Study on the Reactivity of Bis-π-allyl and Related Palladium Intermediates with Functionalized 1,3-Dienes and Carbonyl Compounds
&
Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles

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By

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THIRUVANANTHAPURAM-695 019, KERALA, INDIA

September, 2016

Dedicated to My Parents and Teachers…

DECLARATION

I hereby declare that the Ph.D. thesis entitled **"Study on the Reactivity of Bis-π-allyl and Related Palladium Intermediates with Functionalized 1,3-Dienes and Carbonyl Compounds & Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles"** is an independent work carried out by me at the Chemical Sciences and Technology Division, CSIR-National Institute for Interdisciplinary Science and Technology (CSIR-NIIST), Thiruvananthapuram under the supervision of Dr. K. V. Radhakrishnan, Principal Scientist, and it has not been submitted anywhere else for any other degree, diploma or title.

Baiju T. V.

Thiruvananthapuram
September, 2016

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CERTIFICATE

This is to certify that the work incorporated in this Ph.D. thesis entitled ***"Study on the Reactivity of Bis-π-allyl and Related Palladium Intermediates with Functionalized 1,3-Dienes and Carbonyl Compounds & Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles"*** *submitted by* ***Mr. Baiju T. V.*** *to Academy of Scientific and Innovative Research (AcSIR), New Delhi, in partial fulfillment of the requirements for the award of the* ***Degree of Doctor of Philosophy in Chemical Sciences,*** *embodies original research work under my guidance. I further certify that this work has not been submitted to any other University or Institution in part or full for the award of any degree or diploma.*

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Baiju T. V.

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ABBREVIATIONS

Ar	: Aryl group
Å	: Angstrom
ACMP	: *O*-Anisylcyclohexylmethylphosphine
AcOH	: Acetic acid
OAc	: Acetyl
BDPP	: 2,4-Diphenylphosphinopentane
BQ	: Benzoquinone
Bu	: *n*-Butyl
^{t}Bu	: *tert*-butyl
Bz	: Benzoyl
bpy	: Bipyridine
Calcd.	: Calculated
COSY	: Correlation spectroscopy
Cp	: Cyclopentadiene
d	: Doublet
dd	: Doublet of doublet
dba	: Dibenzylideneacetone
DCM	: Dichloromethane
DEPT	: Distortionless enhancement by polarisation transfer
DMIP	: Dimethylisopropylphosphine
DMBQ	: 2,6-Dimethoxy-1,4-benzoquinone
DDQ	: 2,3-dichloro-5,6dicyanobenzoquinone
DIOP	: 2,3-*O*-isopropylidene-2,3-dihydroxy-l,4-bis(diphenylphosphino)butane
DMA	: N,N-dimethylacetamide
IDcA	: Interceptive decarboxylative allylation
J	: Coupling constant
DMAD	: Dimethyl acetylene dicarboxylate
DMF	: Dimethylformamide
DMSO	: Dimethylsulphoxide
dppf	: 1,1'-(Bisdiphenylphosphino)ferrocene
dppp	: 1,3-(Bisdiphenylphosphino) propane
dppb	: 1,4-(Bisdiphenylphosphino) butane
dppe	: 1,4-(Bisdiphenylphosphino) ethane
DcA	: Decarboxylative allylation

dr : Diastereomeric ratio

°C : Degree celsius

EDG : Electron donating group

ee : Enantiomeric excess

ESI : Electron spray ionization

Et : Ethyl

EtOH : Ethanol

EtOAc : Ethyl acetate

equiv : Equivalents

Et_3N : Triethylamine

h : Hour

Hz : Hertz

HRMS : High-resolution mass spectrometry

HMBC : Heteronuclear multiple-bond correlation

HMQC : Heteronuclear multiple quantum correlation

HOMO : Highest occupied molecular orbital

IR : Infrared

IEDDA : Inverse electron demand Diels-Alder reaction

^{i}Pr : Isopropyl

In : Indium

IMDA : Intramolecular Diels-Alder reaction

LDA : Lithium diisopropyl amide

LG : Leaving group

LA : Lewis acid

LUMO : Lowest unoccupied molecular orbital

Me : Methyl

MHz : Megahertz

MeOH : Methanol

mp : Melting point

mL : Milliliter

mg : Milligram

MS : Molecular sieves

m : Multiplet

N : Normality

NMR : Nuclear magnetic resonance

NHOMO : Next highest occupied molecular orbital

NMP : N-methyl pyrrolidinone

Nu : Nucleophile

O_2 : Oxygen

OTf : Triflate

p : para

ppm : Parts per million

pin : Pinacol

Ph : Phenyl

PTSA : *para*-toluene sulphonic acid

q : Quartet

rt : Room temperature

s : Singlet

t : triplet

TBAB : Tetrabutylammonium bromide

THF : Tetrahydrofuran

THQ : Tetrahydroquinoline

TFA : Trifluoroacetic acid

TFAA : Trifluoroacetic anhydride

TON : Turnover number

UV : Ultraviolet

PREFACE

Reactions involving the construction of new carbon-carbon and carbon-heteroatom bonds have a significant role in synthetic organic chemistry as it allows the synthesis of complex organic molecules with potent biological and material properties using short synthetic procedures. Transition metal catalyzed reactions played a major role in carbon-carbon and carbon-heteroatom bond forming reactions, which allow the economically benign synthetic transformation with readily available starting materials. Among the various transition metals investigated for coupling reactions, palladium catalyst stands out because of its easily convertible stable oxidation states (0 and +2) and the reactions proceeded with very high turnover numbers.

The prominent palladium-catalyzed cross coupling reactions that are widely employed in organic synthesis include Suzuki coupling, Heck coupling, Negishi coupling, Stille coupling, Kumada coupling, *etc*. In addition, palladium catalyzed allylic alkylation reaction accomplished a significant position among other palladium catalyzed coupling reactions and is popularly known as Tsuji-Trost reaction. Tsuji-Trost reaction proceeds through the formation of electrophilic π-allyl palladium intermediate and subsequently allylation occurs by the attack of a nucleophile to π-allyl palladium intermediate. Subsequent investigation on the palladium-catalyzed allylation reactions lights the way to nucleophilic allylation of ketones and imines. The nucleophilic allylation reaction proceeds through the generation of bis-π-allyl palladium complex from allyl stannanes in the presence of palladium catalyst. Further study on the reactivity of bis-π-allyl palladium intermediate disclosed the di-allylation reaction of activated olefins. Amphiphilicity of the bis-π-allyl palladium intermediate leads to the bis-allylation reaction. The reactivity of bis-π-allyl palladium and related amphiphilic palladium complexes with functionalized conjugated dienes and carbonyl compounds forms the main theme of this thesis entitled "**Study on the Reactivity of Bis-π-allyl and Related Palladium Intermediates with Functionalized 1,3-Dienes and Carbonyl Compounds & Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles.**"

The thesis is divided into four chapters. Appropriate references are given at the end of each chapter**.** A brief overview on the reactivity of mono- and bis-π-allyl palladium complexes is discussed in the first chapter. Bis-functionalization of activated alkenes using

bis-π-allyl palladium and related complexes were well studied. However, conjugate addition of these amphiphilic palladium complexes with substrates containing conjugated double bonds is less explored. The second chapter of the thesis describes the conjugate 1,4-addition of bis-π-allyl palladium and related complexes with functionalized dienes. The third chapter outlines palladium catalyzed interceptive decarboxylative 1,4-addition of allyl carbonates with the carbonyl group of squaric acid esters. The developed method is also compatible for the 1,2-interceptive addition of C-3 carbonyl group of N-substituted isatin derivatives and other electrophilic carbonyl group containing substrates such as acenaphthenequinone and diethylketomalonate.

Lewis acid catalyzed [4+2] cycloaddition between aromatic imines and electron-rich alkenes is known as Povarov reaction. The cycloaddition strategy is well utilized for synthesizing tetrahydroquinoline derivatives. The tetrahydroquinoline ring system is a very common structural motif and is found in numerous biologically active natural products and pharmacologically relevant therapeutic agents. Pentafulvenes are considered to be excellent candidates for constructing fused ring systems through intra- and intermolecular cycloaddition reactions. Cycloaddition reactions involving pentafulvenes are well studied, and they can participate as 2π, 4π or 6π candidates in various cycloaddition reactions. The detailed investigation on Lewis acid catalyzed Povarov reaction involving pentafulvenes and aromatic imines generated from phenylglyoxal and anilines constitute the subject matter of the fourth chapter of the thesis.

It may be mentioned that each chapter of the thesis is presented as an independent unit and therefore the structural formulae, schemes and figures are numbered chapter wise. A summary of the work is given towards the end of the thesis.

CHAPTER 1

Palladium-Catalyzed Allylation Reactions: A Brief Overview

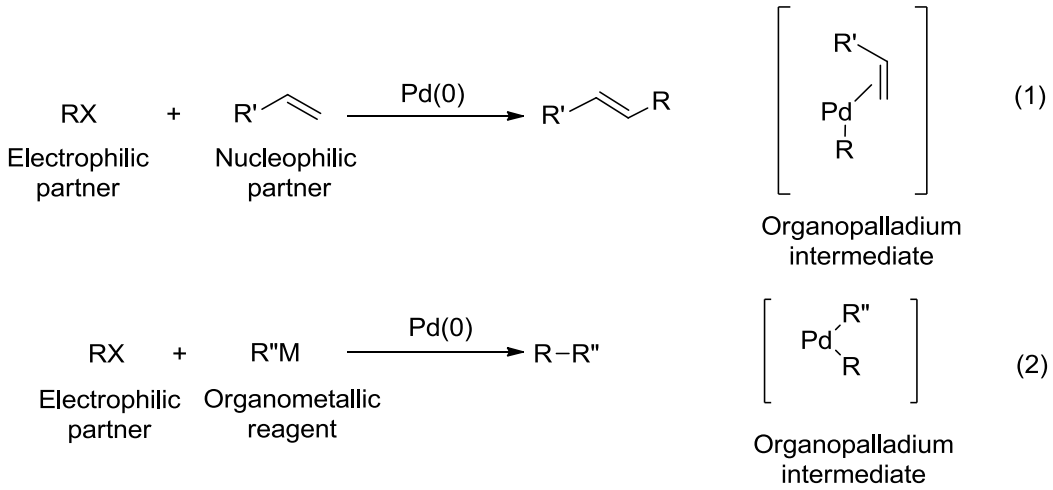
1.1. Introduction

Organic reactions involving the formation of carbon-carbon bond has been emerged as a valuable tool for the synthesis of both biologically relevant molecular scaffolds and organic materials with excellent mechanical and electrical properties. Among the various methods, transition metal catalyzed carbon-carbon bond forming strategy stands out since they require mild reaction conditions.[1] Over the last few decades, palladium has emerged as one of the most versatile and useful metals in organic synthesis, in particular for the formation of carbon-carbon bonds. The ready accessibility of two interconvertible stable oxidation states (0 and +2) and the simultaneous availability of one or more empty and filled nonbonding orbitals are the important factors responsible for the versatility and usefulness of palladium complexes as catalysts in organic synthesis.[2] Palladium can readily participate in reductive elimination, carbometallation, migratory insertion and nucleophilic substitution reactions which makes palladium as an efficient catalyst for carbon-carbon bond formation.

The importance of the palladium catalyzed carbon-carbon bond formation is reflected by 2010 Nobel Prizes in Chemistry, which was awarded jointly to Heck, Negishi and Suzuki for the invention of palladium-catalyzed cross coupling reactions in organic synthesis. Within a short time, the area of palladium-catalyzed coupling reactions has experienced a tremendous growth.[3] The transition of stoichiometric use of palladium based reagents to catalysts with impressive turnover numbers (TONs) has achieved in just a few decades. Discovery of the palladium-catalyzed oxidation of ethylene to acetaldehyde, later became the industrially relevant Wacker process has made a significant influence in organic synthesis. Subsequent investigation on palladium-catalyzed reactions paved the way for the discovery of new methods for the creation of carbon-carbon and carbon-hetero atom bonds.[1]

1.2. Palladium Catalyzed Cross Coupling

The main principle of palladium-catalyzed cross coupling is that two molecules are assembled on the metal *via* the formation of metal-carbon bonds.[1] In this way, the carbon atoms bound to palladium are brought very close to one another. In the next step, they couple to one another and this leads to the formation of a new carbon-carbon single bond.[1] There are two types of cross coupling reactions according to this principle that has become important in organic synthesis. These two categories of reactions are shown in Scheme 1.1.

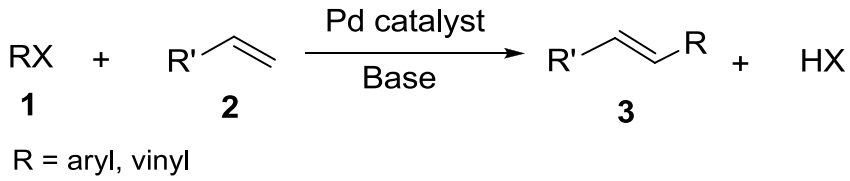


Scheme 1.1

Zero-valent palladium catalyzes both reactions, and both reactions employ an organohalide RX (or analogous compound) as the electrophilic coupling partner. However, the nucleophilic coupling partner differs in the two reactions. In the first type (eq. 1) it is an olefin whereas in the second category (eq. 2) it is an organometallic compound R"M.[1] In this way, the palladium-catalyzed cross coupling reactions in equations 1 and 2 complements one another with regards to the nucleophilic coupling partner. A common feature of the two types of cross couplings is that the organic groups from the reagents are assembled on palladium. Furthermore, both reactions begin by generating an organopalladium complex RPdX from the reaction of the organic halide with Pd(0). The organopalladium species RPdX will subsequently react with the nucleophilic coupling partner. The reaction conditions are very mild since they utilize organic halides and olefins/organometallic compounds R"M, where M is typically zinc, boron or tin.[1] A brief overview of various palladium catalyzed cross-coupling reactions is discussed in the successive sections.

1.2.1. Heck reaction

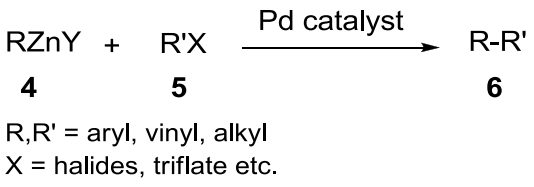
The palladium catalyzed Mizoroki-Heck reaction is the most efficient route for the vinylation of aryl/vinyl halides or triflates. In the late 1960s, Heck reported that arylated alkenes were formed in the reaction of alkenes with a stoichiometric amount of [Ar-Pd-Cl] or [Ar-Pd-OAc], generated *in situ* by reacting ArHgCl with $PdCl_2$ or ArHgOAc with $Pd(OAc)_2$ respectively.[4,5,6] In 1971, Mizoroki *et al.* reported preliminary results on the $PdCl_2$ catalyzed arylation of alkenes by iodobenzene in the presence of potassium acetate as a base.[6,7] In 1972, Heck and Nolley improved the reactions by using $Pd(OAc)_2$ as catalyst and *n*-Bu_3N as a base.[8] The reactions were performed without any solvent or in N-methyl pyrrolidone (NMP) at 100 ^oC.[6] In general, the palladium catalyzed carbon-carbon coupling between aryl halides or vinyl halides **1** and activated alkenes **2** in the presence of a base is referred as the Heck Reaction.



Scheme 1.2

1.2.2. Negishi coupling

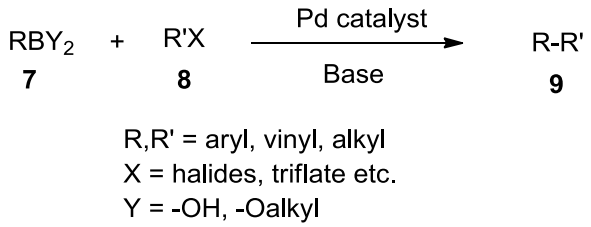
In 1976, Negishi initiated studies to explore more chemoselective organometallic species in the palladium-catalyzed couplings with organohalides. In the earlier attempts, Negishi employed organozirconium or organoaluminum compounds as coupling partners.[9] Motivated from the results of these studies Negishi and coworkers tried even less reactive organometallic species as coupling partners. The breakthrough came in 1977 when Negishi introduced organozinc compounds **4** as the nucleophilic coupling partners in palladium-catalyzed cross coupling, and now it is popularly known as the Negishi reaction.[1,10]



Scheme 1.3

1.2.3. Suzuki coupling

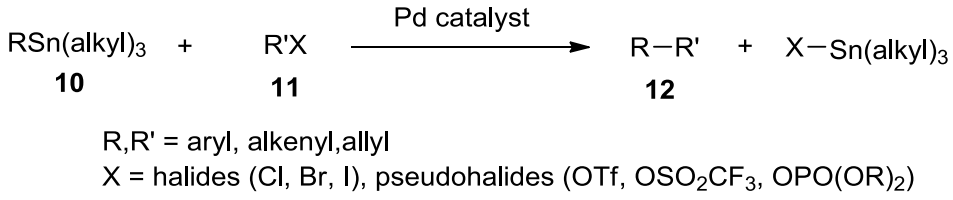
In 1979 Suzuki and co-workers reported the use of organoboron compounds **7** as coupling partners with vinyl and aryl halides **8** in palladium catalyzed cross coupling reaction.[11] Base activates organoboron reagents to boronate intermediates and facilitates the transfer of organic group from boron to palladium (transmetallation). A significant advancement came after the observation that aryl boronic acids can participate as coupling partners in the palladium catalyzed cross coupling reaction. Boron compounds are non-toxic, and the reaction can be performed under very mild conditions which have made the reaction popular in the pharmaceutical industry.



Scheme 1.4

1.2.4. Stille reaction

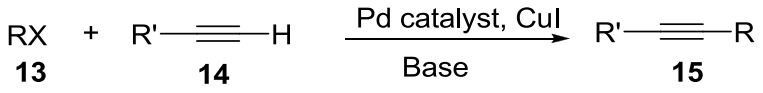
The palladium catalyzed coupling of organotin compounds (organostannanes) **10** with various organic electrophiles **11** is known as Stille coupling.[12] The reaction takes place generally under mild conditions and is compatible with different electrophiles like halides, triflates, sulfonates or phosphates. However, the toxicity of organostannanes limits its application in pharmaceutical industry.



Scheme 1.5

1.2.5. Sonogashira reaction

Sonogashira coupling reaction is the palladium catalyzed coupling of vinyl or aryl halides **13** with terminal alkynes **14** in the presence of copper(I) co-catalyst and an amine base.[13] This coupling reaction is widely used to synthesize conjugated enynes or aryl alkynes, which have applications in natural product chemistry, pharmaceuticals and material science.[14]

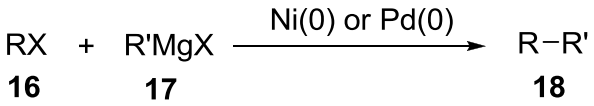


R' = alkyl, aryl, vinyl
R = aryl, benzyl, vinyl
X = halides (Br, Cl, I), OTf

Scheme 1.6

1.2.6. Kumada coupling

Kumada cross coupling reaction is the reaction of an organohalide **16** with an organomagnesium compound (Grignard reagent) **17** to give the coupled product **18** using a palladium or nickel catalyst.[15]

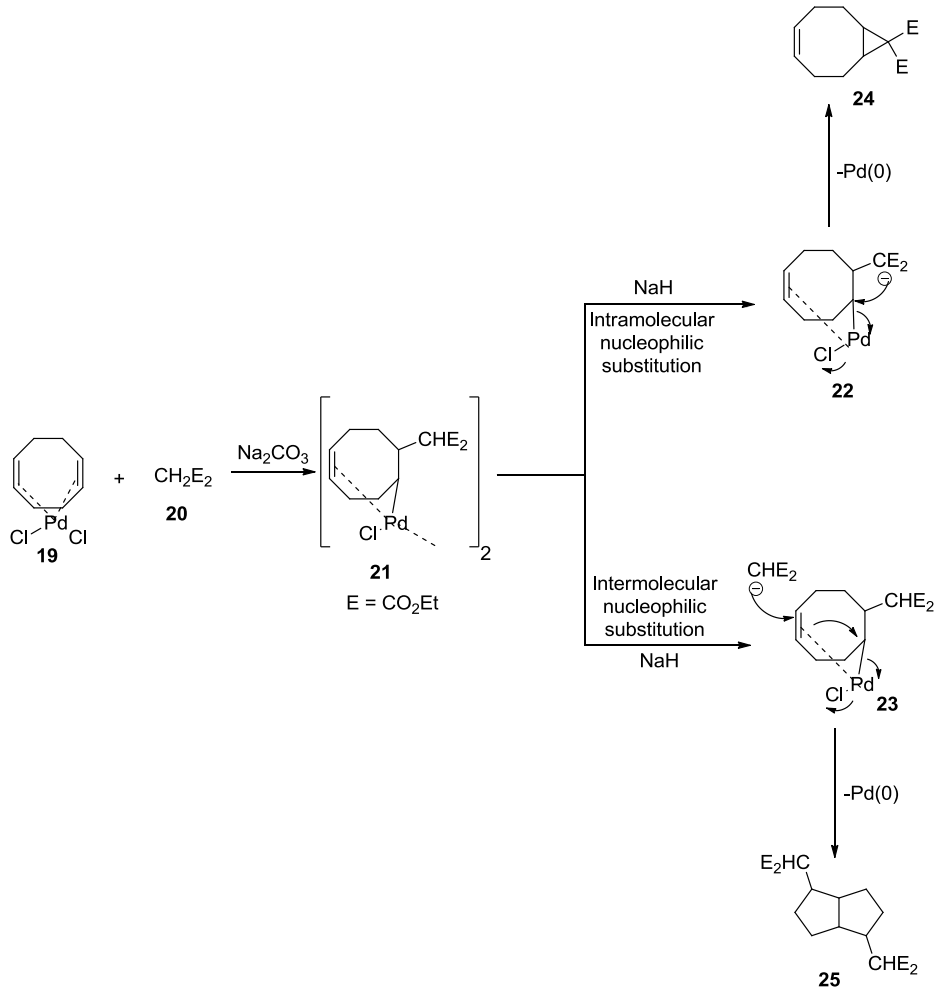


R = alkyl, aryl, vinyl
R' = aryl, vinyl
X = halides (Br, Cl, I)

Scheme 1.7

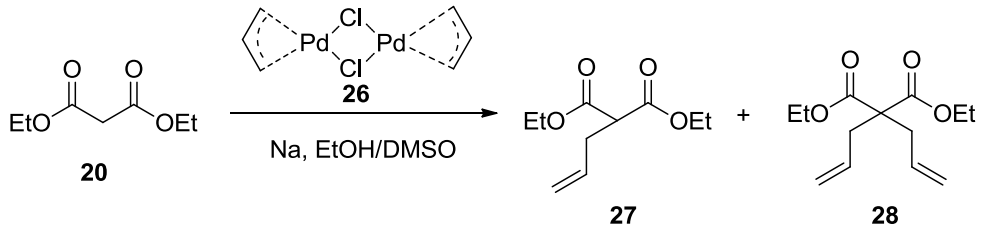
1.3. Palladium Catalyzed Allylation: Tsuji-Trost Reaction

The palladium mediated carbon-carbon bond forming reactions started with the pioneering work reported by Tsuji in 1965.[16] A mixture of $PdCl_2$(cyclooctadiene) complex **19** and diethyl malonate **20** under basic conditions successfully generated the carbo-palladation products **24** and **25** at room temperature by intra- and intermolecular nucleophilic substitution. This discovery led to the development of the powerful palladium chemistry.



Scheme 1.8

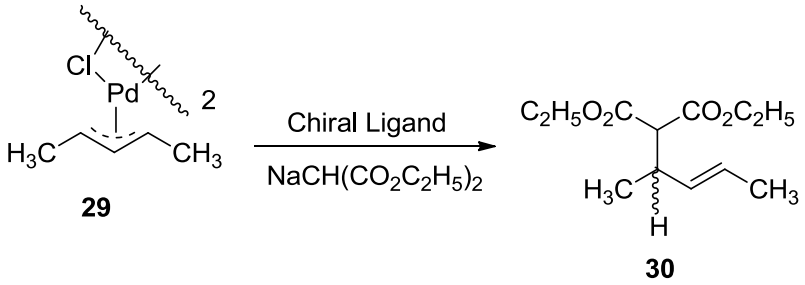
Subsequently, Tsuji investigated the reaction of allylpalladium chloride dimer **26** with the sodium salt of diethyl malonate **20**. The reaction afforded a mixture of mono- and di-allyl ethyl malonate **27** and **28**.[17] Construction of carbon-carbon bonds to generate secondary and tertiary centers is a powerful method in synthetic chemistry.



Scheme 1.9

The catalytic version of the allylation of nucleophiles *via* π-allylpalladium intermediates was reported independently by Hata *et al.* and Atkin *et al.* in 1970 using allylic alcohol as well as esters and allyl phenyl ethers as substrates.[18,19] Trost later introduced asymmetric allylic

alkylation reaction with the aid of chiral phosphine ligands in 1973.[20] Among the various chiral ligands tried, Trost observed that sparteine and (+)-ACMP [*o*-anisylcyclohexylmethylphosphine] furnished higher optical yields compared to (+)-DIOP [2,3-*O*-isopropylidene-2,3-dihydroxy-l,4-bis(diphenylphosphino)butane] and (-)-DMIP [dimenthylisopropylphosphine].



Scheme 1.10

Thus, the palladium catalyzed allylation of nucleophiles *via* π-allylpalladium complex **31** (figure 1.1) has been widely referred as Tsuji-Trost reaction.

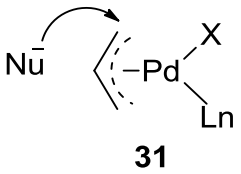
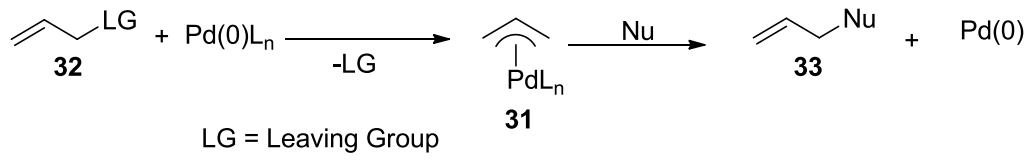


Figure 1.1 π-allylpalladium intermediate

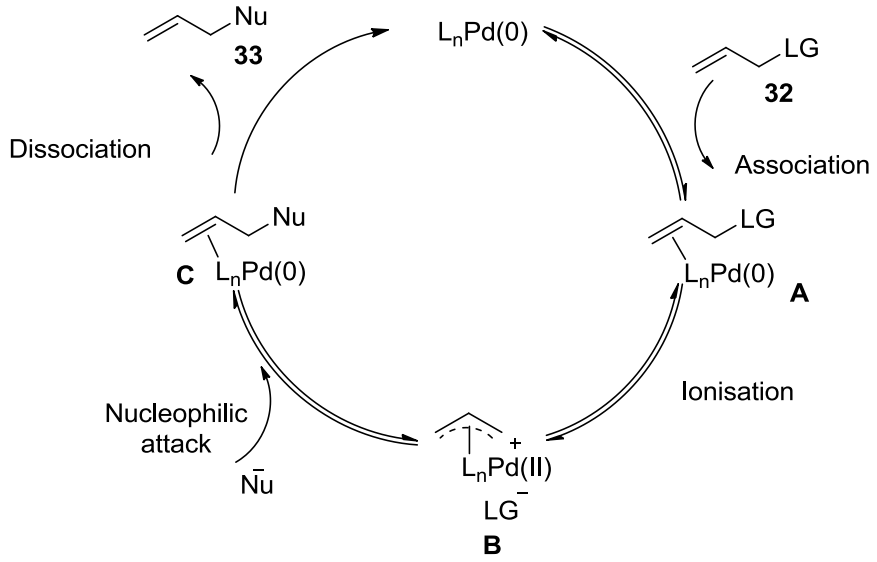
Tsuji-Trost reaction has been well utized for architecting synthetically and medicinally valuable compounds by employing various carbon, nitrogen and oxygen based nucleophiles. Also, the reaction compatible with allylic functionality containing different leaving groups such as acetates, halides, carbonates, epoxides and phosphates.[21] Introduction of phosphine ligands to the catalytic system of allylation reaction improved the reactivity of reactants and enabled numerous asymmetric allylic alkylation strategies. This modification greatly expands the utility of this reaction for many synthetic applications. A schematic representation of the Tsuji-Trost reaction is shown in Scheme 1.11.



Scheme 1.11

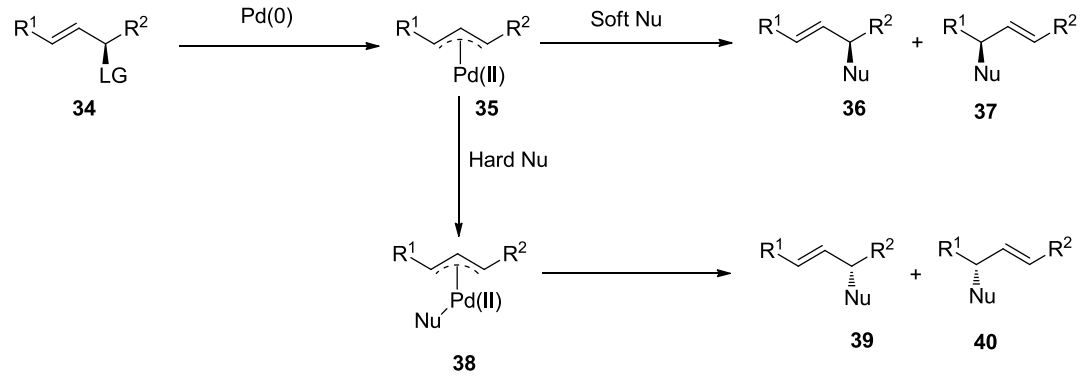
1.3.1. Mechanism and catalytic Cycle

The initial step of the Tsuji-Trost reaction involves the co-ordination of the Pd(0) complex to the allylic substrate **32** to generate a η^2- palladium complex **A** (Scheme 1.12). Thereafter, *via* oxidative addition, a (η^3-allyl)Pd complex **B** with the leaving group as a counter ion is formed. The oxidative addition of these types of complexes is also referred as ionization. The resulting (η^3-allyl)Pd complex reacts with the nucleophile, yielding a η^2-complex **C**. In the final step, the product is released after dissociation from the Pd(0) complex.



Scheme 1.12 Catalytic cycle for palladium catalyzed allylic alkylation

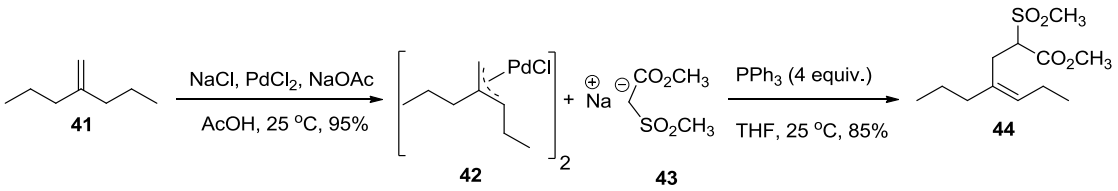
The ionization step occurs with inversion of configuration and the nucleophilic attack also proceeds with inversion when using soft, stabilized carbon nucleophiles (e.g. malonates) forming the final product with an overall retention of stereochemistry (Scheme 1.13). Hard unstabilized carbon nucleophiles (e.g. organometallic reagents) react with the η^3-allyl complex by another mechanism: first a transmetallation to Pd occurs and then transfer to an allylic carbon atom by reductive elimination. Thus the final product forms with an overall inversion of stereochemistry (Scheme 1.13).[22] Heteroatom based nucleophiles such as amines[23] and alcohols[24] are also feasible, and they usually react *via* inversion, as for the stabilized carbon nucleophiles. Carboxylates can react with both soft and hard nucleophiles, depending on the reaction conditions.[25]



Scheme 1.13 Stereochemical outcome with soft and hard nucleophiles

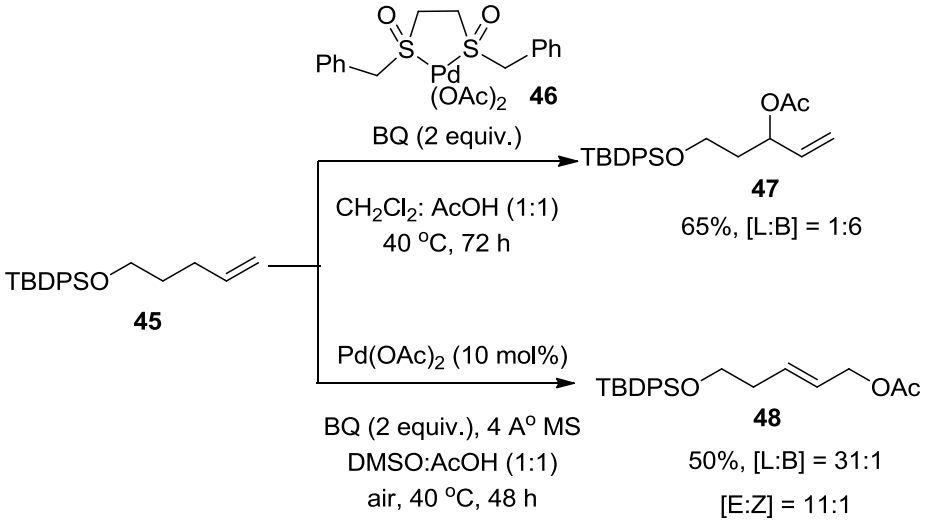
1.4. Palladium Catalyzed Allylic C-H Alkylation

In 1973, Trost and Fullerton observed that allylic alkylation of non-functionalized alkenes could proceed in the presence of stoichiometric amounts of palladium(II) reagent.[26] The reaction of alkene **41** with $PdCl_2$ in the presence of sodium chloride and sodium acetate in acetic acid furnished the dimeric palladium complex **42** in almost quantitative yield. Treatment of the palladium complex with the anion of methyl (methylsulfonyl)acetate afforded **44** as a single stereoisomer. Furthermore, the addition of ligand, triphenylphosphine increased the electrophilic character of the π-allylpalladium and facilitated the nucleophilic alkylation.



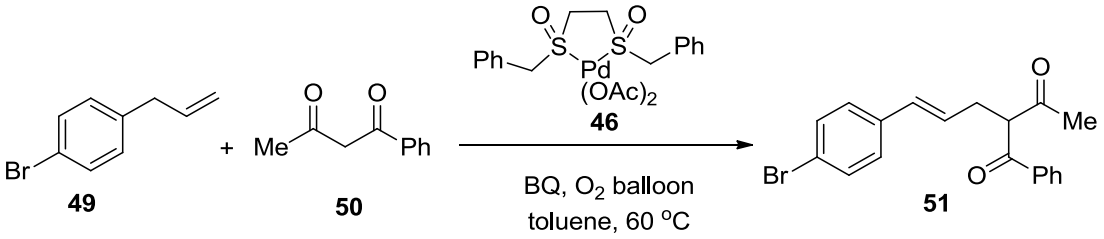
Scheme 1.14

After nearly half a century, significant progress has been made by White *et al.* in the area of allylic C-H functionalization of acyclic alkenes by introducing a bis-sulfoxide/$Pd(OAc)_2$ catalyst **46**.[27] One of the difficulties in the oxidation of olefinic compound is the formation of Wacker type products. White *et al.* demonstrated a sulfoxide ligated Pd(II) salts which selectively promote C-H oxidation over Wacker oxidation and control the regioselectivity in C-H functionalization reactions.[27] This system has proven general for allylic C-H functionalization, esterification, amination, alkylation, Heck addition and dehydrogenation of terminal olefins *via* a π-allylpalladium intermediate.[28, 29]



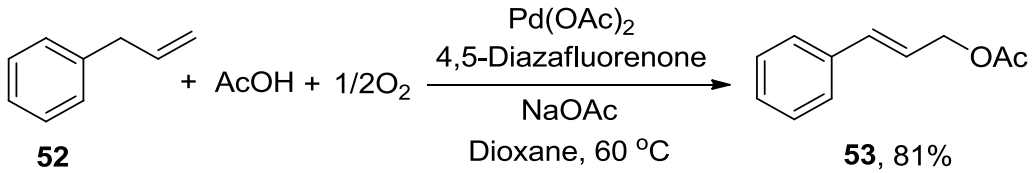
Scheme 1.15

Shi *et al*. demonstrated the intra/intermolecular palladium(II) catalyzed allylic alkylation between allylic sp^3 C-H bond and methylenic sp^3 C-H bond *via* C-H activation.[30] In presence of 1,2-bis(benzylsulfinyl)ethane palladium acetate **46** catalyst and the oxidant benzoquinone, allylbenzene **49** was alkylated with benzoyl acetone **50**.



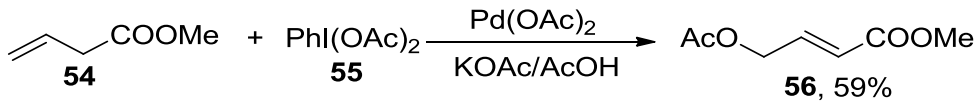
Scheme 1.16

Later on, Kaneda *et al.*[31] and Stahl *et al.*[32] independently developed palladium catalyzed acetoxylation of terminal alkenes under aerobic conditions in the absence of BQ. The ligand 4,5-diazafluorenone was found to be essential for the allylic C-H bond functionalization. 4,5-Diazafluorenone facilitates C-O reductive elimination from π-allyl-Pd(II) intermediate and successfully replaced benzoquinone oxidant in the catalytic step.



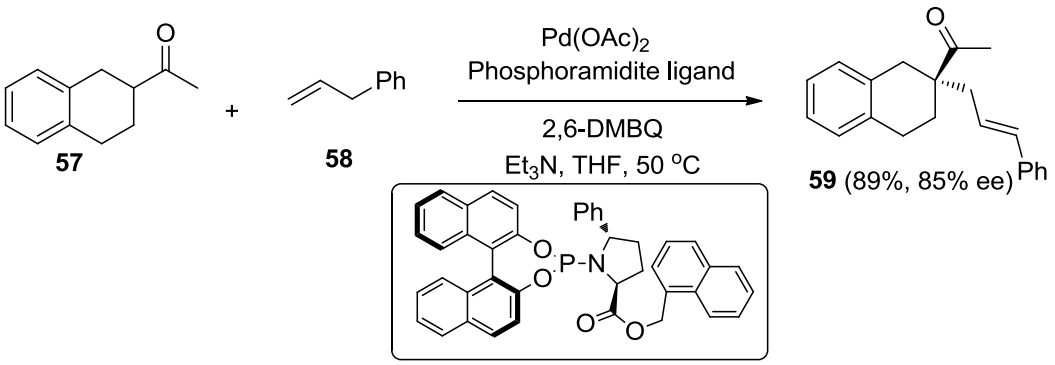
Scheme 1.17

Recently hypervalent iodine **55** has been explored as an oxidant to achieve allylic C-H oxygenation and amination.[33,34,35] Szabo and co-workers proposed that the allylic C-H acetoxylation proceeds through a Pd(II/IV) catalytic cycle and the (η^3-allyl)palladium(IV) complex is the key intermediate in iodonium salt mediated oxidation reactions.[33]



Scheme 1.18

Very recently, Trost and co-workers designed pyroglutamic acid derived phosphoramidite ligands for the enantioselective allylic C-H activation and demonstrated the synthesis of chiral 2,2,-dialkyl-1,2-diketones.[36] The ligand is also compatible for the traditional palladium-catalyzed asymmetric allylic alkylation. Covell and White reported that phosphine ligands were unsuitable for allylic C-H activation under the oxidative conditions.[37]



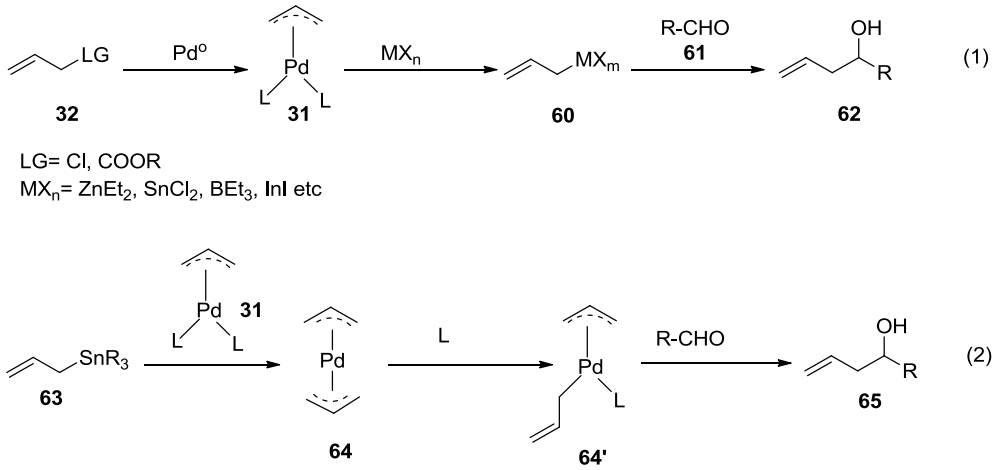
Scheme 1.19

1.5. Nucleophilic Reactivity of π-Allyl Palladium Complex

Palladium-catalyzed nucleophilic allylic substitution is a well explored area in synthetic organic chemistry. In the traditional palladium catalyzed allylic alkylation reactions, the allyl moiety has an electrophilic character which reacts with nucleophilic substrates. Application of electrophilic reagents in allylic substitution requires umpolung electrophilic reactivity for the allylic moiety in η^3-allylpalladium complexes. Possibilities to extend the synthetic scope of the allyl-palladium chemistry to electrophilic reagents, such as aldehydes, imines and Michael acceptors have been the subject of great interest in mechanistic and in synthetic organic chemistry. The most significant challenge in these processes is to generate an allyl-palladium intermediate with a nucleophilic allyl moiety. There exist two major strategies to achieve this

umpolung reactivity of the allyl functionality. The first strategy involves the transformation of the electrophilic η^3-allylpalladium intermediate **31** into nucleophilic allyl-metal species by treatment with low valent metal reagents (such as $ZnEt_2$, BEt_3, InI, or $SnCl_2$).[38] These highly reactive species subsequently react with electrophiles such as aldehydes **61** directly. The latter approach is based on the generation of bis-π-allylpalladium intermediates **64** from allylstannanes **63** followed by the nucleophilic attack of one of the allyl moieties with various types of electrophiles (Scheme 1.20).

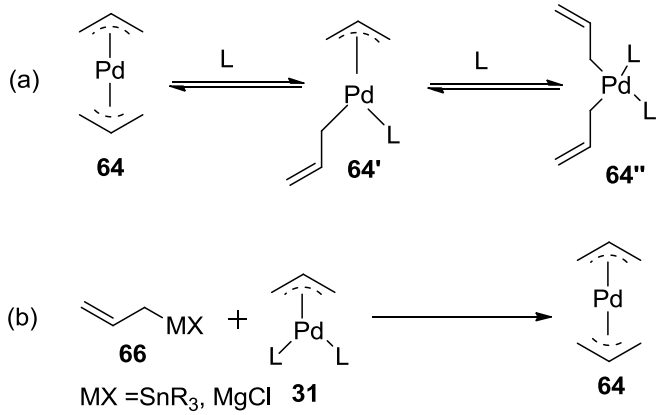
The difference between these two strategies is that in the second process (eq. 2, Scheme 1.20) the electrophile reacts directly with the allyl moiety of the bis-π-allylpalladium complex, while in the former case (eq. 1, Scheme 1.20) the highly reactive allyl-metal species attack the electrophile without any assistance of palladium. This mechanistic difference leads to difference in reactivity and selectivity in catalytic applications.[39]



Scheme 1.20

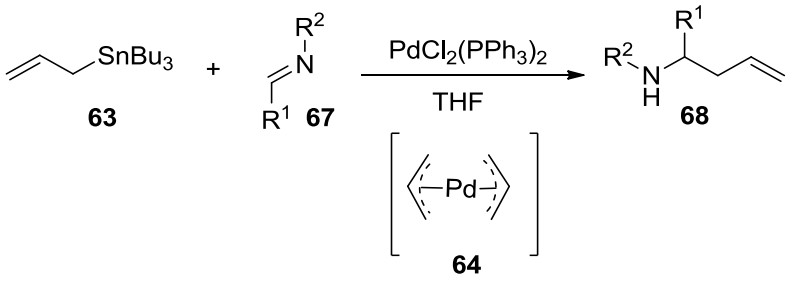
1.5.1. Bis-π-allyl palladium complexes

A wide range of palladium catalyzed allylation reactions of electrophiles involving bis-π-allylpalladium intermediates **64** has been established. These complexes incorporate with two allyl moieties that can bind with different hapticity to palladium (Scheme 1.21). These π-allyl palladium complexes may interconvert by ligand coordination. Bis-π-allylpalladium complexes can easily be generated by the reaction of mono-allylpalladium complexes and allyl-metal species, such as Grignard reagents (Scheme 1.21).[40]



Scheme 1.21. (a) Bis-π-allylpalladium complexes with different hapticity; (b) Generation of bis-π-allyl palladium complexes from allyl-metal species and mono-allylpalladium complexes

Yamamoto and co-workers generated bis-π-allylpalladium intermediate **64** from allyltributylstannane **63** in the presence of catalytic amount of palladium reagent. The bis-π-allylpalladium complex formed is readily attacked by electrophiles such as aldehydes or imines and delivers the corresponding homoallylic alcohols and homoallylic amines respectively.[41] NMR spectroscopic analysis supports that the reaction is proceeding through the formation of intermediate $(\eta^3\text{-allyl})_2$ palladium complex **64.**[40]

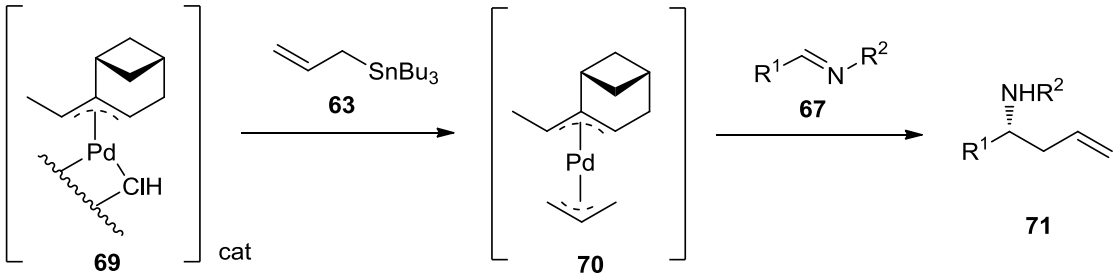


Scheme 1.22

Since phosphine ligand, such as PPh_3, is also present under applied conditions, it was assumed that **64** coordinates with a phosphine ligand and the actual substrate of the electrophilic attack is the η^1,η^3- allylpalladium complex **64'** (Scheme 1.21). The nature of the allyl-metal interactions is fundamentally different in $(\eta^3\text{-allyl})$palladium and $(\eta^1\text{-allyl})$palladium complexes. In $(\eta^3\text{-allyl})$palladium complexes, the allyl system donates electrons to the PdL_2 fragment, and therefore, π-acceptor ligands (L) such as phosphines, activate the allyl moiety towards the nucleophilic attack. On the other hand, in $(\eta^1\text{-allyl})$palladium complexes the palladium atom donates electrons to the allyl moiety.

Accordingly, the allyl moiety can be activated toward electrophilic reagents by the employment of electron donating ligands on palladium.[42]

Yamamoto and co-workers also described a catalytic asymmetric version of the allylation reaction of aldimines.[43] In this process, the bis-π-allylpalladium intermediate **70** is formed from (1S)-*β*-(-)pinene based mono-allylpalladium complex **69** (Scheme 1.23). Subsequently, this complex underwent electrophilic attack by aldimine **67** afforded homoallylamine **71** up to 91% enantiomeric excess. The best results were accomplished by using benzylimine derivatives. It was found that the chiral information from the η^3-allyl ligand is propagated in the electrophilic attack involving bis-π-allylpalladium intermediate **70**. The sterically bulky π-allyl group acts as a nontransferable π-allyl ligand, whereas the other allylic moiety reacts with imines in an asymmetric fashion.



Scheme 1.23

1.5.2. Amphiphilicity of bis-π-allyl palladium complex: A double allylation strategy

Bis-π-allylpalladium complex **64** reacts with electrophiles such as aldehydes and imines to form the carbon-carbon bond.[40] In this reaction, one of the two allyl groups of the bis-π-allylpalladium complex reacts with electrophiles and the other stays on the palladium atom. In 1997, Yamamoto and co-workers introduced the catalytic amphiphilic reactivity of bis-π-allylpalladium complex; it reacted with both nucleophilic and electrophilic carbons at once resulting the double allylated products.[44]

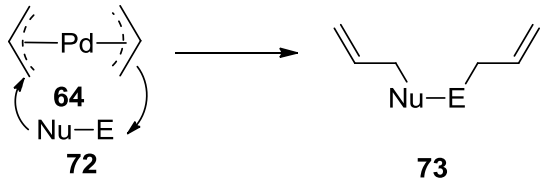
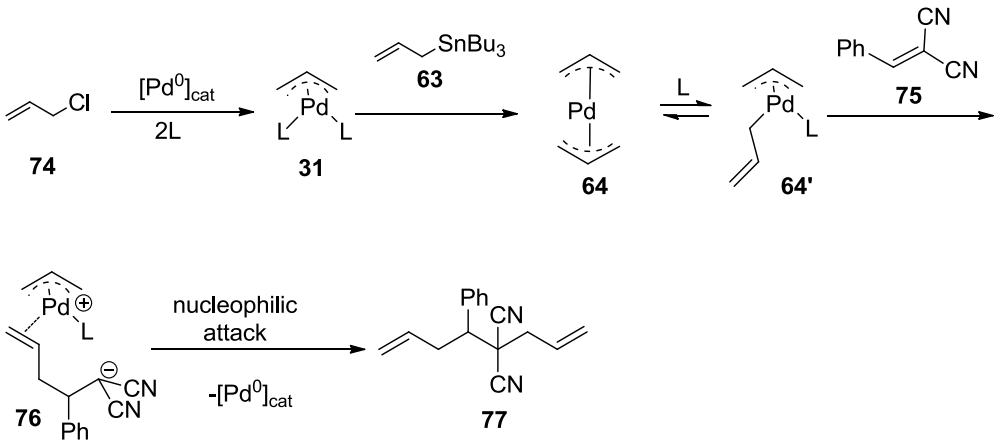


Figure 1.2. Amphiphilic reactivity of bis-π-allyl palladium complex

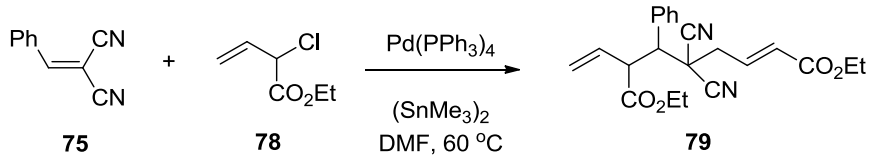
The bis-allylation of activated electrophilic olefin was achieved by reacting with *in situ* generated bis-π-allyl palladium complex from allyl chloride **74** and allyltributylstannane **63**. The reaction of phenylethylidene malononitrile **75**, allyltributylstannane **63** and allyl chloride **74** in THF was carried out in the presence of $PdCl_2(PPh_3)_2$ under an argon atmosphere at room temperature afforded the intercepted diallyl product 4,4-dicyano-5-phenyl-1,7-octadiene **77** in excellent yield (Scheme 1.24). Allylic bromide, iodide, acetate and alcohol were found to be less efficient to replace allyl chloride. Different substituted activated olefins underwent the double allylation and furnished the corresponding 1,7-octadienes in high yields. Among the electron withdrawing groups, one group must be -CN and the other group can be -CN, $-SO_2Ph$ or $-CO_2Et$.[44]



Scheme 1.24

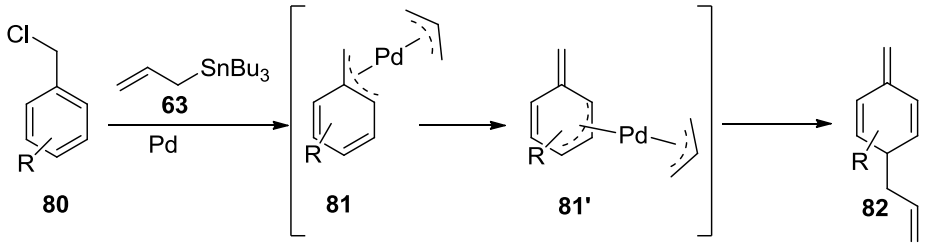
Mechanism of this reaction is particularly interesting. The first step of the reaction is the oxidative addition of the palladium(0) catalyst to allyl chloride to give a mono-allylpalladium complex **31** (Scheme 1.24). This complex undergoes transmetallation providing the bis-π-allylpalladium intermediate **64** which is in equilibrium with η^1,η^3- allylpalladium complex **64'**. Subsequently, the η^1-allyl moiety of **64'** reacts with alkylidene malononitrile **75** generating a π-allylpalladium complex and a malononitrile anion **76**. This malononitrile derivative undergoes the second allylation by the nucleophilic attack with cationic π-allyl palladium counter ion to give compound **77**. This peculiar behavior of bis-π-allylpalladium complexes involving an initial nucleophilic attack followed by an electrophilic attack is classified as amphiphilic (or ambiphilic) reactivity. Control of the regioselectivity became an important issue when substituted allyl chlorides and allyl stannanes were employed as reagents. An important feature is that the reaction with mono-alkyl-substituted precursors usually gives a poor regioselectivity.[42]

Bis-allylation reactions can also be performed by using the functionalized allyl chloride precursor together with hexamethylditin (Scheme 1.25).[45] This catalytic transformation proceeds with very high regioselectivity. A particularly interesting mechanistic aspect of this reaction is that palladium catalyzes three processes in each catalytic cycle: (a) generation of the allylstannane precursor from allyl chloride and hexamethylditin, (b) the electrophilic attack and (c) the nucleophilic attack.[45]



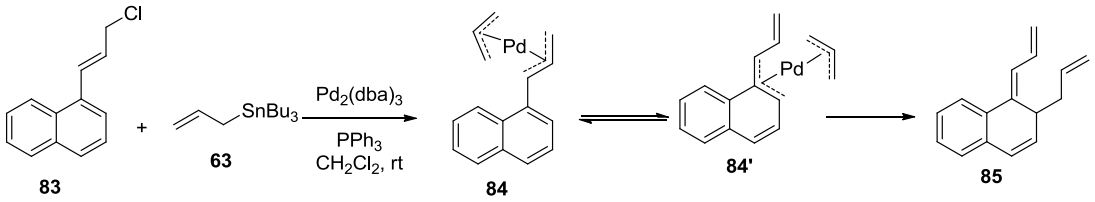
Scheme 1.25

In 2001, Yamamoto and Bao reported an interesting palladium catalyzed allylative de-aromatization reaction of benzylic chlorides **80** with allyltributyltin **63** through the formation of bis-π-allylpalladium intermediate.[46] This process appears to involve the formation and isomerization of the η^3-allyl-η^3-benzylpalladium intermediate **81** and **81'** which led to **82**, where an allyl group is linked at *para* position relative to the exocyclic methylene group.



Scheme 1.26

Recently, Bao *et al.* extended the allylative de-aromatization strategy to naphthalene derivatives bearing allyl chloride units.[47] The reaction is proceeding through the formation and isomerization of bis-π-allylpalladium intermediate **84** to **84'**, which is then converted to *ortho*-allylated product **85** (Scheme 1.27). The de-aromatization of the benzene derivatives bearing allyl chloride was not feasible and afforded only the Stille cross-coupling product.[47]



Scheme 1.27

1.5.3. Bis-functionalization of activated olefins by related π-allyl palladium complexes

Yamamoto and co-workers conducted a detailed investigation on the reactivity of π-allyl palladium complexes with activated olefins.[48] These reactions worked when the olefins contain at least one electron withdrawing groups such as nitrile, which indicate the special nature of those olefins in the palladium catalyzed processes. The basic principle of bis-functionalization reactions relates to the amphiphilic nature of π-allylpalladium complexes **A** and **B** (figure 1.3). These complexes react with both nucleophilic and electrophilic carbons of activated olefins at once to produce bis-functionalized products. Some of the palladium catalyzed bis-functionalization of activated olefins are described in the following sections.

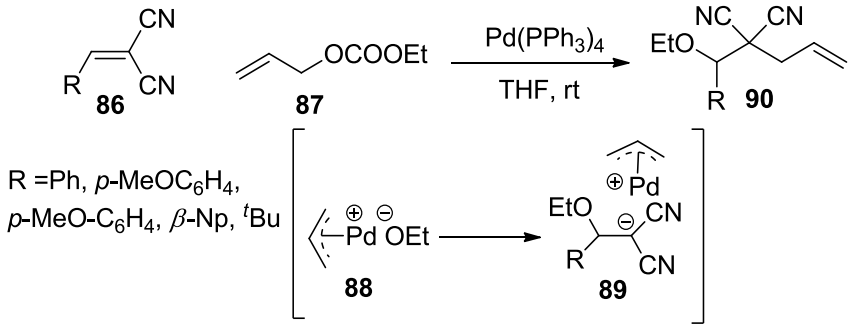
A **B**

X, Y, Z = carbon or heteroatom

Figure 1.3 Amphiphilic π-allylpalladium complexes

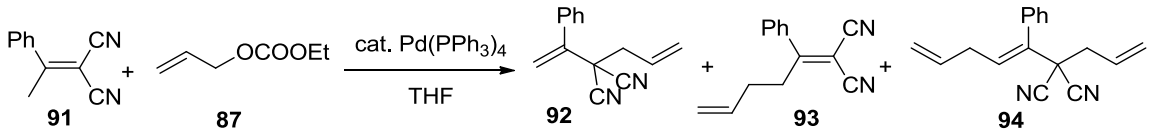
1.5.3.1. Alkoxy-allylation

In 1998, Yamamoto and co-workers reported the *β*-alkoxy-α-allylation of activated olefins by the interceptive addition of allyl carbonate in the presence of a palladium catalyst.[49] The reaction is proceeding through *in situ* generation of π-allylpalladium complex **88** by the oxidative addition of the allylic carbonate **87** to palladium(0) catalyst. A subsequent attack of alkoxide anion of intermediate **88** with olefin **86** gives the intermediate **89**. Further, reductive elimination of palladium(0) from **89** delivers the product **90** (Scheme 1.28).



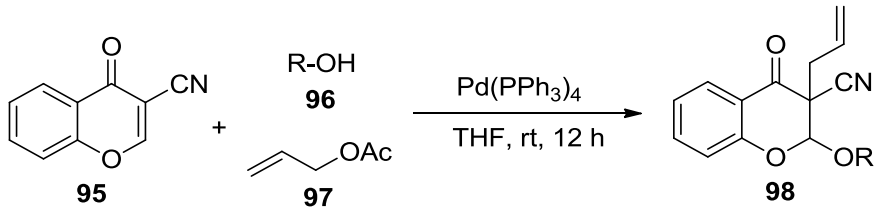
Scheme 1.28

When the decarboxylative alkoxy allylation reaction performed with tetra-substituted activated olefins **91**, afforded a mixture of α-adduct **92**, β-adduct **93** and α,γ-adduct **94** (Scheme 1.29). The alkoxy allylation adduct, which was the sole product in the previous case of trisubstituted olefins, was not observed.



Scheme 1.29

In 2007, the same research group had reported the alkoxy allylation of chromone by palladium catalyzed three component coupling with allyl acetate and alcohols.[50] This method is useful for the diversity-oriented synthesis of chromones. However, these reactions are limited to 2-cyano and 2-formyl chromones.

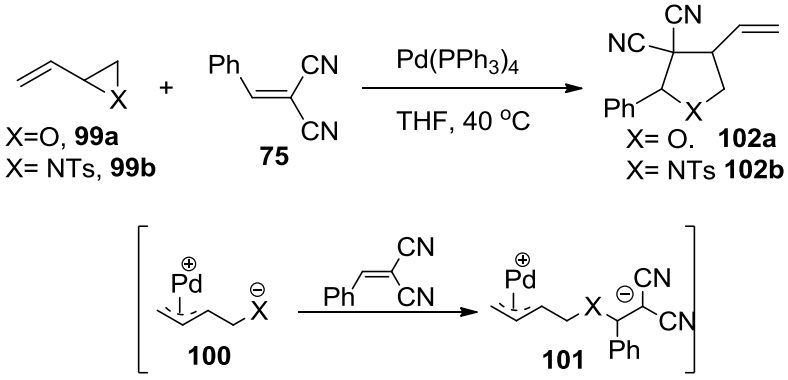


Scheme 1.30

1.5.3.2. Cycloaddition reactions of π-allyl palladium complex

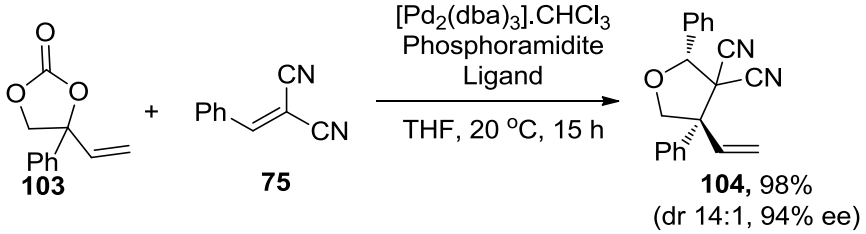
Yamamoto and co-workers also utilized the π-allyl palladium chemistry for cycloaddition reactions. Palladium-catalyzed [3+2] cycloaddition of vinylic oxirane **99a** and aziridine **99b** with activated olefin **75** provided five-membered cyclic ether **102a** and pyrrolidine derivative **102b**, respectively.[51,52] Oxidative addition of Pd(0) to **99** generates the π-allylpalladium complex **100**. The Michael addition of the heteroatomic nucleophile in **100**

to activated olefin **75** gives **101**, which undergoes intramolecular nucleophilic attack at the π-allylic carbon atom provided cyclized products **102**.



Scheme 1.31

Recently Zhang *et al.* developed an efficient method for the diastereo- and enantioselective construction of vicinal all-carbon quaternary stereocenters through palladium catalyzed decarboxylative cycloaddition of vinyl ethylene carbonates **103** with activated Michael acceptors.[53] In the presence of $[Pd_2(dba)_3]\cdot CHCl_3$ and a phosphoramidite ligand, the reaction furnished multi-functionalized tetrahydrofurans **104** bearing vicinal quaternary stereocenters in high yields with a high level of absolute and relative stereocontrol (Scheme 1.32).

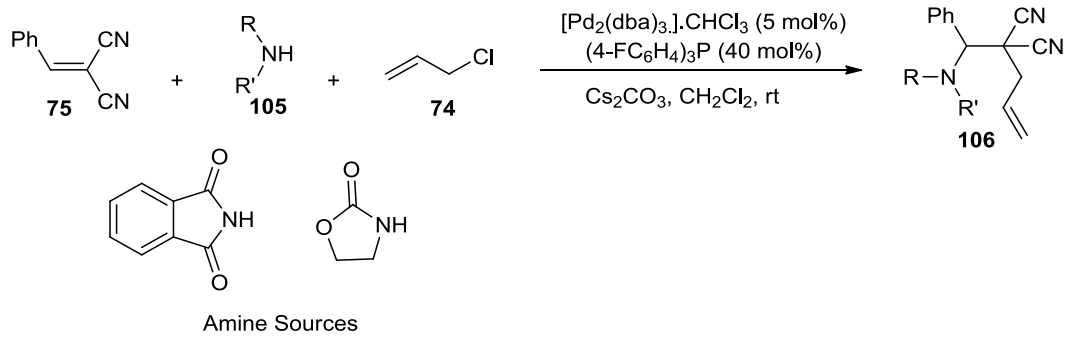


Scheme 1.32

1.5.3.3. Aminoallylation

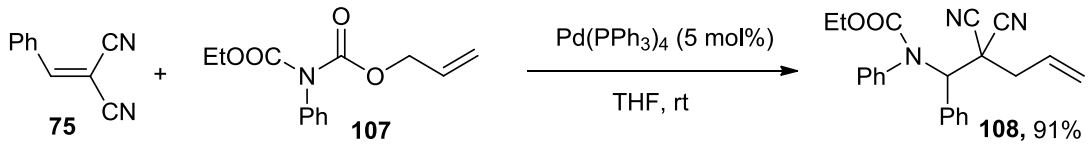
Palladium-catalyzed aminoallylation reaction of activated olefins has been realized by using phthalimide and oxazolidinone as amine sources. The three component aminoallylation reaction of the activated olefins with the phthalimide and allyl chloride **74** was achieved by $[Pd_2(dba)_3].CHCl_3/P(4\text{-}FC_6H_4)_3/Cs_2CO_3$ catalyst system at room temperature.[52] Cyclic amines having an electron withdrawing group is essential for the reaction, since higher electron density on a nitrogen atom induces the direct allylation to the π-allylpalladium

complex, and the palladium(II) complex promotes the Michael addition of the nitrogen nucleophiles to the activated olefins. Authors also demonstrated the feasibility of aminoallylation with activated olefins derived from Meldrum's acid yielding the corresponding adducts in good to excellent yields.[53]



Scheme 1.33

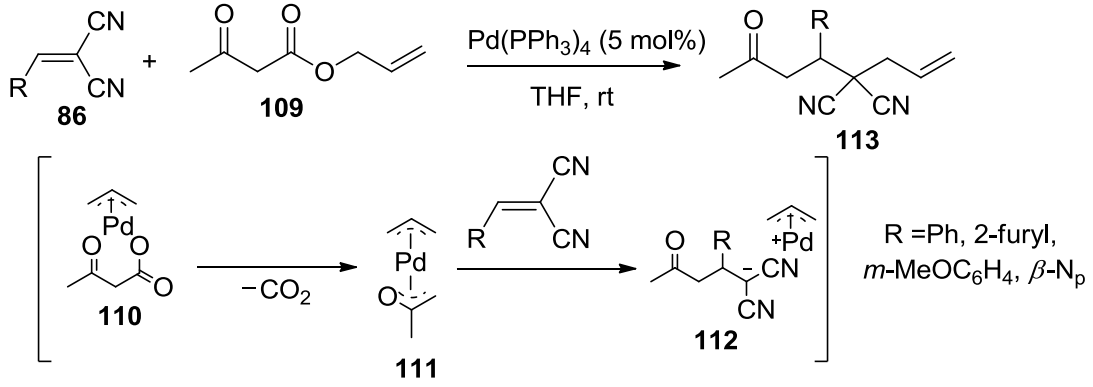
Another strategy for amino-allylation is the decarboxylative addition of allyl carbamates **107** with activated olefins in the presence of $Pd(PPh_3)_4$ catalyst in THF.[54] Activated olefins containing two nitrile groups as well as 2-cyano enones underwent aza-Michael addition-allylation with various allylic carbamates affording the corresponding *β*-amino-α-allylated products in high yields with high diastereoselectivities.



Scheme 1.34

1.5.3.4. Acetonation-allylation

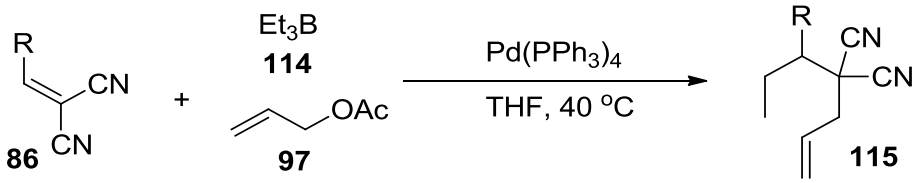
Another significant development in the palladium catalyzed bis-functionalization of activated olefin was the use of allyl acetoacetate **109** as an amphiphilic reagent.[55] In the presence of catalytic amounts of $Pd(PPh_3)_4$ in THF at room temperature, the reaction afforded *β*-acetonated-*α*-allylated products **113** in good yields. Furthermore, the three-component version of *β*-acetonation-*α*-allylation reaction was established by using *α*-halo ketone and allyltributylstannane as an acetonate and an allyl source respectively. It is proposed that the reaction is proceeding through oxa-π-allyl-π-allylpalladium intermediate **111**.



Scheme 1.35

1.5.3.5. Alkyl-allylation

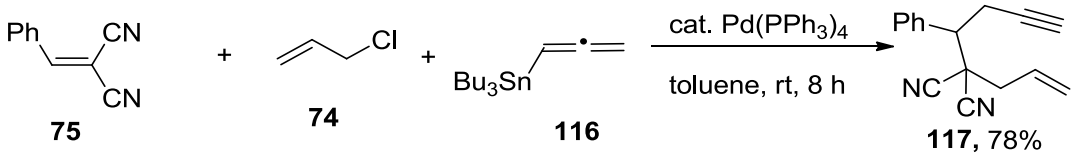
The palladium catalyzed three component *β*-alkyl-*α*-allylation reaction of activated olefins was reported by Yamamoto *et al.* in 2006.[56] In the presence of 5 mol% of $Pd(PPh_3)_4$, the reaction of activated olefins **86** with triethyl borane **114** and allyl acetate **97** in THF at 40 °C yielded the corresponding alkyl-allylated products **115**.



Scheme 1.36

1.5.3.6. Propargylallylation

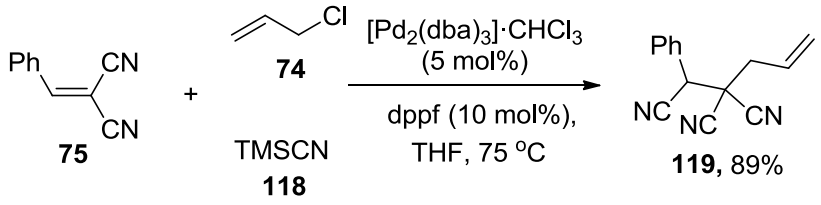
An efficient method for the synthesis of 1,7-enyne derivative **117** *via* a palladium-catalyzed three-component assembling of activated olefin **75**, allylic chloride **74** and allenylstannane **116** has been described by Cheng *et al.*[57] In this propargylallylation reaction, the η^1-allenyl η^3-allyl palladium intermediate which is generated *in situ* reacted with the activated olefins faster than the coupling of the allenyl and allyl groups in the intermediate.



Scheme 1.37

1.5.3.7. Cyanoallylation

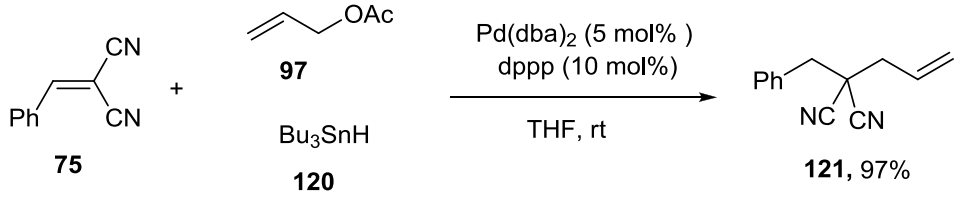
Cyanoallylation was achieved by the three-component coupling reaction of the activated olefins **75**, allylic chlorides **74** and trimethylsilyl cyanide **118**.[58] In the presence of $[Pd_2(dba)_3]\cdot CHCl_3$-dppf catalyst in THF, the reaction proceeded smoothly and afforded the cyanoallylation products **119** in good to excellent yields. The key factor in cyanoallylation strategy is the stability of the π-allylpalladium cyanide complex during the reaction pathway.



Scheme 1.38

1.5.3.8. Hydroallylation

Yamamoto and co-workers developed a palladium catalyzed β-hydro-α-allylation of activated olefins using tributylstannane and allyl acetate.[59] Activated olefins reacted with allyl acetate **97** and tributylstannane **120** in the presence of catalytic amounts of a palladium reagent [$Pd(dba)_2$ and dppp ligand] in THF at room temperature to give the corresponding hydroallylated products. The key step in the reaction mechanism is the transmetallation of η^3-allylpalladium acetate with tributylstannane to produce π-allylpalladium hydride.



Scheme 1.39

1.6. Conclusion and Present Work

The creation of carbon-carbon bonds through palladium catalysis is widely used in synthetic organic chemistry and has recently been highlighted by the 2010 Nobel Prize to Heck, Negishi and Suzuki for their ground-breaking discoveries of palladium catalyzed carbon-carbon bond formation. Another strategy which is exceptionally useful for carbon-carbon and carbon-heteroatom bond formation is palladium catalyzed allylic alkylation

(Tsuji-Trost reaction). In Tsuji-Trost reaction, the allyl moiety has an electrophilic character and it reacts with various nucleophilic substrates. The discovery of catalytic amphiphilic bis-π-allyl palladium complex makes it possible to achieve the palladium catalyzed allylation of a range of electrophiles. The normally used Michael acceptor is arylidene malononitrile which is a suitable substrate for palladium catalyzed bis-functionalization reactions including bis-allylation, alkoxy-allylation, acetonation-allylation, cyanoallylation, *etc*. under mild and neutral conditions.

The functionalization of activated alkenes by bis-π-allylpalladium complexes is well explored in organic synthesis, but their reactivity towards the functionalized conjugated systems remains unexplored. Encouraged by the results of our earlier investigation on the 1,8-conjugate addition of cyclic cross-conjugated dicyanoheptafulvenewith bis-π-allyl palladium and relaed complexes,[60] we envisioned the 1,4-functionalization of 1,3-diene bearing electron withdrawing ester groups would be feasible. Our investigations in this direction led to a simple and efficient method for the bis-functionalization of 1,3-butadiene derivatives by amphiphilic bis-π-allyl palladium and related complexes and the results are described in the second chapter.[61]

The third chapter outlines the results of our investigations on the palladium-catalyzed interceptive decarboxylative 1,4-addition of allyl carbonates with squaric acid esters.[62] Interceptive decarboxylative 1,2-addition of allyl carbonates with N-substituted isatins, acenaphthenequinone and diethylketomalonate, are also discussed. The ring closing metathesis of bis-allylaoxy-2-oxindole derivatives offers an efficient approach for the preparation of biologically relevant spirooxindole derivatives.

Cycloadditions of fulvenes offer versatile and powerful approaches to synthesize various natural products and biologically active molecules.[63] Povarov reaction, which was developed in the 1960s by the Russian Scientist L. S. Povarov, one of the most powerful Lewis acid catalyzed [4+2] cycloaddition strategies for synthesizing tetrahydroquinoline derivatives.[64] The tetrahydroquinoline ring system is a very common structural motif and is found in numerous biologically active natural products and pharmacologically relevant therapeutic agents. Our group has made significant achievements in the cycloaddition chemistry of pentafulvenes[65] and Lewis acid catalyzed regioselective hydroheteroarylation of pentafulvenes with indole.[66] Lewis acid catalyzed Povarov reaction of aromatic imines using pentafulvene as dienophile has a severe disadvantage because of the lower product yield and

substrate scope.[67] Given this more demanding background, we undertook a detailed investigation on Povarov reaction of pentafulvenes with aryl imines generated from phenylglyoxal and various substituted anilines. Our effort in this line is discussed in the final chapter.

1.7. References

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CHAPTER 2

Bis-functionalization of 1,3-Dienes *via* 1,4-Conjugate Addition of Amphiphilic Bis-π-Allyl and Related Palladium Intermediates

2.1. Introduction

Functionalization of 1,3-dienes in regio- and stereoselective fashion has found widespread applications in organic synthesis. There exist different strategies for 1,4-functionalization of 1,3-dienes which include classical cycloaddition reactions involving singlet oxygen,[1] hetero dienophiles such as nitroso compounds[2] and azodicarboxylates.[3] The transition metal catalyzed transformations of 1,3-dienes are useful reactions in organic synthesis. In contrast to cycloaddition reaction of 1,3-dienes with dienophiles, transition metal catalyzed regioselective difunctionalization process yields molecular frameworks such as skipped polyenes with high regio- and stereoselectivity.[4,5] Synthesis of stereochemically defined skipped polyenes still remains as a challenge in modern synthetic organic chemistry.[4] Some of the biologically relevant terpenoid natural products with polyene skeleton are shown in figure 2.1.[5]

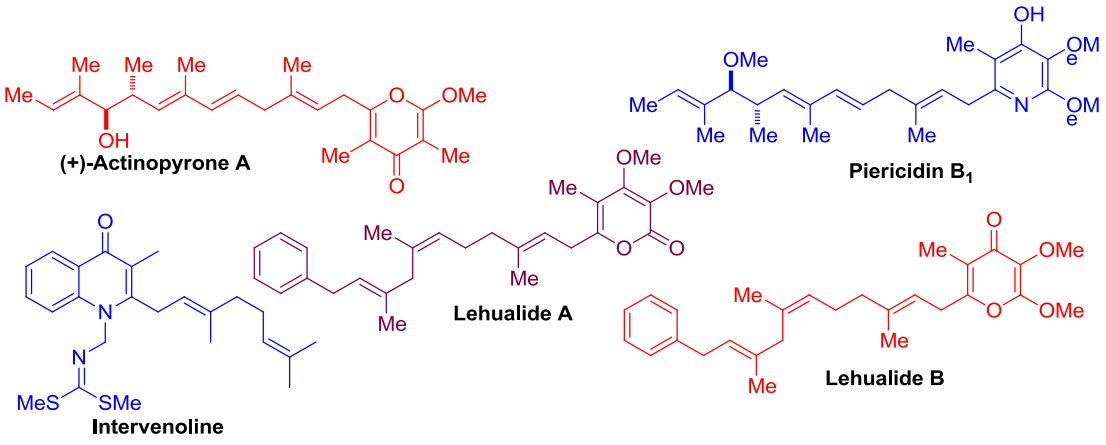


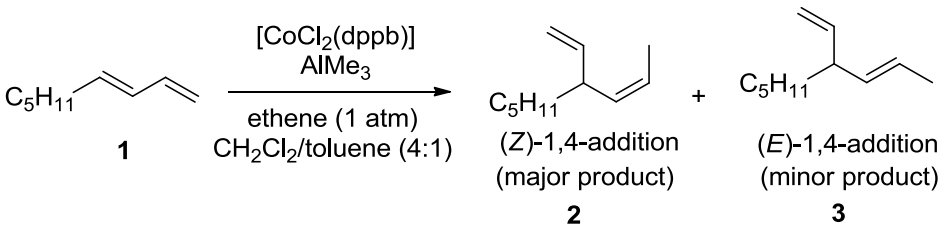
Figure 2.1. Natural products containing polyenes

Transition metal catalyzed 1,2- and 1,4-functionalization of 1,3-dienes have been investigated by different research groups. A brief discussion on the transition metal catalyzed regioselective functionalization of 1,3-dienes will be presented in the following sections. In this chapter, we wish to describe bis-functionalization of 1,3-butadiene derivatives *via* 1,4-conjugate addition of amphiphilic bis-π-allyl and related palladium intermediates which resulted in functionalized triene and diene derivatives.

2.1.1. Bis-functionalization of 1,3-dienes under transition metal catalysis

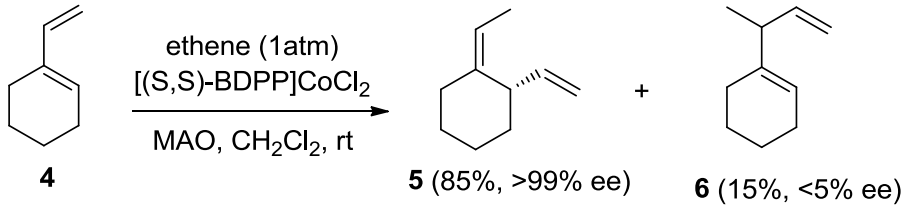
2.1.1.1. Hydrovinylation of 1,3-dienes

The transition metal catalyzed co-dimerization of 1,3-dienes with alkenes is known as hydrovinylation. The hydrovinylation reaction was first reported by Alderson *et al.* in 1965.[6] They employed rhodium and ruthenium salts under high ethylene pressure with a variety of substrates. Subsequently, other metals such as iron, cobalt, nickel and palladium have been used.[7] Styrene has been used as a standard substrate in many studies especially for asymmetric variants of the reaction. Hydrovinylation of 1,3-diene with ethene using cobalt catalyst was reported by Sharma and Rajan Babu in 2010 (Scheme 2.1).[8] By conducting the hydrovinylation reaction using (*E*)-1,3- nonadiene **1** as the substrate at -10 °C, a mixture of (*Z*)-1,4- and (*E*)-1,4-hydrovinylation products were obtained in 93% and 7% yields respectively. The other regioselective product distribution was found to be strongly dependent on the nature of the ligand and temperature.



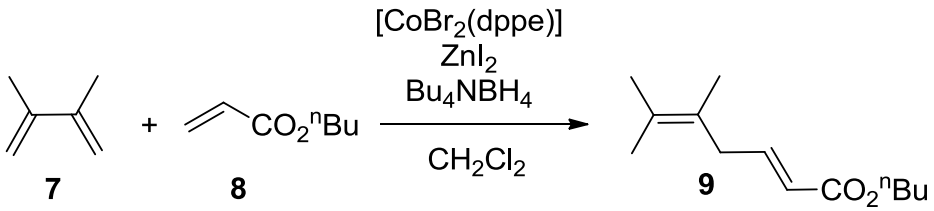
Scheme 2.1

Further, they have extended the cobalt catalyzed 1,4-hydrovinylation reaction to vinyl cycloalkenes **4** using ethylene as a source of alkene.[9] In addition to the 1,4-conjugate addition product **5**, a slight amount of 1,2-hydrovinylation product **6** was also observed (Scheme 2.2).



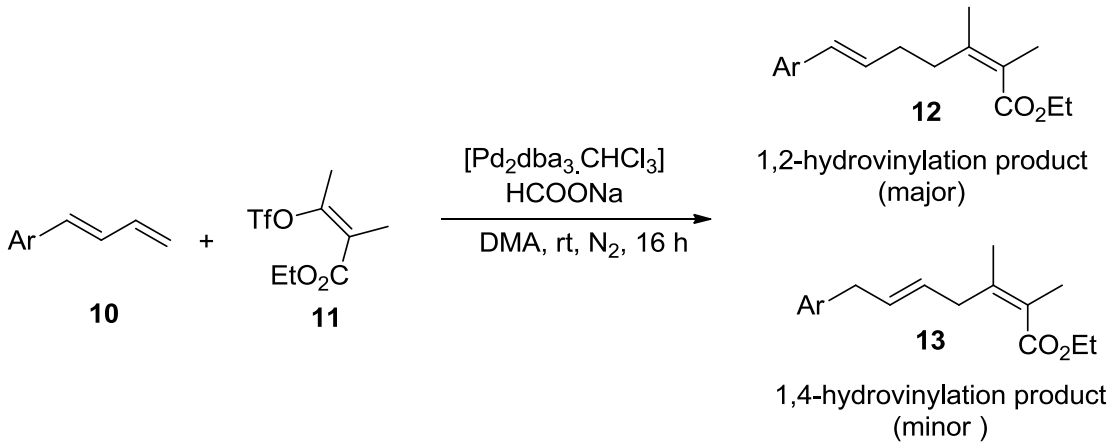
Scheme 2.2

Hilt *et al*. also contributed to the cobalt catalyzed 1,4-hydrovinylation reaction of 1,3-butadienes with alkenes.[10] Linear and branched 1,4-dienes were obtained under mild reaction conditions with good regioselectivity and in good to excellent yields (Scheme 2.3).



Scheme 2.3

Recently, Sigman and co-workers reported palladium catalyzed intermolecular 1,2-hydrovinylation of 1,3-dienes.[11] The reaction of 1,3-dienes **10** and vinyl triflates **11** in the presence of sodium formate as the reductant under mild reaction conditions provided highly functionalized tri- and tetrasubstituted alkenes.

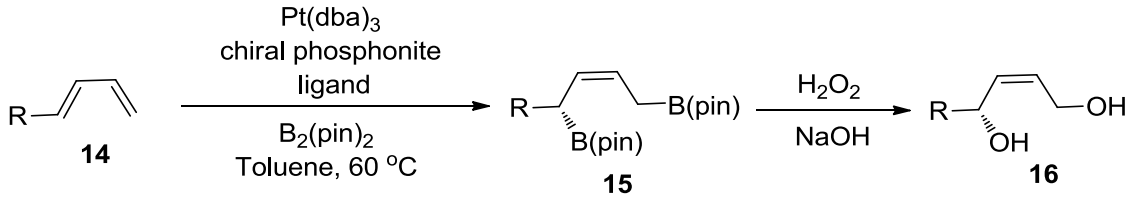


Scheme 2.4

2.1.1.2. 1,4-Diboration reaction in 1,3-dienes

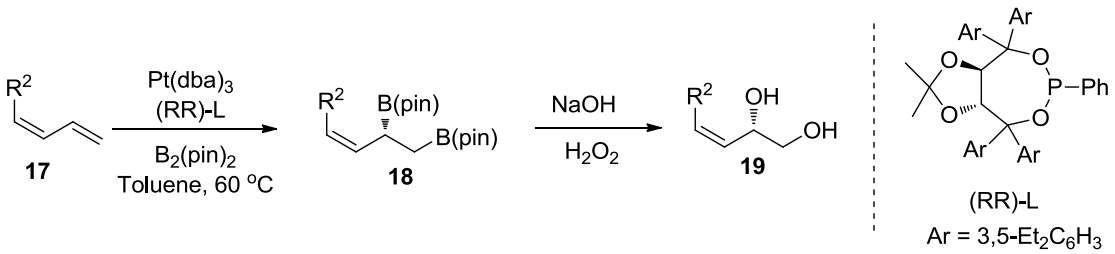
The dimetalation of unsaturated substrates is an effective tool for enriching the functional and stereochemical complexity of simple hydrocarbon substrates. Diboration reaction of dienes provides reactive intermediates which can be transformed to synthetically useful organic compounds. Morken *et al.* reported the enantioselective 1,4-diboration of *trans*

1,3-dienes using [Pt(dba)$_3$] and a chiral phosphonite ligand.[12] This method provides a synthetic route for the preparation of chiral 2-buten-1,4-diols. Extension of the enantioselective 1,4-diboration reaction to cyclic dienes was achieved by using a taddol-derived phosphonite ligand.[13]



Scheme 2.5

Further, regio-and enantioselective catalytic 1,2-diboration of 1,3-dienes was realized by replacing the *trans* diene with *cis* diene substrate.[14]

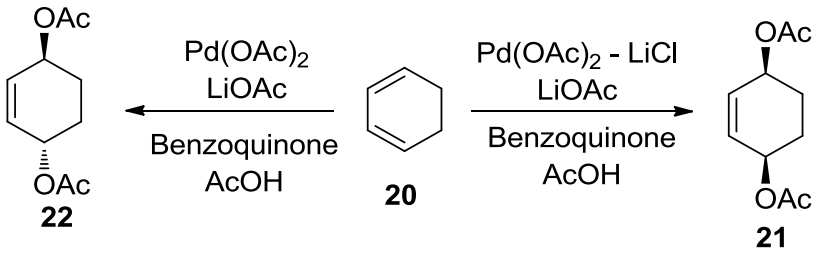


Scheme 2.6

2.1.1.3. Palladium catalyzed functionalization of dienes

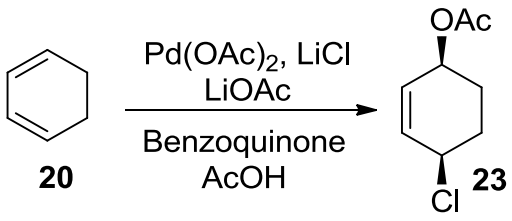
Conjugated dienes coordinated to a transition metal can readily be transformed into a π-allyl metal complex by functionalization at the 4th-position. This strategy makes dienes as useful substrates for catalytic transformations since the π-allyl complex can undergo further transformations. In many cases, palladium-catalyzed reactions of conjugated dienes are proceed *via* π-allylpalladium intermediate and which leads to 1,4- or 1,2- functionalization of the diene.[15] Bäckvall *et al.* extensively studied the palladium catalyzed 1,4-functionalizations of conjugated dienes which mainly involves the regioselective nucleophilic additions to π-allylpalladium intermediates. One of the well-studied 1,4-functionalization of diene is 1,4-diacetoxylation reaction.[16] The 1,4-addition to the diene is highly regio- and stereoselective, and the ligand plays a major role in controlling the stereoselectivity. The chloride and acetate ligands (as LiC1 and LiOAc) significantly influences the stereochemical outcome of the reaction.[16]

Palladium-catalyzed oxidation of 1,3-cyclohexadiene in acetic acid in the absence of LiCl and LiOAc gave a 1:1 mixture of *cis*- and *trans*- 1,4-diacetoxy-2-cyclohexene.[16] If the oxidation was performed in the presence of lithium acetate, the reaction yielded *trans*-diacetoxylated cyclohexene stereoselectively. Oxidation of 1,3-cyclohexadiene in the presence of lithium acetate and catalytic amounts of lithium chloride gave exclusively *cis*-diacetoxylated cyclohexene **21**.[16] In the presence of chloride ligands, mainly *trans* attack on the π-allylpalladium complex takes place whereas in the absence of chloride ligands both *cis*- and *trans* attack can occur depending on the acetate concentration. The explanation for the dual stereo control in the presence of catalytic amounts of LiCl and the in absence of LiCl is that chloride blocks the coordination of acetate to palladium in the catalytic intermediate, thus suppressing the *cis* migration of acetate in the presence of LiCl. The 1,4-diacetoxylation is quite general for all cyclic dienes such as 1,3-cycloheptadiene and 1,3-cyclopentadiene.[16]



Scheme 2.7

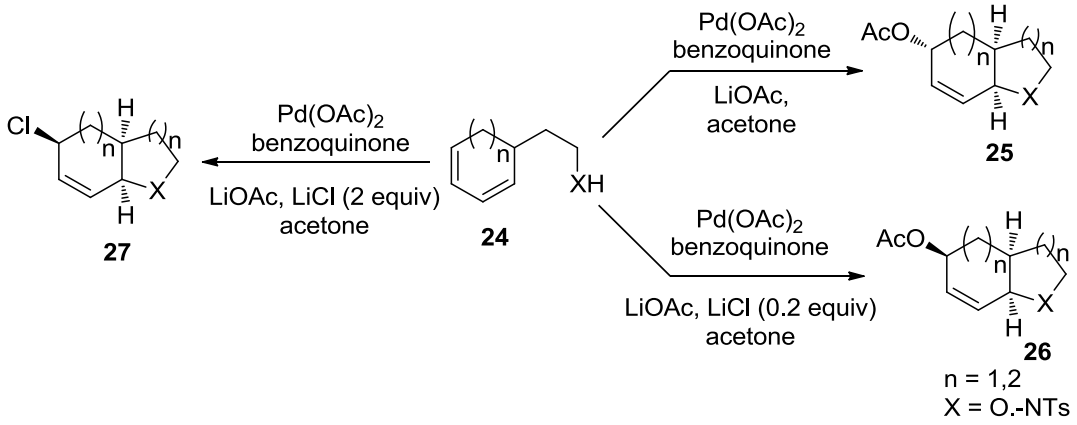
If the palladium catalyzed oxidation of 1,3-dienes in acetic acid is performed at a slightly higher chloride concentration, the product pattern changes and 1,4-chloroacetate **23** becomes the sole product. This reaction is highly stereospecific which proceeds with overall *cis*-stereochemistry with cyclic dienes.[16]



Scheme 2.8

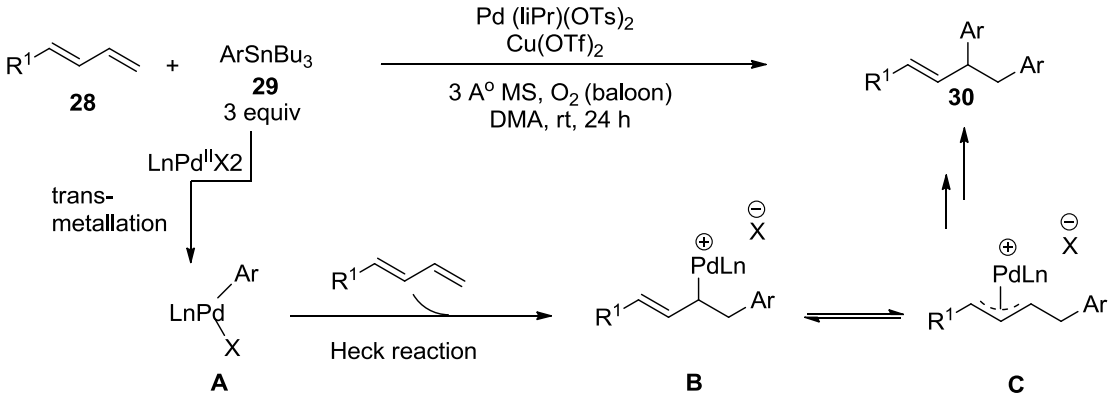
The intramolecular 1,4-oxidation of conjugated dienes offered efficient pathways to synthesize fused carbocyclic and heterocyclic rings in a stereocontrolled manner.[17] The intramolecular oxyacetoxylation and oxychlorination worked well for six- and seven-

membered dienes containing amide and alcohol nucleophilic moiety to afford the corresponding heterocyclic products. Bäckvall *et al.* performed the reaction under three different reaction conditions: (a) without adding LiCl, (b) by adding a catalytic amount of LiCl and (c) by adding two equiv. of LiCl. These slight variations of reaction conditions had a dramatic effect on the outcome of the reaction and furnished different product with complete product control.[18,19]



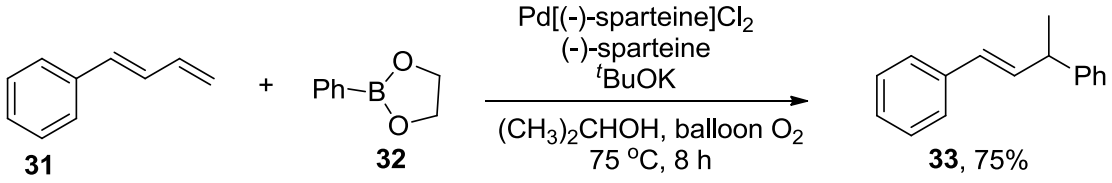
Scheme 2.9

Palladium-catalyzed regioselective 1,2-diarylation of conjugated terminal 1,3-dienes using organostannanes was reported by Sigman and co-workers.[20] In this reaction, two aryl groups originating from an arylstannane **29** are added across a 1,3-diene **28** to yield 1,2-diarylation product **30**. Mechanistically, this reaction is proposed to be initiated by trans-metalation to form Pd-aryl species **A** followed by Heck insertion of a conjugated diene yielding **B** which is then stabilized as a π-allyl intermediate **C** (Scheme 2.10). Subsequent cross-coupling of the other equivalent of an aryl stannane results in the product formation. The introduction of two identical aryl groups from the arylstannane and reasonably complex reaction conditions limits the synthetic utility of this 1,2-alkene difunctionalization reaction.



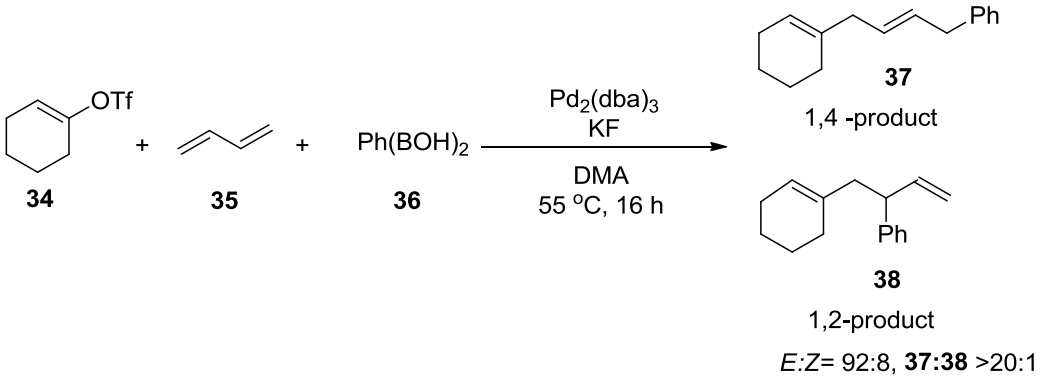
Scheme 2.10

In 2010, the same research group developed 1,2-hydroarylation of 1,3-dienes by generating π-allyl palladium intermediates directly using a coupled aerobic alcohol oxidation to access a palladium hydride.[21] Aryl boronic ester **32** couples with the π-allyl intermediate and furnishes the regioselective 1,2-addition product **33**.



Scheme 2.11

Sigman and co-workers further developed the 1,2-difunctionalization of terminal 1,3-dienes by a three-component coupling of vinyl triflates and boronic acids.[22] The reaction proceeds through the initial formation of π-allylpalladium intermediate from Heck insertion to diene, which is faster than the probable Suzuki cross coupling. By utilizing the same strategy, they could achieve the 1,4-addition across the commodity chemical 1,3-butadiene (Scheme 2.12).[4] Through a palladium σ → π → σ allyl isomerization, two new carbon-carbon bonds are formed with high regioselectivity and *trans* stereoselectivity. Very recently, they have reported a palladium catalyzed 1,4-difunctionalization of isoprene by utilizing pyrox ligands and established a synthetic route for the preparation of skipped polyenes.[5]

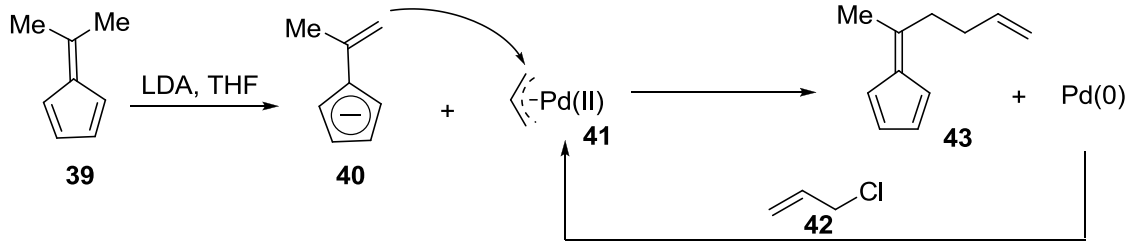


Scheme 2.12

2.1.2. Palladium catalyzed allylation reactions in conjugated system

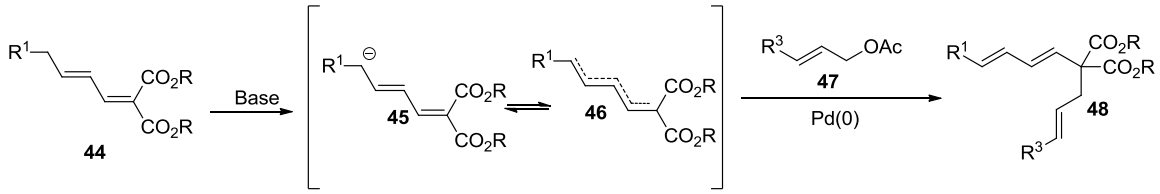
The Pd(0) catalyzed allylic substitution reaction has been studied in cyclic cross-conjugated systems such as pentafulvene. In 1991, Nystrom and co-workers reported a

regioselective allylation reaction in pentafulvene. Vinyl cyclopentadienyl anion **40** generated by the reaction of dimethyl fulvene **39** with LDA underwent palladium catalyzed allylation at the exocyclic position in presence allyl chloride, allyl acetate or allyl carbonate.[23]



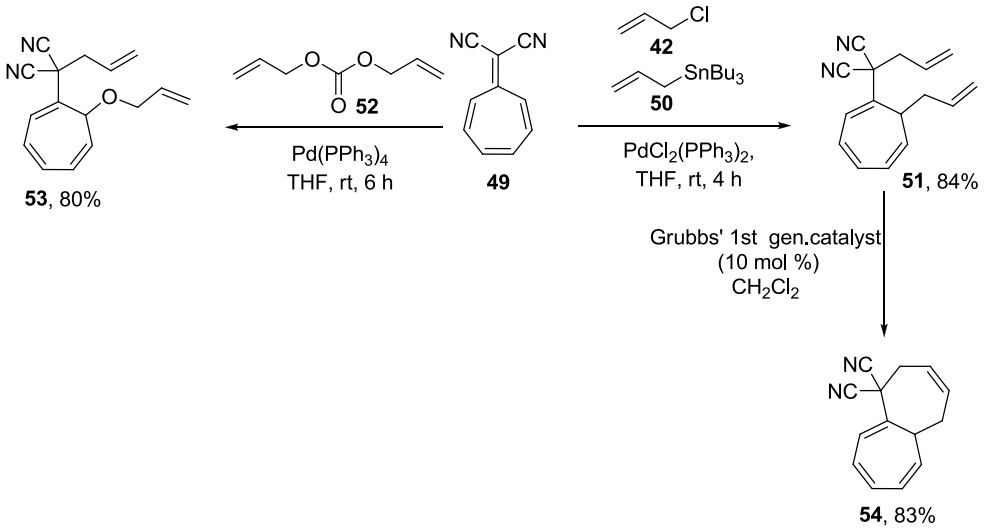
Scheme 2.13

Later, Sato and co-workers succeeded in developing a Pd(0)-catalyzed deconjugative allylation of functionalized diene derivatives like alkenylidenemalonates (Scheme 2.14).[24] This finding provided a useful method for synthesizing conjugated diene **48** that contains a 1,3-diene unit attached to a quaternary carbon center.



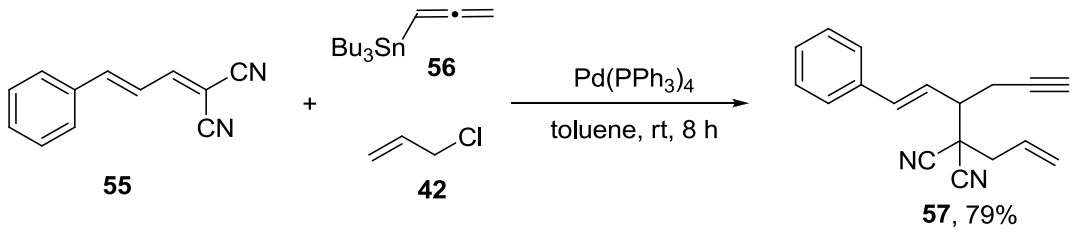
Scheme 2.14

Our group also investigated the reactivity of cyclic conjugated heptafulvene system towards palladium catalyzed allylation. We have disclosed the 1,8-conjugate addition of bis-π-allyl palladium complex to dicyanoheptafulvenes which furnished cycloheptatriene derivatives (Scheme 2.15).[25] We explored the synthetic potential of this methodology towards the synthesis of heptalene by the ring closing metathesis of **51** using Grubbs' first generation catalyst. 1,8-Alkoxy allylation of dicyanoheptafulvenes **49** was also achieved by conducting the reaction with diallyl carbonate **52**.



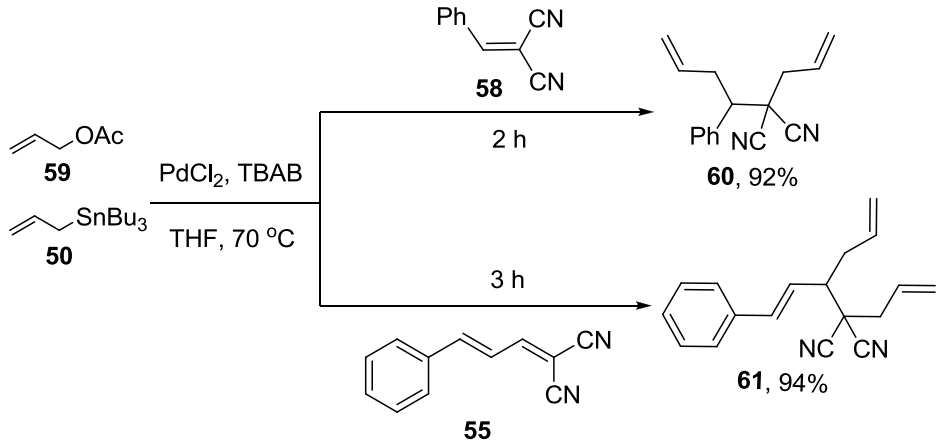
Scheme 2.15

In 2004, Cheng and co-workers conducted a detailed study on the palladium catalyzed bisfunctionalization reaction of alkene as well as conjugated diene with allyl chloride **42** and allenyl stannane **56**.[26] This propargyl allylation reaction proceeds with high regio- and chemoselectively affording 1,2 addition product **57** in the case of conjugated diene (Scheme 2.16).



Scheme 2.16

Ranu *et al*. demonstrated the palladium nanoparticle catalyzed vicinal double allylation of activated alkenes by reacting with allyl acetates and allyl stannanes (Scheme 2.17).[27] 1,3-Butadiene **55** derived from cinnamaldehyde and malononitrile was reacted with bis-π-allyl palladium complex generated *in situ* from allyl acetates and allyl stannanes afforded regioselective 1,2-diallylated product **61** in good yield.



Scheme 2.17

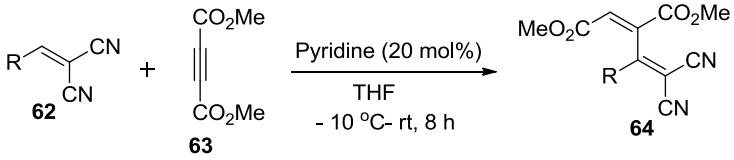
2.2. Statement of the Problem

The functionalization of activated alkenes by bis-π-allylpalladium complexes is well explored in organic synthesis,[28] but their reactivity towards the functionalized conjugated system remains unexplored. Investigation from our laboratory has exposed the reactivity of bis-*π*-allyl palladium and related complexes with isatylidenes[29] and dicyanoheptafulvenes.[25] It is evident from the literature background presented above that, the reactions of functionalized 1,3-diene **55** derived from cinnamaldehyde and malononitrile underwent regioselective 1,2-addition with bis-π-allylpalladium and related complexes. Prompted by this, we reasoned that 1,4-difunctionalization of 1,3- diene could be achieve by installing an electron withdrawing group. A detailed investigation of the 1,4-functionalization of 1,3-dienes by utilizing bis-π-allylpalladium and related complexes forms the central theme of the present chapter.

2.3. Results and Discussion

2.3.1. Bis-functionalization of 1,3-dienes *via* 1,4-conjugate addition of bis-π-allyl palladium complexes

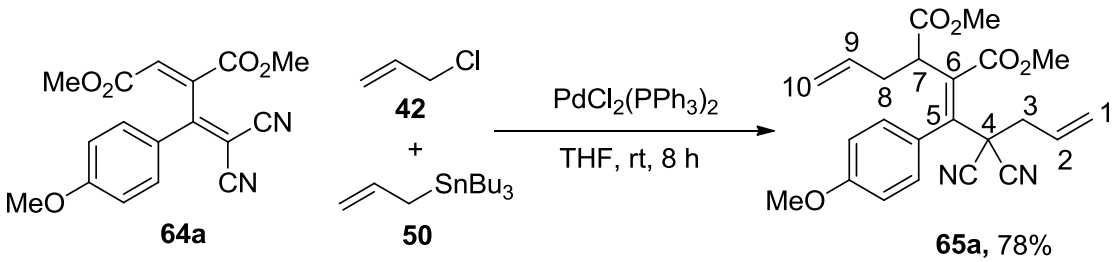
The 1,3-butadiene derivatives, starting material for our investigation was prepared from dicyanostyrene **62** through a pyridine catalyzed reaction with dimethyl acetylene dicarboxylate (DMAD) **63**.[30] Different substituted functionalized dienes (**64a-h**) were prepared from various substituted arylidene malononitriles **62** using this strategy.



R= *p*-MeO-C_6H_4, 78%, **64a**
R= Ph, 59%, **64b**
R= *p*-Me-C_6H_4, 59%, **64c**
R= *p*-Cl-C_6H_4, 87%, **64d**
R= 2-furyl, 46%, **64e**
R= 2-thiophenyl, 51%, **64f**
R= 3,4-dimethoxyphenyl, 21%, **64g**
R= 2,4-dimethylphenyl, 44%, **64h**

Scheme 2.18

We commenced our investigations with the reaction of 1,3-butadiene derivative **64a** with allyl chloride **42** and allyltributylstannane **50** in the presence of 5 mol% $PdCl_2(PPh_3)_2$ in THF at room temperature. The reaction afforded 1,4-bis-allylated product **65a** in 78% yield.



Scheme 2.19

The structure of the compound **65a** was characterized by various spectroscopic analysis. In the IR spectrum, the peak at 2225 cm^{-1} was assigned to the cyano group, and a sharp signal at 1730 cm^{-1} was attributed to the ester carbonyl group. The ^1H NMR spectrum of **65a** (Figure 2.2) provided clear indication of the formation of the bis-allylated product. In ^1H NMR spectrum, protons at C-2 and C-9 appeared as multiplets in the region δ 5.94-5.86 and 5.56-5.47 ppm respectively. The sp^2 -CH_2 protons at C-1 and C-10 observed as two multiplets in the region δ 5.42-5.35 and 5.05-4.98 ppm respectively. The sp^3 CH_2 protons at C-3 resonated as multiplet in the region δ 2.87-2.75 ppm and protons at C-8 appeared as two separate multiplets in the region δ 2.63-2.58 and 2.27-2.21 ppm. The proton attached to C-7 resonated as a multiplet in the region δ 3.18-3.15 ppm and two carbomethoxy protons discernible as singlets at δ 3.89 and 3.72 ppm, while the methoxy group attached to the aromatic ring observed as a singlet at δ 3.85 ppm.

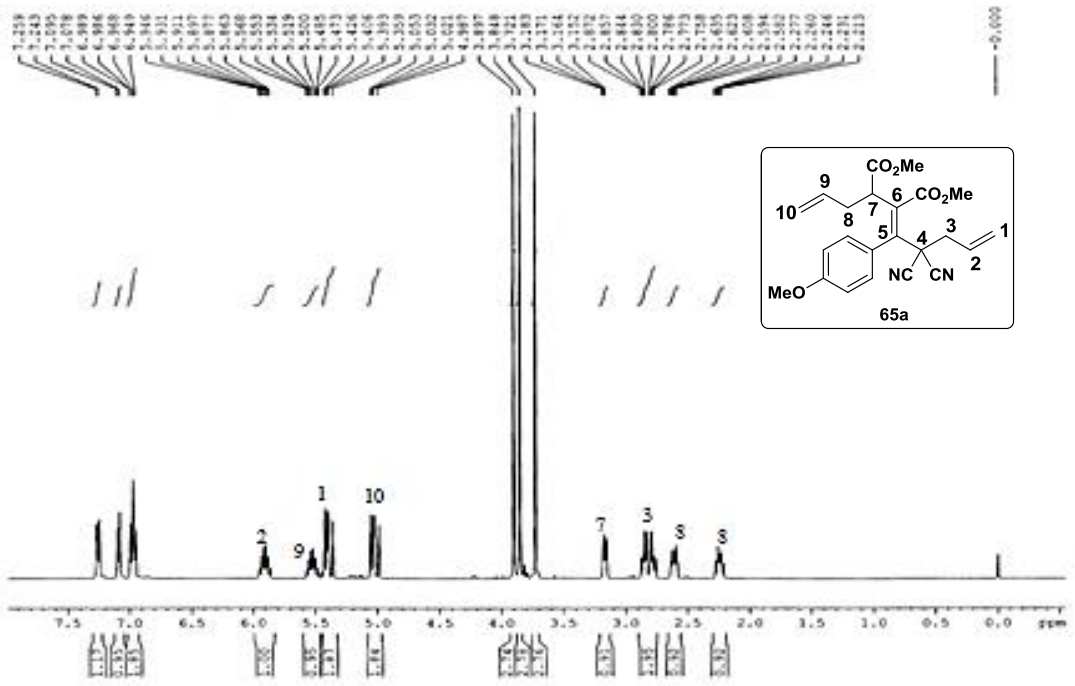


Figure 2.2. ^{1}H NMR spectrum of compound **65a**

In ^{13}C NMR spectrum (Figure 2.3), the cyanide carbons resonated at δ 113.74 and 113.71 ppm. The peaks visible at 42.7 and 33.8 ppm correspond to C-3 and C-8 carbons respectively. The quaternary carbons C-5 and C-6 resonated at 137.4 and 126.0 ppm respectively. The sp^2 carbons C-2 and C-9 observed at δ 114.5 and 114.3 ppm and sp^2 carbons C-1 and C-10 resonated at δ 123.5 and 118.1 ppm. Characteristic peaks of two carbomethoxy carbonyl groups observed at δ 171.0 and 166.0 ppm. Further evidence for the structure was obtained from the high-resolution mass spectral analysis which showed the molecular ion peak at *m/z* 431.15646 $[M+Na]^+$.

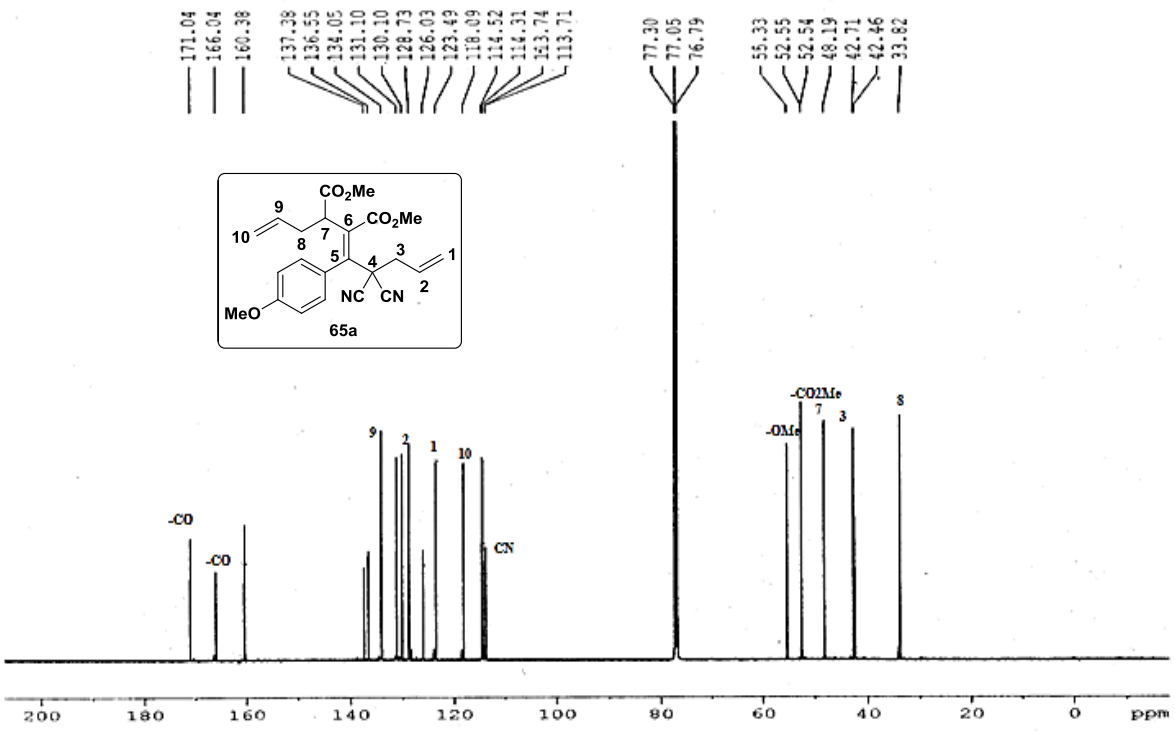
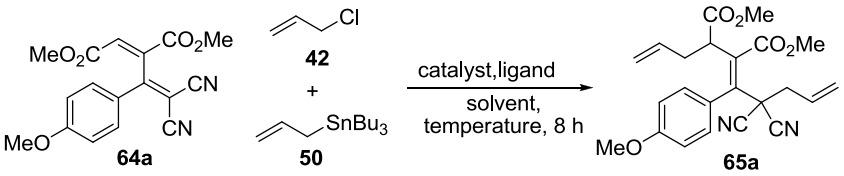


Figure 2.3. ^{13}C NMR spectrum of compound **65a**

The reaction was then optimized for the best conditions, and the efforts are summarized in Table 2.1. Among different catalysts screened, $PdCl_2(PPh_3)_2$ gave the product in 78% yield. THF was found to be the best solvent for the transformation. Based on the studies, the optimal condition for the transformation was found to be a combination of 1.0 equiv. diene, 2.0 equiv. allyl chloride, 2.0 equiv. allyltributylstannane and 5 mol% $PdCl_2(PPh_3)_2$ in 3 mL THF at room temperature.

Table 2.1. Reaction optimization studies

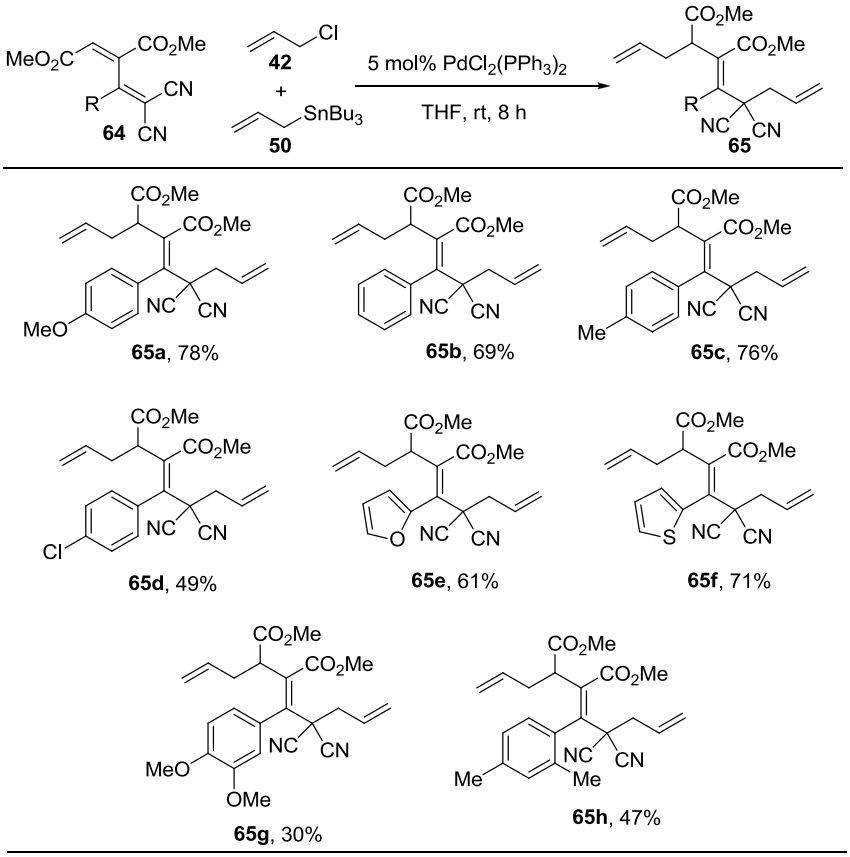


Entry	Catalyst	Ligand	Solvent	Yield (%)[a]
1	$PdCl_2(PPh_3)_2$	-	THF	78
2	$PdCl_2$	PPh_3	THF	44
3	$Pd_2(dba)_3$	PPh_3	THF	20
4	$PdCl_2(PPh_3)_2$	PPh_3	THF	69
5	$Pd(PPh_3)_4$	-	THF	30
6	$PdCl_2(PPh_3)_2$	-	DCM	39
7	$PdCl_2(PPh_3)_2$	-	Toluene	No reaction
8	$PdCl_2(PPh_3)_2$	-	DMF	45
9	$PdCl_2(PPh_3)_2$	-	CH_3CN	77
10	$PdCl_2(PPh_3)_2$	-	THF	74[b]

[a]Conditions: 1,3-diene **64a** (1.0 equiv), allyl chloride **42** (2.0 equiv), allyl tributylstannane **50** (2.0 equiv), catalyst (5 mol%), ligand (10 mol %), solvent (3 mL), rt, 8 h. [b] THF at 60 °C.

The substrate scope for the bis-allylation strategy was investigated by utilizing various functionalized 1,3-butadienes. A variety of 1,3-dienes derived from substituted benzylidene malononitriles (**64a-d**, **64g** and **64h**) and heteroaryl malononitriles (**64e** and **64f**) showed moderate to good compatibility. The use of highly substituted 1,3-butadienes makes this method potentially valuable towards the synthesis of functionalized triene derivatives, and the results are summarized in Table 2.2.

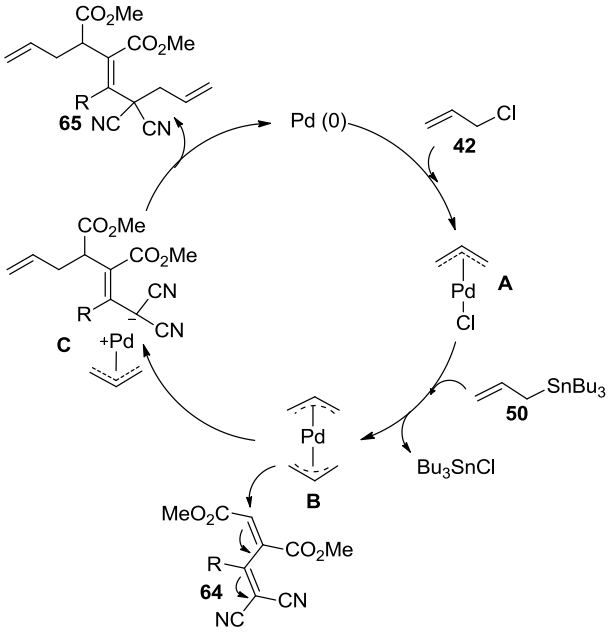
Table 2.2. Palladium-catalyzed bis-allylation of various 1,3-butadiene derivatives



Reaction conditions: 1,3-diene **64** (1.0 equiv), allyl chloride **42** (2.0 equiv), allyl tributylstannane **50** (2.0 equiv), $PdCl_2(PPh_3)_2$ (5 mol%), THF (3 mL), rt, 8 h.

2.3.1.1. Mechanistic considerations

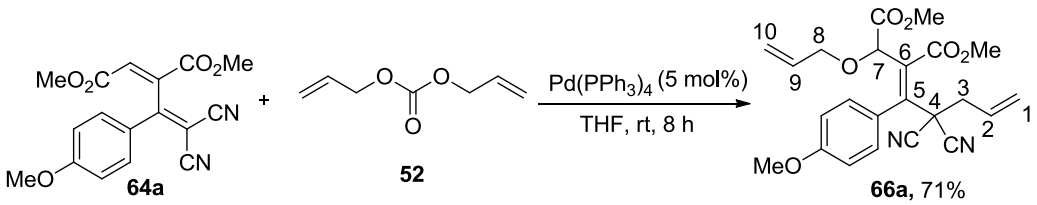
A plausible mechanistic pathway for bis-allylation is illustrated in Scheme 2.20. The initial event involves the oxidative addition of the allyl chloride **42** to palladium(0) species to produce the η^3-allylpalladium intermediate **A**. The intermediate **A** undergo ligand exchange with allyltributylstannane **50** to generate bis-η^3-allylpalladium intermediate **B**, which subsequently undergo nucleophilic 1,4-addition with diene **64** to form intermediate **C**. Further, the reductive elimination of palladium from **C** gives the 1,4-bis-allylated product **65**.



Scheme 2.20

2.3.2. Palladium catalyzed allylation-oxyallylation reaction of 1,3-dienes using diallyl carbonate

To demonstrate the further application of the developed method, we evaluated the reactivity of other amphiphilic bis-π-allyl palladium complexes. With this idea in mind, we initiated our investigations with allylation-oxyallylation reaction of dimethyl 2-(2,2-dicyano-1-(4-methoxyphenyl)vinyl)maleate **64a** and diallyl carbonate **52** in the presence of $Pd(PPh_3)_4$ as the catalyst and THF as the solvent (Scheme 2.21). The reaction provided the desired 1,4-allylated-oxyallylated product **66a** in 71% yield.



Scheme 2.21

The structure of the allyl-oxyallylated product **66a** was assigned on the basis of spectral data. The compound showed characteristic –CN stretching at 2247 cm^{-1} and carbonyl stretching at 1727 cm^{-1} in the IR spectrum. In the ^1H NMR spectrum of compound **66a** (Figure 2.4), protons at C-2 and C-9 appeared as multiplets in the region δ 5.93-5.82 and 5.76-5.63 ppm respectively. The sp^2 methylene protons at C-1 and C-10 observed as two

separate multiplets in the region δ 5.43-5.34 and 5.10-5.04 ppm respectively. The proton at C-7 appeared as a singlet at δ 4.28 ppm. Protons at C-8 observed as a multiplet at δ 3.90 ppm. The protons at C-3 were visible as two separate multiplets at δ 2.99-2.92 and 2.77-2.74 ppm. The methoxy protons were discernible at δ 3.87, 3.83 and 3.78 ppm.

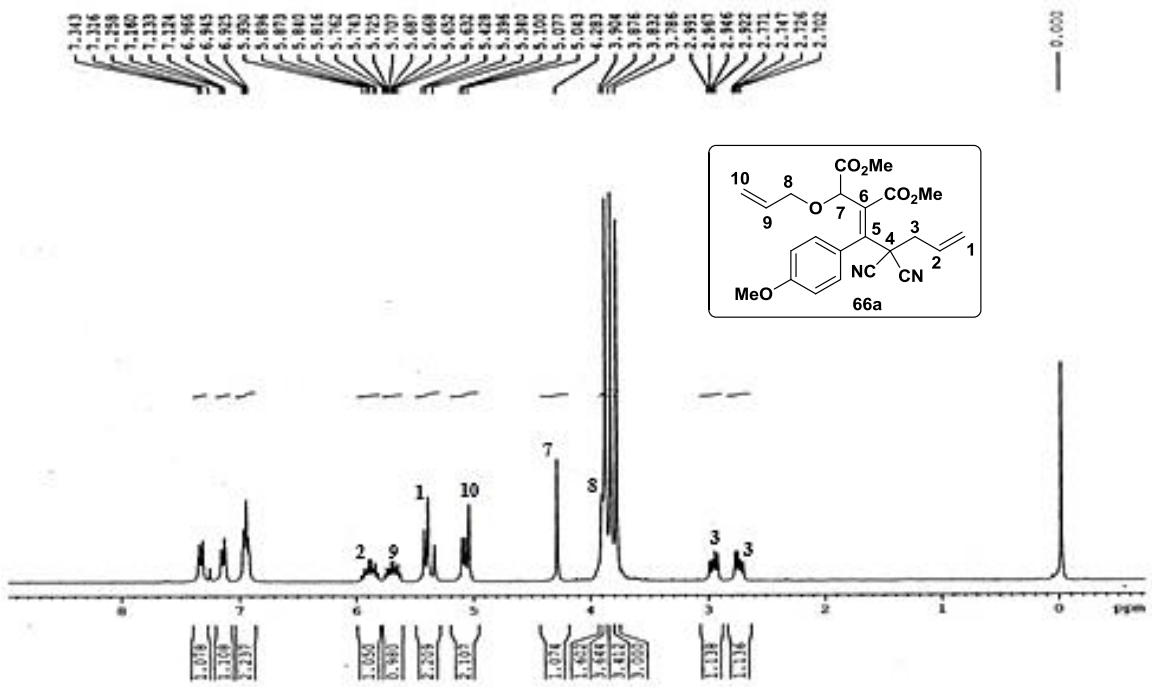


Figure 2.4. ^{1}H NMR spectrum of compound **66a**

In ^{13}C NMR spectrum (Figure 2.5), the nitrile carbons were observed at δ 113.48 and 113.45 ppm. The peak visible at δ 42.6 corresponds to C-3 carbon. The quaternary carbons C-5 and C-6 resonated at δ 138.2 and 135.9 ppm respectively. The sp^2 carbons C-2 and C-9 observed at δ 132.1 and 133.0 ppm and sp^2 carbons C-1 and C-10 resonated at δ 123.6 and 118.6 ppm. The sp^3 C-8 carbon resonated at δ 70.9 ppm. The carbon at C-7 resonated at δ 76.4 ppm and the characteristic peaks of two carbomethoxy carbonyl groups observed at δ 168.9 and 165.2 ppm.

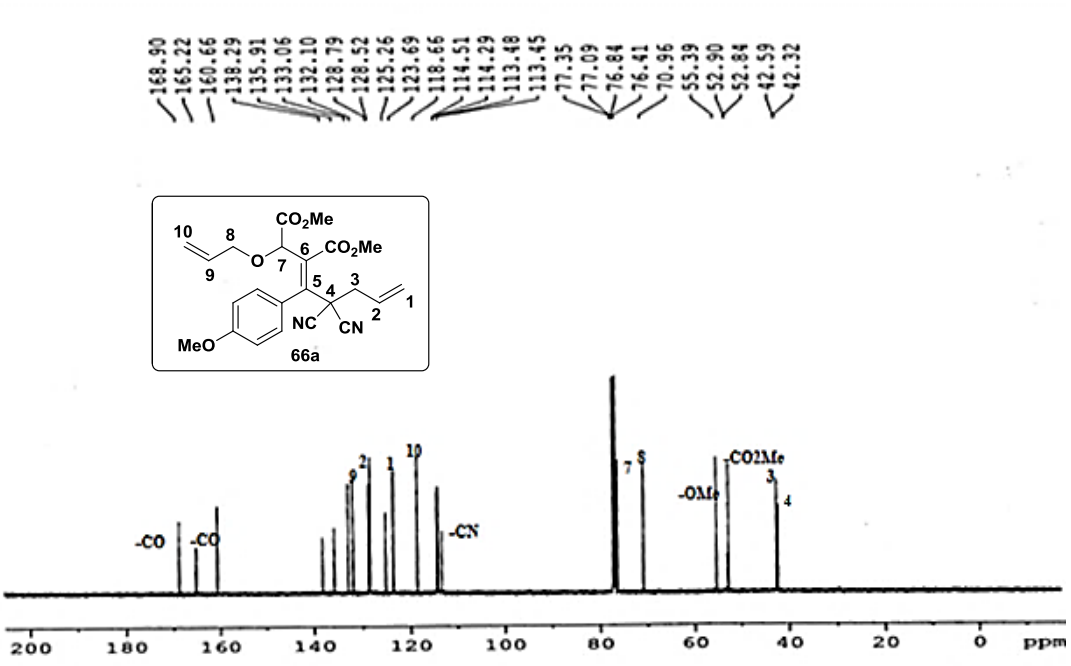


Figure 2.5. ^{13}C NMR spectrum of compound **66a**

Further evidence for the structure was obtained from the mass spectral analysis which showed molecular ion peak at *m/z* 447.15103, $[M+Na]^+$. Finally, the proposed structure of the product (**66b**) formed from the diene derived from benzylidene malononitrile (**64b**) was confirmed unambiguously by single crystal X-ray analysis (Figure 2.6).[31]

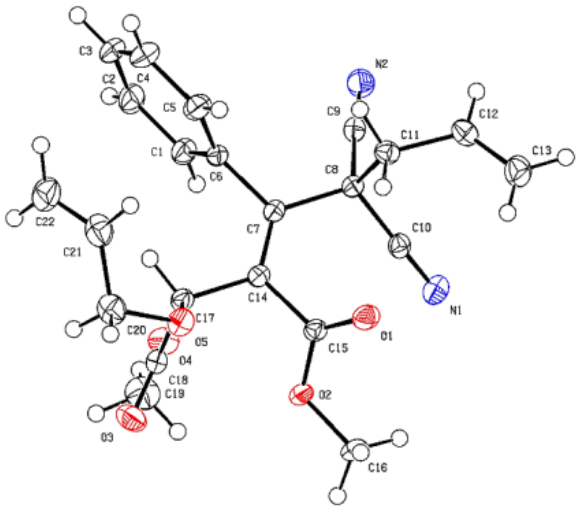
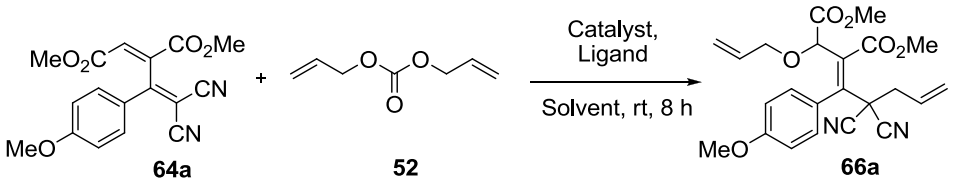


Figure 2.6. ORTEP diagram of compound **66b**

To develop conditions suitable for this transformation, we surveyed a variety of palladium catalysts and solvents, and the optimization results are summarized in Table 2.3. Among various palladium catalysts tested, $Pd(OAc)_2$, $PdCl_2$ and $PdCl_2(PPh_3)_2$ were totally

ineffective for the reaction and $Pd(PPh_3)_4$ was found to be the best catalyst. THF was found to be the best solvent for the transformation. After screening various catalysts and solvents, the optimal conditions for this reaction are as follows: 1:2 mixture of 1,3-diene/diallyl carbonate with 5 mol% $Pd(PPh_3)_4$ in 3 mL THF at room temperature for 8 h (Entry 1, Table 2. 3).

Table 2.3. Reaction optimization studies

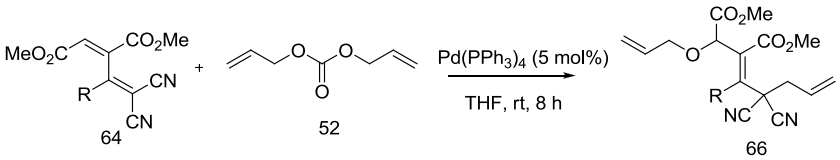


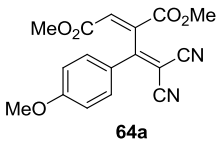
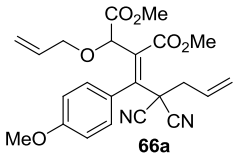
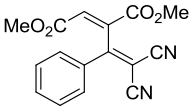
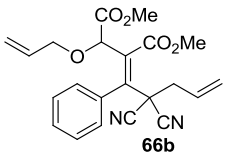
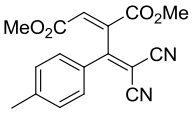
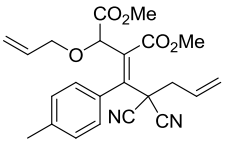
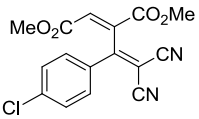
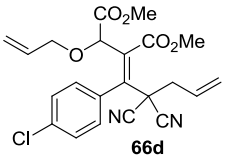
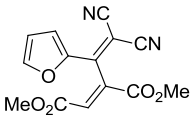
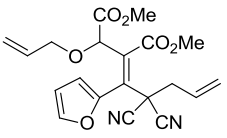
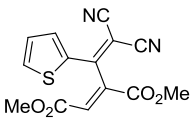
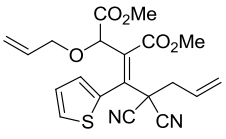
Entry	Catalyst	Ligand	Solvent	Yield (%)
1	$Pd(PPh_3)_4$	-	THF	71
2	$Pd(OAc)_2$	PPh_3	THF	No reaction
3	$PdCl_2$	PPh_3	THF	No reaction
4	$[Pd(allyl)Cl]_2$	PPh_3	THF	9
5	$Pd_2(dba)_3$	PPh_3	THF	30
6	$PdCl_2(PPh_3)_2$	PPh_3	THF	No reaction
7	$Pd_2(dba)_3.CHCl_3$	PPh_3	THF	7
8	$Pd(PPh_3)_4$	PPh_3	THF	67
9	$Pd(PPh_3)_4$	-	DCM	8
10	$Pd(PPh_3)_4$	-	Toluene	28
11	$Pd(PPh_3)_4$	-	CH_3CN	11
12	$Pd(PPh_3)_4$	-	DMF	22

Reaction conditions: 1,3-diene **64a** (1.0 equiv), diallyl carbonate **52** (2.0 equiv), catalyst (5 mol%), ligand (10 mol%), solvent (3 mL), rt, 8 h

A detailed study was performed under the optimized condition to expand the scope of 1,4-allylation-oxyallylation strategy to other 1,3-dienes **(64b-f),** which proved that a wide range of substitution patterns are tolerated. This reaction is compatible with a range of substituents including phenyl, substituted phenyl (electron-donating and electron-withdrawing groups), furyl, and thiophenyl group containing 1,3-dienes. The results of the investigation are summarized in Table 2.4.

Table 2.4. Palladium-catalyzed allylation-oxyallylation reaction of 1,3-dienes

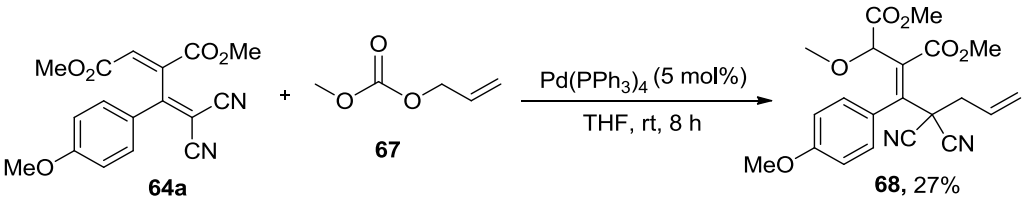


Entry	Substrate	Product	Yield (%)
1	 **64a**	 **66a**	71
2	 **64b**	 **66b**	55
3	 **64c**	 **66c**	66
4	 **64d**	 **66d**	31
5	 **64e**	 **66e**	69
6	 **64f**	 **66f**	43

Reaction conditions: 1,3-diene **64** (1.0 equiv), diallyl carbonate **52** (2.0 equiv), $Pd(PPh_3)_4$ (5 mol%), THF (3 mL), rt, 8 h

2.3.2.1. Palladium catalyzed 1,4-difunctionalization of 1,3-butadiene derivative using allyl methyl carbonate and dimethallyl carbonate

We were then interested in checking the reactivity of allyl methyl carbonate **67** with 1,3-butadiene derivative **64a**. Under similar reaction condition employed for diallyl carbonate, the reaction afforded the expected decarboxylative 1,4-conjugate methoxy-allylated product **68** in 27% yield.



Scheme 2.22

The structure of the product **68** was elucidated by spectroscopic analysis. The IR spectrum showed characteristic carbonyl absorptions at 1731 cm^{-1}. In the ^{1}H NMR spectrum of the compound **68** (Figure 2.7), sp^2 methylene protons of allyl part resonated as multiplet in the region δ 5.45-5.38 ppm. The multiplet in the region δ 5.95-5.87 ppm was assigned to the sp^2 methine CH proton of allyl group. Four methoxy protons were discernible as singlets at δ 3.90, 3.86, 3.81 and 3.27 ppm. The proton on the carbon attached to the methoxy and carbomethoxy group resonated as a singlet at δ 4.15 ppm. In the ^{13}C NMR spectrum (Figure 2.8), the ester carbonyl carbons observed at δ 168.4 and 164.9 ppm. All other signals in ^{1}H and ^{13}C NMR spectra were in agreement with the proposed structure. The molecular ion peak at *m/z* 421.13844, $[M+Na]^+$ in the mass spectrum, provided further information about the proposed structure.

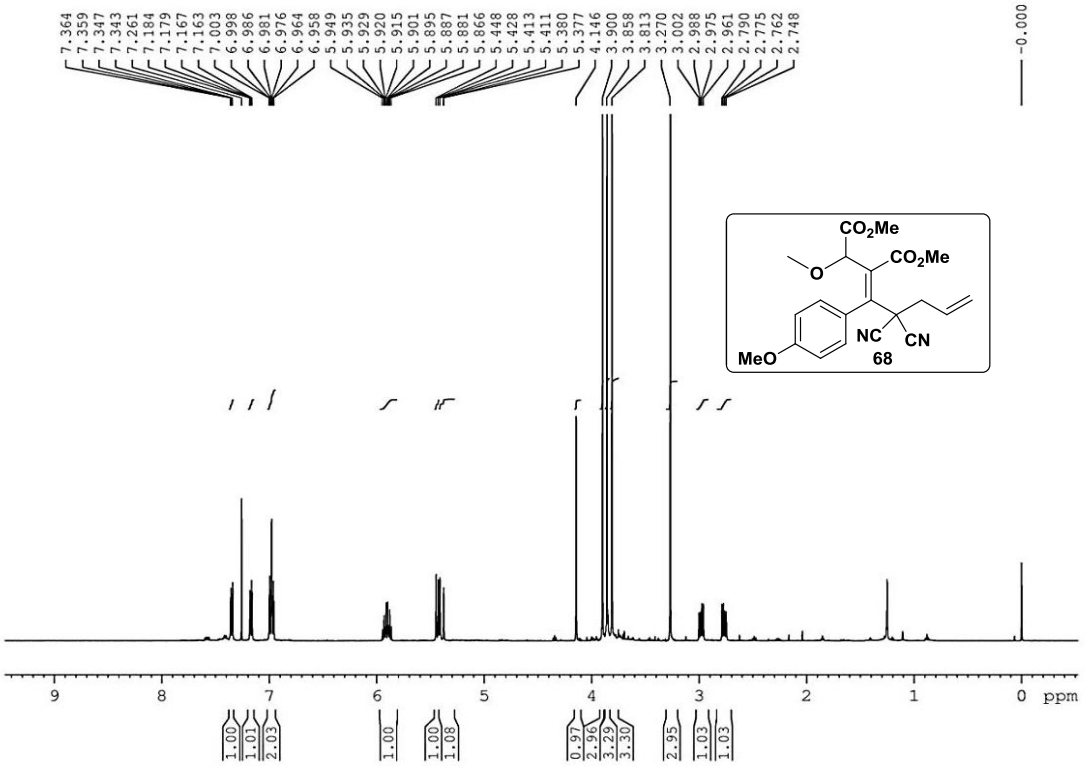


Figure 2.7. ^{1}H NMR spectrum of compound **68**

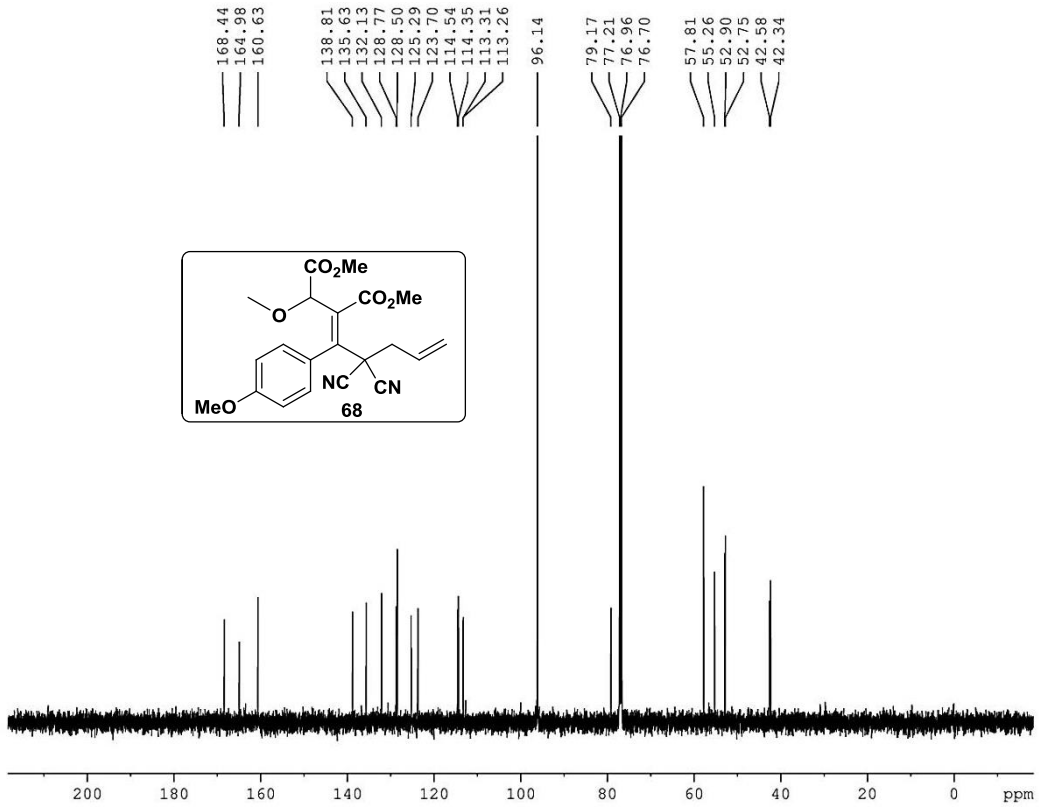
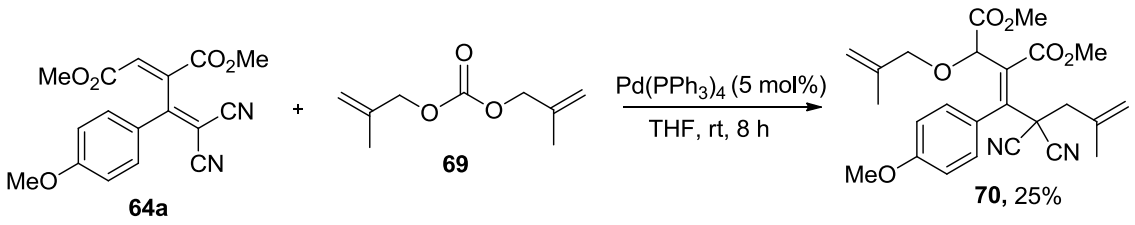


Figure 2.8. ^{13}C NMR spectrum of compound **68**

Dimethallyl carbonate **69** also reacted in the same fashion with 1,3-butadiene derivative **64a** under similar reaction conditions and provided the 1,4- addition product **70** in 25% yield (Scheme 2.23).



Scheme 2.23

The structure of the product **70** was assigned based on various spectroscopic analysis. The strong absorption at 1732 cm^{-1} in the IR spectrum indicates the presence of carbonyl group. In ^{1}H NMR spectrum (Figure 2.9), terminal olefin protons resonated as doublets at δ 5.15 and 4.75 ppm. The proton on the carbon attached to the oxygen atom and the carbomethoxy group resonated as a singlet at δ 4.29 ppm. Sharp singlets observed at δ 1.93 and 1.65 ppm were characteristic of the methyl protons of methallyl group. The carbonyl carbons resonated at δ 168.9 and 165.3 ppm in the ^{13}C NMR spectrum (Figure 2.10). All

other peaks in the ^{1}H and ^{13}C NMR spectra were in agreement with the proposed structure. The structure of **70** further supported by the mass spectral analysis which showed a molecular ion peak at *m/z* 475.18565, $[M+Na]^{+}$.

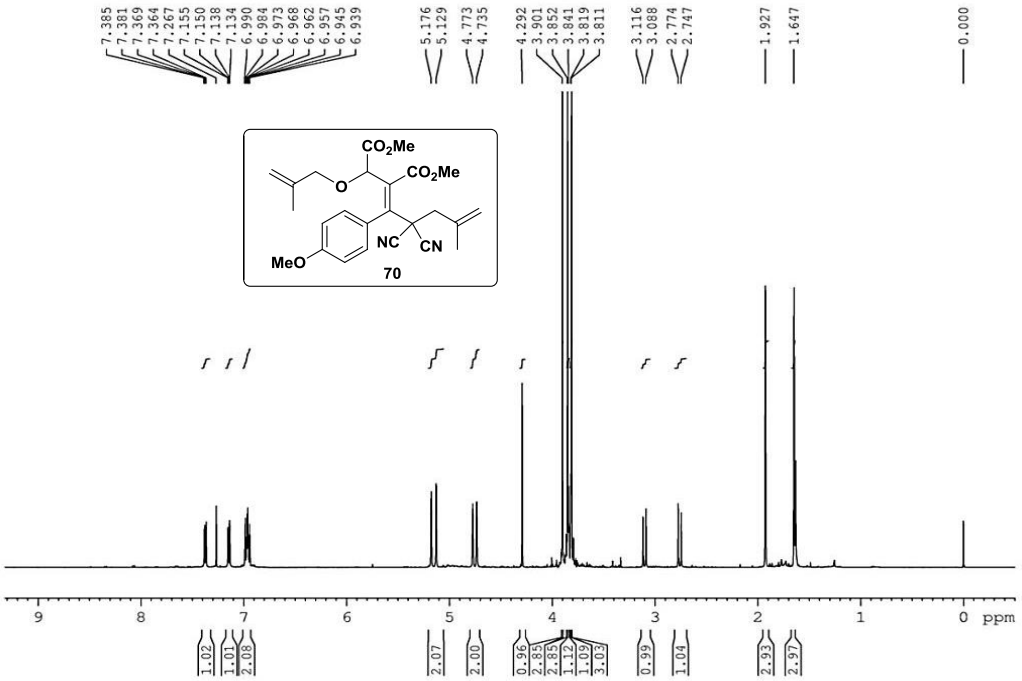


Figure 2.9. ^{1}H NMR spectrum of compound **70**

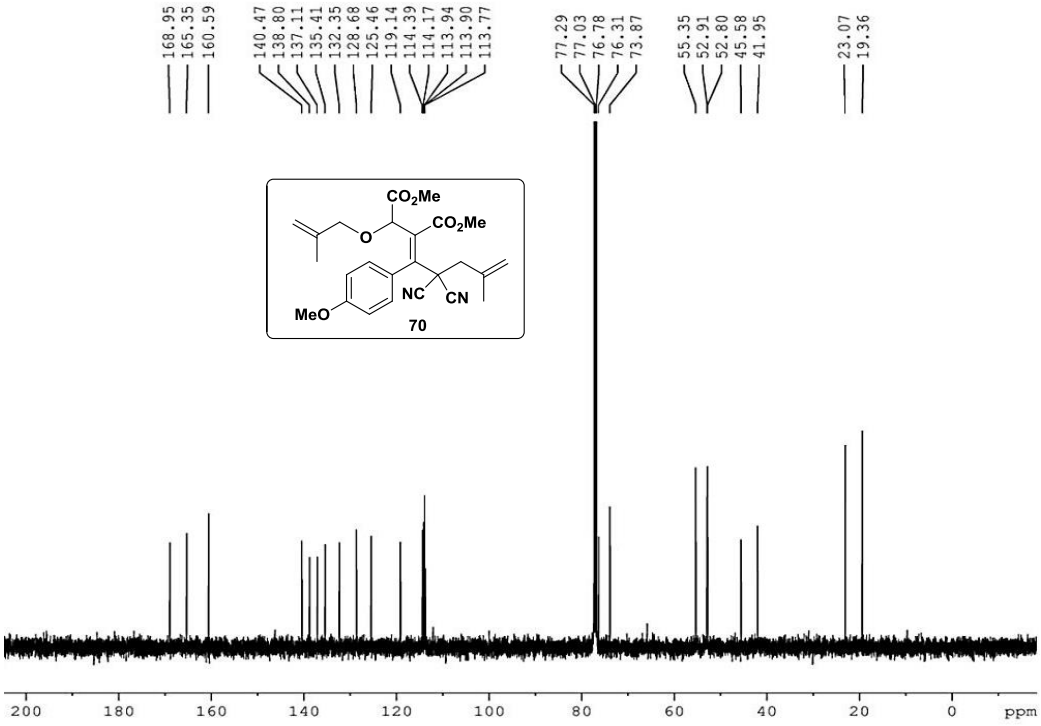
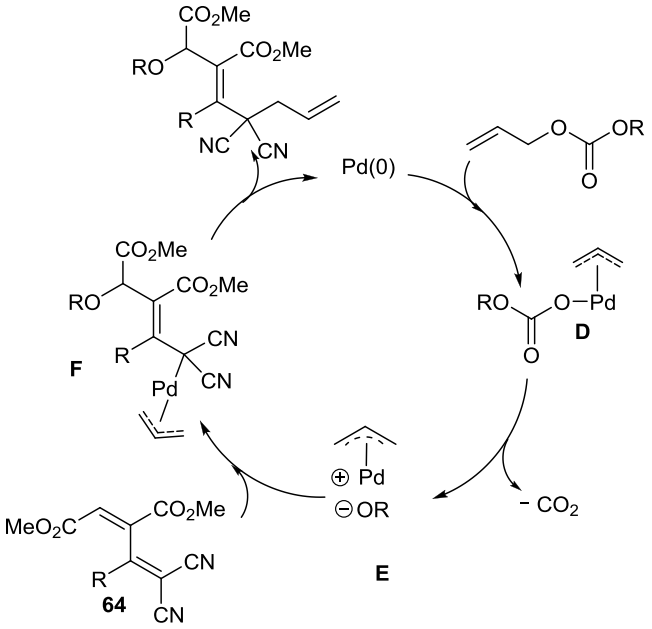


Figure 2.10. ^{13}C NMR spectrum of compound **70**

2.3.3. Mechanistic considerations

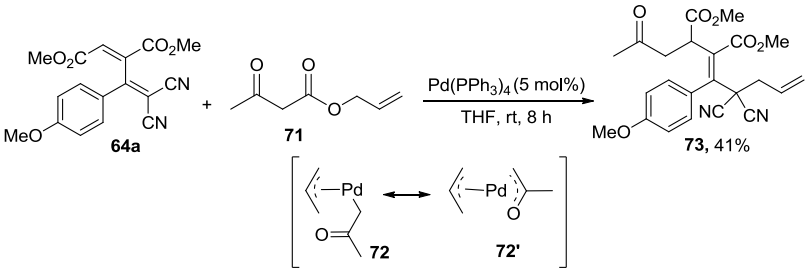
A mechanistic postulate suggested for this reaction would involve the oxidative addition of palladium(0) to allyl carbonate to afford the intermediate **D** which then will undergo decarboxylation to produce the π-allylpalladium intermediate **E**. The alkoxy anion of intermediate **E** will then undergo 1,4-addition with diene **64** producing intermediate **F**. The final step involves reductive elimination of palladium from **F** to give the 1,4-double addition product (Scheme 2.24).



Scheme 2.24

2.3.4. Palladium catalyzed decarboxylative allylation-acetonation reaction in 1,3-butadiene derivatives

In the next phase, we evaluated the reactivity of allyl acetoacetate **71** with the functionalized diene **64a**. We were pleased to find that 1,4-difunctionalization occurs by the decarboxylative addition of allyl acetoacetate. The reaction was carried out in the presence of 5 mol% $Pd(PPh_3)_4$ in 3 mL THF at room temperature, which after 8 h furnished the 1,4-acetonation-allylated product **73** in 41% yield. The reaction is presumed to be proceeding through oxa-π-allyl-π-allylpalladium complex **72'** derived from allyl acetoacetate.



Scheme 2.25

Spectral analysis was carried out to assign the structure of **73**. The IR spectrum displayed the characteristic carbonyl absorption at 1724 cm^{-1}. In the ^{1}H NMR spectrum (Figure 2.11), terminal olefin protons of allyl group resonated as multiplet in the region δ 5.43-5.30 ppm. The sp^2 -CH proton of the allyl moiety was located at δ 5.92-5.85 ppm as a multiplet. A sharp singlet observed at δ 2.13 ppm corresponds to sp^3 methyl protons.

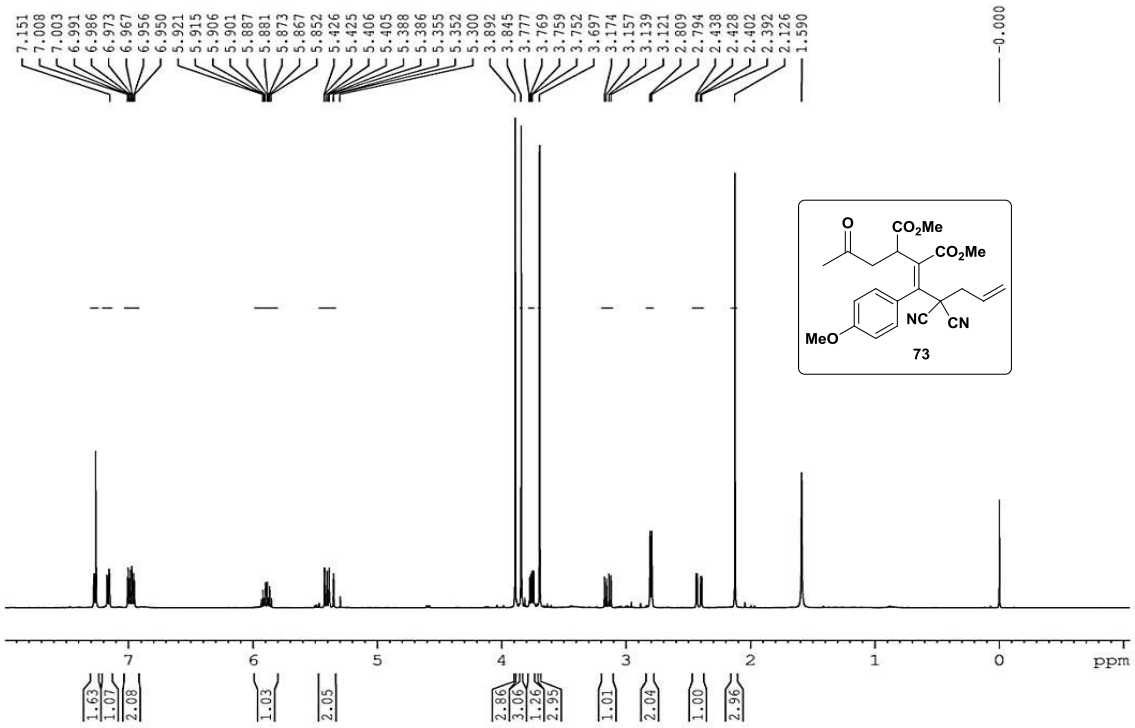


Figure 2.11. ^{1}H NMR spectrum of compound **73**

In the ^{13}C NMR spectrum (Figure 2.12), the carbonyl carbon was detected at δ 204.4 ppm whereas the ester carbonyls observed at δ 170.9 and 166.1 ppm. The nitrile carbons resonated at δ 113.7 and 113.6 ppm. The signal corresponding to methyl carbon attached to carbonyl group appeared at δ 30.1 ppm. All other peaks in the spectrum were in agreement

with the proposed structure. The high-resolution mass spectral analysis which showed $[M+Na]^+$ peak at *m/z* 447.15299 provided further proof for the structure.

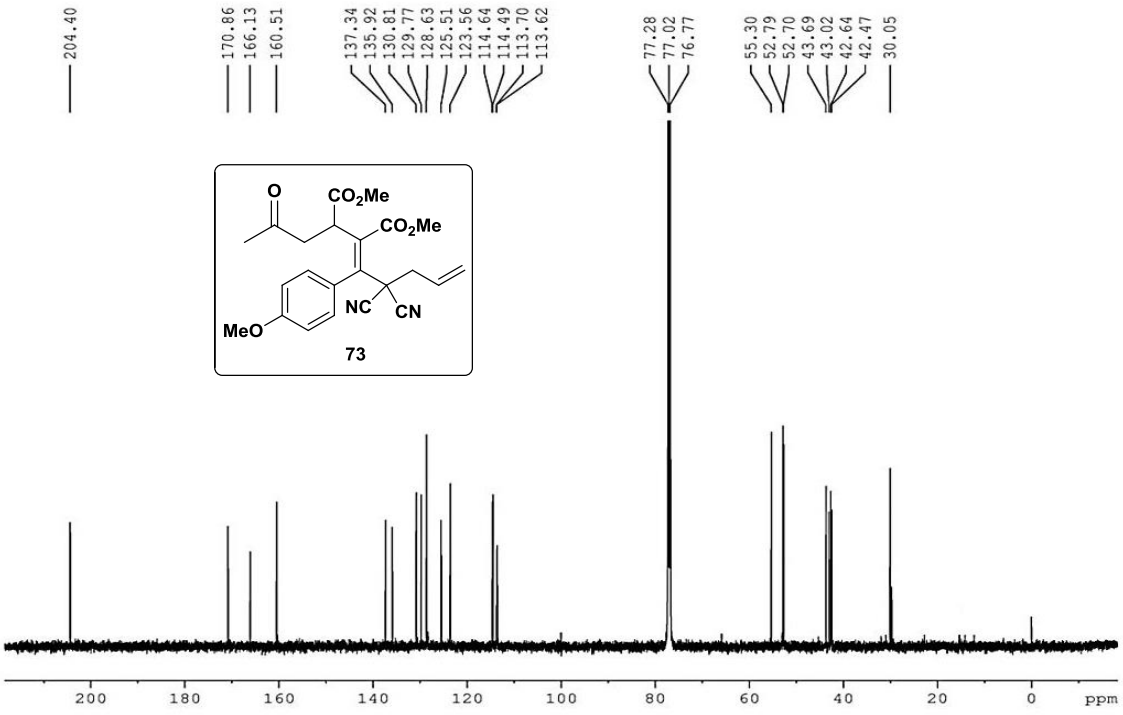
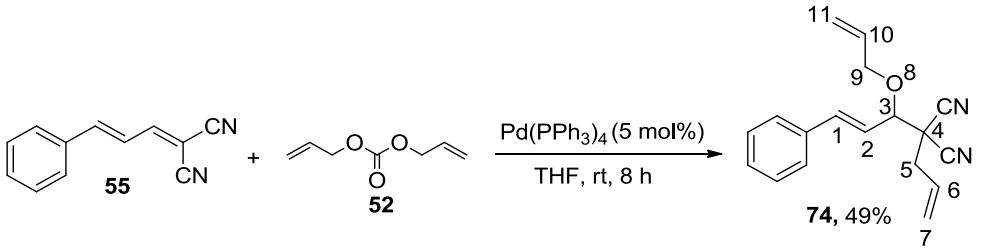


Figure 2.12. ^{13}C NMR spectrum of compound **73**

2.3.5. Reactivity of other functionalized dienes toward π-allyl palladium related complexes

To further understand the regioselectivity of this catalytic bis-functionalization reaction, we have investigated the reactivity of bis-π-allyl palladium and related complexes with other functionalized dienes. We have synthesized diene **55** from cinnamaldehyde and malononitrile. The reactivity of bis-π-allylpalladium complex with this diene is already reported.[29] We have performed palladium catalyzed allylation-oxyallylation reaction in diene **55** using diallyl carbonate **52**. Treatment of diene **55** with diallyl carbonate **52** in the presence of 5 mol% $Pd(PPh_3)_4$ afforded exclusively 1,2-addition product **74** in 49% yield. No other regioisomer or 1,4-addition product was observed, indicating that 1,4-addition can only be achieved by introducing suitable electron withdrawing group on the conjugated system.



Scheme 2.26

The structure of the product **74** was elucidated by spectroscopic techniques. The IR spectrum of the compound showed characteristic -CN stretching at 2259 cm^{-1}. In the ^{1}H NMR spectrum (Figure 2.13), the aromatic protons resonated as a multiplet in the region δ 7.47-7.34 ppm. Olefinic protons at C-1 resonated as a doublet at δ 6.79 (J = 15.5 Hz) ppm and proton at C-2 resonated as multiplet at δ 6.17-6.12 ppm. The sp^2 methine protons of allyl group at C-6 and C-10 observed as a multiplet at δ 5.94-5.87 ppm. The peak at δ 5.43-5.26 ppm corresponds to sp^2 -CH_2 protons of the allyl group at C-7 and C-11.

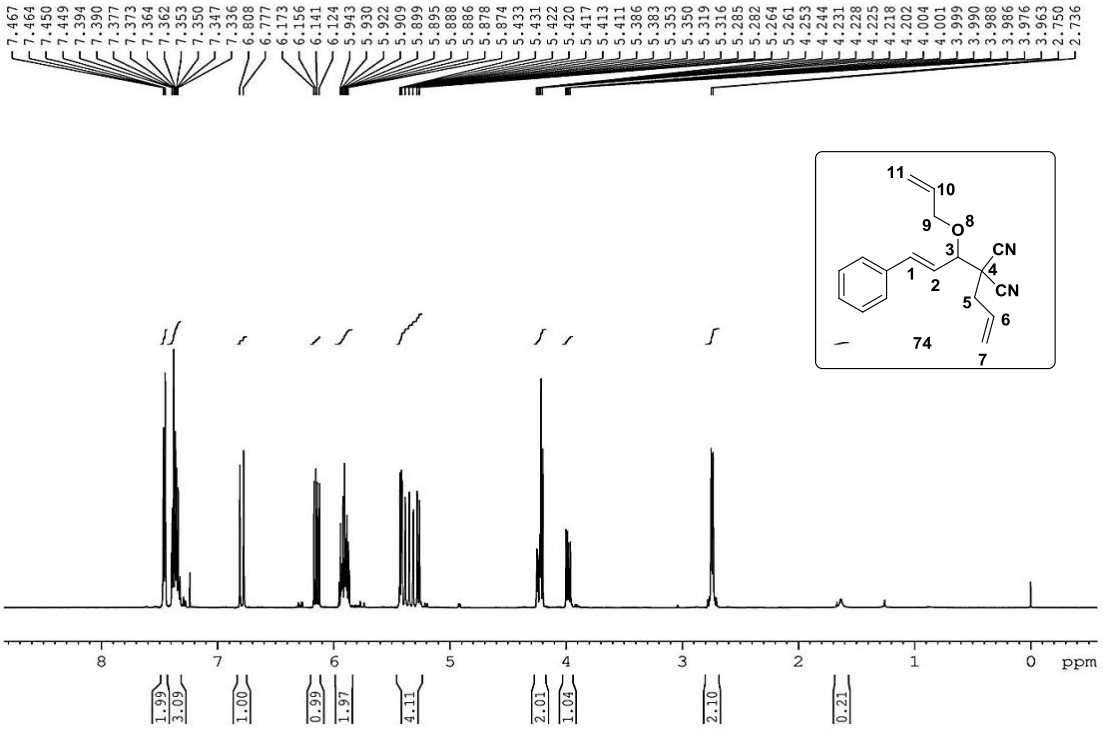


Figure 2.13. ^{1}H NMR spectrum of compound **74**

In the ^{13}C NMR spectrum (Figure 2.14), the nitrile carbons were discernible at δ 114.0 and 113.8 ppm. The olefinic carbons at C-1 and C-2 were located at δ 138.9 and 121.1ppm respectively. The quaternary C-4 carbon resonated at δ 43.7 ppm and the signals

corresponding to C-3 and C-9 appeared at δ 80.1 and 70.1 ppm respectively. All other signals in the ^{1}H and ^{13}C NMR spectra were in agreement with the proposed structure.

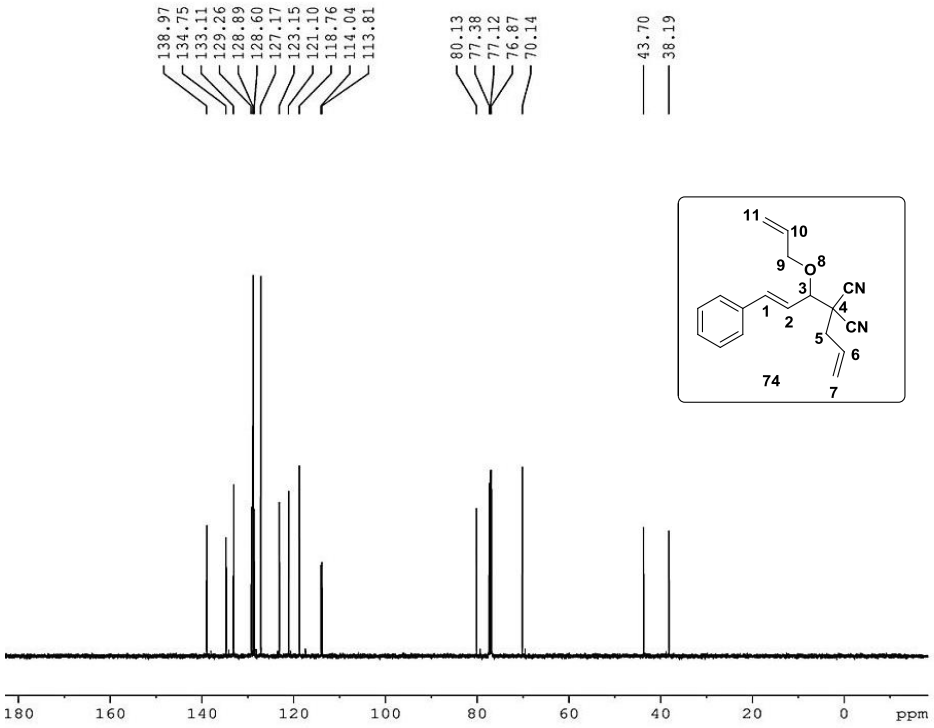
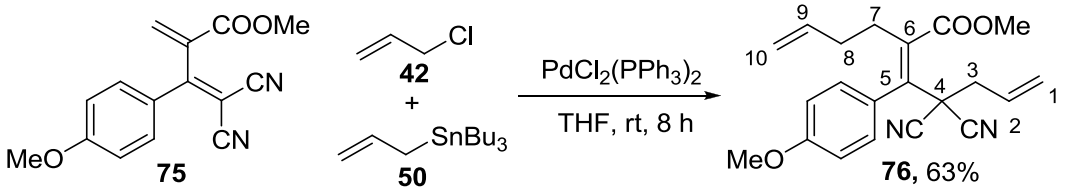


Figure 2.14. ^{13}C NMR spectrum of compound **74**

Further, we synthesized 1,3-butadiene derivative **75** containing an electron withdrawing ester group on the conjugated system by PPh_3-catalyzed reaction of methyl propiolate with 2-(4-methoxybenzylidene)malononitrile.[32] The reaction of conjugated diene **75** with allyl chloride and allyltributyltin in the presence of $PdCl_2(PPh_3)_2$ exclusively afforded 1,4-conjugate addition product **76** in 63% yield.



Scheme 2.27

Spectral data provided sufficient information for the structural analysis of the product **76**. The IR spectrum of the compound **76** showed characteristic carbonyl absorptions at 1741 cm^{-1}. The absorption indicative of the -CN stretching was seen at 2234 cm^{-1}. In the ^{1}H NMR spectrum of **76** (Figure 2.15), the alkene protons at C-2 and C-9 were identified as two

multiplets at δ 5.94-5.85 and 5.59-5.52 ppm. The sp^2 methylene protons of the allyl groups at C-1 and C-10 resonated as multiplets in the region δ 5.41-5.34 and 4.94-4.89 ppm. Two methoxy protons were discernible as singlets at δ 3.92 and 3.85 ppm. The sp^3 methylene protons at C-7 appeared as multiplet at δ 2.21-2.18 ppm. All other signals were in good agreement with the assigned structure.

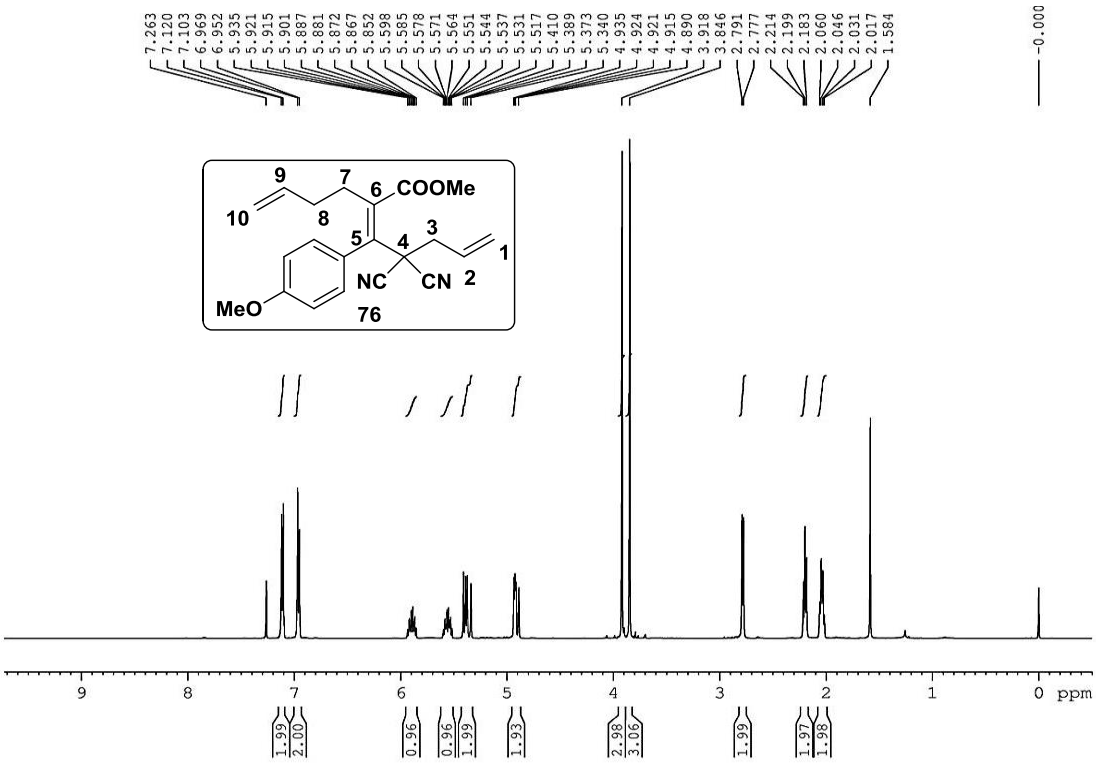


Figure 2.15. ^{1}H NMR spectrum of compound **76**

The ^{13}C NMR spectrum (figure 2.16) positioned the carbonyl peak at δ 168.1 ppm. A signal at δ 160.1 ppm was ascribed to the aromatic carbon attached to the methoxy group. The sp^3 carbons at C-3, C-4, C-7 and C-8 appeared at δ 42.8, 42.3, 32.7 and 32.0 ppm respectively. Two cyano carbons resonated at δ 114.4 and 113.9 ppm. The methine carbons of allyl group C-2 and C-9 were located at δ 126.3 and 136.3 ppm respectively. The sp^2 methylene carbons at C-1 and C-10 resonated at δ 123.3 and 115.9 ppm. The structure was further confirmed by high-resolution mass spectral analysis which showed a molecular ion peak at *m/z* 351.17142, $[M+1]^+$.

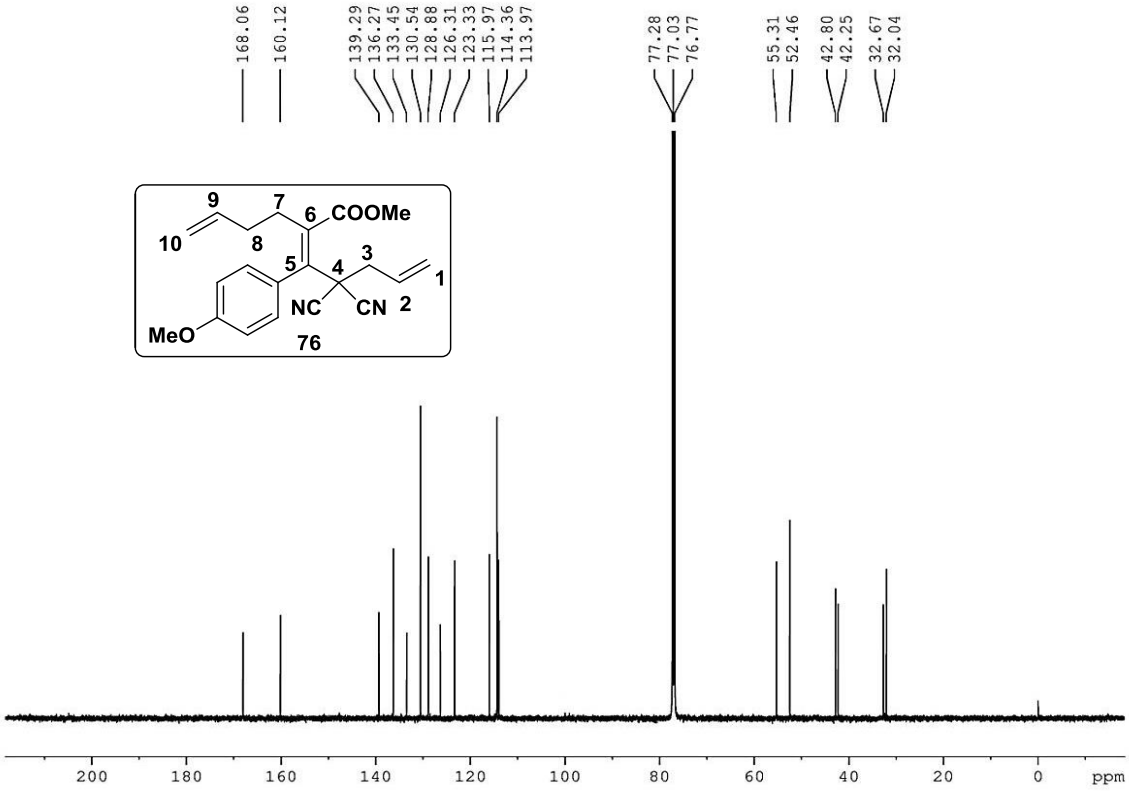
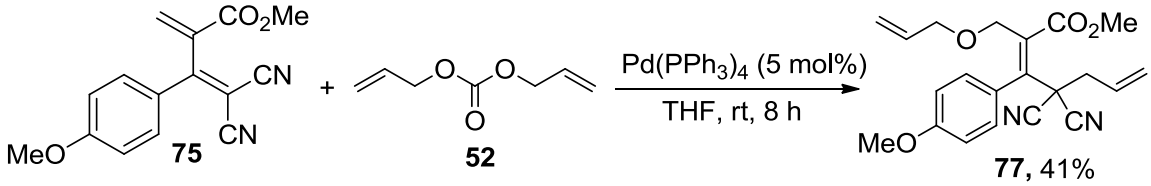


Figure 2.16. ^{13}C NMR spectrum of compound **76**

In similar fashion, the reaction of diallyl carbonate **52** with diene **75** in the presence of 5 mol% $Pd(PPh_3)_4$ provided the 1,4-allyloxy allylation product **77** in 41% yield.

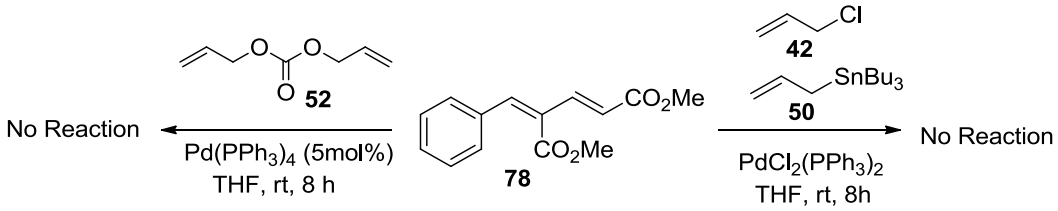


Scheme 2.28

The structure of the product **77** elucidated with the help of spectroscopic data. The IR spectrum of the compound showed characteristic carbonyl absorption at 1738 cm^{-1}. In ^{1}H NMR spectrum, the two sp^2 methylene protons of allyl groups were resonated as multiplets in the region δ 5.29-5.22 and 5.12-5.03 ppm. The sp^2 methine protons of allyl groups located at δ 5.88-5.83 and 5.58-5.49 ppm as multiplets. The ^{13}C NMR spectrum presented the carbonyl carbon at δ 170.4 ppm. The carbons of methoxy groups located at δ 55.3 and 52.8 ppm. All other signals in the ^{1}H and ^{13}C NMR spectra were in agreement with the proposed structure.

The structure was further supported by high-resolution mass spectral analysis which showed a molecular ion peak at *m/z* 367.16639 $[M+1]^+$.

In the light of the results obtained with different dienes containing nitrile group as the essential functional group, we attempted the allylation reaction of diene **78** derived from glutaconic diester. The diene **78** was prepared by reacting glutaconic dimethyl ester with benzaldehyde in the presence of piperidine base.[33] We have carried out both bis-allylation and allylation-oxyallylation reaction with diene **78** under the standard reaction conditions. In both cases the reactions were unsuccessful, and the diene was recovered as such. The reason for the failure of the reaction might be the destabilization of intermediate due to the lack of nitrile group.[34]



Scheme 2.29

2.4. Conclusion

In conclusion, we have developed a simple, clean and efficient strategy for the bis-functionalization of the 1,3-butadiene derivative using bis-π-allyl palladium and related complexes. To the best of our knowledge, this is the first report on a palladium catalyzed 1,4-conjugate addition reaction of 1,3-butadiene derivative *via* amphiphilic bis-π-allylpalladium and associated complexes. Functionalized trienes and dienes were synthesized by introducing allyl, oxyallyl and acetonyl groups. The reactivity of π-allylpalladium complex with different functionalized dienes was verified, and a 1,4-conjugate addition was achieved only by installing electron withdrawing group such as ester on the conjugated system. Although these reactions are limited to highly activated dienes, the use of cyano group for further structural manipulation is noteworthy.

2.5. Experimental Details

General methods: All reactions were conducted in oven-dried glass wares. Solvents used for the experiments were distilled and dried as specified. All chemicals were commercially available and are used without further purification. The progress of the reaction was

monitored by thin layer chromatography, which was performed on Merck pre-coated plates (silica gel 60 F254, 0.25 mm), and was visualized with UV light. Gravity column chromatography was done using 100-200 mesh silica gel or neutral aluminium oxide and mixtures of hexane-ethyl acetate were used for elution. The solvents were removed using Buchi E.L. rotary evaporator.

The melting point of the solid compounds was determined on a Buchi melting point apparatus and are uncorrected. IR spectra were recorded on Bruker Alpha FT-IR spectrometer. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 500 MHz spectrophotometers ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.25, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (double doublet); m (multiplet). Coupling constants are reported as *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.03, triplet). Mass spectra were recorded under ESI/HRMS at 60000 resolution using Thermo Scientific Exactive mass spectrometer.

2.5.1. General experimental procedure for the preparation of arylidene malononitrile derivatives (62)

A solution of aromatic aldehyde (1.0 equiv.), malononitrile (3.0 equiv.) and ammonium acetate (1.0 equiv.) were taken together in 10 mL of benzene. To this, a drop of glacial acetic acid was added and refluxed for 6 hours. Then the solvent was removed and extracted with dichloromethane and dried over Na_2SO_4. Products were purified by silica gel column chromatography using hexane-ethyl acetate mixture.

2.5.2. General experimental procedure for the preparation of substituted 1,3-butadienes (64a-h)

A solution of dimethyl acetylenedicarboxylate (1.2 equiv.) and dicyanostyrene (1.0 equiv.) in dry THF (6 mL) under an argon atmosphere was cooled to -10 ^{o}C. To this pyridine (0.2 equiv.) was added and the reaction mixture was stirred for 3-4 hours at room temperature, and the completion of the reaction was monitored by TLC analysis. The solvent

was then removed under vacuum and the residue on chromatographic separation on silica gel column using hexane-ethyl acetate mixture afforded dienes in good yields.

2.5.3. General experimental procedure for bis-allylation of 1,3-butadiene derivatives

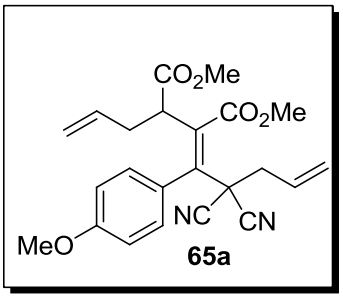
To a degassed solution of $PdCl_2(PPh_3)_2$ (5 mol%) in dry THF (2 mL) in a Schlenk tube, allyltributylstannane **50** (2 equiv.) was added followed by allyl chloride **42** (2 equiv.). The reaction mixture stirred at room temperature till the yellow colour turns to colourless. Then 1,3-buadiene derivative (1 equiv.) was added (in THF) and stirred at room temperature for 8 hours. After completion of the reaction (as evident by TLC), the solvent was removed under reduced pressure, and the residue on silica gel (100-200 mesh) column chromatography yielded functionalized 1,4-addition products (**65a-h)**.

2.5.4. General experimental procedure for allylation-oxyallylation reaction of 1,3-butadiene derivative

1,3-butadiene derivatives (1 equiv.) and $Pd(PPh_3)_4$ (5 mol%) were taken in a Schlenk tube, degassed and diallyl carbonate **52** (2 equiv.) was added followed by 3 mL THF. Argon gas is purged into the reaction mixture and stirred at room temperature for 8 hours. After the completion of reaction (as evident by TLC), the solvent was evaporated *in vacuo* and the residue on silica gel (100-200 mesh) column chromatography afforded the 1,4-allyl-oxyallylated products (**66a-f**).

(*Z*)-Dimethyl-2-allyl-3-(2,2-dicyano-1-(4-methoxyphenyl)pent-4-enylidene)succinate (65a)

Following the general experimental procedure, 1,3-diene **64a** (42 mg, 0.12 mmol), allyl chloride **42** (19 mg, 0.25 mmol), allyltributylstannane **50** (85 mg, 0.25 mmol) and $PdCl_2(PPh_3)_2$ (4 mg, 0.0064 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65a** as a pale yellow viscous liquid in 78% (41 mg) yield.

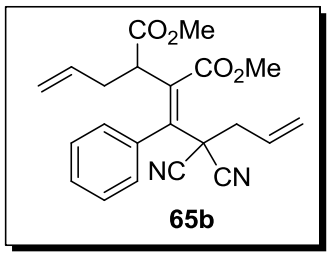


65a

R_f: 0.46 (4:6 Ethyl acetate/hexane). **IR (neat) υ_{max}:** 3079, 2955, 2919, 2850, 2313, 2246, 1734, 1604, 1510, 1461, 1376, 1290, 1248, 1177, 1118, 1032 cm^{-1}.;**^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.26–7.24 (m, 1 H), 7.08 (d, *J* = 8.5 Hz, 1 H), 6.98-6.94 (m, 2 H), 5.94-5.86 (m, 1 H), 5.56-5.47 (m, 1 H), 5.42-5.35 (m, 2 H), 5.05-4.98 (m, 2 H), 3.89 (s, 3 H), 3.84 (s, 3 H), 3.72 (s, 3 H), 3.18-3.15 (m, 1 H), 2.87-2.75(m,2 H), 2.63-2.58(m, 1 H), 2.27-2.21(m,1 H); **^{13}C NMR (125MHz, $CDCl_3$):** δ 171.0, 166.0, 160.4, 137.4, 136.6, 134.0, 131.1, 130.1, 128.7, 126.0, 123.5, 118.1, 114.5, 114.3, 113.7 (2C), 55.3, 52.6, 52.5, 48.2, 42.7, 42.5, 33.8. **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}N_2NaO_5$ $[M+Na]^+$: 431.15829; Found: 431.15646.

(*Z*)-Dimethyl 2-allyl-3-(2,2-dicyano-1-phenylpent-4-enylidene)succinate (65b)

Following the general experimental procedure, 1,3-diene **64b** (61 mg, 0.21mmol), allyl chloride **42** (32 mg, 0.42 mmol), allyl tributyl tin **50** (139 mg, 0.42 mmol) and $PdCl_2(PPh_3)_2$ (4 mg, 0.010 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65b** as a pale yellow viscous liquid in 69% (54 mg) yield.

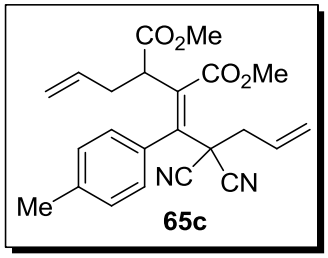


65b

R_f: 0.49 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3083, 2954, 2922, 2853, 2312, 2243, 1735, 1645, 1599, 1437, 1252, 1120, 933, 849 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.47-7.43 (m, 3 H), 7.37-7.31 (m, 1 H), 7.16-7.15 (m, 1 H), 5.96-5.82 (m, 1 H), 5.57-5.33 (m, 3 H), 5.04-4.95 (m, 2 H), 3.89 (s, 3 H), 3.71 (s, 3 H), 3.11-3.06 (m, 1 H), 2.91-2.71 (m, 2H), 2.63-2.54 (m, 1 H), 2.27-2.17 (m, 1 H).; **^{13}C NMR (75MHz, $CDCl_3$)**: δ 170.6, 165.7, 137.3, 136.4, 134.3, 134.0, 129.7, 129.6, 129.2, 128.9, 128.7, 128.3, 123.4, 118.1, 113.5, 113.4, 52.5, 52.4, 48.2, 42.7, 42.0, 33.8.; **HRMS (ESI):** *m/z* calcd. for $C_{22}H_{22}N_2NaO_4$ $[M+Na]^+$: 401.14773, Found: 401.14563.

(*Z*)-Dimethyl 2-allyl-3-(2,2-dicyano-1-p-tolylpent-4-enylidene)succinate (65c)

Following the general experimental procedure, 1,3-diene **64c** (72 mg, 0. 23mmol), allyl chloride **42** (35 mg, 0.46 mmol), allyltributylstannane **50** (152 mg, 0.46 mmol) and $PdCl_2(PPh_3)_2$ (8 mg, 0.012 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65c** as a pale yellow viscous liquid in 76% (105 mg) yield.

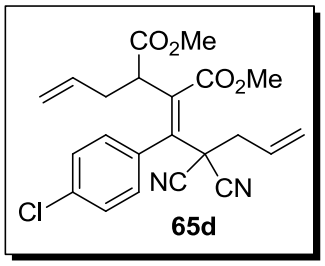


65c

R_f: 0.50 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3080, 2921, 2868, 2377, 2312, 1725, 1639, 1510, 1435, 1258, 1111, 1022, 826 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.27-7.18 (m, 3 H), 7.04 (d, *J* = 7.8 Hz, 1 H), 5.96-5.82 (m, 1 H), 5.58-5.44 (m, 1 H), 5.42-5.33 (m, 2 H), 5.03-4.95 (m, 2 H), 3.88 (s, 3 H), 3.71 (s, 3 H), 3.14-3.09 (m, 1 H), 2.86-2.72 (m, 2 H), 2.63-2.54 (m, 1 H), 2.39 (s, 3 H), 2.28-2.20 (m,1 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 170.8, 165.9, 139.7, 137.4, 136.3, 134.1, 131.2, 129.9, 129.6, 129.5, 128.8, 128.7, 123.4, 118.0, 113.6, 52.4, 48.2, 42.7, 42.2, 33.9, 21.3.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}N_2NaO_4$ $[M+Na]^+$: 415.16338, Found: 415.16123.

(*Z*)-Dimethyl 2-allyl-3-(1-(4-chlorophenyl)-2,2-dicyanopent-4-enylidene)succinate (65d)

Following the general experimental procedure, 1,3-diene **64d** (106 mg, 0.32mmol), allyl chloride **42** (49 mg, 0.64 mmol), allyltributylstannane **50** (211 mg, 0.64 mmol) and $PdCl_2(PPh_3)_2$ (11 mg, 0.016 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65d** as a pale yellow viscous liquid in 49% (65 mg) yield.

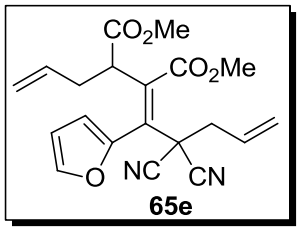


65d

R_f: 0.56 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2924, 2856, 2378, 2221, 1745, 1730, 1650, 1591, 1470, 1266, 1158, 1020, 852, 776 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.44-7.41 (m, 2 H), 7.30-7.25 (m, 1 H), 7.13-7.10 (m,1 H), 5.95-5.81 (m, 1 H), 5.57-5.34 (m, 3 H), 5.05-4.96 (m, 2 H), 3.89 (s, 3 H), 3.71 (s, 3 H), 3.06-3.01 (m, 1 H), 2.87-2.71 (m, 2 H), 2.63-2.54 (m, 1 H), 2.34-2.17 (m,1 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 170.3, 165.6, 142.0, 137.0, 136.1, 133.8, 132.5, 131.4, 130.3, 129.6, 129.2, 128.5, 123.7, 118.4, 113.3, 52.6, 48.3, 42.7, 42.5, 42.0, 34.1.; **HRMS (ESI):** *m/z* calcd. for $C_{22}H_{21}ClN_2NaO_4$ $[M+Na]^+$: 435.10875, Found: 435.10675.

(*E*)-Dimethyl 2-allyl-3-(2,2-dicyano-1-(furan-2-yl)pent-4-enylidene)succinate (65e)

Following the general experimental procedure, 1,3-diene **64e** (70 mg, 0.24 mmol), allyl chloride **42** (36 mg, 0.48 mmol), allyltributylstannane **50** (159 mg, 0.48 mmol) and $PdCl_2(PPh_3)_2$ (9 mg, 0.012 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65e** as a pale yellow viscous liquid in 61% (54 mg) yield.

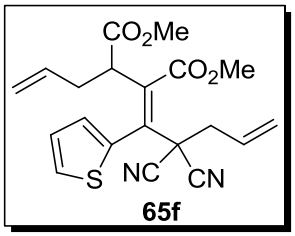


65e

R_f: 0.37 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3146, 3083, 2954, 2918, 2850, 2630, 2339, 2255, 2210, 1735, 1640, 1578, 1435, 1290, 1260, 1139, 1055, 1016, 913, 794 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.55 (s, 1 H), 6.66 (d, *J* = 2.7 Hz, 1 H), 6.51-6.49 (m, 1 H), 5.98-5.87 (m, 1 H), 5.58-5.41 (m, 3 H), 5.04-4.97 (m, 2 H), 3.87 (s, 3 H), 3.75 (s, 3 H), 3.53-3.48(m, 1 H), 3.08-3.01 (m, 2 H), 2.68-2.63 (m, 1 H), 2.34-2.19 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 170.5, 165.3, 145.7, 144.2, 139.4, 133.7, 128.8, 128.2, 127.6, 123.4, 118.0, 113.9, 113.0, 111.2, 52.7, 52.3, 48.5, 42.8, 42.0, 34.0.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{20}N_2NaO_5$ $[M+Na]^+$: 391.12699, Found: 391.12476.

(*E*)-Dimethyl 2-allyl-3-(2,2-dicyano-1-(thiophen-2-yl)pent-4-enylidene)succinate (65f)

Following the general experimental procedure, 1,3-diene **64f** (91 mg, 0.30 mmol), allyl chloride **42** (46 mg, 0.61 mmol), allyltributylstannane **50** (201 mg, 0.61 mmol) and $PdCl_2(PPh_3)_2$ (11 mg, 0.015 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **65f** as a pale yellow viscous liquid in 71% (82 mg) yield.

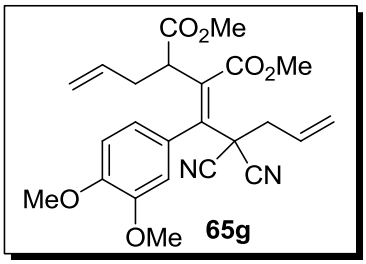


65f

R_f: 0.48 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2981, 2925, 2245, 1587, 1463, 1418, 1363, 1315, 1266, 1121, 1037 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.48 (dd, *J* = 4.8Hz, 1.2Hz, 1 H), 7.13-7.08 (m, 2 H), 5.90-5.84 (m, 1 H), 5.62-5.48 (m, 1 H), 5.45-5.38 (m, 2 H), 5.05-4.98 (m, 2 H), 3.88 (s, 3 H), 3.72 (s, 3 H), 3.33-3.28 (m, 1 H), 3.03-2.87 (m, 2 H), 2.68-2.59 (m, 1 H), 2.28-2.18 (m, 1 H).; **^{13}C NMR (75MHz, $CDCl_3$)**: δ 170.4, 165.4, 139.8, 133.7, 133.4, 130.6, 130.4, 128.6, 128.4, 127.6, 123.6, 118.2, 113.1, 52.7, 52.5, 48.6, 42.9, 42.7, 33.8.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{20}N_2NaO_4S$ $[M+Na]^+$: 407.10415, Found: 407.10220.

(*Z*)-Dimethyl 2-allyl-3-(2,2-dicyano-1-(3,4-dimethoxyphenyl)pent-4-enylidene)succinate (65g)

Following the general experimental procedure, 1,3-diene **64g** (52 mg, 0.14 mmol), allyl chloride **42** (22 mg, 0.29 mmol), allyltributylstannane **50** (96 mg, 0.29 mmol) and $PdCl_2(PPh_3)_2$ (5 mg, 0.007 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **65g** as a pale yellow viscous liquid in 30% (19 mg) yield.

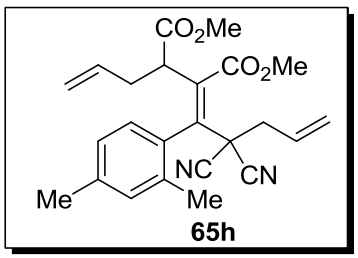


65g

R_f: 0.35 (4:6 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3742, 3079, 2955, 2918, 2850, 2584, 2379, 2312, 2246, 1733, 1640, 1598, 1511, 1458, 1248, 1135, 1023, 818 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 6.92-6.82 (m, 2 H), 6.70-6.62 (m, 1 H), 5.94-5.83 (m, 1 H), 5.61-5.46 (m, 1 H), 5.43-5.34 (m, 2 H), 5.04-4.96 (m, 2 H), 3.90-3.87 (m, 9 H), 3.71 (s, 3 H), 3.20-3.15 (m, 1 H), 2.92-2.72 (m, 2 H), 2.62-2.55 (m, 1 H), 2.33-2.15 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 170.8, 165.8, 149.9, 149.1, 137.2, 136.6, 134.3, 133.9, 128.8, 126.3, 123.4, 122.3, 121.0, 118.0, 113.6, 112.2, 55.9, 55.8, 52.5, 52.4, 48.3, 42.7, 42.3, 33.9.; **HRMS (ESI):** *m/z* calcd. for $C_{24}H_{26}N_2NaO_6$ $[M+Na]^+$: 461.16886, Found: 461.16669.

(*Z*)-Dimethyl-2-allyl-3-(2,2-dicyano-1-(2,4-dimethylphenyl)pent-4-enylidene)succinate (65h)

Following the general experimental procedure, 1,3-diene **64h** (53 mg, 0.16 mmol), allyl chloride **42** (19 mg, 0.25 mmol), allyltributyltin **50** (81 mg, 0.25 mmol) and $PdCl_2(PPh_3)_2$ (8 mg, 0.008 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **64h** as a pale yellow viscous liquid in 47% (31 mg) yield.



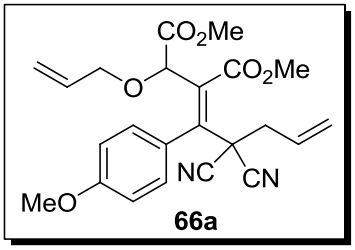
65h

R_f: 0.53 (4:6 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3582**,** 3078, 2921, 2853, 2380, 2311, 2245, 1731, 1609, 1434, 1257, 1205, 1032, 990, 925, 826, 747cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.13 (s, 1 H), 7.03 (d, *J* = 7.5 Hz, 1 H), 6.87 (d, *J* = 7.8 Hz, 1H), 5.96-5.85 (m, 1 H), 5.61-5.49 (m, 1 H), 5.43-5.36 (m, 2 H), 5.04-4.95 (m, 2 H), 3.88 (s, 3 H), 3.68 (s, 3 H), 3.08-3.02 (m, 1 H), 2.75-2.68 (m, 1 H), 2.64-2.55 (m, 1 H), 2.38-2.32 (m, 8 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 170.8, 165.8, 139.8, 138.5, 137.3, 136.3, 134.3, 132.1, 130.9, 129.0, 128.9, 126.7, 123.4, 118.0, 113.6, 113.5, 52.6, 52.3, 52.1, 48.0, 42.5, 34.3, 21.2, 20.0.; **HRMS (ESI):** *m/z* calcd. for $C_{24}H_{26}N_2NaO_4$ $[M+Na]^+$: 429.17903, Found: 429.17688.

(*Z*)-Dimethyl-2-(allyloxy)-3-(2,2-dicyano-1-(4-methoxyphenyl)pent-4-enylidene)succinate (66a)

Following the general experimental procedure, 1,3-diene **64a** (110 mg, 0.33 mmol), diallyl carbonate **52** (95 mg, 0.67 mmol) and $Pd(PPh_3)_4$ (19 mg, 0.016 mmol) in 3 mL THF at

room temperature under argon atmosphere for 8h gave the product **66a** as a pale yellow viscous liquid in 71% (99 mg) yield.

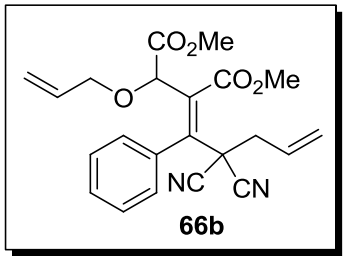


66a

R_f: 0.31 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2954, 2921, 2852, 2377, 2312, 1727, 1604, 1507, 1456, 1378, 1246, 1178, 1023, 838 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.34-7.32 (m, 1 H), 7.16-7.12 (m, 1 H), 6.97-6.93 (m, 2 H), 5.93-5.82 (m, 1 H), 5.76-5.63 (m, 1 H), 5.43-5.34 (m, 2 H), 5.10-5.04 (m, 2 H), 4.28 (s, 1 H), 3.90 (m, 2 H), 3.88 (s, 3 H), 3.83 (s, 3 H), 3.79 (s, 3 H), 2.99-2.92 (m, 1 H), 2.77-2.70 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 168.9, 165.2, 160.6, 138.2,135.9, 133.0, 132.1, 128.7, 128.5, 125.2, 123.6, 118.6, 114.5, 114.2, 113.5, 113.4, 76.4, 71.0, 55.3, 52.9, 52.8, 42.6, 42.3.; **HRMS (ESI)**: *m/z* calcd. for $C_{23}H_{24}N_2NaO_6$ $[M+Na]^+$: 447.15321, Found: 447.15103.

(*Z*)-Dimethyl-2-(allyloxy)-3-(2,2-dicyano-1-phenylpent-4-enylidene)succinate (66b)

Following the general experimental procedure, 1,3-diene **64b** (161 mg, 0.54 mmol), diallyl carbonate **52** (155 mg, 1.09 mmol) and $Pd(PPh_3)_4$ (31 mg, 0.027 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **66b** as a pale yellow solid in 55% (118 mg) yield.



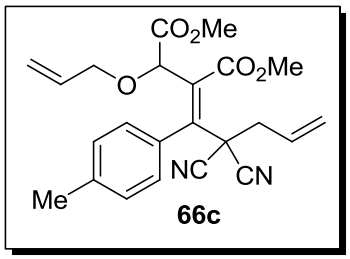
66b

R_f: 0.37 (4:6 Ethyl acetate/hexane); **mp:** 82-85 ^oC; **IR (neat) υ_{max}:** 3320, 3045, 2962, 2926, 2862, 2378, 2309, 1658, 1591, 1153, 1111, 1020, 853 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.49-7.46 (m, 3 H), 7.43-7.42 (m, 1 H), 7.27-7.24 (m, 1 H), 5.93-5.87 (m, 1 H), 5.71-5.66 (m, 1 H), 5.44-5.37 (m, 2 H), 5.07-5.03 (m, 2 H), 4.24 (s, 1 H), 3.93-3.90 (m, 5 H), 3.81 (s, 3 H), 2.97-2.93 (m, 1 H), 2.77-2.73 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 168.6, 164.9, 138.1, 135.7, 133.4, 130.7, 129.9, 129.0, 128.9, 128.5, 127.4, 123.7, 118.6, 113.2 (2C), 76.2, 70.9, 52.8, 52.7, 42.5, 41.9.; **HRMS (ESI) :** *m/z* calcd. for $C_{22}H_{22}N_2NaO_5$ $[M+Na]^+$: 417.14264, Found: 417.14075.

(*Z*)-Dimethyl-2-(allyloxy)-3-(2,2-dicyano-1-p-tolylpent-4-enylidene)succinate (66c)

Following the general experimental procedure, 1,3-diene **64c** (87 mg, 0.28 mmol), dially lcarbonate **52** (80 mg, 0.56 mmol) and $Pd(PPh_3)_4$ (16 mg, 0.014 mmol) in 3 mL THF at

room temperature under argon atmosphere for 8h gave the product **66c** as a pale yellow viscous liquid in 66% (76 mg) yield.

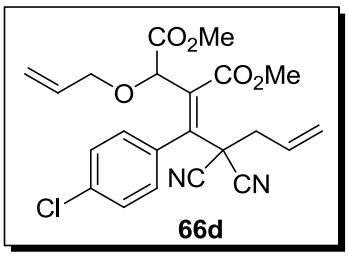


66c

R_f: 0.41 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3083, 2924, 2856, 2313, 2247, 1732, 1641, 1604, 1511, 1431, 1253, 1208, 1121, 1017, 933, 826 cm^{-1}; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.26-7.12 (m, 3 H), 7.10 (d, *J*= 6.6 Hz, 1 H), 5.95-5.81 (m, 1 H), 5.75-5.62 (m, 1 H), 5.42-5.33 (m, 2 H), 5.09-5.03 (m, 2 H), 4.25 (s, 1 H), 4.02-3.87 (m, 5 H), 3.78 (s, 3 H), 2.98-2.91 (m, 1 H), 2.77-2.70 (m, 1 H), 2.39 (s, 3 H).; **^{13}C NMR (75 MHz, $CDCl_3$)**: δ 168.6, 165.0, 140.0, 138.3, 135.7, 133.2, 130.6, 130.5, 129.8, 129.5, 128.6, 127.4, 123.6, 118.4, 113.3, 76.5, 70.9, 52.7, 52.6, 42.6, 42.1,21.3.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}N_2NaO_5$ $[M+Na]^+$: 431.15829,found: 431.15616.

(*Z*)-Dimethyl-2-(allyloxy)-3-(1-(4-chlorophenyl)-2,2-dicyanopent-4-enylidene)succinate (66d)

Following the general experimental procedure, 1,3-diene **64d** (64 mg, 0.19 mmol), diallyl carbonate **52** (55 mg, 0.38 mmol) and $Pd(PPh_3)_4$ (11 mg, 0.009 mmol) in 2 mL THF at room temperature under argon atmosphere for 8h gave the product **66d** as a pale yellow viscous liquid in 31% (26 mg) yield.



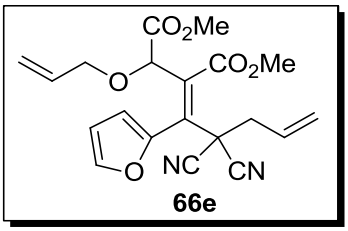
66d

R_f: 0.40 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2956, 2919, 2851, 2309, 2232, 1735, 1646, 1589, 1490, 1462, 1376, 1260, 1214, 1093, 1016 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.49-7.35 (m, 3 H), 7.21-7.18 (m, 1 H), 5.94-5.82 (m, 1 H), 5.75-5.64 (m, 1 H), 5.47-5.37 (m, 2 H), 5.12-5.07 (m, 2 H), 4.21 (s, 1 H), 3.94-3.91 (m, 5 H), 3.84 (s, 3 H), 3.01- 2.94 (m, 1 H), 2.78-2.71 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 168.4, 164.7, 136.8, 136.5, 133.0, 132.3, 131.8, 129.5, 129.2, 128.9, 128.3, 123.9, 118.7, 113.0, 76.3, 71.1, 53.0, 52.8, 42.6, 42.0.; **HRMS (ESI):** *m/z* calcd. for $C_{22}H_{21}ClN_2NaO_5$ $[M+Na]^+$: 451.10367, Found: 451.10156.

(*E*)-Dimethyl-2-(allyloxy)-3-(2,2-dicyano-1-(furan-2-yl)pent-4-enylidene)succinate (66e)

Following the general experimental procedure, 1,3-diene **64e** (47 mg, 0.16 mmol), diallyl carbonate **52** (47 mg, 0.33 mmol) and $Pd(PPh_3)_4$ (9 mg, 0.008 mmol) in 3 mL THF at

room temperature under argon atmosphere for 8h gave the product **66e** as a pale yellow viscous liquid in 69% (42 mg) yield.

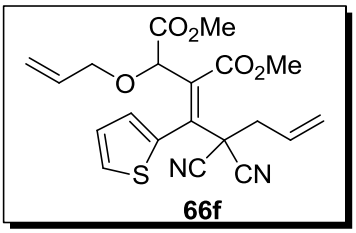


66e

R_f: 0.27 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3583, 3145, 3082, 2952, 2921, 2852, 2378, 2313, 2224, 1729, 1650, 1570, 1434, 1242, 1213, 1092, 1016, 955, 925, 846, 757, 719 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 7.60 (d, *J* = 1.2 Hz, 1 H), 6.84 (d, *J* = 3.0 Hz, 1 H), 6.52-6.51 (m, 1 H), 6.07-5.93 (m, 1 H), 5.78-5.64 (m, 1 H), 5.53-5.47 (m, 2 H), 5.09-4.96 (m, 2 H), 4.84 (s, 1 H), 4.08-4.02 (m, 1 H), 3.96-3.83 (m, 7 H), 3.40-3.33 (m, 1 H), 3.25-3.18 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 168.4, 164.6, 145.1, 144.5, 136.8, 132.7, 128.8, 123.6, 119.4, 115.8, 112.8, 112.7, 111.3, 75.4, 70.8, 53.1, 52.9, 42.8, 41.9.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{20}N_2NaO_6$ $[M+Na]^+$:407.12191, Found: 407.11987.

(*E*)-Dimethyl-2-(allyloxy)-3-(2,2-dicyano-1-(thiophen-2-yl)pent-4-enylidene)succinate (66f)

Following the general experimental procedure, 1,3-diene **64f** (97 mg, 0.32 mmol), diallyl carbonate **52** (91 mg, 0.64 mmol) and $Pd(PPh_3)_4$ (19 mg, 0.016 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **66f** as a pale yellow viscous liquid in 43% (55 mg) yield.

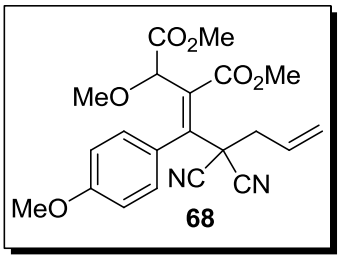


66f

R_f: 0.33 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3088, 2955, 2921, 2309, 2224, 1727, 1593, 1420, 1377, 1118, 1018, 852 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS)** : δ 7.84-7.77 (m, 1 H), 7.51-7.11 (m, 2 H), 6.00-5.86 (m, 1 H), 5.79-5.66 (m, 1 H), 5.47-5.42 (m, 2 H), 5.14-5.08 (m, 2 H), 4.47 (s, 1 H), 4.01-3.97 (m, 2 H), 3.95-3.83 (m, 6 H), 3.20-3.13 (m, 1 H), 2.97-2.90 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 168.3, 164.6 138.8, 132.9, 132.5, 131.7, 131.2, 128.4, 127.6, 123.8, 118.7, 112.9, 112.8, 71.1, 53.0, 52.8, 42.9, 42.5.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{20}N_2NaO_5S$ $[M+Na]^+$: 423.09906, Found: 423.09714.

(*Z*)-Dimethyl-2-(2,2-dicyano-1-(4-methoxyphenyl)pent-4-enylidene)-3-methoxysuccinate (68)

Following the general experimental procedure, 1,3-diene **64a** (72 mg, 0.22 mmol), allyl methylcarbonate **67** (51 mg, 0.44 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.011 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **68** as a pale yellow viscous liquid in 27% (24 mg) yield.

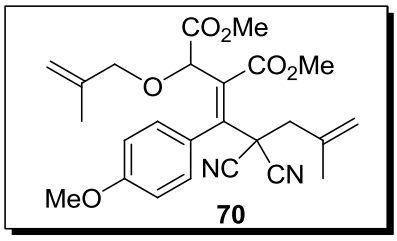


68

R_f: 0.38 (4:6 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2960, 2840, 2227, 1763, 1731, 1511, 1437, 1290, 910 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.36-7.34 (m, 1 H), 7.18-7.16 (m, 1 H), 7.00-6.96 (m, 2 H), 5.95-5.87 (m, 1 H), 5.45-5.38 (m, 2 H), 4.15 (s, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.81(s, 3 H), 3.27 (s, 3 H), 3.00-2.96 (m, 1 H), 2.79-2.75 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 168.4, 164.9, 160.6, 138.8, 135.6, 132.1, 128.8, 128.5, 125.3, 123.7, 114.5, 114.4, 113.3(2C), 79.2, 57.8, 55.3, 52.9, 52.8, 42.6, 42.3.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{22}N_2O_6Na$ $[M+Na]^+$: 421.13756, Found: 421.13844.

(*Z*)-Dimethyl-2-(2,2-dicyano-1-(4-methoxyphenyl)-4-methylpent-4-enylidene)-3-(2-methylallyloxy)succinate (70)

Following the general experimental procedure, 1,3-diene **64a** (104 mg, 0.32 mmol), dimethallyl carbonate **69** (108 mg, 0.64 mmol) and $Pd(PPh_3)_4$ (18 mg, 0.015 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **70** as a pale yellow viscous liquid in 25% (36 mg) yield.



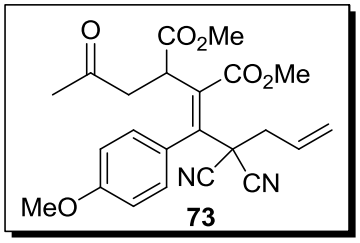
70

R_f: 0.41 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2953, 2840, 1758, 1732, 1511, 1435, 1290, 1250, 1138, 1093, 909 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.39-7.36 (m, 1 H), 7.16-7.13 (m, 1 H), 6.99-6.94 (m, 2 H), 5.15 (d, *J* = 23.5 Hz, 2 H), 4.75 (d, *J* = 19.0 Hz, 2 H), 4.29 (s, 1 H), 3.90 (s, 3 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.84-3.82 (m, 2 H), 3.10 (d, *J* = 14.0 Hz, 1 H), 2.76 (d, *J* = 13.5 Hz, 1 H), 1.93 (s, 3 H), 1.65 (s, 3 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 168.9, 165.4, 160.6, 140.5, 138.8, 137.1, 135.4, 132.4, 128.7, 125.5, 119.1, 114.4, 114.2, 113.9,

113.8, 113.7, 76.3, 73.9, 55.4, 52.9, 52.8, 45.6, 41.9, 23.1, 19.4.; **HRMS (ESI):** *m/z* calcd. for $C_{25}H_{28}N_2O_6Na$ $[M+Na]^+$: 475.18451, Found: 475.18565.

(*Z*)-Dimethyl-2-(2,2-dicyano-1-(4-methoxyphenyl)pent-4-enylidene)-3-(2-oxopropyl)succinate (73)

Following the general experimental procedure, 1,3-diene **64a** (53 mg, 0.16 mmol), allylacetoacetate **71** (46 mg, 0.32 mmol) and $Pd(PPh_3)_4$ (9 mg, 0.008 mmol) in 2 mL THF at room temperature under argon atmosphere for 8h gave the product **73** as a pale yellow viscous liquid in 41% (28 mg) yield.

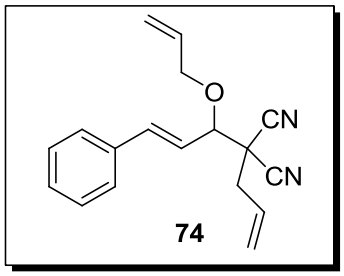


73

R_f: 0.38 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2955, 2847, 1724, 1606, 1510, 1291, 1250, 1180, 1163, 1029, 735 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.28-7.26 (m, 1 H), 7.16 (dd, *J* = 8.0, 2.0 Hz, 1 H), 6.99 (dq. *J* = 8.5, 2.5 Hz, 2 H), 5.92-5.85 (m, 1 H), 5.43-5.30 (m, 2 H), 3.89 (s, 3 H), 3.85 (s, 3 H), 3.78-3.75 (m, 1 H), 3.69 (s, 3 H), 3.17-3.12 (m, 1 H), 2.80 (d, *J* = 7.5 Hz, 2 H), 2.43 (dd, *J* = 18.0, 5.0 Hz, 1 H), 2.13 (s, 3 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 204.4, 170.9, 166.1, 160.5, 137.3, 135.9, 130.8, 129.8, 128.6, 125.5, 123.6, 114.6, 114.5, 113.7, 113.6, 55.3, 52.8, 52.7, 43.7, 43.0, 42.6, 42.5, 30.1.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}N_2O_6Na$ $[M+Na]^+$: 447.15321, Found: 447.15299.

(*E*)-2-Allyl-2-(1-(allyloxy)-3-phenylallyl)malononitrile (74)

Following the general experimental procedure, 1,3-diene **55** (100 mg, 0.55 mmol), diallylcarbonate **52** (157 mg, 1.09 mmol) and $Pd(PPh_3)_4$ (32mg, 0.028 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **74** as a colourless viscous liquid in 49% (75 mg) yield.



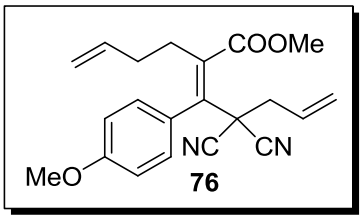
74

R_f: 0.59 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 3086, 2927, 2874, 2253, 1648, 1495, 1449, 1263, 1030, 990, 975, 764 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.47-7.45 (m, 2 H), 7.39-7.34 (m, 3 H), 6.79 (d, *J* = 15.5 Hz, 1 H), 6.17-6.12 (m, 1 H), 5.94-5.87 (m, 2 H), 5.43-5.26 (m, 4 H), 4.25-4.20 (m, 2 H), 4.00-3.96 (m, 1 H), 2.74 (d, *J* = 7.0 Hz, 2 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 138.9, 134.8, 133.1, 129.3, 128.9, 128.6, 127.2, 123.2, 121.1, 118.8, 114.0,

113.8, 80.1, 70.1, 43.7, 38.2.; **HRMS (ESI):** *m/z* calcd for $C_{18}H_{18}N_2O$ $[M+Na]^+$: 301.1317, Found: 301.1374.

(*Z*)-Methyl 2-(but-3-enyl)-4,4-dicyano-3-(4-methoxyphenyl)hepta-2,6-dienoate (76)

Following the general experimental procedure, 1,3-diene **75** (45 mg, 0.26 mmol), allyl chloride **42** (26 mg, 0.35 mmol), allyltributylstannane **50** (115 mg, 0.35 mmol) and $PdCl_2(PPh_3)_2$ (6 mg, 0.008 mmol) in 3 mL THF at room temperature under argon atmosphere for 8 h gave the product **76** as a colourless viscous liquid in 63% (39 mg) yield.

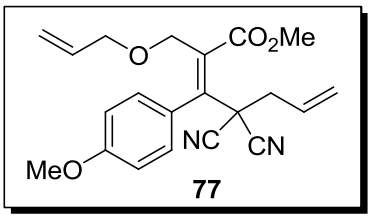


76

R_f: 0.62 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2957, 2843, 2234, 1741, 1604, 1508, 1293, 1251, 1216, 1178, 1029, 927, 840, 823 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.11 (d, *J* = 8.5 Hz, 2 H), 6.96(d, *J* = 8.5 Hz, 2 H), 5.94-5.85 (m, 1 H), 5.59-5.52 (m, 1 H), 5.41-5.34 (m, 2 H), 4.94-4.89 (m, 2 H), 3.92 (s, 3 H), 3.85 (s, 3 H), 2.78 (d, *J* = 7.0 Hz, 2 H), 2.21-2.18 (m, 2 H), 2.06-2.02 (m, 2 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 168.1, 160.1, 139.3, 136.3, 133.5, 130.5, 128.9, 126.3, 123.3, 115.9, 114.4, 113.9, 55.3, 52.5, 42.8, 42.3, 32.7, 32.0.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{23}N_2O_3$ $[M^+ +1]$: 351.17087, Found: 351.17142.

(*Z*)-Methyl 2-(allyloxymethyl)-4,4-dicyano-3-(4-methoxyphenyl)hepta-2,6-dienoate (77)

Following the general experimental procedure, 1,3-diene **75** (69 mg, 0.26 mmol), diallylcarbonate **52** (76 mg, 0.54 mmol) and $Pd(PPh_3)_4$ (14 mg, 0.013 mmol) in 3 mL THF at room temperature under argon atmosphere for 8h gave the product **77** as a pale yellow viscous liquid in 41% (40 mg) yield.

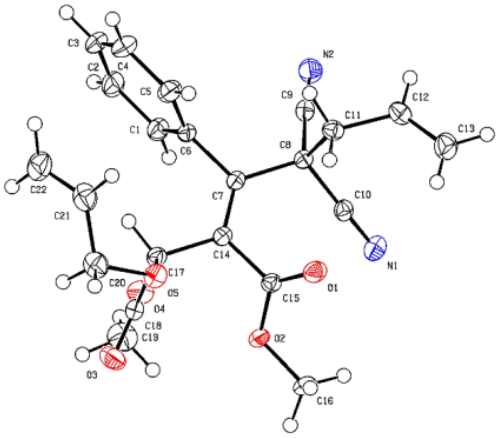


77

R_f: 0.59 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2951, 2831, 1738, 1613, 1287, 1249, 1211, 819 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.22 (d, *J* = 7.0 Hz, 2 H), 6.96-6.94 (m, 2 H), 5.88-5.83 (m, 1 H), 5.58-5.49 (m, 1 H), 5.29-5.22 (m, 2 H), 5.12-5.03 (m, 2 H), 4.05-3.96 (m, 3 H), 3.85 (s, 3 H), 3.79-3.76 (m, 4 H), 2.67-2.63 (m, 1 H), 2.42-2.38 (m, 1 H).; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 170.4, 161.0, 133.7, 131.3, 128.9, 127.4, 120.5, 117.9, 114.1, 112.3, 111.4, 72.6,

71.2, 55.3, 52.8, 39.0.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{22}N_2O_4$ [M^++1]: 367.16578, Found: 367.16639.

Crystal Data: Compound 66b



CCDC Number 933875

Chemical formula moiety	$C_{22}H_{22}N_2O_5$
Chemical formula sum	$C_{22}H_{22}N_2O_5$
Chemical formula weight	394.42
Symmetry cell setting	Monocilinic
Symmetry space group name	P21/c
Cell length a	9.6286 (9)
Cell length b	26.124 (2)
Cell length c	9.2040 (8)
Cell angle alpha	90.00
Cell angle beta	118.2250 (10)
Cell angle gamma	90.00
Cell volume	2039.8 (3)
Cell formula units Z	3
Cell measurement temperature	110 K(2)
Cell measurement reflns used	8313
Cell measurement theta min	2.40
Cell measurement theta max	28.19
Exptl crystal description	Block
Exptl crystal size max	0.30
Exptl crystal size mid	0.28

Exptl crystal size min	0.22
Exptl crystal density diffrn	1.284
Exptl crystal_density_method	'not measured'
Exptl crystal colour	colourless
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Exptl absorpt coefficient mu	0.092
Exptl absorpt correction-type	Multi-Scan
Exptl absorpt correction T min	0.9730
Exptl absorpt correction T max	0.980
Diffrn ambient temperature	110 (2)
Diffrn radiation wavelength	0.71073

2.6. References

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CHAPTER 3

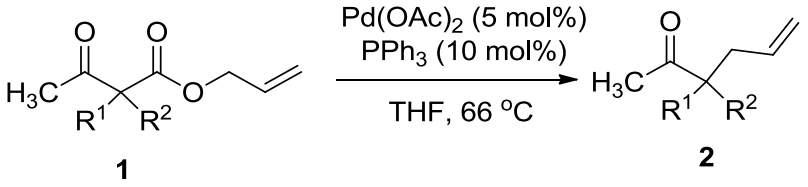
Palladium-Catalyzed Interceptive Decarboxylative Addition of Allyl Carbonates to Squarates, Isatins and Other Electrophilic Carbonyl Compounds

3.1. Introduction

Catalytic cross-coupling reactions have had a profound impact on the synthesis of pharmaceuticals, biologically active natural products and materials. In this scenario, transition metals were employed as reagents or catalysts because they permit the reactions to proceed under mild conditions, with high functional group compatibility and often proceed in a chemo-, regio- and stereoselective manner. Among the various metal catalyzed cross coupling reactions, transition metal catalyzed decarboxylative coupling is an important environmentally benign strategy.[1] Decarboxylative coupling takes place by generating an organometallic intermediate *via* decarboxylative metallation, and further reductive elimination provides coupled product. Decarboxylative coupling reaction has numerous advantages over the traditional cross-coupling methods: (i) the reactants, carboxylic acid derivatives, are ubiquitous and inexpensive, (ii) decarboxylation can generate reactive intermediates under neutral conditions, and (iii) the by-product formed is CO_2, which is non-flammable, non-toxic and easily removed from the reaction medium.[1] Another advantage of decarboxylative allylation (DcA) is the ability to generate both nucleophile and electrophile *in situ*.

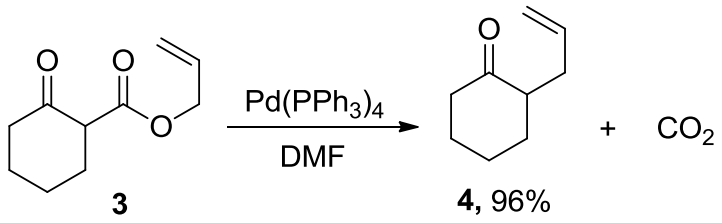
Since the pioneering work of Tsuji[2] and Saegusa,[3] palladium catalyzed decarboxylative allylations have emerged as an important strategy for constructing complex molecular frameworks under mild reaction conditions. They almost simultaneously reported the decarboxylative allylation of β-keto allyl esters. Tsuji and co-workers disclosed the

decarboxylative allylation of allyl esters of acetoacetic acid **1** in the presence of catalytic amount of $Pd(OAc)_2$ and PPh_3 rendered γ,δ-unsaturated methyl ketones **2** in high yield.[2]



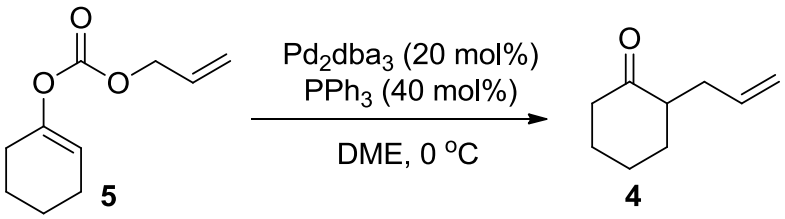
Scheme 3.1

Alternatively, Saegusa and co-workers demonstrated the decarboxylative coupling with a variety of acyclic and cyclic ketoesters using 5 mol% $Pd(PPh_3)_4$ as the catalyst. A Pd(II) enolate intermediate was proposed to be involved in the reaction.[3]



Scheme 3.2

A few years after this initial report on the decarboxylative coupling of β-ketoesters, Tsuji demonstrated the potential of allyl vinyl carbonate **5** to undergo a decarboxylative allylation to generate product identical to those observed from the decarboxylative allylation of the β-ketoester.[4]

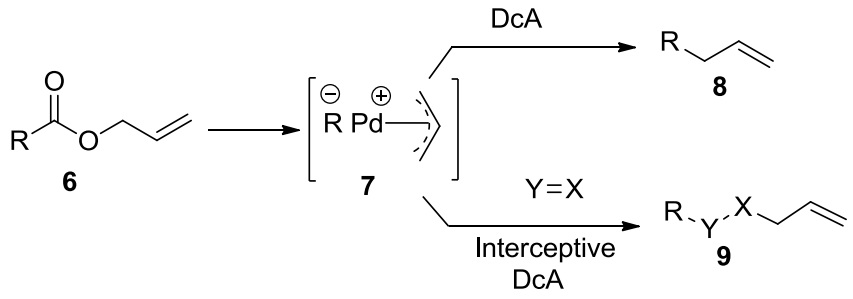


Scheme 3.3

3.1.1. Interceptive decarboxylative allylations (IDcA)

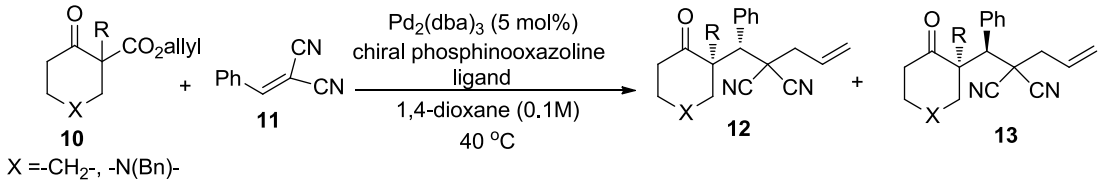
Decarboxylative allylation reactions performed in the presence of an electrophile are termed as Interceptive Decarboxylative Allylations. Electrophilic and nucleophilic intermediate species are generated from allyl esters and carbonates upon treatment with transition metal catalyst. These intermediates can be intercepted with an externally added

electrophile before their combination to form decarboxylative allylation products (Scheme 3.4).[1]



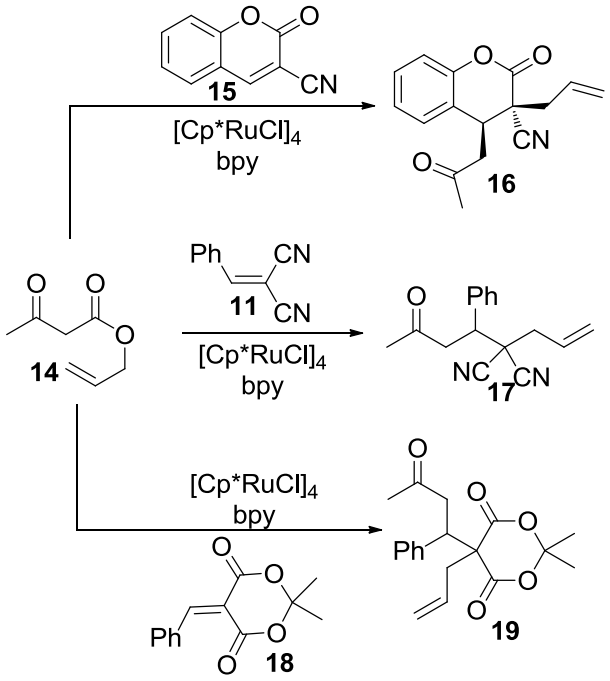
Scheme 3.4. Representation of DcA and IDcA

Yamamoto and co-workers conducted a detailed study on the decarboxylative addition of allyl acetoacetate, allyl carbonates and allyl carbamates with activated olefins which are already discussed in chapter 1.[5] Later on, the asymmetric decarboxylative addition of cyclic *β*-keto ester **10** with activated olefin **11** was reported by Stoltz and co-workers.[6] Cyclic *β*-ketoesters and arylidene malononitriles smoothly underwent the interceptive addition in the presence of the phosphinooxazoline ligated palladium catalyst, allowing generation of adjacent quaternary and tertiary carbon stereocenters with high enantioselectivity and diastereoselectivity.



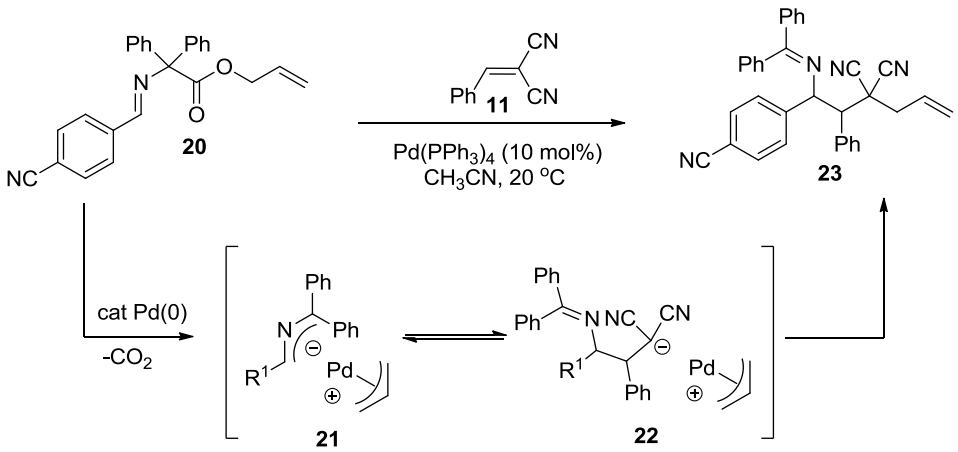
Scheme 3.5

Ruthenium-catalyzed decarboxylative insertion of electrophiles into allyl *β*-ketoesters is reported by Tunge *et al.* in 2005.[7] In addition to the olefin containing electron withdrawing nitrile groups, the Knoevenagel adduct of benzaldehyde and Meldrum's acid is also an effective Michael acceptor for the interceptive decarboxylative addition. In the presence of 2.5 mol% $[Cp^*RuCl]_4$ and 10 mol% bipyridine, the interceptive addition of allyl *β*-ketoesters with sufficiently electrophilic Michael acceptors occur to give Michael addition-allylation product.



Scheme 3.6

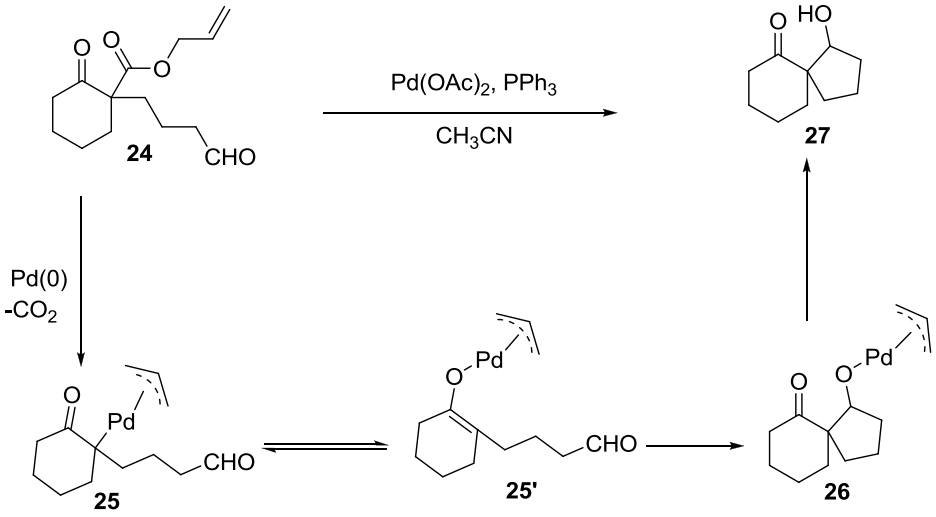
Chruma *et al.* reported palladium catalyzed interceptive decarboxylative allylation of allyl diphenylglycinate ester **20** with benzylidene malononitrile **11**.[8] The reaction proceeds through the formation of 2-aza-allyl anion **21** which is generated by the ionization of allyl ester **20** followed by decarboxylation in the presence of catalytic amount of palladium catalyst. The formed intermediate **21** is then intercepted by benzylidene malononitrile **11** and the resultant anion reacts with π-allyl palladium intermediate to give allylated imine **23** (Scheme 3.7).



Scheme 3.7

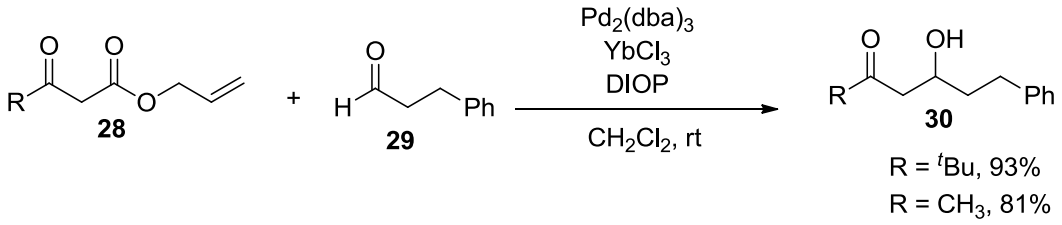
3.1.2. Reactivity of π-allyl palladium intermediates towards carbonyl compounds

In 1989, Tsuji and co-workers reported palladium-catalyzed intramolecular aldol reaction of aldehydes with ketone enolate generated from the allyl-*β*-keto ester under neutral conditions (Scheme 3.8).[9] The reaction proceeds through the formation of π-allylpalladium enolate **25** and **25'**.



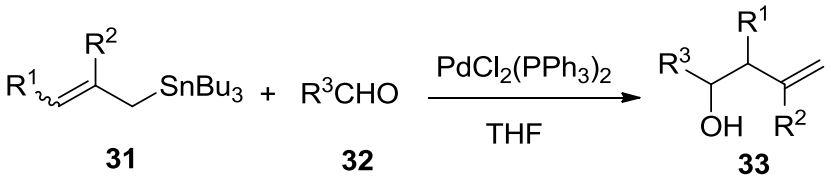
Scheme 3.8. Intramolecular decarboxylative aldol reaction

Later, the intermolecular version of palladium catalyzed decarboxylative aldol reaction of allyl-*β*-keto esters **28** and aldehyde **29** is reported by Schaus and co-workers.[10] The reaction involves the *in situ* formation of a ketone enolate from allyl *β*-keto esters followed by the addition of the enolate to aldehydes and generate the product in good yield.



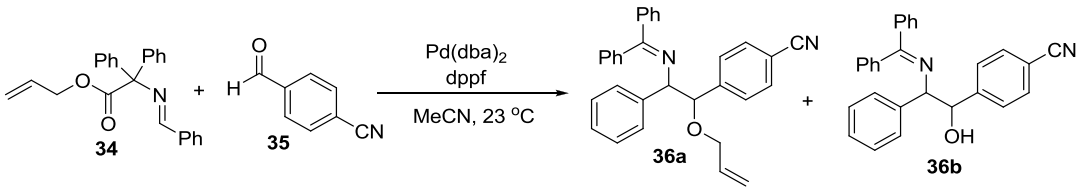
Scheme 3.9

Palladium-catalyzed allylation of aldehydes using bis-π-allylpalladium intermediate was reported by Yamamoto *et al.* for the first time.[11] The reaction of allylstannanes **31** with aldehydes **32** catalyzed by Pd(II) complex produced the corresponding homoallylic alcohols **33**.



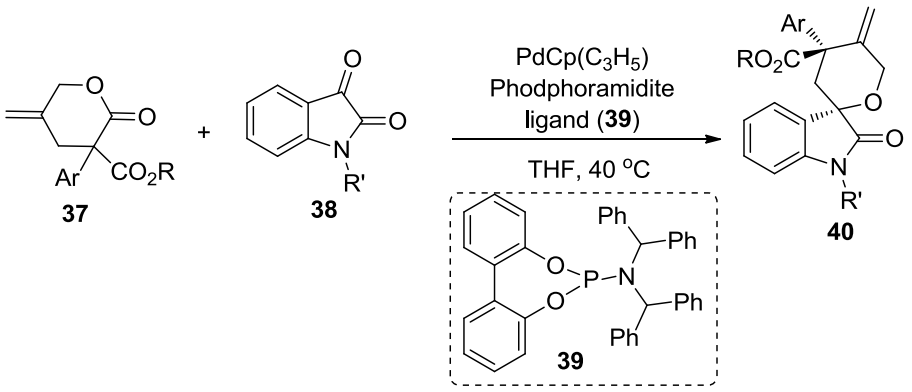
Scheme 3.10

Chruma and co-workers investigated the interceptive addition of aldehydes with *α*-imino anions, generated under neutral reaction conditions *via* Pd-mediated decarboxylation of allyl diphenylglycinate imines.[12] Treatment of benzaldimine **34** with $Pd(dba)_2$/dppf in the presence of *p*-cyanobenzaldehyde **35** afforded the allyl ether **36a** in 53% isolated yield as an inseparable mixture of diastereomers and the remaining mass balance was the 1,2-imino alcohol **36b**. The latter product, **36b** presumably formed by the protonation of the intermediate alkoxide with adventitious water.



Scheme 3.11

Hayashi and co-workers reported various synthetic transformations of malonate derived valerolactones by utilizing palladium catalyzed decarboxylation chemistry.[13] Palladium-catalyzed decarboxylation of *γ*-methylidene-*δ*-valerolactones generates 1,4-dipole which is the key intermediate for the synthetic transformations. They have reported [4+2] decarboxylative cycloadditions of *γ*-methylidene-*δ*-valerolactones with isatins and other activated ketones.[14] Treatment of *γ*-methylidene-*δ*-valerolactones **37** with isatins **38** in the presence of palladium catalyst and phosphoramidite ligand **39** afforded the spiro-oxindoles **40** in excellent yields and diastereoselectivities (Scheme 3.12). The methodology developed is used for the straightforward synthesis of pharmaceutically relevant spiro-oxindoles. In order to expand the scope of the decarboxylative cycloaddition reaction, various activated ketones such as acenaphthenequinone and diethylketomalonate were used as coupling partners. This is an interesting transformation because ketones are usually not competent partners for Pd-catalyzed interceptive additions reactions.

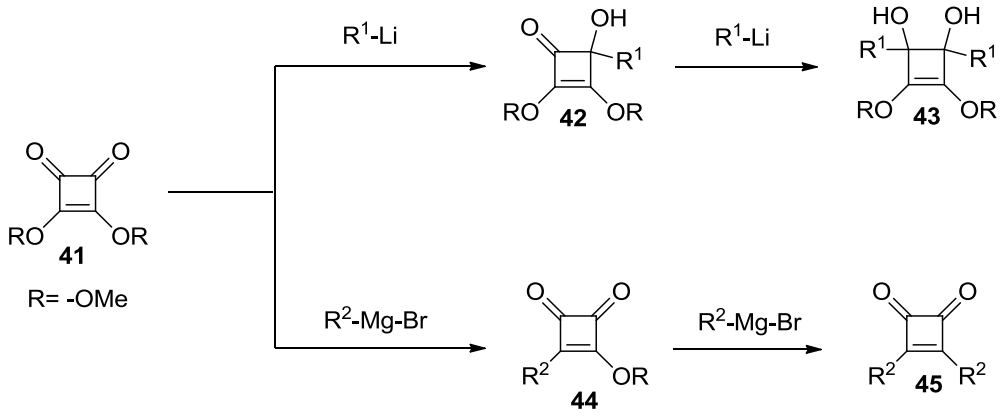


Scheme 3.12

3.1.3. Squarates: A brief discussion

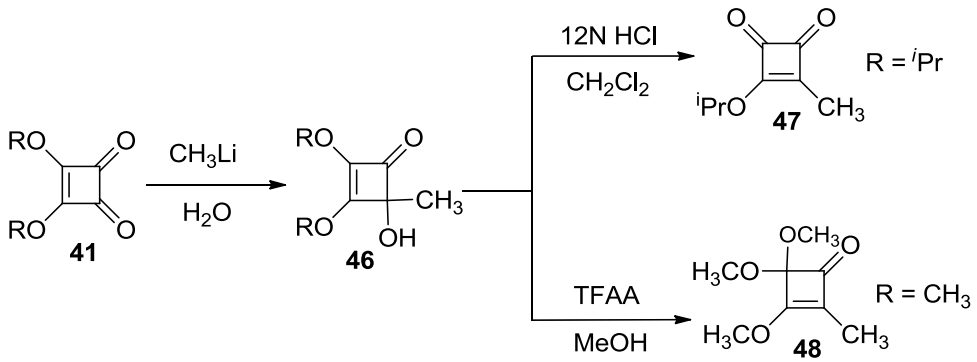
During the last few years, cyclobutene-l,2-diones have emerged as theoretically and synthetically interesting molecules to serve as useful synthetic intermediates. The reactivity is due to the resident functionality and high ring strain present in the four-membered dicarbonyl compounds. The addition of nucleophiles across electrophilic C=O bond using transition metal catalysis is especially interesting since it provides alternatives to the more strongly nucleophilic and basic main group metal reagents such as organomagnesium and organolithium compounds.[15]

Due to the presence of two carbonyl groups, squarate esters are sufficiently electrophilic in nature. Many early investigations have been done based on the mono addition of an organometallic reagent in advance of further structural change or ring expansion. In 1985, Kraus reported the reactivity of organolithium as well as organomagnesium reagents with dimethyl squarate.[16] By reacting with organolithium reagent, dimethylsquarate **41** underwent 1,2-addition leading to 2-hydroxy-3,4-dimethoxy-3-cyclobutenone **42**. The excess organolithium reagent led to double 1,2-addition and afforded dihydroxy dimethoxy dialkyl cyclobutene derivative **43**. The reaction of Grignard reagents with dimethyl squarate **41** resulted in the mono- or dialkyl-cyclobutene dione derivatives according to a 1,4-addition process. The use of excess Grignard reagent leads to the dialkyl cyclobutene dione **45**.[16]



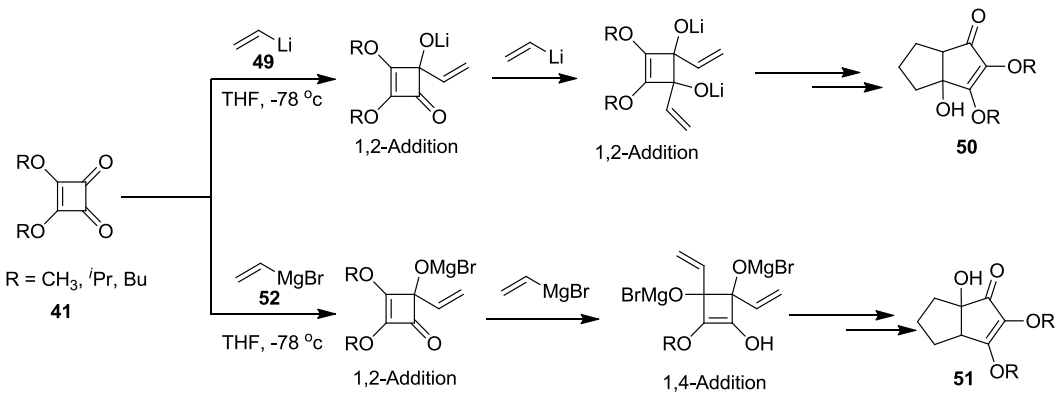
Scheme 3.13

The 1,2-adduct of squarate ester obtained by reacting dialkyl squarate with CH_3Li is further transformed to semisquarate derivative **47** by reacting with HCl[17] and cyclobutenedione mono acetal **48** by reacting with TFAA in methanol (Scheme 3.14).[18]



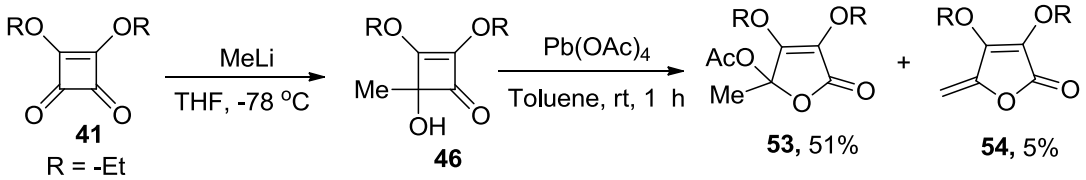
Scheme 3.14

The two-fold addition of alkenyl magnesium or lithium derivatives to squarate esters is a known method for preparation of cyclopentenone moiety. Paquette *et al.* extensively studied the two-fold addition of organolithium reagent to squarate ester.[19] Squarate ester **41** on reaction with two equivalents of vinyl lithium afforded bicyclooctenone **50** whereas the two-fold addition of vinyl magnesium bromide with squarate ester furnished the regioisomer **51**.[20] Bicyclooctenone derivative **50** was formed by 1,2-1,2 double addition of vinyl lithium followed by ring expansion whereas the regioisomer **51** formed by the 1,2-1,4 addition of vinyl magnesium bromide and further ring expansion (Scheme 3.15).



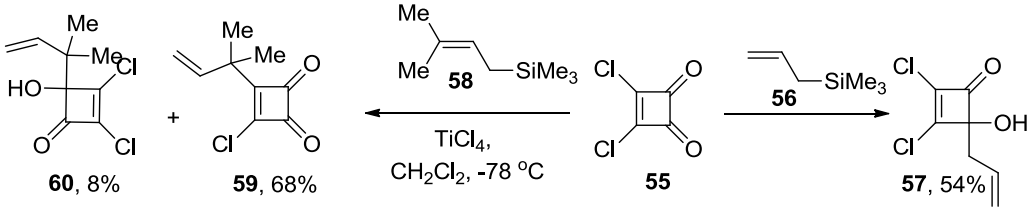
Scheme 3.15

In 1994, Eguchi *et al.* developed a versatile method for the synthesis of highly substituted furanones by the oxidative rearrangement of 4-hydroxycyclobutenones **46**.[21] The intermediate 4-hydroxycyclobutenone was generated by the 1,2-addition of methyl lithium to diethyl squarate. The synthesis of furanone **53** involves oxy-radical triggered ring opening of 4-hydroxycyclobutenone and subsequent intramolecular radical addition to the carbonyl oxygen.



Scheme 3.16

$TiCl_4$ catalyzed carbon-carbon bond forming reaction of squaryl chloride with allyl silanes and silyl enol ether was reported by the same group.[22] The reaction of allylsilane **56** with squaryl chloride **55** afforded the 1,2-addition product **57**. In contrast, prenylsilane **58** underwent l,4-addition followed by dechlorosilylation to give 3-allyl-4-chlorocyclobut-3-ene-1,2-dione **59** as the predominant product along with minor 1,2-addition product **60**. The regioselectivity is determined by the substitution pattern on the organosilanes (Scheme 3.17).



Scheme 3.17

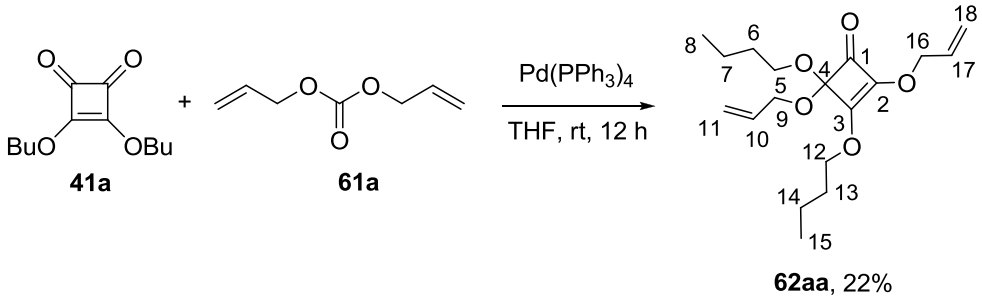
3.2. Present Work

Palladium-catalyzed decarboxylative allylation has emerged as an important method for the construction of new carbon-carbon bonds. Recent advances toward palladium catalyzed interceptive decarboxylative allylation include the reactions of allyl-*β*-keto esters, allyl carbonates, allyl carbamates and allyl diphenylglycinate esters with electrophilic olefins. Squarate, a fascinating and versatile C-4 synthons, offer the prospect of serving as useful starting materials for the synthesis of a wide variety of compounds. The mono-addition and two-fold addition to the carbonyl group of squarates by organometallic reagents such as organolithium and Grignard reagents to synthesize polycyclic compounds are well-documented in the literature. However, there have been only a few reports on palladium-catalyzed reactions of squarates.[23] In this context, we decided to explore the reactivity of allyl palladium intermediate generated *in situ* from allyl carbonates with squarates. Also, we extended the investigation on the reactivity of allyl palladium intermediates to isatins and other electrophilic carbonyl compounds. The results of these studies are discussed in the following section.

3.3. Results and Discussion

3.3.1. Palladium catalyzed interceptive decarboxylative 1,4-addition of allyl carbonates to squarates

Our studies commenced with the reaction of dibutyl squarate **41a** and diallyl carbonate **61a** in the presence of $Pd(PPh_3)_4$ (5 mol%) in THF at room temperature. The reaction afforded 1,4-addition product 2,4-bis(allyloxy)-3,4-dibutoxycyclobut-2-enone **62aa** as a colourless liquid in 22% yield.



Scheme 3.18

The structure of the product **62aa** was established by usual spectroscopic techniques. In the IR spectrum, the peak at 1778 cm^{-1} assigned to the carbonyl group. In the ^{1}H NMR spectrum (Figure 3.1), the sp^2 methine protons of the two allyl groups at C-10 and C-17 were visible as a multiplet in the region δ 5.98-5.91 ppm and the sp^2 methylene protons at C-11 and C-18 appeared as multiplet in the area δ 5.39-5.15 ppm. The sp^3 methylene protons on C-9 and C-16 were discernible as two doublets at δ 4.27 (*J* = 5.5 Hz) and 4.77 (*J* = 5.5 Hz) ppm respectively. Two methyl protons of butyl groups at C-8 and C-15 appeared as triplets at δ 0.96 (*J* = 7.5 Hz) and 0.91(*J* = 7.5 Hz) ppm. The sp^2 methylene protons of the two butyl groups at C-5 and C-12 were visible as triplets at δ 3.71 (*J* = 6.5 Hz) and δ 4.40 (*J* = 6.5 Hz) ppm respectively.

In ^{13}C NMR (Figure 3.2), the carbonyl peak observed at δ 184.9 ppm. Signals appeared at δ 118.8 and δ 116.8 ppm corresponds to sp^2 methylene carbons C-11 and C-18. The peaks observed at δ 134.3 and 132.6 ppm assigned to C-10 and C-17 respectively. The quaternary carbons assigned with the help of DEPT-135 and HMQC spectral analysis. The quaternary carbon at C-3 resonated at δ 167.4 ppm. The peak visible at δ 137.08 ppm corresponds to C-2 carbon. The quaternary C-4 carbon attached to the two oxygen atoms resonated at δ 108.2 ppm. All other signals were in good agreement with the assigned structure.

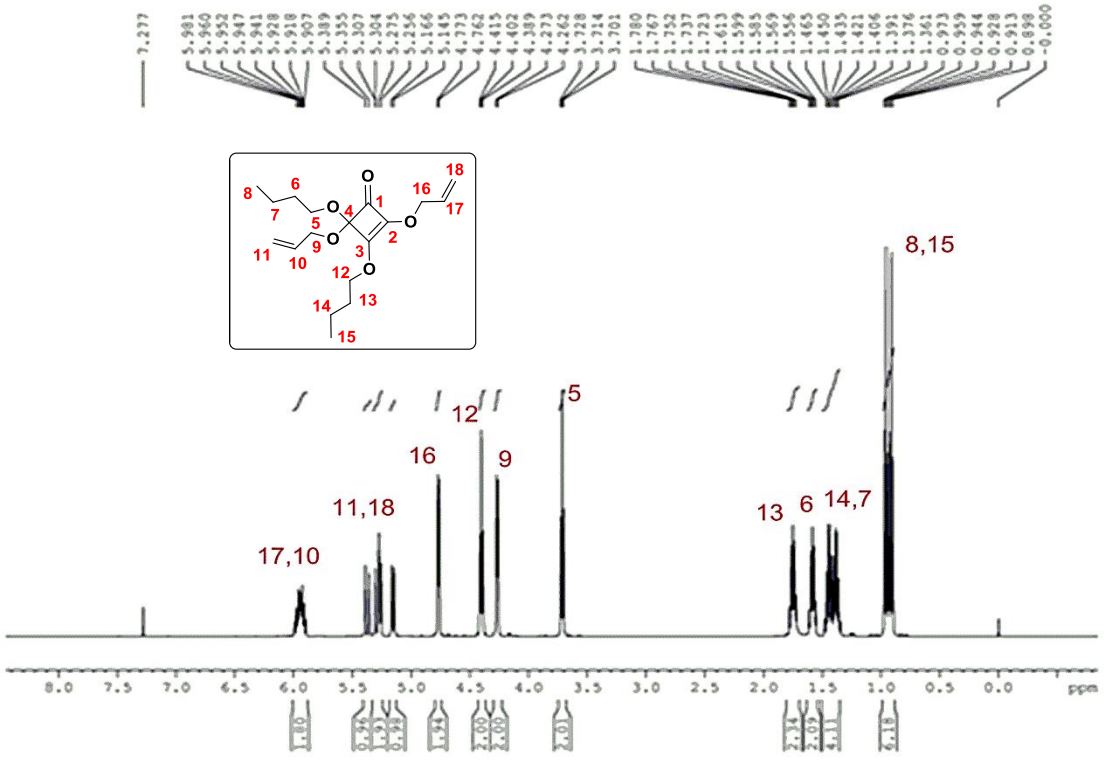


Figure 3.1. ^{1}H NMR spectrum of compound **62aa**

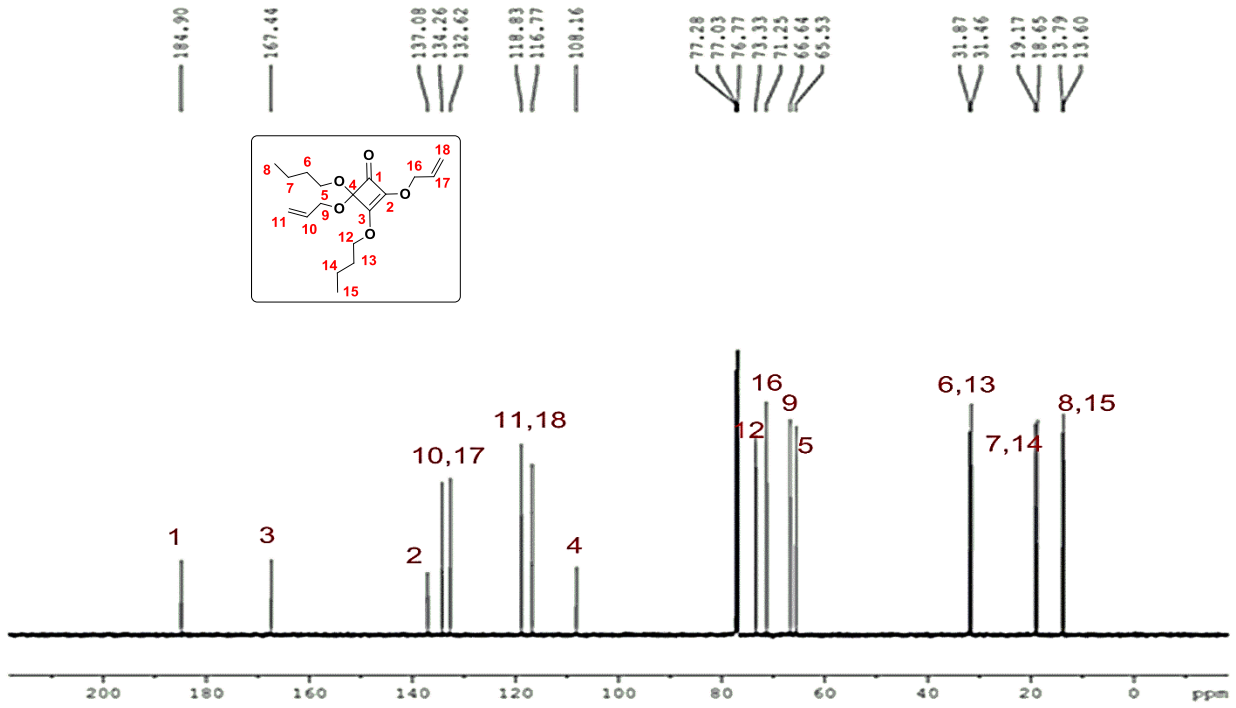


Figure 3.2. ^{13}C NMR spectrum of compound **62aa**

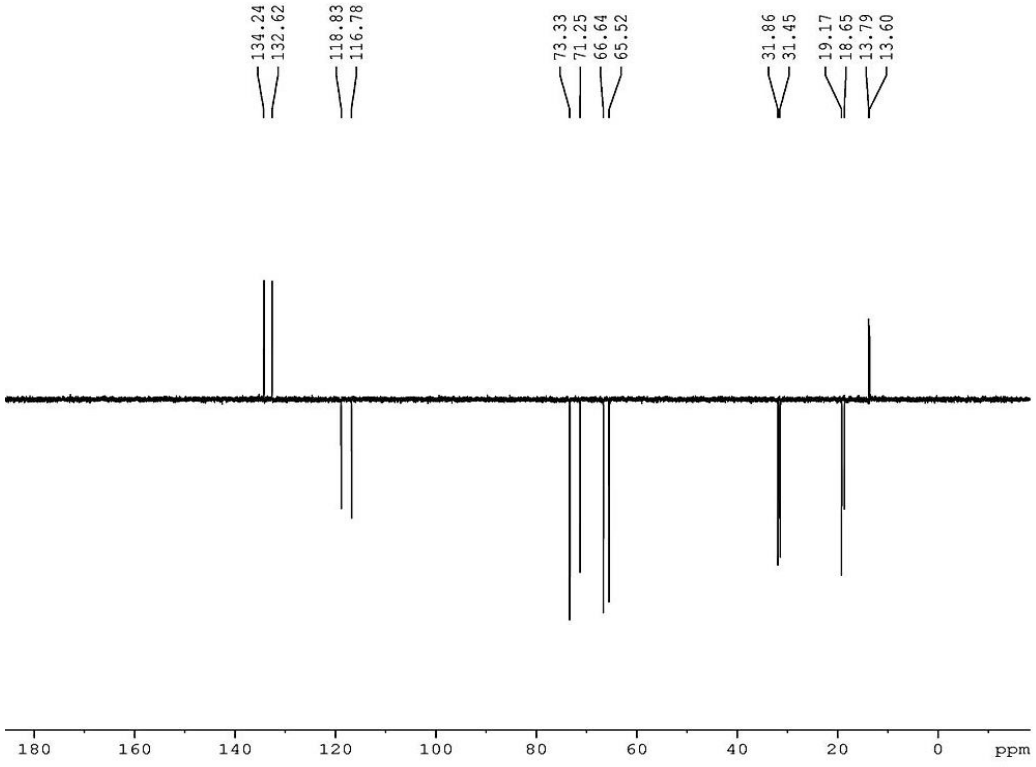


Figure 3.3. DEPT-135 NMR spectrum of compound **62aa**

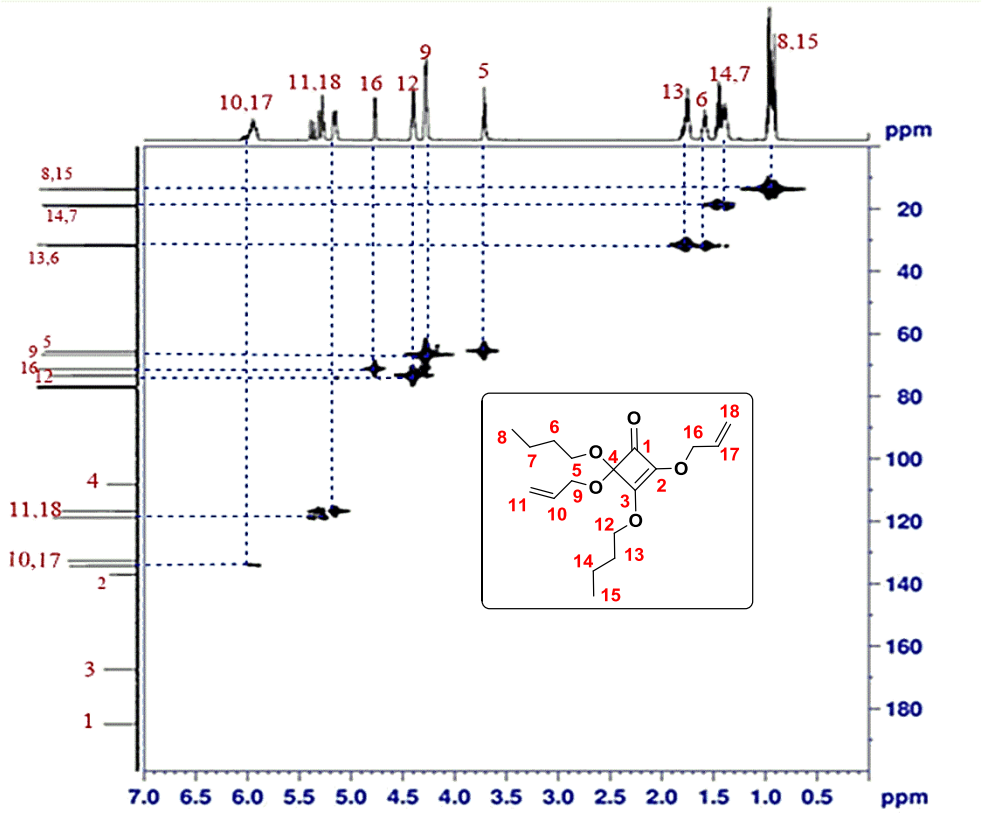


Figure 3.4. ^{1}H-^{13}C HMQC spectrum of compound **62aa**

Further, the regiochemical 1,4-addition was confirmed by HMBC spectral analysis. From HMBC spectral analysis, it is clear that the sp^3 methylene protons at C-5 and C-9 show correlation with the quaternary carbon C-4. This correlation confirms that both are attached to the same carbon atom. Also, the sp^2 methylene protons of butyl group at C-12 shows correlation with C-3 carbon and sp^2 methylene protons of allyl group at C-16 shows correlation with C-2 carbon.

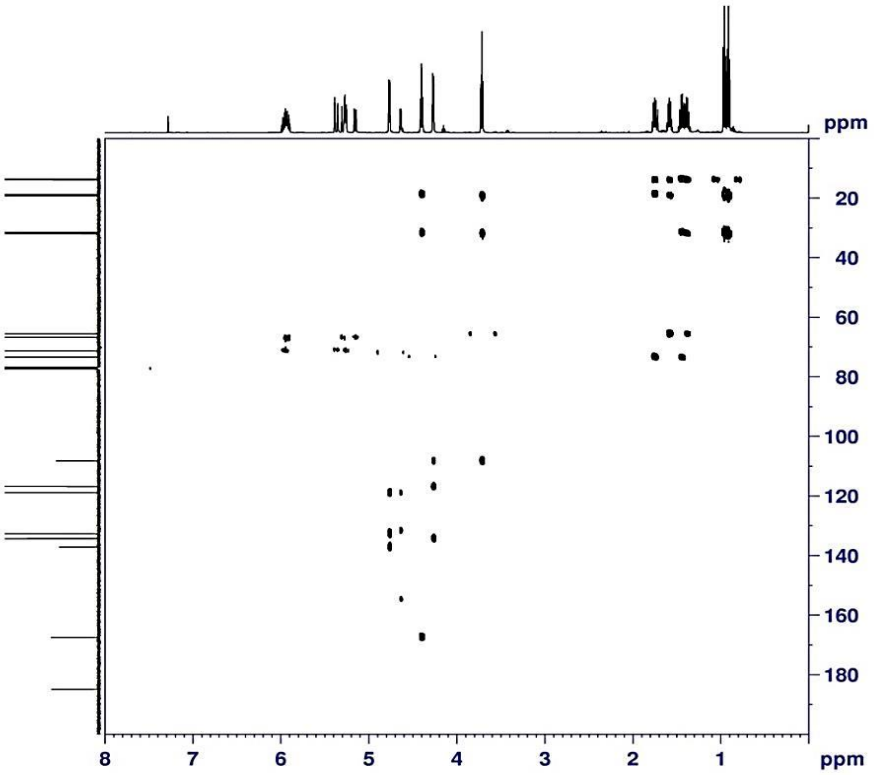


Figure 3.5. ^{1}H-^{13}C HMBC spectrum of compound **62aa**

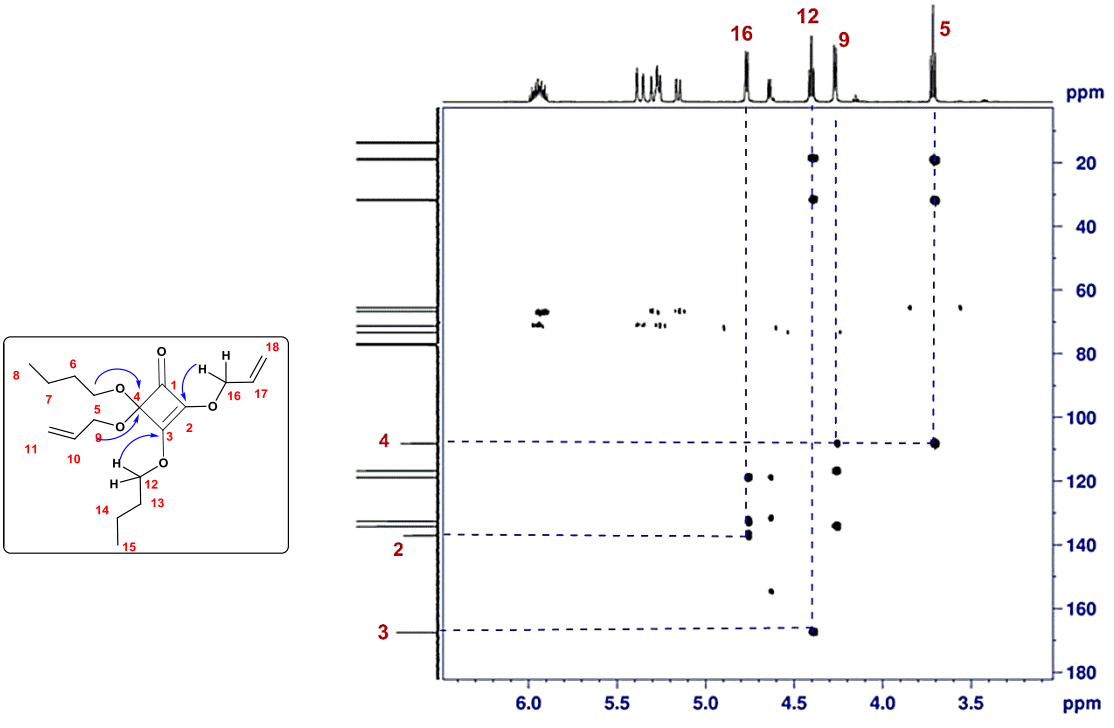
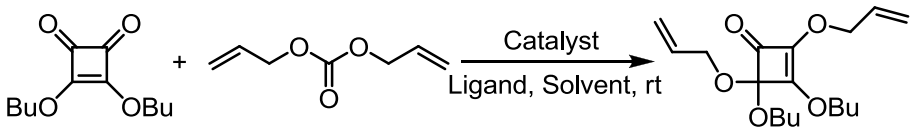


Figure 3.6. Expansion of ^{1}H-^{13}C HMBC spectrum of compound **62aa**

The molecular ion peak at *m/z* 347.18249 $[M+Na]^{+}$, observed in the mass spectrum provided further supporting information for the proposed structure.

Detailed optimization studies were carried out to find the best condition for the reaction.Various catalysts such as $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $PdCl_2$, $Pd(OAc)_2$, $[Pd_2(dba)_3].CHCl_3$ and $[Pd(allyl)Cl]_2$ were screened, from which $Pd(PPh_3)_4$ gave the highest yield. We then turned our attention to other parameters such as solvent and ligand. Among the solvents screened, dichloromethane was found to be best. The ligands examined were PPh_3, dppe, dppm, dppf and phosphoramidite ligand and found that none of the ligand favour to improve the yield. Temperature does not considerably impact this transformation. After the optimization studies, the best condition for the reaction was found to be a 1:2 mixture of dibutyl squarate and diallyl carbonate in the presence of 10 mol% $Pd(PPh_3)_4$ in dry dichloromethane as solvent at room temperature. The results are summarized in Table 3.1.

Table 3.1. Screening of parameters for best catalyst system

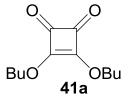
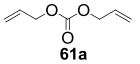
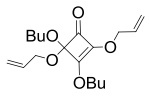
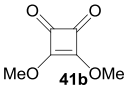
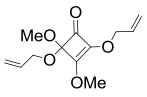
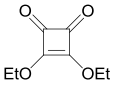
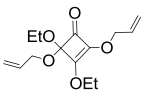
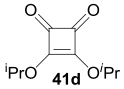
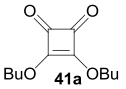
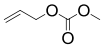
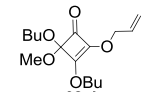
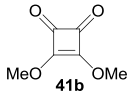
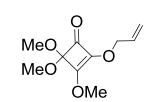
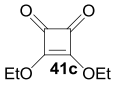
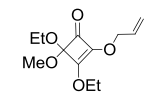
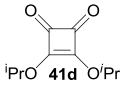
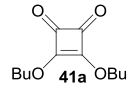
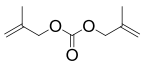
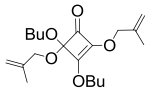
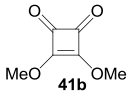
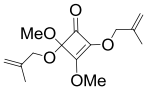
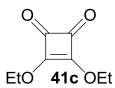
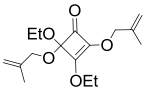


Entry	Catalyst	Equiv. of Catalyst	Ligand	Solvent	Yield (%)[a]
1	$Pd(PPh_3)_4$	5 mol%	-	THF	22
2	$[Pd_2(dba)_3].CHCl_3$	5 mol%	PPh_3	”	14
3	$PdCl_2$	5 mol%	PPh_3	”	No Reaction
4	$Pd_2(OAc)_2$	5 mol%	PPh_3	”	No Reaction
5	$Pd_2Cl_2(PPh_3)_2$	5 mol%	PPh_3	”	No Reaction
6	$[Pd(allyl)Cl]_2$	5 mol%	PPh_3	”	No Reaction
7	$Pd(PPh_3)_4$	10 mol%	-	”	29
8	$Pd(PPh_3)_4$	15 mol%	-	”	31
9	$Pd(PPh_3)_4$	10 mol%	-	”	21[b]
10	$Pd(PPh_3)_4$	10 mol%	-	CH_3CN	23
11	$Pd(PPh_3)_4$	10 mol%	-	Toluene	39
12	$Pd(PPh_3)_4$	10 mol%	-	DCM	42
13	$Pd(PPh_3)_4$	10 mol%	-	DMF	No Reaction
14	$Pd(PPh_3)_4$	10 mol%	dppe	DCM	38
15	$Pd(PPh_3)_4$	10 mol%	dppf	”	19
16	$Pd(PPh_3)_4$	10 mol%	dppm	”	13
17	$Pd(PPh_3)_4$	10 mol%	Phosphoramidite Ligand[c]	”	38

Reaction Conditions: dibutyl squarate (1.0 equiv.), diallylcarbonate (2.0 equiv.), solvent (2 mL), rt, 12 h, [a]isolated, [b]performed the reaction at 60 °C, [c]N,N-Bis-((S)-1-phenylethyl)dibenzo[d,f][1.3.2]dioxaphosphepin-6-amine

Under this optimized condition, the reaction was found to be general with different alkyl squarates (**41a-c**) and the results are summarized in Table 3.2. The scope of the reaction was further expanded by using different allyl carbonates such as allyl methyl carbonate **61b** and dimethallyl carbonate **61c**. All the reactions proceeded smoothly at room temperature to produce the desired ketals **62aa-62cc** in moderate yields (Table 3.2). Regioselective 1,4-addition achieved using the alkyl squarate 4**1b-c**, but the 1,4-addition was not observed for isopropyl squarate **41d.** The branched isopropyl group placed on the olefinic carbon makes the 1,4-conjugate addition difficult.[20]

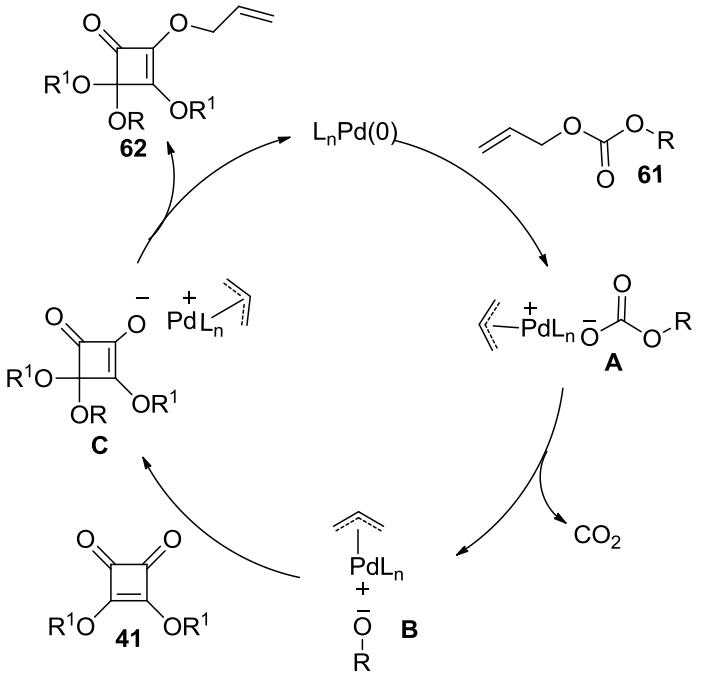
Table 3.2 Decarboxylative 1,4-addition of allyl carbonates with squarates

Entry	Squarate	Allylcarbonate	Product	Yield(%)
1	 **41a**	 **61a**	 **62aa**	42[a] (62)[b]
2	 **41b**	**61a**	 **62ba**	59[a] (74)[b]
3	 **41c**	**61a**	 **62ca**	21[a] (69)[b]
4	 **41d**	**61a**	No Reaction	
5	 **41a**	 **61b**	 **62ab**	18[a] (67)[b]
6	 **41b**	**61b**	 **62bb**	45[a] (75)[b]
7	 **41c**	**61b**	 **62cb**	29[a] (63)[b]
8	 **41d**	**61b**	No Reaction	
9	 **41a**	 **61c**	 **62ac**	36[a] (69)[b]
10	 **41b**	**61c**	 **62bc**	43[a] (73)[b]
11	 **41c**	**61c**	 **62cc**	44[a] (71)[b]

Reaction Conditions: squarate (1.0 equiv), carbonate (2.0 equiv), catalyst (10 mol%), CH_2Cl_2 (2 mL), rt, 12 h.[a]Isolated Yield, [b]Yield based on recovered starting material.

3.3.2. Mechanistic pathway

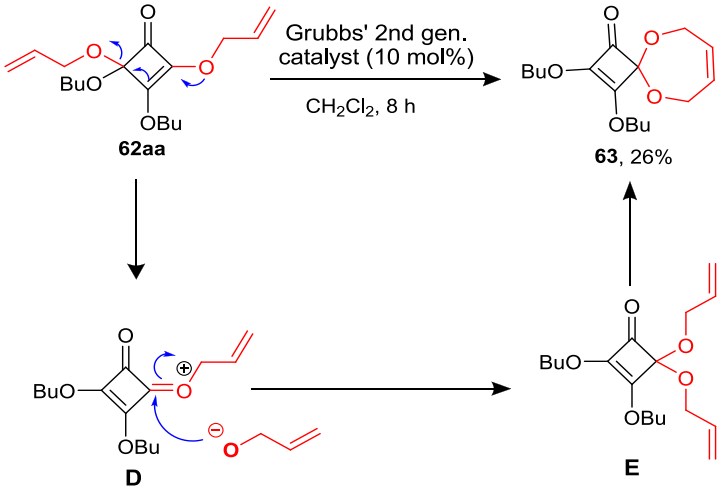
Based on the results, we propose a plausible mechanism for the 1,4-interceptive addition of allyl carbonates to squarates and is illustrated in Scheme 3.19. The catalytic cycle is initiated by the oxidative addition of Pd(0) to allyl carbonate **61** followed by decarboxylation to generate π-allylpalladium complex **B**. The alkoxy anion undergoes 1,4-addition with squarate **41** to give cationic π- allylpalladium complex **C** having oxyanion of squarate as the counter ion. Reductive elimination of palladium from **C** results in the formation of allylated product **62** and regenerates the catalyst.



Scheme 3.19

3.3.3. Synthesis of spiro 4,7-dihydro-1,3-dioxepine

We have carried out a straightforward synthetic transformation of 2,4-bis(allyloxy)-3,4-dibutoxycyclobut-2-enone **62aa**. The ring-closing metathesis of compound **62aa** with Grubbs' second generation catalyst afforded spiro-4,7-dihydro-1,3-dioxepine fused 2-butenone derivative **63** in 26% yield (Scheme 3.20). The formation of product **63** is presumed to form through the 1,3-allyloxy migration and subsequent ring closing metathesis of the intermediate **E** (Scheme 3.20).



Scheme 3.20

The structure of the product **63** was elucidated by spectroscopic techniques. In the IR spectrum, the sharp band at 1779 cm^{-1} assigned to the carbonyl group. In the ^{1}H NMR spectrum (Figure 3.7), the olefinic protons at C-6 and C-7 discernible as a singlet at δ 5.69 ppm. Two sp^2 methylene protons at C-5 and C-8 observed as doublets at δ 4.59 (*J* = 14.5 Hz) and 4.47 (*J* = 15.0 Hz) ppm respectively. All other proton signals were in good agreement with the assigned structure.

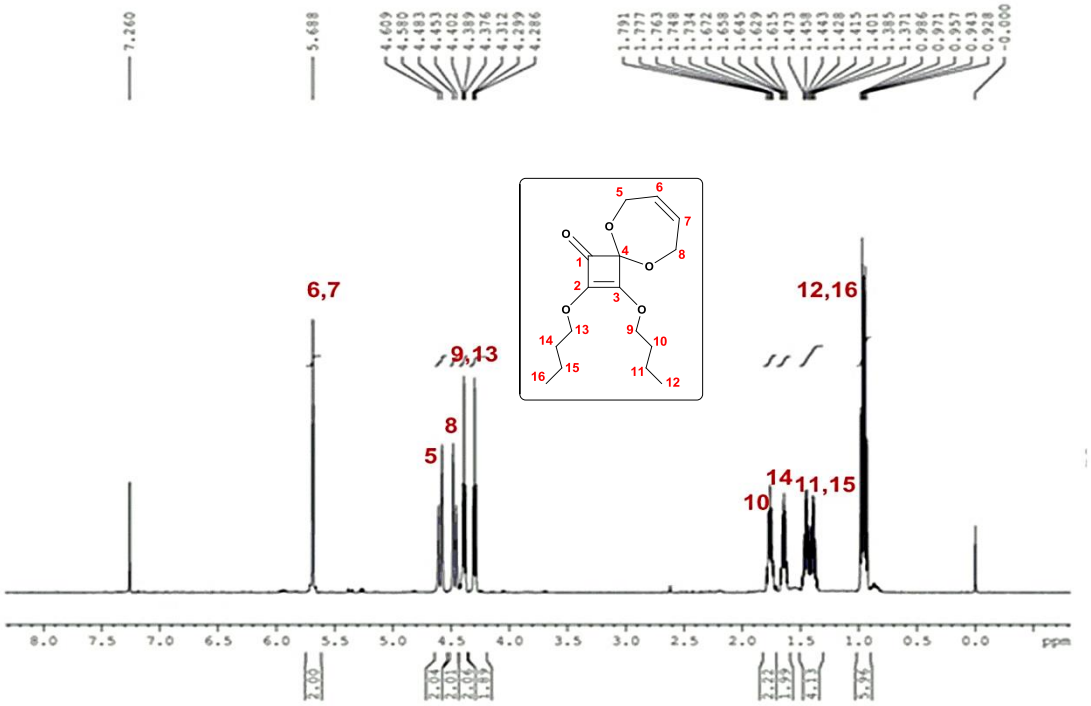


Figure 3.7. ^{1}H NMR spectrum of compound **63**

In the ^{13}C NMR spectrum (Figure 3.8), the characteristic carbonyl peak was observed at δ 184.6 ppm. The sp^2 carbons present in the cyclobutenone ring C-2 and C-3 were observed at δ 137.4 and 166.8 ppm respectively. The characteristic peak corresponds to the spiro carbon C-4 appeared at δ 107.9 ppm. The peak observed at δ 65.5 ppm corresponds to C-5 and C-8 carbons. All other signals were in good agreement with the proposed structure.

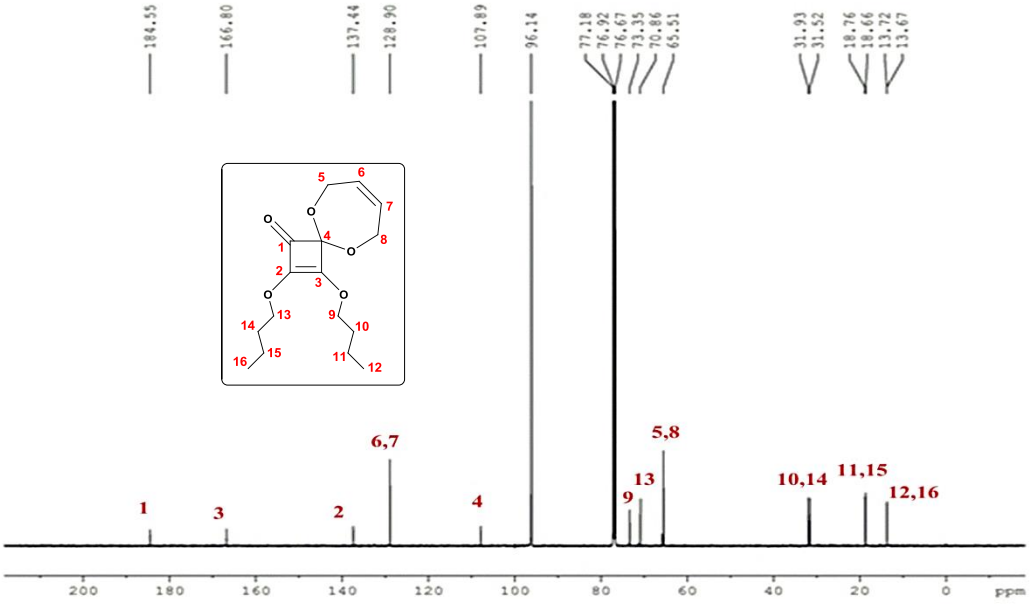


Figure 3.8. ^{13}C NMR spectrum of compound **63**

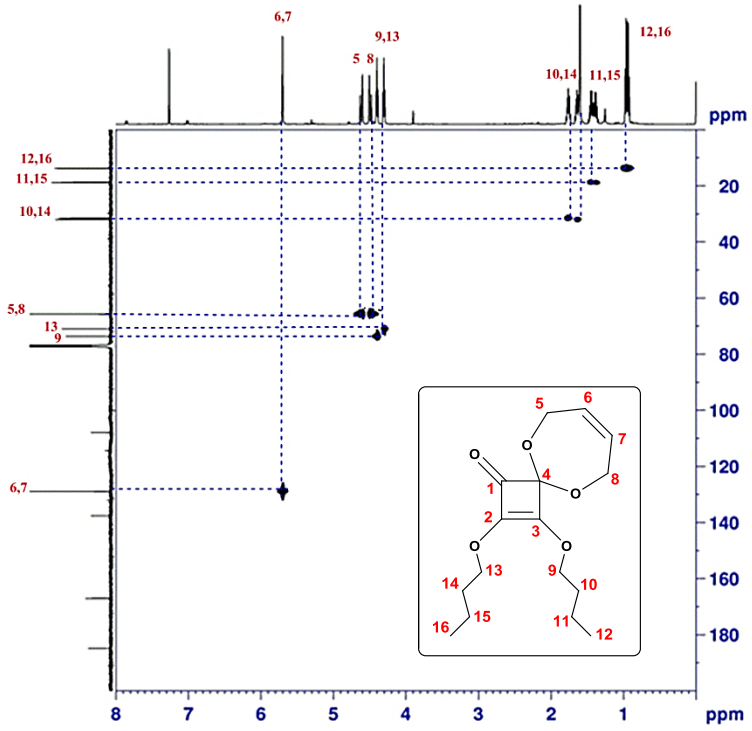


Figure 3.9. ^{1}H-^{13}C HMQC Spectrum of Compound **63**

Further evidence for the proposed structure was obtained from the HMBC spectral analysis (Figure 3.10). The sp^3 methylene protons at C-5 and C-8 show good correlation with C-4 carbon, which indicates that the formed compound is a spirocyclic one. The sp^3 methylene protons of butyl groups at C-9 and C-13 show correlation with carbon atoms C-3 and C-2 respectively. All other correlations are in good agreement with the proposed structure.

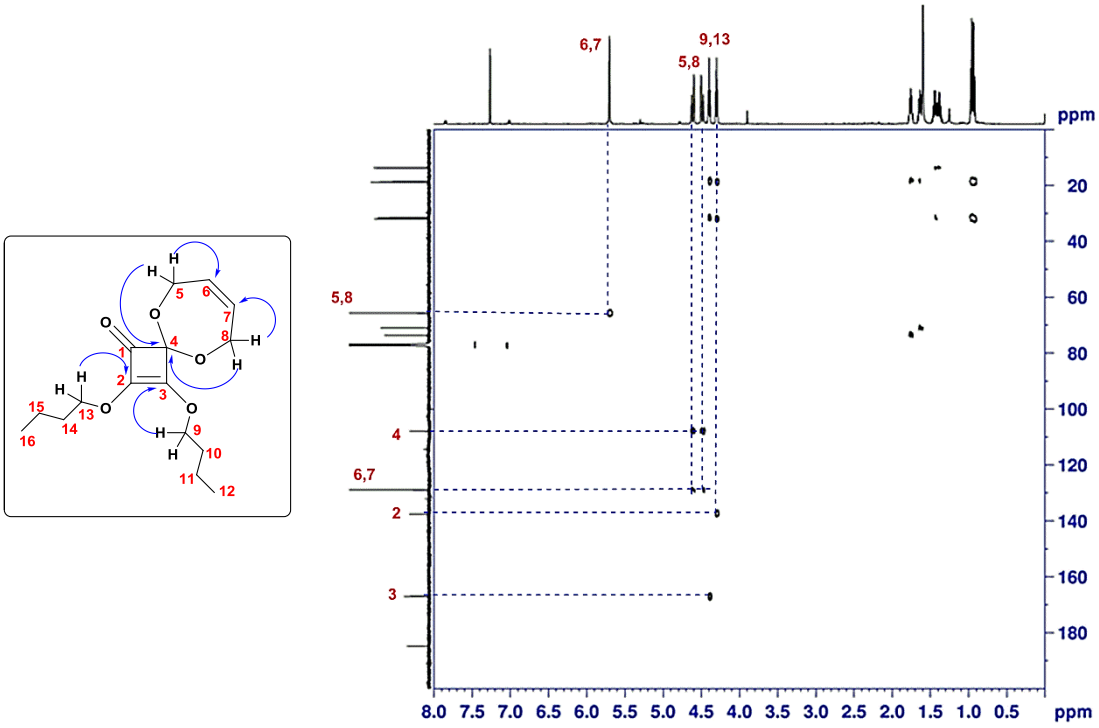
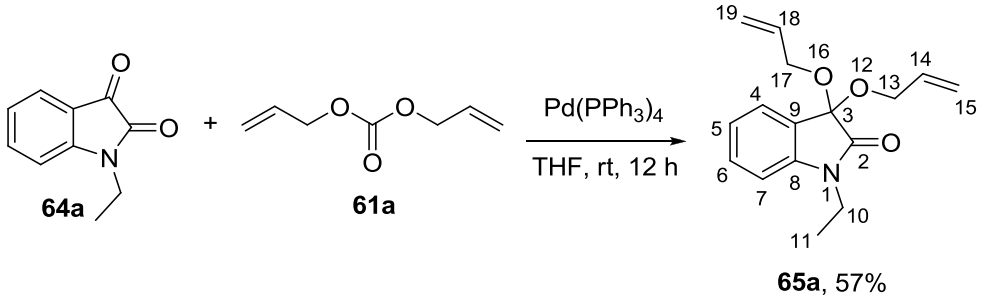


Figure 3.10. ^{1}H-^{13}C HMBC spectrum of compound **63**

Further evidence for the structure was obtained from the high-resolution mass spectral analysis, which showed the molecular ion peak at *m/z* 319.15134 $[M+Na]^+$.

3.3.4. Palladium catalyzed interceptive decarboxylative 1,2-addition of allyl carbonates with isatins

To examine the possibility of interceptive decarboxylative 1,2-addition, we carried out the reaction of allyl carbonates with isatins. Isatins have been widely used as precursors for the synthesis of spiro-oxindoles and many other natural products.[24] In an initial attempt, we carried out the reaction of 1-ethyl isatin **64a** with diallyl carbonate **61a** in the presence of 5 mol% $Pd(PPh_3)_4$ in THF at room temperature. The C-3 carbonyl group of isatin underwent smooth allylation-oxyallylation to afford 3,3-bis(allyloxy)-1-ethylindolin-2-one **65a** in 57% yield (Scheme 3.21).



Scheme 3.21

The structure of the product was established with the aid of various spectroscopic analyses. IR spectrum confirmed the carbonyl absorptions in the region 1729 cm^{-1}. In the ^{1}H NMR spectrum (Figure 3.11), the sp^2 methine protons of the two allyl groups at C-14 and C-18 were visible as a multiplet in the region δ 5.95-5.89 ppm and the sp^2 methylene protons at C-15 and C-19 appeared as multiplet in the area δ 5.31-5.26 ppm. The sp^3 methylene protons at C-13 and C-17 resonated as two separate multiplets in the region δ 5.15-5.13 and δ 4.47-4.43 ppm.

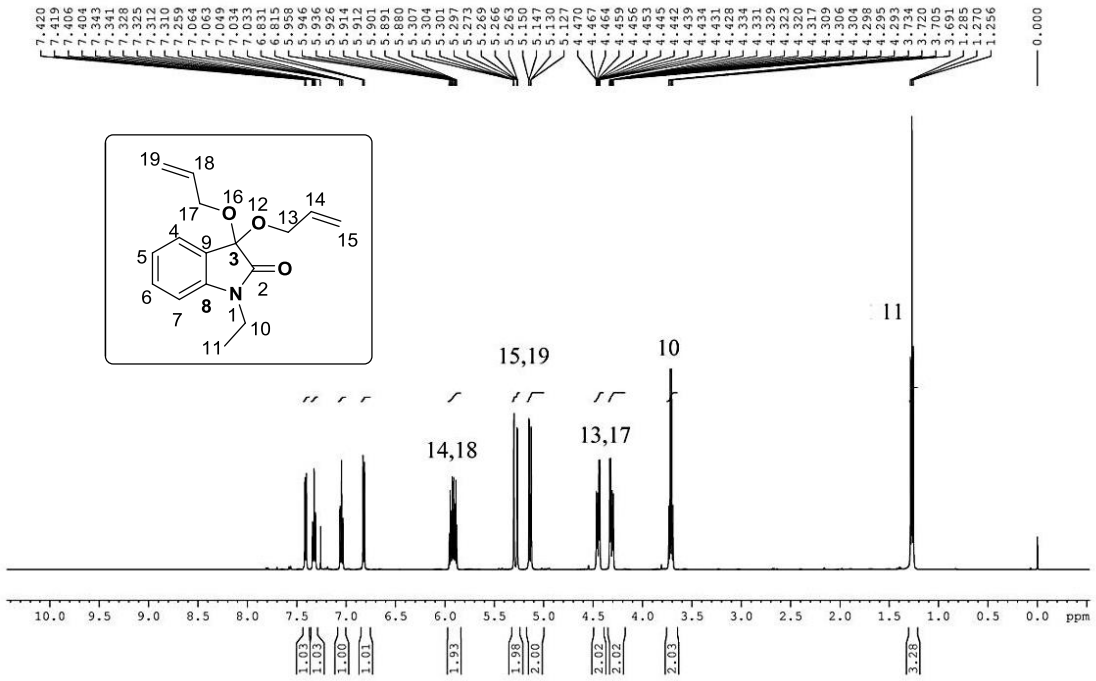


Figure 3.11. ^{1}H NMR spectrum of compound **65a**

In the ^{13}C NMR spectrum (Figure 3.12), the carbonyl carbon at C-2 resonated at δ 170.1 ppm. The quaternary carbon at C-3 was located at δ 96.5 ppm. The sp^2 carbons C-13 and C-17 were seen at δ 64.2 ppm. The signal corresponding to sp^2 methine carbons C-14 and

C-18 appeared at δ 134.0 ppm and sp^2 methylene carbons C-15 and C-19 resonated at δ 116.8 ppm. All other signals were in good agreement with the assigned structure.

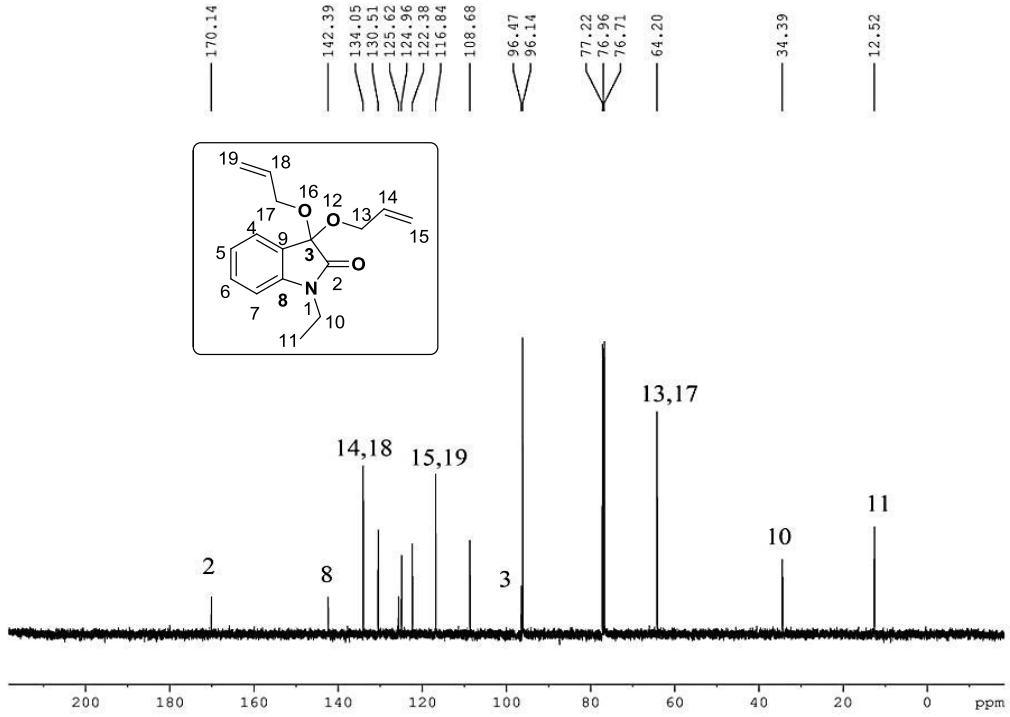


Figure 3.12. ^{13}C NMR spectrum of compound **65a**

The structure was further supported by high-resolution mass spectral analysis, which showed a molecular ion peak at *m/z* 296.12634 $[M+Na]^+$.

Finally, the structure of bis-allyloxy oxindole derivative was unambiguously confirmed by single crystal X-ray analysis of one of the derivatives **71a** (Figure 3.13).[25]

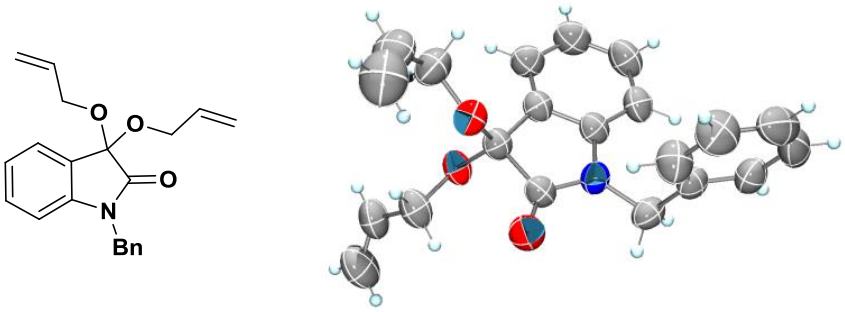
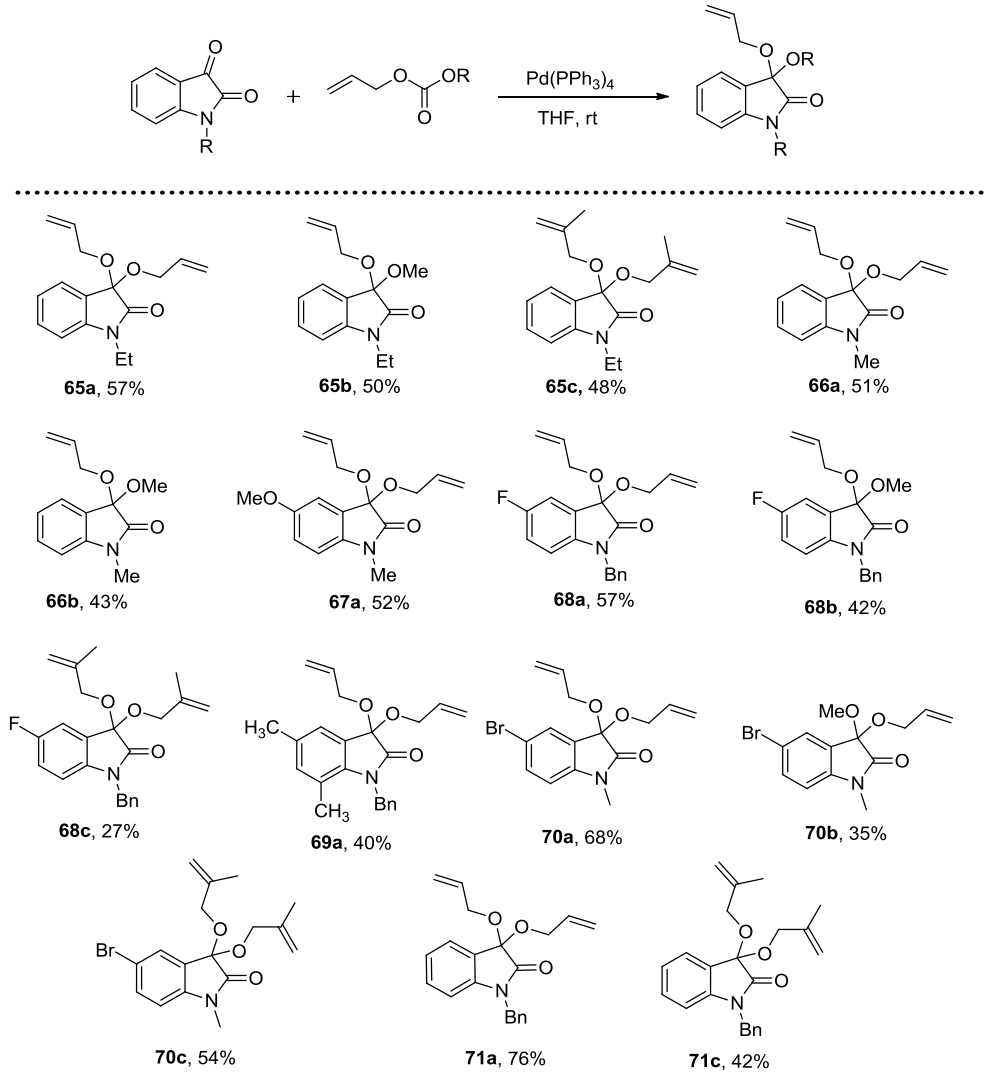


Figure 3.13. ORTEP diagram of compound **71a**

The method was also proved to be very convenient and general for the palladium catalyzed decarboxylative 1,2-addition of allyl carbonates such as diallyl carbonate, allyl

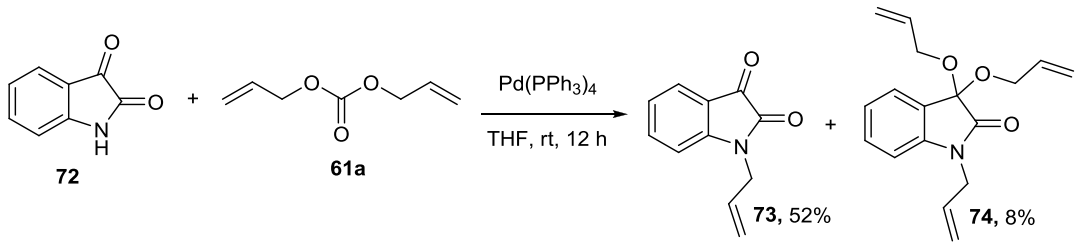
methyl carbonate and dimethallyl carbonate with the C-3 carbonyl group of a range of isatins. The reactions proceeded very efficiently under the same catalytic condition to furnish the desired 1,2-addition products **65a-71c** in good yields (Table 3.3).

Table 3.3. Decarboxylative addition of allyl carbonates with N-substituted isatins



Reaction Conditions: isatin (1.0 equiv), allyl carbonate (2.0 equiv), catalyst (5 mol%), THF (2 mL), rt, 12 h

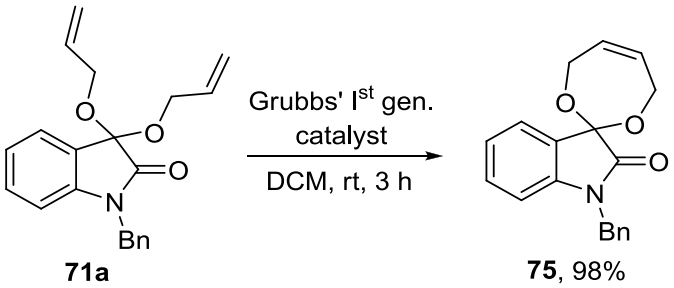
The reaction of isatin **72** with diallyl carbonate **61a** was conducted under similar conditions. The reaction afforded 1-allylindoline-2,3-dione **73** in 52% yield along with 1-allyl-3,3-bis(allyloxy)indolin-2-one **74** in 8% yield (Scheme 3.22). From our investigations, it is noticeable that the C-3 functionalization takes place only after the N-protection.



Scheme 3.22

3.3.5. Synthesis of dioxepine fused spiro-oxindole

Synthetic utility of this chemistry is further highlighted by synthesizing spiro-dioxepine fused 2-oxindole. Ring-closing metathesis of **71a** using Grubbs' first generation catalyst afforded dioxepine fused spiro-oxindole **75** in 98% yields.



Scheme 3.23

Spectroscopic analysis established the structure of the product 75. In the IR spectrum, the peak visible at 1726 cm^{-1} showed the presence of carbonyl group. In the ^{1}H NMR spectrum (Figure 3.14), the olefinic protons resonated as a singlet at δ 5.85 ppm. The methylene protons attached to oxygen atom resonated as two separate doublets at δ 5.09 (*J* = 15.0 Hz) and 4.61 (*J* = 15.0 Hz) ppm. In the ^{13}C NMR spectrum (Figure 3.15), the characteristic carbonyl peak was observed at δ 172.0 ppm. The peak corresponding to the spiro carbon appeared at δ 96.9 ppm. The peak observed at δ 63.8 ppm corresponds to methylene carbons attached to two oxygen atom. All other signals in the ^{1}H and ^{13}C-NMR spectra were in accordance with the expected structure. Mass spectra clearly showed molecular ion peak at *m/z* 330.11101 $[M+Na]^{+}$, which further supported the assigned structure.

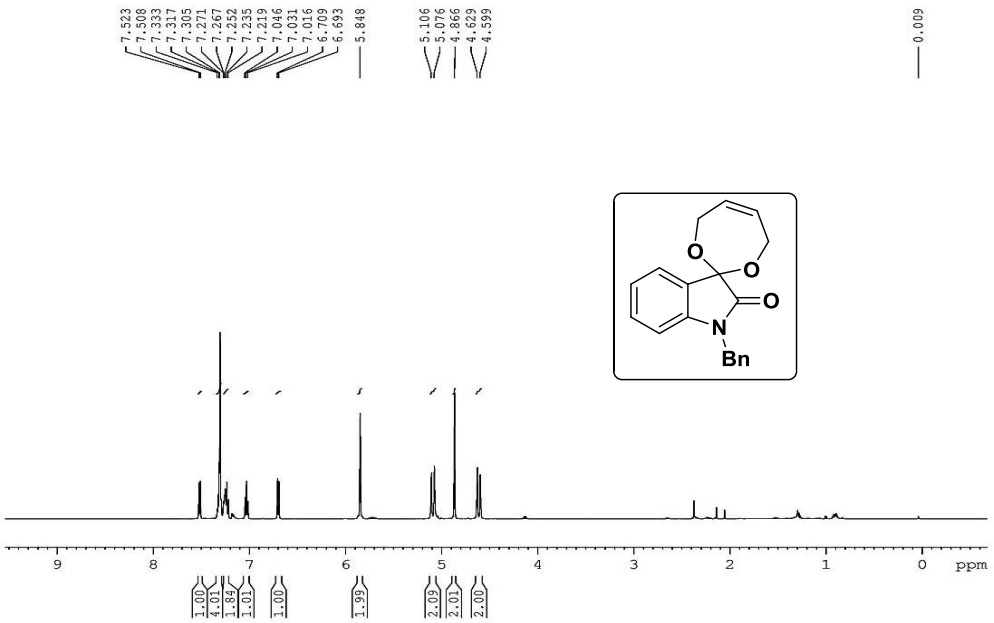


Figure 3.14. ^{1}H NMR Spectrum of compound **75**

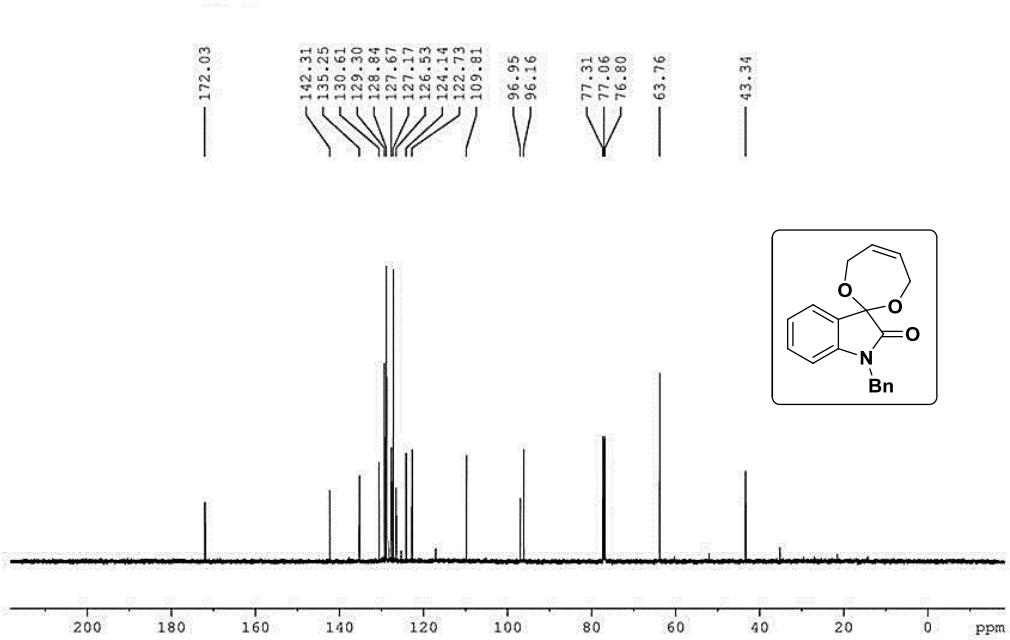
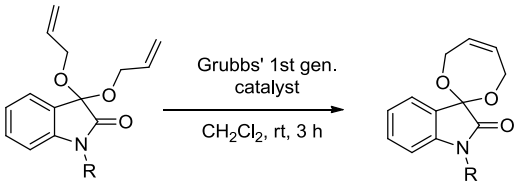
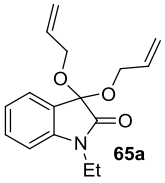
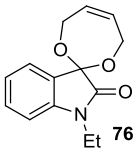
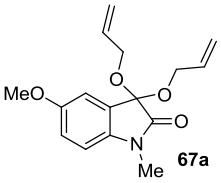
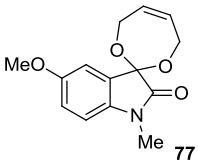
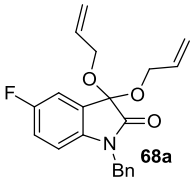
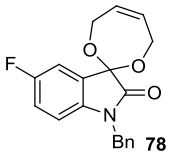
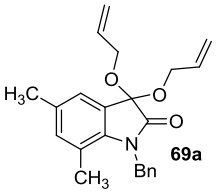
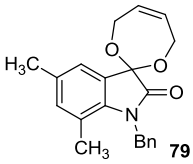


Figure 3.15. ^{13}C NMR Spectrum of compound **75**

Analogous results were obtained with various N-protected bis-allyloxy indolin-2-one and the spiro-oxindoles (**76-79**) were formed in good to excellent yields. The results obtained are shown in Table 3.4. It is noteworthy that spirocyclic oxindole compounds are valuable pharmaceuticals. Spiro-oxindoles have been reported to possess a broad range of biological activities.[24]

Table 3.4. Ring closing metathesis of bis-allyloxy-2-oxindoles

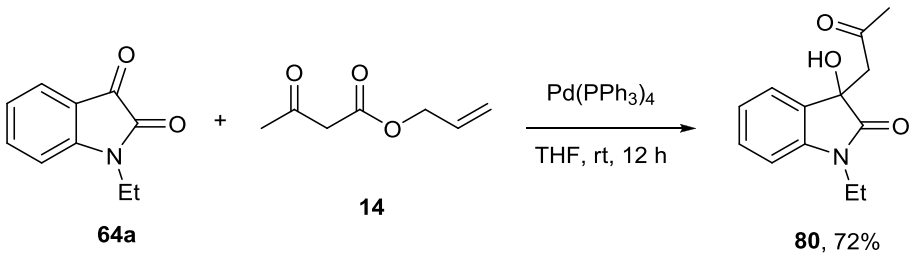


Entry	Substrate	Product	Yield(%)
1	 **65a**	 **76**	76
3	 **67a**	 **77**	97
4	 **68a**	 **78**	96
5	 **69a**	 **79**	88

Reaction Conditions: bis-allyloxy oxindole (1.0 equiv), catalyst (5 mol%), CH_2Cl_2 , rt, 3 h

3.3.6. Decarboxylative addition of allyl acetoacetate with N-substituted isatins

Encouraged by the interceptive decarboxylative 1,2- addition of allyl carbonates with carbonyl groups, we were interested in studying the reactivity of allyl acetoacetate **14** with N-substituted isatins. In an initial attempt, we have tried the reaction of 1-ethyl isatin **64a** with allyl acetoacetate **14**. Instead of the intercepted addition product the reaction afforded 1-ethyl-3-hydroxy-3-(2-oxopropyl)indolin-2-one **80** in 72% yield.



Scheme 3.24

The structure of the product **80** was established by various spectroscopic analysis. In the IR spectrum, the characteristic O-H stretching observed at 3381 cm^{-1} and the carbonyl stretching was visible at 1694 cm^{-1}. In the ^{1}H NMR spectrum (Figure 3.16), a broad singlet observed at δ 4.30 ppm was assigned to the proton of hydroxyl group attached to the C-3 carbon. The sp^3methylene protons resonated as two separate doublets at δ 3.19 (*J* = 17.0 Hz) and 2.97 (*J* = 17.0 Hz) ppm and the methyl protons of acetonyl group were observed as a singlet at δ 2.15 ppm.

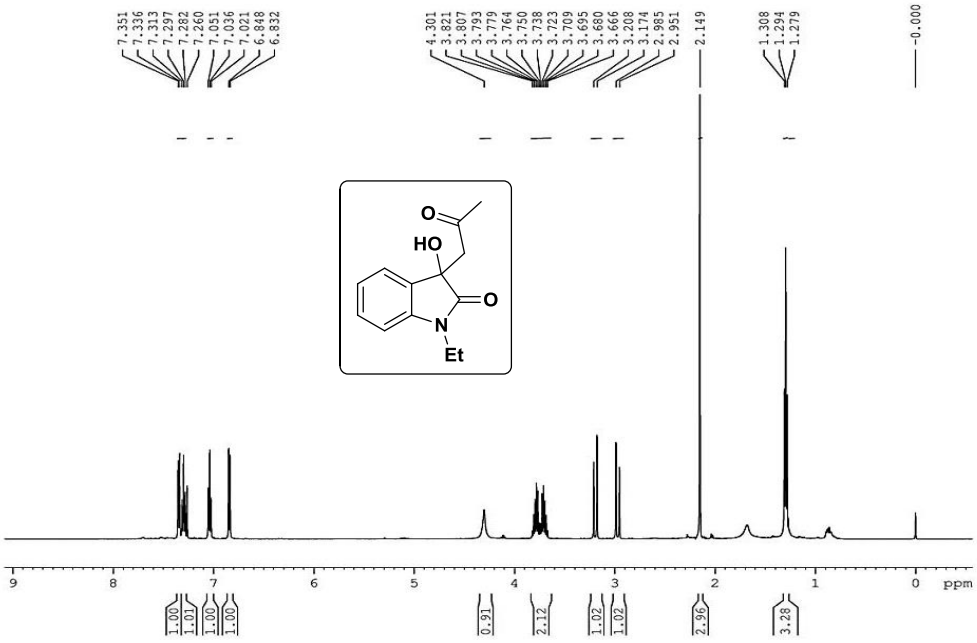


Figure 3.16. ^{1}H NMR Spectrum of compound **80**

In ^{13}C NMR spectrum, amide carbonyl was observed at δ 175.9 ppm, while the signal due to the carbonyl of acetonyl group appeared at δ 206.5 ppm. The quaternary carbon bearing hydroxyl group was located at δ 73.9 ppm. All other signals of ^{1}H NMR and ^{13}C NMR were in agreement with the proposed structure.

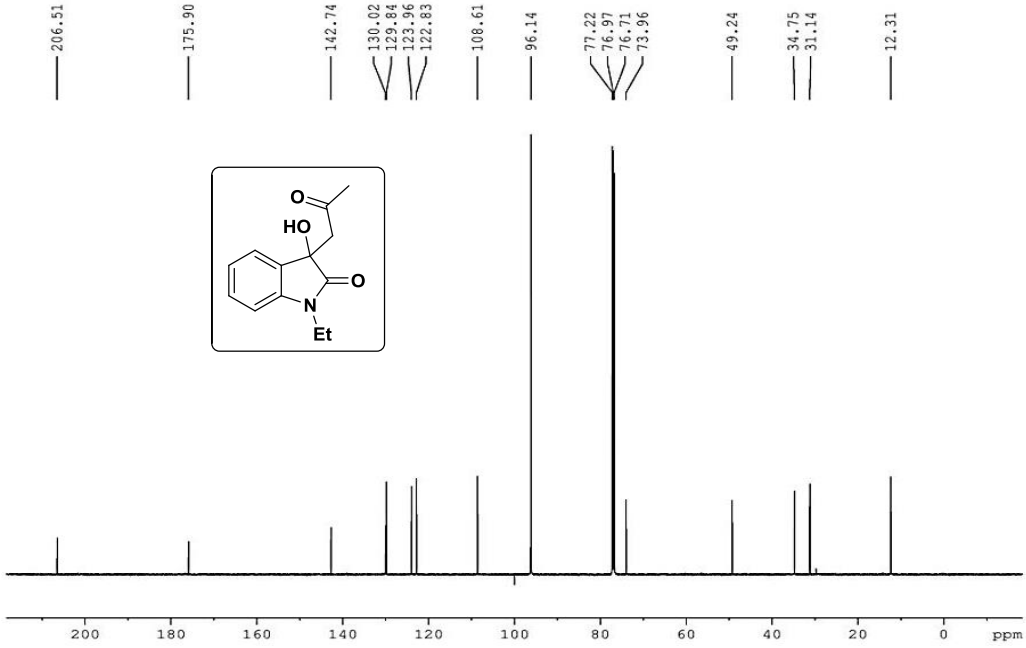


Figure 3.17. ^{13}C NMR Spectrum of compound **80**

Supporting evidence for the structure was obtained from the high-resolution mass spectrum which showed the molecular ion peak at *m/z* 256.09497 $[M+Na]^+$. Further, the structure of the product **80** was unambiguously confirmed by single crystal X-ray analysis (Figure 3.18).[26]

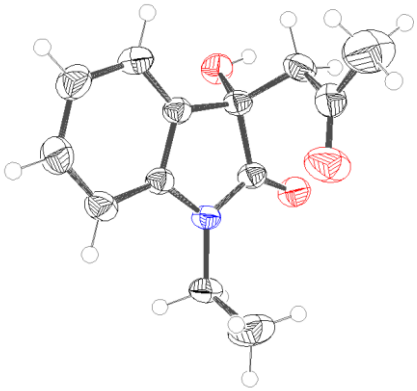
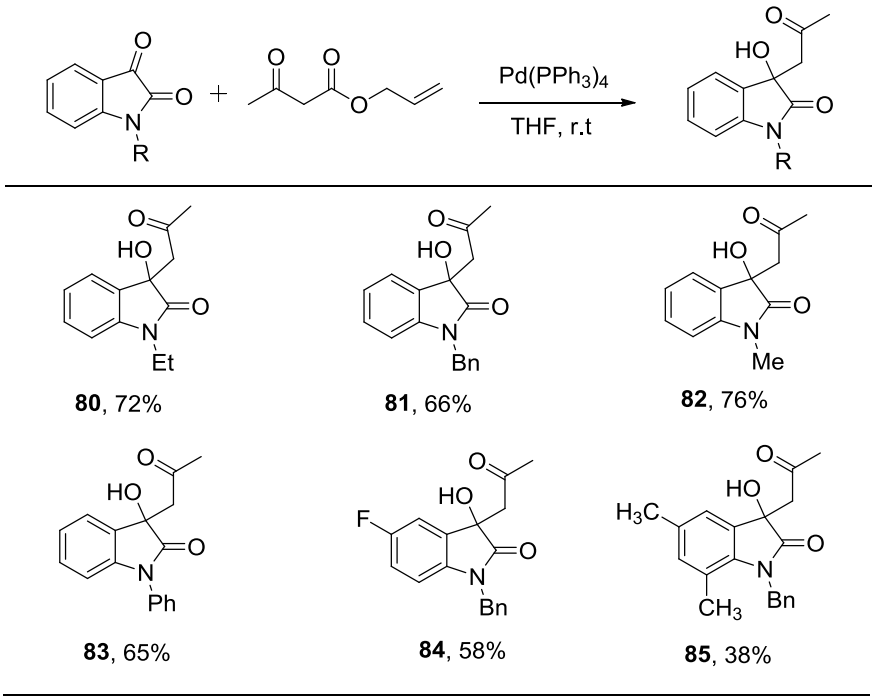


Figure 3.18. ORTEP Diagram of compound **80**

The generality of the reaction was examined by reacting different N-substituted isatins with allyl acetoacetate **13** under identical reaction conditions, and the products were obtained in good yields. The results obtained are shown in Table 3.5

Table 3.5. Decarboxylative addition of allyl acetoacetate to C-3 carbonyl group of isatin



Reaction Conditions: isatin (1.0 equiv), allylacetotate (2.0 equiv), catalyst (5 mol%), THF (2 mL), rt, 12 h

The synthesized compounds, 3-hydroxy-3-substituted oxindoles, are significant structural motifs in medicinal chemistry. Some of the biologically significant hydroxyl substituted 2-oxindoles are shown in figure 3.19.

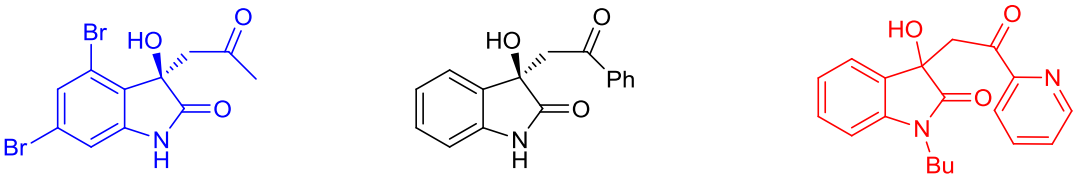
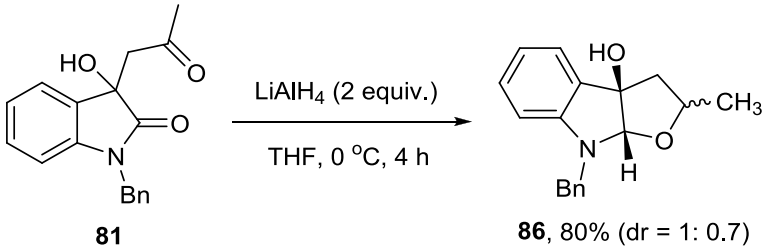


Figure 3.19. Bioactive 3-hydroxy-3-substituted oxindoles

3.3.7. Reductive cyclization of 3-hydroxy oxindoles

To demonstrate the utility of the present method in synthetic chemistry, further transformations of the obtained oxindoles were then investigated. The treatment of compound **81** with lithium aluminum hydride (LAH) in THF at 0 ^{o}C led to product **86** as inseparable diastereomers (dr = 1: 0.7) in 80% yield (Scheme 3.25).[27]

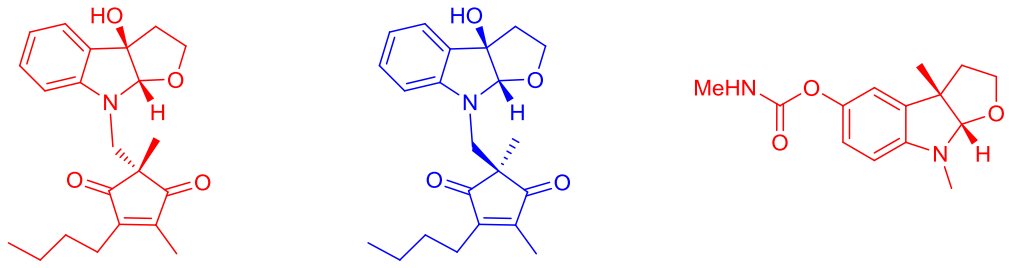


81 **86**, 80% (dr = 1: 0.7)

Scheme 3.25

The structure of product **86** was assigned with the help of various spectral data. The compound showed characteristic O-H stretching at 3390 cm^{-1} in the IR spectrum. In the ^{1}H NMR spectrum, the ring junction proton which is attached to both oxygen and nitrogen was observed as a singlet at δ 5.19 ppm. The hydroxyl proton was discernible as a singlet at δ 4.76 ppm. The proton attached to an oxygen atom in the furan ring was observed as a multiplet in the area δ 4.39-4.32 ppm. In the ^{13}C NMR spectrum, the methyl carbon was seen at δ 20.4 ppm. All other signals in the ^{1}H and ^{13}C NMR spectra were in agreement with the proposed structure. The mass spectral analysis showed a peak at *m/z* 282.14932 $[M+Na]^{+}$, which also supported the proposed structure.

The formed furoindoline skeleton was found in indole alkaloid physovenine and it also analogue to the half fragment of natural products madindoline A and B (Figure 3.20).



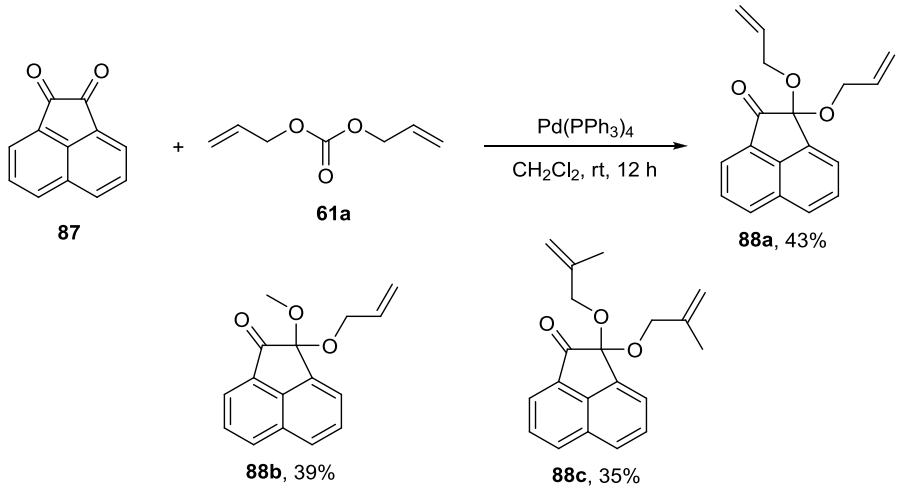
(+)-Madindoline A (+)-Madindoline B (±)-Physovenine

Figure 3.20 Natural products containing furoindoline skelton

3.3.8. Interceptive decarboxylative addition of allyl carbonates with other carbonyl compounds

3.3.8.1. Interceptive addition with acenaphthenequinone

Interceptive decarboxylative addition of allyl carbonates was also proved to be general with electrophilic acenaphthenequinone under the similar reaction conditions. Allyl carbonates **61a-c** reacted smoothly with **87** and furnished corresponding ketals **88a-c** in moderate yields (Scheme 3.26).

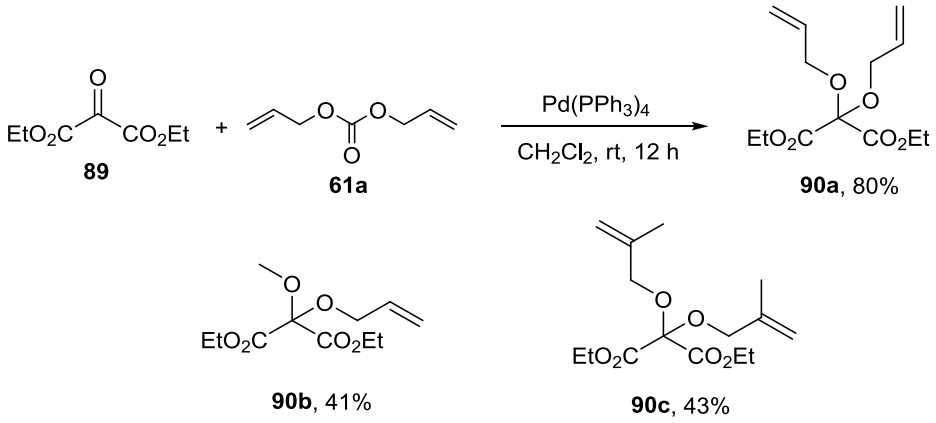


87 + **61a** → **88a**, 43%; **88b**, 39%; **88c**, 35%

Scheme 3.26 Decarboxylative addition of allyl carbonate with acenaphthenequinone

3.3.8.2. Interceptive addition with diethyl ketomalonate

The interceptive decarboxylative addition of allyl carbonates is further extended to diethyl ketomalonate. Diethyl ketomalonate **89** underwent smooth decarboxylative 1,2-interceptive addition with allyl carbonates **61a-c** under the optimized reaction conditions to give corresponding ketals **90a-c** in good yields.

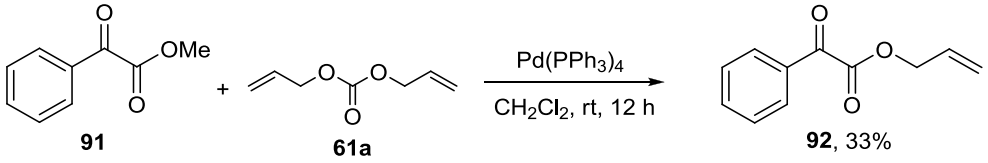


89 + **61a** → **90a**, 80%; **90b**, 41%; **90c**, 43%

Scheme 3.27

3.3.8.3. Reaction of diallyl carbonate with methyl benzoylformate

We proceeded to examine the reactivity of methyl benzoyl formate **91** towards the interceptive addition with diallyl carbonate **61a**. In this case, instead of the expected intercepted product the reaction afforded transesterification product allyl benzoylformate **92** in 33% yield.



Scheme 3.28

3.4. Conclusion

In summary, we have developed for the first time a palladium catalyzed interceptive decarboxylative 1,4-addition of allyl carbonates to squarates. Interceptive decarboxylative 1,2-addition of allyl carbonates with N-substituted isatins, acenaphthenequinone and diethyl ketomalonate are also described. Furthermore, the ring-closing metathesis of bis allyloxy oxindole derived from the 1,2-interceptive addition of diallyl carbonate with isatin derivatives furnished the corresponding spiro-dioxepine fused 2-oxindoles in good yields. The addition of allyl acetoacetate with isatins provided the 3-hydroxy oxindole derivatives. Synthesized 3-hydroxy oxindole derivative could be transformed into heterocyclic furoindoline skeleton.

3.5. Experimental Section

3.5.1. General experimental procedure for the palladium catalyzed interceptive decarboxylative allylation of squaric acid esters

Dialkyl squarate (1.0 equiv.) and $Pd(PPh_3)_4$ (10 mol%) were taken in a Schlenk tube, degassed, and allyl carbonate (2.0 equiv.) was added followed by 2 mL dichloromethane . Argon gas is purged into the reaction mixture and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue on silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture afforded the product in moderate yields.

3.5.2. General experimental procedure for the palladium catalyzed decarboxylative addition of allyl carbonates to isatin

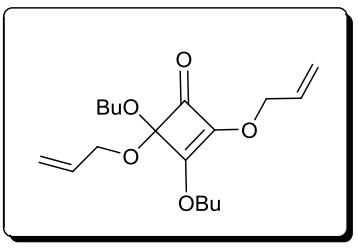
N-substituted isatin (1 equiv.) and $Pd(PPh_3)_4$ (5 mol %) were taken in a Schlenk tube, degassed, and allyl carbonate (2 equiv.) was added followed by 2 mL THF. Argon gas is purged into the reaction mixture and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue on silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent afforded the product.

3.5.3. General experimental procedure for the palladium catalyzed decarboxylative addition of allyl acetoacetate to isatins

N-protected isatin (1 equiv.) and $Pd(PPh_3)_4$ (5 mol%) were taken in a Schlenk tube, degassed, and allyl acetoacetate (2 equiv) was added followed by 2 mL THF. Argon gas is purged into the reaction mixture and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue on silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent to afford the product.

2,4-Bis(allyloxy)-3,4-dibutoxycyclobut-2-enone (62aa)

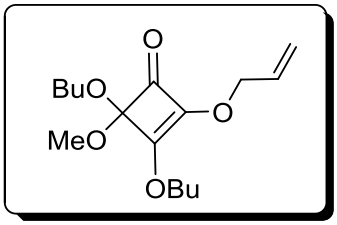
Dibutyl squarate **41a** (40 mg, 0.18 mmol), diallyl carbonate **2a** (50 mg, 0.35 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.018 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 97:3), compound **62aa** was obtained as a colourless viscous oil in 42% yield (24 mg) and the unreacted dibutyl squarate (13 mg) was recovered.



R_f : 0.61 (3:7 Ethyl acetate/hexane); **IR (neat) υ_{max}:** 2961, 2935, 2874, 1778, 1638, 1460, 1331, 1061 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.98-5.91 (m, 2 H), 5.39-5.15 (m, 4 H), 4.77 (d, *J* = 5.5 Hz, 2 H), 4.40 (t, *J* = 6.5 Hz, 2 H), 4.27 (d, *J* = 5.5 Hz, 2 H), 3.71 (t, *J* = 6.5 Hz, 2 H), 1.75 (quin, *J* = 7.0 Hz, 2 H), 1,58 (quin, *J* = 7.0 Hz, 2), 1.47-1.36 (m, 4 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 0.91 (t, *J* = 7.5 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.9, 167.4, 137.1, 134.3, 132.6, 118.8, 116.8, 108.2, 73.3, 71.2, 66.6, 65.5, 31.9, 31.5, 19.2, 18.7, 13.8, 13.6.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{28}O_5Na$ $[M+Na]^+$: 347.18344; Found: 347.18249.

2-(Allyloxy)-3,4-dibutoxy-4-methoxycyclobut-2-enone (62ab)

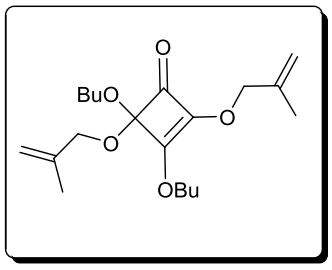
Dibutyl squarate **41a** (40 mg, 0.18 mmol), allyl methyl carbonate **61b** (41 mg, 0.35 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.018 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 95:5), compound **62ab** was obtained as a colourless viscous oil in 18% yield (9 mg) and the unreacted dibutyl squarate (30 mg) was recovered.



R_f : 0.23 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2960, 2937, 2874, 1778, 1638, 1458, 1331, 1070 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.99-5.91 (m, 1 H), 5.39-5.26 (m, 2 H), 4.76 (d, *J* = 6.0 Hz, 2 H), 4.38 (t, *J* = 6.5 Hz, 2 H), 3.69 (t, *J* = 6.5 Hz, 2 H), 3.49 (s, 3 H), 1.75 (quin, *J* = 7.0 Hz, 2 H), 1.58 (quin, *J* = 7.0 Hz, 2 H), 1.47-1.37 (m, 4 H), 0.97 (t, *J* = 7.0 Hz, 3 H), 0.92 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 184.2, 167.3, 137.4, 134.2, 118.9, 108.2, 74.1, 70.8, 65.8, 53.2, 31.9, 31.8, 18.7, 18.5, 13.7, 13.6.; **HRMS (ESI):** *m/z* calcd. for $C_{16}H_{26}O_5Na$ $[M+Na]^+$: 321.16779; Found: 321.16608.

3,4-Dibutoxy-2,4-bis((2-methylallyl)oxy)cyclobut-2-enone (62ac)

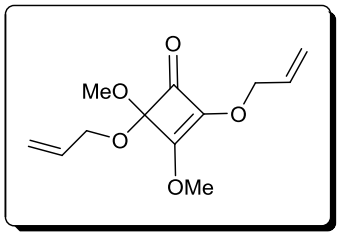
Dibutyl squarate **41a** (50 mg, 0.22 mmol), dimethallyl carbonate **61c** (75 mg, 0.44 mmol) and $Pd(PPh_3)_4$ (25 mg, 0.022 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 95:5), compound **62ac** was obtained as a colourless viscous oil in 36% yield (28 mg) and the unreacted dibutyl squarate (24 mg) was recovered.



R_f : 0.54 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2960, 2933, 2874, 1778, 1638, 1460, 1407, 1331, 1060, 1030 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.03-4.86 (m, 4 H), 4.69 (s, 2 H), 4.40 (t, *J* = 6.5 Hz, 2 H), 4.16 (s, 2H), 3.73 (t, *J* = 6.5 Hz, 2 H), 1.78-1.75 (m, 8 H), 1.65-1.56 (m, 2 H), 1.48-1.35 (m, 4 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 0.91(t, *J* = 7.5 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 185.0, 167.3, 141.7, 140.3, 137.2, 113.5, 111.8, 108.3, 74.0, 73.3, 69.5, 65.5, 31.9, 31.5, 19.5, 19.3, 19.1, 18.7, 13.7, 13.6.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{32}O_5Na$ $[M+Na]^+$: 375.21474; Found: 375.21385.

2,4-Bis(allyloxy)-3,4-dimethoxycyclobut-2-enone (62ba)

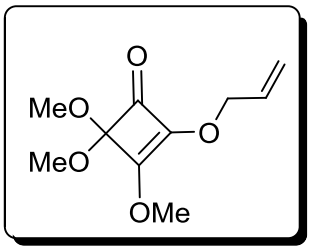
Dimethyl squarate **41b** (50 mg, 0.35 mmol), diallyl carbonate **61a** (100 mg, 0.70 mmol) and $Pd(PPh_3)_4$ (41 mg, 0.035 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 90:10), compound **62ba** was obtained as a colourless viscous oil in 59% yield (51 mg) and the unreacted dimethyl squarate (10 mg) was recovered.



R_f : 0.48 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2927, 1718, 1647, 1587, 1320, 1019 cm^{-1}.; **^{1}H NMR (300 MHz, $CDCl_3$, TMS):** δ 6.02-5.88 (m, 2 H), 5.41-5.15 (m, 4 H), 4.76(d, *J* = 5.7 Hz, 2 H), 4.27 (d, *J* = 5.4 Hz, 2 H), 4.14 (s, 3 H), 3.51(s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.5, 167.3, 137.8, 134.0, 132.5, 118.9, 116.9, 108.5, 71.4, 66.8, 60.2, 53.3.; **HRMS (ESI):** *m/z* calcd. for $C_{12}H_{16}O_5Na$ $[M+Na]^+$: 263.08954; Found: 263.08845.

2-(Allyloxy)-3,4,4-trimethoxycyclobut-2-enone (62bb)

Dimethyl squarate **41b** (100 mg, 0.70 mmol), allylmethyl carbonate **61b** (163 mg, 1.41 mmol) and $Pd(PPh_3)_4$ (82 mg, 0.074 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 95:5), compound **62bb** was obtained as a colourless viscous oil in 45% yield (68 mg) and the unreacted dimethyl squarate (19 mg) was recovered.

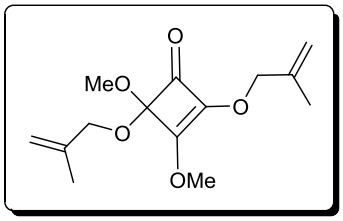


R_f : 0.28 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2924, 2854, 1743, 1683, 1646, 1568, 1119, 1048 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.99-5.92 (m, 1 H), 5.40-5.27 (m, 2 H), 4.77 (d, *J* = 5.5 Hz, 2 H), 4.14 (s, 3 H), 3.51 (s, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.6, 167.3, 137.8, 132.5, 118.9, 108.9, 71.4, 60.2, 53.3.; **HRMS (ESI):** *m/z* calcd. for $C_{10}H_{14}O_5Na$ $[M+Na]^+$: 237.07389; Found: 237.07271.

3,4-Dimethoxy-2,4-bis((2-methylallyl)oxy)cyclobut-2-enone (62bc)

Dimethyl squarate **41b** (100 mg, 0.70 mmol), dimethallyl carbonate **61c** (239 mg, 1.41 mmol) and $Pd(PPh_3)_4$ (82 mg, 0.074 mmol) were treated according to

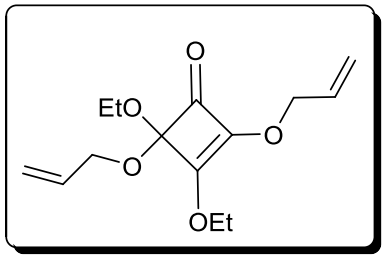
the general method. After purification by column chromatography (hexane/Ethyl acetate 95:5), compound **62bc** was obtained as a colourless viscous oil in 43% yield (80 mg) and the unreacted dimethyl squarate (42 mg) was recovered.



R_f : 0.31 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2924, 1779, 1746, 1655, 1625, 1471, 1337, 1021cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.04-4.88 (m, 4 H), 4.69 (s, 2 H), 4.16 (s, 2 H), 4.15 (s, 3 H), 3.51 (s, 3 H), 1.77 (s, 3 H), 1.76 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.6, 167.2, 141.6, 140.1, 137.9, 113.7, 111.9, 108.6, 74.1, 69.5, 60.1, 53.3, 19.5, 19.1.; **HRMS (ESI):** *m/z* calcd. for $C_{14}H_{20}O_5Na$ $[M+Na]^+$: 291.12084; Found: 291.12021.

2,4-Bis(allyloxy)-3,4-diethoxycyclobut-2-enone (62ca)

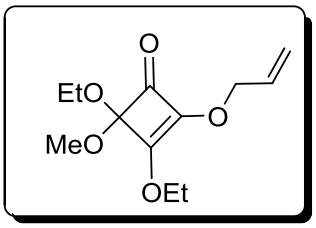
Diethyl squarate **41c** (100 mg, 0.64 mmol), diallyl carbonate **61a** (181 mg, 1.27 mmol) and $Pd(PPh_3)_4$ (73 mg, 0.074 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 90:10), compound **62ca** was obtained as a colourless viscous oil in 21% yield (35 mg) and the unreacted diethyl squarate (71 mg) was recovered.



R_f : 0.30 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2984, 2930, 1812, 1731, 1602, 1418, 1335, 1021 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.97-5.89 (m, 2 H), 5.39-5.14 (m, 4 H), 4.77 (d, *J* = 5.5 Hz, 2 H), 4.46 (q, *J* = 7.0 Hz, 2 H), 4.25 (d, *J* = 5.5 Hz, 2 H), 3.78 (q, *J* = 7.0 Hz, 2 H), 1.43 (t, *J* = 7.0 Hz, 3 H), 1.23 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.5, 166.9, 137.0, 134.2, 132.6, 118.9, 116.7, 107.9, 71.2, 69.3, 66.5, 61.3, 15.4, 15.2.; **HRMS (ESI):** *m/z* calcd. for $C_{14}H_{20}O_5Na$ $[M+Na]^+$: 291.12084; Found: 291.12021.

2-(Allyloxy)-3,4-diethoxy-4-methoxycyclobut-2-enone (62cb)

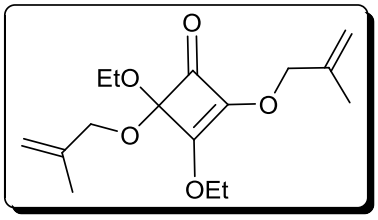
Diethyl squarate **41c** (100 mg, 0.64 mmol), allylmethyl carbonate **61b** (147 mg, 1.27 mmol) and $Pd(PPh_3)_4$ (73 mg, 0.074 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 90:10), compound **62cb** was obtained as a colourless viscous oil in 29% yield (44 mg) and the unreacted diethyl squarate (55 mg) was recovered.



R_f : 0.30 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2924, 1744, 1590, 1423, 1318, 1119, 1020 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.99-5.91 (m, 1 H), 5.39-5.26 (m, 2 H), 4.77 (d, *J* = 5.5 Hz, 2 H), 4.45 (q, *J* = 7.0 Hz, 2 H), 3.77 (q, *J* = 7.0 Hz, 2 H), 3.49 (s, 3 H), 1.43 (t, *J* = 7.0 Hz, 3 H), 1.24 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.7, 166.9, 137.0, 132.6, 118.9, 108.4, 71.2, 69.3, 61.3, 53.1, 15.4, 15.2.; **HRMS (ESI):** *m/z* calcd. for $C_{12}H_{18}O_5Na$ $[M+Na]^+$: 265.10519; Found: 265.10367.

3,4-Diethoxy-2,4-bis((2-methylallyl)oxy)cyclobut-2-enone (62cc)

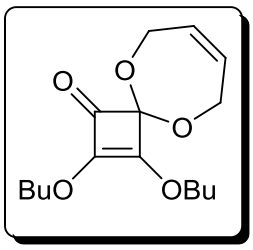
Diethyl squarate **41c** (100 mg, 0.64 mmol), dimethallyl carbonate **41c** (216 mg, 1.27 mmol) and $Pd(PPh_3)_4$ (73 mg, 0.074 mmol) were treated according to the general method. After purification by column chromatography (hexane/Ethyl acetate 90:10), compound **62cc** was obtained as a colourless viscous oil in 44% yield (83 mg) and the unreacted diethyl squarate (38 mg) was recovered.



R_f : 0.26 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2931, 2866, 1779, 1641, 1462, 1343, 1074 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.03-4.85 (m, 4 H), 4.69(s, 2 H), 4.46 (q, *J* = 7.0 Hz, 2 H), 4.13 (s, 2 H), 3.78 (q, *J* = 7.0 Hz, 2 H), 1.77 (s, 3 H), 1.75 (s, 3 H), 1.44 (t, *J* = 7.0 Hz, 3 H), 1.23 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.7, 166.8, 141.6, 140.2, 137.1, 113.6, 111.9, 108.1, 73.9, 69.3, 66.8, 61.3, 19.6, 19.2, 15.5, 15.3.; **HRMS (ESI):** *m/z* calcd. for $C_{16}H_{24}O_5Na$ $[M+Na]^+$:319.15214; Found: 319.15131.

Typical Procedure for the RCM of 2,4-bis(allyloxy)-3,4-dibutoxycyclobut-2-enone 62aa for the synthesis of 2,3-dibutoxy-5,10-dioxaspiro[3.6]deca-2,7-dien-1-one (63)

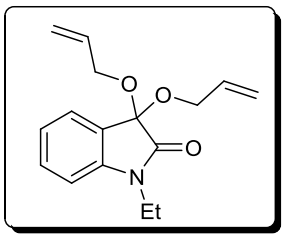
2,4-Bis(allyloxy)-3,4-dibutoxycyclobut-2-enone **62aa** (43 mg, 0.13 mmol) was dissolved in 6 mL dichloromethane. To this Grubbs' second generation catalyst (12 mg, 0.013 mmol) was added and stirred at room temperature for 8 hours. The reaction was monitored by Thin Layer Chromatography. The solvent was evaporated *in vacuo* and the residue on silica gel (100 – 200 mesh) column chromatography using 5% ethyl acetate in hexane afforded the product **63** as colourless viscous oil in 26% (10 mg) yield.



R_f : 0.33 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}**: 2960, 2871, 1779, 1638, 1465, 1413, 1334, 1071, 1049 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.69 (s, 2 H), 4.59 (d, *J* = 14.5 Hz, 2 H), 4.47 (d, *J* = 15.0 Hz, 2 H), 4.39 (t, *J* = 6.5 Hz, 2 H), 4.30 (t, *J* = 6.5 Hz, 2 H), 1.76 (quin, *J* = 7.0 Hz, 2 H), 1.64 (quin, *J* = 7.0 Hz, 2 H), 1.47-1.37 (m, 4 H), 0.99-0.93 (m, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.5, 166.8, 137.4, 128.9, 107.9, 73.4, 70.9, 65.5, 31.9, 31.5, 18.7, 18.6, 13.7, 13.6.; **HRMS (ESI)**: *m/z* calcd. for $C_{16}H_{24}O_5Na$ $[M+Na]^+$: 319.15214; Found: 319.15134.

3,3-Bis(allyloxy)-1-ethylindolin-2-one (65a)

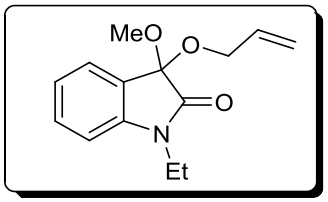
Following the general experimental procedure, N-ethyl isatin **64a** (100 mg, 0.57 mmol), diallyl carbonate **61a** (142 mg, 1.14 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **65a** as a pale yellow viscous liquid (89 mg, 57% yield) after column chromatography (5% Ethyl acetate-Hexane).



R_f : 0.78 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3077, 2979, 2933, 2875, 1729, 1613, 1465, 1366, 1264, 1212, 1159, 1117, 1048, 927, 754 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.41 (d, *J* = 7.0 Hz, 1 H), 7.33 (t, *J* = 8.0 Hz, 1 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.82 (d, *J* = 8.0 Hz, 1 H), 5.95-5.89 (m, 2 H), 5.31-5.26 (m, 4 H), 5.15-5.13 (m, 2 H), 4.47-4.43 (m, 2 H), 4.33-4.29 (m, 2 H), 1.27 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.1, 142.4, 134.1, 130.5, 125.6, 124.9, 122.4, 116.8, 108.7, 96.5, 64.2, 34.4, 12.5.; **HRMS (ESI):** *m/z* calcd. for $C_{16}H_{19}O_3NNa$ $[M+Na]^+$: 296.12626; Found: 296.12634.

3-(Allyloxy)-1-ethyl-3-methoxyindolin-2-one (65b)

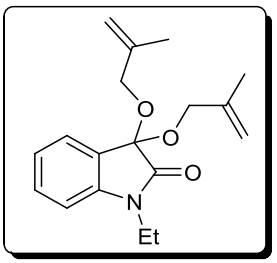
Following the general experimental procedure, N-ethyl isatin **64a** (100 mg, 0.57 mmol), allylmethyl carbonate **61b** (133 mg, 1.14 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **65b** as a pale yellow viscous liquid (71 mg, 50% yield) after column chromatography (15% Ethyl acetate-Hexane).



R_f : 0.39 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3061, 2980, 2940, 1729, 1614, 1489, 1466, 1371, 1288, 1263, 1213, 1155, 1121, 1050, 931, 756 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.43 (d, *J* = 7.0 Hz, 1 H), 7.35 (t, *J* = 8.0 Hz, 1 H), 7.08 (t, *J* = 7.5 Hz, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 5.99-5.91 (m, 1 H), 5.32-5.15 (m, 2 H), 4.49-4.46 (m, 1 H), 4.36-4.33 (m, 1 H), 3.72 (q, *J* = 7.5 Hz, 2 H), 3.55 (s, 3 H), 1.26 (t, *J* = 7.5 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.3, 142.4, 134.1, 130.6, 125.3, 124.9, 122.5, 116.9, 108.9, 96.8, 64.2, 50.9, 34.4, 12.5.; **HRMS (ESI):** *m/z* calcd. for $C_{14}H_{17}O_3NNa$ $[M+Na]^+$: 270.11061; Found: 270.11057.

1-Ethyl-3,3-bis(2-methylallyloxy)indolin-2-one (65c)

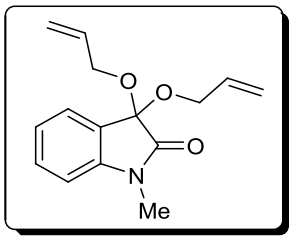
Following the general experimental procedure, N-ethyl isatin **64a** (100 mg, 0.57 mmol), dimethallyl carbonate **61c** (194 mg, 1.14 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **65c** as a pale yellow viscous liquid (82 mg, 48% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.57 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3074, 2975, 2927, 2867, 1729, 1654, 1613, 1463, 1368, 1212, 1119, 1043, 901, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.42 (d, *J* = 7.5 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 1 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.82 (d, *J* = 8.0 Hz, 1 H), 4.98 (s, 2 H), 4.83 (s, 2 H), 4.34-4.18 (m, 4 H), 3.72 (q, *J* = 7.0 Hz, 2 H), 1.75 (s, 6 H), 1.27 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.2, 142.4, 141.5, 130.4, 125.8, 124.9, 122.4, 111.8, 108.6, 96.5, 66.8, 34.4, 19.7, 12.5.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{23}O_3NNa$ $[M+Na]^+$: 324.15756; Found: 324.15765.

3,3-Bis(allyloxy)-1-methylindolin-2-one (66a)

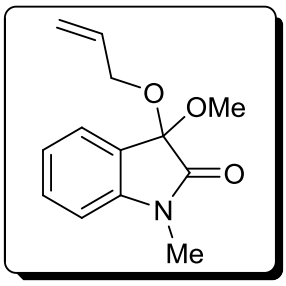
Following the general experimental procedure, N-methyl isatin (100 mg, 0.62 mmol), diallyl carbonate **61a** (176 mg, 1.24 mmol), $Pd(PPh_3)_4$ (36 mg, 0.031 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **66a** as a brown viscous liquid (83 mg, 51% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.46 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3062, 2874, 2377, 2310, 1728, 1610, 1468, 1369, 1349, 1234, 1110, 1039, 925, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.40 (d, *J* = 7.0 Hz, 1 H), 7.34-7.31 (m, 1 H), 7.06-7.03 (m, 1 H), 6.79 (d, *J* = 7.5 Hz, 1 H), 5.95-5.87 (m, 2 H), 5.28 (d, *J* = 17.0 Hz, 2 H), 5.13 (d, *J* = 10.0 Hz, 2 H), 4.48-4.44 (m, 2 H), 4.33-4.29 (m, 2 H), 3.13 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.5, 143.2, 133.9, 130.6, 125.3, 124.7, 122.6, 116.9, 108.6, 96.5, 64.2, 25.8.; **HRMS (ESI):** *m/z* calcd. for $C_{15}H_{17}O_3NNa$ $[M+Na]^+$: 282.11061; Found: 282.11102.

3-(Allyloxy)-3-methoxy-1-methylindolin-2-one (66b)

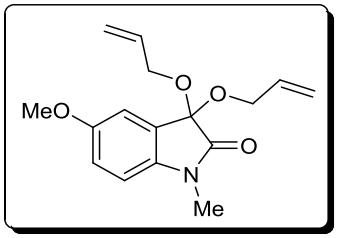
Following the general experimental procedure, N-methyl isatin (50 mg, 0.03 mmol), allyl methyl carbonate **61b** (72 mg, 0.62 mmol), $Pd(PPh_3)_4$ (18 mg, 0.015 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **66b** as a yellow viscous liquid (31 mg, 43% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.43 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2955, 2922, 2089, 1725, 1648, 1612, 1465, 1369, 1612, 1465, 1369, 1347, 1234, 1112, 1040, 749 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.42 (d, *J* = 7.5 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 6.83 (d, *J* = 8.0 Hz, 1 H), 5.99-5.91 (m, 1 H), 5.31 (d, *J* = 17.0 Hz, 1 H), 5.16 (d, *J* = 10.5 Hz, 1 H), 4.49-4.46 (m, 1 H), 4.36-4.33 (m, 1 H), 3.56 (s, 3 H), 3.18 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.5, 143.3, 134.0, 130.6, 125.2, 124.8, 122.6, 116.9, 108.6, 96.8, 64.2, 50.8, 25.8.; **HRMS (ESI):** m/z calcd. for $C_{13}H_{15}NO_3Na$ $[M+Na]^+$: 256.09496, Found: 256.09527.

3,3-Bis-allyloxy-5-methoxy-1-methylindolin-2-one (67a)

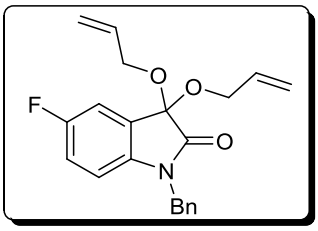
Following the general experimental procedure, 5-methoxy-N-methyl isatin (100 mg, 0.52 mmol), diallyl carbonate **61a** (149 mg, 1.24 mmol), $Pd(PPh_3)_4$ (30 mg, 0.026 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **67a** as a yellow viscous liquid (80 mg, 52% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.41 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3064, 2871, 2371, 2308, 1727, 1610, 1464, 1369, 1349, 1231, 1110, 1031, 924, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.02 (s, 1 H), 6.85 (d, *J* = 8.5 Hz, 1 H), 6.71 (d, *J* = 8.5 Hz, 1 H), 5.96-5.88 (m, 2 H), 5.29 (d, *J* = 17.5 Hz, 2 H), 5.14 (d, *J* = 10.5 Hz, 2 H), 4.45-4.42 (m, 2 H), 4.33-4.29 (m, 2 H), 3.79 (s, 3 H), 3.13 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.3, 155.9, 136.5, 133.9, 126.4, 116.9, 114.7, 112.3, 108.9, 96.8, 64.3, 55.8, 25.9.; **HRMS (ESI):** m/z calcd. for $C_{16}H_{19}NO_4Na$ $[M+Na]^+$: 312.12118, Found: 312.12145.

3,3-Bis(allyloxy)-1-benzyl-5-fluoroindolin-2-one (68a)

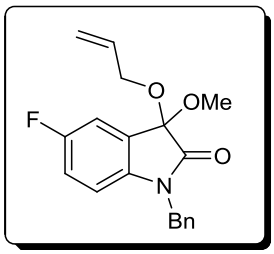
Following the general experimental procedure, 5-fluoro-N-benzyl isatin (100 mg, 0.41 mmol), diallyl carbonate **61a** (118 mg, 0.83 mmol), $Pd(PPh_3)_4$ (24 mg, 0.021 mmol), in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **68a** as a yellow viscous liquid (84 mg, 57% yield) after column chromatography (15% Ethyl acetate-Hexane).



R_f : 0.62 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3071, 3027, 2925, 2873, 2311, 1727, 1616, 1487, 1452, 1344, 1271, 1179, 1131, 1103, 1043, 923, 806, 752, 695, 600, 555 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.31-7.28 (m, 2 H), 7.25-7.24 (m, 3 H), 7.17 (dd, J_1 = 7.5Hz, J_2 = 2.5 Hz, 1 H), 6.90 (dt, J_1 = 9.0 Hz, J_2 = 2.5 Hz, 1 H), 6.58 (dd, J_1 = 8.5 Hz, J_2 = 4.0 Hz, 1 H), 5.97-5.91 (m, 2 H), 5.31 (d, *J* = 17.5 Hz, 2 H), 5.17 (d, *J* = 10.5 Hz, 2 H), 4.83 (s, 2 H), 4.51-4.47 (m, 2 H), 4.37-4.34 (m, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.5, 159.9, 158.0, 138.2 (2C), 135.0, 133.8, 128.9, 127.8, 127.2, 127.0, 126.9, 117.2, 116.8, 116.6, 113.1, 112.9, 110.4, 110.3, 96.5, 64.3, 43.6.; **HRMS (ESI):** m/z calcd. for $C_{21}H_{20}FNO_3Na$ $[M+Na]^+$: 376.13249, Found: 376.13315.

3-(Allyloxy)-1-benzyl-5-fluoro-3-methoxyindolin-2-one (68b)

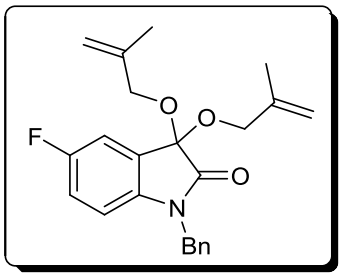
Following the general experimental procedure, the 5-fluoro-N-benzyl isatin (100 mg, 0.41 mmol), allyl methyl carbonate **61b** (96 mg, 0.83 mmol), $Pd(PPh_3)_4$ (24 mg, 0.021 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **68b** as a yellow solid (55 mg, 42% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.59 (3:7 Ethyl acetate/hexane).; **mp:** 78-83 ^{0}C.; **IR (neat) υ_{max}:** 2952, 2916, 2841, 2311, 1728, 1612, 1486, 1451, 1342, 1270, 1172, 1035, 975, 925, 803, 752, 670 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.35-7.32 (m, 2 H), 7.29-7.26 (m,3 H), 7.18 (dd, J_1 = 7.5 Hz, J_2 = 2.5 Hz, 1 H), 6.94 (dt, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1 H), 6.61 (dd, J_1 = 8.5 Hz, J_2 = 4.0 Hz, 1 H), 6.01-5.93 (m, 1 H), 5.35 (d, J = 17.0 Hz, 1 H), 5.21 (d, J = 10.5 Hz, 1 H), 4.92-4.82 (m, 2 H), 4.55-4.51 (m, 1 H), 4.42-4.38 (m, 1 H), 3.57 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.5, 159.9, 158.0, 138.2 (2C), 134.9, 133.8, 128.9, 127.8, 127.1, 126.8, 126.7, 117.1, 116.8, 116.6, 113.1, 112.9, 110.4, 110.3, 96.7, 64.3, 50.9, 43.5.; **HRMS (ESI):** *m/z* calcd. for $C_{19}H_{18}FNO_3Na$ $[M+Na]^+$: 350.11684, Found: 350.11762.

1-Benzyl-5-fluoro-3,3-bis((2-methylallyl)oxy)indolin-2-one (68c)

Following the general experimental procedure, 5-fluoro-N-benzyl isatin (100 mg, 0.41 mmol), dimethallyl carbonate **61c** (141 mg, 0.83 mmol), $Pd(PPh_3)_4$ (24 mg, 0.021 mmol), in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **68c** as a pale yellow solid (43 mg, 27% yield) after column chromatography (8% Ethyl acetate-Hexane).

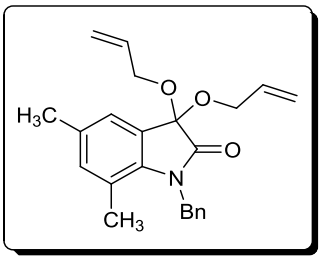


R_f : 0.69 (3:7 Ethyl acetate/hexane).; **mp:** 76-80 °C.; **IR (neat) υ_{max}:** 3070, 3032, 2986, 2912, 1730, 1604, 1487, 1452, 1343, 1271, 1179, 1038, 900, 813, 753, 696, 670, 601 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.35-7.32 (m, 2 H), 7.29-7.26 (m, 3 H), 7.19 (dd, J_1 = 7.5 Hz, J_2 = 2.5 Hz, 1 H), 6.94 (dt, J_1 = 8.5 Hz,J_2 = 2.0 Hz, 1 H), 6.60 (dd, J_1 = 8.5 Hz, J_2 = 4.0 Hz, 1 H), 5.03 (s, 2 H), 4.89-4.87 (m, 4 H), 4,39 (d, J = 12.0 Hz, 2 H), 4.26 (d, J = 12.0 Hz, 2 H), 1.79 (s, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 170.5, 159.9, 158.0, 141.2, 138.2, 138.1, 135.0, 128.9, 127.8, 127.1, 127.0, 116.7, 116.5, 113.1, 112.9, 112.1, 110.3, 110.2, 96.6, 66.9, 43.5, 19.7.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}FNO_3Na$ $[M+Na]^+$: 404.16379, Found: 404.16459.

3,3-Bis(allyloxy)-1-benzyl-5,7-dimethylindolin-2-one (69a)

Following the general experimental procedure, 5,7-dimethyl N-benzyl isatin (100 mg, 0.37 mmol), diallyl carbonate **61a** (107 mg, 0.75 mmol), $Pd(PPh_3)_4$ (22 mg, 0.019 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **69a** as a

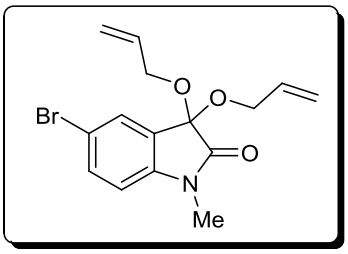
brown viscous liquid (55 mg, 40% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.54 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2309, 1723, 1600, 1482, 1451, 1344, 1272, 1145, 1013, 921, 861, 751, 671 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.29-7.27 (m, 2 H), 7.24-7.19 (m, 1 H), 7.14-7.12 (m, 3 H), 6.79 (s, 1 H), 5.99-5.92 (m, 2 H), 5.32 (dd, J_1 = 17.0 Hz, J_2 = 1.0 Hz, 2 H), 5.16 (dd, J_1 = 10.5 Hz, J_2 = 1.0 Hz, 2 H), 5.10 (s, 2 H), 4.49-4.46 (m, 2 H), 4.38-4.34 (m, 2 H), 2.28 (s, 3 H), 2.17 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 171.9, 137.9, 137.2, 134.9, 134.2, 132.4, 128.9, 128.3, 127.9, 127.2, 126.2, 125.6, 123.5, 120.1, 116.9, 96.4, 64.3, 44.7, 20.8, 18.7.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{25}NO_3Na$ $[M+Na]^+$: 386.17321, Found: 386.17373.

3,3-bis(allyloxy)-5-bromo-1-methylindolin-2-one (70a)

Following the general experimental procedure, N-Methyl-5-bromo isatin (80 mg, 0.25 mmol), diallyl carbonate **61a** (72 mg, 0.51 mmol), $Pd(PPh_3)_4$ (15 mg, 0.028 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **70a** as a pale yellow viscous liquid (57 mg, 68% yield) after column chromatography (10% Ethyl acetate-Hexane).

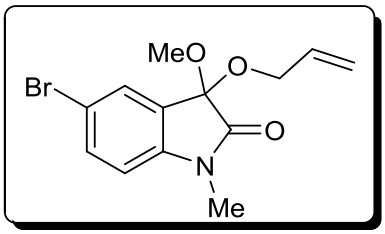


R_f : 0.56 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3078, 2933, 2876, 1739, 1645, 1610, 1487, 1465, 1426, 1358, 1343, 1262, 1231, 1114, 1059, 1037, 977, 926, 812 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.52 (s, 1 H), 7.47 (d, J = 8.5 Hz, 1 H), 6.69 (d, J = 7.0 Hz, 1 H), 5.95-5.87 (m, 2 H), 5.32-5.28 (m, 2 H), 5.18-5.15 (m, 2 H), 4.47-4.43 (m, 2 H), 4.33-4.28 (m, 2 H), 3.15 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 169.9, 142.2, 133.6, 133.3, 127.9, 127.3, 117.2, 115.4, 110.1, 96.2, 64.3, 25.9.; **HRMS (ESI):** *m/z* calcd. for $C_{15}H_{16}O_3BrNNa$ $[M+Na]^+$: 360.02113; Found: 360.02155.

3-(Allyloxy)-5-bromo-3-methoxy-1-methylindolin-2-one (70b)

Following the general experimental procedure, N-Methyl-5-bromo isatin (50 mg, 0.21 mmol), allyl methyl carbonate **61b** (48 mg, 0.42 mmol), $Pd(PPh_3)_4$ (12 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **70b** as a pale

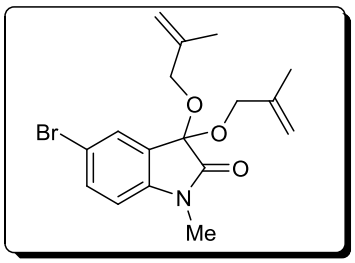
yellow viscous liquid (23 mg, 35% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.56 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 2940, 1735, 1610, 1487, 1464, 1427, 1357, 1263, 1234, 114, 1062, 972, 928, 813 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.51 (s, 1 H), 7.48 (d, *J* = 7.75 Hz, 1 H), 6.69 (d, *J* = 8.5 Hz, 1 H), 5.95-5.89 (m, 1 H), 5.33-5.16 (m, 2 H), 4.48-4.44 (m, 1 H), 4.34-4.31 (m, 1 H), 3.54 (s, 3 H), 3.15 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 169.9, 142.3, 133.7, 133.3, 127.9, 127.1, 117.2, 115.4, 110.0, 96.4, 64.2, 50.9, 25.9.; **HRMS (ESI):** *m/z* calcd. for $C_{13}H_{14}O_3BrNNa$ $[M+Na]^+$: 334.00548; Found: 334.00577.

5-Bromo-1-methyl-3,3-bis(2-methylallyloxy)indolin-2-one (70c)

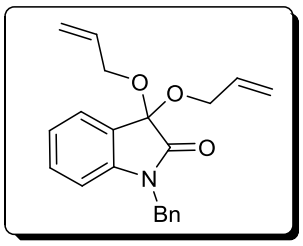
Following the general experimental procedure, N-Methyl-5-bromo isatin (50 mg, 0.21 mmol), dimethallyl carbonate **61c** (71 mg, 0.42 mmol), $Pd(PPh_3)_4$ (12 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **70c** as a pale yellow viscous liquid (41 mg, 54% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.58 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3077, 2920, 1738, 1654, 1610, 1488, 1465, 1429, 1359, 1342, 1262, 1230, 1114, 1039, 901, 812 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.52 (s, 1 H), 7.47 (d, *J* = 8.5 Hz, 1 H), 6.69 (d, *J* = 8.5 Hz, 1 H), 4.99 (s, 2 H), 4.86 (s, 2 H), 4.32 (d, *J* = 12.0 Hz, 2 H), 4.19 (d, *J* = 12.0 Hz, 2 H), 3.15 (s, 3 H), 1.76 (s, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 169.9, 142.3, 141.2, 133.3, 127.9, 127.4, 115.4, 112.2, 110.0, 96.3, 66.9, 25.9, 19.7.; **HRMS (ESI):** *m/z* calcd. for $C_{17}H_{20}O_3BrNNa$ $[M+Na]^+$: 388.05243; Found: 388.05270.

3,3-Bis(allyloxy)-1-benzylindolin-2-one (71a)

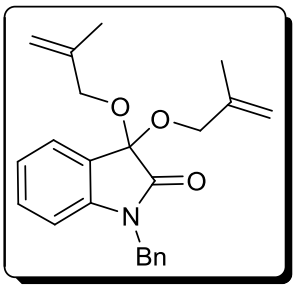
Following the general experimental procedure, N-benzyl isatin (50 mg, 0.21 mmol), diallyl carbonate **61a** (60 mg, 0.42 mmol), $Pd(PPh_3)_4$ (12 mg, 0.011 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **71a** as a pale yellow viscous liquid (53 mg, 76% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.49 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3063, 3030, 2926, 2873, 1729, 1646, 1614, 1488, 1468, 1425, 1360, 1300, 1255, 1161, 1102, 1014, 925, 847, 698 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.44 (d, *J* = 7.5 Hz, 1 H), 7.34-7.22 (m, 6 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.69 (d, *J* = 8.0 Hz, 1 H), 6.01-5.93 (m, 2 H), 5.33 (d, J = 17.5 Hz, 2 H), 5.18 (d, *J* = 10 Hz, 2 H), 4.87 (s, 2 H), 4.55-4.51 (m, 2 H), 4.41-4.37 (m, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.7, 142.4, 135.3, 134.0, 130.5, 128.8, 127.7, 127.2, 125.5, 124.8, 122.7, 116.9, 109.7, 96.6, 64.3, 43.4.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{21}NO_3Na$ $[M+Na]^+$: 358.14191; Found: 358.14163.

1-Benzyl-3,3-bis((2-methylallyl)oxy)indolin-2-one (71c)

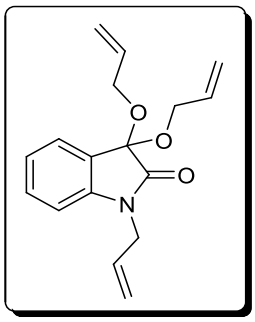
Following the general experimental procedure, N-benzyl isatin (50 mg, 0.21 mmol), dimethallyl carbonate **61c** (71 mg, 0.42 mmol), $Pd(PPh_3)_4$ (12 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **71c** as a pale yellow viscous liquid (30 mg, 42% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.53 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3064, 3032, 2974, 2918, 2866, 1731, 1655, 1614, 1490, 1467, 1361, 1300, 1254, 1184, 1138, 1077, 1041, 943, 900, 752, 698 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.44 (d, *J* = 7.5 Hz, 1 H), 7.33-7.22 (m, 6 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.69 (d, *J* = 7.5 Hz, 1 H), 5.02 (s, 2 H), 4.88 (s, 4 H), 4.39 (d, *J* = 12.0 Hz, 2 H), 4.26 (d, *J* = 12.0 Hz, 2H), 1.78 (s, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.8, 142.4, 141.5, 135.4, 130.4, 128.8, 127.7, 127.2, 125.6, 124.8, 122.6, 111.9, 109.6, 96.7, 66.9, 43.4, 19.7.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{25}NO_3Na$ $[M+Na]^+$: 386. 17321; Found: 386.17374.

1-Allyl-3,3-bis(allyloxy)indolin-2-one (74)

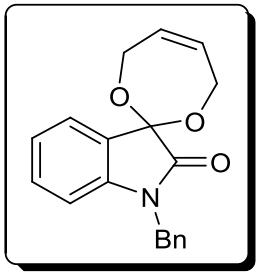
Following the general experimental procedure, isatin **72** (50 mg, 0.17 mmol), diallyl carbonate (50 mg, 0.35 mmol), $Pd(PPh_3)_4$ (10 mg, 0.008 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 gave the product **74** as a pale yellow viscous liquid after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.32 (3:7 Ethyl acetatehexane).; **IR (neat) υ_{max}:** 3083, 2922, 2871, 1728, 1612, 1466, 1427, 1361, 1258, 1191, 1125, 1045, 925, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.42 (d, *J* = 7.5 Hz, 1 H), 7.30(t, *J* = 7.5 Hz, 1 H), 7.06 (t, *J* = 7.5 Hz, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 5.96-5.89 (m, 2 H), 5.85-5.79 (m, 1 H), 5.31-5.22 (m, 4 H), 5.15 (d, *J* = 10.5 Hz, 2 H), 4.48-4.44 (m, 2 H), 4.35-4.29 (m, 4 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 170.3, 142.5, 133.9, 131.1, 130.5, 125.4, 124.8, 122.6, 117.8, 116.9, 109.5, 96.5, 64.3, 42.0.; **HRMS (ESI):** *m/z* calcd. for $C_{17}H_{19}O_3NNa$ $[M+Na]^+$: 308.12626; Found: 308.12668.

1'-Benzyl-4,7-dihydrospiro[[1,3]dioxepine-2,3'-indolin]-2'-one (75)

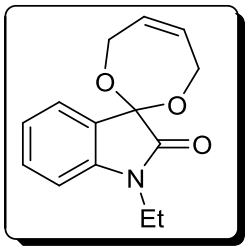
Following the general experimental procedure, the compound **71a** (150 mg, 0.44 mmol), Grubb's first generation catalyst (18 mg, 0.02 mmol) in 5 mL dichloromethane at room temperature under argon atmosphere for 3 h gave the product **75** as a pale yellow viscous liquid (134mg, 98% yield) after column chromatography (15% Ethyl acetate-Hexane).



R_f : 0.42 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3782, 3062, 3033, 2936, 2872, 1726, 1611, 1489, 1465, 1360, 1257, 1185, 1140, 1083, 1040, 1015, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.52 (d, *J* = 7.5 Hz, 1 H), 7.33-7.31 (m, 4 H), 7.27-7.22 (m, 2 H), 7.03 (t, *J* = 7.5 Hz, 1 H), 6.70 (d, *J* = 8.0 Hz, 1 H), 5.85 (s, 2 H), 5.09 (d, *J* = 15.0 Hz, 2 H), 4.87 (s, 2 H), 4.61 (d, *J* = 15.0 Hz, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 172.0, 142.3, 135.3, 130.6, 129.3, 128.8, 127.7, 127.2, 126.5, 124.1, 122.7, 109.8, 96.9, 63.8, 43.3.; **HRMS (ESI):** *m/z* calcd. for $C_{19}H_{17}NO_3Na$ $[M+Na]^+$: 330.11061, Found: 330.11101.

1'-Ethyl-4,7-dihydrospiro[[1,3]dioxepine-2,3'-indolin]-2'-one (76)

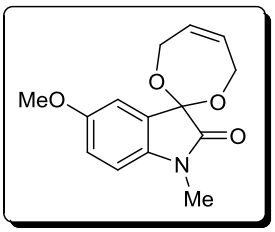
Following the general experimental procedure, the compound **65a** (25 mg, 0.0915 mmol) and Grubbs' first generation catalyst (4 mg, 0.0046 mmol), in 4 mL dichoromethane at room temperature under argon atmosphere for 3 h gave the product **76** as a pale yellow viscous liquid (17 mg, 76% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.48 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3031, 29708, 2936, 2873, 1727, 1613, 1489, 1467, 1371, 1259, 1213, 1123, 1084, 1051, 1024, 754 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.49 (d, *J* = 7.5 Hz, 1 H), 7.34 (t, *J* = 8.0 Hz, 1 H), 7.04 (t, *J* = 8.0 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 5.81(s, 2 H), 5.03 (d, *J* = 14.5 Hz, 2 H), 4.56 (d, *J* = 15.0 Hz, 2 H), 3.72 (q, *J* = 7. 5 Hz, 2 H), 1.28 (t, *J* = 7.5 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 171.4, 142.3, 130.6, 129.3, 126.7, 124.3, 122.5, 108.8, 96.8, 63.7, 34.4, 12.4.; **HRMS (ESI):** *m/z* calcd. for $C_{14}H_{15}NNaO_3$ $[M+Na]^+$: 268.09496; Found: 268.09503.

5'-Methoxy-1'-methyl-4,7-dihydrospiro[[1,3]dioxepine-2,3'-indolin]-2'-one (77)

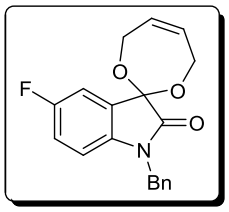
Following the general experimental procedure, the compound **67a** (95 mg, 0.33 mmol) and Grubbs' first generation catalyst (14 mg, 0.016 mmol), in 5 mL dichloromethane at room temperature under argon atmosphere for 3 h gave the product **77** as a colourless solid (83 mg, 97% yield) after column chromatography (20% Ethyl acetate-Hexane).



R_f : 0.43 (4:6 Ethyl acetate/hexane).; **mp:** 113-117 ^oC.; **IR (neat) υ_{max}:** 3071, 2964, 2858, 2312, 1723, 1606, 1495, 1452, 1359, 1290, 1207, 1180, 1120, 1086, 1046, 1019, 966, 882, 797, 650 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.09 (d, *J* = 2.5 Hz, 1 H), 6.85 (dd, J_1= 8.5, 2.5 Hz, 1 H), 6.71 (d, *J* = 8.5 Hz, 1 H), 5.79 (s, 2 H), 5.01 (d, *J* = 15.0 Hz, 2 H), 4.54 (d, *J* = 15.0 Hz, 2 H), 3.79 (s, 3 H), 3.12 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 171.5, 155.9, 136.5, 129.2, 127.5, 114.6, 111.8, 109.0, 97.0, 63.6, 55.8, 25.8.; **HRMS (ESI):** *m/z* calcd. for $C_{14}H_{15}NO_4Na$ $[M+Na]^+$: 284.08988, Found: 284.09018.

1'-Benzyl-5'-fluoro-4,7-dihydrospiro[[1,3]dioxepine-2,3'-indolin]-2'-one (78)

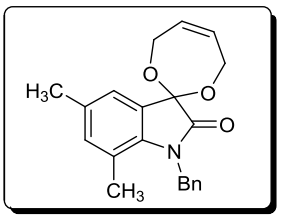
Following the general experimental procedure, the compound **68a** (135 mg, 0.38 mmol) and Grubb's first generation catalyst (16 mg, 0.019 mmol), in 5 mL dichloromethane at room temperature under argon atmosphere for 3 h gave the product **78** as a brown viscous liquid (120 mg, 96% yield) after column chromatography (15% Ethyl acetate-Hexane).



R_f : 0.57 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3038, 2985, 2876, 2311, 1727, 1619, 1489, 1454, 1348, 1275, 1180, 1132, 1083, 984, 956, 926, 877, 815, 795, 745, 699, 645 cm^{-1}.; **^{1}HNMR (500 MHz, $CDCl_3$, TMS):** δ 7.33-7.30 (m, 2 H). 7.28-7.25 (m, 4 H), 6.93 (dt, J_1 = 9.0 Hz, J_2 = 2.0 Hz, 1 H), 6.61 (dd, J_1 = 8.5 Hz, J_2 = 4.0 Hz, 1 H), 5.84 (s, 2 H), 5.08 (d, J = 15.0 Hz, 2 H), 4.85 (s, 2 H), 4.58 (d, J = 15.0 Hz, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 171.8, 159.9, 158.0, 138.1 (2C), 135.9, 129.2, 128.9, 127.9, 127.8, 127.1, 116.8, 116.6, 112.6, 112.4, 110.5, 110.4, 96.8, 63.8, 43.5.; **HRMS (ESI):** *m/z* calcd. for $C_{19}H_{16}FNO_3Na$ $[M+Na]^+$: 348.10119, Found: 348.10162.

1'-Benzyl-5',7'-dimethyl-4,7-dihydrospiro[[1,3]dioxepine-2,3'-indolin]-2'-one (79)

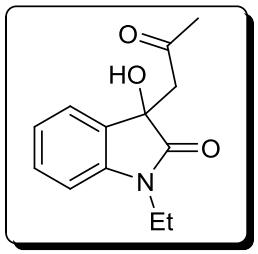
Following the general experimental procedure, the compound **69a** (63 mg, 0.17 mmol) and Grubb's first generation catalyst (7 mg, 0.008 mmol), in 5 mL dichloromethane at room temperature under argon atmosphere for 3 h gave the product **79** as a pale brown viscous liquid (51 mg, 88% yield) after column chromatography (20% Ethyl acetate-Hexane).



R_f : 0.46 (3:7 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3029, 2936, 2870, 1725, 1602, 1482, 1448, 1352, 1271, 1215, 1156, 1078, 1022, 863, 751 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.33-7.24 (m, 4 H), 7.18 (d, J = 7.5 Hz, 2 H), 6.85 (s, 1 H), 5.86 (s, 2 H), 5.14 (s, 2 H), 5.10 (d, J = 15.5 Hz, 2 H), 4.65 (d, J = 15.5 Hz, 2 H), 2.29 (s, 3 H), 2.21 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.3, 137.7, 137.0, 135.1, 132.6, 129.3, 128.9, 127.2 (2C), 125.6, 122.8, 120.5, .96.3, 63.7, 44.7, 20.7, 18.8.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{21}NO_3Na$ $[M+Na]^+$: 358.14191, Found: 358.14215.

1-Ethyl-3-hydroxy-3-(2-oxopropyl)indolin-2-one (80)

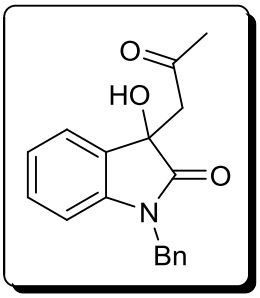
Following the general experimental procedure, N-ethyl isatin **64a** (50 mg, 0.285 mmol), allyl acetoacetate (81 mg, 0.57 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol), in 3 mL dichloromethane at room temperature under argon atmosphere for 12 h gave the product **80** as a colourless crystals (48 mg, 72% yield) after column chromatography (35% Ethyl acetate-Hexane).



R_f : 0.39 (8:2 Ethyl acetate/hexane).; **mp**: 144-148 °C.; **IR (neat) υ_{max}:** 3381, 2924, 2821, 1694, 1615, 1546, 1492, 1466, 1419, 1376, 1359, 1205, 1102, 1080, 755 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** 7.34 (d, *J* = 7.5 Hz, 1 H), 7.29 (t, *J* = 7.5 Hz, 1 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 4.30 (s, 1 H), 3.82-3.67 (m, 2 H), 3,19 (d, *J* = 17.0 Hz, 1 H), 2.97 (d, *J* = 17.0 Hz, 1 H), 2.15 (s, 3 H), 1.29 (t, *J* = 7.5 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 206.5, 175.9, 142.7, 130.0, 129.8, 123.9, 122.8, 108.6, 73.9, 49.2, 34.8, 31.1, 12.3.; **HRMS (ESI):** *m/z* calcd. for $C_{13}H_{15}NO_3Na$ $[M+Na]^+$: 256.09496; Found: 256.09497.

1-Benzyl-3-hydroxy-3-(2-oxopropyl)indolin-2-one (81)

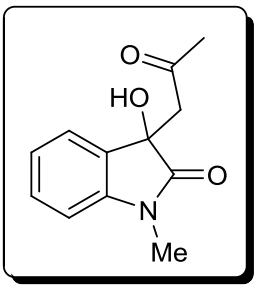
Following the general experimental procedure, N-benzyl isatin (50 mg, 0.21 mmol), allyl acetoacetate (61 mg, 0.42 mmol), $Pd(PPh_3)_4$ (12 mg, 0.011 mmol), in 2 mL dichloromethane at room temperature under argon atmosphere for 12 h gave the product **81** as a colourless crystals (41 mg, 66% yield) after column chromatography (35% Ethyl acetate-Hexane).



R_f : 0.48 (8:2 Ethyl acetate/hexane).; **mp:** 148-152 °C.; **IR (neat) υ_{max}:** 3359, 2956, 2922, 2853, 1707, 1612, 1490, 1466, 1359, 1173, 1075, 966, 751, 696 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** 7.38-7.32 (m, 5 H), 7.29-7.27 (m, 1 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.03 (t, *J* = 7.5 Hz, 1 H), 6.71 (d, *J* = 8.0 Hz, 1 H), 4.96 (d, *J* = 15.5 Hz, 1 H), 4.85 (d, *J* = 16.0 Hz, 1 H), 4,47(s, 1 H), 3.27 (d, *J* = 17.0 Hz, 1 H), 3.06 (d, *J* = 17.0 Hz, 1 H), 2.19(s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 207.3, 176.4, 142.7, 135.4, 129.9, 129.7, 128.8, 127.7, 127.2, 123.8, 123.2, 109.7, 74.2, 48.9, 43.9, 31.3.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{17}NO_3Na$ $[M+Na]^+$: 318.11061; Found: 318.11111.

3-Hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (82)

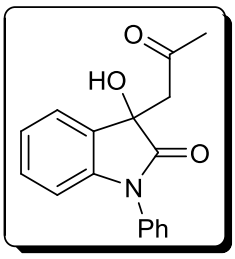
Following the general experimental procedure, N-methyl isatin (50 mg, 0.31 mmol), allyl acetoacetate (88 mg, 0.62 mmol), $Pd(PPh_3)_4$ (18 mg, 0.015 mmol), in 2 mL dichloromethane at room temperature under argon atmosphere for 12 h gave the product **82** as a pale yellow crystals (52 mg, 76% yield) after column chromatography (40% Ethyl acetate-Hexane).



R_f : 0.34 (8:2 Ethyl acetate/hexane).; **mp:** 134-138 °C.; **IR (neat) υ_{max}:** 3302, 2919, 2850, 1696, 1612, 1493, 1468, 1422, 1356, 1258, 1222, 1172, 1094, 1020, 963, 754 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.35-7.28 (m, 2 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.82 (d, *J* = 7.5 Hz, 1 H), 4.62 (s, 1 H), 3.22-3.18 (m, 4 H), 2.99 (d, *J* = 17.0 Hz, 1 H), 2.14 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 206.6, 176.4, 143.6, 129.9, 129.8, 123.8, 123.1, 108.5, 74.0, 49.2, 31.2, 26.3.; **HRMS (ESI):** *m/z* calcd. for $C_{12}H_{13}NO_3Na$ $[M+Na]^+$: 242.07931; Found: 242.07967.

3-Hydroxy-3-(2-oxopropyl)-1-phenylindolin-2-one (83)

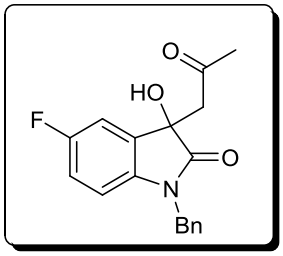
Following the general experimental procedure, N-phenyl isatin (50 mg, 0.22 mmol), allyl acetoacetate (63 mg, 0.44 mmol), $Pd(PPh_3)_4$ (13 mg, 0.011 mmol), in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **83** as a colourless solid (42 mg, 65% yield) after column chromatography (35% Ethyl acetate-Hexane).



R_f : 0.39 (6:4 Ethyl acetate/hexane).; **mp:** 112-114 °C.; **IR (neat) υ_{max}:** 3400, 3060, 2924, 2854, 1713, 1614, 1596, 1501, 1482, 1467, 1371, 1330, 1298, 1200, 1176, 1112, 1068, 1023, 971, 755, 700 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.54-7.51 (m, 2 H), 7.47-7.45 (m, 2 H), 7.43-7.37 (m, 2 H), 7.23 (t, *J* = 8.0 Hz, 1 H), 7.07 (t, *J* =7.5 Hz, 1 H), 6.78 (d, *J* = 8.0 Hz, 1 H), 4.6 (s, 1 H), 3.34 (d, *J* = 17.0 Hz, 1 H), 3.21 (d, *J* = 17.0 Hz, 1 H), 2.11 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 205.9, 176.3, 144.1, 134.2, 129.8, 129.6, 129.4, 128.2, 126.7, 123.8, 123.4, 109.8, 73.9, 50.3, 30.9.; **HRMS (ESI):** *m/z* calcd. for $C_{17}H_{15}NO_3Na$ $[M+Na]^+$: 304.09496, Found: 304.09500.

1-Benzyl-5-fluoro-3-hydroxy-3-(2-oxopropyl)indolin-2-one (84)

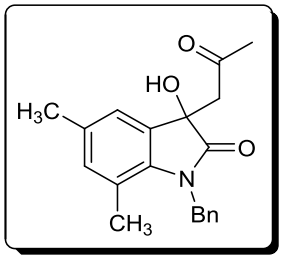
Following general experimental procedure, the 5-flouro-N-benzylisatin (100 mg, 0.42 mmol), allyl acetoacetate (118 mg, 0.83 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol), in 3 mL THF at room temperature under argon atmosphere for 12 h gave the product **84** as a pale yellow viscous liquid (76 mg, 58% yield) after column chromatography (30% Ethyl acetate-Hexane).



R_f : 0.44 (6:4 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3468, 2379, 1708, 1601, 1486, 1455, 1339, 1266, 1172, 754, 696, 669 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.33-7.31 (m, 4 H), 7.29-7.27 (m, 1 H), 7.12 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1 H), 6.87 (dt, J = 8.5, 2.5 Hz, 1 H), 6.61-6.58 (m, 1 H), 4.66 (s, 1 H), 4.95 (d, J = 16.0 Hz, 1 H), 4.81 (d, J = 15.5 Hz, 1 H), 3.31 (d, J = 17.5 Hz, 1 H), 3.15 (d, J = 17.5 Hz, 1 H), 2.15(s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 206.4, 176.8, 160.4, 158.4, 138.8, 135.1, 131.5, 131.4, 128.9, 127.8, 116.1, 112.2, 110.5, 110.4, 74.1, 49.5, 44.1, 30.9.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{16}FNO_3Na$ $[M+Na]^+$: 336.10119, Found: 336.10165.

1-Benzyl-3-hydroxy-5,7-dimethyl-3-(2-oxopropyl)indolin-2-one (85)

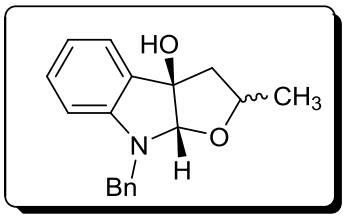
Following the general experimental procedure, 5,7-dimethyl N-benzyl isatin (100 mg, 0.37 mmol), allyl acetoacetate (107 mg, 0.75 mmol), $Pd(PPh_3)_4$ (22 mg, 0.018 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **85** as a brown coloured viscous liquid (43 mg, 38% yield) after column chromatography (35% Ethyl acetate-Hexane).



R_f : 0.41 (6:4 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3393, 3062, 3029, 2922, 1717, 1605, 1452, 1386, 1169, 862, 734 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.31-7.28 (m, 2 H), 7.23-7.21 (m, 3 H), 6.99 (s, 1 H), 6.75 (s, 1 H), 5.11 (s, 2 H), 4.66 (s, 1 H), 3.22 (d, J = 17.0 Hz, 1 H), 3.11 (d, J = 17.0 Hz, 1 H), 2.24 (s, 3 H), 2.16 (s, 3 H), 2.12 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 206.3, 177.9, 138.4, 137.4, 134.3, 132.7, 130.6, 128.8, 127.1, 125.7, 122.3, 119.9, 73.3, 49.6, 45.1, 31.1, 20.7, 18.5.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{21}NO_3Na$ $[M+Na]^+$: 346.14191, Found: 346.14200.

8-Benzyl-2-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indol-3a-ol (86)

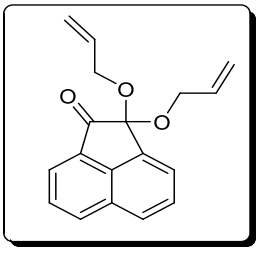
Following the general experimental procedure, the compound **81** (160 mg, 0.54 mmol) and $LiAlH_4$ (41 mg, 1.08 mmol) in 6 mL THF at 0 °C under argon atmosphere for 4 h gave the product **86** as a brown coloured solid (122 mg, 80% yield) after column chromatography (15% Ethyl acetate-Hexane).



R_f : 0.41 (3:7 Ethyl acetate/hexane).; **mp:** 98-102 °C.; **IR (neat) υ_{max}:** 3390, 2965, 2923, 1609, 1468, 1453, 1355, 1260, 1125, 1021, 947, 742, 696 cm^{-1}.; **^{1}H NMR (500 MHz, Acetone-d_6):** δ 7.41 (d, *J* = 7.5 Hz, 2 H), 7.37 (d, *J* = 7.5 Hz, 1.4 H), 7.31 (t, *J* = 7.5 Hz, 3 H), 7.25-7.22 (m,3 H), 7.06-7.01 (m, 2 H), 6.67-6.62 (m, 2 H), 6.37 (d, *J* = 8.0 Hz, 1 H), 6.32 (d, *J* = 8.0 Hz, 0.7 H), 5.31 (s, 0.7 H), 5.19 (s, 1 H), 4.81 (s, 0.7 H), 4.76 (s, 1 H), 4.58-4.52 (m, 2 H), 4.47-4.36 (m, 2 H), 4.39-4.32 (m, 1 H), 3.90-3.84 (m, 0.7 H), 2.53 (dd, J_1 = 12.5 Hz, J_2 = 5.5 Hz, 1 H), 2.39 (dd, J_1 = 12.0 Hz, J_2 = 4.5 Hz, 0.7 H), 2.05- 2.04 (m, 0.7 H), 1.86-1.81 (m, 1 H), 1.24 (d, *J* = 6.0 Hz, 2.2 H), 1.12 (d, *J* = 6.0 Hz, 3 H).; **^{13}C NMR (125 MHz, Acetone-d_6):** δ 150.6, 149.1, 139.0, 138.8, 133.0, 131.7, 129.4, 129.1, 128.3, 128.2, 127.5, 127.3, 126.8, 126.8, 126.7, 123.8, 123.4, 117.5, 117.3, 106.6, 105.5, 105.0, 103.8, 87.7, 87.5, 74.3, 74.2, 49.7, 49.1, 48.6, 48.3, 20.4, 19.2.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{20}NO_2$ $[M+1]^+$: 282.14940, Found: 282.14932.

2,2-Bis(allyloxy)acenaphthylen-1(2H)-one (88a)

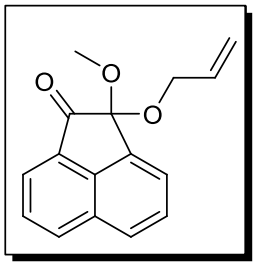
Following the general experimental procedure, acenaphthenequinone **87** (50 mg, 0.27mmol), diallyl carbonate **61a** (100 mg, 0.54 mmol), $Pd(PPh_3)_4$ (16 mg, 0.013 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **88a** as a yellow viscous liquid (33 mg, 43% yield) after column chromatography (4% Ethyl acetate-Hexane).



R_f : 0.63 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3081, 2926, 2875, 1729, 1647, 1607, 1434, 1422, 1271, 1196, 1062, 1049, 1028, 1015, 989, 925, 834, 782 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 8.10 (d, *J* = 8.0Hz, 1 H), 7.95-7.91 (m, 2 H), 7.73-7.70 (m, 2 H), 7.68-7.65 (m, 1 H),5.97-5.89 (m, 2 H), 5.28 (dd, J_1 = 17.0 Hz, J_2 = 1.5 Hz, 2 H), 5.13 (d, *J* = 10.5 Hz, 2 H), 4.57-4.54 (m, 2 H), 4.45-4.41 (m, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 197.4, 141.0, 135.3, 134.1, 131.8, 130.8, 130.2, 128.2, 128.1, 126.2, 122.1, 121.3, 116.8, 99.3, 64.6.; **HRMS (ESI):** *m/z* calcd. for $C_{18}H_{16}O_3Na$ $[M+Na]^+$: 303.09971; Found: 303.10001.

2-(Allyloxy)-2-methoxyacenaphthylen-1(2H)-one (88b)

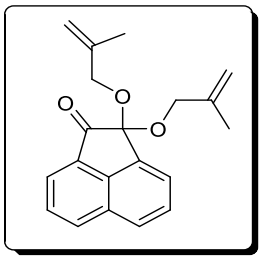
Following the general experimental procedure, acenaphthenequinone **87** (50 mg, 0.27mmol), allyl methyl carbonate **61b** (64 mg, 0.54 mmol), $Pd(PPh_3)_4$ (16 mg, 0.013 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **88b** as a yellow viscous liquid (27 mg, 39% yield) after column chromatography (8% Ethyl acetate-Hexane).



R_f : 0.56 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3054, 2943, 1731, 1607, 1494, 1465, 1271, 1196, 1065, 1049, 1031, 932, 834, 782 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 8.11 (d, *J* = 8.0 Hz, 1 H), 7.96-7.92 (m, 2 H), 7.74-7.66 (m, 3 H), 5.98-5.93 (m, 1 H), 5.30 (dd, J_1 = 17.0 Hz, J_2 = 1.5 Hz, 1 H), 5.15 (dd, J_1 = 10.5 Hz, J_2 = 1.5 Hz, 1 H), 4.56-4.53 (m, 1 H), 4.46-4.43 (m, 1 H), 3.65 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 197.6, 141.1, 135.0, 134.1, 131.9, 130.8, 130.2, 128.3, 128.2, 126.2, 122.1, 121.3, 116.9, 99.5, 64.6, 51.3.; **HRMS (ESI):** *m/z* calcd. for $C_{16}H_{14}O_3Na$ $[M+Na]^+$: 277.08406; Found: 277.08401.

2,2-Bis((2-methylallyl)oxy)acenaphthylen-1(2H)-one (88c)

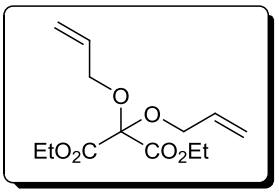
Following the general experimental procedure, acenaphthenequinone **87** (50 mg, 0.27mmol), dimethallyl carbonate **61c** (93 mg, 0.54 mmol), $Pd(PPh_3)_4$ (16 mg, 0.013 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **88c** as a yellow viscous liquid (29 mg, 35% yield) after column chromatography (8% Ethyl acetate-Hexane).



R_f : 0.49 (2:8 Ethyl acetate/hexane).; **IR (neat) υ_{max}:** 3075, 2920, 2867, 1732, 1654, 1609, 1494, 1453, 1434, 1374, 1270, 1196, 1072, 1060, 899, 784 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 8.12(d, *J* = 8.0 Hz, 1 H), 7.96-7.93 (m, 2 H), 7.75-7.73 (m, 2 H), 7.69-7.67 (m, 1 H), 4.98 (s, 2 H), 4.83 (s, 2 H), 4.44 (d, *J* = 12.0 Hz, 2 H), 4.32 (d, *J* = 12.5 Hz, 2 H), 1.75 (s, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 197.8, 141.6, 141.0, 135.4, 131.8, 130.7, 130.2, 128.2, 128.1, 126.2, 122.0, 121.3, 111.8, 99.3, 67.2, 19.7.; **HRMS (ESI):** *m/z* calcd. for $C_{20}H_{20}O_3Na$ $[M+Na]^+$: 331.13101; Found: 331.13068.

Diethyl 2,2-bis(allyloxy)malonate (90a)

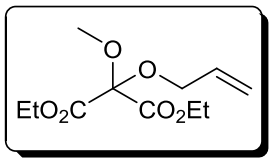
Following the general experimental procedure, diethylketomalonate **89** (50 mg, 0.29 mmol), diallyl carbonate **61a** (82 mg, 0.57 mmol), $Pd(PPh_3)_4$ (17 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **90a** as a colourless viscous liquid (63 mg, 80% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.48 (2:8 Ethyl acetate/hexane).; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.94-5.87 (m, 2 H), 5.31 (d, *J* = 17.5 Hz, 2 H), 5.17 (d, *J* = 10.5 Hz, 2 H), 4.26 (q, *J* = 7.0 Hz, 4 H), 4.07 (d, *J* = 5.5 Hz, 4 H), 1.28 (t, *J* = 7.0 Hz, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.0, 132.9, 117.6, 97.7, 65.2, 62.1, 13.9.; **HRMS (ESI):** *m/z* calcd. for $C_{13}H_{20}O_6Na$ $[M+Na]^+$: 295.11576; Found: 295.11581.

Diethyl 2-(allyloxy)-2-methoxymalonate (90b)

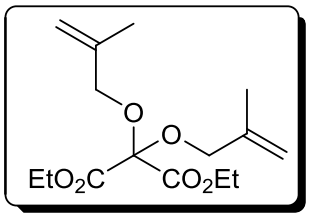
Following the general experimental procedure, diethylketomalonate **89** (50 mg, 0.29 mmol), allyl methyl carbonate **61b** (67 mg, 0.57 mmol), $Pd(PPh_3)_4$ (17 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **90b** as a colourless viscous liquid (29 mg, 41% yield) after column chromatography (10% Ethyl acetate-Hexane).



R_f : 0.44 (2:8 Ethyl acetate/hexane).; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.97-5.90 (m, 1 H), 5.33 (d, *J* = 17.0 Hz, 1 H), 5.19 (d, *J* = 10.0 Hz, 1 H), 4.28 (q, *J* = 7.0 Hz, 4 H), 4.06 (d, *J* = 5.5 Hz, 2 H), 3.36 (s, 3 H), 1.30 (t, *J* = 7.0 Hz, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 164.9, 132.9, 117.7, 98.2, 65.0, 62.2, 51.6, 14.0.; **HRMS (ESI):** *m/z* calcd. for $C_{11}H_{18}O_6Na$ $[M+Na]^+$: 269.10011; Found: 269.10018.

Diethyl 2,2-bis(2-methylallyloxy)malonate (90c)

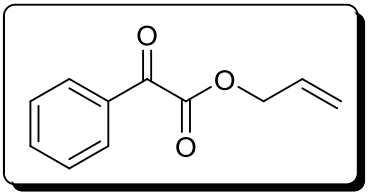
Following the general experimental procedure, diethylketomalonate **89** (50 mg, 0.29 mmol), dimethallyl carbonate **61c** (98 mg, 0.57 mmol), $Pd(PPh_3)_4$ (17 mg, 0.014 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **90c** as a colourless viscous liquid (36 mg, 43% yield) after column chromatography (5% Ethyl acetate-Hexane).



R_f : 0.52 (2:8 Ethyl acetate/hexane).; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 5.05 (s, 2 H), 4.90 (s, 2 H), 4.28 (q, *J* = 7.0 Hz, 4 H), 3.99 (s, 4 H), 1.77 (s, 6 H), 1.29 (t, *J* = 7.0 Hz, 6 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.2, 140.4, 112.6, 97.6, 67.6, 62.1, 19.5, 13.9.; **HRMS (ESI):** *m/z* calcd. for $C_{15}H_{24}O_6Na$ $[M+Na]^+$: 323.14706; Found: 323.14717.

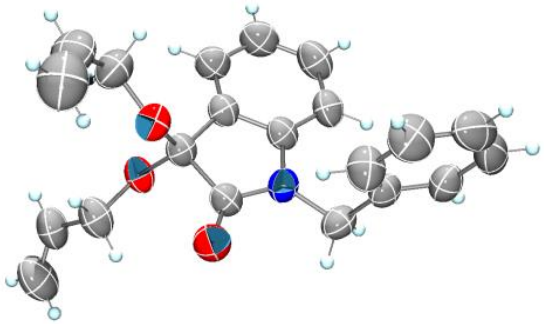
Allyl 2-oxo-2-phenylacetate (92)

Following the general experimental procedure, methyl benzoylformate **91** (50 mg, 0.30 mmol), diallyl carbonate **61a** (87mg, 0.61 mmol), $Pd(PPh_3)_4$ (18 mg, 0.015 mmol) in 2 mL THF at room temperature under argon atmosphere for 12 h gave the product **92** as a colourless viscous liquid (19 mg, 33% yield) after column chromatography (3% Ethyl acetate-Hexane).



R_f : 0.59 (1:9 Ethyl acetate/hexane).; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ 8.08 (d, *J* = 8.0 Hz, 2 H), 7.66 (t, *J* = 7.5 Hz, 1 H), 7.51(t, *J* = 7.5 Hz, 2 H), 6.06-5.98 (m, 1 H), 5.46 (d, *J* = 17.0 Hz, 1 H), 5.35 (d, *J* = 10.5 Hz, 1 H), 4.87 (d, *J* = 5.5 Hz, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 185.8, 163.3, 134.8, 132.5, 130.8, 130.0, 128.9, 119.9, 66.5.; **HRMS (ESI):** *m/z* calcd. for $C_{11}H_{10}O_3Na$ $[M+Na]^+$: 213.05276; Found: 213.05243.

Crystal Data: Compound 71a

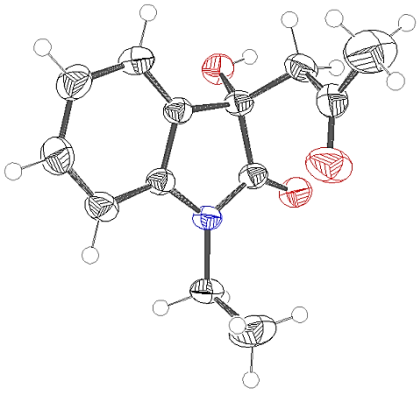


CCDC number: 984183

Chemical formula moiety $C_{21}H_{21}NO_3$

Chemical formula sum	$C_{21}H_{21}NO_3$
Chemical formula weight	335.39
Symmetry cell setting	Monoclinic
Symmetry space group name	P21/n
Cell length a	9.894 (2)
Cell length b	9.031 (1)
Cell length c	20.891 (3)
Cell angle alpha	90
Cell angle beta	93.28(3)
Cell angle gamma	90
Cell volume	1863.6
Cell formula units Z	4
Cell measurement temperature	571K
Cell measurement reflns used	28744
Cell measurement theta min	3.1
Cell measurement theta max	27.5
Exptl crystal description	Block
Exptl crystal size max	0.30
Exptl crystal size med	0.30
Exptl crystal size min	0.20
Exptl crystal density diffrn	1.195
Exptl crystal_density_method	'not measured'
Exptl crystal colour	colourless
Exptl crystal F 000	712
Exptl absorpt coefficient mu	0.080
Exptl absorpt correction-type	Empirical
Exptl absorpt correction T min	0.9765
Exptl absorpt correction T max	0.9842
Diffrn ambient temperature	571(2)
Diffrn radiation wavelength	0.71073

Crystal Data: Compound 80



CCDC number: 984187

Chemical formula moiety	$C_{13}H_{15}NO_3$
Chemical formula sum	$C_{13}H_{15}NO_3$
Chemical formula weight	233.26
Symmetry cell setting	Tricilinic
Symmetry space group name	P-1
Cell length a	8.344(4)
Cell length b	8.833(5)
Cell length c	8.917(5)
Cell angle alpha	113.075(9)
Cell angle beta	93.003(4)
Cell angle gamma	92.983(9)
Cell volume	601.9(5)
Cell formula units Z	2
Cell measurement temperature	300K
Cell measurement reflns used	1024
Cell measurement theta min	3.4
Cell measurement theta max	27.5
Exptl crystal description	Block
Exptl crystal size max	0.40
Exptl crystal size mid	0.40
Exptl crystal size min	0.20
Exptl crystal density diffrn	1.287

Exptl crystal_density_method	'not measured'
Exptl crystal colour	colourless
Exptl crystal F 000	248
Exptl absorpt coefficient mu	0.092
Exptl absorpt correction-type	Empirical
Exptl absorpt correction T min	0.964
Exptl absorpt correction T max	0.981
Diffrn ambient temperature	300 (2)
Diffrn radiation wavelength	0.71073

3.6. References

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25. CCDC 984183
26. CCDC 984187
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CHAPTER 4

Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles

4.1. Introduction

Fulvenes are cyclic cross-conjugated molecules with an odd number of carbon atoms in the ring and are highly colored compounds. Fulvenes and their derivatives are at the center stage of research attributed to their theoretical, mechanistic and synthetic viewpoints.[1] Fulvene backbone possesses an exocyclic carbon-carbon double bond which generates a unique polar system. According to the ring size, fulvenes are named as triafulvenes, pentafulvenes, heptafulvenes *etc.* (Figure 4.1). Among them, pentafulvenes stands out because of its peculiar reactivity pattern and the versatility of the reaction products. Pentafulvenes are excellent candidates for the preparation of polycyclic compounds through a diverse array of cycloaddition reactions.[2] Pentafulvenes are mainly utilized as synthetic intermediates to access new carbo- as well as heterocyclic systems, containing one or more five-membered rings such as natural products pallambins A and B,[3] kigelinol, neoamphilectane and kempane skeletons.[4]

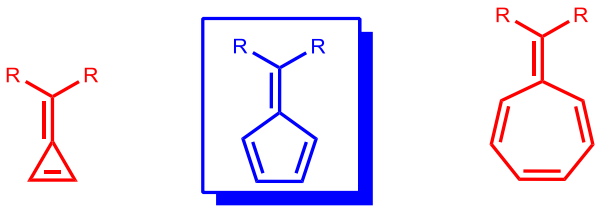
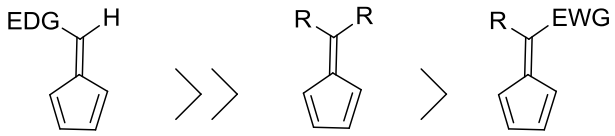


Figure 4.1. Common fulvenoids

Pentafulvenes possess high polarizability and non-benzenoid aromaticity. The ground state of fulvenes presents a strong polyolefinic character as compared to the aromaticity exhibited by a benzene ring. The electronic nature of substituents at the exocyclic position significantly influences the aromatic character of pentafulvenes.[5] Electron donating groups on the exocyclic position of pentafulvenes strongly stabilizes the five-membered ring leading to

a substantial increase in aromatic character (Figure 4.2). This is evidently due to the electron accepting power of the five-membered ring to satisfy the Huckel 4n+2 rule.



EDG = Electron donating groups EWG = Electron withdrawing groups

Figure 4.2. Order of aromaticity of pentafulvenes

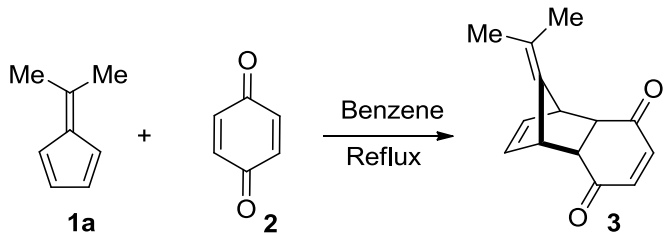
4.1.1. Reactivity of pentafulvenes

Fulvenes display a broad range of reactions with nucleophiles, electrophiles and various cycloaddition partners.[6] The terminal exocyclic carbon of pentafulvenes is electrophilic and can be attacked by suitable nucleophiles. On the other hand, fulvenes with N- or O- functions at the exocyclic carbon show a marked tendency for electrophilic and nucleophilic substitution reactions like the isomeric anilines or phenols.[7] However, the synthetic potential of pentafulvenes was mainly exploited in periselective cycloaddition reactions.

4.1.1.1. Cycloaddition reactions in pentafulvenes

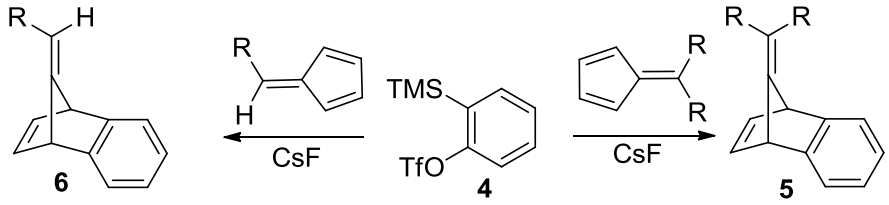
In cycloaddition reactions, pentafulvenes can act as 2π, 4π or 6π component, depending on the number of electrons furnished by the competing partner.[4] For example [2+2], [4+2], [2+4], [6+4] and [6+2] cycloadditions of pentafulvenes provided efficient approaches towards polycyclic systems and natural products. The periselectivity of these reactions is controlled by the substituents on the fulvene and the substrates engaged in the reaction.[8] Cycloadditions of fulvenes offer a versatile and powerful approach to synthesize various natural products and biologically active molecules.[3,9] Some of the key examples of cycloaddition reactions of pentafulvene are discussed in the following section.

Pentafulvenes can function as highly reactive dienes with various dienophiles. Pentafulvenes undergo smooth Diels-Alder reaction with dienophiles like maleimide, maleic anhydride, *p*-quinone and dialkyl azodicarboxylates to afford the corresponding bicyclic adducts in good yields. A typical Diels-Alder cycloaddition of pentafulvene with quinone is presented in Scheme 4.1.[10]



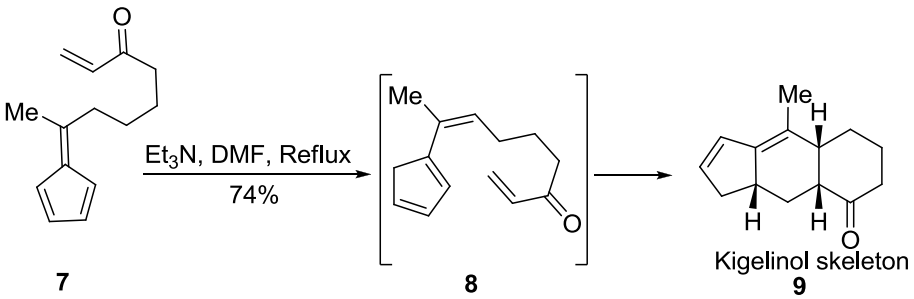
Scheme 4.1

In 2012, Biju *et al.* reported a high-yielding, versatile and practical Diels-Alder reaction of pentafulvenes with arynes under mild reaction conditions. The arynes generated by the fluoride-induced 1,2-elimination of 2-(trimethylsilyl)aryl triflates underwent efficient cycloaddition with 6-substituted and 6,6-disubstituted pentafulvenes led to the formation of benzonorbornadiene derivatives **5,6** (Scheme 4.2).[11]



Scheme 4.2

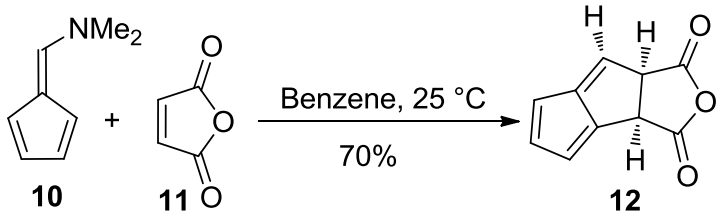
Hong and co-workers developed intramolecular Diels-Alder (IMDA) cycloaddition in simple acyclic fulvenes towards a variety of polycyclic ring skeletons such as kigelinol, neoamphilactane, kempane *etc.* An example for the synthesis of kigelinol skeleton **9** from the fulvene **7** is depicted in Scheme 4.3.[4]



Scheme 4.3

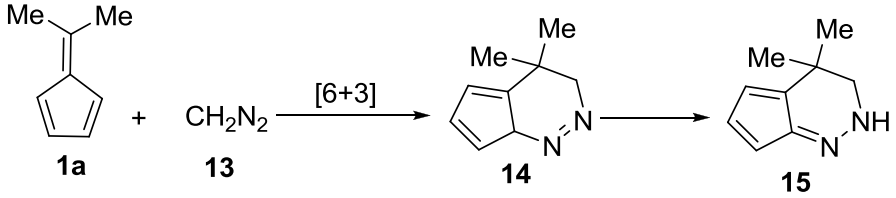
The reactivity of fulvenes mainly depends on the polarity of the exocyclic double bond. Fulvenes having electron rich substituents at the exocyclic position show different behavior towards dienophiles. 6-(N,N-dimethylamino)fulvene **10** acted like a 6π candidate in

cycloaddition reaction with maleic anhydride **11** and furnished the [6+2] cycloadduct **12** in 70% yield (Scheme 4.4).[10]



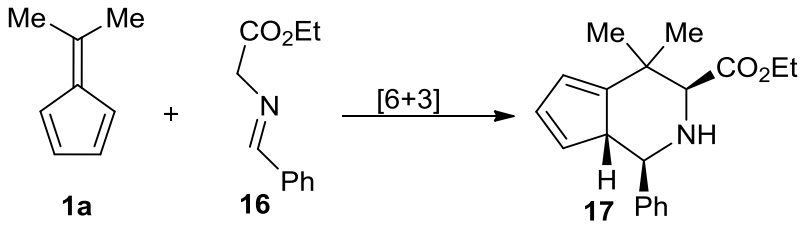
Scheme 4.4

The reactions of pentafulvenes with various dipolar systems are also exploited for the construction of many biologically relevant polycycles. Diazomethane, a 1,3-dipole with well-established nucleophilic character adds to 6,6-dimethyl fulvene **1a** exclusively in a [6+3] fashion to yield the fused product **15**, after tautomerization of the initially formed cycloadduct **14**.[12]



Scheme 4.5

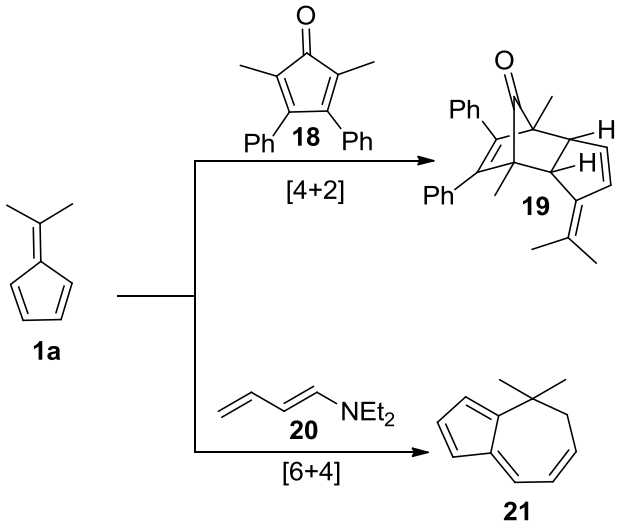
In 2003, Hong *et al.* reported a [6+3] cycloaddition of azomethine ylides with fulvenes, in which fulvenes served as 6π components.[13] This reaction is providing a synthetic route for the construction of racemic six-membered piperidine derivatives. Later, Wang and co-workers reported the asymmetric version of this reaction by using Cu(I)/TF-BiphamPhos catalyst.[14]



Scheme 4.6

Electron deficient dienes normally engage with fulvenes in a [4+2] cycloaddition at one of the endocyclic double bonds,[15] while electron rich dienes react as 4π components in a

[6+4] process.[16] An illustration of each of these modes of reaction is given Scheme 4.7. The reaction of dimethylfulvene **1a** with electron deficient 2,5-dimethyl-3,4-diphenylcyclopentadienone **18** in refluxing THF afforded [4+2] adduct **19** whereas the reaction of dimethylfulvene with electron rich 1-diethylaminobutadiene **20** furnished [6+4] adduct **21**.



Scheme 4.7

Factors governing reactivity of fulvenes have been elucidated out by employing frontier molecular orbital considerations. The relevant molecular orbitals of fulvene that are generally participating in the reaction are displayed in the figure 4.3.

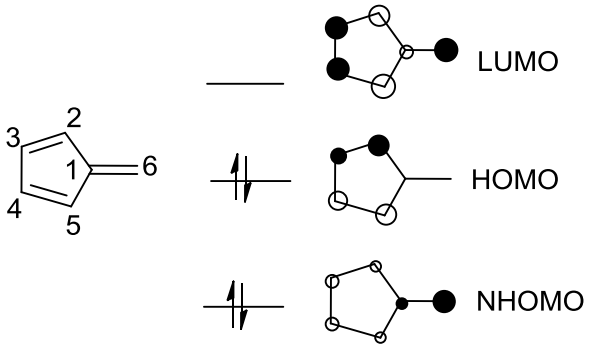
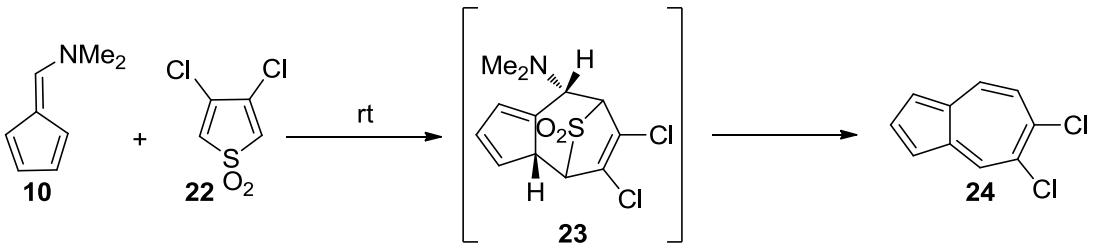


Figure 4.3. Frontier molecular orbitals of fulvene

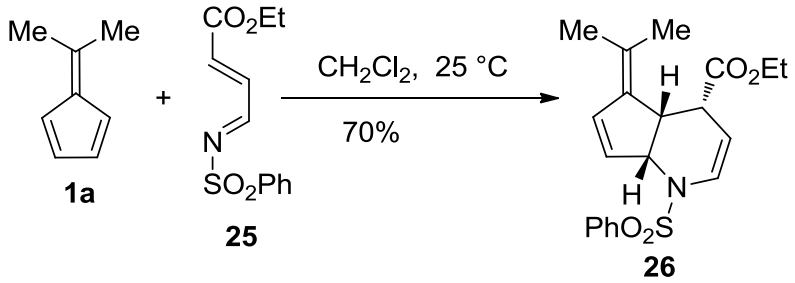
The controlling orbitals involved in the reaction of fulvene with an electron deficient diene are the HOMO of fulvene and LUMO diene. The large frontier density at C-2 and C-3, as well as the node through C-1 and C-6, dictate that the fulvene will participate as a 2π partner. On the other hand, LUMO controlled reactions with electron-rich diene partners

should react at C-6 and C-2, affording [6+4] adducts. Furthermore, strongly electron donating substituents located at the C-6 position of fulvene elevate the next highest occupied molecular orbital (NHOMO) sufficiently to permit the [6+4] mode of cycloaddition to prevail with electron deficient 4π systems. An example of this type of reaction is presented in Scheme 4.8. Electron rich N,N-dimethylaminofulvene **10** known to react with electron deficient diene partners primarily in the [6+4] mode.[17]



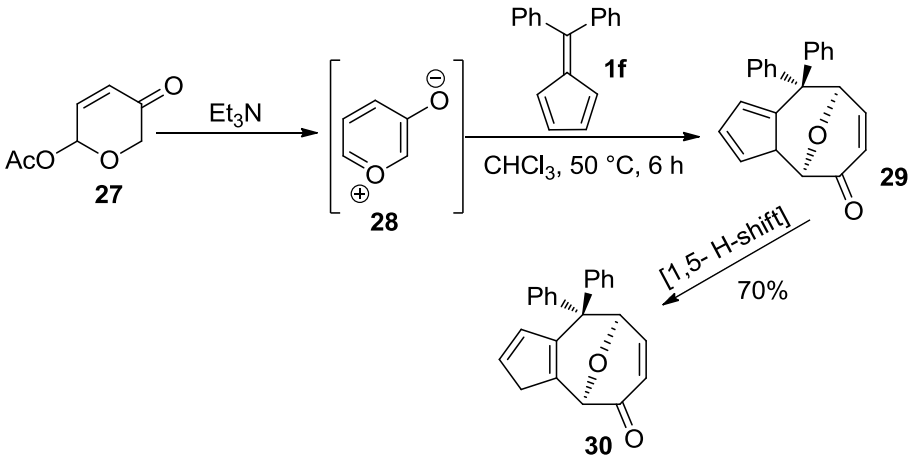
Scheme 4.8

In 2004, Hong and co-workers investigated the reactivity of fulvene with electron deficient azadiene N-sulfonyl-1-aza-1,3-butadiene **25**.[4] This inverse electron demand Diels-Alder reaction furnished tetrahydra-[1]-pyridine derivative **26**. The [4+2] cycloaddition reaction also verifies the reactivity of fulvene as 2π component with electron deficient azadienes.



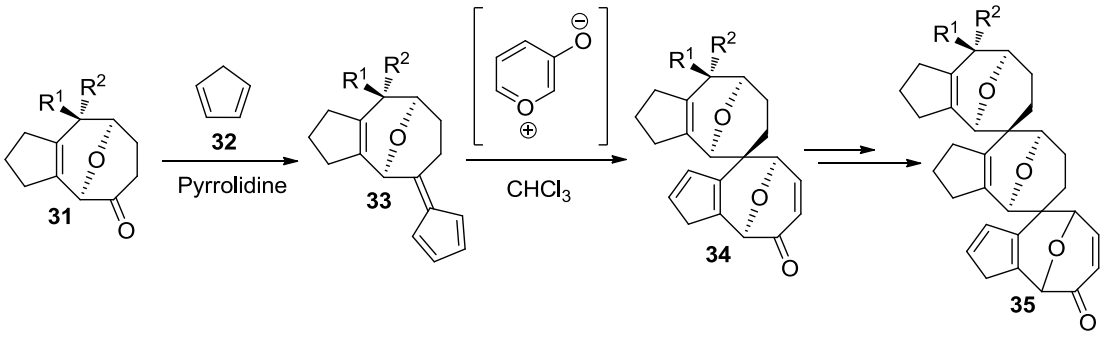
Scheme 4.9

Our group also significantly contributed to the cycloaddition chemistry of pentafulvenes. We have reported a straightforward and efficient synthetic strategy for the construction of 5-8 fused cyclo-octanoids by [6+3] cycloaddition reaction of pentafulvenes with 3-oxidopyrylium betaines.[18]



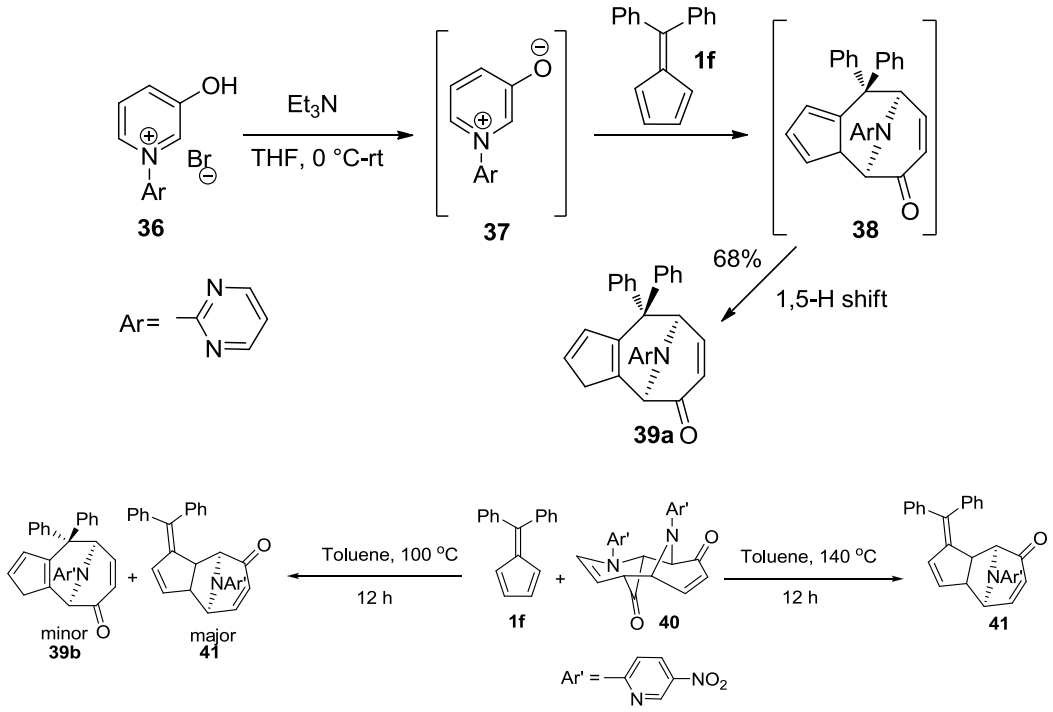
Scheme 4.10

Utilizing the cycloaddition potential of pentafulvenes, we developed an efficient spiro-annulation reaction that allows the expeditious synthesis of spirocyclic compounds.[19]



Scheme 4.11

Later, we extended the cycloaddition profile of pentafulvenes with various 3-oxidopyridinium betaines. The adopted methodology involved [6+3] and [3+2] cycloaddition reactions of pentafulvenes with 3-oxidopyridinium betaines generated either by the action of a base on the pyridinium salt or thermally from pyridinium betaine dimer. A careful manipulation of the reaction conditions paved the way for the efficient synthesis of bicyclo[6.3.0]undecane **39** as the kinetic adduct and bicyclo[5.3.0]undecane **41** as the thermodynamic adduct.[20]

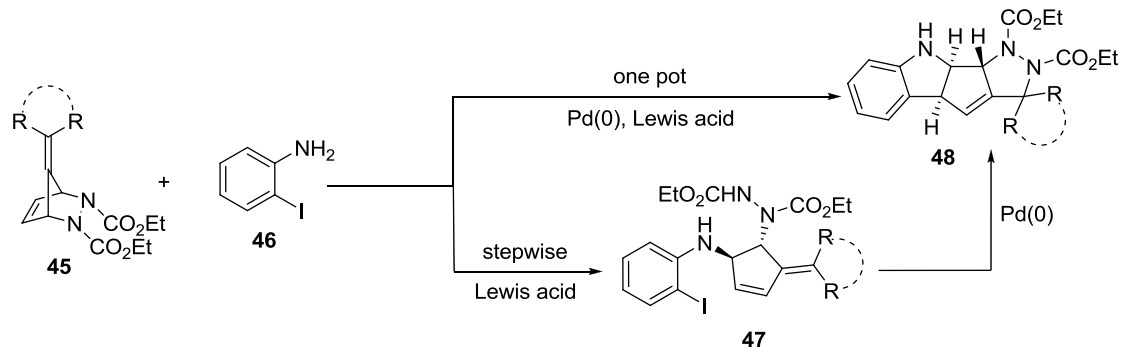


Scheme 4.12

Further, synthesis of alkylidene cyclopentenes from [4+2] cycloadduct of pentafulvenes was established by Palladium/Lewis acid catalyzed ring-opening of fulvene derived azabicyclic olefins with hard nucleophiles like organostannanes, silanes, boronic acids and allylindium reagents. These reactions provide an efficient method for the synthesis of *trans*-3,4-disubstituted alkylidene cyclopentene **44** in good yields (Scheme 4.13).[21]

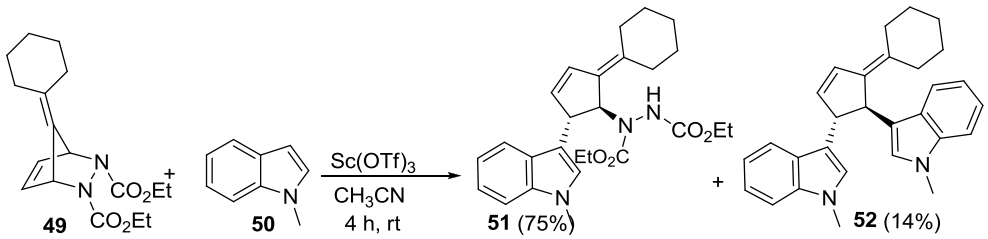
Scheme 4.13

Synthesis of spiro-pentacyclic motifs with an indoline and pyrazolidine fused to cyclopentene was accomplished by the Palladium/Lewis acid mediated domino reaction of pentafulvene derived diazabicyclic olefins with various *ortho*-functionalized aryl iodides such as 2-iodoanilines, 2-iodophenols and 2-iodobenzene thiols.[22]



Scheme 4.14

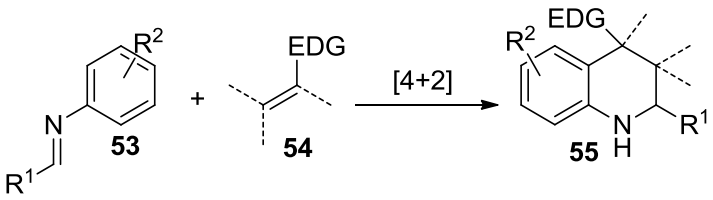
Very recently, we reported a Lewis acid catalyzed ring opening of pentafulvene derived diazabicyclic olefins using indoles, and the reaction yielded C-3 alkylidene cyclopentene substituted indole and bisindole derivatives.[23]



Scheme 4.15

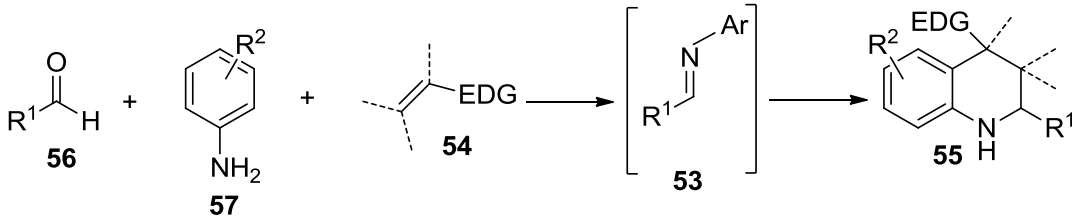
4.1.2. Povarov reaction: A brief introduction

In the early 1960s, during the investigation of the reactivity of electron rich olefins towards different substrates, Povarov and co-workers discovered that alkyl vinyl ethers and thioethers reacted with N-arylimines activated by coordination with boron trifluoride to give 1,2,3,4-tetrahydroquinolines (THQs).[24] Povarov classified the reaction as a [4+2] hetero-Diels–Alder cycloaddition reaction. The requirement of a Lewis acid for coordinating the 2-azadiene and enhancing its electron-deficient character was rationalized by considering a [4+2] cycloaddition between an electron deficient hetero-diene and an electron rich dienophile, with a reversal of the typical pattern followed by Diels-Alder reactions. In recognition of the discovery and the substantial contributions to its development reported later in the 1960s by Povarov,[25] cycloadditions of N-aryl imines with electron-rich olefins, and variants thereof, are now called Povarov reactions (Scheme 4.16).



Scheme 4.16. The Povarov cycloaddition reaction (EDG = electron donating group)

The three-component ABC combination, typical of other multicomponent reactions involving imines generated *in situ*, is the most popular version of the multicomponent Povarov reaction (Scheme 4.17). Importantly, this three component strategy can be employed to overcome the low stability of N-aryl imines derived from enolizable aliphatic aldehydes, by avoiding their isolation.



Scheme 4.17. Multicomponent Povarov reaction

Povarov reaction is utilized for the synthesis of natural products such as martinelline and martinellic acid.[26] Moreover, the reaction has been a very useful tool, especially in its multicomponent variant, for the preparation of biologically active agents, such as the selective antagonist G protein-coupled receptor GPR30 which is formed as a result of three-component Povarov reaction between 2-bromopiperonal, aniline and cyclopentadiene.[27]

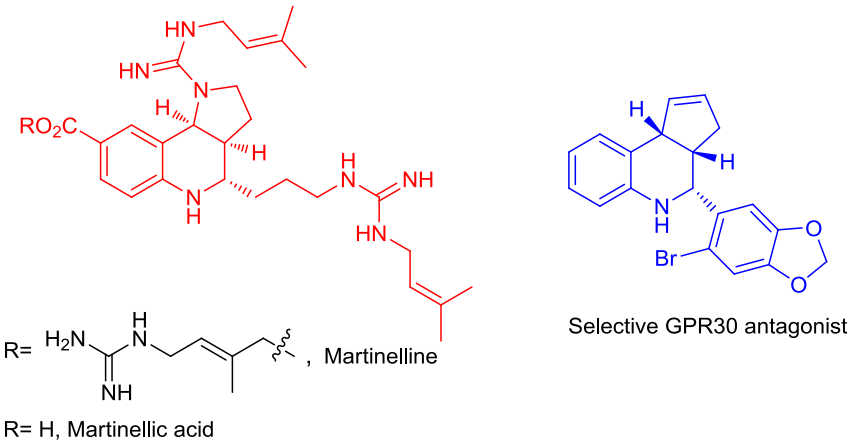
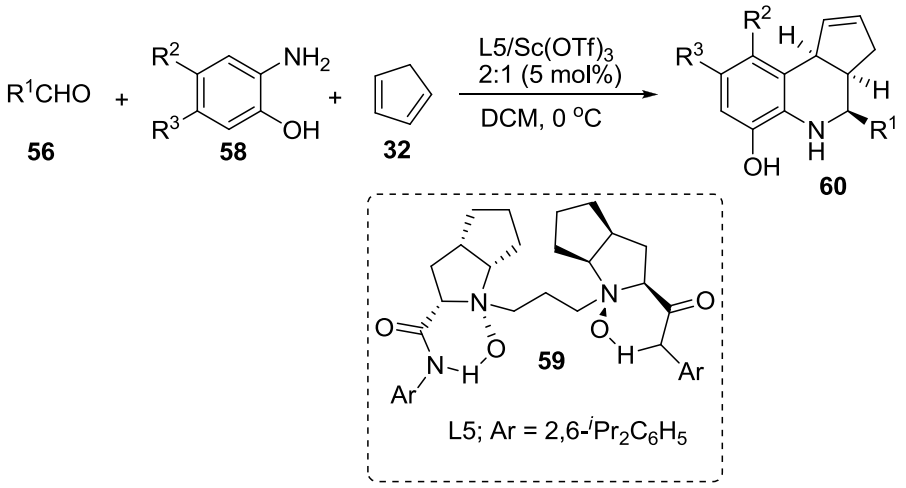


Figure 4.4. Natural product and biologically active THQs synthesized by Povarov cycloaddition reaction.

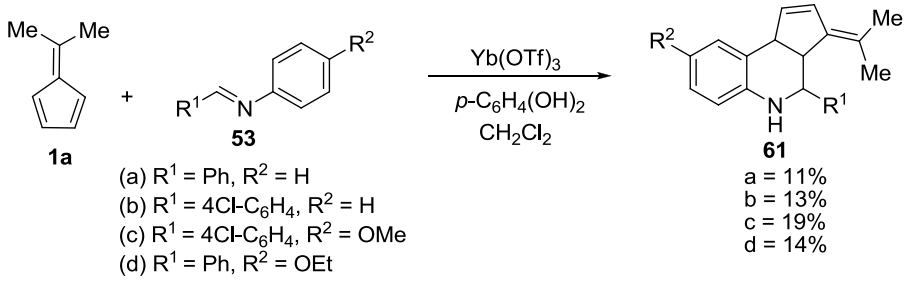
Povarov reaction using cyclopentadiene as a 2π component is well documented in the literature.[28] Recently, Feng and co-workers reported an asymmetric three-component Inverse Electron Demand Diels-Alder Reaction (IEDDA) with cyclopentadiene **32** as the dienophile.[29] The asymmetric Povarov reaction is catalyzed by chiral N,N'-dioxide–$Sc(OTf)_3$ complex **59** and furnished the ring fused tetrahydroquinolines **60** in good to high yields with excellent diastereo- and enantioselectivities.



Scheme 4.18

4.2. Present Work

As already discussed in the previous section, our group has made significant involvement in the cycloaddition chemistry of pentafulvenes. As part of our research program in the field of Lewis acid catalysis in fulvenes, we envisioned the Povarov type hetero Diels-Alder reaction using fulvene as the dienophile. We have done a thorough literature survey and noted a report from Stepakov *et al.* on the two component Povarov reaction of 6,6-dimethyl fulvene **1a** and aromatic imines (Scheme 4.19).[30] Even though the reaction is known but the scope of the reaction is limited to only 6,6-dimethyl fulvene and the products afforded in low yield because of side polymerization of fulvenes.

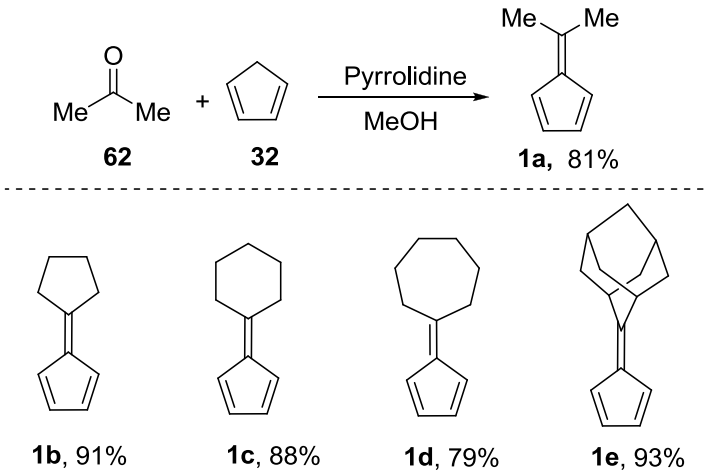


Scheme 4.19

In continuation of our consistent interest in cycloaddition reactions of fulvenes and to expand the scope of the reaction by using electron deficient imines generated from phenylglyoxal and aromatic amines, we undertook a detailed investigation of Povarov reaction in various substituted fulvenes. The results of these studies are discussed in the following sections.

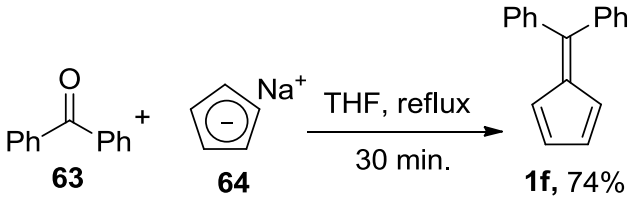
4.3. Results and Discussion

Fulvenes used for our investigations were prepared by the base catalyzed condensation between cyclopentadiene and carbonyl compounds.[31] For example, synthesis of dimethylfulvene **1a** from acetone **62** and cyclopentadiene **32** is shown in Scheme 4.20. Using this method we have synthesized various 6-substituted cyclic fulvenes (**1b-e**) by condensing cyclopentadiene and corresponding ketones.



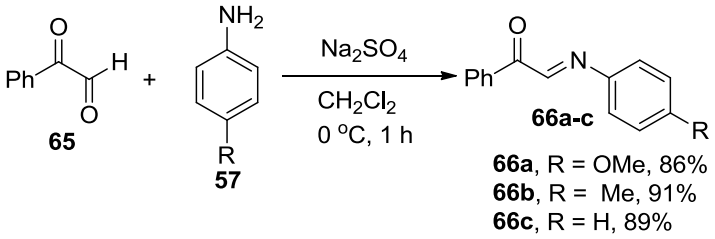
Scheme 4.20

Even though, this procedure is widely accepted for the synthesis of fulvenes regarding the generality and high yields; the reaction was unsuccessful with bulky ketones such as diaryl ketones. Ottoson described an improved synthesis of fulvenes through reaction of sodium cyclopentadienide with the appropriate ketones refluxing in THF and they showed that alkyl or aryl substituted fulvenes are formed rapidly in high yields.[32] Diphenylfulvene **1f** was synthesized by using this procedure.



Scheme 4.21

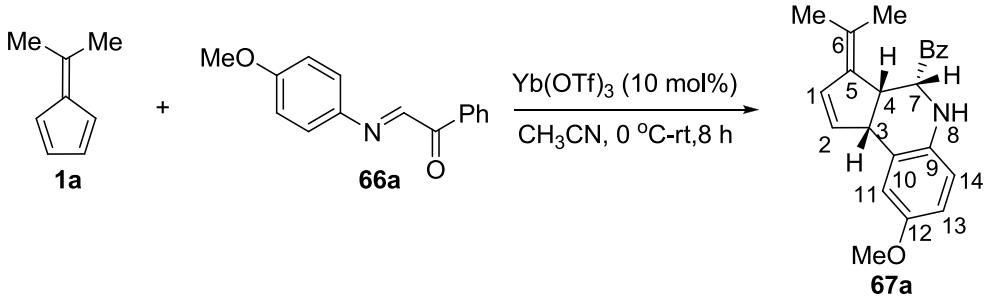
The starting material imines desired for our studies were prepared according to the literature procedure.[33] Imines derived from phenylglyoxal synthesized by simple condensation with aryl amines in the presence of magnesium sulfate in dichloromethane at 0 °C.



Scheme 4.22

4.3.1. Lewis acid catalyzed aza Diels-Alder cycloaddition reaction of fulvenes with aryl imines generated from phenylglyoxal

We commenced our investigation by reacting the imine generated from phenylglyoxal and *p*-anisidine **66a** with dimethyl fulvene **1a** in the presence of 10 mol% $Yb(OTf)_3$ in acetonitrile at 0 ^oC for 8 h. The reaction afforded *cis*-alkylidene cyclopentene fused tetrahydroquinoline **67a** in 55% yield with diastereomeric ratio 91:9.



Scheme 4.23

The structure of the product was characterized by various spectroscopic analyses. In IR spectrum, the peak at 3363 cm^{-1} assigned to the –NH stretching and –CO stretching

absorption observed at 1682 cm^{-1}. The ^{1}H NMR of **67a** (Figure 4.5) shows two alkene protons at C-1 and C-2 appeared as a doublet at δ 6.02 and a quartet at 5.88 ppm respectively. Two methyl groups attached to the exocyclic double bond found to be resonated as singlets at δ 1.82 and 1.21 ppm. The singlet at δ 3.79 ppm was attributed to methoxy protons attached to an aryl group. The proton at C-3 resonated at δ 4.03 ppm as a singlet, and C-7 proton was discernible at δ 4.95 ppm as a doublet.

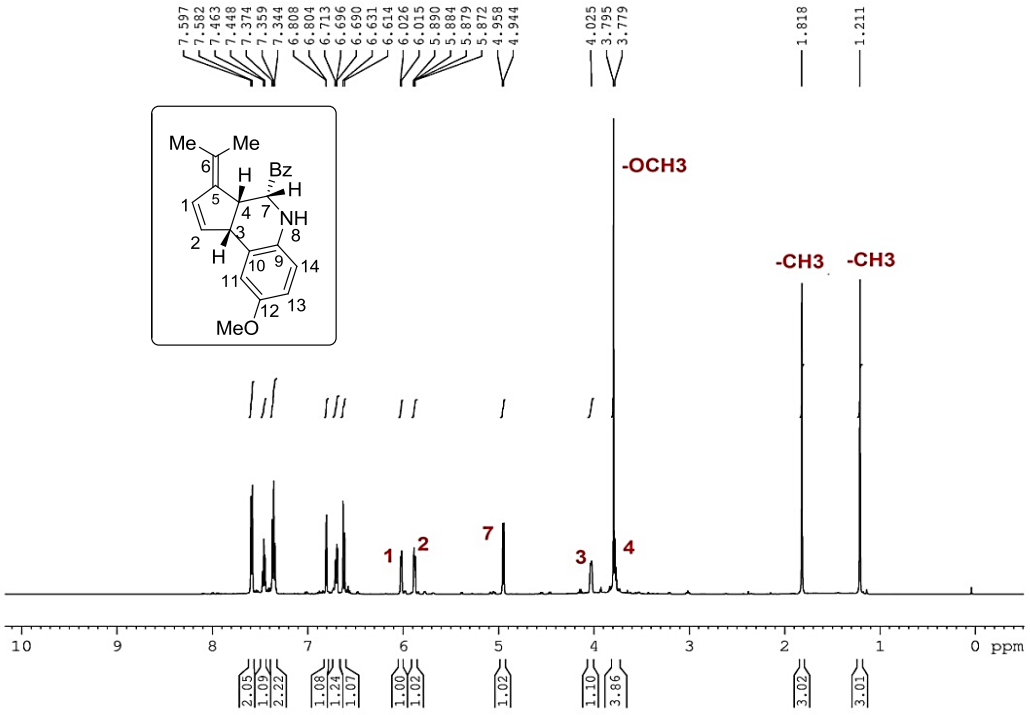


Figure 4.5. ^{1}H NMR of compound **67a**

In ^{13}C NMR spectrum (Figure 4.6), characteristic carbonyl peak was visible at δ 203.1 ppm. The olefinic carbons observed at δ 139.7 and 129.9 ppm. The aromatic carbon C-12 bearing the methoxy group resonated at δ 152.5 ppm. C-7, C-3 and C-4 carbons are found to be resonated at δ 55.8, 45.2 and 44.1 ppm respectively. The methoxy carbon was discernible at δ 55.7 ppm. The peaks observed at δ 21.9 and 20.2 ppm corresponds to the exocyclic methyl carbons. All other signals are in good agreement with the assigned structure.

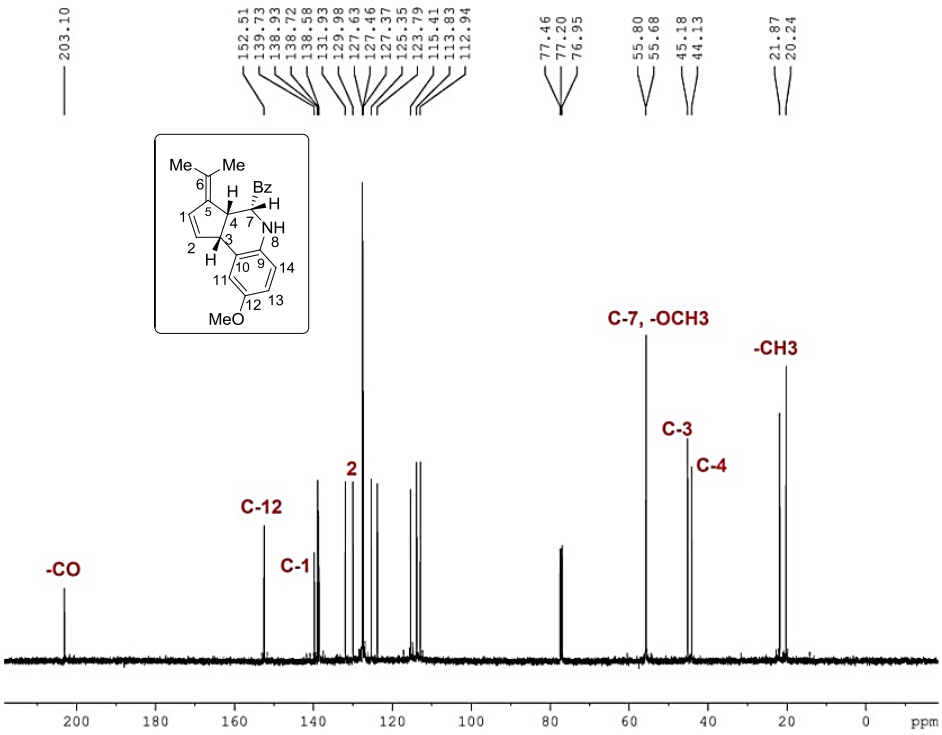


Figure 4.6. ^{13}C NMR of compound **67a**

Further proof for the structure was obtained from the mass spectrum which showed a peak at *m/z*, $[M+1]^+$: 346.18133. The relative stereochemistry of the product **67a** was unambiguously established by single crystal X-ray analysis (Figure 4.7).[34]

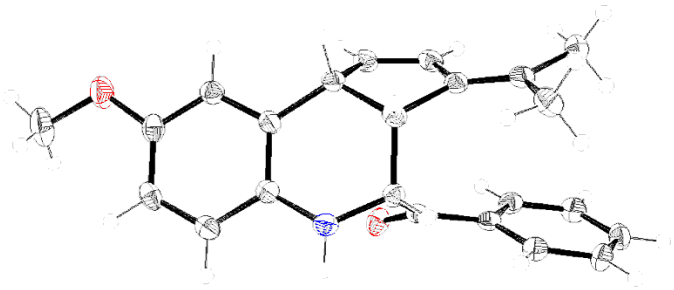
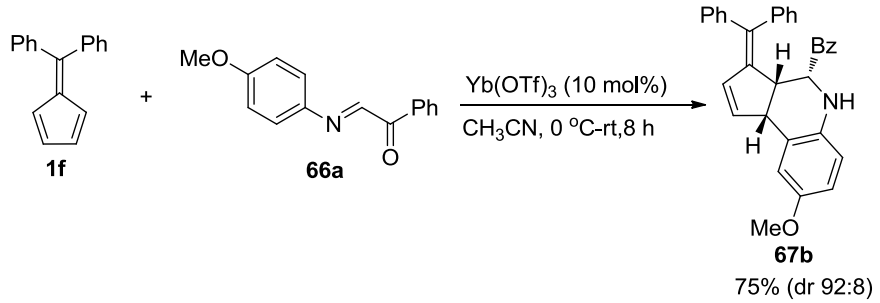


Figure 4.7. ORTEP diagram of compound **67a**

After successful reaction in dimethylfulvene, next we performed the reaction with the stable diphenyl fulvene **1f** and imine **66a** under similar reaction conditions and the reaction furnished the corresponding tetrahydroquinoline derivative **67b** in 75% yield.



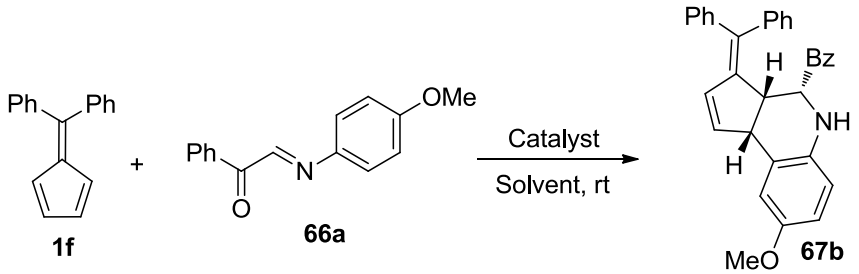
Scheme 4.24

The structure of the product **67b** was established by IR, ^{1}H and ^{13}C NMR and mass spectral analyses. IR spectrum of the compound **67b** showed the characteristic carbonyl absorptions at 1667 cm^{-1} and –NH stretching at 3360 cm^{-1}. In the ^{1}H NMR spectrum, the protons adjacent to the nitrogen resonated at δ 4.63 (J = 7.0 Hz) ppm as a doublet. A sharp singlet observed at δ 3.79 ppm assigned to methoxy protons. Two ring junction protons were visible in the region δ 4.42-4.21 ppm. ^{13}C NMR of **67b** displayed the benzoyl carbonyl at δ 197.6 ppm. The peak at δ 153.4 ppm corresponds to the aryl carbon attached to the methoxy group. The structure was further supported by the mass spectral analysis which showed a molecular ion peak at *m/z*, $[M+1]^{+}$ = 470.21144.

4.3.2. Optimization studies

Next, we turned our attention to optimizing the reaction condition to find out the best catalyst by choosing diphenyl fulvene **1f** and imine **66a** as the model substrates. In this regard, several Brønsted and Lewis acid catalysts were screened and the results are summarized in Table 4.1. Various lanthanide triflates were screened and among which initially used $Yb(OTf)_3$ was found to be the best. $Yb(OTf)_3$ already proved to be an efficient LA catalyst for this type of reaction. Using $BF_3.Et_2O$, Povarov adduct was obtained in 69% yield. Brønsted acid catalysts such as PTSA and TFA were also screened, but the yield was found to be lower as compared to Lewis acids. When the solvent switched from CH_3CN to CH_2Cl_2 yield was lowered to 58%, and also there is no appreciable change in diastereomeric ratio. In the absence of a catalyst, the reaction did not afford any product.

Table 4.1. Optimization studies

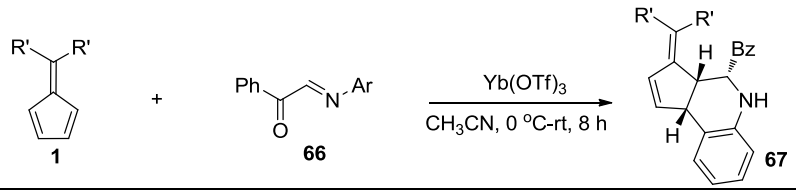


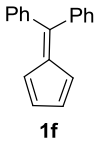
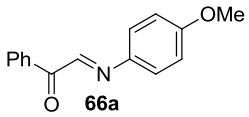
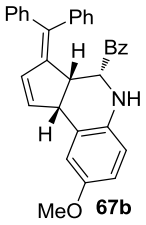
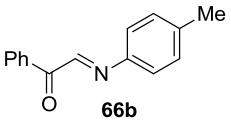
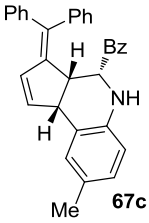
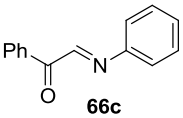
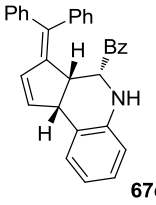
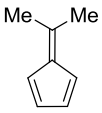
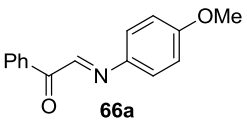
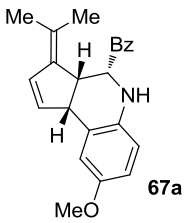
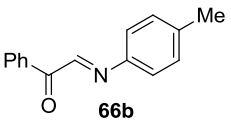
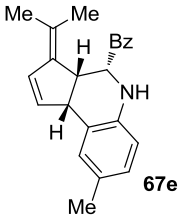
Entry	Catalyst	Solvent	Yield[a] (dr)[b]
1	$Yb(OTf)_3$	CH_3CN	75 (92:8)
2	$Sc(OTf)_3$	CH_3CN	58 (93:7)
3	$Cu(OTf)_2$	CH_3CN	46 (88:12)
4	$BF_3.OEt_2$	CH_2Cl_2	69
5	PTSA	CH_3CN	28
6	TFA	CH_3CN	31 (93:7)
7	$Yb(OTf)_3$	CH_2Cl_2	52 (96:4)
8	-	CH_3CN	No Reaction

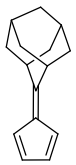
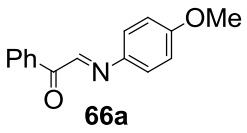
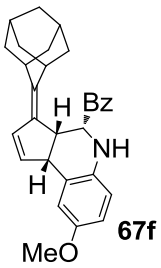
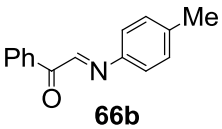
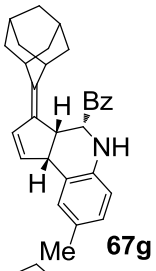
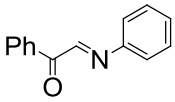
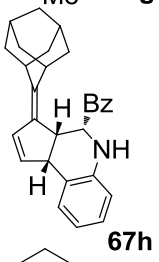
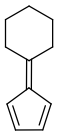
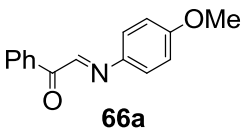
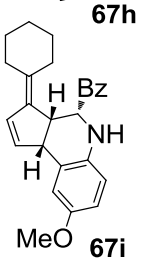
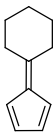
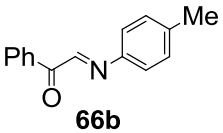
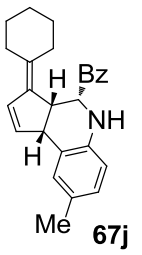
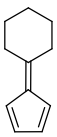
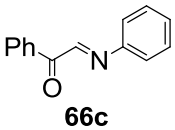
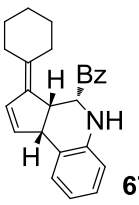
[a] Isolated yield [b] Determined by ^1H NMR analysis of the crude mixture

With this optimized reaction condition in hand, next we examined the scope of the reaction with respect to different imines derived from phenylglyoxal and substituted anilines and various 6,6-disubstituted fulvenes. Pentafulvenes derived from benzophenone, acetone, adamantanone, cyclopentanone and cyclohexanone reacted with imines **66a-c** and afforded the corresponding tetrahydroquinoline derivatives in moderate to good yields, and the results of the investigation are summarized in Table 4.2.

Table 4.2. Povarov reaction of fulvenes with phenyl glyoxal derived imines



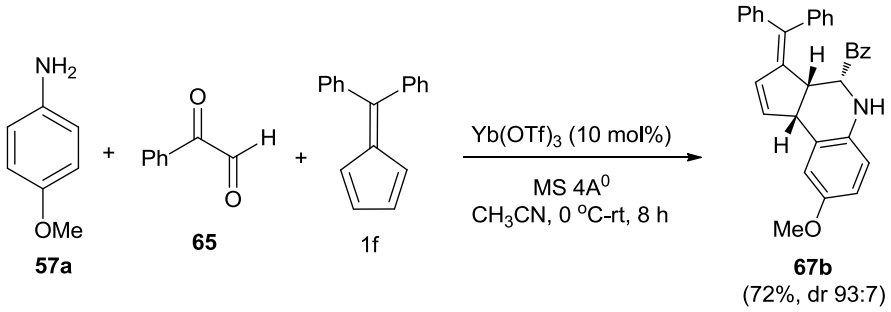
Entry	Fulvene	Imine	Product	Yield (dr)
1	 **1f**	 **66a**	 **67b**	75% (92:8)
2	**1f**	 **66b**	 **67c**	66% (93:7)
3	**1f**	 **66c**	 **67d**	46% (91:9)
4	 **1a**	 **66a**	 **67a**	55% (91:9)
5	**1a**	 **66b**	 **67e**	43% (92:8)

Entry	Fulvene	Imine	Product	Yield (dr)
6	 **1e**	 **66a**	 **67f**	72% (97:3)
7	**1e**	 **66b**	 **67g**	64% (94:6)
8	**1e**	 **66c**	 **67h**	26% (91:9)
9	 **1c**	 **66a**	 **67i**	64% (90:10)
10	 **1c**	 **66b**	 **67j**	59% (92:8)
11	 **1c**	 **66c**	 **67k**	52% (80:20)

Reaction Conditions: fulvene (1.0 equiv.), imine (1.0-1.5 equiv.), $Yb(OTf)_3$ (10 mol%), CH_3CN, 0 ^oC-rt, 8 h

4.3.3. Three component Povarov reaction

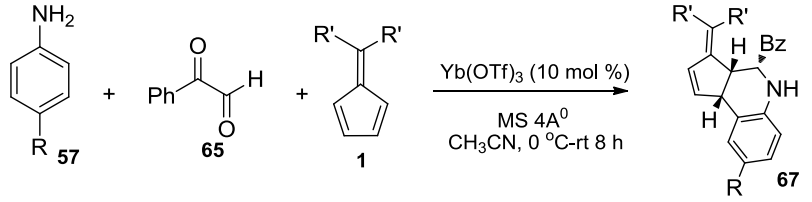
Next, we focused on carrying out this reaction in a multicomponent one-pot fashion which was highly desirable over the multi-step procedure with respect to atom-economic transformation of easily available starting materials into complex organic building blocks. To our delight, we obtained comparable results when we set up a three-component reaction of phenylglyoxal monohydrate **65**, *p*-anisidine **57a** and diphenyl fulvene **1f** under similar optimized conditions (Scheme 4.25).

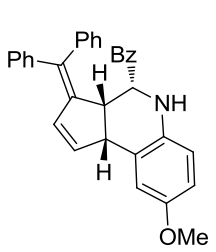


Scheme 4.25

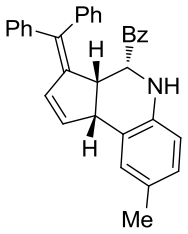
The scope of the reaction was then explored with different substituted anilines and various pentafulvenes. Evaluation of the reactivity of a series of fulvenes established that the hetero-Diels-Alder reaction with imines which is generated *in situ* is effective under the optimal catalyst system. Phenylglyoxals bearing different substituents on the phenyl ring furnished the corresponding products in good yields. The structures of all the products were established by employing usual spectral analyses. The results obtained are summarized in Table 4.3.

Table 4.3. Three component Povarov reaction

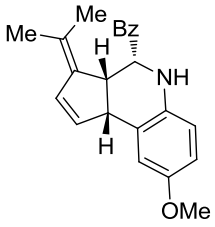




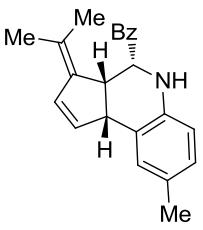
67b
(68%, dr 93:7)



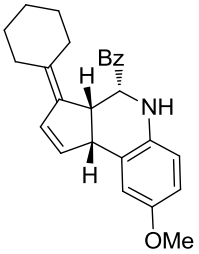
67c
(54%, dr 91:9)



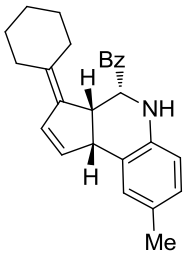
67a
(78%, dr 90:10)



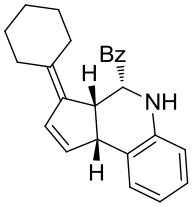
67e
(52%, dr 89:11)



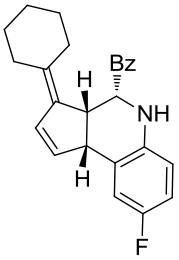
67i
(56%, dr 89:11)



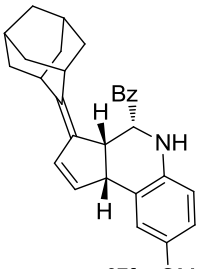
67j
(51%, dr 93:7)



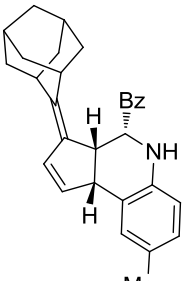
67k
(21%, dr 90:10)



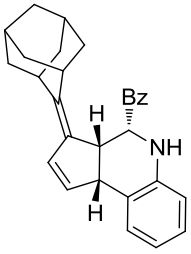
67l
(31%, dr 91:9)



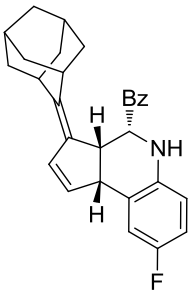
67f
(57%, dr 95:5)



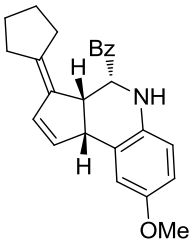
67g
(53%, dr 96:4)



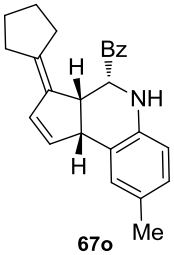
67h
(42%, dr 93:7)



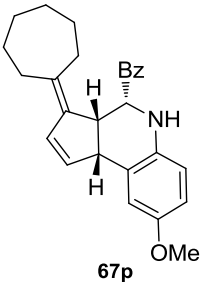
67m
(40%, dr 91:9)



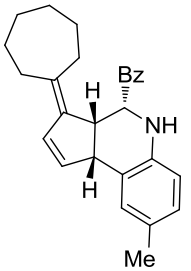
67n
(77%, dr 96:4)



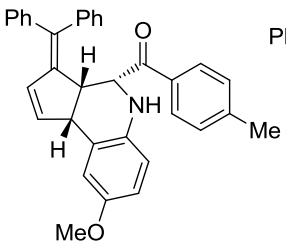
67o
(58%, dr 93:7)



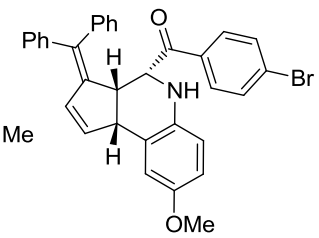
67p
(45%, dr 90:10)



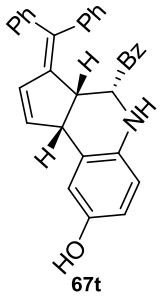
67q
(34%, dr 92:8)



67r
(46%, dr 91:9)



67s
(58%, dr 96:4)

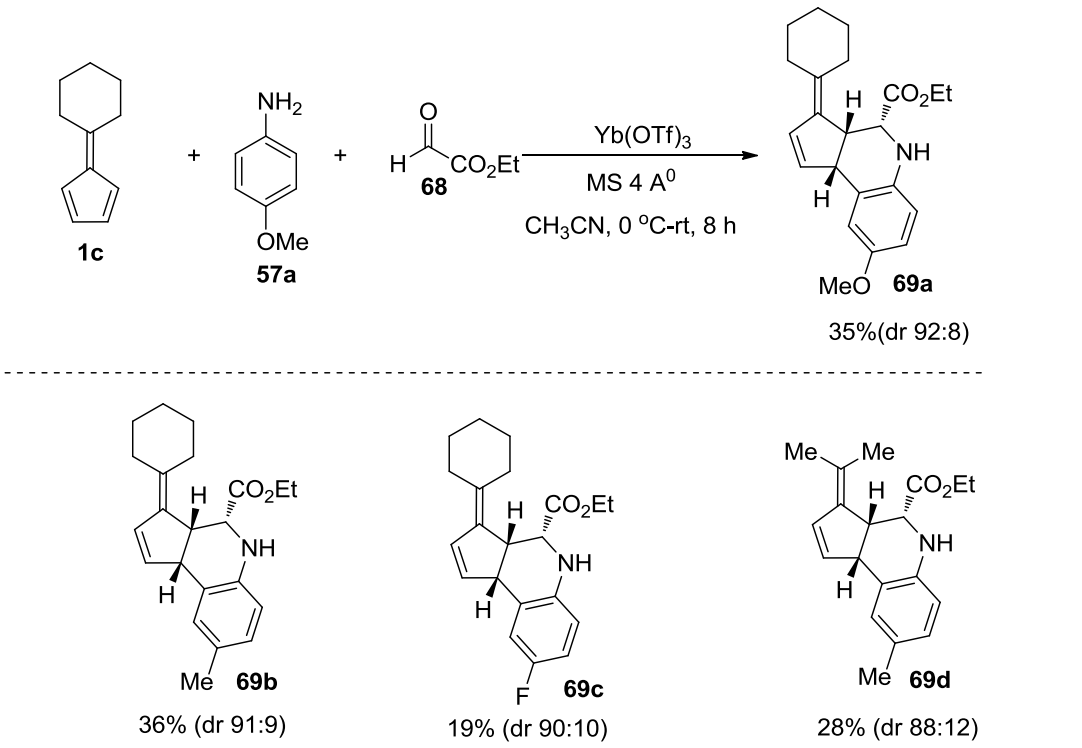


67t
(47%, dr 90:10)

Reaction Conditions: fulvene (1.0-2.0 equiv.), phenylglyoxal (1.0 equiv.), aryl amine (1.0 equiv.), CH_3CN, 0 °C-rt, 8 h

4.3.4. Three component Povarov reaction using ethyl glyoxalate as aldehyde component

After successful attempts with phenylglyoxal, to broaden the scope, we extended the Povarov cycloaddition by using ethyl glyoxalate **68** as aldehyde component. Three component reaction of fulvene **1c**, *p*-anisidine **57a** and ethyl glyoxalate **68** under the optimal reaction conditions provided the product **69a** in 35% yield (dr 92:8).



Scheme 4.26. Three component Povarov reaction using ethyl glyoxalate as aldehyde component

Various spectroscopic techniques were utilized for the structural characterization of the product **69a**. In the IR spectrum, ester carbonyl absorption was observed at 1725 cm^{-1}. In the ^1H NMR spectrum (Figure 4.8), olefinic protons resonated in the region δ 6.29-6.27 and 6.02-6.04 ppm. The proton on the carbon attached to the ester group appeared as a doublet at δ 3.95 ppm. The ring junction protons resonated as a doublet at δ 3.99 ppm and a triplet at δ 3.62 ppm. The methoxy protons resonated as a sharp singlet at δ 3.73 ppm. The methyl protons of the carboethoxy groups resonated as a triplet at δ 1.07 ppm.

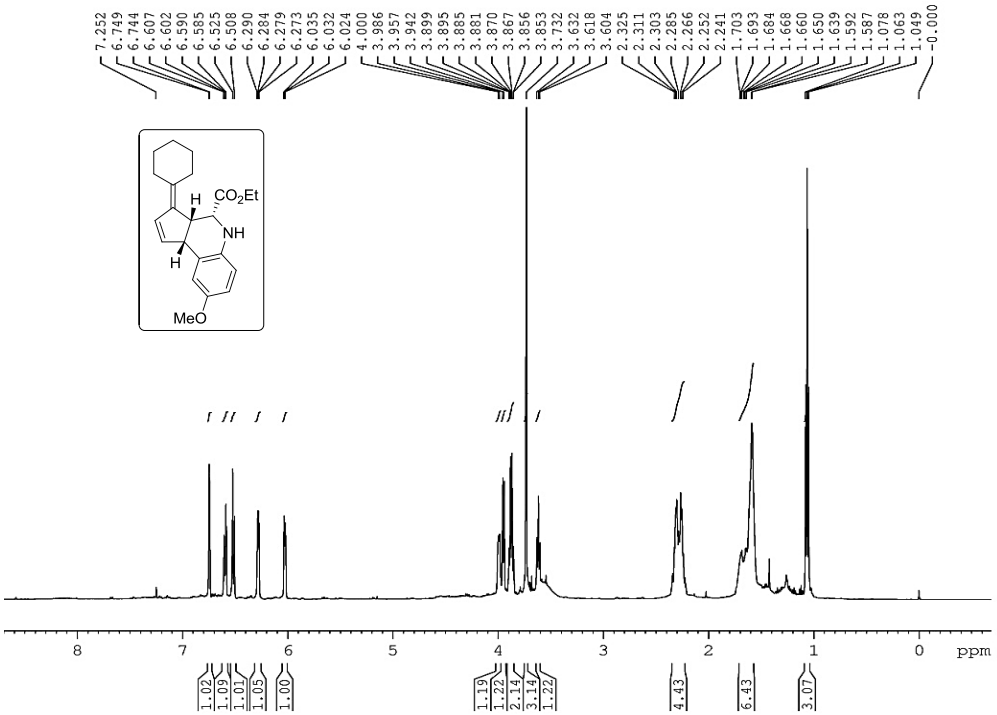


Figure 4.8. ^{1}H NMR spectrum of compound **69a**

^{13}C NMR of **69a** (Figure 4.9) displayed the characteristic ester carbonyl peak at δ 172.5 ppm. The aromatic carbon attached to the methoxy group found at δ 152.7 ppm. The peaks observed at δ 44.5 and 42.3 ppm were assigned to the ring junction carbons. The methyl carbon of the ester group resonated at δ 14.1 ppm. Further proof for the structure was obtained from the mass spectral analysis which showed a peak at *m/z* = 354.20715, $[M+1]^{+}$.

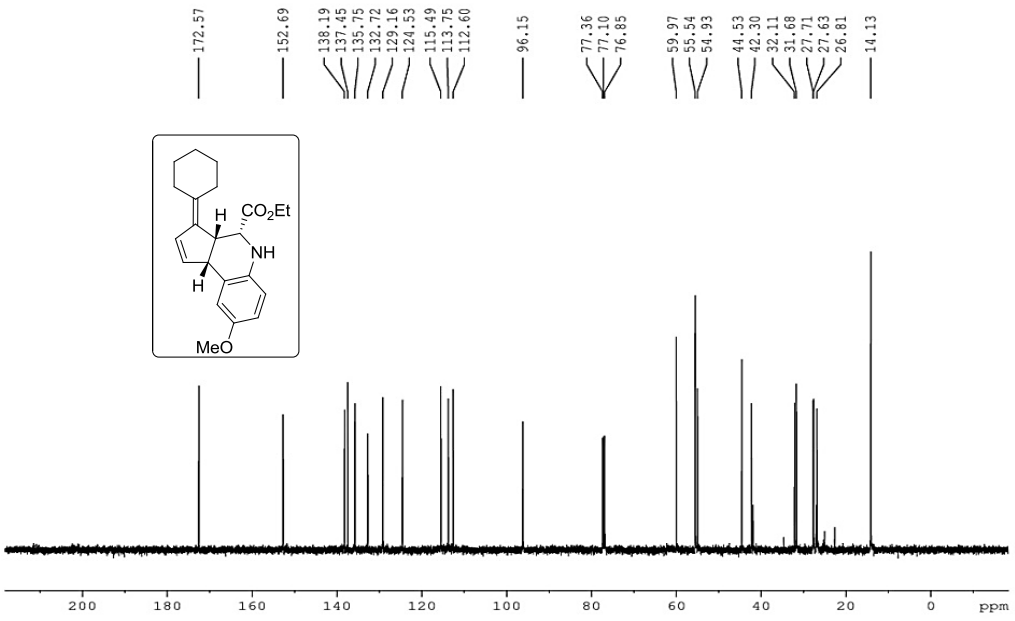
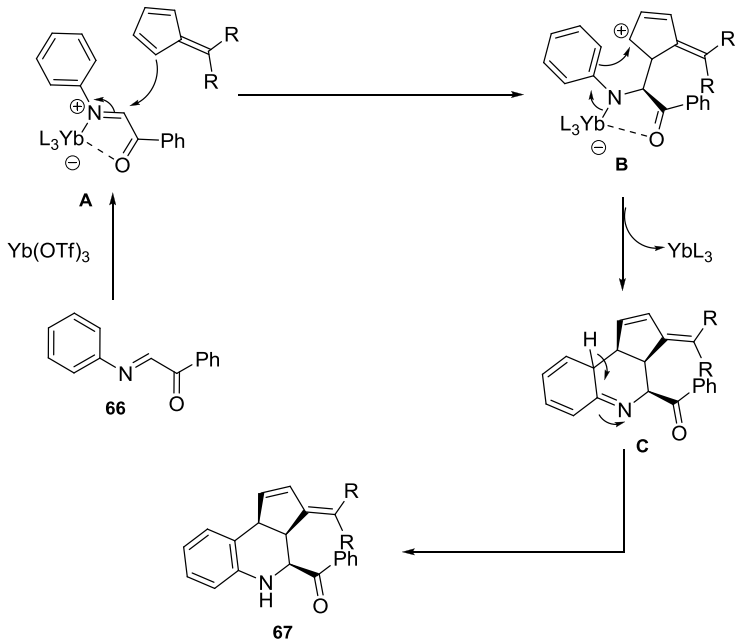


Figure 4.9. ^{13}C NMR spectrum of compound **69a**

In the same fashion, Povarov reaction of ethyl glyoxalate and fulvene derived from cyclohexanone was conducted in the presence of *p*-toluidine and 4-fluoroaniline and afforded corresponding cycloadducts **69b-c** in moderate yields. Similarly, dimethylfulvene **1a** also provided the corresponding product **69d** in the presence of ethyl glyoxalate and *p*-toluidine under the optimal reaction conditions (Scheme 4.26).

4.3.5. Mechanistic proposal

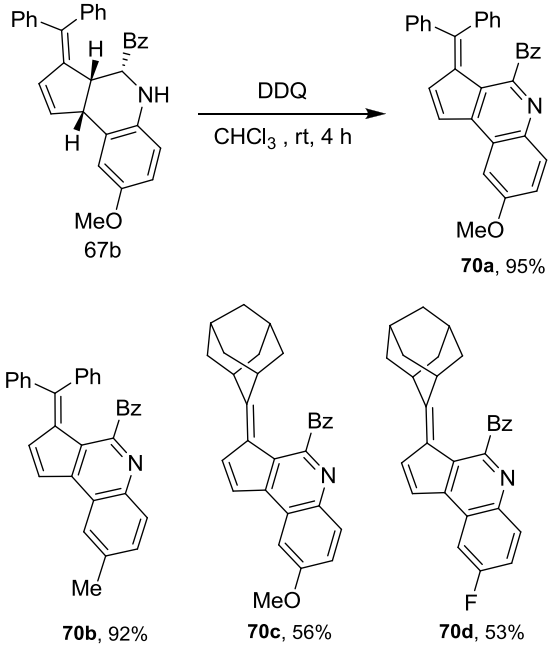
Although the Povarov reaction is defined as an Inverse Electron Demand aza-Diels-Alder process, there have been doubts regarding the pathway (cycloaddition or stepwise) that the reaction is followed.[35,24] A more likely explanation is that a common reaction mechanism is operating, involving a step-wise Lewis acid catalyzed process, which only appears to behave similarly to alternative concerted cycloaddition reactions.[35] Initially Lewis acid coordinates to the imine nitrogen and carbonyl oxygen of benzoyl group. This bidentate chelation of Yb(III) substantially lock the imine in the S-trans configuration and increases the electrophilicity of the imine carbon atom.[35] Fulvene attacks the imine carbon providing the cationic intermediate **B**. Further, the Friedel-Crafts type cyclization occurs to give the intermediate **C** by the concurrent regeneration of $Yb(OTf)_3$. Subsequent proton transfer from **C** resulted tetrahydroquinoline derivative **67**. Bidentate chelation favors the diastereoselective formation of the *cis*-product.



Scheme 4.27

4.3.6. Oxidation of Povarov adduct: Access of quinoline derivatives

Our attention next turned to the conversion of the tetrahydroquinoline derivatives to the corresponding quinoline derivatives. DDQ oxidation of the Povarov adduct **67b** was performed in chloroform and the reaction provided quinoline derivative **70a** in 95% yield.



Scheme 4.28

Spectral analysis was carried out to assign the structure of **70a**. The IR spectrum showed the characteristic carbonyl absorptions at 1667 cm^{-1}. In ^{1}H NMR spectrum (Figure 4.10), the methoxy protons resonated as a singlet at δ 3.99 ppm. In the ^{13}C NMR spectrum (Figure 4.11), the carbonyl carbon was detected at δ 192.1 ppm and the methoxy carbon resonated at δ 55.7 ppm. Further supporting evidence for the structure was obtained from the high-resolution mass spectral analysis which showed the molecular ion peak at *m/z* 466.18106 $[M+1]^{+}$. In a similar fashion, quinoline derivatives **70b-d** were synthesized in good yields from corresponding tetrahydroquinoline derivatives and is illustrated in Scheme 4.28.

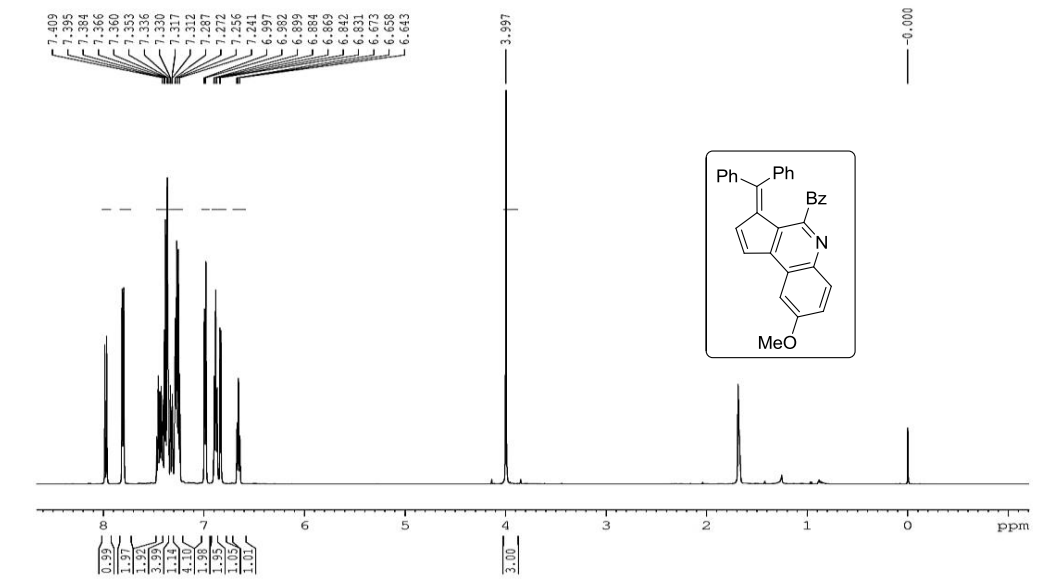


Figure 4.10. ^{1}H NMR spectrum of compound **70a**

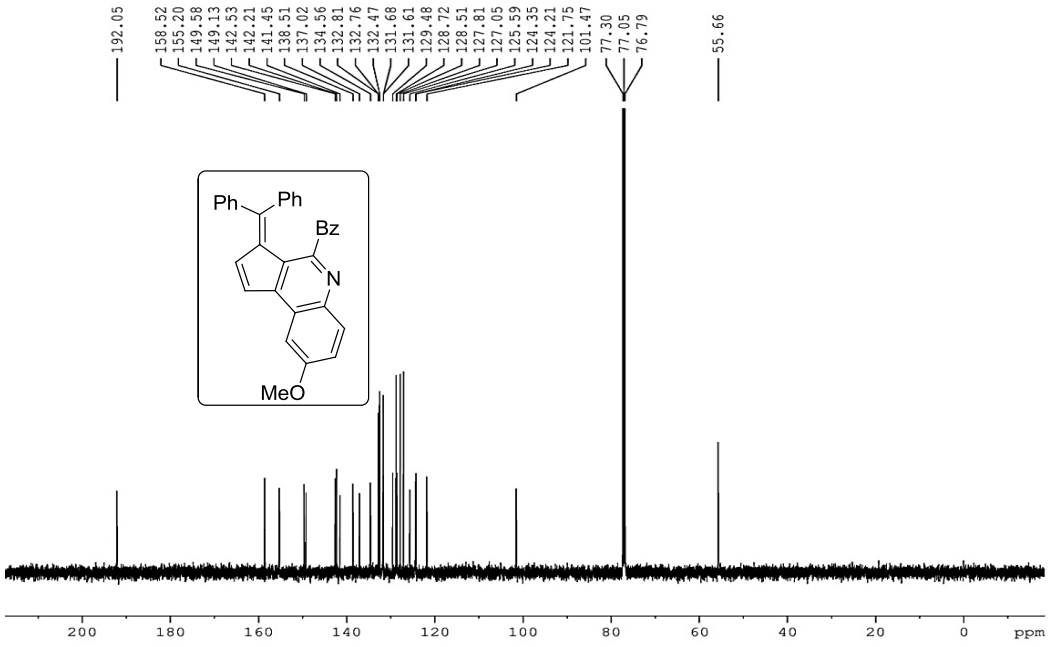


Figure 4.11. ^{13}C NMR spectrum of compound **70a**

4.4. Conclusion

In summary, we have developed the Lewis acid-catalyzed three-component Povarov reaction of α-oxo aldehydes, anilines and pentafulvenes.We have demonstrated the Povarov reaction in both two component as well as three component fashion and in each cases the reaction afforded tethahydroquinoline derivatives in comparable yields. The synthetic utility

is further highlighted by the synthesis of quinoline fused fulvene derivatives by DDQ oxidation.

4.5. Experimental Section

General information regarding the experiments is given in Section 2.5 of Chapter 2.

4.5.1. General experimental procedure for two component Povarov reaction of imine and pentafulvenes (Method A)

$Yb(OTf)_3$ (10 mol%) and imine derived from phenylglyoxal (1.0-1.5 equiv.) were stirred in acetonitrile at 0 °C. To this reaction mixture, fulvene (1.0 equiv.) in acetonitrile was added and stirred at room temperature for 8 h. The solvent was evaporated in *vacuo* and the residue on silica gel (100-200 mesh) column chromatography yielded tetrahydroquinoline derivatives.

4.5.2. General experimental procedure for three component Povarov reaction of aniline, phenyl glyoxal/ethyl glyoxalate and pentafulvenes (Method B)

To a suspension of 10 mol% $Yb(OTf)_3$ and $4A^o$ molecular sieves in dry acetonitrile was added a solution of phenylglyoxal monohydrate (1.0 equiv.) and aniline (1.0 equiv.) in acetonitrile followed by addition of fulvene (1.0-2.0 equiv.) in acetonitrile solution at 0 °C. The reaction mixture was stirred for 8 h at room temperature. The reaction was monitored by TLC and quenched with water. The aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue on column chromatography (silica gel) using hexane-ethyl acetate mixtures (95:5 hexane-ethyl acetate or 90:10 hexane-ethyl acetate) yielded tetrahydroquinolines in good yields.

4.5.3. General experimental procedure for the oxidation of tetrahydroquinoline derivatives to quinoline derivatives

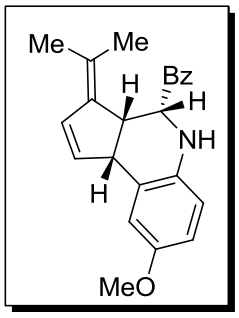
To a solution of tetrahydroquinoline derivative in $CHCl_3$, DDQ (2 equiv.) was added and the mixture was stirred for 4 h at room temperature. An aqueous saturated $NaHCO_3$ solution (10 mL) was added, and the resulting mixture was extracted with $CHCl_3$ (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in

vacuo. The reaction mixture was purified by column chromatography (hexane-ethyl acetate) to afford the desired product.

8-Methoxy-3-(propan-2-ylidene)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67a)

Following the general experimental procedure (method A), the dimethyl fulvene **1a** (164 mg, 0.69 mmol), imine **66a** (72 mg, 0.69 mmol) and $Yb(OTf)_3$ (43 mg, 0.069 mmol) in 5 mL CH_3CN at room temperature for 8 h gave the product **67a** as a yellow solid in 55% (132 mg) yield with dr 91:9.

Following the general experimental procedure (method B), the dimethyl fulvene **1a** (264 mg, 2.49 mmol), phenylglyoxal monohydrate **65** (189 mg, 1.24 mmol), *p*-anisidine (152 mg, 1.24 mmol), $Yb(OTf)_3$ (77 mg, 0.124 mmol) and 4A° MS (200 mg) in 5 mL CH_3CN at room temperature for 8 h gave the product **67a** as a yellow solid in 78% (334 mg) yield with dr 90:10.

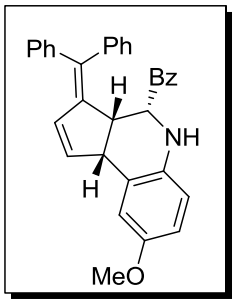


R_f: 0.32 (20% Ethyl acetate-hexane).; **mp**: 180-185 °C.; **IR (neat) υ_{max}:** 3363, 2907, 2851, 2830, 1682, 1504, 1444, 1217 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$, TMS):** δ **7**.59 (d, *J* = 7.5 Hz, 2 H), 7.46 (m, 1 H), 7.36 (t, *J*= 7.5 Hz, 2 H), 6.81 (d, *J* = 2.0 Hz, 1 H), 6.70 (m, 1 H), 6.62 (d, *J* = 8.5 Hz, 1 H), 6.02 (d, *J* = 5.5 Hz, 1 H), 5.88 (q, *J* = 3.0 Hz, 1 H), 4.95 (d, *J* = 7.0 Hz, 1 H), 4.03 (s, 1 H), 3.79 (s, 3 H), 3.78 (m, 1 H), 1.82 (s, 3 H), 1.21 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 203.1, 152.5, 139.7, 138.9, 138.7, 138.6, 131.9, 129.9, 127.6, 127.5, 127.4, 125.4, 123.8, 115.4, 113.8, 112.9, 55.8, 55.7, 45.2, 45.1, 21.9, 20.2.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}NO_2$ [M+1]: 346.18016; Found: 346.18133.

3-(Diphenylmethylene)-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67b)

Following the general experimental procedure (method A), the diphenyl fulvene **1f** (100 mg, 0.43 mmol), imine **66a** (125 mg, 0.52 mmol) and $Yb(OTf)_3$ (27 mg, 0.043 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67b** as a reddish brown solid in 75% (153 mg) yield with dr 92:8.

Following the general experimental procedure (method B), the diphenyl fulvene **1f** (100 mg, 0.43 mmol), phenylglyoxal monohydrate **65** (55 mg, 0.36 mmol), *p*-anisidine (44 mg, 0.36 mmol), $Yb(OTf)_3$ (22 mg, 0.036 mmol) and MS $4A^0$ (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67b** as a reddish brown solid in 72% (122 mg) yield with dr 93:7.

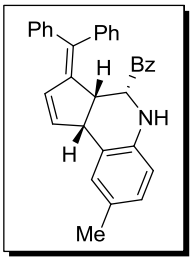


R_f: 0.28 (20% Ethyl acetate-hexane).; **mp:** 212-216 ^oC.; **IR (neat) υ_{max}:** 3360, 2836, 1667, 1599, 1495, 1265, 1233, 1226, 1210, 1206 cm^{-1}.; **^1H NMR (500 MHz, $CDCl_3$, TMS):** δ 7.56-7.51 (m, 3 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.33-7.31 (m, 3 H), 7.19-7.16 (m, 5 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 6.80-6.78 (m, 2 H), 6.59 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.51(dd, *J* = 5.75, 2.5 Hz, 1 H), 6.42-6.41 (m, 1 H), 6.38 (d, *J* = 8.5 Hz, 1 H), 4.63 (d, *J* = 7.0 Hz, 1 H), 4.41 (t, *J* = 8.0 Hz, 1 H), 4.23-4.21 (m, 1 H), 3.79 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 197.6, 153.4, 145.2, 142.5, 142.4, 140.9, 137.4, 136.2, 133.8, 132.8, 132.7, 129.7, 128.5(2C), 128.2, 127.8, 127.1, 126.6, 126.3, 115.9, 113.2, 112.4, 55.7, 53.7, 44.9, 42.4.; **HRMS (ESI):** *m/z* calcd. for $C_{33}H_{28}NO_2$ $[M+1]^+$: 470.21146; Found: 470.21144.

3-(Diphenylmethylene)-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67c)

Following the general experimental procedure (method A), the diphenyl fulvene **1f** (88 mg, 0.38 mmol), imine **66b** (129 mg, 0.58 mmol) and $Yb(OTf)_3$ (27 mg, 0.038 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67c** as a reddish brown solid in 66% (114 mg) yield with dr 93:7.

Following the general experimental procedure (method B), diphenyl fulvene **1f** (100 mg, 0.43 mmol), phenylglyoxal monohydrate **65** (65 mg, 0.43 mmol), *p*-toluidine (46 mg, 0.43 mmol), $Yb(OTf)_3$ (26 mg, 0.043 mmol) and 4 A^0 MS (100 mg) in 5 mL CH_3CN at room temperature for 8 h gave the product **67c** in 54% (106 mg) yield with dr 91:9.

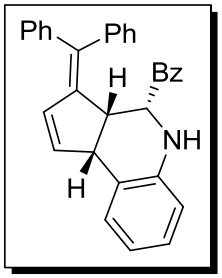


R_f: 0.26 (20% Ethyl acetate-hexane).; **mp:** 198-202 ^oC.; **IR (neat) υ_{max}:** 3368, 3054, 3024, 2861, 1682, 1589, 1507, 1444, 1306, 1263, 1215, 812, 756, 698 cm^{-1}.; **^1H NMR (500 MHz, $CDCl_3$):** δ 7.49-7.45 (m, 3 H), 7.35-7.32 (m, 2 H), 7.27-7.26 (m, 3 H), 7.16-7.14 (m, 2 H), 7.10-7.06 (m, 4 H),

6.74 (d, *J* = 8.0 Hz, 1 H), 6.69-6.68 (m, 2 H), 6.46-6.45 (m, 1 H), 6.33-6.29 (m, 2 H), 4.58 (d, *J* = 7.0 Hz, 1 H), 4.36 (t, *J* = 7.5 Hz, 1 H), 4.14 (d, *J* = 7.5 Hz, 1 H), 2.25 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 197.5, 145.3, 142.6, 142.5, 141.4, 140.1, 137.5, 133.7, 132.6, 132.5, 129.7(2C), 128.6, 128.5, 128.4, 128.2, 128.1, 127.7, 127.3, 127.0, 126.6, 124.7, 115.0, 53.5, 44.6, 42.6, 20.8.; **HRMS (ESI):** *m/z* calcd. for $C_{33}H_{28}NO$ $[M+1]^+$: 454.21654; Found: 454.21686.

3-(Diphenylmethylene)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67d)

Following the general experimental procedure (method A), the diphenyl fulvene **1f** (100 mg, 0.43 mmol), imine **66c** (135 mg, 0.65 mmol) and $Yb(OTf)_3$ (27 mg, 0.043 mmol) in 3 mL CH_3CN at room temperature for 8 h gave the product **67d** as a reddish brown solid in 46% (88 mg) yield with dr 91:9.



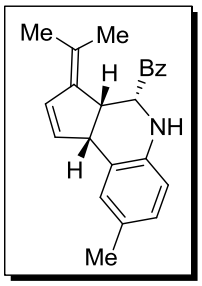
R_f: 0.27 (20% Ethyl acetate-hexane).; **mp:** 204-208 ^oC.; **IR (neat) υ_{max}:** 3362, 2872, 1684, 1598, 1502, 1434, 1301, 1269, 1217 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.54 (d, *J* = 7.5 Hz, 2 H), 7.50-7.47 (m, 1 H), 7.35 (t, *J* = 7.5 Hz, 2 H), 7.30-7.27 (m, 3 H), 7.25-7.24 (m, 2 H), 7.17-7.16 (m, 2 H), 7.10-7.09 (m, 2 H), 6.97-6.94 (m, 1 H), 6.79 (t, *J* = 7.5 Hz, 1 H), 6.65-6.64 (m, 2 H), 6.45-6.41 (m, 2 H), 6.31-6.29 (m, 1 H), 4.61(d, *J* = 7.0 Hz, 1 H), 4.37 (t, *J* = 7.5 Hz, 1 H), 4.17 (d, *J* = 7.5 Hz, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 197.8, 145.0, 142.7, 142.5, 142.4, 141.6, 137.6, 133.9, 132.6, 132.3, 129.7, 129.6, 128.5, 128.4, 128.3, 127.7, 127.5, 127.1, 126.7, 126.6, 124.5, 119.5, 114.9, 53.4, 44.6, 42.6.; **HRMS (ESI):** *m/z* calcd. for $C_{32}H_{26}NO$ $[M+1]^+$: 440.20089; Found: 440.20087.

8-Methyl-3-(propan-2-ylidene)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67e)

Following the general experimental procedure (method A), the dimethyl fulvene **1a** (84 mg, 0.79 mmol), imine **66b** (266 mg, 1.19 mmol) and $Yb(OTf)_3$ (49 mg, 0.079 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67e** as a yellow solid in 43% (114 mg) yield with dr 92:8.

Following the general experimental procedure (method B), the dimethyl fulvene **1a** (153 mg, 1.44 mmol), phenylglyoxal monohydrate **65** (183 mg, 1.20 mmol), *p*-toluidine (128

mg, 1.20 mmol), $Yb(OTf)_3$ (74 mg, 0.12 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67e** in 52% (205 mg) yield with dr 89:11.

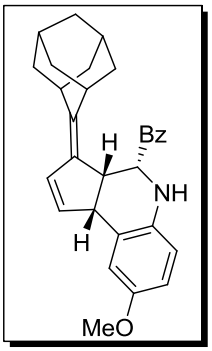


R_f: 0.21 (20% Ethyl acetate-hexane).; **mp:** 202-204 ^oC.; **IR (neat) υ_{max}:** 3362, 2981, 2930, 2851, 1680, 1477, 1442, 1220 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ **7**.55 (d, *J* = 7.0 Hz, 2 H), 7.42 (m, 1 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 6.97 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.55 (d, *J* = 8.0 Hz, 1 H), 5.98 (m, 1 H), 5.81 (m, 1 H), 4.91 (d, *J* = 7.0 Hz, 1 H), 3.97 (s, 1 H), 3.74 (t, *J* = 7.0 Hz, 1 H), 2.27 (s, 3 H), 1.79 (s, 3 H), 1.16 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.6, 142.2, 139.8, 139.3, 139.1, 131.8, 129.7, 128.9, 127.6, 127.5, 127.4, 124.9, 122.5, 114.6, 55.7, 44.9, 44.3, 21.9, 20.8, 20.2.; **HRMS (ESI):** *m/z* calcd. for $C_{23}H_{24}NO$ $[M+H]^+$: 330.18524; Found: 330.18555.

Compound 67f

Following the general experimental procedure (method A), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), imine **66a** (145 mg, 0.61 mmol) and $Yb(OTf)_3$ (31 mg, 0.051 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67f** as a yellow solid in 72% (159 mg) yield with dr 97:3.

Following the general experimental procedure (method B), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), phenylglyoxal monohydrate **65** (77 mg, 0.50 mmol), *p*-anisidine (62 mg, 0.50 mmol), $Yb(OTf)_3$ (31 mg, 0.051 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67f** in 57% (125 mg) yield with dr 95:5.



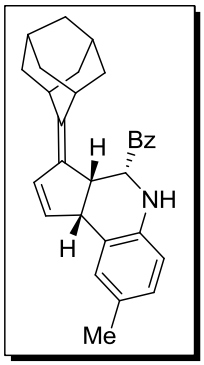
R_f: 0.41 (20% Ethyl acetate-hexane).; **mp:** 79-84 ^oC.; **IR (neat) υ_{max}:** 3361, 2906, 2847, 1684, 1598, 1503, 1446, 1352, 1216, 1158, 1038, 878, 691 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.71 (d, *J* = 7.5 Hz, 2 H), 7.49 (t, *J* = 7.0 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 6.84 (d, *J* = 2.5 Hz, 1 H), 6.63 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.51 (d, *J* = 8.5 Hz, 1 H), 6.19-6.17 (m, 1 H), 6.04-6.03 (m,1 H), 4.90 (d, *J* = 6.5 Hz, 1 H), 4.08 (d, *J* = 7.0 Hz, 1 H), 3.81-3.79 (m, 4 H), 2.76 (s, 1 H), 2.58 (s, 1 H), 1.92-1.86 (m, 2 H), 1.77 (s, 6 H), 1.68 (d, *J* = 12.0 Hz, 1 H), 1.62-1.58 (m, 2 H), 1.12 (d, *J* = 12.0 Hz, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 200.6, 152.9, 140.9, 138.9, 137.8, 137.3, 132.2, 131.9, 129.5, 128.2,

128.1, 125.8, 115.6, 113.7, 112.4, 56.8, 55.6, 45.4, 43.2, 40.1, 39.7, 37.7, 37.5, 37.1, 35.2, 34.6, 28.4, 27.9.; **HRMS (ESI):** *m/z* calcd. for $C_{30}H_{32}NO_2$ $[M+1]^+$: 438.24330; Found: 438.24316.

Compound 67g

Following the general experimental procedure (method A), pentafulvene derived from adamantanone **1e** (75 mg, 0.38 mmol), imine **66b** (110 mg, 0.49 mmol) and $Yb(OTf)_3$ (24 mg, 0.038 mmol) in 3 mL CH_3CN at room temperature for 8 h gave the product **67g** as a yellow solid in 64% (102 mg) yield with dr 94:6.

Following the general experimental procedure (method B), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), phenylglyoxal monohydrate **65** (77 mg, 0.50 mmol), *p*-toluidine (54 mg, 0.50 mmol), $Yb(OTf)_3$ (31 mg, 0.051 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67g** in 53% (111 mg) yield with dr 96:4.

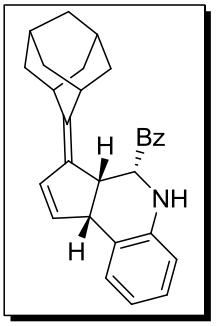


R_f: 0.53 (20% Ethyl acetate-hexane).; **mp:** 66-70 °C.; **IR (neat) υ_{max}:** 3360, 2908, 2849, 1710, 1687, 1611, 1507, 1447, 1353, 1217, 810, 713, 690 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 7.5 Hz, 2 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.34 (t, *J* = 7.5 Hz, 2 H), 7.01 (s, 1 H), 6.80 (d, J = 8.0 Hz, 1 H), 6.46 (d, *J* = 8.0 Hz, 1 H), 6.11-6.09 (m, 1 H), 6.00-5.99 (m, 1 H), 4.86 (d, *J* = 7.0 Hz, 1 H), 4.02 (d, *J* = 7.0 Hz, 1 H), 3.76 (t, *J* = 7.0 Hz, 1 H), 2.74 (s, 1 H), 2.53 (s, 1 H), 2.27 (s, 3 H), 1.89-1.83 (m, 2 H), 1.76-1.74 (m, 6 H), 1.66-1.60 (m, 2 H), 1.56-1.54 (m, 1 H), 1.07 (d, *J* = 12.0 Hz, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 200.7, 141.6, 140.7, 139.1, 137.8, 132.1, 129.3, 128.7, 128.2, 128.1, 127.9, 127.3, 124.3, 114.8, 56.6, 45.1, 43.4, 40.1, 39.7, 37.7, 37.5, 37.2, 35.2, 34.6, 28.4, 27.9, 20.8.; **HRMS (ESI):** *m/z* calcd. for $C_{30}H_{32}NO$ $[M+1]^+$: 422.24784; Found: 422.24792.

Compound 67h

Following the general experimental procedure (method A), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), imine **66c** (157 mg, 0.76 mmol) and $Yb(OTf)_3$ (31 mg, 0.05 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67h** as a yellow solid in 26% (54 mg) yield with dr 91:9.

Following the general experimental procedure (method B), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), phenylglyoxal monohydrate **65** (77 mg, 0.50 mmol), aniline (47 mg, 0.50 mmol), $Yb(OTf)_3$ (31 mg, 0.051 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67h** in 42% (85 mg) yield with dr 93:7.

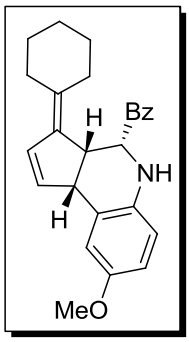


R_f: 0.50 (20% Ethyl acetate-hexane).; **mp:** 205-210 ^oC.; **IR (neat) υ_{max}:** 3353, 2907, 2848, 1715, 1682, 1494, 1445, 1266, 1222, 1173, 1102, 752 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 7.5 Hz, 2 H), 7.46 (d, *J* = 7.0 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 2 H), 7.20-7.16 (m, 1 H), 6.99 (t, *J* = 7.5 Hz, 1 H), 6.77 (t, *J* = 7.0 Hz, 1 H), 6.56 (d, *J* = 8.0 Hz, 1 H), 6.10-6.08 (m, 1 H), 5.99-5.98 (m, 1 H), 4.88 (d, *J* = 6.5 Hz, 1 H), 4.06 (d, *J* = 7.0 Hz, 1 H), 3.78 (t, *J* = 7.0 Hz, 1 H), 2.75 (s, 1 H), 2.52 (s, 1 H), 1.89-1.84 (m, 2 H), 1.77-1.71 (m, 6 H), 1.65-1.55 (m, 2 H), 1.54-1.53 (m, 1 H), 1.05 (d, *J* = 7.0 Hz, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 201.1, 144.1, 140.9, 139.1, 137.9, 132.1, 131.8, 130.2, 129.2, 128.5, 128.2, 126.7, 119.5, 119.1, 114.8, 56.5, 45.1, 43.4, 40.2, 39.7, 37.6, 37.4, 37.2, 35.2, 34.6, 28.4, 27.9.; **HRMS (ESI):** *m/z* calcd. for $C_{29}H_{30}NO$ $[M+1]^+$: 408.23219; Found: 408.23267.

3-Cyclohexylidene-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67i)

Following the general experimental procedure (method A), pentafulvene derived from cyclohexanone **1c** (74 mg, 0.51 mmol), imine **66a** (145 mg, 0.61 mmol) and $Yb(OTf)_3$ (31 mg, 0.051 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67i** as a yellow solid in 64% (124 mg) yield with dr 90:10.

Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (102 mg, 0.69 mmol), phenylglyoxal monohydrate **65** (88 mg, 0.58 mmol), *p*-anisidine (72 mg, 0.58 mmol), $Yb(OTf)_3$ (36 mg, 0.058 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67i** in 56% (125 mg) yield with dr 89:11.

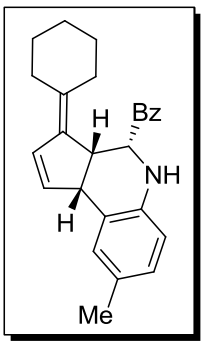


R_f: 0.46 (30% Ethyl acetate-hexane).; **mp:** 194-197 ^oC.; **IR (neat) υ_{max}:** 3363, 2927, 2851, 2828, 1683, 1503, 1469, 1444, 1251, 1215, 1159, 1095, 1038, 915, 809, 693 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.58 (d, *J* = 7.5 Hz, 2 H), 7.44 (t, *J* = 7.5 Hz, 1 H), 7.34 (t, *J* = 7.5 Hz, 2 H), 6.76 (d, *J* = 2.0 Hz, 1 H), 6.64 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.56 (d, *J* = 8.5 Hz, 1 H), 6.01-5.99 (m, 1 H), 5.94-5.93 (m, 1 H), 4.87 (d, *J* = 7.0 Hz, 1 H), 4.01 (d, *J* = 6.5 Hz, 1 H), 3.79-3.77 (m, 4 H), 2.50-2.46 (m, 1 H), 2.01-1.94 (m, 2 H), 1.68-1.65 (m, 1 H), 1.60-1.58 (m, 1 H), 1.43-1.41 (m, 1 H), 1.38-1.29 (m, 3 H), 1.26-1.21(m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 202.2, 152.7, 139.5, 138.8, 138.2, 136.1, 133.1, 131.9, 129.4, 127.7, 127.6, 124.2, 115.4, 113.8, 112.7, 56.2, 55.5, 45.0, 43.5, 32.2, 30.8, 27.3, 27.1, 26.5.; **HRMS (ESI):** *m/z* calcd. for $C_{26}H_{28}NO_2$ $[M+1]^+$: 386.21146; Found: 386.21176.

3-Cyclohexylidene-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67j)

Following the general experimental procedure (method A), pentafulvene derived from cyclohexanone **1c** (93 mg, 0.63 mmol), imine **66b** (170 mg, 0.76 mmol) and $Yb(OTf)_3$ (39 mg, 0.063 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67j** as a yellow solid in 59% (138 mg) yield with dr 92:8.

Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (120 mg, 0.82 mmol), phenylglyoxal monohydrate **65** (104 mg, 0.68 mmol), *p*-toluidine (73 mg, 0.68 mmol), $Yb(OTf)_3$ (42 mg, 0.068 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67j** in 51% (128 mg) yield with dr 93:7.



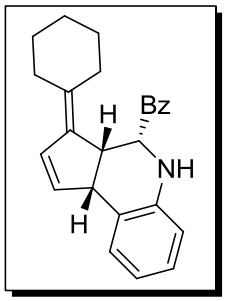
R_f: 0.32 (30% Ethyl acetate-hexane).; **mp:** 185-188 ^oC.; **IR (neat) υ_{max}:** 3366, 3054, 2924, 2825, 2827, 1682, 1612, 1594, 1507, 1443, 1298, 1260, 1216, 1070, 808, 772, 730, 692 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.56 (d, *J* = 7.5 Hz, 2 H), 7.43 (t, *J* = 7.5 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 2 H), 6.98 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H), 6.00-5.99 (m, 1 H), 5.91-5.89 (m, 1 H), 4.88 (d, *J* = 7.0 Hz, 1 H), 3.99 (d, *J* = 6.5 Hz, 1 H), 3.78 (t, *J* = 7.0 Hz, 1 H), 2.52-2.45 (m, 1 H), 2.27 (s, 3 H), 2.01-1.92 (m, 2 H), 1.69-1.66 (m, 1 H), 1.61-1.57 (m, 1 H), 1.46-1.43 (m, 1 H), 1.41-1.33 (m, 4 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 202.3, 141.7, 139.6, 139.2, 136.1, 133.0, 131.8, 129.2, 128.9,

127.8, 127.7, 127.6, 123.0, 114.8, 56,0, 44.7, 43.6, 32.2, 30.7, 27.3, 27.1, 26.5, 20.8.; **HRMS (ESI):** *m/z* calcd. for $C_{26}H_{28}NO$ $[M+1]^+$: 370.21654; Found: 370.21695.

3-Cyclohexylidene-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67k)

Following the general experimental procedure (method A), pentafulvene derived from cyclohexanone **1c** (69 mg, 0.47mmol), imine **66c** (98 mg, 0.47 mmol) and $Yb(OTf)_3$ (29 mg, 0.047 mmol) in 4 mL CH_3CN at room temperature for 8 h gave the product **67k** as a yellow solid in 52% (86 mg) yield with dr 80:20.

Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (141 mg, 0.96 mmol), phenyl glyoxal monohydrate **65** (121 mg, 0.80mmol), aniline (73 mg, 0.80mmol), $Yb(OTf)_3$ (49 mg, 0.08 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67k** in 21% (59 mg) yield with dr 90: 10.

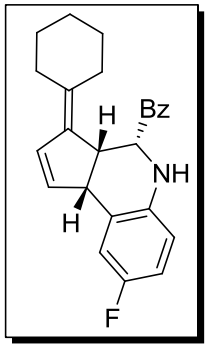


R_f: 0.35 (30% Ethyl acetate-hexane).; **mp:** 168-172 ^oC.; **IR (neat) υ_{max}:** 3375, 3060, 2925, 2859, 1682, 1573, 1496, 1483, 1477, 1219, 751, 730 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.56-7.54 (m, 2 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 7.15 (d, *J* = 7.5 Hz, 1 H), 7.02 (t, *J* = 7.5 Hz, 1 H), 6.77-6.74 (m, 1 H), 6.60 (d, *J* = 7.5 Hz, 1 H), 5.99 (d, *J* = 5.5 Hz, 1 H), 5.89-5.88 (m, 1 H), 4.87 (d, *J* = 7.0 Hz, 1 H), 4.01 (d, *J* = 6.5 Hz, 1 H), 3.77 (t, *J* = 7.0 Hz, 1 H), 2.49-2.46 (m, 1 H), 1.99-1.92 (m, 2 H), 1.69-1.67 (m, 1 H), 1.60-1.57 (m, 1 H), 1.43-1.40 (m, 1 H), 1.34-1.30 (m, 1 H), 1.28-1.19 (m, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 202.4, 144.6, 139.6, 139.4, 136.1, 133.0, 131.9, 129.1, 128.3, 127.7, 126.8, 122.9, 118.6, 114.6, 55.8, 44.7, 43.6, 32.3, 30.7, 27.1, 26.5.; **HRMS (ESI):** *m/z* calcd. for $C_{25}H_{26}NO$ $[M+1]^+$: 356.20089; Found: 356.20164.

3-Cyclohexylidene-8-fluoro-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67l)

Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (285mg, 1.9 mmol), phenyl glyoxal monohydrate **65** (197 mg, 1.29 mmol), 4-fluoroaniline (144 mg, 1.29 mmol), $Yb(OTf)_3$ (81 mg, 0.129 mmol) and MS 4 A^0 (200 mg)

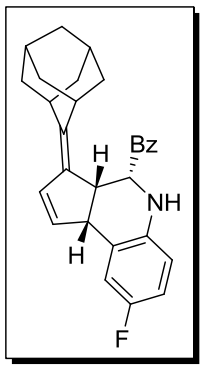
in 6 mL CH_3CN at room temperature for 8 h gave the product **67l** as a yellow solid in 31% (150 mg) yield with dr 91:9.



R_f: 0.29 (20% Ethyl acetate-hexane).; **mp:** 178-172 ^oC.; **IR (neat) υ_{max}:** 3360, 2924, 2859, 2829, 1681, 1504, 1486, 1246, 1234, 1208, 810 cm^{-1}.; **^1H NMR (500 MHz, $CDCl_3$):** 7.55 (d, *J* = 7.5 Hz, 2 H), 7.44 (t, *J* = 7.5 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 2 H), 6.89 (dd, *J* = 9.0, 2.0 Hz, 1 H), 6.75-6.72 (m, 1 H), 6.54-6.51 (m, 1 H), 5.96-5.90 (m, 2 H), 4.87 (d, *J* = 6.5 Hz, 1 H), 3.99 (d, *J* = 6.5 Hz, 1 H), 3.75 (t, *J* = 6.5 Hz, 1 H), 2.49-2.46 (m, 1 H), 2.01-1.93 (m, 2 H), 1.69-1.66 (m, 1 H), 1.61-1.57 (m, 1 H), 1.43-1.41 (m, 1 H), 1.36-1.19 (m, 4 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 202.4, 157.2, 155.3, 140.6, 139.5, 138.4, 135.8, 133.5, 132.0, 129.5, 127.7, 127.6, 124.3, 124.2, 115.2, 115.1, 114.7, 114.5, 113.6, 113.4, 55.8, 44.8, 43.3, 32.3, 30.8, 27.3, 27.1, 26.5.; **HRMS (ESI):** *m/z* calcd. for $C_{25}H_{25}FNO$ $[M+1]^+$: 374.19147; Found: 374.19147.

Compound 67m

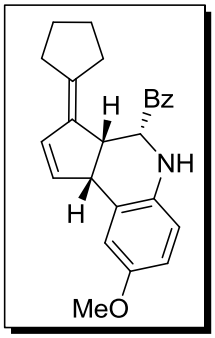
Following the general experimental procedure (method B), pentafulvene derived from adamantanone **1e** (100 mg, 0.50 mmol), phenylglyoxal monohydrate **65** (64 mg, 0.42 mmol), 4-fluoroaniline (47 mg, 0.42 mmol), $Yb(OTf)_3$ (26 mg, 0.042 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67m** as a yellow solid in 40% (72 mg) yield with dr 91:9.



R_f: 0.50 (20% Ethyl acetate-hexane).; **mp:** 212-216 ^oC.; **IR (neat) υ_{max}:** 3362, 2913, 2854, 1708, 1685, 1611, 1504, 1449, 1351, 1223 cm^{-1}.; **^1H NMR (500 MHz, $CDCl_3$):** δ 7.69 (d, *J* = 7.0 Hz, 2 H), 7.50 (t, *J* = 7.0 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 6.95 (dd, *J* = 9.5, 2.0 Hz, 1 H), 6.74 (m, 1 H), 6.52-6.49 (m, 1 H), 6.16-6.15 (m, 1 H), 5.99 (dd, *J* = 5.5 Hz, 2.0 Hz, 1 H), 4.91 (d, *J* = 6.5 Hz, 1 H), 4.06 (d, *J* = 7.0 Hz, 1 H), 3.78 (t, *J* = 7.0 Hz, 1 H), 2.77 (s, 1 H), 2.55 (s, 1 H), 1.93-1.87 (m, 2 H), 1.78 (m, 6 H), 1.68-1.63 (m, 2 H), 1.59-1.57 (m, 1 H), 1.08 (d, *J* = 7.0 Hz, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 200.7, 157.5, 155.6, 141.2, 140.1, 138.9, 136.9, 132.3, 131.6, 129.6, 128.2, 128.1, 125.8(2C), 115.3(2C), 115.2, 114.6, 114.4, 113.4, 113.2, 56.4, 45.2, 42.9, 40.1, 39.7, 37.6, 37.4, 37.1, 35.2, 34.6, 28.3, 27.9.; **HRMS (ESI):** *m/z* calcd. for $C_{29}H_{29}FNO$ $[M+1]^+$: 426.22277; Found: 426.22325.

3-Cyclopentylidene-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67n)

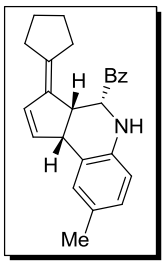
Following the general experimental procedure (method B), pentafulvene derived from cyclopentanone **1b** (40 mg, 0.30 mmol), phenyl glyoxal monohydrate **65** (31 mg, 0.20 mmol), *p*-anisidine (24 mg, 0.20 mmol), $Yb(OTf)_3$ (13 mg, 0.020 mmol) and MS 4 A^0 (100 mg) in 3 mL CH_3CN at room temperature for 8 h gave the product **67n** as a viscous liquid in 77% (58 mg), with dr 96:4.



R_f: 0.61 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3368, 3064, 2946, 2832, 1682, 1599, 1507, 1503, 1444, 1245, 1223, 1171, 1030 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.60 (d, *J* = 7.0 Hz, 2 H), 7.45 (t, *J* = 7.0 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 2 H), 6.77 (d, *J* = 2.0 Hz, 1 H), 6.66-6.64 (m, 1 H), 6.59 (d, *J* = 8.5 Hz, 1 H), 5.96 (d, *J* = 5.0 Hz, 1 H), 5.78-5.77 (m, 1 H), 4.98 (d, *J* = 6.5 Hz, 1 H), 4.02 (s, 1 H), 3.77 (s, 3 H), 3.66 (t, *J* = 7.0 Hz, 1 H), 2.36-2.32 (m,1 H), 2.27-2.22 (m, 1 H), 2.01-1.98 (m, 1 H), 1.62-1.58 (m, 2 H), 1.53-1.50 (m, 2 H), 1.39-1.35 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.2, 152.8, 139.4, 138.2, 137.7, 136.2, 135.2, 133.5, 131.9, 130.9, 130.2, 128.4, 127.8, 127.5, 115.5, 113.8, 112.8, 55.7, 55.6, 45.6, 45.2, 31.6, 30.7, 26.7, 26.1.; **HRMS (ESI):** *m/z* calcd for $C_{25}H_{26}NO_2$ $[M+1]^+$: 372.19581; Found: 372.19635.

3-Cyclopentylidene-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67o)

Following the general experimental procedure (method B), pentafulvene derived from cyclopentanone **1b** (47 mg, 0.35 mmol), phenyl glyoxal monohydrate **65** (36 mg, 0.24 mmol), *p*-toluidine (25 mg, 0.24 mmol), $Yb(OTf)_3$ (15 mg, 0.024 mmol) and MS 4 A° (100 mg) in 3 mL CH_3CN at room temperature for 8 h gave the product as a viscous liquid **67o** in 58% (49 mg) yield with dr 93:7.

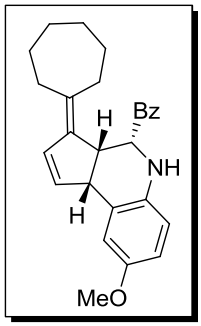


R_f: 0.58 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3362, 3054, 2928, 2825, 1684, 1612, 1594, 1443, 1288, 1267, 1216 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.58 (d, *J* = 7.5 Hz, 2 H),7.43 (t, *J* = 7.5 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 6.99 (s, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 6.57-6.55 (m, 1 H), 5.96 (d, *J* = 5.0 Hz, 1 H), 5.74-5.73 (m, 1 H), 4.98 (d, *J* = 7.0 Hz, 1 H), 4.01 (d, *J* = 6.5

Hz, 1 H), 3.64 (t, *J* = 7.0 Hz, 1 H), 2.38-2.33 (m, 1 H), 2.27-2.23 (m, 4 H), 2.02-1.95 (m, 1 H), 1.78-1.73 (m, 2 H), 1.63-1.56 (m, 2 H), 1.38-1.34 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.4, 142.1, 139.6, 138.3, 137.4, 136.1, 135.3, 132.7, 131.8, 131.0, 130.1, 128.9, 127.7, 127.5, 114.7, 55.4, 45.3, 45.2, 31.6, 30.6, 26.8, 26.2, 20.8.; **HRMS (ESI):** *m/z* calcd. for $C_{25}H_{26}NO$ $[M+1]^+$: 356. 20089; Found: 356.20169.

3-Cycloheptylidene-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67p)

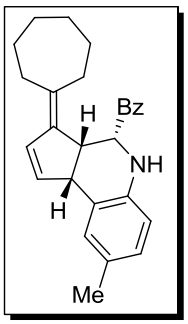
Following the general experimental procedure (method B), pentafulvene derived from cycloheptanone **1d** (159 mg, 0.99 mmol), phenyl glyoxal monohydrate **65** (100 mg, 0.66 mmol), *p*-anisidine (81 mg, 0.66 mmol), $Yb(OTf)_3$ (41 mg, 0.066 mmol) and MS 4 A^0 (200 mg) in 5 mL CH_3CN at room temperature for 8 h gave the product **67p** as a yellow viscous liquid in 45% (118 mg) yield with dr 90:10.



R_f: 0.56 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3364, 2926, 2865, 2812, 1683, 1507, 1479, 1251, 1231, 1215 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.52 (d, *J* = 7.0 Hz, 2 H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.29-7.26 (m, 2 H), 6.74 (d, *J* = 2.5 Hz, 1H), 6.64-6.62 (m, 1 H), 6.53 (d, *J* = 8.5 Hz, 1 H), 5.98-5.97 (m, 1 H), 5.86-5.84 (m, 1 H), 4.91 (d, *J* = 7.0 Hz, 1 H), 3.96 (d, *J* = 5.5 Hz, 1 H), 3.74 (s, 3 H), 3.69 (t, *J* = 7.5 Hz, 1 H), 2.61-2.56 (m, 1 H), 2.16-1,94 (m, 1 H), 1.94-1.88 (m, 1 H), 1.70-1.66 (m, 1 H), 1.52-1.39 (m, 5 H), 1.35-1.32 (m, 1 H), 1.31-1.23 (m, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.8, 152.5, 139.6, 138.6 (2C), 138.4, 134.9, 131.9, 129.9, 127.7, 127.6, 123.9, 115.4, 113.9, 112.8, 55.6, 55.4, 45.2, 43.9, 33.3, 31.9, 29.8, 29.5, 27.9, 27.2.; **HRMS (ESI):** *m/z* calcd for $C_{27}H_{30}NO_2$ $[M+1]^+$: 400.22711; Found: 400.22769.

3-Cycloheptylidene-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67q)

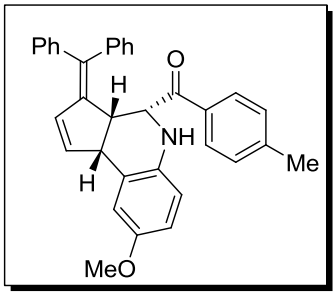
Following the general experimental procedure (method B), pentafulvene derived from cycloheptanone **1d** (251 mg, 1.57 mmol), phenyl glyoxal monohydrate **65** (159 mg, 1.05 mmol), *p*-toluidine (112 mg, 1.05 mmol), $Yb(OTf)_3$ (65 mg, 0.105 mmol) and MS 4 A^0 (200 mg) in 5 mL CH_3CN at room temperature for 8 h gave the product **67q** as a yellow solid in 34% (138 mg) yield with dr 92:8.



R_f: 0.51 (30% Ethyl acetate-hexane).; **mp:** 208-212 °C.; **IR (neat) υ_{max}:** 3373, 2924, 2860, 1683, 1577, 1494, 1482, 1478, 1221 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.55 (d, *J* = 7.0 Hz, 2 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.30 (t, *J* = 7.5 Hz, 2 H), 6.98 (s, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 6.55 (d, *J* = 8.0 Hz, 1 H), 5.99 (d, *J* = 5.5 Hz, 1 H), 5.85-5.83 (m, 1 H), 4.95 (d, *J* = 6.5 Hz, 1 H),3.97 (s, 1 H), 3.72 (t, *J* = 7.0 Hz, 1 H), 2.65-2.59 (m, 1 H), 2.27 (s, 3 H), 2.19-2,14 (m,1 H), 1.94-1.89 (m, 1 H), 1,73-1.69 (m, 1 H), 1.54-1.51 (m, 3 H), 1.49-1.41 (m, 2 H), 1.36-1.33 (m, 1 H), 1.31-1.25 (m, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.7, 142.1, 139.7, 139.1, 138.7, 134.8, 131.8, 129.7, 128.9, 127.7, 127.6, 127.5, 122.7, 114.6, 55.3, 44.9, 44.1, 33.3, 31.9, 29.8, 29.6, 27.9, 27.2, 20.8.; **HRMS (ESI):** *m/z* calcd for $C_{27}H_{30}NO$ $[M+1]^+$: 384.23219; Found: 384.23331.

3-(Diphenylmethylene)-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(p-tolyl)methanone (67r)

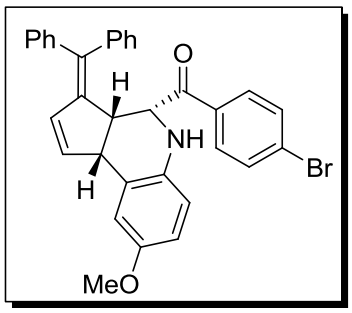
Following the general experimental procedure (method B), diphenylfulvene **1f** (97 mg, 0.40 mmol), 2-oxo-2-*p*-tolylacetaldehyde (50 mg, 0,34 mmol), *p*-anisidine (42 mg, 0.34 mmol), $Yb(OTf)_3$ (21 mg, 0.034 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67r** as a viscous liquid in 46% (75 mg) yield with dr 91:9.



R_f: 0.59 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3368, 2831, 1668, 1599, 1496, 1261, 1241, 1232, 1209 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 (d, *J* = 8.0 Hz, 2 H), 7.27-7.26 (m, 3 H), 7.15-7.09 (m, 7 H), 6.83 (d, *J* = 2.5 Hz, 1 H), 6.73-6.71 (m, 2 H), 6.52 (dd. *J* = 8.5, 3.0 Hz, 1 H), 6.44 (dd, *J* = 6.0, 3.0 Hz, 1 H), 6.35-6.31 (m, 2 H), 4.53 (d, *J* = 7.0 Hz, 1 H), 4.33 (t, *J* = 7.5 Hz, 1 H), 4.14 (d, *J* = 8.0 Hz, 1 H), 3.73 (s, 3 H), 2.36 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 196.9, 153.3, 145.4, 143.2, 142.6, 142.5, 140.9, 136.3, 134.9, 133.6, 132.8, 129.8, 129.1, 128.5, 128.4, 127.7, 126.9, 126.6, 126.1, 115.8, 113.1, 112.3, 55.5, 53.7, 44.9, 42.4.; **HRMS (ESI):** *m/z* calcd. for $C_{34}H_{30}NO_2$ $[M+H]^+$: 484.22765; Found: 484.22784.

(4-Bromophenyl)-3-(diphenylmethylene)-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)methanone (67s)

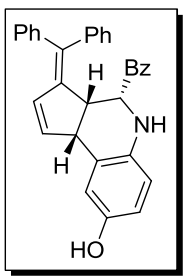
Following the general experimental procedure (method B), diphenylfulvene **1f** (100 mg, 0.43 mmol), 2-(4-bromophenyl)-2-oxoacetaldehyde (77 mg, 0.36 mmol), *p*-anisidine (44 mg, 0.36 mmol), $Yb(OTf)_3$ (22 mg, 0.036 mmol) and MS 4 A° (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **67s** as a yellow solid in 58% (114 mg) yield with dr 96:4.



R_f: 0.41 (20% Ethyl acetate-hexane).; **mp:** 86-90 °C.; **IR (neat) υ_{max}:** 3356, 3064, 2836, 1671, 1583, 1504, 1447, 1424, 1272, 1166, 836, 760 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.48 (d, *J* = 8.5 Hz, 2 H), 7.37-7.35 (m, 2 H), 7.29-7.28 (m, 3 H), 7.18-7.13 (m, 5 H), 6.86 (dd, *J* = 8.0, 2.0 Hz, 1 H), 6.76-6.74 (m, 2 H), 6.58-6.55 (m, 1 H), 6.45 (dd, *J* = 6.0, 2.5 Hz, 1 H), 6.37-6.35 (m, 2 H), 4.52 (d, *J* = 7.0 Hz, 1 H), 4.38 (t, *J* = 7.5 Hz, 1 H), 4.18-4.17 (m, 1 H), 3.75 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 196.4, 153.5, 145.1, 142.4, 140.7, 135.9, 133.9, 132.9, 131.7, 129.7 (2C), 129.1, 128.6, 128.2, 127.9, 127.8, 127.2, 126.7, 126.3, 115.9, 113.1, 112.4, 55.6, 53.9, 44.9, 42.5.; **HRMS (ESI):** *m/z* calcd for $C_{33}H_{26}BrNO_2$ M^+: 547.11469; Found: 547.09266.

3-(Diphenylmethylene)-8-hydroxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (67t)

Following the general experimental procedure (method B), the diphenyl fulvene **1f** (100 mg, 0.43 mmol), phenyl glyoxal monohydrate **65** (65 mg, 0.43 mmol), 4-hydroxy aniline (47 mg, 0.43 mmol), $Yb(OTf)_3$ (26 mg, 0.043 mmol) and 4 A^0 MS (100 mg) in 5 mL CH_3CN at room temperature for 8 h gave the product **67t** as a viscous liquid in 47% (92 mg) yield with dr 90: 10.

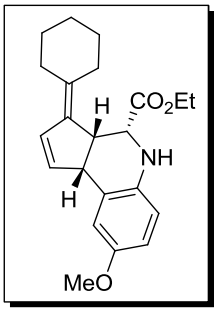


R_f: 0.38 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3356, 3056, 1667, 1593, 1503, 1491, 1443, 1214, 1209 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.48-7.46 (m, 2 H)**,** 7.31 (t, *J* = 7.5 Hz, 2 H), 7.26-7.16 (m, 3 H), 7.13-7.09 (m, 5 H), 6.75-6.71 (m, 3 H), 6.39-6.36 (m, 2 H), 6.34-6.32 (m, 1 H), 6.23 (d, *J* = 8.5 Hz, 1 H), 4.56 (d, *J* = 7.0 Hz, 1 H), 4.34 (t, *J* = 7.5 Hz, 1 H),

4.11-4.09 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 197.7, 149.5, 145.2, 142.5(2C), 140.8, 137.2, 135.5, 133.7, 132.8, 132.7, 129.0, 128.5, 128.4, 128.2, 127.8, 127.0, 126.6, 126.5, 125.3, 116.1, 114.5, 113.9, 53.7, 44.7, 42.3.; **HRMS (ESI):** *m/z* calcd. for $C_{32}H_{26}NO_2$ $[M+1]^+$: 456.19635; Found: 456.21693.

Ethyl 3-cyclohexylidene-8-methoxy-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinoline-4-carboxylate (69a)

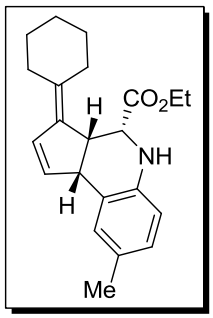
Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (150 mg, 1.03 mmol), ethyl glyoxalate **68** (139 mg, 1.37 mmol), *p*-anisidine (84 mg, 0.68 mmol), $Yb(OTf)_3$ (42 mg, 0.068 mmol) and MS $4A^0$ (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **69a** as a yellow solid in 35% (84 mg) yield with dr 92:8.



R_f: 0.55(30% Ethyl acetate-hexane).; **mp:** 108-112 °C.; **IR (neat) υ_{max}:** 3374, 2932, 2857, 1725, 1509, 1449, 1382, 1258, 1189, 814 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 6.74 (d, *J* = 2.5 Hz, 1 H), 6.59 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.51 (d, *J* = 8.5 Hz, 1 H), 6.29-6.27 (m, 1 H), 6.04-6.02 (m, 1 H), 3.99 (d, *J* = 7.0 Hz, 1 H), 3.95 (d, *J* = 7.5 Hz, 1 H), 3.89-3.85 (m, 2 H), 3.73 (s, 3 H), 3.62 (t, *J* = 7.0 Hz, 1 H), 2.33-2.24 (m, 4 H), 1.70-1.59 (m, 6 H), 1.07 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 172.5, 152.7, 138.2, 137.4, 135.7, 132.7, 129.1, 124.5, 115.5, 113.7, 112.6, 59.9, 55.5, 54.9, 44.5, 42.3, 32.1, 31.7, 27.7, 27.6, 26.8, 14.1.; **HRMS (ESI):** *m/z* calcd for $C_{22}H_{28}NO_3$ $[M+1]^+$: 354.20637; Found: 354.20715.

Ethyl 3-cyclohexylidene-8-methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinoline-4-carboxylate (69b)

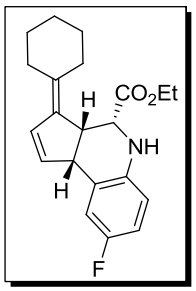
Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (145 mg, 0.99 mmol), ethyl glyoxalate **68** (134 mg, 1.32 mmol), *p*-toluidine (70 mg, 0.66 mmol), $Yb(OTf)_3$ (41mg, 0.066 mmol) and MS $4A^0$ (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **69b** as a yellow solid in 36% (80 mg) yield with dr 91:9.



R_f: 0.53 (30% Ethyl acetate-hexane).; **mp:** 94-98 °C.; **IR (neat) υ_{max}:** 3379, 2933, 2859, 1724, 1621, 1504, 1451, 1375, 1249, 1185, 817 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.02 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H), 6.32-6.30 (m, 1 H), 6.08-6.07 (m, 1 H), 4.03-3.99 (m, 2 H), 3.95-3.90 (m, 2 H), 3.66 (t, *J* = 7.0 Hz, 1 H), 2.37-2.33 (m, 2 H), 2.31-2.27 (m, 5 H), 1.73-1.57 (m, 6 H), 1.11 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 172.6, 141.2, 138.7, 135.8, 132.6, 128.9, 128.8, 127.6, 127.3, 123.3, 114.7, 60.0, 54.7, 44.2, 42.4, 32.1, 31.7, 27.7, 27.6, 26.8, 20.7, 14.1.; **HRMS (ESI):** *m/z* calcd. for $C_{22}H_{28}NO_2$ $[M+1]^+$: 338.21146; Found: 338.21158.

Ethyl 3-cyclohexylidene-8-fluoro-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinoline-4-carboxylate (69c)

Following the general experimental procedure (method B), pentafulvene derived from cyclohexanone **1c** (155 mg, 1.06 mmol), ethyl glyoxalate **68** (145mg, 1.42 mmol), 4-fluoroaniline (78 mg, 0.71mmol), $Yb(OTf)_3$ (49mg, 0.071 mmol) and MS 4 A° (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **69c** as a yellow viscous liquid in 19% (46 mg) yield with dr 90:10.

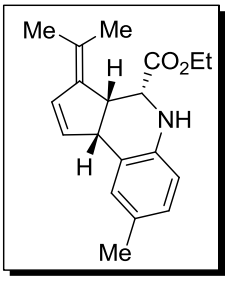


R_f: 0.55 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3371, 2929, 2855, 2832, 1725, 1503, 1475, 1435, 1235, 1181, 1033, 809 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** 6.92 (dd, *J* = 9.0, 2.0 Hz, 1 H), 6.77-6.73 (m, 1 H), 6.56-6.53 (m, 1 H), 6.33-6.32 (m, 1 H), 6.02 (dd, *J* = 5.5, 1.5 Hz, 1 H), 4.03-3.99 (m, 2 H), 3.93-3.89 (m, 2 H), 3.65 (t, *J* = 7.0 Hz, 1 H), 2.37-2.26 (m, 4 H), 1.74-1.62 (m, 6 H), 1.09 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** 172.3, 157.3, 155.4, 139.7, 137.7, 135.4, 133.2, 129.4, 124.9, 124.8, 115.3, 115.2, 114.6, 114.5, 113.4, 113.2, 60.1, 54.8, 44.4, 42.1, 32.1, 31.7, 27.7, 27.6, 26.8.; **HRMS (ESI):** *m/z* calcd. for $C_{21}H_{25}FNO_2$ $[M+H]^+$: 342.18638; Found: 342.18738.

Ethyl 8-methyl-3-(propan-2-ylidene)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinoline-4-carboxylate (69d)

Following the general experimental procedure (method B), dimethyl fulvene **1a** (125 mg, 1.17 mmol), ethyl glyoxalate **68** (160mg, 1.57 mmol), *p*-toluidine (84 mg, 0.78mmol),

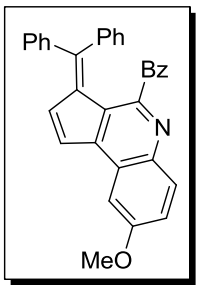
$Yb(OTf)_3$ (48mg, 0.078 mmol) and MS 4 A^0 (100 mg) in 4 mL CH_3CN at room temperature for 8 h gave the product **69d** as a yellow viscous liquid in 28% (66 mg) yield with dr 88:12.



R_f: 0.57 (30% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3375, 2929, 2846, 1726, 1627, 1500, 1459, 1255, 1179 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7. 02 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.55 (d, *J* = 8.0 Hz, 1 H), 6.29-6.27 (m, 1 H), 6.07 (d, *J* = 5.5 Hz, 1 H), 4.08 (d, *J* = 7.0 Hz, 1 H), 4.04 (d, *J* = 6.5 Hz, 1 H), 3.96-3.91 (m, 1 H), 3.90-3.85 (m, 1 H), 3.66 (t, *J* = 7.0 Hz, 1 H), 2.28 (s, 3 H), 1.91 (s, 3 H), 1.83 (s, 3 H), 1.09 (t, *J* = 7.0 Hz, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 172.6, 141.1, 138.8, 129.5, 128.8, 127.7, 127.4, 124.4, 123.3, 114.7, 60.0, 54.2, 44.4, 43.1, 21.4, 21.0, 20.7, 14.0.; **HRMS (ESI):** *m/z* calcd. for $C_{19}H_{24}NO_2$ $[M+1]^+$: 298.18016; Found: 298.18031.

(3-(Diphenylmethylene)-8-methoxy-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (70a)

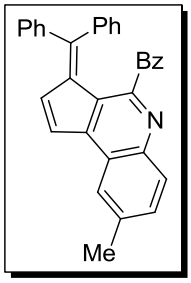
Following the general experimental procedure, tetrahydroquinoline derivative **67b** (50 mg, 0.11 mmol) and DDQ (48 mg, 0.21 mmol) in 5 mL $CHCl_3$ at room temperature for 4 h gave the product **70a** as a red solid in 95% (47 mg) yield.



R_f: 0.51 (20% Ethyl acetate-hexane).; **mp:** 234-236 °C.; **IR (neat) υ_{max}:** 3060, 2931, 2832, 1667, 1620, 1578, 1559, 1498, 1456, 1428, 1280, 1222, 1050, 833, 730 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 9.5 Hz, 1 H), 7.81-7.79 (m, 2 H), 7.47-7.41 (m, 2 H), 7.39-7.35 (m, 4 H), 7.34-7.31 (m, 1 H), 7.29-7.24 (m, 4 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 6.88 (t, *J* = 7.5 Hz, 2 H), 6.84 (d, *J* = 5.5 Hz, 1 H), 6.66 (t, *J* = 7.5 Hz, 1 H), 3.99 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 192.1, 158.5, 155.2, 149.6, 149.1, 142.5, 142.2, 141.5, 138.5, 137.0, 134.6, 132.8, 132.5, 131.7, 131.6, 129.5, 128.7, 128.5, 127.8, 127.1, 125.6, 124.4, 124.2, 121.8, 101.5, 55.7.; **HRMS (ESI):** *m/z* calcd for $C_{33}H_{24}NO_2$ $[M+1]^+$: 466.18016; Found: 466.18106.

(3-(Diphenylmethylene)-8-methyl-3H-cyclopenta[c]quinolin-4-yl)(phenyl)methanone (70b)

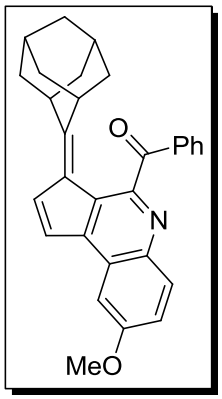
Following the general experimental procedure, tetrahydroquinoline derivative **67c** (70 mg, 0.15 mmol) and DDQ (70 mg, 0.31mmol) in 5 mL $CHCl_3$ at room temperature for 4 h gave the product **70b** as a red coloured liquid in 92% (64 mg) yield.



R_f: 0.49 (20% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 3027, 2920, 2861, 1668, 1558, 1497, 1446, 1390, 1315, 1243, 1180, 1054, 1002, 901 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 9.0 Hz, 1 H), 7.88 (s, 1 H), 7.81-7.79 (m, 2 H), 7.48 (dd, *J* = 9.0, 2.0 Hz, 1 H), 7.44-7.39 (m, 3 H), 7.35 (t, *J* = 7.0 Hz, 2 H), 7.28-7.22 (m, 4 H), 6.98 (d, *J* = 7.5 Hz, 2 H), 6.87-6.82 (m, 3 H), 6.62 (t, *J* = 7.5 Hz, 1 H), 2.58 (s, 3 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 191.7, 154.9, 150.9, 149.7, 144.1, 142.6, 142.3, 138.6, 137.2, 136.9, 134.6, 132.8, 132.6, 132.5, 131.7, 131.4, 129.9, 129.4, 128.7, 128.4, 127.8, 126.9, 125.3, 124.4, 123.2, 122.5, 21.9.; **HRMS (ESI):** *m/z* calcd. for $C_{33}H_{24}NO$ $[M+1]^+$: 450.18524; Found: 450.18466.

Compound 70c

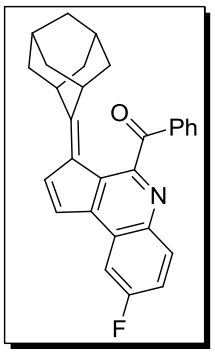
Following the general experimental procedure, tetrahydroquinoline derivative **67f** (150 mg, 0.34 mmol) and DDQ (156 mg, 0.69mmol) in 5 mL $CHCl_3$ at room temperature for 4 h gave the product **70c** as a yellow solid in 56% (84 mg) yield.



R_f: 0.34 (20% Ethyl acetate-hexane).; **mp:** 184-188 ^oC.; **IR (neat) υ_{max}:** 2911, 2852, 1670, 1606, 1562, 1497, 1427, 1324, 1220, 1163, 1053, 1025, 969, 911, 784, 729 cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.24-8.23 (m, 2 H), 7.95 (d, *J* = 9.0 Hz, 1 H), 7.60-7.57 (m, 1 H), 7.48 (t, *J* = 8.0 Hz, 2 H), 7.31-7.27 (m, 2 H), 7.25-7.22 (m, 2 H), 3.96 (s, 3 H), 3.41 (s, 1 H), 3.07 (s, 1 H), 2.06-2.03 (m, 2 H), 1.99-1.95 (m, 4 H), 1.85-1.81 (m, 3 H), 1.74-1.72 (m, 1 H), 1.51 (dd, *J* = 12.5, 2.5 Hz, 2 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 192.6, 167.4, 158.3, 149.9, 148.8, 140.9, 136.1, 133.1, 131.3(2C), 130.9, 130.6, 128.3, 124.3, 124.1, 122.3, 121.5, 101.3, 55.4, 40.3, 39.3, 38.2, 38.1, 36.5, 27.8.; **HRMS (ESI):** *m/z* calcd. for $C_{30}H_{28}NO_2$, $[M+1]^+$: 434.21146; Found: 434.20996.

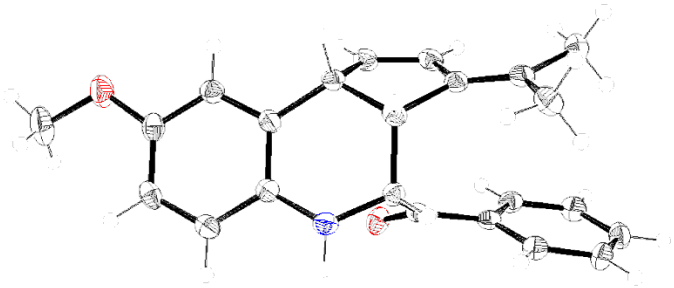
Compound 70d

Following the general experimental procedure, tetrahydroquinoline derivative **67m** (70 mg, 0.16 mmol) and DDQ (75 mg, 0.33mmol) in 5 mL $CHCl_3$ at room temperature for 4 h gave the product **70d** as a yellow viscous liquid in 53% (37 mg) yield.



R_f: 0.47 (20% Ethyl acetate-hexane).; **IR (neat) υ_{max}:** 2986, 2837, 1668, 1601, 1508, 1424, 1327, 1219, 1186, 1055, 1085, 931cm^{-1}.; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.23 (d, *J* = 7.5 Hz, 2 H), 8.09-8.06 (m, 1 H), 7.71 (dd, *J* = 9.0, 2.5Hz, 1 H), 7.62 (t, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 8.0 Hz, 2 H), 7.42 (m, 1 H), 7.30 (d, *J* = 5.5 Hz, 1 H), 7.25 (d, *J* = 5.5 Hz, 1 H), 3.44 (s, 1 H), 3.08 (s, 1 H), 2.09-2.06 (m, 2 H), 1.99-1.96 (m, 4 H), 1.87-1.79 (m, 3 H), 1.74 (d, *J* = 12.5 Hz, 1 H), 1.65 (s, 1 H), 1.54-1.51 (m, 1 H).; **^{13}C NMR (125 MHz, $CDCl_3$):** δ 192.6, 169.6, 161.9, 159.9, 151.5, 149.7, 149.6, 141.9, 135.7, 133.5, 132.3, 132.2, 131.3, 130.9(2C), 128.4, 124.2, 123.9, 123.8, 122.1, 119.1, 118.9, 107.1, 106.9, 40.4, 39.6, 38.4, 38.2, 36.4, 27.8.; **HRMS (ESI):** *m/z* calcd. for $C_{29}H_{25}FNO_2$, $[M+1]^+$: 422.19147; Found: 422.19220.

Crystal Data: Compound 67a



CCDC 1451008

Chemical formula moiety	$C_{23}H_{23}NO_2$
Chemical formula sum	$C_{23}H_{23}NO_2$
Chemical formula weight	345.42
Symmetry cell setting	monoclinic
Symmetry space group name	P21/c
Cell length a	12.604 (4)
Cell length b	10.100 (5)

Cell length c	14.236 (5)
Cell angle alpha	90.00
Cell angle beta	94.478 (9)
Cell angle gamma	90.00
Cell volume	1806.7 (16)
Cell formula units Z	4
Cell measurement temperature	150K
Cell measurement reflns used	2654
Cell measurement theta min	3.0
Cell measurement theta max	27.5
Exptl crystal description	Block
Exptl crystal size max	0.20
Exptl crystal size mid	0.20
Exptl crystal size min	0.10
Exptl crystal density diffrn	1.270
Exptl crystal_density_method	'not measured'
Exptl crystal colour	colourless
Exptl crystal F 000	736
Exptl absorpt coefficient mu	0.080
Exptl absorpt correction-type	Empirical
Exptl absorpt correction T min	0.984
Exptl absorpt correction T max	0.992
Diffrn ambient temperature	150K
Diffrn radiation wavelength	0.71073

4.6. References

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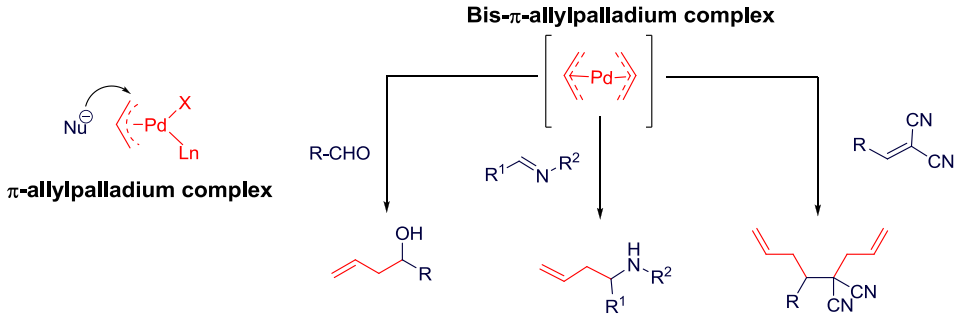
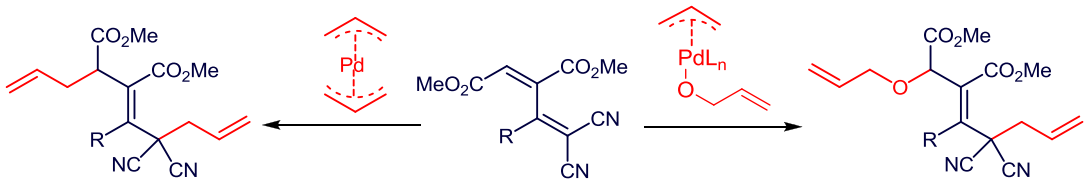
SUMMARY

The thesis entitled **"Study on the Reactivity of Bis-π-allyl and Related Palladium Intermediates with Functionalized 1,3-Dienes and Carbonyl Compounds & Lewis Acid Catalyzed Povarov Reaction Using Pentafulvenes as Dienophiles**" presents the results of our investigations on the reactivity of bis-π-allyl palladium and related complexes with functionalized conjugated dienes and carbonyl compounds and synthesis of tetrahydroquinoline derivatives by Lewis acid catalyzed Povarov reaction of pentafulvenes and aryl imines.

The first chapter deals with a brief overview on the reactivity of π-allyl palladium complex (Tsuji-Trost reaction) and amphiphilic bis-π-allyl and related palladium complexes with various substrates.

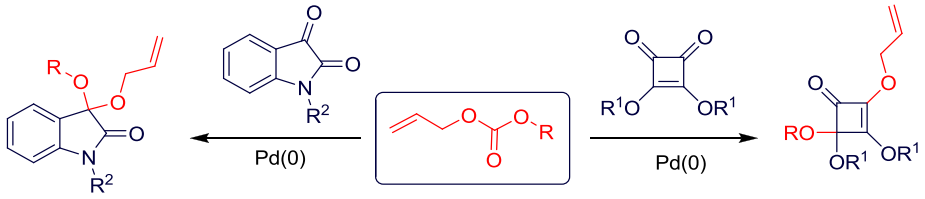


The second chapter describes the reaction of bis-π-allyl palladium and related complexes with functionalized dienes. Amphiphilic π-allyl palladium complexes reacted with conjugated dienes and provided regioselective 1,4-intercepted products.

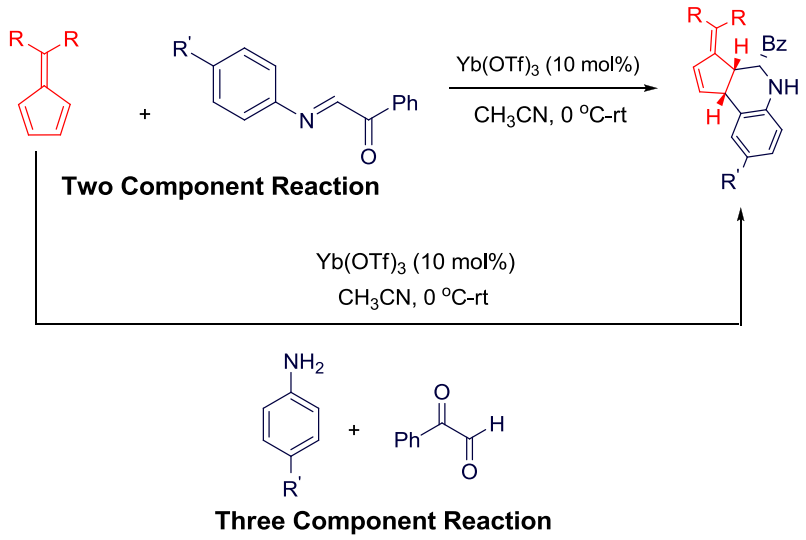


The third chapter outlines the results of our investigations on the palladium-catalyzed interceptive decarboxylative 1,4-addition of allyl carbonates with squarates. Decarboxylative allylation reaction of allyl carbonates is further extended to functionalize C-3 carbonyl group of N-substituted isatins and furnished oxindole derivatives by 1,2-interceptive addition. Compounds containing electrophilic carbonyl group such as acenaphthenequinone and

diethylketomalonate also underwent decarboxylative 1,2-addition by reacting with allyl carbonates in the presence of palladium catalyst.



The detailed investigation of the inverse-electron-demand aza-Diels-Alder reaction of aryl imines generated from phenylglyoxal and anilines with pentafulvenes constitutes the subject matter of the fourth chapter of the thesis. Lewis acid catalyzed Povarov reaction of pentafulvenes was conducted in both two component as well as in three component fashion and the reaction afforded tethahydroquinoline derivatives in moderate to good yields. Synthetic utility of this reaction is further highlighted by constructing quinoline fused fulvene derivatives by DDQ oxidation.



In conclusion, we have conducted a detailed investigation on the reactivity of bis-π-allyl palladium and related complexes with functionalized 1,3-butadienes and studied the palladium catalyzed interceptive decarboxylative addition of allyl carbonates with squaric acid esters and N-substituted isatins. Lewis acid catalyzed Povarov reaction of pentafulvenes was carried out with aryl imines generated from phenylglyoxal and anilines and the reaction furnished ring fused tetrahydroquinoline derivatives.

List of publications

1. Bis-functionalization of 1,3-Dienes *via* 1,4-Conjugate Addition of Amphiphilic Bis-π-allyl and Related Palladium Intermediates. **T. V. Baiju**; Ajesh Vijayan; Nayana Joseph; Preethanuj Preethalayam; K. V. Radhakrishnan; E. Suresh; Yoshinori Yamamoto *Synlett*. **2014**, *25*, 359-364.

2. Palladium Catalyzed Interceptive Decarboxylative Addition of Allyl Carbonates with Carbonyl group. **T. V. Baiju**; Nayana Joseph; Jainu Ajit; Praveen Prakash; K. V. Radhakrishnan; Yoshinori Yamamoto *Synlett.* **2014**, *25*, 1246-1252.

3. Palladium Catalyzed Ring Opening of Cyclopropane Appended Spirotricyclic Olefins with Soft Nucleophiles and Organoboronic Acids: Facile Synthesis of Functionalized Spiro[2.4]heptenes. E. Jijy; Praveen Prakash; **T. V. Baiju**; M. Shimi; Y. Yamamoto; E. Suresh; K. V. Radhakrishnan *Synthesis* **2014**, 46, 2629-2643.

4. Transition Metal Free Intramolecular Approach for the Synthesis of Cyclopenta[b]chromene Derivatives from Phenol Substituted Fulvene Derived Azabicyclic Olefins. Ajesh Vijayan; **T. V. Baiju;** Sunil Varughese; K. V. Radhakrishnan *Tetrahedron Lett*. **2016**, *57*, 2965-2968.

5. Rhodium Catalyzed Oxidative Coupling of Salicylaldehydes with Heterobicyclic Olefins towards the Synthesis of Fused Chromanones. Ajesh Vijayan; **T. V. Baiju;** E. Jijy; Praveen Prakash; M. Shimi; Petri M. Pihko; Nayana Joseph; K. V. Radhakrishnan *Tetrahedron* **2016**, *72*, 4007-4015.

6. Lewis acid Catalyzed Povarov Reaction Using Pentafulvenes and Spiro-cyclopentadienes as Dienophiles. **T. V. Baiju;** S. Saranya; K. V. Radhakrishnan [To be submitted to *Synthesis*]

Papers presented at conferences

1. Palladium Catalyzed Interceptive Decarboxylative Addition of Allyl carbonates to Squarates and Isatins, **Baiju T. V**. and K. V. Radhakrishnan, a poster presented at National Symposium on Transcending Frontiers in Organic Chemistry (TFOC), held at CSIR-National Institute for Interdisciplinary Science & Technology, Thiruvananthapuram, October **2014**

2. Palladium Catalyzed Interceptive Decarboxylative Addition of Allyl carbonates with Carbonyl group, **Baiju T. V**. and K. V. Radhakrishnan, a poster presented at CRSI National Symposium in Chemistry, held at CSIR-North East Institute of Science & Technology, Jorhat, July **2014**

3. Synthesis of Alkylidene Cyclopentenes by Palladium Catalyzed Desymmetrization of Pentafulvene Derived Bicyclic Hydrazine with Soft Nucleophiles, **Baiju T. V**., Rani Rajan and K. V. Radhakrishnan, a poster presented at International Conference on Drug Development for Orphan/Neglected Diseases, held at CSIR-Central Drug Research Institute, Lucknow, February **2013**.

4. Palladium Catalyzed 1,8-Conjugate Addition to Heptafulvene *via* Bis-π-allyl Palladium Complexes, **Baiju T. V.**, Sholly Clair George., Jijy, E., Praveen Prakash and K. V. Radhakrishnan**,** a poster presented at International Conference on Heterocyclic Chemistry, held at University of Rajasthan, Jaipur, December, **2011**.