 1.370(2), C(11)-C(15) 1.427(3), C(12)-N(2) 1.360(2), C(13)-C(16) 1.486(2) [Å].

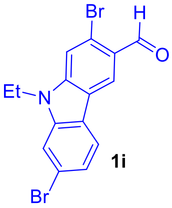
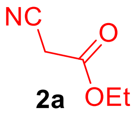
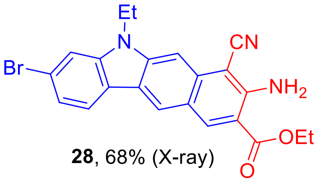
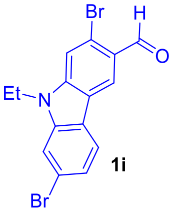
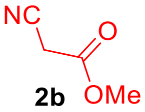
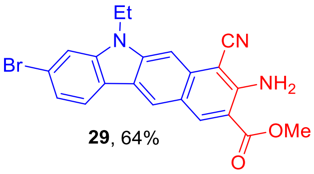
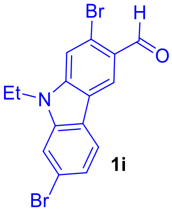
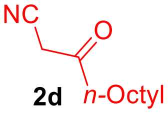
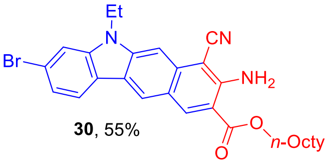
In a manner similar to above, we subsequently examined the reaction of 2-bromo-3-pyridinecarboxaldehyde **1h** with alkyl cyanoacetates **2a**, **2b** and **2d**. Satisfyingly, the reaction furnished the desired products **25-27** in moderate to good yields of 52-72% (Table 3) along with < 17% yield of **25a**' and **27a**'. X-ray structures of compounds **25a**' are **26** shown Figure 2 (left and center, respectively). We successfully extended this methodology to the synthesis of alkyl 7-amino-8-cyano-5-ethyl-5*H*-benzo[*b*]carbazole-9-carboxylate **28** (X-ray; Figure 2, right), **29** and **30** by using precursor **1i** (Table 3)**.**



Scheme 3: Synthesis of poly functionalized quinolines and benzo[*b*]carbazoles

Table 3. [Cu]-Catalyzed Tandem Synthesis of Quinolines and Benzo[*b*]carbazoles 25-30[a]

Entry	2-Bromoaryl aldehydes	Alky cyanoacetates	Quinolines/ Benzo[*b*]carbazoles (yield)[b]	Quinolines/ Benzo[*b*]carbazoles (yield)[b]
1	 **1h**	 2a	 **25a**, 66%	 **25a**', 12% (X-ray)
2	 **1h**	 **2b**	 **26**, 72% (X-ray)	Not formed
3	 **1h**	 **2d**	 **27a**, 61%	 **27a**', 17%

4	 1i	 **2a**	 **28**, 68% (X-ray)	Not formed
5	 1i	 **2b**	 **29**, 64%	Not formed
6	 1i	 **2d**	 **30**, 55%	Not formed

[a] Reaction conditions: **1** (0.5 mmol), **2** (1.0 mmol), K_2CO_3 (1.6 mmol), CuI (0.05 mmol), DMSO (2 mL), in a stoppered Schlenk tube in air at 120 °C (oil bath) for 3 h.

[b] Yield of product **25-30**.

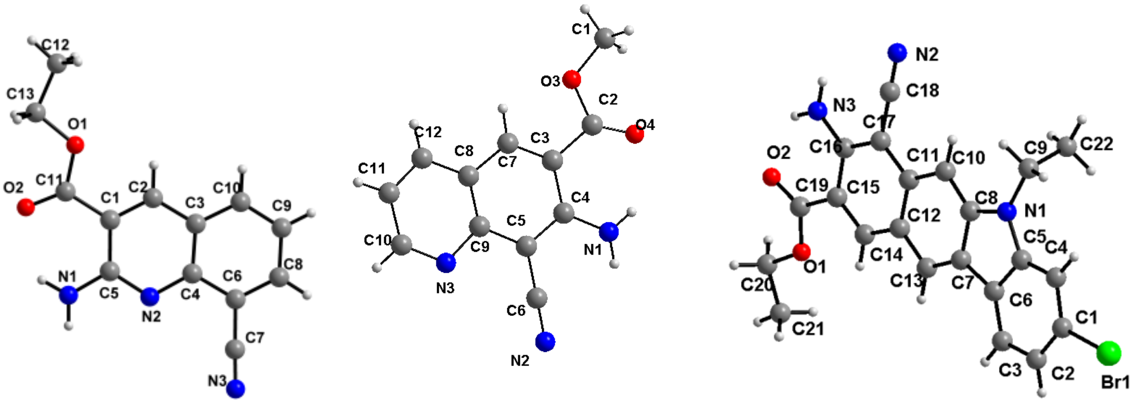
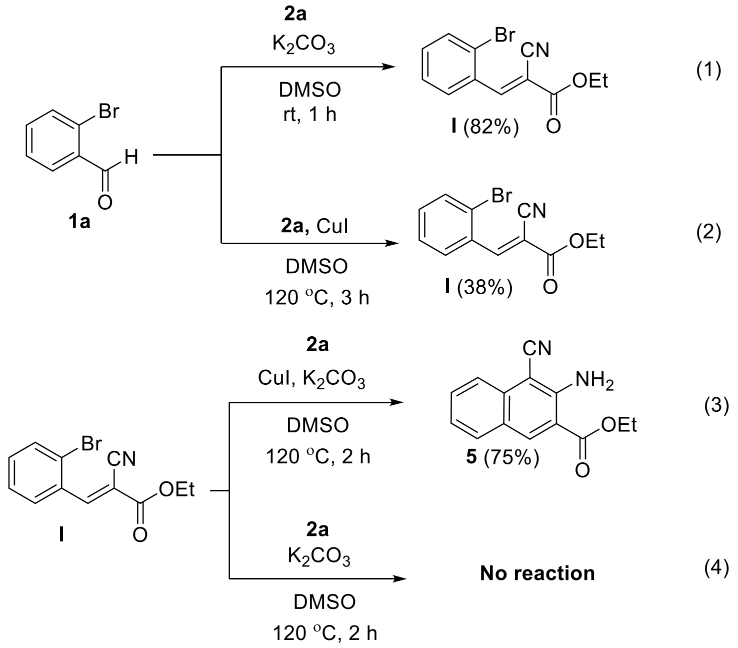


Figure 2. Molecular structures of compouds **25a'**, **26** and **28**. Selected bond parameters: Compoud **25a'** C(5)-N(1) 1.343(7), C(1)-C(11) 1.489(8), C(3)-C(10) 1.405(7), C(10)-C(9) 1.365(8), C(9)-C(8) 1.402(8), C(8)-C(6) 1.378(7), C(6)-C(7) 1.440(8), C(6)-C(4) 1.415(8) [Å]. Compound **26** C(5)-C(9) 1.430(11), C(5)-C(6) 1.410(12), C(5)-C(4) 1.420(11), C(4)- N(1) 1.374(12), C(4)-C(3) 1.433(12), C(3)-C(7) 1.366(12), C(7)-C(8) 1.440(12) [Å]. Compound **28** C(11)-C(17) 1.424(5), C(17)-C(18) 1.436(6), C(17)-C(16) 1.387(5), C(16)- N(3) 1.341(5), C(16)- C(15) 1.444(6), C(15)- C(14) 1.379(5), C(14)-C(12) 1.389(5) [Å].

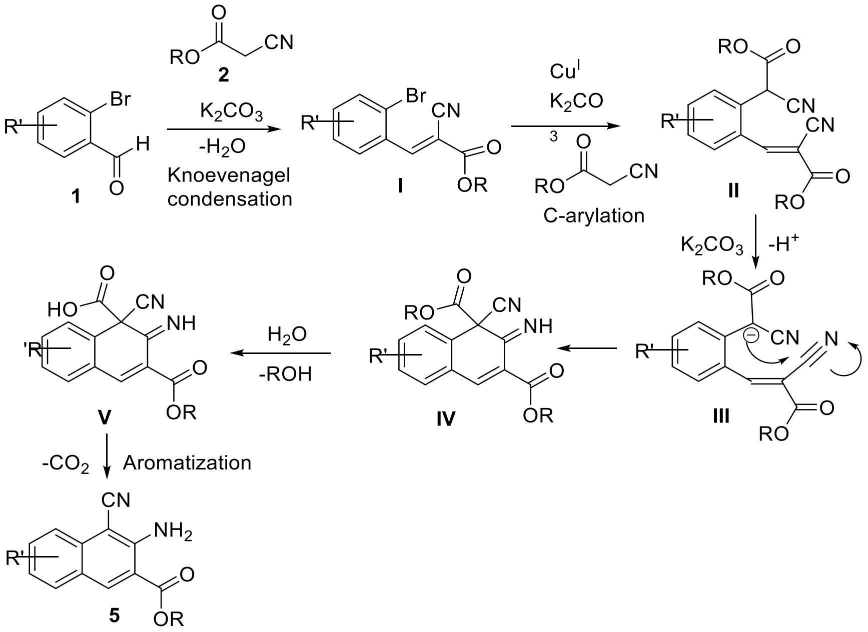
5.2.2 Plausible pathway for the formation of products 5-30

In order to decipher the reaction pathway, we performed the reaction of 2-bromobenzaldehyde **1a** (1.0 mmol) with ethyl cyanoacetate **2a** (1.0 mmol) using K_2CO_3 (1.0 mmol) in DMSO at rt (25 °C) for 1 h that provided the Knoevenagel adduct **I** in 82% yield (Scheme 5, eq 1). In the absence of K_2CO_3, only the Knoevenagel adduct **I** was obtained in 38% yield, along with unreacted starting material **1a** (Scheme 4, eq 2). When we treated **I** (1 mmol) with ethyl cyanoacetate **2a** (1 mmol), CuI (0.1 mmol), and K_2CO_3 (2.0 mmol) at 120 °C for 2 h, the desired product **5** was obtained in excellent yield (Scheme 4, eq 3). In the absence of CuI, the reaction did not proceed (Scheme 4, eq 4). These simple observations clearly showed that copper mediated C-arylation is the key step in this tandem process.



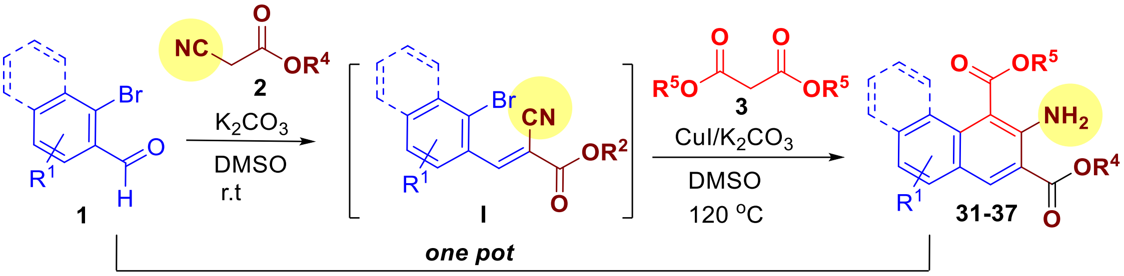
Scheme 4: Control experiments for ascertaining the mechanism

On the basis of the above control experiments and literature reports,[33] a plausible pathway for the formation of **5-30** is illustrated in Scheme 5. Initially, the reaction of 2-bromobenzaldehyde **1** and alkyl cyanoacetate **2** in the presence of base generates Knoevenagel adduct **I**. Copper-catalyzed coupling of **I** with **2** leads to C-arylation product **II**. Then, the base abstracts a proton from an active methine carbon of **II** forming the highly nucleophilic carbanion **III** that attacks the nitrile leading to the cyclized intermediate **IV** which undergoes hydrolysis to give **V**. Decarboxylation, followed by aromatization of **V** affords alkyl 3-amino-4-cyano-2-naphthoate (**5**). We wish to emphasize here that (i) the later stages of this reaction pathway as well as the resulting products differ from the one reported using *β*-keto-esters wherein an oxetane intermediate and elimination of carboxylate species is proposed[33e] and (ii) the formation of **25a'** and **27a'** albeit in very low yields perhaps offers a different type of mechanism for their formation but currently it is a puzzling observation.



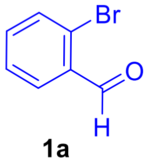
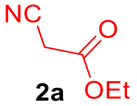
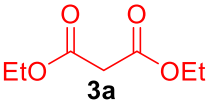
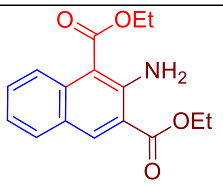
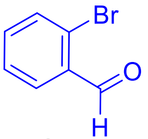
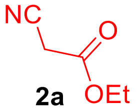
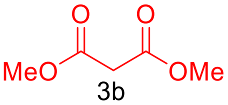
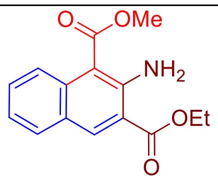
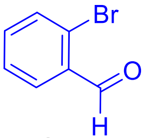
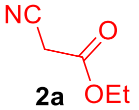
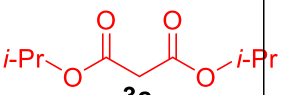
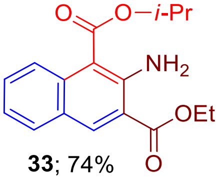
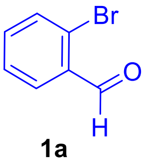
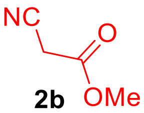
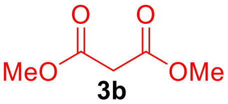
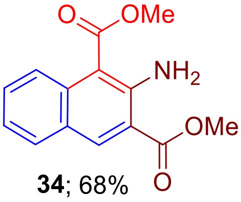
Scheme 5: Probable pathway for the formation of multifunctional naphthalenes

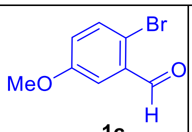
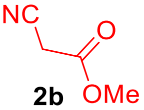
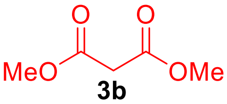
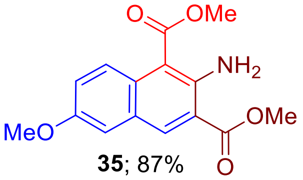
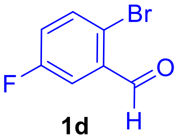
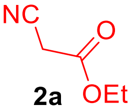
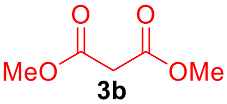
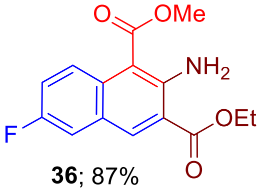
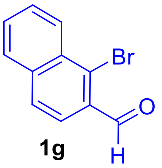
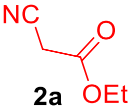
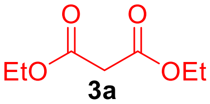
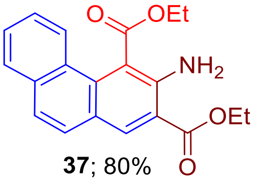
To extend our concept by expanding the scope of substrates, we treated 2-bromobenzaldehyde **1a** (1.0 mmol) with methyl cyanoacetate **2b** (1.0 mmol**)** and K_2CO_3 (1.0 mmol) in DMSO at rt for 1 h to generate intermediate **I**; after consumption of all of **1a** (TLC), CuI (10 mol%), K_2CO_3 (2.0 mmol) and diethylmalonate (**3a**, 1.0 mmol) were added and the contents heated at 120 ^{o}C for 2 h. The overall reaction proceeded smoothly to afford diethyl 2-aminonaphthalene-1,3-dicarboxylate **31** in 68% yield (Table 4). The scope of this protocol was examined using diverse 2-bromobenzaldehydes (**1a**, **1c, 1d** and **1g**), alkyl 2-cyanoacetates (**2a-b**) and dialkyl malonates (**3a-c**; R^5 = Et, Me, *i*-Pr). The corresponding products **31-37** were isolated in good yields (Scheme 6; Table 4). X-ray structure of compound **34** shown in Figure 3. This new one-pot sequence also allowed for the synthesis of polysubstituted phenanthrene **37** in 80% yield (Table 4).



Scheme 6: Cu-catalyzed one- pot synthesis of dialkyl-2-aminonaphthalene-1,3-dicarboxylates

Table 4. Cu(I)-Catalyzed One-Pot Sequential Synthesis of Amino-naphthalene/phenanthrene-dicarboxylates 31-37^{a,b}

Entry	2-bromoaryl aldehydes	Alky cyano acetates	Dialkylmalonate	Amino-naphthalene/phenanthrene-dicarboxylates (yield)^b
1	 **1a**	 **2a**	 **3a**	 **31**; 80%
2	 **1a**	 **2a**	 3b	 **32**; 79%
3	 **1a**	 **2a**	 **3c**	 **33**; 74%
4	 **1a**	 **2b**	 **3b**	 **34**; 68% (X-ray)

5	 **1c**	 **2b**	 **3b**	 **35**; 87%
6	 **1d**	 **2a**	 **3b**	 **36**; 87%
7	 **1g**	 **2a**	 **3a**	 **37**; 80%

[a]Reaction conditions: **1** (~0.5 mmol), **2** (0.5 mmol), K_2CO_3 (0.5 mmol), DMSO (2 mL), at rt for 1 h in a stoppered Schlenk tube in air; then CuI (0.05 mmol), **3** (0.5 mmol), and K_2CO_3 (1.0 mmol) were added in air and contents heated at 120 °C (oil bath) for 2 h.

[b] Yield of products **31-37**.

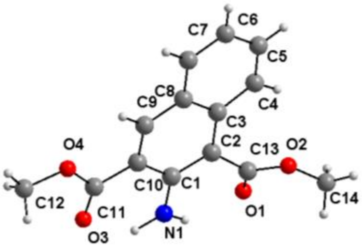
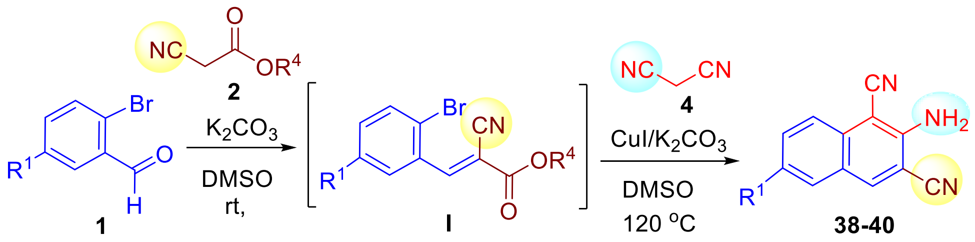


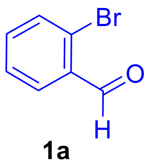
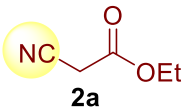
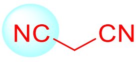
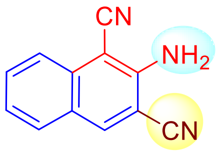
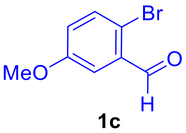
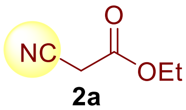
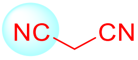
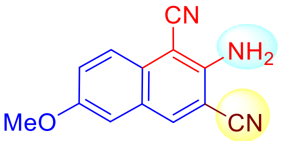
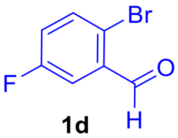
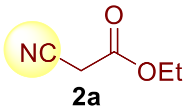
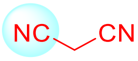
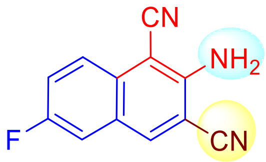
Figure 3. Molecular structure of compoud **34**. Selected bond parameters: C(8)-C(9) 1.405(3), C(9)-C(10) 1.360(3), C(10)-C(11) 1.490(3), C(10)-C(1) 1.441(3), C(1)- N(1) 1.352(3), C(1)-C(2) 1.406(3), C(2)-C(3) 1.432(3) [Å].

In order to explore the above one-pot sequential method further, malononitrile (**4**; 1 mmol) was used to replace dialkyl malonate **3**. Very interestingly, this reaction afforded 2-aminonaphthalene-1,3-dicarbonitriles **38-40** (X-ray structure of **38** in Figure 4) in 67-82% yield (Scheme 7 and Table 5).



Scheme 7: [Cu]-catalyzed synthesis of 2-aminonaphthalene-1,3-dicarbonitriles

Table 5. Cu(I)-Catalyzed One-Pot Sequential Synthesis of 2-Aminonaphthalene-1,3-dicarbonitriles 38-40^{a,b}

Entry	2-bromoaryl aldehyde	Alky cyano acetate	Other active methylene compd	2-Aminonaphthalene-1,3-dicarbonitriles (yield)^b
1	 **1a**	 **2a**	 **4**	 **38**; 70% (X-ray)
2	 **1c**	 **2a**	 **4**	 **39**: 82%
3	 **1d**	 **2a**	 **4**	 **40**: 67%

^{a}Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), K$_2$CO$_3$ (0.5 mmol), DMSO (2 mL), at rt for 1h, in a stoppered Schlenk tube in air; then CuI (0.05 mmol), **4** (0.5 mmol), and K$_2$CO$_3$ (1.0 mmol) were added in air and the contents heated at 120 °C (oil bath) for 2h.

^{b} Yield of products **38-40**.

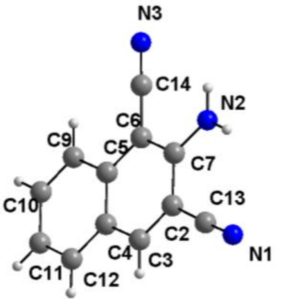
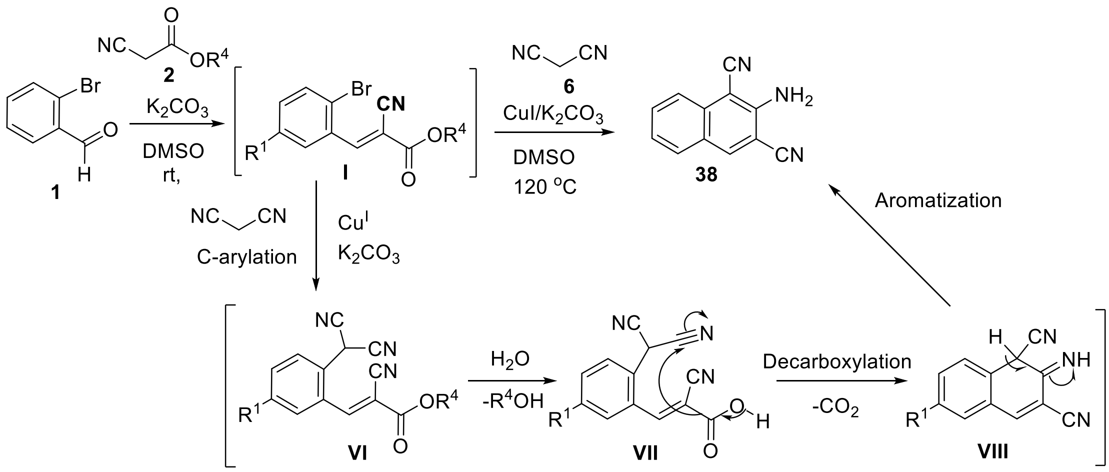


Figure 4. Molecular structure of compoud **38**: Selected bond parameters: C(4)-C(3) 1.408(4), C(3)-C(2) 1.369(4), C(2)-C(7) 1.424(4), C(7)- N(2) 1.354(4), C(7)-C(6) 1.386(4), C(5)-C(6) 1.425(4), C(2)-C(13) 1.423(4), C(6)-C(14) 1.413(4) [Å].

5.2.3 Plausible pathway for the formation of products 38-40

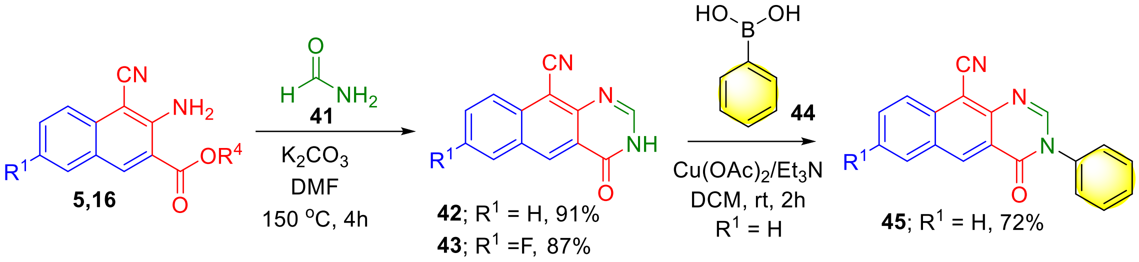
Mechanistically, the reaction seems to involve an initial C-arylation *via* copper-catalyzed coupling of **I** with **4** to give intermediate **VI** (Scheme 8). Hydrolysis of ester on **VI** leads to **VII**. Decarboxylation followed by cyclization of **VII** leads to intermediate **VIII**. Finally, aromatization of **VIII** afforded products **38-40**. Thus the later stages of this pathway appears to be slightly different from that shown in Scheme 6 or the one involving *β*-ketoesters.[32e]



Scheme 8: Plausible mechanism for the formation of products **38-40**

5.2.4 Utilization of the multifunctional naphthalenes

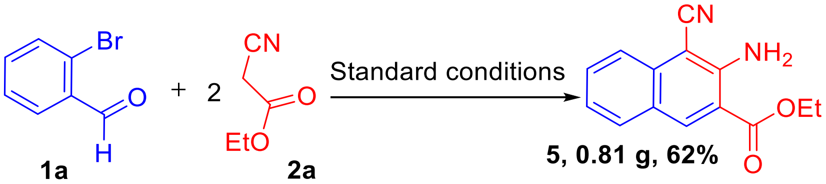
To demonstrate the utility of the present protocol, further structural elaboration of compounds **5** and **16** was performed *via* the reaction with formamide **41** in the presence of K_2CO_3 to give the corresponding benzo[*g*]quinazoline **42-43**. Later, the compound **42** was converted to 4-oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile **45** by using a reported Cu-mediated C-N bond forming reaction (cf. Scheme 9);[33] there was no perceptible reaction using CuI under the conditions given in Table 2.



Scheme 9: Synthesis of 4-oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile from prepared multifunctional naphthalenes

5.2.5 Gram-Scale Transformation

To examine the scalability of the optimized method, the tandem reaction between 2-bromobenzaldehyde **1a** and ethyl cyanoacetate **2a** was carried out under standard conditions on a gram scale. To our delight, the expected product ethyl 3-amino-4-cyano-2-naphthoate **5** could be obtained in 62% isolated yield (Scheme 10).



Scheme 10: Gram-scale synthesis of ethyl 3-amino-4-cyano-2-naphthoate under optimized conditions

5.2.6. Photophysical properties of the obtained phenanthrenes 22, 24 and 37

We expected phenanthrene-2-carboxylates **22, 24** and **37** to be photochemically active and perhaps could be used later. Hence the UV-visible and fluorescence spectra were recorded. The emission spectra of compounds **22**, **24**, and **37** were recorded upon excitation at 330 nm. As expected, these compounds show moderate fluorescence emission intensity (cf. Figure 5). The absorption peak wavelengths (λ_{abs}), molar extinction coefficient (Ɛ), emission peak wavelengths (λ_{em}) in solution are summarized in Table 6 and Figure 5.

Table 6. UV−Visible Absorption and Fluorescence Emission Properties of Phenanthrene Carboxylates 22, 24 and 37

entry	compound	λ_{abs} (nm)[a]	Ɛ (10^4 $M^{-1}cm^{-1}$)	λ_{em} (nm)[b]
1	**22**	435	1.0	461
2	**24**	435	3.3	467
3	**37**	427	1.9	488

[a]UV-visible absorption wavelengths, [b]Emission wavelengths at rt in toluene at concentration of 1 × 10^{-5}M.

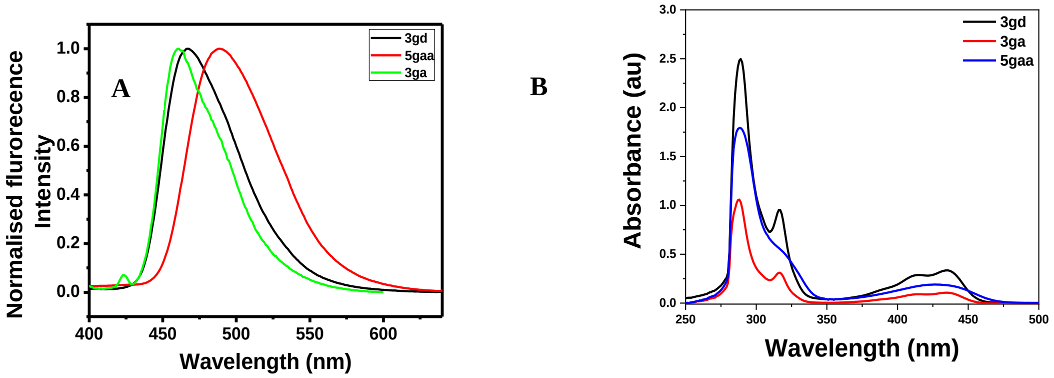


Figure 5. (A) Absorbance and (B) Fluorescence emission spectra of compounds **22**, **24** and **37** in toluene (10^{-5} M) at rt (25 °C). (3gd, 3ga and 5gaa in figure refers to compounds **22**, **24** and **37**)

SUMMARY

We have developed a simple and highly efficient ligand-free one pot Cu(I)-mediated tandem or sequential protocol for the synthesis of multifunctional naphthalenes, phenanthrenes, quinolines and benzo[*b*]carbazoles. The protocol entails readily available substrates such as *o*-bromoarylaldehydes, alkyl cyanoacetates, dialkylmalonates and active methylene nitriles. The developed methodology was utilized further for the synthesis of 4-oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile. The photophysical properties of phenanthrene carboxylates reveal possible applications as highly fluorescent materials.

EXPERIMENTAL SECTION

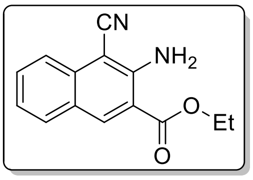
Details of equipment used for most of the measurements have already been given in Chapter 3

The precursors, 2-haloarylaldehydes **1a-h**, alkyl cyanoacetates **2a-d**, dialkylmalonates **3a-c** and malononitrile **4** are commercially available, and 2,7-dibromo-9-ethyl-9H-carbazole-3-carbaldehyde, **1i** [31] was prepared following literature reports.

6.1 Synthesis of Multifunctional Naphthalenes and Phenanthrenes 5-30

To an oven dried Schlenk tube equipped with a magnetic stirrer bar was added 2-bromobenzalaldehyde **1a** (0.1 g, ~0.5 mmol, 1 equiv) CuI (0.103 g, 0.05 mmol, 10 mol %), K_2CO_3 (0.220 g, 1.6 mmol, 3 equiv), ethyl cyanoacetate **2a** (0.115 mL, 1.0 mmol, 2 equiv) and DMSO (2 mL). The tube with the contents was stoppered and heated at 120 °C (oil bath) for 3h. After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to rt (25 ^{o}C), diluted with ethyl acetate (20 mL) and passed through a short celite column. The resulting solution was washed with water (2 x 20 mL) and the aqueous part extracted twice with ethyl acetate (20 mL). The combined organic layer was washed with brine solution (2 x 20 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (9:1) as eluent to afford the pure desired compound **5**. Compounds **5-30** were prepared from the appropriate *o*-bromoaryl aldehyde **1** and alkyl cyanoacetate **2** by using the same procedure using same molar quantities.

Compound 5



Yield: 0.106 g (81%).

Mp: 146-148 ^{o}C.

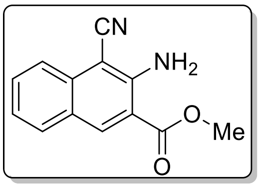
IR (Neat): 3427, 3327, 2967, 2926, 2203, 1739, 1613, 1366, 1210, 1072, 1029, 787, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.66-7.63 (m, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 6.71 (br s, 2H), 4.46 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.7, 151.0, 138.8, 136.1, 131.5, 130.1, 124.8, 123.8, 122.9, 116.9, 114.1, 88.9, 61.6, 14.3 .

HRMS (ESI): Calcd. for $C_{14}H_{12}N_2NaO_2$ [M^++Na] *m/z* 263.0796, found 263.0792.

Compound 6



Yield: 0.095 g (77%).

Mp: 152-154 °C.

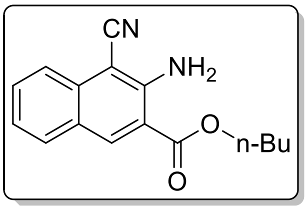
IR (Neat): 3440, 3337, 3015, 2962, 2218, 1739, 1625, 1366, 1213, 1076, 790, 744 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.0Hz, 1H), 7.68-7.64 (m, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 6.70 (br s, 2H), 4.01 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.1, 151.0, 138.9, 136.2, 131.6, 130.1, 124.8, 123.9, 123.0, 116.8, 113.8, 89.0, 52.5.

HRMS (ESI): Calcd. for $C_{13}H_{11}N_2O_2$ [M^++H] *m/z* 227.0821, found 227.0815.

Compound 7



Yield: 0.105 g (72%).

Mp: 142-144 °C.

IR (Neat): 3433, 3330, 2957, 2927, 2864, 2207, 1695, 1613, 1455, 1304, 1210, 1077, 794, 750cm^{-1}.

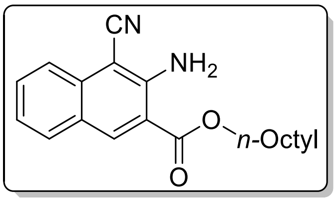
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.66-7.62 (m, 1H), 7.35-7.31 (m, 1H), 6.70 (br s, 2H), 4.40 (t, *J* =

6.4 Hz, 2H), 1.87-1.80 (m, 2H), 1.58-1.49 (m, 2H), 1.04 (t, *J* = 7.6Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 151.1, 138.7, 136.1, 131.5, 130.1, 124.8, 123.8, 122.9, 116.9, 114.1, 89.0, 65.4, 30.7, 29.7, 19.3, 13.8.

HRMS (ESI): Calcd for $C_{16}H_{16}N_2O_2$ [M^++H] *m/z* 269.1290, found 269.1283.

Compound 8



Yield: 0.120 g (68 %).

Mp: 149-151 °C.

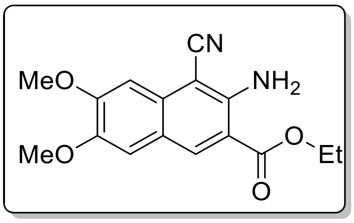
IR (Neat): 3436, 3334, 2924, 2857, 2208, 1737, 1699, 1616, 1573, 1456, 1367, 1303, 1211, 1170, 1083, 794, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 8.67 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.67-7.63 (m, 1H), 7.36-7.32 (m, 1H), 6.71 (br s, 2H), 4.40 (t, *J* = 6.8 Hz, 2H), 1.88-1.81 (m, 2H), 1.53-1.32 (m, 10H), 0.92 (t, *J* = 6.4 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 151.1, 138.8, 136.1, 131.6, 130.1, 124.8, 123.9, 123.0, 116.9, 114.2, 88.9, 65.8, 31.8, 29.3, 29.2, 28.6, 26.1, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{20}H_{25}N_2O_2$ [M^++H] *m/z* 325.1916, found 325.1917.

Compound 9



Yield: 0.104 g (85%).

Mp: 161-163 °C.

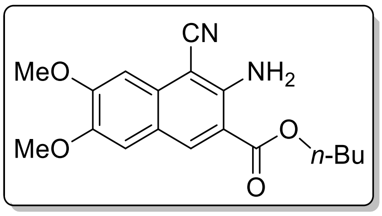
IR (Neat): 3481, 3352, 2924, 2854, 2214, 1673, 1614, 1435, 1323, 1295, 1013, 814 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.96 (s, 1H), 6.96 (s, 1H), 6.28 (s, 2H), 4.53 (q, *J* = 7.0 Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 1.53 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.5, 153.2, 147.7, 147.3, 137.8, 131.8, 121.6, 117.3, 107.6, 105.1, 104.9, 98.4, 61.2, 55.9, 55.8, 14.5.

HRMS (ESI): Calcd for $C_{16}H_{16}N_2O_4$ [M^++H]: *m/z* 301.1188, found 301.1189.

Compound 10



Yield: 0.107 g (80%).

Mp: 157-159 °C.

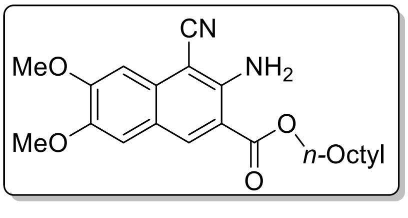
IR (Neat): 3437, 3336, 2959, 2926, 2873, 2203, 1686, 1614, 1461, 1299, 1094, 1039, 974,752 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (s, 1H), 7.15 (s, 1H), 7.06 (s, 1H), 6.57 (s, 2H), 4.38 (t, *J* = 6.5 Hz, 2H), 4.07 (s, 3H), 3.99 (s, 3H), 1.85-1.79 (m, 2H), 1.57-1.50 (m, 2H), 1.03 (t, *J* = 7.5 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.0, 154.3, 150.3, 147.9, 136.3, 133.3, 119.9, 117.3, 111.5, 108.2, 102.0, 88.4, 65.0, 56.2, 56.0, 30.7, 19.3, 13.8.

HRMS (ESI): Calcd for $C_{18}H_{20}N_2O4$ [M^++H] *m/z* 329.1501, found 329.1502.

Compound 11



Yield: 0.129 g (82%);

Mp: 149-151 °C .

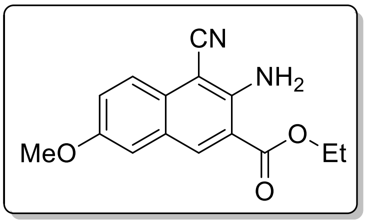
IR (Neat): 3440, 3343, 2955, 2925, 2855, 2204, 1688, 1611, 1509, 1331, 1298, 1039, 1022, 787, 754 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.48 (s, 1H), 7.15 (s, 1H), 7.06 (s, 1H), 6.57 (s, 2H), 4.36 (t, *J* = 6.5 Hz, 2H), 4.07 (s, 3H), 3.99 (s, 3H), 1.85-1.80 (m, 2H), 1.51-1.32 (m, 10H), 0.91 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 167.0, 154.3, 150.3, 147.9, 136.4, 133.3, 119.9, 117.3, 111.6, 108.3, 102.1, 88.4, 65.4, 56.3, 56.0, 31.8, 29.3, 29.2, 28.7, 26.1, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{22}H_{29}N_2O_4$ [M$^+$+H] *m/z* 385.2127, found 385.2128.

Compound 12



Yield: 0.100 g (79 %).

Mp: 165-167 °C.

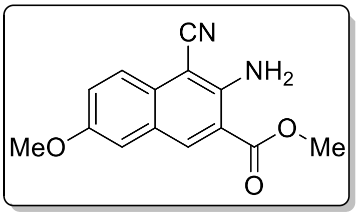
IR (Neat): 3429, 3329, 2979, 2205, 1739, 1614, 1366, 1211, 1074, 1031, 787, 749 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.60 (s, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.33 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.11 (d, *J* = 2.8 Hz, 1H), 6.54 (s, 2H), 4.46 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H). 1.49 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.7, 155.9, 150.1, 137.8, 131.3, 125.5, 124.6, 123.7, 117.2, 114.7, 109.3, 88.0, 61.8, 55.8, 14.5.

HRMS (ESI): Calcd for $C_{15}H_{15}N_2O_3$ [M$^+$+H] *m/z* 271.1083, found 271.1077.

Compound 13



Yield: 0.085 g (71 %).

Mp: 170-172 °C.

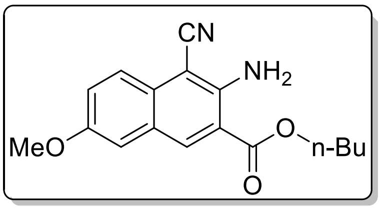
IR (Neat): 3446, 3345, 2959, 2922, 2209, 1738, 1704, 1617, 1505, 1374, 1289, 1215, 1142, 1089, 1012, 824, 787 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (s, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.33 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.10 (d, *J* = 3.0 Hz, 1H), 6.52 (br s, 2H), 3.99 (s, 3H), 3.91 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.2, 156.2, 149.5, 137.3, 131.5, 125.7, 124.5, 124.3, 116.9, 114.2, 108.0, 89.5, 55.4, 52.4.

HRMS (ESI): Calcd for $C_{14}H_{13}N_2O_3$ [M^++H] *m/z* 257.0926, found 257.0929.

Compound 14



Yield: 0.085 g (71 %).

Mp: 170-172 °C.

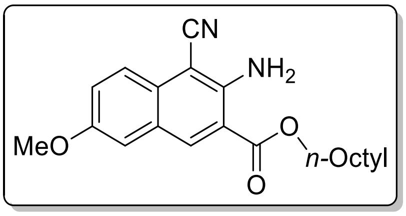
IR (Neat): 3437, 3335, 2925, 2858, 2207, 1738, 1691, 1609, 1459, 1375, 1227, 1080, 1024, 799 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.33 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.11 (d, *J* = 2.8 Hz, 1H), 6.53 (br s, 2H), 4.40 (t, *J* = 6.4 Hz, 2H), 3.92 (s, 3H), 1.87-1.80 (m, 2H), 1.57-1.49 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 156.1, 149.6, 137.1, 131.4, 125.7, 124.4, 124.2, 117.0, 114.5, 107.9, 89.5, 65.3, 55.4, 30.7, 19.3, 13.8.

HRMS (ESI): Calcd for $C_{17}H_{19}N_2O_3$ [M^++H] *m/z* 299.1396, found: 299.1390.

Compound 15



Yield: 0.121 g (73%).

Mp: 153-155 °C.

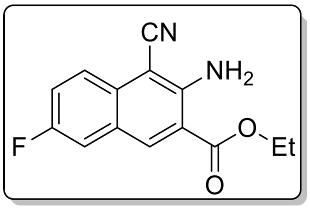
IR (Neat): 3440, 3337, 2924, 2854, 2207, 1694, 1611, 1505, 1463, 1380, 1296, 1233, 1184, 1170, 1086, 1005, 818, 731 cm^{-1} cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.56 (s, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.33 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.10 (d, *J* = 2.4 Hz, 1H), 6.53 (br s, 2H), 4.39 (t, *J* = 6.8 Hz, 2H), 3.92 (s, 3H), 1.88-1.81 (m, 2H), 1.53-1.27 (m, 10H), 0.92 (t, *J* = 6.8 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.8, 156.1, 149.6, 137.1, 131.4, 125.6, 124.4, 124.2, 117.0, 114.4, 107.9, 89.4, 65.7, 55.4, 31.8, 29.2$_4$, 29.1$_8$, 28.6, 26.0, 22.6, 14.1.

HRMS (ESI): Calcd for $C_{21}H_{26}N_2O_3$ [M$^+$+H] *m/z* 355.2022, found 355.2019.

Compound 16



Yield: 0.089 g (70 %).

Mp: 161-163 °C.

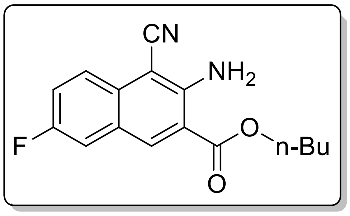
IR (Neat): 3429, 3330, 2958, 2922, 2858, 2209, 1739, 1696, 1616, 1506, 1372, 1281, 1220, 1162, 1087, 1025, 823, 794 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.59 (s, 1H), 7.90-7.86 (m, 1H), 7.45-7.40 (m, 2H), 6.65 (br s, 2H), 4.46 (q, *J* = 7.2 Hz, 2H), 1.49 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.4, 159.0 (*J* = 243.6 Hz), 150.5, 137.6 (*J* = 5.0 Hz), 132.9, 125.2 (*J* = 8.3 Hz), 125.1,121.6 (*J* = 25.2 Hz), 116.6, 115.2, 113.1 (*J* = 20.8 Hz), 89.2, 61.7, 14.3

HRMS (ESI): Calcd for $C_{14}H_{11}FN_2NaO_2$ [M$^+$+Na] *m/z* 281.0697, found 281.0696.

Compound 17



Yield: 0.095 g (67 %).

Mp: 154-156 °C.

IR (Neat): 3440, 3338, 2961, 2208, 1738, 1609, 1506, 1373, 1297, 1225, 1082, 1036, 818, 740 cm^{-1}.

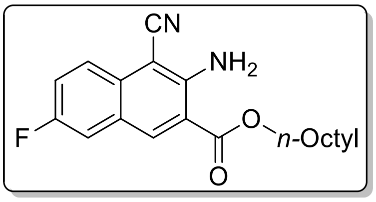
^{1}H NMR (400 MHz, CDCl$_3$): δ 8.60 (s, 1H), 7.92-7.88 (m, 1H), 7.46-7.41 (m, 2H), 6.67 (s, 2H), 4.41 (t, *J* = 6.8 Hz, 2H), 1.87-1.80 (m, 2H), 1.56-1.48 (m, 2H), 1.04 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.5, 159.0 (*J* = 243.7 Hz), 150.5, 137.6 (*J* = 5.1 Hz), 132.9, 125.2 (*J* = 8.2 Hz), 125.1 (*J* = 8.8 Hz), 121.6 (*J* = 25.3 Hz), 116.7, 115.2, 113.2 (*J* = 20.1 Hz), 89.2, 65.6, 30.6, 19.3, 13.8.

HRMS (ESI): Calcd for $C_{16}H_{16}FN_2O_2$ (M$^+$ + H) *m/z* 287.1196, found 287.1183.

This compound was crystallized from dichloromethane–hexane (1:4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 18



Yield: 0.110 mg (65 %).

Mp: 149-151 °C.

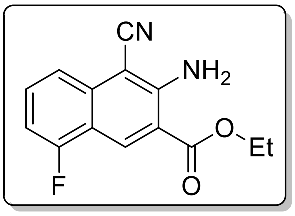
IR (Neat): 3483, 3363, 2958, 2927, 2856, 2204, 1796, 1693, 1609, 1572, 1376, 1279, 1216, 1157, 1077, 1024, 831, 732 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.59 (s, 1H), 7.91-7.88 (m, 1H), 7.45-7.41 (m, 2H), 6.66 (s, 2H), 4.40 (t, *J* = 6.5 Hz, 2H), 1.87-1.81 (m, 2H), 1.51-1.45 (m, 2H), 1.43-1.31 (m, 8H), 0.92 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.5, 159.0 (*J* = 243.6 Hz), 150.5, 137.6 (*J* = 5.0 Hz), 132.9, 125.2 (*J* = 8.4 Hz), 125.1 (*J* = 8.8 Hz), 121.6 (*J* = 25.1 Hz), 116.7, 115.2, 113.2 (*J* = 20.1 Hz), 89.2, 65.9, 31.8, 29.2_4, 29.2_0, 28.6, 26.0, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{20}H_{24}FN_2O_2$ [M$^+$+H] *m/z* 343.1822, found 343.1814.

Compound 19



Yield: 0.078 g (61%).

Mp: 160-162 ^{o}C.

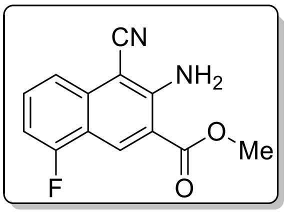
IR (Neat): 3429, 3327, 2984, 2926, 2207, 1735, 1696, 1616, 1574, 1438, 1376, 1273, 1181, 1122, 1048, 866, 796, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.95 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 1H),7.61-7.55 (m, 1H), 7.01-6.97 (m, 1H), 6.83 (s, 2H), 4.48 (q, *J* = 7.2 Hz, 2H), 1.50 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.5, 160.0 (*J* = 254.2 Hz), 151.6, 137.3 (*J* = 3.4 Hz), 132.0 (*J* = 9.3 Hz), 131.5 (*J* = 5.6 Hz), 118.8 (*J* = 4.1 Hz),116.5, 115.1, 114.3, 107.5 (*J* = 19.6 Hz), 88.9, 61.8, 14.3.

HRMS (ESI): Calcd for $C_{14}H_{11}FNaN_2O_2$ [M^{+}+Na] *m/z* 281.0702, found 281.0700.

Compound 20



Yield: 0.082 g (68 %).

Mp: 165-167 ^{o}C.

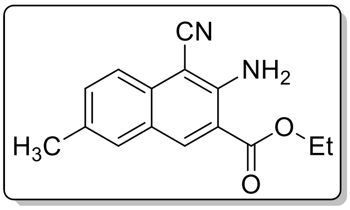
IR (Neat): 3440, 3335, 2960, 2922, 2846, 2215, 1710, 1624, 1571, 1443, 1365, 1306, 1208, 1077, 791cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.95 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.61-7.55 (m, 1H), 7.01-6.97 (m, 1H), 6.81 (s, 2H), 4.02 (s, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.9, 160.0 (*J* = 254.5 Hz), 151.5, 137.3, 132.1 (*J* = 9.3 Hz), 131.7 (*J* = 5.8 Hz), 118.8 (*J* = 4.2 Hz),116.5, 115.2 (*J* = 17.2 Hz), 114.0, 107.1 (*J* = 19.6 Hz), 88.9, 52.6.

HRMS (ESI): Calcd for $C_{13}H_{10}FN_2O_2$ [M^{+}+H] *m/z* 245.0726, found 245.0726.

Compound 21



Yield: 0.103 g (80 %).

Mp: 140-142 °C.

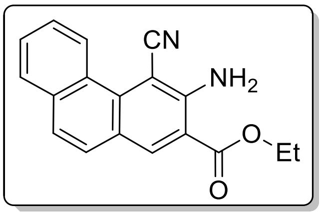
IR (Neat): 3427, 3328, 2974, 2931, 2203, 1739, 1705, 1612, 1572, 1366, 1209, 1151, 1071, 1030, 786, 749 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.63 (s, 1H), 7.69-7.67 (m, 2H), 7.17(dd, *J* = 8.4, 1.6 Hz, 1H), 6.68 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 2.54 (s, 3H), 1.48 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.8, 151.2, 142.4, 138.5, 136.4, 129.9, 126.2, 123.1, 122.2, 117.1, 113.1, 88.4, 61.4, 22.2, 14.3.

HRMS (ESI): Calcd for $C_{15}H_{15}N_2O_2$ [M$^+$+H] *m/z* 255.1134, found 255.1137.

Compound 22



Yield: 0.089 g (72%).

Mp: 176-180 °C.

IR (Neat): 3427, 3328, 2974, 2931, 2203, 1739, 1705, 1612, 1572, 1366, 1209, 1151, 1071, 1030, 786, 749 cm^{-1}.

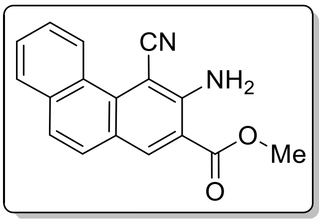
^{1}H NMR (400 MHz, CDCl$_3$): δ 9.74-9.71 (m, 1H), 8.61 (s, 1H), 7.87-7.85 (m, 1H), 7.70-7.66(m, 2H), 7.59-7.54 (m, 2H), 7.00 (br s, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.49 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 166.8, 153.1, 138.5, 134.9, 134.3, 128.9, 127.5, 127.3, 126.6, 125.3, 123.2, 119.9, 112.3, 88.7, 61.5, 14.3.

HRMS (ESI): Calcd for $C_{18}H_{14}N_2NaO_2$ [M$^+$+Na] *m/z* 313.0953, found: 313.0945.

This compound was crystallized from chloroform–hexane (1: 4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 23



Yield: 0.073 g (62%).

Mp: 178-182 °C.

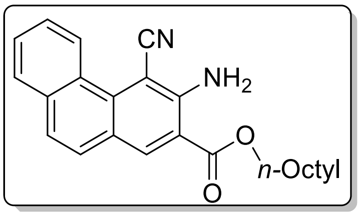
IR (Neat): 3447, 3339, 2958, 2921, 2010, 1702, 1610, 1459, 1609, 1459, 1316, 1279, 1260, 1219, 1092, 1026, 909, 803, 748, 563 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 9.74-9.72 (m, 1H), 8.61 (s, 1H), 7.88-7.86 (m, 1H), 7.71-7.68 (m, 2H), 7.56 (s, 2H), 6.99 (br s, 2H), 4.01 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 167.2, 153.0, 138.5, 134.9, 134.3, 128.9_4, 128.9_1, 127.4, 127.2, 126.6, 125.3_4, 125.2_8, 123.2, 120.0, 111.9, 88.7, 52.4.

HRMS (ESI): Calcd for $C_{17}H_{13}N_2O_2$ [M$^+$+H] *m/z* 277.0977, found 277.0979.

Compound 24



Yield: 0.104 g (65%).

Mp: 120-124 °C.

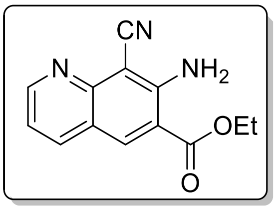
IR (Neat): 3453, 3335, 2923, 2851, 2193, 1737, 1692, 1608, 1581, 1517, 1313, 1282, 1217, 1199, 1122, 1094, 1024, 971, 807, 752, 729, 682, 659 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 9.75-9.74 (m, 1H), 8.61 (s, 1H), 7.89-7.87 (m, 1H), 7.71-7.69 (m, 2H), 7.61-7.57 (m, 2H), 7.02 (br s, 2H), 4.41 (t, *J* = 6.5 Hz, 2H), 1.89-1.83 (m, 2H), 1.54-1.48 (m, 2H), 1.44-1.32 (m, 8H), 0.93 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.8, 153.1, 138.4, 134.9, 134.3, 128.9, 127.4, 127.3, 126.6, 125.3, 123.2, 120.0, 112.3, 88.6, 65.7, 31.8, 29.3, 29.2, 28.7, 26.1, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{24}H_{27}N_2O_2$ [M^++H] *m/z* 375.2073, found: 375.2091.

Compound 25a



Yield: 0.086 g (66%) [R_f 0.3 (ethyl acetate: hexane 1:9)].

Mp: 151-153 °C.

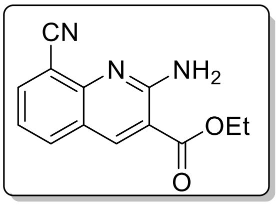
IR (Neat): 3416, 3325, 3301, 2215, 1738, 1628, 1581, 1565, 1370, 1310, 1206, 1083, 1033, 924, 794, 727, 510 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.98 (dd, *J* = 4.0, 1.5 Hz, 1H), 8.65 (s, 1H), 8.08 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.29-7.26 (m, 1H), 6.95 (v br, 2H), 4.48 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.2, 155.0, 153.2, 151.3, 138.1, 137.6, 119.5, 119.4, 116.2, 114.8, 92.0, 61.8, 14.2.

HRMS (ESI): Calcd for $C_{13}H_{12}N_3O_2$ [M^++H] *m/z* 242.0930, found 242.0930.

Compound 25a′



Yield: 0.015 g (12%) [R_f 0.5 (ethyl acetate: hexane 1:9)].

Mp: 142-145 °C.

IR (Neat): 3416, 3294, 3183, 2906, 2221, 1696, 1607, 1564, 1478, 1305, 1281, 1203, 1100, 1020, 795, 755 cm^{-1}.

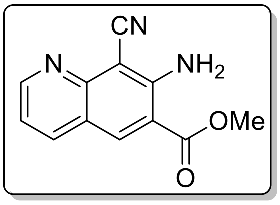
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.01 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.90 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.28 (t, *J* = 6.0 Hz, 1H), 5.88 (s, 2H), 4.46 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 165.9, 157.6, 150.2, 142.5, 137.9, 133.8, 122.4, 121.6, 117.6, 111.8, 109.0, 61.8, 14.2.

HRMS (ESI): Calcd for $C_{13}H_{12}N_3O_2$ [M^++H] *m/z* 242.0930, found 242.0930.

This compound was crystallized from chloroform–hexane (1: 4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 26a



Yield: 0.088 g (72%).

Mp: 134-141 °C.

IR (Neat): 3479, 3410, 3299, 2949, 2210, 1701, 1619, 1581, 1562, 1488, 1428, 1310, 1197, 1071, 1020, 918, 794, 698, 605 cm^{-1}.

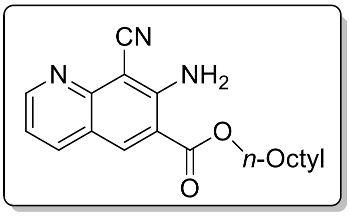
^1H NMR (500 MHz, $CDCl_3$): δ 8.97 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.65 (s, 1H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.29-7.26 (m, 1H), 6.94 (v br, 2H), 4.01 (s, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.7, 155.0, 153.2, 151.2, 138.3, 137.7, 119.5, 116.2, 114.5, 91.8, 52.7.

HRMS (ESI): Calcd for $C_{12}H_{10}N_3O_2$ [M^++H] *m/z* 228.0773, found 228.0774.

This compound was crystallized from chloroform–hexane (1:4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 27a



Yield: 0.107 g (61%) [R_f 0.3 (ethyl acetate:hexane 1:9)].

Mp: 162-164 °C.

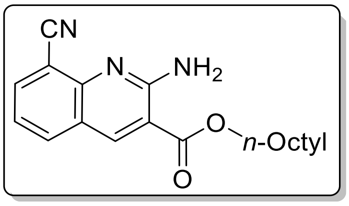
IR (Neat): 3425, 3310, 3059, 2961, 2227, 1702, 1628, 1566, 1488, 1463, 1439, 1278, 1198, 1015, 966, 755, 691 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 8.99-8.98 (m, 1H), 8.63 (s, 1H), 8.10-8.08 (m, 1H), 7.30-7.27 (m, 1H), 6.92 (v br, 2H), 4.41 (t, *J* = 6.8 Hz, 2H), 1.88-1.81 (m, 2H), 1.49-1.32 (m, 10H), 0.91 (t, *J* = 6.0 Hz, 3H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 155.0, 153.2, 151.3, 138.1, 137.7, 119.5, 119.4, 116.3, 114.8, 91.9, 66.0, 31.8, 29.2$_3$, 29.1$_9$, 28.6, 26.0, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{19}H_{24}N_3O_2$ [M^++H] *m/z* 326.1869, found 326.1869.

Compound 27a′



Yield: 0.030 g (17%) [R_f 0.5 (ethyl acetate:hexane 1:9)].

Mp: 169-171 °C.

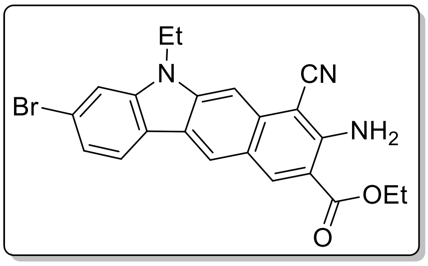
IR (Neat): 3426, 3311, 2954, 2919, 2868, 2226, 1701, 1628, 1565, 1458, 1377, 1305, 1278, 1197, 1081, 966, 892, 799, 758, 590 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.71 (s, 1H), 8.00 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.93 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.29-7.26 (m, 1H), 5.95 (s, 2H), 4.38 (t, *J* = 6.5 Hz, 2H), 1.86-1.80 (m, 2H), 1.50-1.45 (m, 2H), 1.40-1.31 (m, 8H), 0.91.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.0, 157.6, 150.2, 142.5, 138.0, 133.9, 122.3, 121.6, 117.7, 111.8, 108.9, 66.0, 31.8, 29.2$_4$, 29.1$_9$, 28.6, 26.0, 22.7, 14.1.

HRMS (ESI): Calcd for $C_{19}H_{24}N_3O_2$ [M^++H]: m/z 326.1869. Found: 326.1869.

Compound 28



Yield: 0.078 g (68%).

Mp: 208-210 °C.

IR (Neat): 3343, 2921, 2852, 2203, 1734, 1682, 1460, 1254, 1084, 799, 582 cm^{-1}.

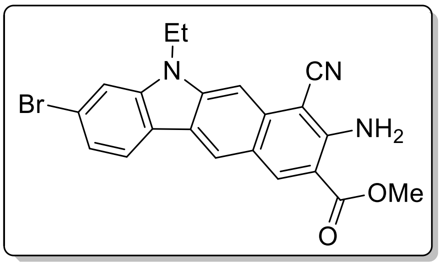
^1H NMR (500 MHz, $CDCl_3$): δ 8.77 (s, 1H),8.34 (s, 1H),7.86 (d, *J* = 8.0 Hz, 1H),7.52 (s, 1H),7.44 (d, *J* = 1.5 Hz, 1H), 7.31 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.68 (br, 2H),4.38 (q, *J* = 7.0 Hz, 2H), 4.27 (q, *J* = 7.0 Hz, 2H), 1.42 (t, *J* = 8.0 Hz, 6H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.9, 151.3, 143.8, 143.1, 139.9, 135.1, 122.9_3, 122.8_9, 122.3, 121.7_0, 121.6_6,121.0, 119.8, 118.0, 111.8, 111.3, 98.5, 86.9, 61.3, 37.9, 14.4, 13.3.

HRMS (ESI): Calcd for $C_{22}H_{18}{}^{79}BrN_3O_2$ and $C_{22}H_{18}{}^{81}BrN_3O_2$ [M$^+$+H] *m/z* 436.0661 and 438.0661, found 436.0658 and 438.0640.

This compound was crystallized from dichloromethane–hexane (1:4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 29



Yield: 0.071 g (64%).

Mp: 195-197 °C.

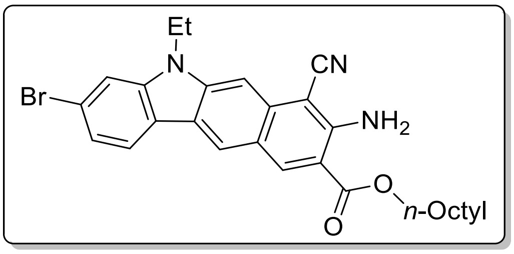
IR (Neat): 3427, 3338, 2921, 2852, 2207, 1707, 1632, 1517, 1433, 1332, 1216, 1187, 1060, 827, 582 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.80 (s, 1H), 8.35 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.51 (d, *J* = 1.5 Hz, 1H), 7.38 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.73 (br, 2H), 4.32 (t, *J* = 7.0 Hz, 2H), 4.01(s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 167.3, 151.2, 143.8, 143.1, 139.9, 135.2, 128.8, 123.0, 122.2, 121.7, 121.6, 121.1, 119.8, 117.8, 111.8, 111.0, 98.5, 87.0, 52.2, 37.9, 13.2.

HRMS (ESI): Calcd for $C_{21}H_{17}BrN_3O_2$ [M$^+$+H] and $C_{21}H_{17}{}^{81}BrN_3O_2$ *m/z* 422.0504 and 424.04, found 422.0505 and 424.0470.

Compound 30



Yield: 0.075 g (55%).

Mp: 229-231 °C .

IR (Neat): 3349, 2923, 2854, 2195, 1699, 1608, 1460, 1332, 1193, 1057, 586 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (s, 1H), 8.45 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H), 7.54 (d, *J* = 1.0 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.77 (s, 2H),4.41-4.35 (m, 4H), 1.89-1.83 (m, 2H), 1.52-1.49 (m, 4H), 1.44-1.27 (m, 9H), 0.93 (t, *J* = 7.0 Hz, 3H).

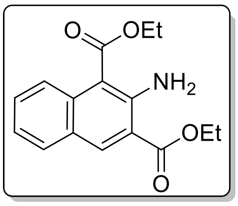
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.0, 151.4, 143.9, 143.2, 139.9, 135.2, 123.0, 122.3, 121.7, 121.0, 119.9, 118.0, 111.8, 111.4, 98.6, 87.0, 65.5, 38.0, 31.8, 29.3, 29.2, 28.7, 26.1, 22.7, 14.1,13.3.

HRMS (ESI): Calcd for $C_{28}H_{31}BrN_3O_2$ [M^++H] and $C_{28}H_{31}{}^{81}BrN_3O_2$ *m/z* 520.1600 and 522.1579, found 520.1600 and 522.1585.

6.2 Synthesis of Multifunctional Amino-naphthalene/phenanthrene-dicarboxylates 31-37 and 2-Aminonaphthalene-1,3-dicarbonitriles 38-40

To an oven dried Schlenk tube equipped with a magnetic stirrer bar was added *o*-bromo aldehyde **1** (~0.5 mmol), K_2CO_3 (0.5 mmol), alkyl cyanoacetate **2** (0.5 mmol) and DMSO (2 mL). The contents were sealed and heated at rt for 1h. Then CuI (0.05 mmol), K_2CO_3 (1.0 mmol) and **3** or **4** (0.5 mmol) was added and the reaction was performed at 120 °C for 2 h. After completion of the reaction as monitored by TLC, the crude reaction mixture was cooled to rt. The mixture was diluted with ethyl acetate (20 mL) and passed through celite. The resulting solution was washed with water and the aqueous part extracted twice with ethyl acetate (20 mL). The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated in vacuum. The residue was then purified by using silica gel column chromatography using hexane-ethyl acetate (9:1) as eluent to afford the pure compounds **31**-**37** and **38**-**40**.

Compound 31



Yield: 0.125 g (80%).

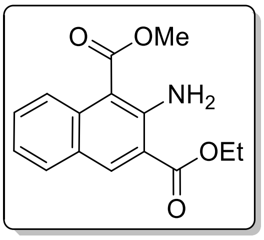
IR (Neat): 3453, 3352, 2926, 1702, 1621, 1561, 1366, 1264, 1204, 1160, 1074, 1027, 804, 747 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.62 (s, 1H), 8.32 (d, *J* = 9.0 Hz, 1H), 7.77 (br s, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.53-7.50 (m, 1H), 7.23 (t, *J* = 7.0 Hz, 1H), 4.52 (q, *J* = 7.0 Hz, 2H), 4.43 (q, *J* = 7.0 Hz, 2H), 1.51-1.45 (m, 6H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 169.2, 167.4, 149.8, 139.0, 135.7, 130.3, 130.2, 125.1, 124.5, 122.4, 114.9, 105.6, 61.2, 60.8, 14.4, 14.3.

HRMS (ESI): Calcd for $C_{16}H_{18}NO_4$ [M$^+$+H] *m/z* 288.1236, found 288.1238.

Compound 32



Yield: 0.117 g (79%).

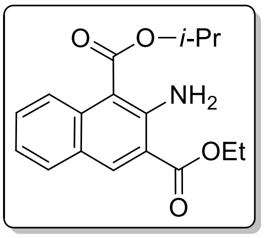
IR (Neat): 3450, 3347, 2981, 2950, 2203, 1697, 1619, 1601, 1556, 1260, 1201, 1158, 1071, 1018, 802, 744 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.63 (s, 1H), 8.29 (d, *J* = 9.0 Hz, 1H), 7.84 (br s, 2H), 7.71 (d, *J* = 8.0Hz, 1H), 7.54-7.51 (m, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 4.44 (q, *J* = 7.0 Hz, 2H), 4.04 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 169.7, 167.4, 150.1, 139.3, 135.7, 130.4, 130.3, 125.1, 124.5, 122.4, 114.8, 105.0, 61.2, 51.7, 14.3.

HRMS (ESI): Calcd for $C_{15}H_{16}NO_4$ [M$^+$+H] *m/z* 274.1079, found 274.1078.

Compound 33



Yield: 0.121 g (74%).

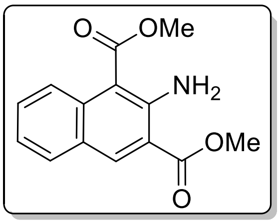
IR (Neat): 2981, 2936, 2203, 1728, 1703, 1622, 1561, 1381, 1204, 1145, 1098, 1018, 805, 750 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.62 (s, 1H), 8.31 (dd, *J* = 8.5, 0.5 Hz, 1H), 7.73-7.71 (m, 1H), 7.68 (br s, 2H), 7.53-7.50 (m, 1H), 7.25-7.22 (m, 1H), 5.48-5.43 (m, 1H), 4.44 (q, *J* = 7.0 Hz, 2H), 1.50-1.46 (m, 9H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 168.8, 167.5, 149.4, 138.8, 135.6, 130.2, 125.1, 124.3, 122.4, 114.8, 106.1, 68.6, 61.2, 22.2, 14.3.

HRMS (ESI): Calcd for $C_{17}H_{19}NO_4$ [M$^+$+H] *m/z* 302.1392, found 302.1393.

Compound 34



Yield: 0.118 g (87 %).

IR (Neat): 3391, 3337, 3181, 2918, 2848, 2360, 1692, 1645, 1608, 1560, 1467, 1428, 1259, 1191, 1038, 950, 824 cm^{-1}.

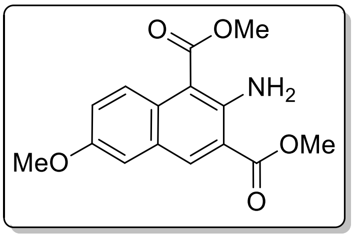
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.57 (s, 1H), 8.22 (d, *J* = 9.5 Hz, 1H), 7.63 (br s, 2H), 7.22 (dd, *J* = 9.5, 2.5 Hz, 1H), 7.04 (d, *J* = 3.0 Hz, 1H), 4.03 (s, 3H), 3.97 (s, 3H), 3.90 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 169.6, 167.9, 154.9, 148.5, 137.9, 131.1, 126.3, 126.0, 122.8, 114.9, 108.0, 105.8, 55.3, 52.2, 51.7.

HRMS (ESI): Calcd for $C_{15}H_{15}NO_5$ [M$^+$+H] *m/z* 290.1028, found 290.1027.

This compound was crystallized from chloroform–hexane (1 : 4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 35



Yield: 0.118 g (87 %).

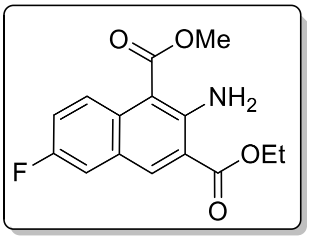
IR (Neat): 3391, 3337, 3181, 2918, 2848, 2360, 1692, 1645, 1608, 1560, 1467, 1428, 1259, 1191, 1038, 950, 824 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.57 (s, 1H), 8.22 (d, *J* = 9.5 Hz, 1H), 7.63 (br s, 2H), 7.22 (dd, *J* = 9.5, 2.5 Hz, 1H), 7.04 (d, *J* = 3.0 Hz, 1H), 4.03 (s, 3H), 3.97 (s, 3H), 3.90 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 169.6, 167.9, 154.9, 148.5, 137.9, 131.1, 126.3, 126.0, 122.8, 114.9, 108.0, 105.8, 55.3, 52.2, 51.7.

HRMS (ESI): Calcd for $C_{15}H_{15}NO_5$ [M$^+$+H] *m/z* 290.1028, found 290.1027.

Compound 36



Yield: 0.125 g (87%).

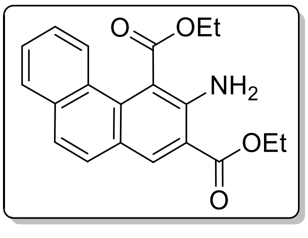
IR (Neat): 3451, 3348, 2923, 2852, 1704, 1612, 1568, 1504, 1462, 1371, 1264, 1222, 1204, 1136, 853, 731 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.56 (s, 1H), 8.30 (dd, *J* = 9.5, 5.0 Hz, 1H), 7.77 (br s, 2H), 7.36 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.32-7.30 (m, 1H), 4.44 (q, *J* = 7.0 Hz, 2H), 4.03 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 169.4, 167.2, 158.1(*J* = 242.3 Hz), 149.5, 138.0 (*J* = 4.8 Hz), 132.5, 127.0 (*J* = 7.5 Hz), 125.5 (*J* = 8.3 Hz), 120.0 (*J* = 24.1 Hz), 116.1, 112.8 (*J* = 20.0 Hz), 105.4, 61.3, 51.7, 14.3.

HRMS (ESI): Calcd for $C_{15}H_{15}FNO_4$ [M$^+$+H] *m/z* 292.0985, found 292.0982.

Compound 37



Yield: 0.115 g (80%).

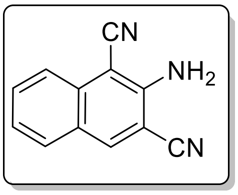
IR (Neat): 3646, 2919, 2850, 1738, 1608, 1367, 1260, 1216, 1023, 799, 750 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.57 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.60-7.58 (m, 2H), 7.53-7.46 (m, 2H), 7.03 (br s, 2H), 4.45 (q, *J* = 7.0 Hz, 2H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 171.5, 167.5, 147.6, 135.9, 134.7, 134.0, 128.3, 128.2, 127.8, 127.6, 127.0, 125.0, 124.3, 123.4, 113.3, 110.9, 61.5, 61.1, 14.4, 13.8.

HRMS (ESI): Calcd for $C_{20}H_{20}NO_4$ [M$^+$+H] *m/z* 338.1392, found 338.1394.

Compound 38



Yield: 0.073 g (70%).

Mp: 140-142 °C.

IR (Neat): 3473, 3359, 3242, 2923, 2853, 2349, 2229, 2208, 1638, 1504, 1220, 770 cm^{-1}.

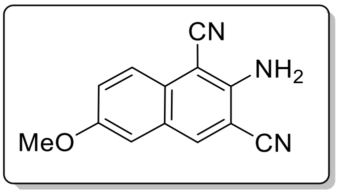
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.24 (s, 1H), 7.97 (dd, *J* = 8.5, 0.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.74-7.71 (m, 1H), 7.46-7.43 (m, 1H), 5.30 (br s, 2H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 148.8, 139.9, 135.2, 132.3, 129.3, 125.4, 125.2, 123.6, 115.6$_0$, 115.5$_7$, 99.8, 89.5.

HRMS (ESI): Calcd for $C_{12}H_7N_3$ [M$^+$] *m/z* 193.0640, found 193.0642.

This compound was crystallized from chloroform–hexane (1 : 4) mixture by slow evaporation at room temperature. X-ray structure has been determined for this compound.

Compound 39



Yield: 0.085 g (82%).

Mp: 147-149 °C.

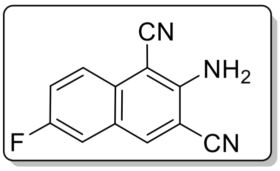
IR (Neat): 3450, 3320, 3240, 2923, 2850, 2221, 2217, 1680, 1612, 1243, 1093, 1020, 792 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.50 (s, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.43-7.38 (m, 2H), 6.74 (br s, 2H), 3.84 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 156.3, 149.2, 140.5, 130.8, 126.0, 124.9, 124.3, 116.5$_5$, 116.4$_6$, 108.6, 100.6, 87.7, 55.9.

HRMS (ESI): Calcd for $C_{13}H_{10}N_3O$ [M$^+$+H] *m/z* 224.0824, found 224.0826.

Compound 40



Yield: 0.070 g (67%).

Mp: 165-169 °C.

IR (Neat): 3472, 3348, 3247, 3050, 2211, 2207, 2027, 1983, 1601, 1224, 1181, 1147, 967, 816, 721 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.18 (s, 1H), 7.99-7.96 (m, 1H), 7.53-7.49 (m, 1H),7.44 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.28.

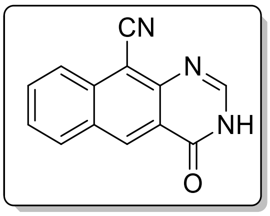
^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 159.7 (*J* = 246.5 Hz), 148.3, 138.7 (*J* = 5.1 Hz), 132.0, 126.0 (*J* = 8.6 Hz), 125.9 (*J* = 9.3 Hz), 122.5, 122.3, 115.3 (*J* = 11.4 Hz), 112.7 (*J* = 21.6 Hz), 101.2, 89.9.

HRMS (ESI): calcd for $C_{12}H_7FN_3$ [M$^+$+H] *m/z* 212.0624, found 212.0624.

6.3 Synthesis of Benzo[*g*]quinazoline 42, 44 and 4-Oxo-3-phenyl-3,4-dihydrobenzo[*g*]quinazoline-10-carbonitrile 45

The compounds **42**, **44** and **45** were prepared by using literature reports.[34]

Compound 42



Yield: 0.083 g (91%).

Mp: 176-178 °C.

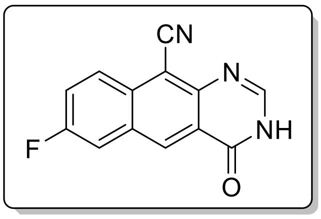
IR (Neat): 3480, 2923, 2853, 2159, 2030, 1976, 1453, 1367, 1228, 1216, 798 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 12.52 (s, 1H), 9.13 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.31(s, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.97-7.93 (m, 1H), 7.77-7.74 (m, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.7, 149.1, 148.7, 135.9, 133.8, 132.4, 131.2, 130.6, 127.9, 124.7, 121.9, 116.2, 105.2.

HRMS (ESI): calcd for $C_{13}H_8N_3O$ [M^++H] *m/z* 222.0667, found: 222.0663.

Compound 43



Yield: 0.077 g (87%).

Mp: 185-187 °C.

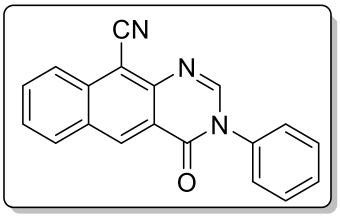
IR (Neat): 3390, 3057, 2920, 2222, 1701, 1609, 1482, 1302, 1231, 1166, 1102, 866, 799, 556 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 12.55 (s, 1H), 9.14-9.08 (m, 1H), 8.31-8.19 (m, 3H), 7.88-7.87 (m, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.0 (*J* = 246.2 Hz), 159.7,148.6, 148.5, 133.0 (*J* = 6.1 Hz), 132.9, 131.4 (*J* = 10.2 Hz), 127.9 (*J* = 9.0 Hz), 122.9 (*J* = 26.4 Hz), 122.7, 116.0, 113.9 (*J* = 21.5 Hz), 105.6.

HRMS (ESI): calcd for $C_{13}H_7FN_3O$ [M^++H] *m/z* 240.0568, found 240.0541.

Compound 45



Yield: 0.096 g (72%).

Mp: 146-148 °C.

IR (Neat): 3066, 2916, 2214, 1691, 1606, 1581, 1259, 1017, 935, 796 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.44 (d, *J* = 8.5 Hz, 1H), 8.31(s, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 7.92-7.89 (m, 1H),7.75-7.72 (m, 1H), 7.64-7.61(m, 2H), 7.58-7.55 (m, 1H) 7.50-7.48 (m, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.1, 148.2, 147.3, 137.0, 136.3, 134.0, 131.7, 131.2, 130.3, 129.9, 129.5, 127.9, 126.9, 125.6, 120.6, 115.5, 107.2.

HRMS (ESI): Calcd for $C_{19}H_{12}N_3O$ [M^++H] *m/z* 298.0980, found 298.0974.

6.4 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **16, 22, 25a'**, **26a**, **28, 34, and 38**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer using Mo-K_α radiation (λ = 0.71073 Å) or Cu- K_α (λ = 1.54184 Å). Structures were solved and refined using standard methods.[35] Absorption corrections were done using SADABS program, where applicable. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier and refined isotropically. Crystal data are summarized in Tables 7-8.

Table 7: Crystal data for compounds **16**, **22,** and **25a'**[a]

Compound	**19**	**22**	**25a'**
Emp. Formula	$C_{14}H_{11}FN_2O_2$	$C_{18}H_{14}N_2O_2$	$C_{13}H_{11}N_3O_2$
Formula weight	258.25	290.31	241.25
Crystal system	Monoclinic	Triclinic	Triclinic
Space group	*P*21/c	*P*-1	*P*-1
a /Å	8.2304(11)	7.300(2)	7.6992(12)
b /Å	13.6434(17)	9.493(4)	8.7622(4)
c /Å	10.9178(12)	10.119(5)	9.7258(6)
α/deg	90	103.93(12)	66.365(5)
β/deg	91.930(4)	98.12(12)	74.766(11)
γ/deg	90	97.41(16)	84.533(8)
V /Å^3	1225.3(30)	707.32(50)	579.93(11)
Z	4	2	2
Dcalc /g cm^{-3}]	1.400	1.363	1.382
μ /mm^{-1}	0.106	0.090	0.097
F(000)	536.0	304.0	252.0
Data/ restraints/ parameters	2145/0/181	2407/0/208	2033/0/164
S	1.042	1.133	1.244
R1 [I>2σ(I)]	0.0363	0.0448	0.0934
wR2 [all data]	0.1043	0.1591	0.3186
Max./min. residual electron dens. [eÅ^{-3}]	0.511/-0.591	0.166/-0.193	0.284/-0.262

[a] $R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 8: Crystal data for compounds **26a**, **28**, **34** and **38** [a]

Compound	**26a**	**28**	**34**	**38**
Emp. formula	$C_{12}H_9N_3O_2$	$C_{22}H_{18}BrN_3O_2$	$C_{14}H_{13}NO_4$	$C_{12}H_7N_3$
Formula weight	227.22	436.30	259.25	193.21
Crystal system	Monoclinic	Orthorhombic	Triclinic	Monoclinic
Space group	P_c	*P*bca	*P*-1	$P2_1$/c
a /Å	10.1364 (8)	20.5404(6)	7.7957(2)	3.8196(5)
b /Å	30.3806 (19)	8.9927(3)	8.5442(3)	16.069(2)
c /Å	7.3026 (5)	20.6948(6)	10.0862(3)	15.350(2)
α/deg	90	90	68.141(3)	90
β/deg	106.248(7)	90	83.048(3)	92.66(1)
γ/deg	90	90	88.471(3)	90
V /Å^3	2159.9 (3)	3822.61(20)	618.81(3)	941.12(20)
Z	8	8	2	4
*D*calc /g cm^{-3}]	1.403	1.516	1.391	1.364
μ /mm^{-1}	0.099	2.174	0.103	0.086
F(000)	944.0	1776.0	272.0	400.0
Data/ restraints/ parameters	7033/2/617	3379/0/255	2177/0/182	1664/0/142
S	0.861	1.057	1.058	1.069
R1 [I>2σ(I)]	0.0697	0.0547	0.0535	0.0433
wR2 [all data]	0.1615	0.1170	0.1784	0.1072
Max./min. residual electron dens. [eÅ^{-3}]	0.275/-0.215	0.422/-0.303	0.216/-0.296	0.438/-0.549

[a] $R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

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A) Copies of $^{1}H/^{13}C$ NMR spectra for representative compounds

Part A: Compounds 9, 18, 30, 35, 41, 40′,45, 51, 53, 55

Part B: Compounds 5, 22, 25a, 28, 31, 38, .

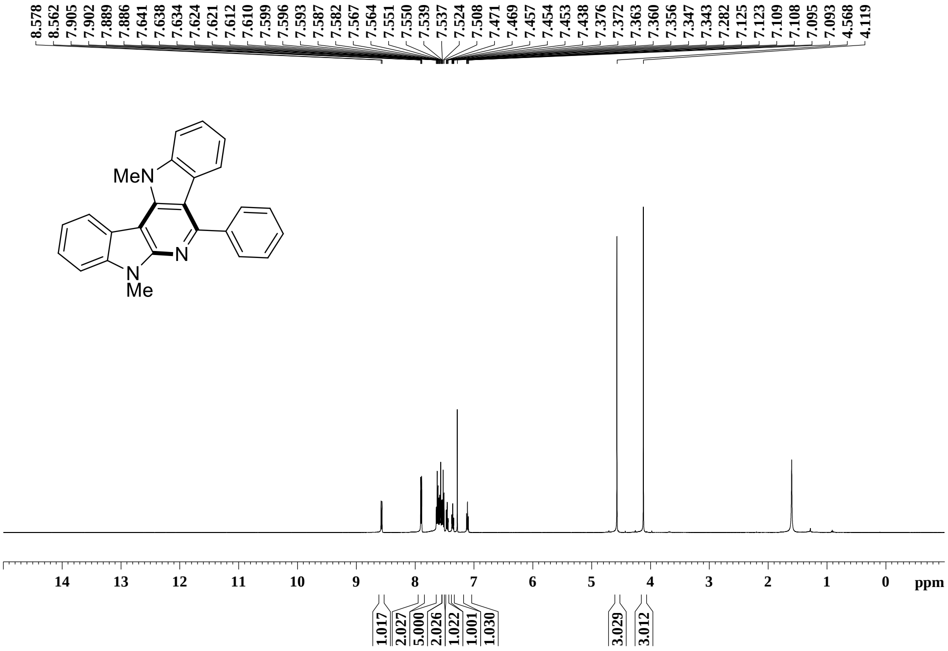

Figure A1. ^{1}H NMR spectrum of compound **9**

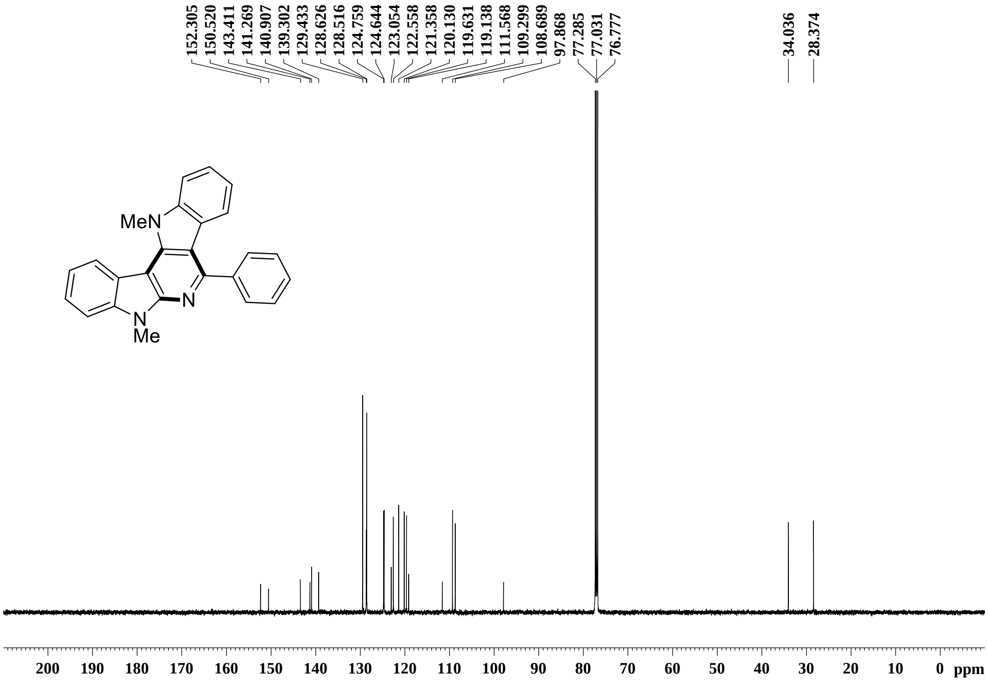

Figure A2. ^{13}C {^{1}H} NMR spectrum of compound **9**

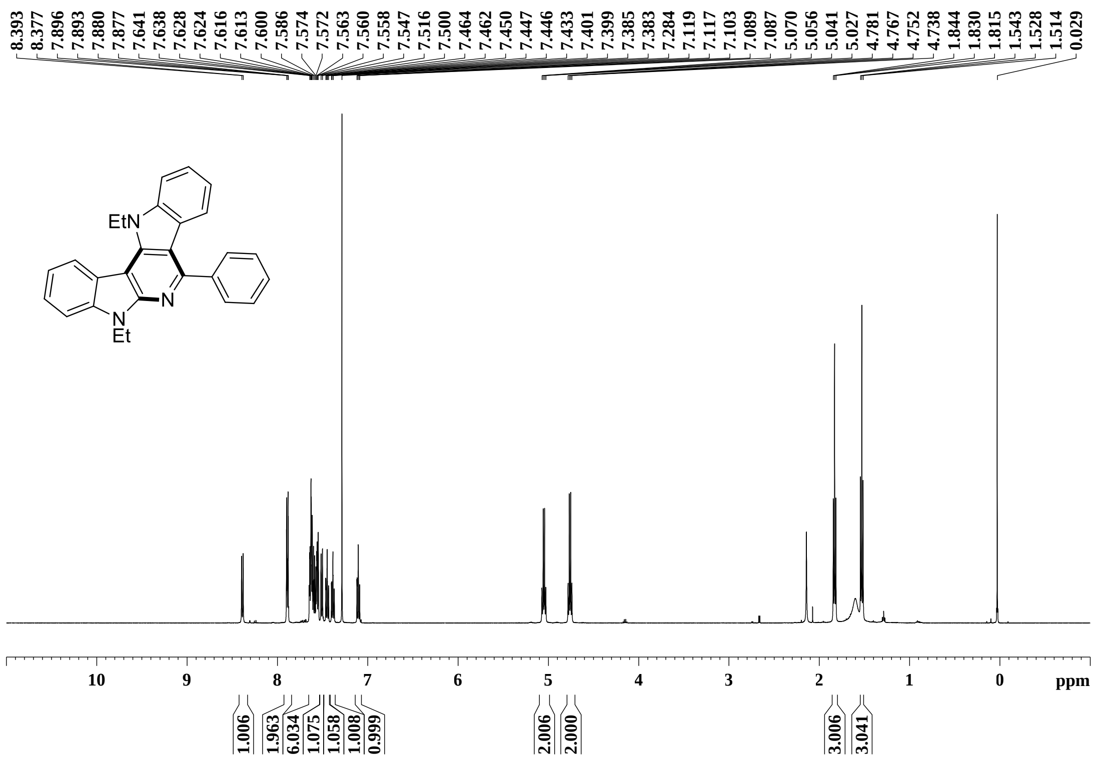

Figure A3. ^{1}H NMR spectrum of compound **18**

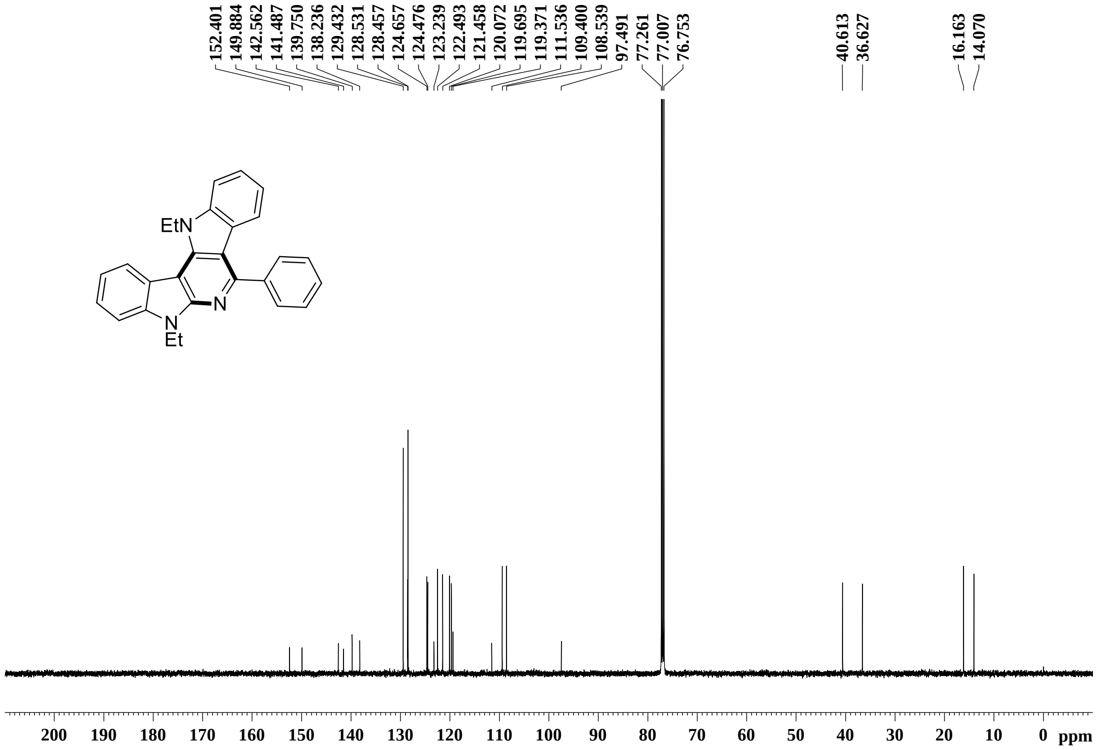

Figure A4. ^{13}C {^{1}H} NMR spectrum of compound **18**

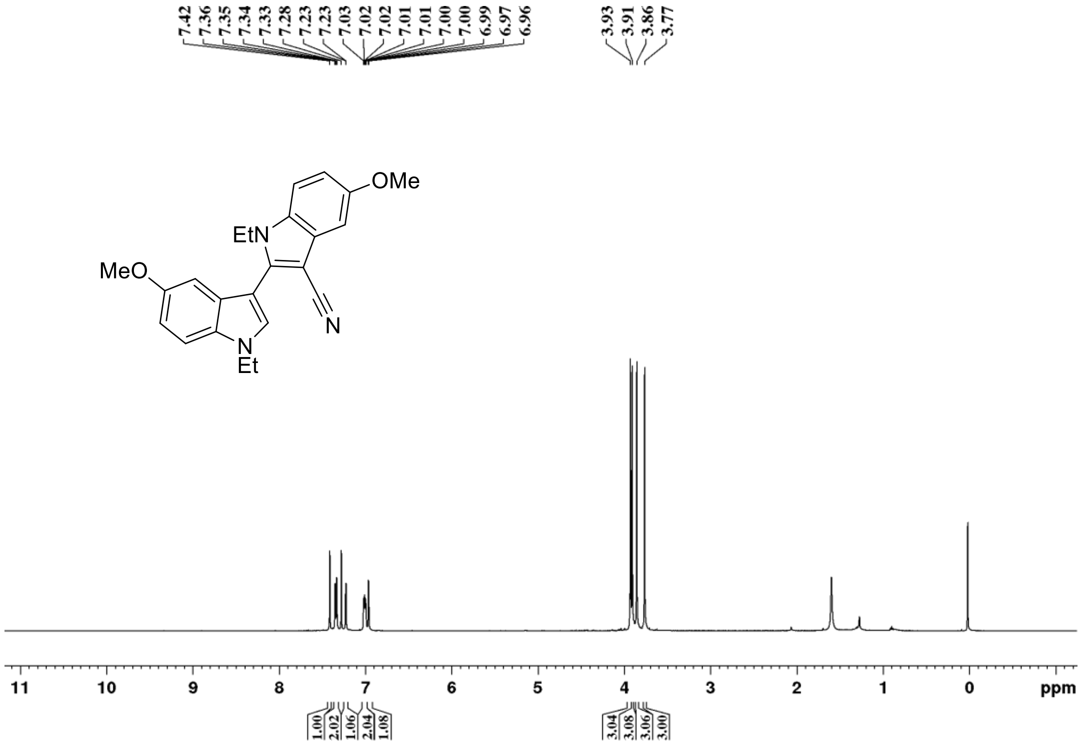

Figure A5. ^{1}H NMR spectrum of compound **30**

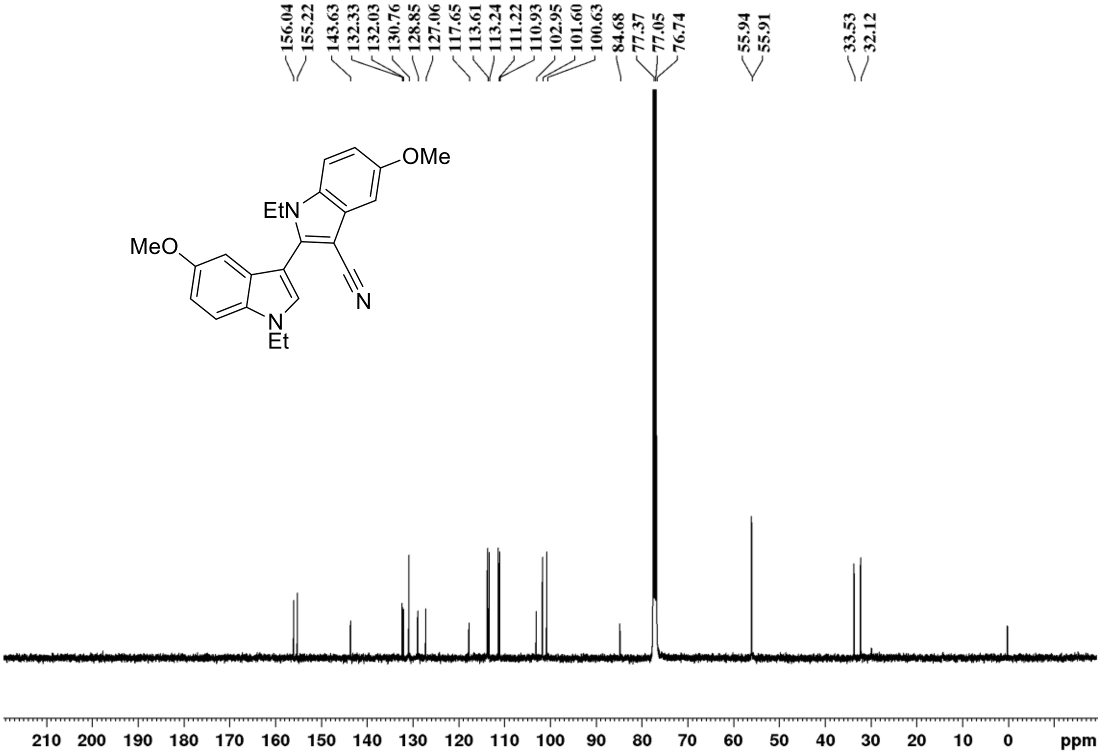

Figure A6. ^{13}C {^{1}H} NMR spectrum of compound **30**

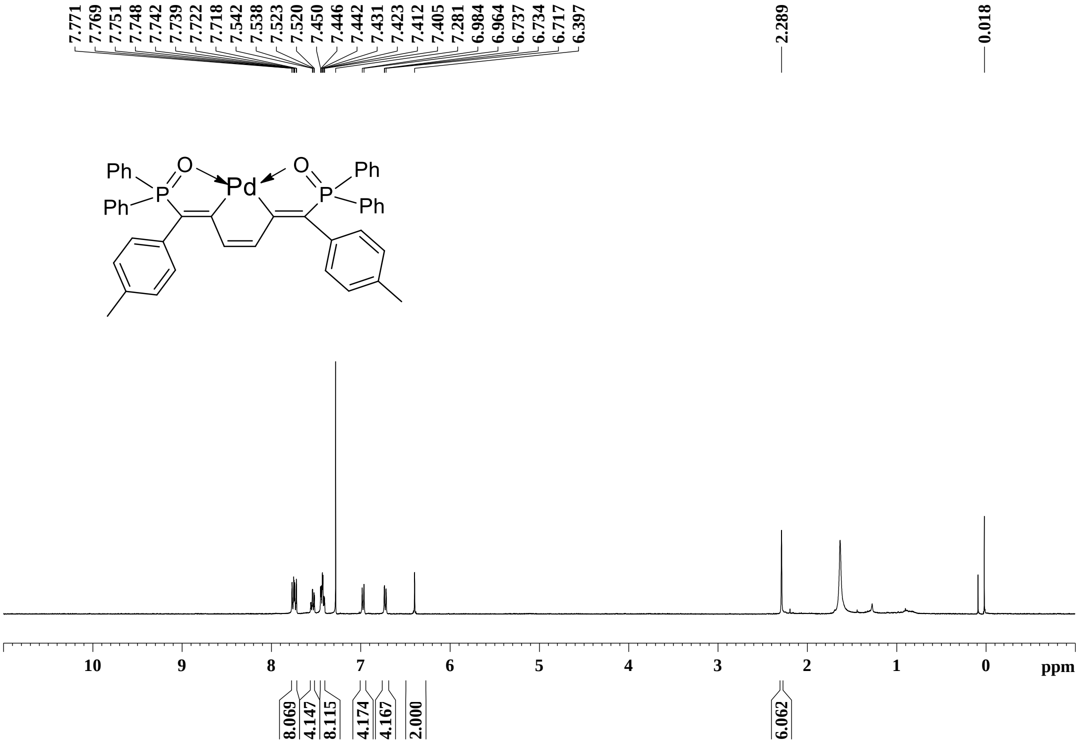

Figure A7. ^{1}H NMR spectrum of compound **35**

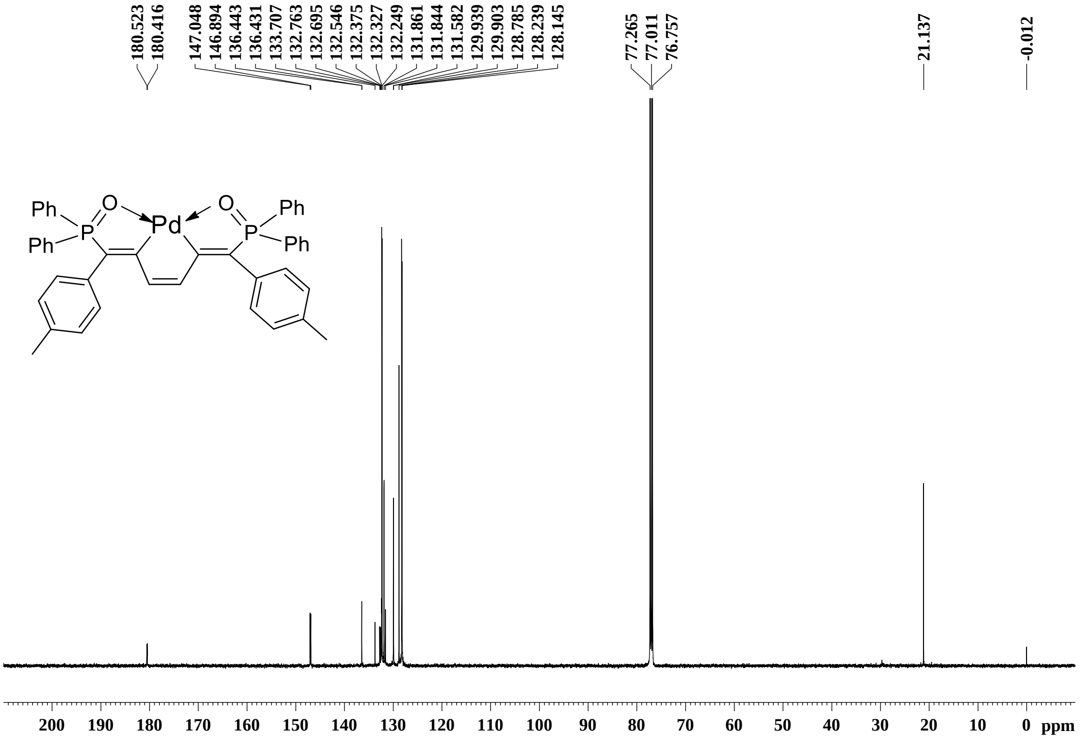

Figure A8. ^{13}C {^{1}H} NMR spectrum of compound **35**

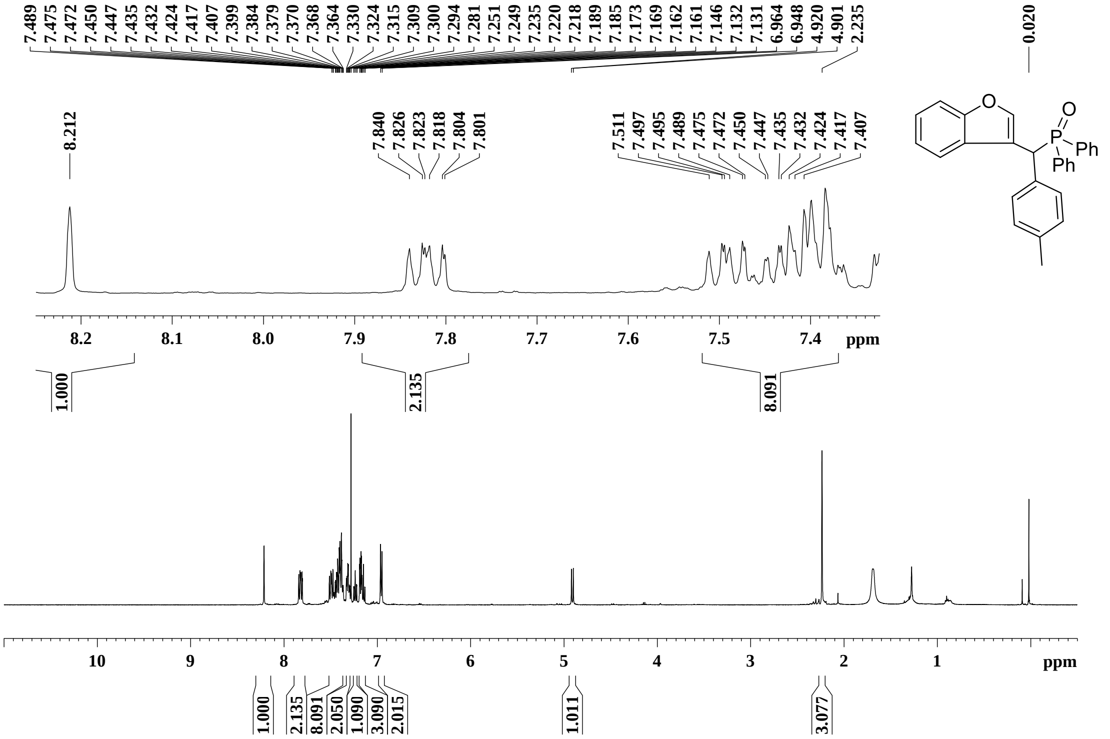

Figure A9. ^{1}H NMR spectrum of compound **41**

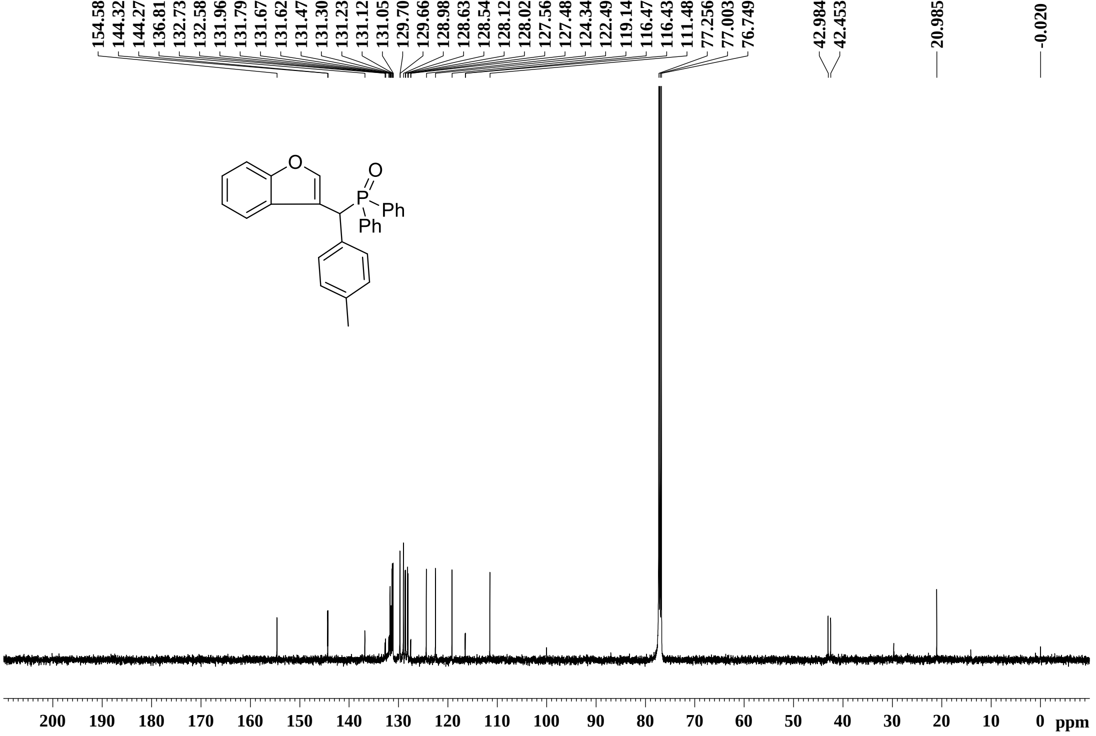

Figure A10. ^{13}C {^{1}H} NMR spectrum of compound **41**

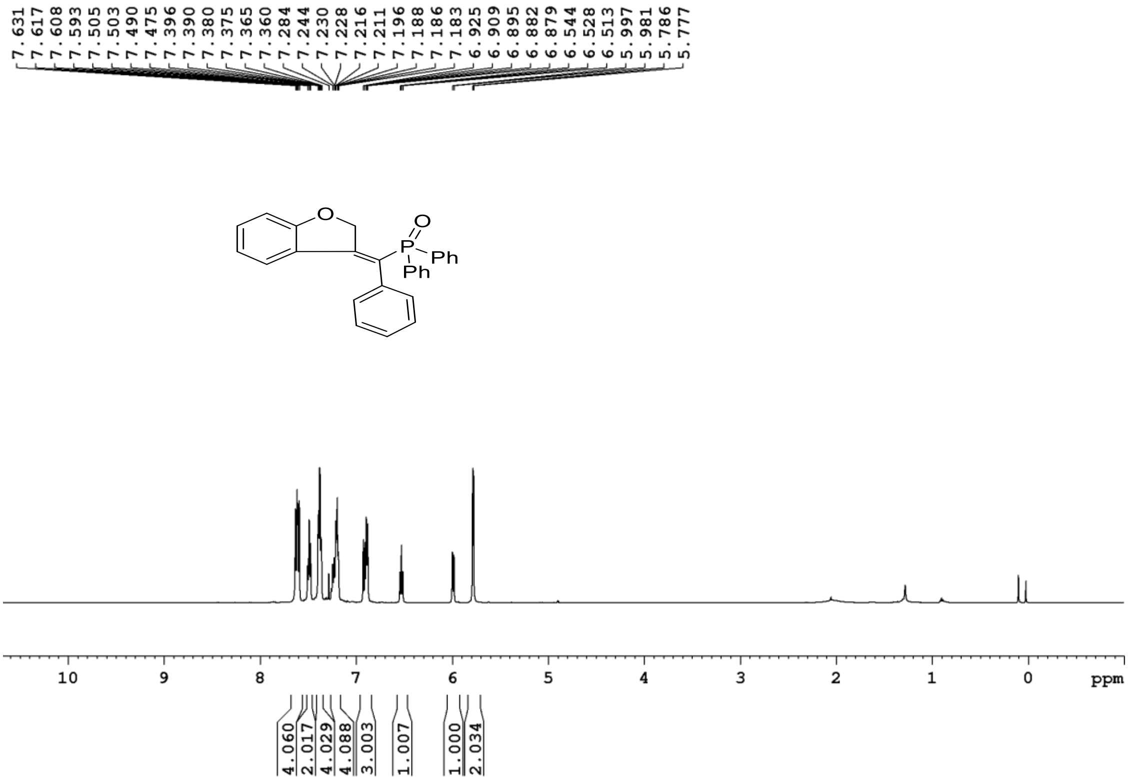

Figure A11. ^{1}H NMR spectrum of compound **40′**

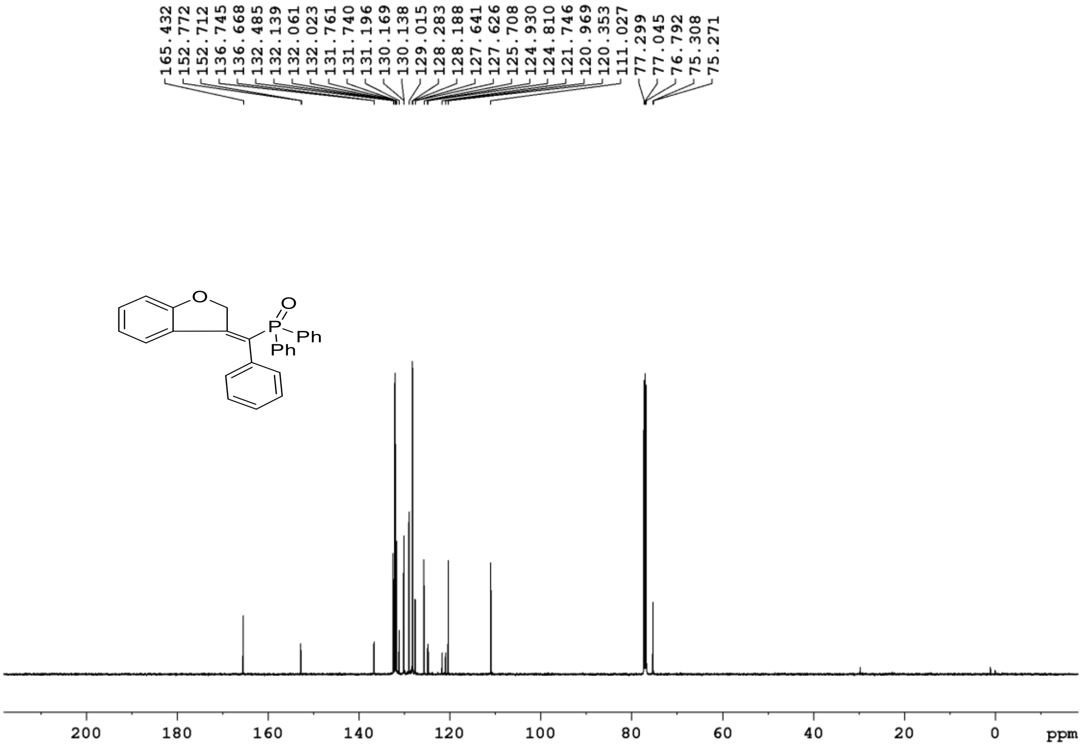

Figure A12. ^{13}C {^{1}H} NMR spectrum of compound **40′**

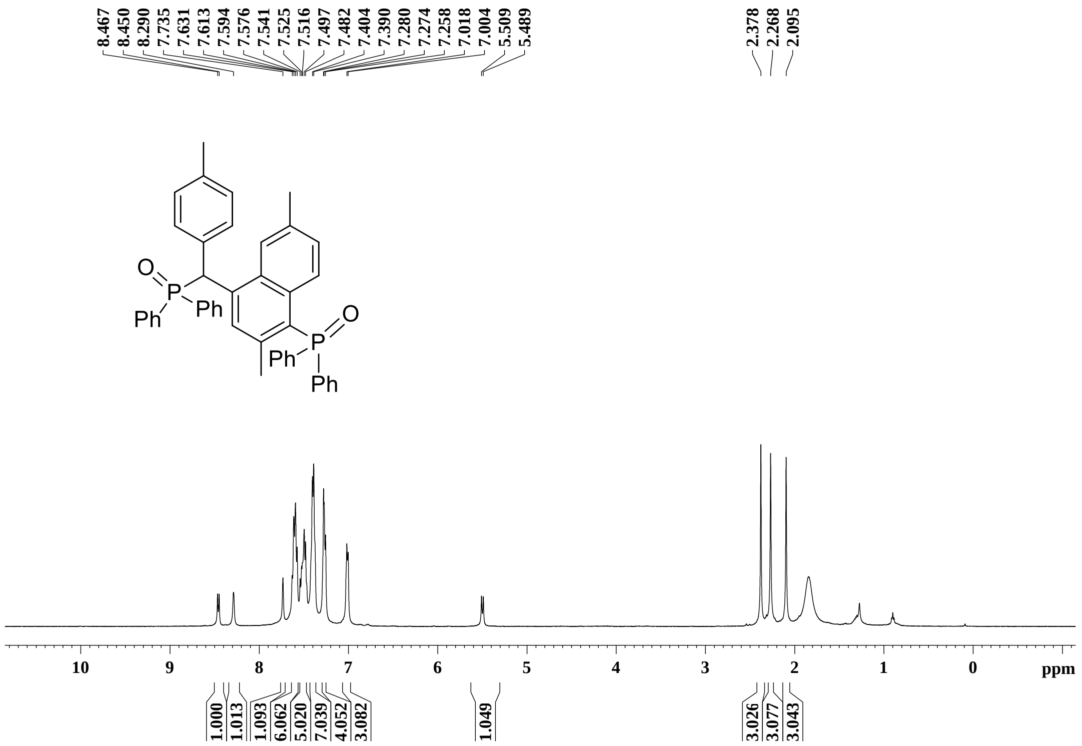

Figure A13. ^{1}H NMR spectrum of compound **45**

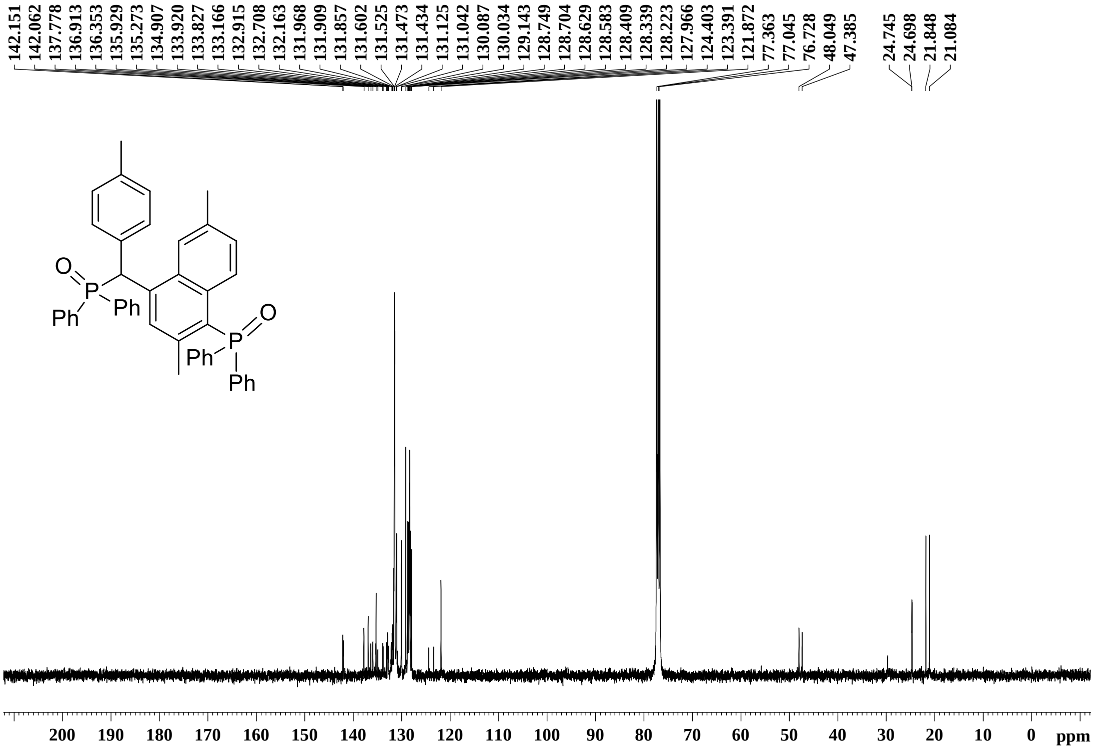

Figure A14. ^{13}C {^{1}H} NMR spectrum of compound **45**

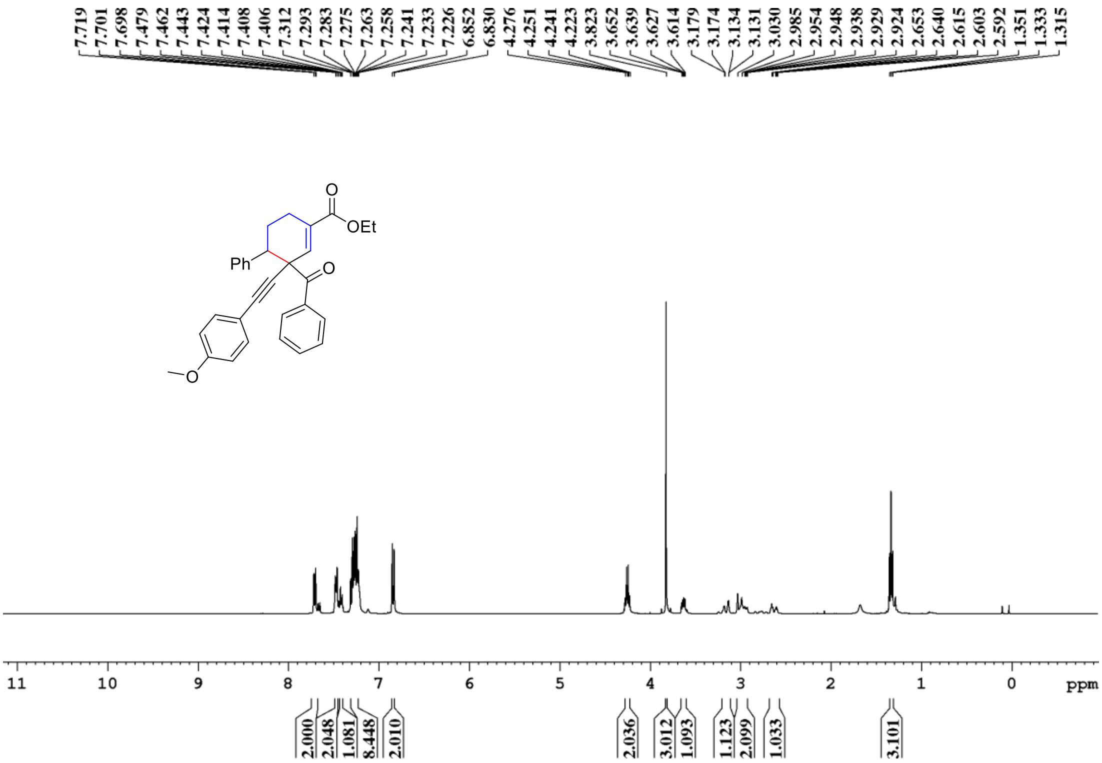

Figure A15. ^{1}H NMR spectrum of compound **51**

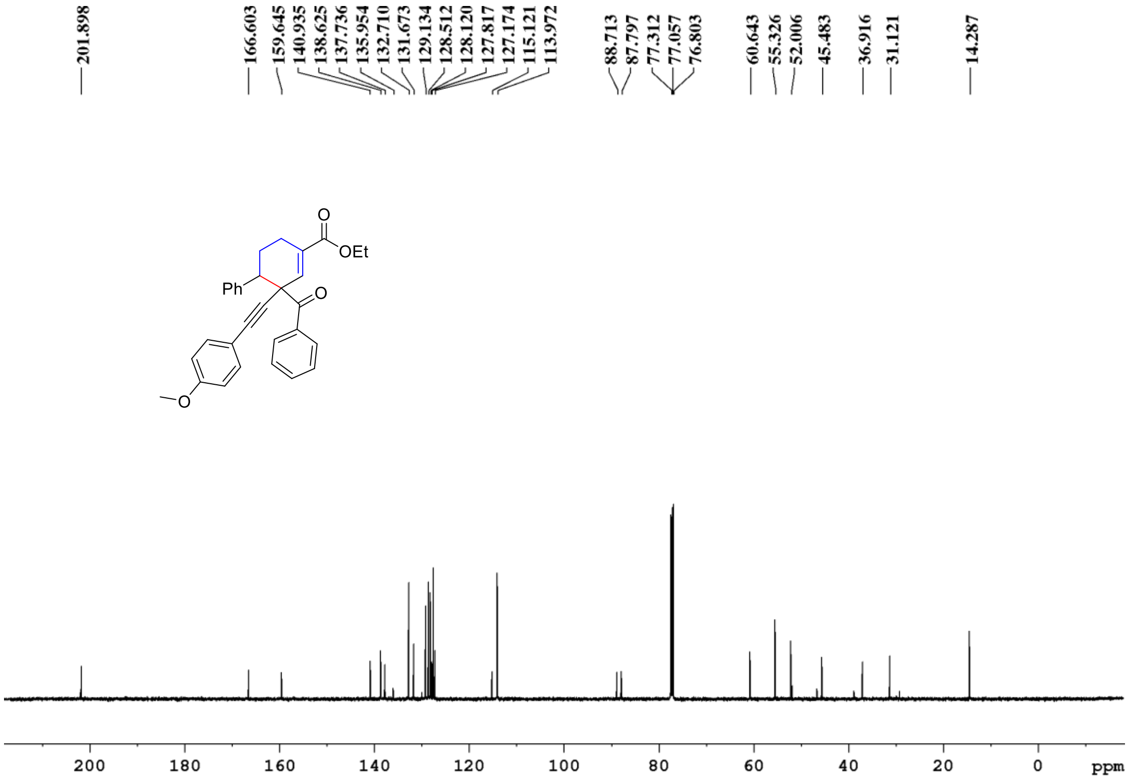

Figure A16. ^{13}C {^{1}H} NMR spectrum of compound **51**

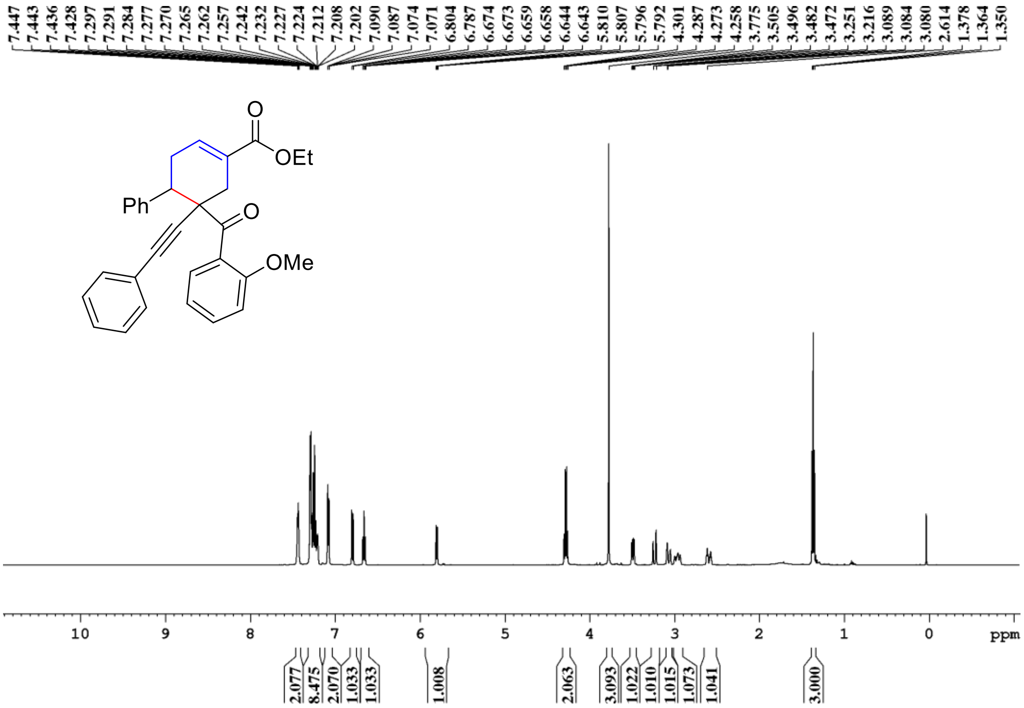

Figure A17. ^{1}H NMR spectrum of compound **53**

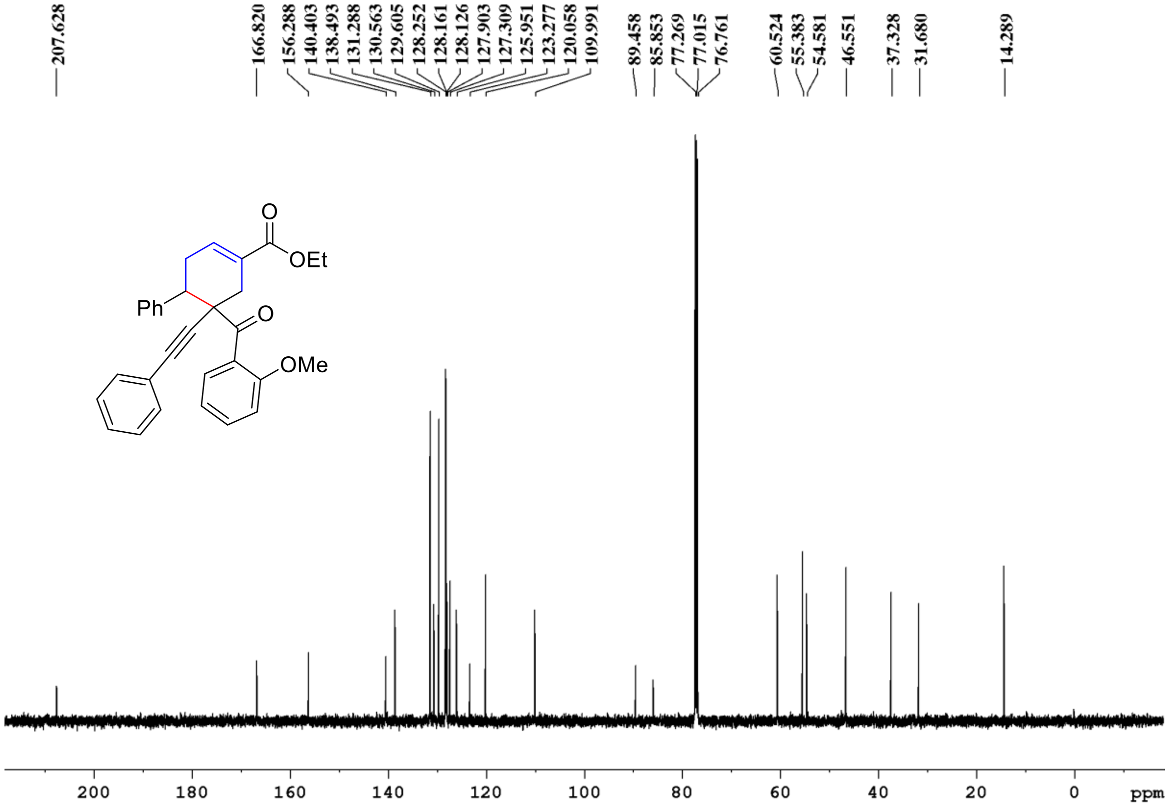

Figure A18. ^{13}C {^{1}H} NMR spectrum of compound **53**

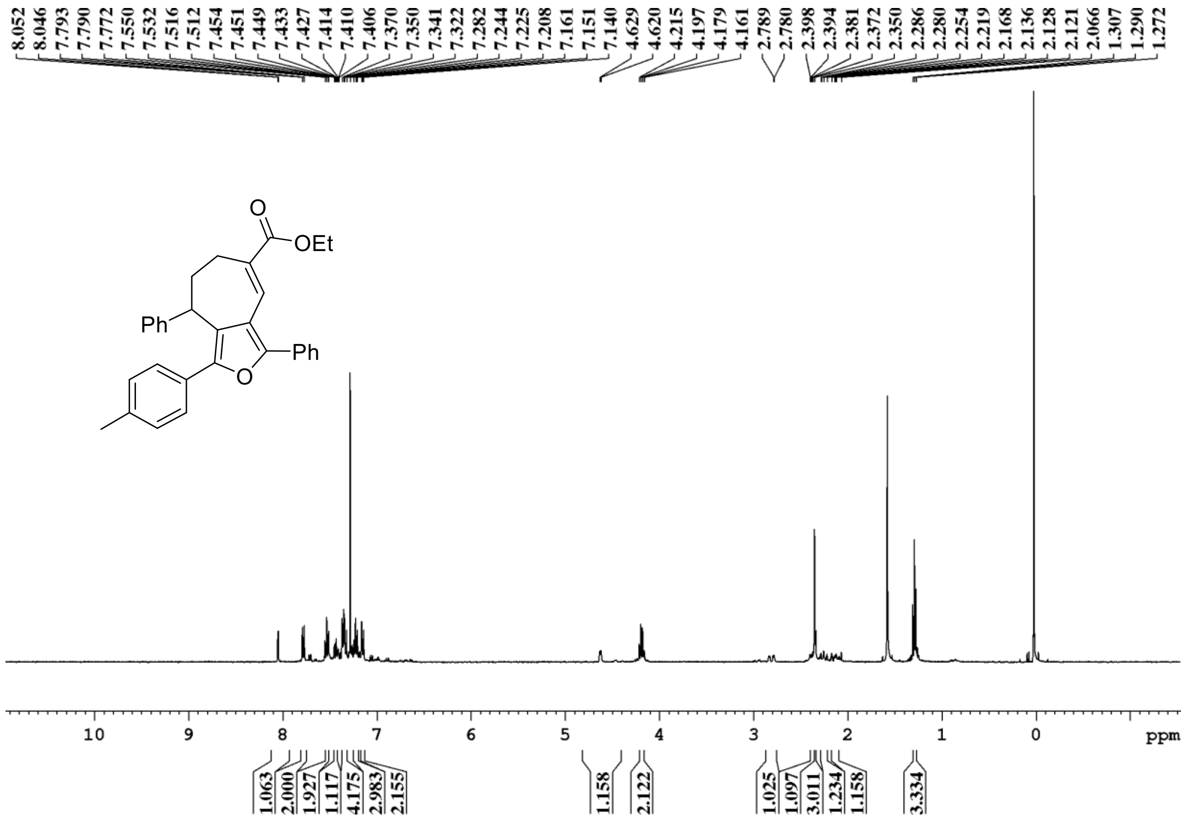

Figure A19. ^{1}H NMR spectrum of compound **55**

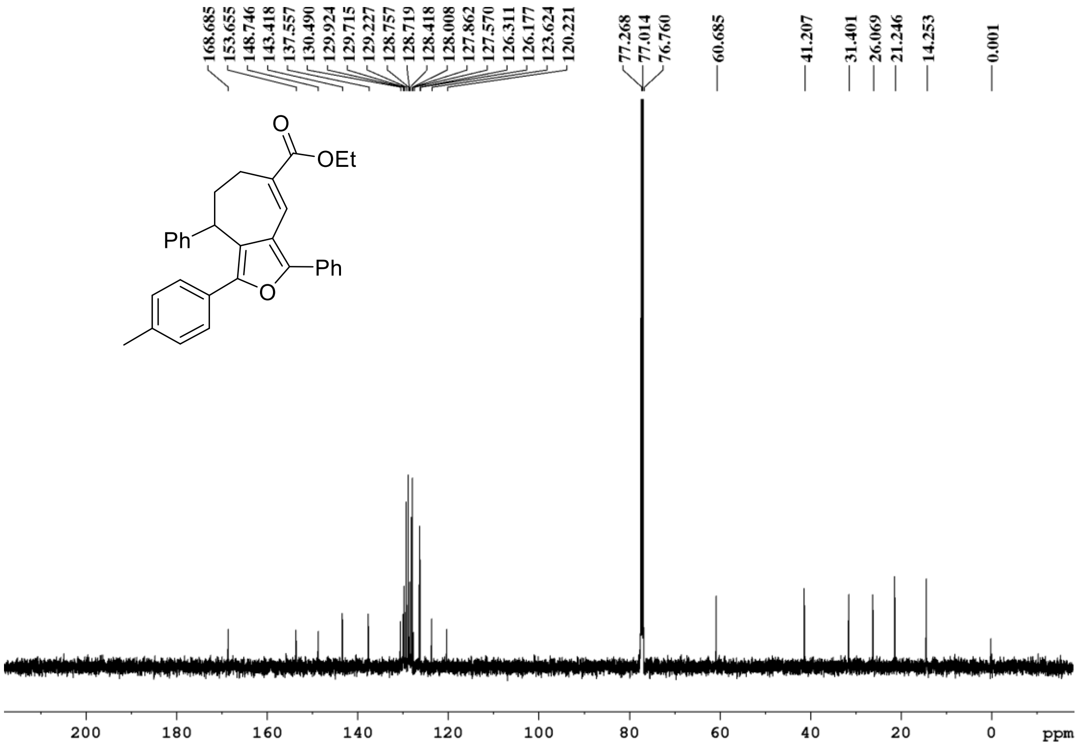

Figure A20. ^{13}C {^{1}H} NMR spectrum of compound **55**

PART-B

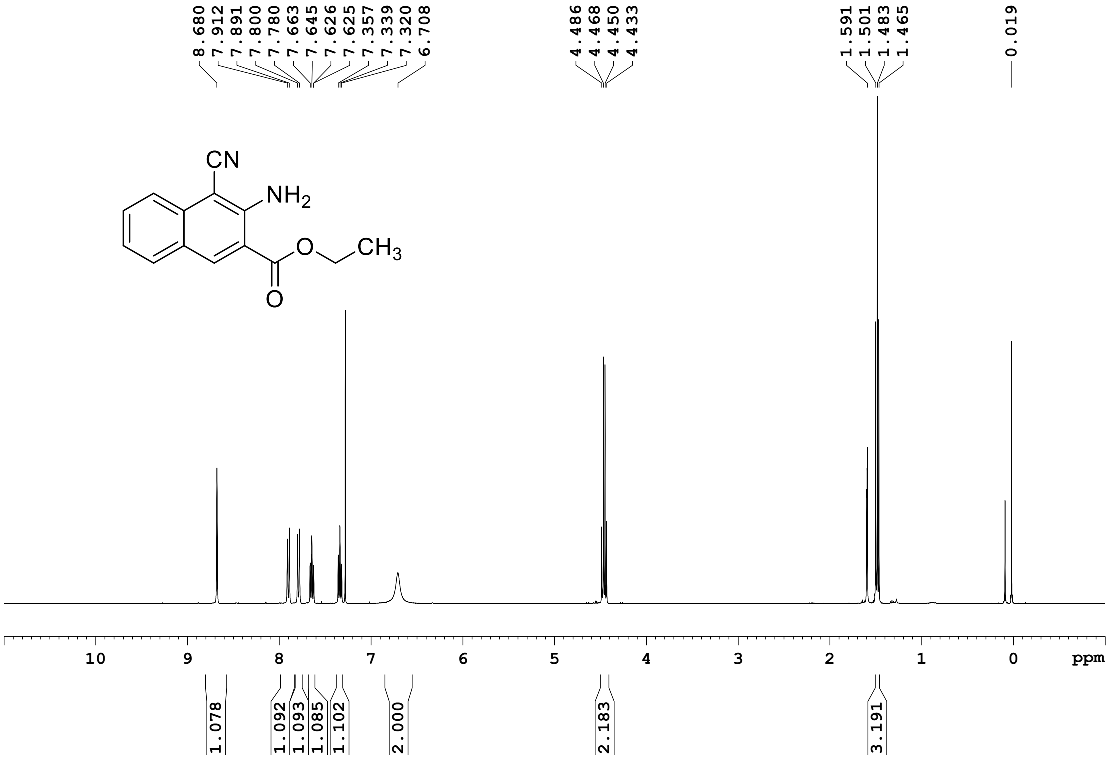

Figure A21. ^{1}H NMR spectrum of compound **5**

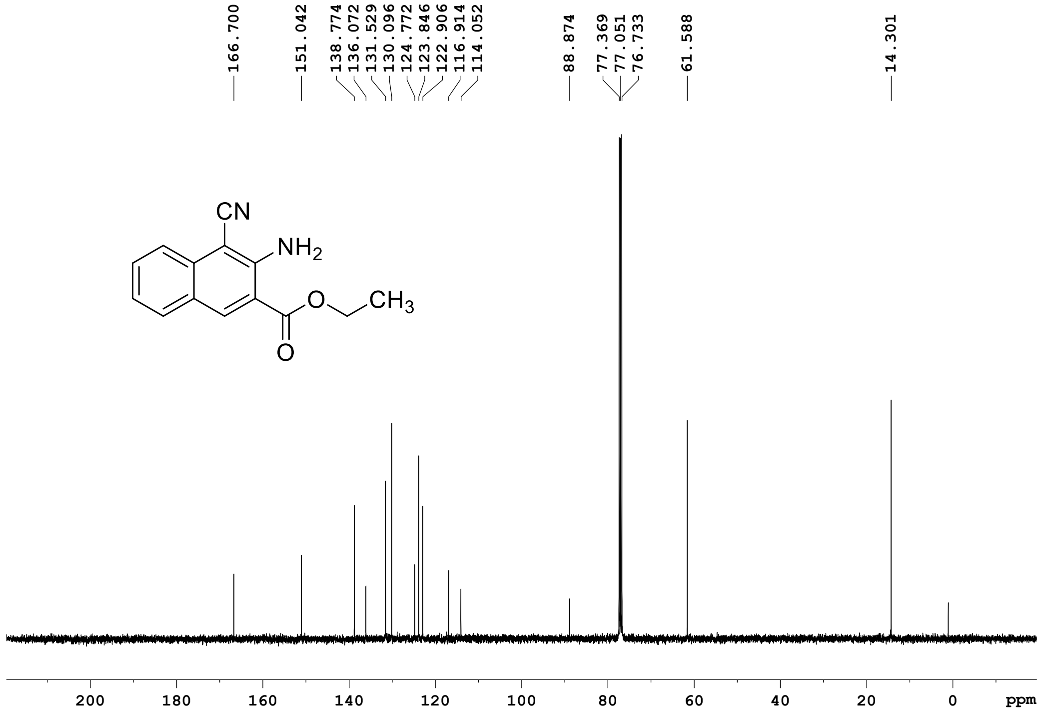

Figure A22. ^{13}C {^{1}H} NMR spectrum of compound **5**

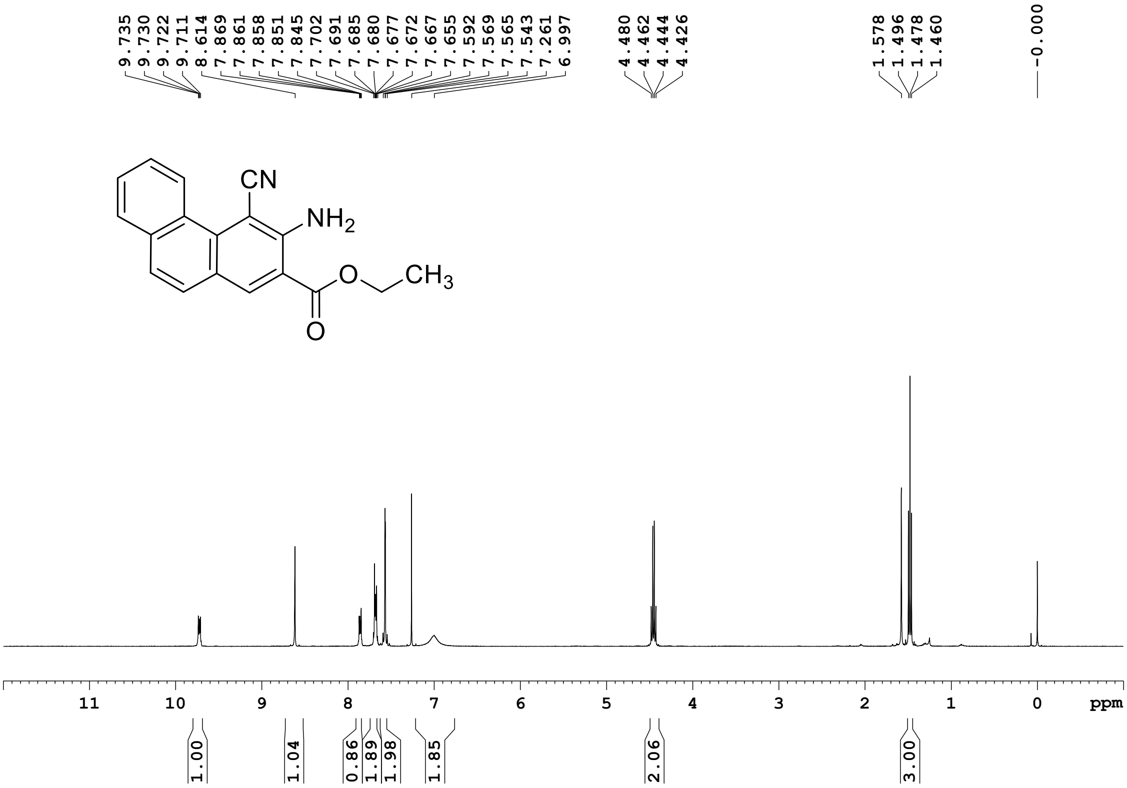

Figure A23. ^{1}H NMR spectrum of compound **22**

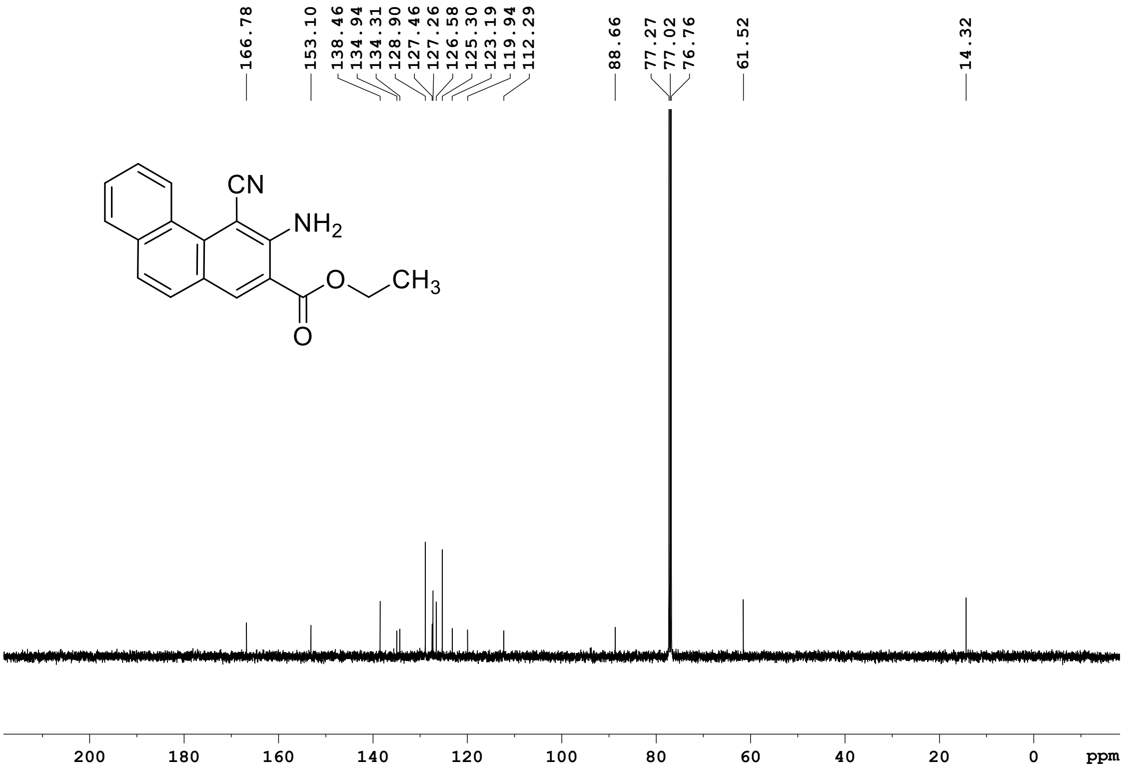

Figure A24. ^{13}C {^{1}H} NMR spectrum of compound **22**

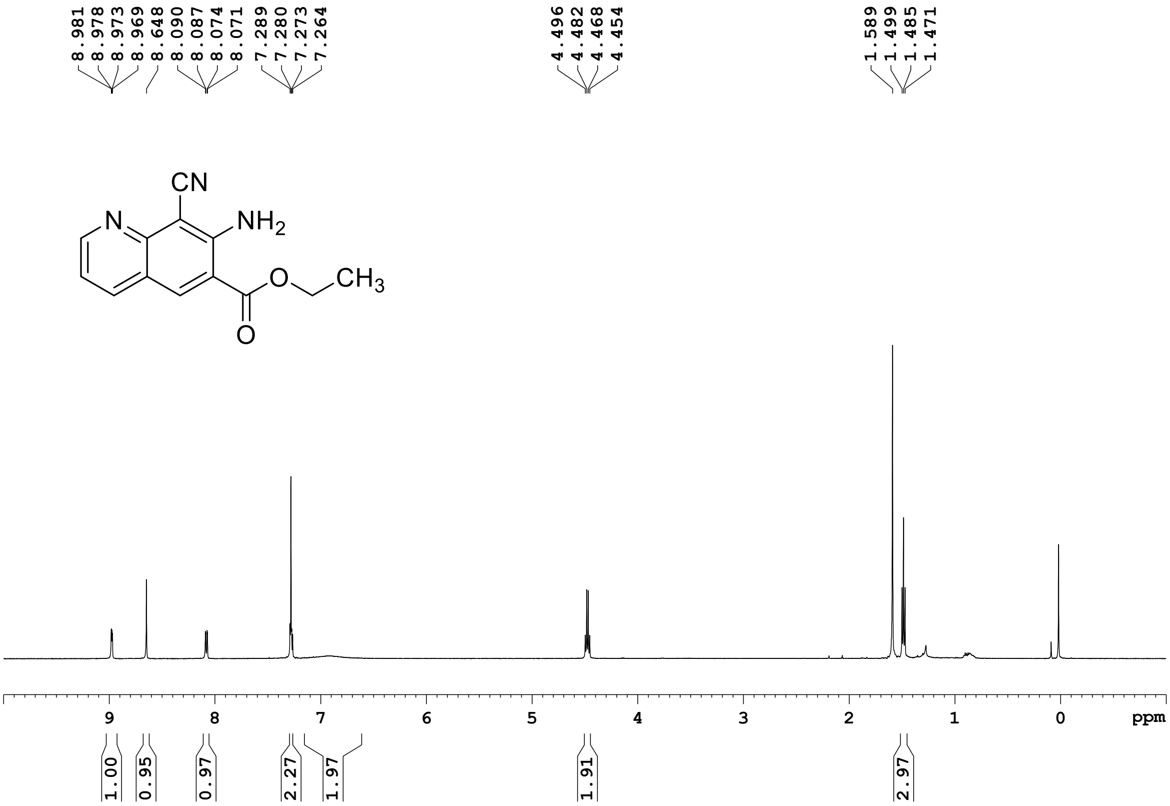

Figure A25. ^{1}H NMR spectrum of compound **25a**

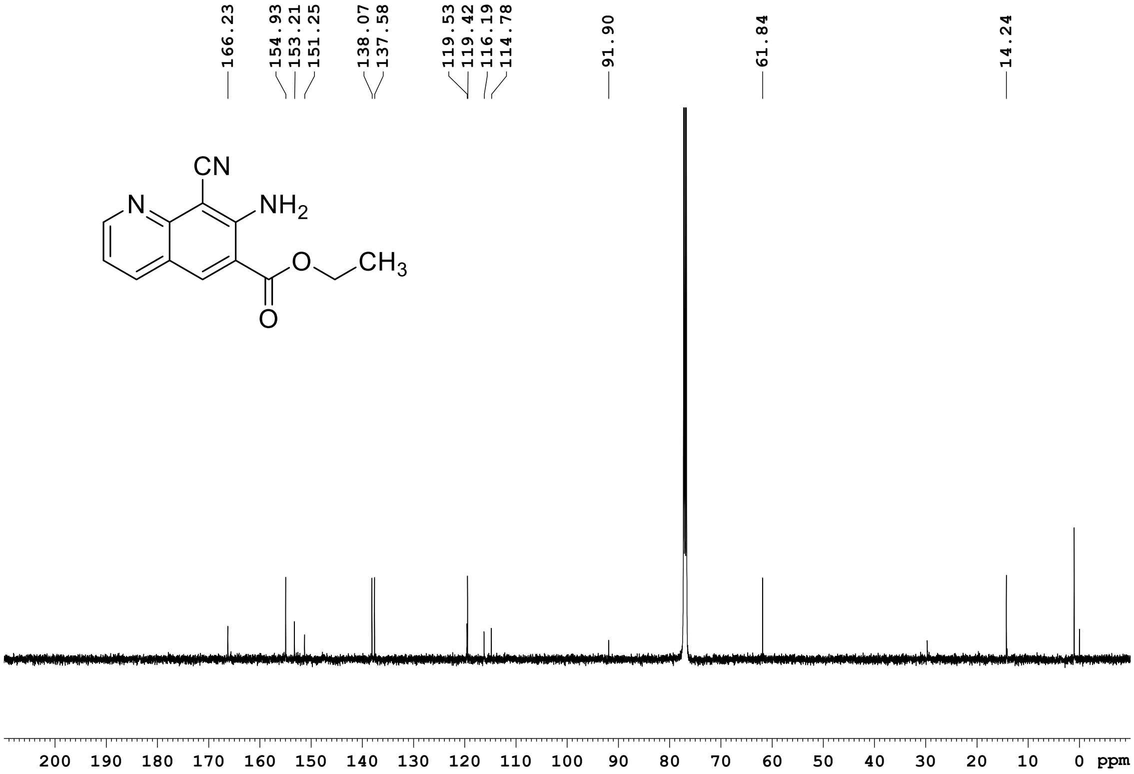

Figure A26. ^{13}C {^{1}H} NMR spectrum of compound **25a**

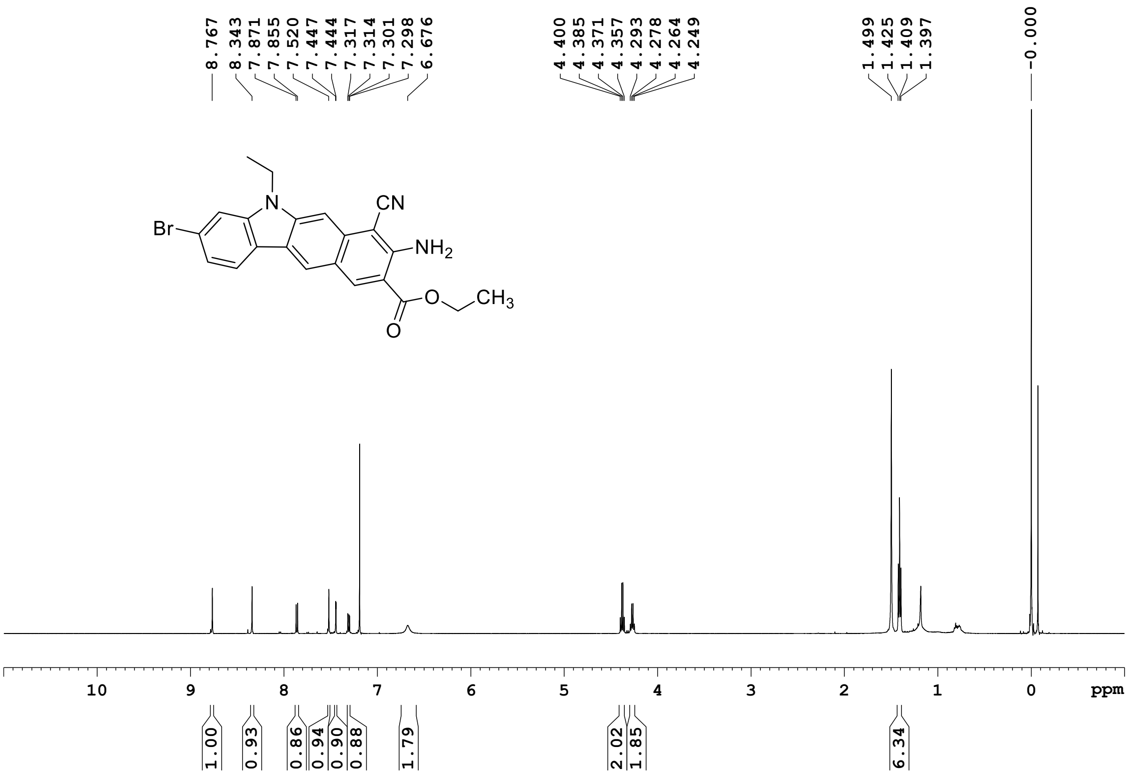

Figure A27. ^{1}H NMR spectrum of compound **28**

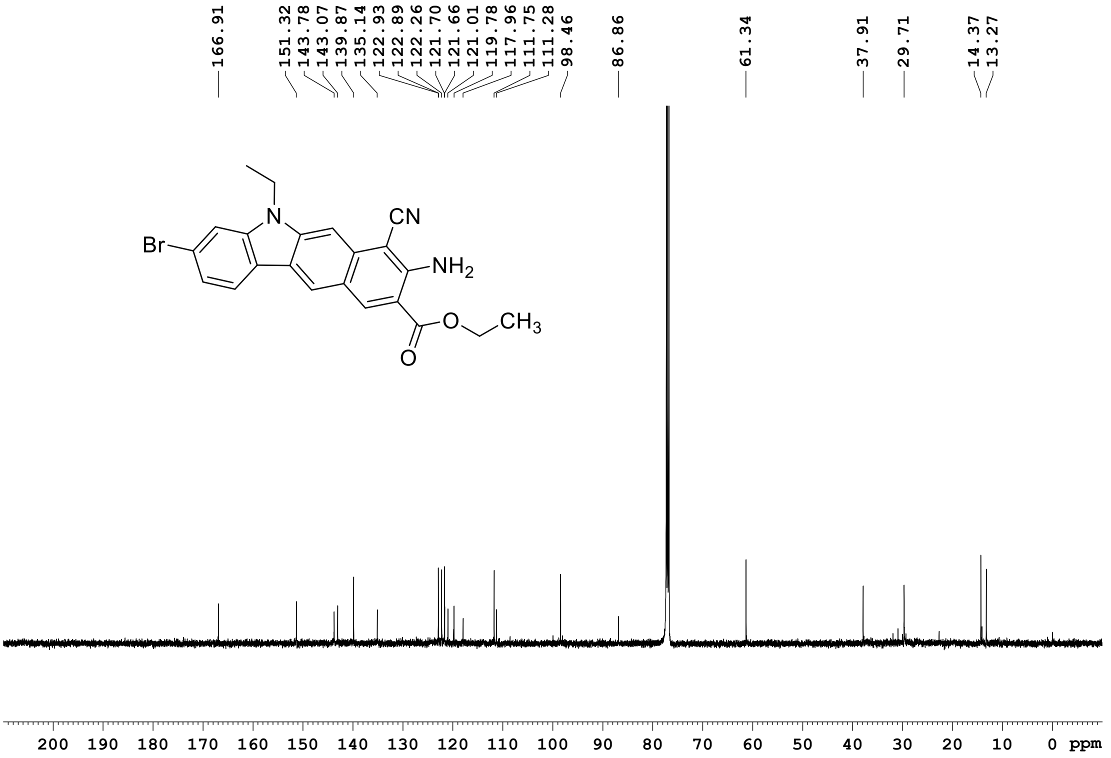

Figure A28. ^{13}C {^{1}H} NMR spectrum of compound **28**

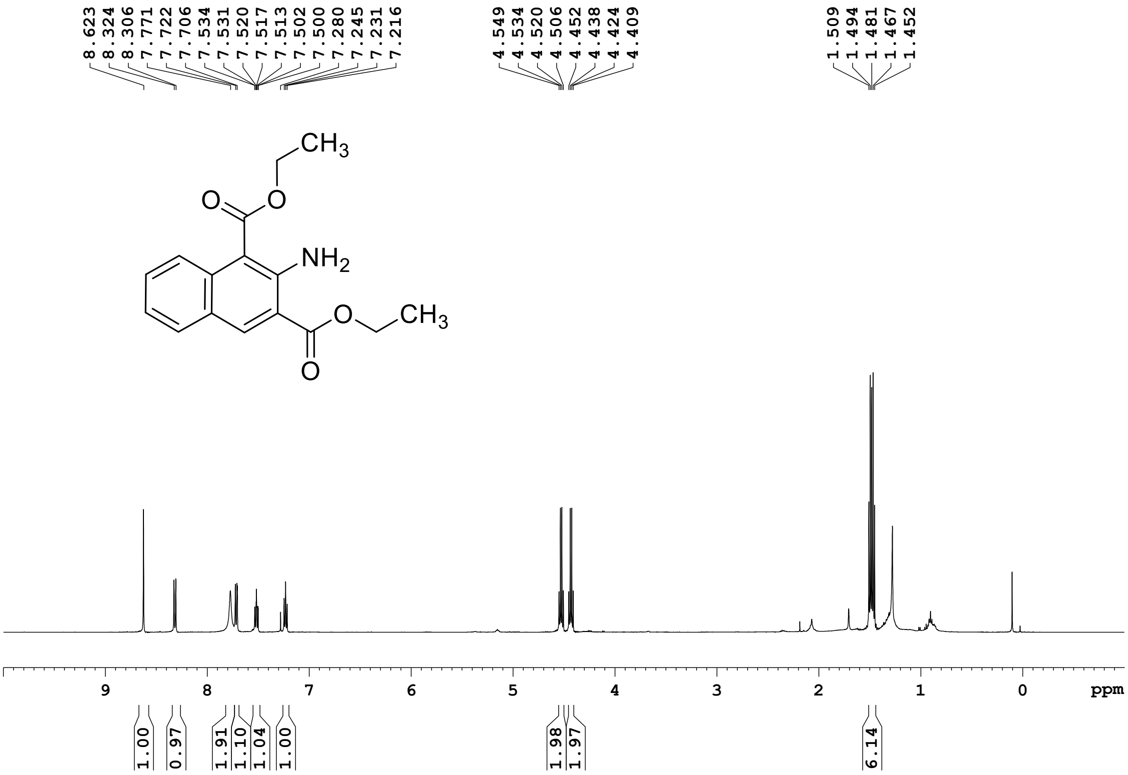

Figure A29. ^{1}H NMR spectrum of compound **31**

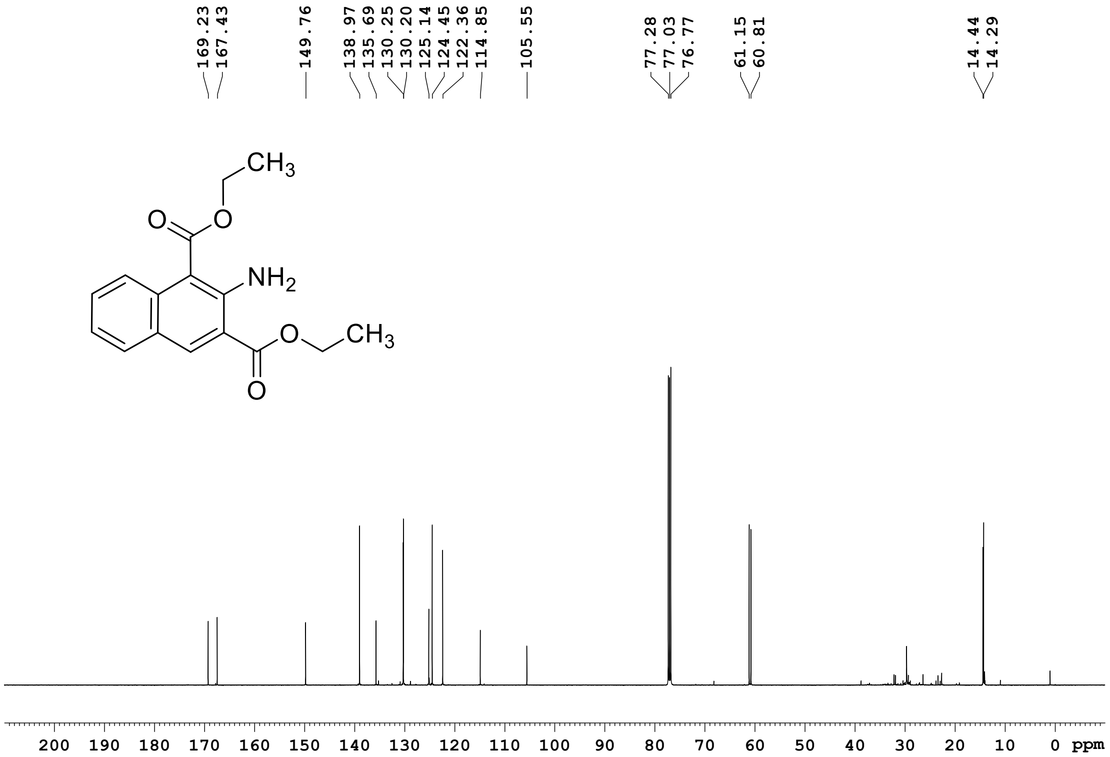

Figure A30. ^{13}C {^{1}H} NMR spectrum of compound **31**

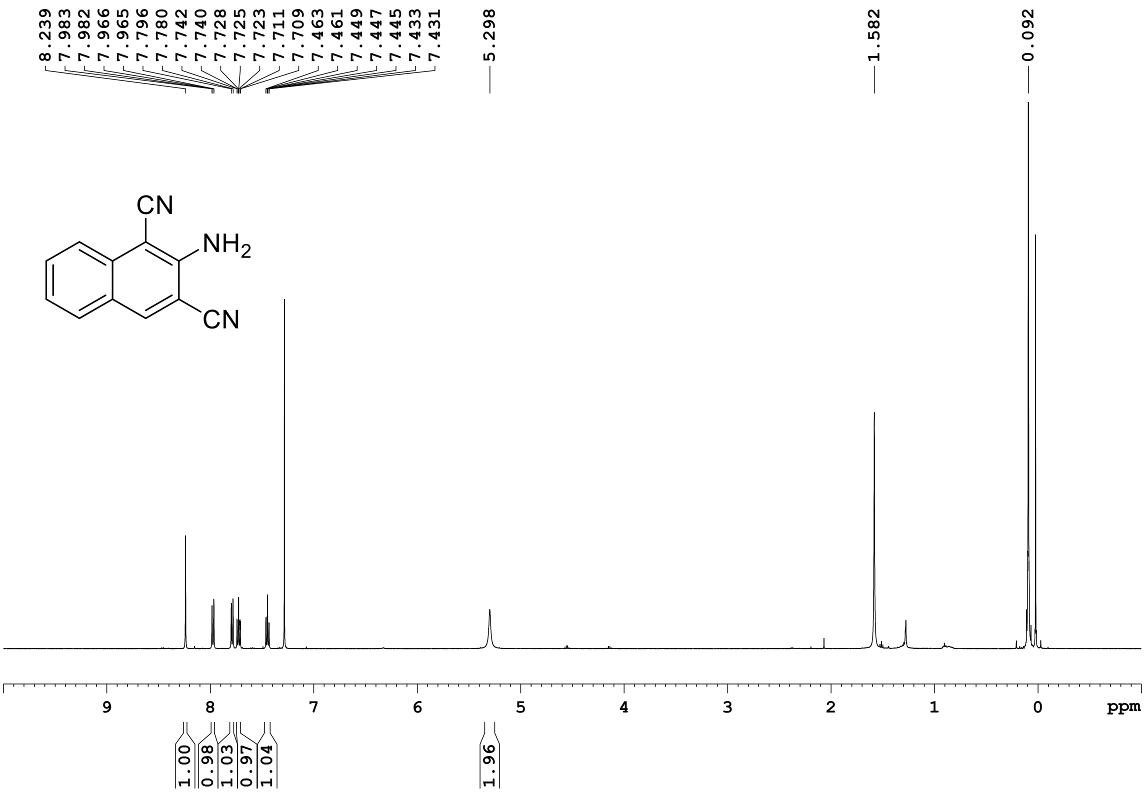

Figure A31. ^{1}H NMR spectrum of compound **38**

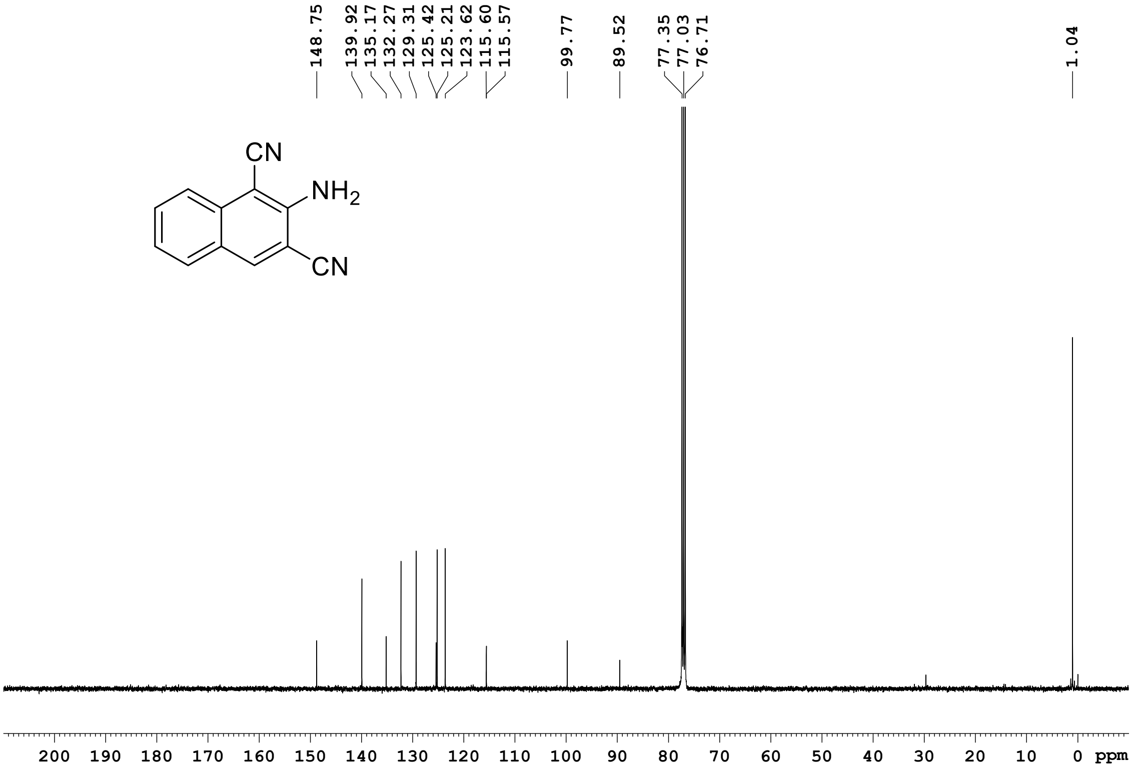

Figure A32. ^{13}C {^{1}H} NMR spectrum of compound **38**

B) Publication numbers and checkcif for X-ray structures reported in this thesis

I. Publication numbers for the published compounds

PART A: **Compounds 10, 14, 19, and 30 Publication no. 1 (Contents, p. xii)**
Compounds 35, 40′, 45, 53 and 55
PART B: **Compounds 16, 22, 25a, 26, 28, 34 and 38 Publication no. 2 (Contents, p. xii)**

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck94_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCEDCRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck 35

Bond precision: C-C = 0.0050 A Wavelength=0.71073

Cell:	a=21.918(3)	b=15.241(2)	c=22.159(4)
	alpha=90	beta=90	gamma=90
Temperature:	301 K		

	Calculated	Reported
Volume Space	7402.3(19)	7402(2)
groupHall	P b c a	Pbca
group	-P 2ac 2ab	?
Moiety formula	C44 H36 O2 P2 Pd	?
Sum formula	C44 H36 O2 P2 Pd	C44 H36 O2 P2 Pd
Mr	765.07	765.07
Dx,g cm-3	1.373	1.373
Z	8	8
Mu (mm-1)	0.624	0.624
F000	3136.0	3136.0
F000’	3130.68	
h,k,lmax	26,18,26	26,18,26
Nref	6512	6489
Tmin,Tmax		
Tmin’		

Correction method= Not given

Data completeness= 0.996 Theta(max)= 25.000

R(reflections)= 0.0309(5189) wR2(reflections)= 0.0900(6489)

S = 1.092 Npar= 444

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B
PLAT919_ALERT_3_B Reflection # Likely Affected by the Beamstop ... 1

Check

Alert level C
PLAT053_ALERT_1_C Minimum Crystal Dimension Missing (or Error) ... Please Check PLAT054_ALERT_1_C Medium Crystal Dimension Missing (or Error) ... Please Check PLAT055_ALERT_1_C Maximum Crystal Dimension Missing (or Error) ... Please Check PLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 3.3 Ratio PLAT241_ALERT_2_C High 'MainMol' Ueq as Compared to Neighbors of C40 Check PLAT910_ALERT_3_C Missing # of FCF Reflection(s) Below Theta(Min). 6 Note PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.595 18 ReportPLAT918_ALERT_3_C Reflection(s) with I(obs) much Smaller I(calc) . 1 Check PLAT934_ALERT_3_C Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers .. 1 Check PLAT977_ALERT_2_C Check Negative Difference Density on H16 -0.36 eA-3

- **Alert level G**

PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please
Do ! PLAT093_ALERT_1_G No s.u.’s on H-positions, Refinement Reported as
mixed Check PLAT720_ALERT_4_G Number of
Unusual/Non-Standard Labels 5
Note PLAT793_ALERT_4_G Model has Chirality at P003 (Centro SPGR) R
VerifyPLAT794_ALERT_5_G Tentative Bond Valency for Pd1 (II).
1.83 Info
PLAT899_ALERT_4_G SHELXL97 is Deprecated and
Succeeded by SHELXL 2018 Note
PLAT909_ALERT_3_G Percentage of I>2sig(I) Data at Theta(Max) Still
63% Note PLAT913_ALERT_3_G Missing # of Very
Strong Reflections in FCF .... 2 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 2
Info PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by
1 Check

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
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10 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

10 **ALERT level G** = General information/check it is not something unexpected

4 ALERT type CIF construction/syntax error, inconsistent or missing data
4 ALERT type Indicator that the structure model may be wrong or deficient
7 ALERT type Indicator that the structure quality may be low
3 ALERT type Improvement, methodology, query or suggestion

3 ALERT type Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of apaper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

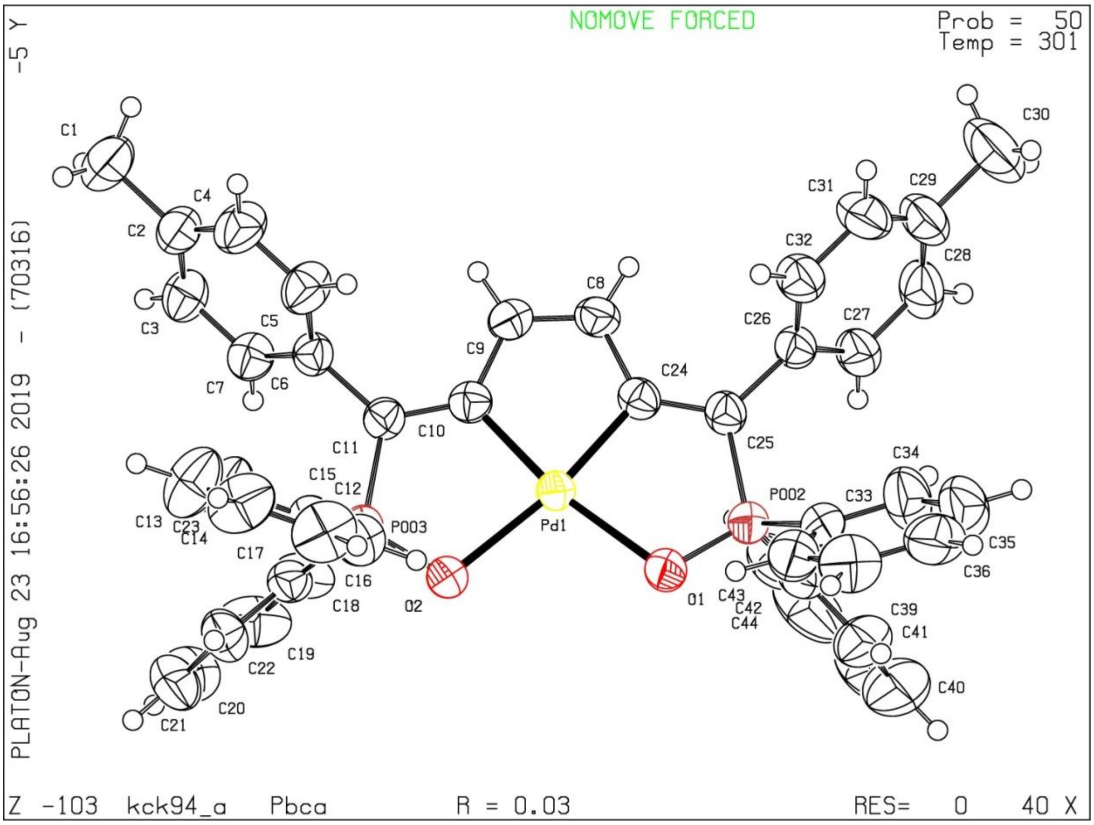
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 07/08/2019; check.def file version of 30/07/2019

Datablock kck 35_a - ellipsoid plot



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) KCK028_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: KCK 40′_0m_a

Bond precision: C-C = 0.0332 A Wavelength=0.71073

Cell:	a=10.001(7)	b=11.138(6)	c=11.883(12)
	alpha=102.420(14)	beta=105.022(19)	gamma=115.73(3)
Temperature:	298 K		

	Calculated	Reported
Volume Space	1066.9(15)	1066.9(15)
groupHall	P -1	P -1
group	-P 1	-P 1
Moiety formula	C27 H21 O2 P	C27 H21 O2 P
Sum formula	C27 H21 O2 P	C27 H21 O2 P
Mr	408.41	408.44
Dx,g cm-3	1.271	1.271
Z	2	2
Mu (mm-1)	0.150	0.150
F000	428.0	428.4
F000’	428.38	
h,k,lmax	12,14,15	12,13,14
Nref	4680	3003
Tmin,Tmax	0.968,0.973	0.388,0.746
Tmin’	0.968	

Correction method= # Reported T Limits: Tmin=0.388 Tmax=0.746AbsCorr = CYLINDER

Data completeness= 0.642 Theta(max)= 27.050

R(reflections)= 0.0992(612) wR2(reflections)

=

0.4027(3003)

S = 0.855 Npar= 271

The following ALERTS were generated. Each ALERT has

the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the

test.

Alert level A

RINTA01_ALERT_3_A The value of Rint is
greater than 0.25Rint given 0.400
PLAT020_ALERT_3_A The Value of Rint is Greater Than 0.12 ....
0.
400 Report PLAT026_ALERT_3_A Ratio Observed / Unique Reflections (too) Low ..
20
% Check PLAT029_ALERT_3_A _diffrn_measured_fraction_theta_full value Low .
0.
641 Why?
PLAT213_ALERT_2_A Atom C24 has ADP max/min Ratio ..... 6.2 oblate

---

Alert level B

DIFMN02_ALERT_2_B The minimum difference density is < -0.1*ZMAX*1.00

_refine_diff_density_min given = -1.574Test value = -1.500
PLAT084_ALERT_3_B High wR2 Value (i.e. > 0.25) .... 0.40 Report
PLAT097_ALERT_2_B Large Reported Max. (Positive) Residual Density
1.58 eA-3 PLAT098_ALERT_2_B
Large Reported Min. (Negative) Residual Density -1.57 eA-3
PLAT213_ALERT_2_B Atom C26 has ADP max/min Ratio .....
4.1 prolat PLAT234_ALERT_4_B
Large Hirshfeld Difference C1 --C6 .
0.28 Ang.
PLAT234_ALERT_4_B Large Hirshfeld Difference C23 --C24 .
0.30 Ang.
PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds 0.03321
Ang. PLAT911_ALERT_3_B Missing FCF Refl Between Thmin & STh/L=
0.600 977
ReportPLAT919_ALERT_3_B Reflection # Likely Affected by the Beamstop ...
1 Check

Alert level C

DIFMN03_ALERT_1_C The minimum difference density is < -0.1*ZMAX*0.75 The relevant atom site should be identified.

DIFMX02_ALERT_1_C The maximum difference density is > 0.1*ZMAX*0.75 The relevant atom site should be identified.

PLAT148_ALERT_3_C s.u. on the c - Axis is (Too) Large .... 0.012 Ang. PLAT213_ALERT_2_C Atom C9 has ADP max/min Ratio ..... 3.2 prolat PLAT213_ALERT_2_C Atom C23 has ADP max/min Ratio ..... 3.3 prolat PLAT234_ALERT_4_C Large Hirshfeld Difference P1 --C9 . 0.17 Ang. PLAT234_ALERT_4_C Large Hirshfeld Difference C17 --C18 . 0.24 Ang. PLAT241_ALERT_2_C High ’MainMol’ Ueq as Compared to Neighbors of C7 Check PLAT241_ALERT_2_C High ’MainMol’ Ueq as Compared to Neighbors of C25 Check PLAT242_ALERT_2_C Low ’MainMol’ Ueq as Compared to Neighbors of C16 Check PLAT331_ALERT_2_C Small Aver Phenyl C-C Dist C16 --C21 . 1.37 Ang. PLAT334_ALERT_2_C Small Aver. Benzene C-C Dist C1 -C6 1.37 Ang. PLAT905_ALERT_3_C Negative K value in the Analysis of Variance ... -1.862 Report PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ...... 12.786 Check PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ...... 3.068 Check PLAT918_ALERT_3_C Reflection(s) with I(obs) much Smaller I(calc) . 1 Check PLAT924_ALERT_1_C The Reported and Calculated Rho(min) Differ by . 1.16 eA-3 PLAT925_ALERT_1_C The Reported and Calculated Rho(max) Differ by . 1.27 eA-3 PLAT934_ALERT_3_C Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers ..1 Check

---

Alert level G

PLAT072_ALERT_2_G SHELXL First Parameter in WGHT Unusually Large 0.14 Report

PLAT073_ALERT_1_G H-atoms ref, but _hydrogen_treatment Reported as constr Check PLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O1 . 108.3 Degree PLAT767_ALERT_4_G INS Embedded LIST 6 Instruction Should be LIST 4 Please Check PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary . Please Do !

PLAT908_ALERT_2_G Max. Perc. Data with I > 2*s(I) per Res.Shell . 63.87% Note

PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 670 Note

PLAT941_ALERT_3_G Average HKL Measurement Multiplicity .... 1.7 Low

PLAT960_ALERT_3_G Number of Intensities with I < - 2*sig(I) ... 8 Check PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.0 Info PLAT980_ALERT_1_G No Anomalous Scattering Factors Found in CIF ... Please Check

---

5 **ALERT level A** = Most likely a serious problem **-** resolve or explain
10 **ALERT level B** = A potentially serious problem, consider carefully
19 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

11 **ALERT level G** = General information/check it is not something unexpected

7 ALERT type CIF construction/syntax error, inconsistent or missing data
16 ALERT type Indicator that the structure model may be wrong or deficient
16 ALERT type Indicator that the structure quality may be low
6 ALERT type Improvement, methodology, query or suggestion
0 ALERT type Informative message, check

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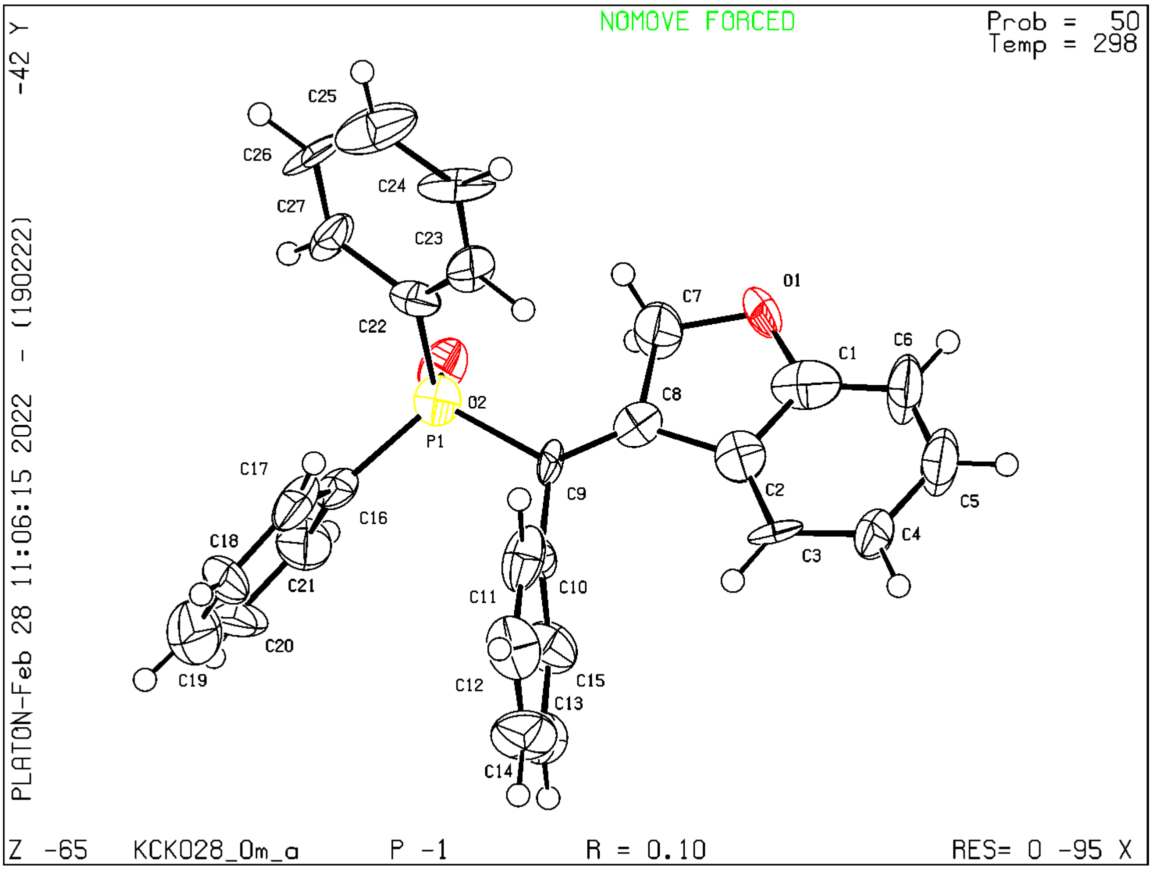
Crystallography, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks arerun on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIFsubmission.

PLATON version of 19/02/2022; check.def file version of 19/02/2022

Datablock KCK 40'_0m_a - ellipsoid plot



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck92a_0m_a

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No syntax errors found.   CIF dictionary   Interpreting this report

Datablock: kck45_0m_a

Bond precision: C-C = 0.0047 A   Wavelength=0.71073

Cell:	a=11.478(3)	b=12.334(3)	c=14.871(4)
	alpha=107.993(10)	beta=111.95(1)	gamma=94.357(10)
Temperature:	300 K		

	Calculated	Reported
Volume Space	1812.9(8)	1813.0(7)P-
groupHall	P -1	1
group	-P 1	?
Moiety formula	C44 H37 O2 P2, H2 O	?
Sum formula	C44 H39 O3 P2	C44 H39 O3 P2
Mr	677.69	677.69
Dx,g cm-3	1.242	1.241
Z	2	2
Mu (mm-1)	0.160	0.160
F000	714.0	714.0
F000’	714.68	
h,k,lmax	13,14,17	13,14,17
Nref	6395	6388
Tmin,Tmax		
Tmin’		

Correction method= Not given

Data completeness= 0.999   Theta(max)= 25.000

R(reflections)= 0.0621(5343)   wR2(reflections)= 0.1776(6388)

S = 1.101   Npar= 453

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

Alert level B

RINTA01_ALERT_3_B The value of Rint is greater than 0.18Rint given 0.222
PLAT919_ALERT_3_B Reflection # Likely Affected by the Beamstop ... 1 Check

---

Alert level C

PLAT053_ALERT_1_C Minimum Crystal Dimension Missing (or Error) ... Please Check PLAT054_ALERT_1_C Medium Crystal Dimension Missing (or Error) ... Please Check PLAT055_ALERT_1_C Maximum Crystal Dimension Missing (or Error) ... Please CheckPLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 4.0 RatioPLAT241_ALERT_2_C High 'MainMol' Ueq as Compared to Neighbors of C35 Check
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds .... 0.0047 Ang.
PLAT355_ALERT_3_C Long O-H (X0.82,N0.98A) O3 - H1B . 1.04 Ang.
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ...... 2.217 Check PLAT910_ALERT_3_C Missing # of FCF Reflection(s) Below Theta(Min). 5 Note
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.595 3 ReportPLAT918_ALERT_3_C Reflection(s) with I(obs) much Smaller I(calc) . 1 Check PLAT934_ALERT_3_C Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers .. 1 Check
PLAT975_ALERT_2_C Check Calcd Resid. Dens. 1.02A From C13 0.74 eA-3

Alert level G

PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please Do ! PLAT020_ALERT_3_G The Value of Rint is Greater Than 0.12 .... 0.222 ReportPLAT154_ALERT_1_G The s.u.'s on the Cell Angles are Equal ..(Note) 0.01 DegreePLAT343_ALERT_2_G Unusual sp? Angle Range in Main Residue for C13 Check PLAT367_ALERT_2_G Long? C(sp?)-C(sp?) Bond C13 - C14 . 1.52 Ang.
PLAT367_ALERT_2_G Long? C(sp?)-C(sp?) Bond C13 - C21 . 1.53 Ang.
PLAT899_ALERT_4_G SHELXL97 is Deprecated and Succeeded by SHELXL 2018 NotePLAT909_ALERT_3_G Percentage of I>2sig(I) Data at Theta(Max) Still 65% Note PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 3 Info

---

0 **ALERT level A** = Most likely a serious problem **-** resolve or explain

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13 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

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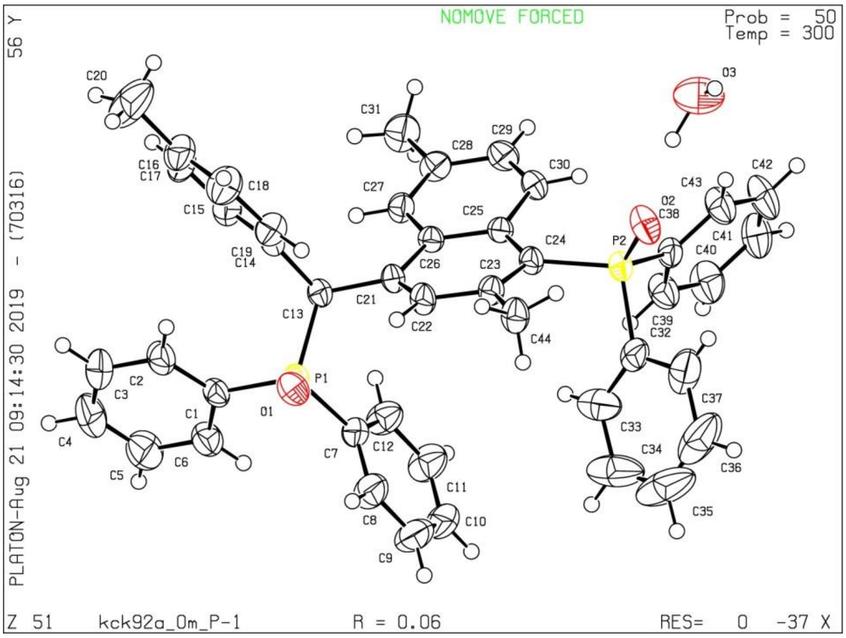
7 ALERT type Indicator that the structure model may be wrong or deficient
11 ALERT type Indicator that the structure quality may be low
1 ALERT type Improvement, methodology, query or suggestion
1 ALERT type Informative message, check



It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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PLATON version of 07/08/2019; check.def file version of 30/07/2019

Datablock kck 45_0m_a - ellipsoid plot

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck65

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck53

Bond precision: C-C = 0.0026 A Wavelength=0.71073

Cell:	a=19.7177(5)	b=7.8743(2)	c=32.7285(9)
	alpha=90	beta=90.299(2)	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	5081.5(2)	5081.4(2)
Space group	I 2/a	I2/a
Hall group	-I 2ya	?
Moiety formula	C31 H28 O4	?
Sum formula	C31 H28 O4	C31 H28 O4
Mr	464.53	464.53
Dx,g cm-3	1.214	1.214
Z	8	8
Mu (mm-1)	0.079	0.079
F000	1968.0	1968.0
F000’	1968.93	
h,k,lmax	23,9,38	23,9,38
Nref	4482	4480
Tmin,Tmax	0.981,0.986	0.634,1.000

Tmin’ 0.981

Correction method= # Reported T Limits: Tmin=0.634 Tmax=1.000 AbsCorr = MULTI-SCAN

Data completeness= 1.000 Theta(max)= 25.000

R(reflections)= 0.0447(3358) wR2(reflections)= 0.1377(4480)

S = 0.987 Npar= 313

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT201_ALERT_2_B Isotropic non-H Atoms in Main Residue(s) 2
ReportC12 C22

Alert level C

ABSTY02_ALERT_1_C An _exptl_absorpt_correction_type has been given without a
literature citation. This should be contained in the
_exptl_absorpt_process_details field.
Absorption correction given as multi-scan
PLAT199_ALERT_1_C Reported _cell_measurement_temperature ..... (K) 293 Check
PLAT200_ALERT_1_C Reported _diffrn_ambient_temperature ..... (K) 293 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ...... 2.491 Check

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Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 2 Note
PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please Do !
PLAT230_ALERT_2_G Hirshfeld Test Diff for C9 --C10 . 6.0 s.u. PLAT371_ALERT_2_G
Long C(sp2)-C(sp1) Bond C11 - C12 . 1.44 Ang.
PLAT793_ALERT_4_G Model has Chirality at C9 (Centro SPGR) S
VerifyPLAT793_ALERT_4_G Model has Chirality at C22 (Centro SPGR) R
VerifyPLAT860_ALERT_3_G Number of Least-Squares Restraints 1
Note PLAT899_ALERT_4_G SHELXL97 is Deprecated and Succeeded by SHELXL/ 2018
Note PLAT909_ALERT_3_G Percentage of I>2sig(I) Data at Theta(Max) Still 42%
Note PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min). 1
Note PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 2
Info

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0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
4 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
11 **ALERT level G** = General information/check it is not something unexpected

3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
5 ALERT type 2 Indicator that the structure model may be wrong or deficient
4 ALERT type 3 Indicator that the structure quality may be low

3 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

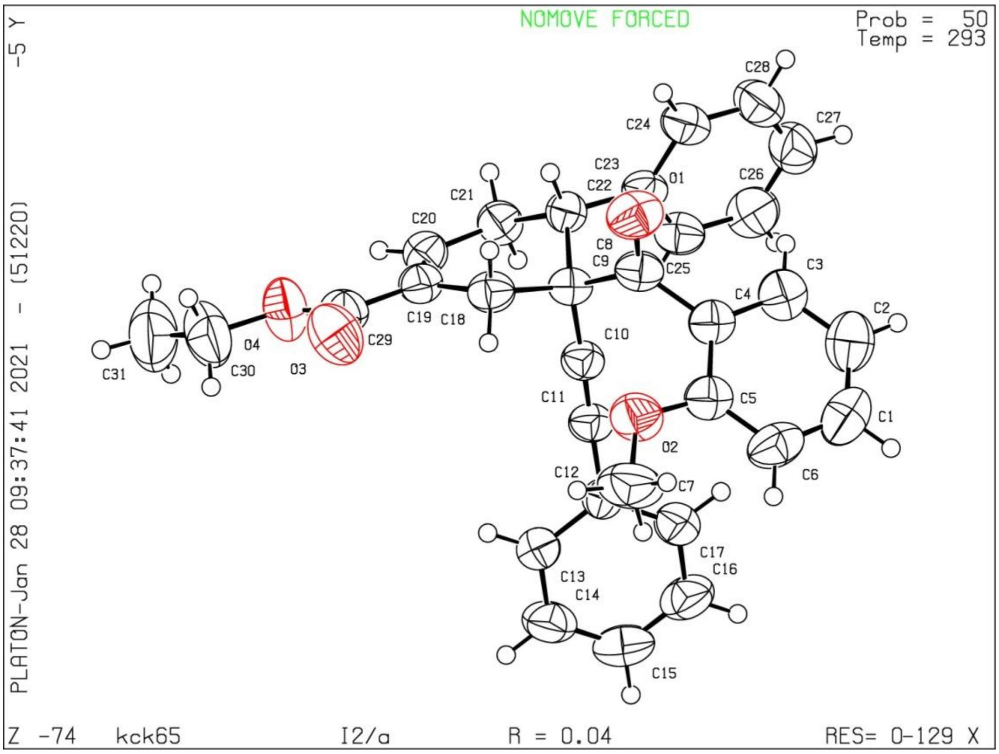
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 05/12/2020; check.def file version of 05/12/2020

Datablock kck 53 - ellipsoid plot



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checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck47a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck55

Bond precision: C-C = 0.0040 A Wavelength=0.71073

Cell:	a=11.6905(5)	b=8.2792(4)	c=25.1517(8)
	alpha=90	beta=97.733(3)	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	2412.24(17)	2412.24(16)

Space group	P 21/n	P2(1)/n
Hall group	-P 2yn	?
Moiety formula	C31 H28 O3	?
Sum formula	C31 H28 O3	C31 H28 O3
Mr	448.53	448.53
Dx,g cm-3	1.235	1.235
Z	4	4
Mu (mm-1)	0.078	0.078
F000	952.0	952.0
F000’	952.42	
h,k,lmax	13,9,29	13,9,29
Nref	4236	4234
Tmin,Tmax	0.983,0.988	0.483,1.000
Tmin’	0.981	

Correction method= # Reported T Limits: Tmin=0.483 Tmax=1.000AbsCorr = MULTI-SCAN

Data completeness= 1.000 Theta(max)= 25.000

R(reflections)= 0.0606(2426) wR2(reflections)= 0.1912(4234)

S = 1.063 Npar= 313

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

Alert level B

PLAT230_ALERT_2_B Hirshfeld Test Diff for O2 --C1 . 18.8 s.u.
PLAT230_ALERT_2_B Hirshfeld Test Diff for C1 --C31 . 12.2 s.u.
PLAT360_ALERT_2_B Short C(sp3)-C(sp3) Bond C1 - C31 . 1.29 Ang.

Alert level C

ABSTY02_ALERT_1_C An _exptl_absorpt_correction_type has been given without a literature citation. This should be contained in the _exptl_absorpt_process_details field. Absorption correction given as multi-scan
PLAT199_ALERT_1_C Reported _cell_measurement_temperature ..... (K) 293 Check PLAT200_ALERT_1_C Reported _diffrn_ambient_temperature ..... (K) 293 CheckPLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 3.7 Ratio
PLAT222_ALERT_3_C Non-Solv. Resd 1 H Uiso(max)/Uiso(min) Range 4.4 RatioPLAT230_ALERT_2_C Hirshfeld Test Diff for O1 -- C11 . 5.5 s.u. PLAT230_ALERT_2_C Hirshfeld Test Diff for C3 --C4 . 5.5 s.u. PLAT230_ALERT_2_C Hirshfeld Test Diff for C12 -- C13 . 5.5 s.u. PLAT241_ALERT_2_C High ’MainMol’ Ueq as Compared to Neighbors of C1 CheckPLAT242_ALERT_2_C Low ’MainMol’ Ueq as Compared to Neighbors of O2 Check PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ...... 5.488 Check

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Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 2 Note PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please Do ! PLAT072_ALERT_2_G SHELXL First Parameter in WGHT Unusually Large 0.10 ReportPLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O1 107.8 DegreePLAT432_ALERT_2_G Short Inter X...Y Contact C14 ..C14 3.12 Ang.
2-x,1-y,2-z = 3_767
Check PLAT793_ALERT_4_G Model has Chirality at C6 (Centro SPGR) S VerifyPLAT860_ALERT_3_G Number of Least-Squares Restraints .... 1 Note PLAT899_ALERT_4_G SHELXL97 is Deprecated and Succeeded by SHELXL 2018 Note PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min). 2 Note PLAT978_ALERT_2_G Number C-C Bonds

with Positive Residual Density. 1 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by
1 Check

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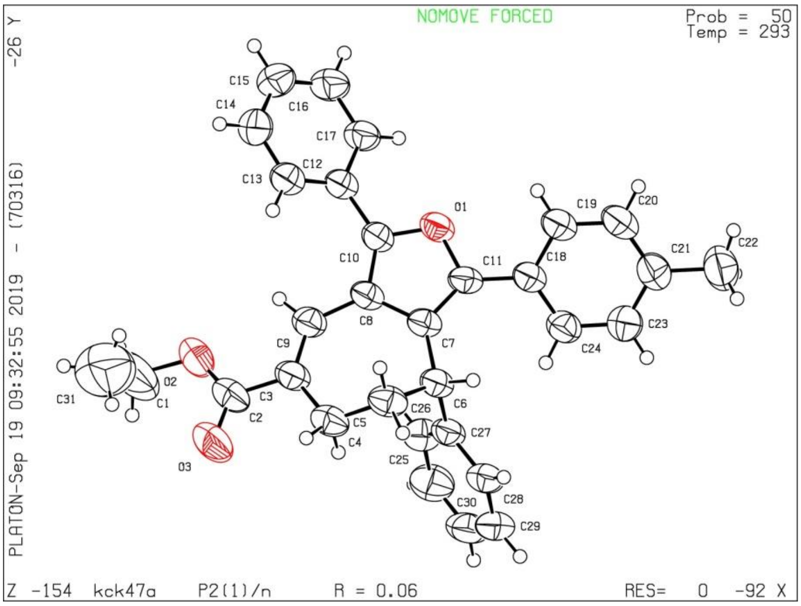
PLATON version of 07/08/2019; check.def file version of 30/07/2019

Datablock kck 55 - ellipsoid plot



Cyclization/ Cycloaddition Reactions of Nitriles, Allenes and Active Methylene Compounds

by Kalyani
A

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