Phosphine-Mediated Annulations of Designed Enones and Ynones

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Dedicated to my mother,
Who taught me how Important
it is for a girl to be educated

Declaration

I do hereby declare that the work presented in this thesis titled "***Phosphine-Mediated Annulations of Designed Enones and Ynones***" has been carried out by me under the supervision of **Dr. S. S. V. Rama Sastry** in the Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, India. This work has not been submitted in part or full for a degree, diploma, or a fellowship to any other university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly with due acknowledgments of collaborative work and discussions. This thesis is a bonafide record of original work done by me and all sources listed within have been detailed in the bibliography.

Lona Dutta

In my capacity as the supervisor of the candidate's thesis work, I certify that the above statements by the candidate are true to the best of my knowledge.

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The thesis entitled as "*Phosphine-mediated annulations of designed enones and ynones*" describes the efforts towards the development of novel metal-free and phosphine-mediated strategies for the annulations of designed enones and ynones for the synthesis of five- and six-membered carbo- and heterocycles. The content of the thesis has been divided into three chapters. In all the chapters, a brief introduction is provided, the compounds are sequentially numbered (bold), and references are marked sequentially as superscript and listed at the end of the thesis.

Cyclopentanoids persist as essential scaffolds in many natural products and pharmaceutically relevant compounds. The importance of the same in the area of synthetic organic chemistry, pharmaceuticals, and material sciences holds the key interest to develop efficient synthetic protocols. Towards this, we developed the first metal- and reductant-free intramolecular reductive aldol reaction of α-substituted dienone-tethered aldehydes to access highly functionalized cyclopentannulated arenes and heteroarenes bearing two contiguous stereogenic centers, one of them being an all-carbon quaternary center, in good yields and diastereoselectivities. After successfully establishing phosphine- and water-promoted reductive aldol product with α-substituted dienone-aldehydes, we were curious about the reductive aldol strategy with α-substituted dienone-ketones. Interestingly, in the presence of stoichiometric tributylphosphine and excess amount of water, α-substituted dienone-ketones undergo intramolecular aldol reaction to afford an unusual class of cyclopentanoids possessing two contiguous stereogenic centres. The mechanistic details were thoroughly elucidated by performing control experiments.

Oxyamination reaction is the deployment of an amino group and a hydroxyl group across the carbon-carbon multiple bond (alkenes, alkynes) and persists as a useful transformation in chemical synthesis. There are enormous transition metal-catalyzed methods reported for oxyamination of olefins. However, the major drawback associated with these transition metals is being expensive, toxic and air sensitive. Moreover, difficulty in removing all the traces of metal from the reaction limited its use on an industrial scale. In response to this, metal-free transformations are gaining attention because they are cheap, less air sensitive and reactive under mild conditions. Towards this, we have developed the first phosphine-mediated intramolecular oxyamination of α,β-ynones. This work encompasses a practical and efficient redox cyclization of 1-(2-nitroaryl)prop-2-ynones to provide a new entry to the synthesis of 3-hydroxyquinoline-4-ones (3HQs) under neutral condition. The mechanistic insights were further gained by performing control experiments. After successfully establishing a phosphine-promoted oxyamination reaction, we intended to illustrate the synthetic utility of

the oxyaminated products. In this regard, we established the synthesis of japonine and its analogs. Japonine was first isolated from the leaves of *Orixa japonica* and shows relaxant activity against rat small intestine. Additionally, the synthetic utility of this methodology was extrapolated to the synthesis of 3,4-dialkoxyquinolines, a less-known class of compound known to have significant biological properties. Furthermore, after realizing the importance of this core, we made a one-pot synthesis of 3,4-di-*tert*-butyloxycarbonyloxy-2-phenylquinolines directly from nitro-ynones. We synthesized 3-hydroxy-3-phenylquinoline-2,4-dione from MnO_2 oxidation of, which is a natural metabolite of some *Pseudomonas* species.

α,β-Ynones are unique synthetic materials that can act as a pool of electrophiles and serve as easily accessible synthons in many chemical transformations. After successfully developing phosphine-mediated oxyamination of ynones tethered to a nitro group, we wanted to further study the field of phosphine-promoted ynone chemistry. In this regard, after a detailed literature survey, we took α,β-ynone having α′-hydrogens available. On the other hand, cyclopenta[*b*]indole moiety resides as a part structure of various bioactive natural products and pharmaceutically relevant compounds. Moreover, to synthesize the same, [3+2] annulation of nitroindoles were explored only with allenoates. Nitroolefins with ynones have not been employed yet to synthesize cyclopenta[*b*]indole moiety. Hence, we aspired to explore 3-nitroindoles in the [3+2] annulation process involving designed ynones and phosphines. We have disclosed the first phosphine-catalyzed denitrative rearomatizing [3+2] annulation of α,β-ynones with 3-nitroindole to access an unprecedented α-arylidene cyclopenta[*b*]indoles in good yields. In continuation, we extended this methodology by establishing [3+2] annulation reaction with 2-nitroheteroaromatic core to synthesize 3-benzylidene-cyclopenta[*b*]benzofuran-2-ones, 3-benzylidene-cyclopenta[*b*]-fused benzothiophenes. Furthermore, after exhaustive studies with the role of substituent around the ynone part bearing α′-hydrogen and nitroheteroarenes, we were curious about the fate of the reaction with ynones lacking α′-hydrogen and 3-nitroindole under our optimized condition. Interestingly, we isolated a separable mixture of α- and β-N-indolyl enones with 1:1 regioisomeric ratio, establishing their first synthesis. Furthermore, the utility of this methodology was extended to the synthesis of natural product, Bruceolline E in two steps.

Ac	acetyl
ACN	acetonitrile
aq	aqueous
atm	atmospheric
BINOL	1,1′-binaphthalene-2,2′-diol
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
brs	broad singlet
^{n}Bu	butyl
^{t}Bu	*tert*-butyl
calcd	calculated
COD	cyclooctadiene
Cy	cyclohexyl
d	day(s)
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of a doublet
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*'-dimethyl formamide
DMSO	dimethyl sulfoxide
dq	doublet of a quartet
dr	diastereomeric ratio
dt	doublet of a triplet
ee	enantiomeric excess
eq	equivalents
ESI	electron spray ionization
FT-IR	Fourier-transform infrared spectroscopy
h	hour(s)
HFIP	1,1,1,3,3,3-hexafluoroisopropanol
HPLC	high-performance liquid chromatograp

HRMS	high-resolution mass spectrum
Hz	Hertz
IBX	2-iodoxybenzoic acid
ICD	isocupredine
J	coupling constant
LDA	lithium diisopropylamide
m	multiplet
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mmol	millimole(s)
M.P	melting point
MS	molecular sieves
m/z	mass/charge
NMR	*nuclear magnetic resonance*
ppm	parts per million
^{n}Pr	*n*-propyl
^{i}Pr	isopropyl
p-TSA	*para*-toluenesulfonic acid
q	quartet
rt	room temperature
s	singlet
sept	septet
t	triplet
td	triplet of a doublet
tert	tertiary
TFE	2,2,2-trifluoroethanol
TFT	α,α,α-trifluorotoluene
THF	tetrahydrofuran
TMS	trimethylsilyl
TMS	tetramethylsilane
TLC	thin layer chromatography

Chapter 1

Phosphine- and Water-Promoted Pentannulative Aldol Reaction

The selective formation of carbon-carbon bond is the root to the art of organic synthesis. Although a myriad of carbon-carbon bond forming reactions are available, the advancement of alternative methodologies in terms of selectivity, availability, operational simplicity, and environmental sustainability is of perpetual interest. Towards this, the utmost importance for an organic chemist is synthesizing complex molecules like drugs, natural products, and dyes in the absence of toxic metals.

Aldol reaction is a classic C-C bond forming reaction involving two carbonyl compounds, one of which behaves as a latent enolate under acidic or basic condition and results in the

formation of β-hydroxy carbonyl compound. It serves as the widely utilized transformation in chemical synthesis. Discovered over 180 years ago by Kane[1] in 1838, but independently attributed to Borodin[2] and Würtz,[3] the development of the organic synthetic chemistry from its provenience to the modern state of the art may be perceived through the lens of aldol chemistry and its variants. Consequently, considerable efforts have been bestowed upon to regulate the stereocontrolled version of this process.[4] The repertoire of its synthetic utility has been valued over decades in transforming structurally articulated complex molecules. Hence, owing to the prevalence of the biologically active compounds containing β-hydroxy carbonyls, significant advancement has been made to the chemo-, regio- and stereoselective variants and applying them to the total synthesis of natural products.[5]

Cyclopentanoids persist as an essential scaffold in many natural products and pharmaceutically relevant compounds, Figure A.[6] For example, donepezil, usually traded as Aricept, is used for treating Alzheimer's disease. Standishinal, a novel skeletal diterpene, isolated from the bark of *Thuja standishii* has a significant aromatase inhibitory activity.[6e] Chromodorolide B bearing ten contiguous stereocenters, is among the most structurally complex members of the rearranged spongian diterpenoids, isolated from nudibranchs in the genus *Chromodoris*, and has nematocidal, antimicrobial activities.[6f] CR-31-B, a synthetic rocaglate, is therapeutic potential against *SARS-CoV2*.[6g]

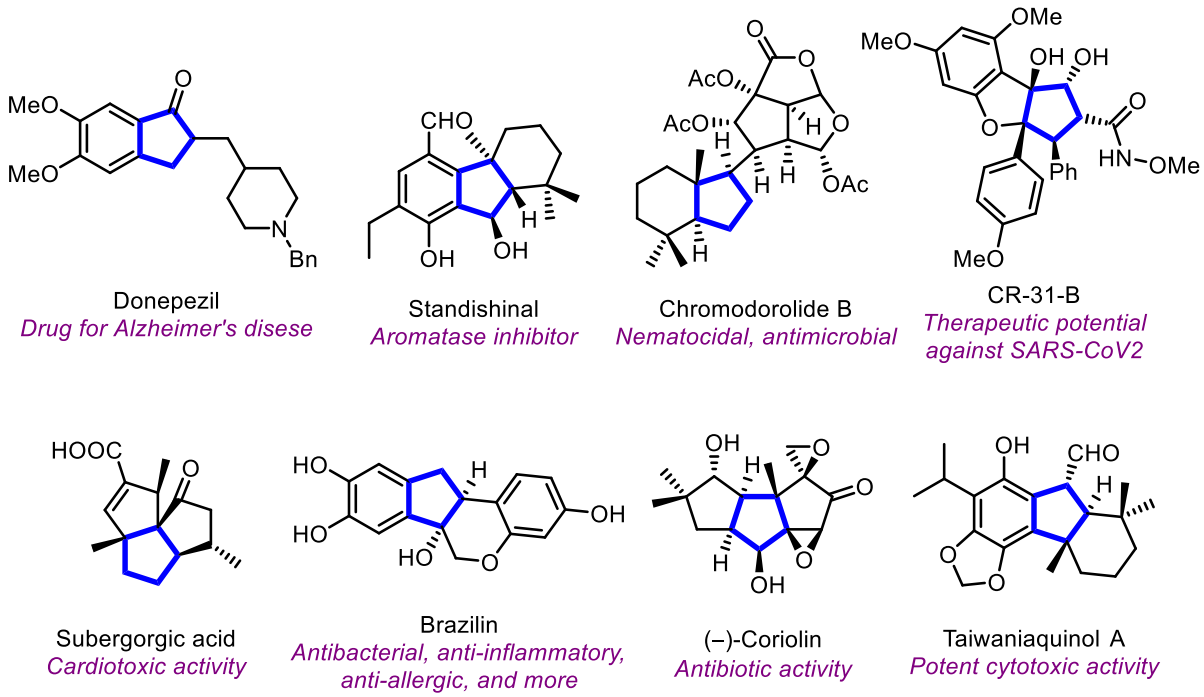


Figure A: Natural product containing cyclopentane moiety.

Subergorgic acid, anangular triquinane sesquiterpene isolated from the Pacific gorgian coral *Subergorgia suberosa*, has cardiotoxic activity.[6h] Brazilin is one of the important bioactive natural products isolated from *Caesalpinia sappan L*. heartwood; having biological activities like antibacterial, anti-inflammatory, anti-allergic, and more.[6i] Coriolin, isolated from *Coriolus consors*, has antibiotic activity against the growth of *Gram-positive* bacteria and *Trichomonas vaginalis*. Taiwaniaquinol A bearing cyclopentane core, isolated from *Taiwania cryptomerioides*, exhibits potent cytotoxicity against the epidermoid carcinoma (KB) cancer cell line. Hence, developing a method for synthesizing structurally defined cyclopentanes has a pronounced impact on the field of organic synthetic chemistry.[7]

These aforementioned importances of cyclopentanoids described in Figure A in the area of synthetic organic chemistry, pharmaceuticals, and material sciences hold the key interest to develop efficient synthetic protocols. Towards this, many methods have been reported for synthesizing this motif by employing precious metal (Pd, Pt, Au, Rh, Ru, and Ir) catalysis.[8] Despite their high levels of stereoselectivity; toxicity and limited stock of the metal led the organic chemists to shift to the metal-free approaches. Recently, organocatalytic approaches (organophosphines, N-heterocyclic carbenes (NHCs), and amines) gained huge attention due to their operational simplicity, atom economic and less toxic nature.

Organophosphorus compounds are widely used in synthetic organic chemistry. While triphenylphosphine and its derivatives have historically been most often used due to their low cost and air-stability, they are surmounted by the more air-sensitive trialkylphosphines, in cases where greater nucleophilicity is demanded. As a comparison, both tertiary phosphines and amines are pyramidal, although the inversion is rapid in amines at room temperature whereas phosphines are configurationally stable above room temperature. Thus, acyclic phosphines retain chirality at phosphorus at room temperature. Phosphines are generally less basic and more nucleophilic than similarly substituted amines. Nucleophilicity is strongest in trialkylphosphines and decreases with aryl substitution. The nucleophilicity of phosphines in their reaction with alkyl halides has been studied extensively and their rates measured by Henderson and Buckler.[9a] Pearson calculated relative reactivity parameters (or Swain–Scott parameters) to provide a nucleophilicity scale.[9b,c] The data presented in Table 1A indicate that there is only slight correlation between the strength of the nucleophile in the reaction with MeI and its basicity. While triphenylphosphine was among the weakest nucleophiles examined, the trialkylphosphines exhibit strong nucleophilicity. However, it is important that nucleophilic

scales be considered only in the context of how they were generated; use of electrophiles other than methyl iodide, such as hard electrophiles, may give different relationships.[9d]

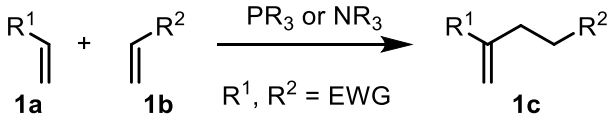
Table 1A: Nucleophilicity and basicity properties of some nucleophiles.

Nucleophile	^{n}MeI	*p*Ka (H_2O)
PEt_3	8.7	8.7
PBu_3	8.7	8.4
PPh_3	1.3	2.7
$P(OMe)_3$	5.2	2.6

Organophosphine-mediated transformations for the construction of cyclopentanes are reported, such as Rauhut-Currier (RC) reaction, Morita-Baylis-Hillman (MBH) reaction, cycloaddition, etc.[9e-i, 44] In the few subsections, organo-phosphine-mediated reactions for the synthesis of a wide variety of cyclopentanoids are discussed.

1.1: Rauhut-Currier (RC) reaction: a tool for cyclopentane synthesis

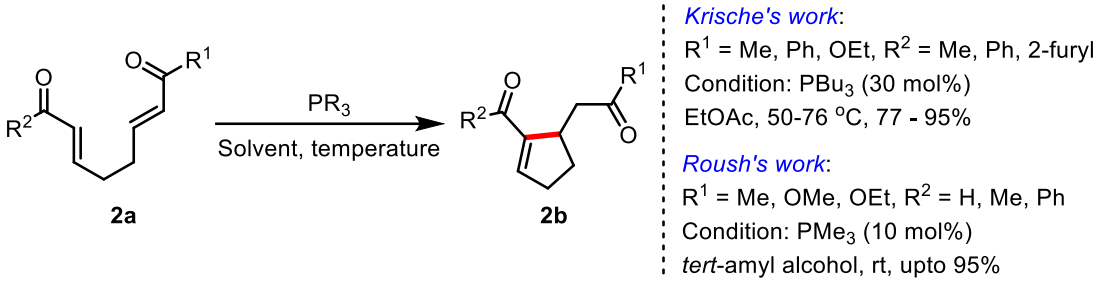
Initially disclosed by Rauhut and Currier in 1963,[10] later reported by many others,[11] Rauhut-Currier reaction is the dimerization of electron-deficient activated alkenes. The transformation proceeds via a reversible conjugate addition of a nucleophilic catalyst (PR_3 or NR_3) to an activated alkene **1a** and then subsequent Michael addition of the enolate to another activated alkene **1b**. Though there are reports of RC reaction mediated by amines,[12] but those were not encouraging because of their inherent lack of stereoselectivity and regioselectivity. A general presentation of Rauhut-Currier reaction is outlined in Scheme 1. RC reaction has been an important tool for the construction of cyclopentane cores.



Scheme 1: General representation of Rauhut-Currier reaction.

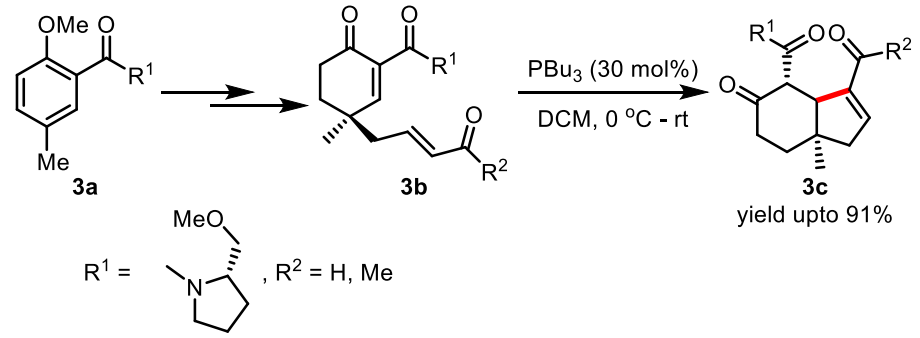
Following Rauhut and Currier's seminal work, an intramolecular version of RC reaction was developed by Krische[13] and Roush[14] independently in 2002 by strategically devising substrates **2a** tethered with coupling partners possessing different electrophilicity, Scheme 2. It is demonstrated by both groups that the reaction undergoes trialkylphosphine

catalyzed chemo- and stereo-induced cycloisomerization of symmetric and unsymmetric bis-enones to furnish cyclopentanoides **2b** with high level of efficacy.



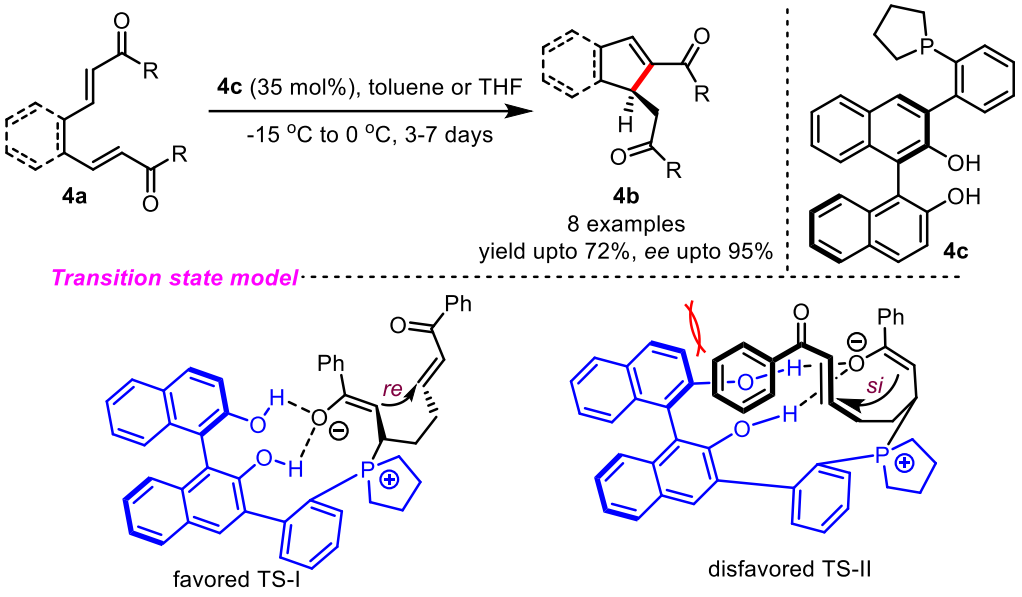
Scheme 2: Krische and Roush's work toward intramolecular RC reaction.

In 2010, Malachowski[15] group reported a phosphine-catalyzed intramolecular RC reaction of **3b** through a two-step sequence starting from **3a** for the synthesis of highly functionalised, fused bicarbocyclic structure bearing an all-carbon quaternary center **3c**, Scheme 3. Interestingly, the scope of this methodology is limited to α,β-unsaturated carbonyls, while replacing the carbonyls with α,β-unsaturated acids and sulfones fails to generate the respective RC products.



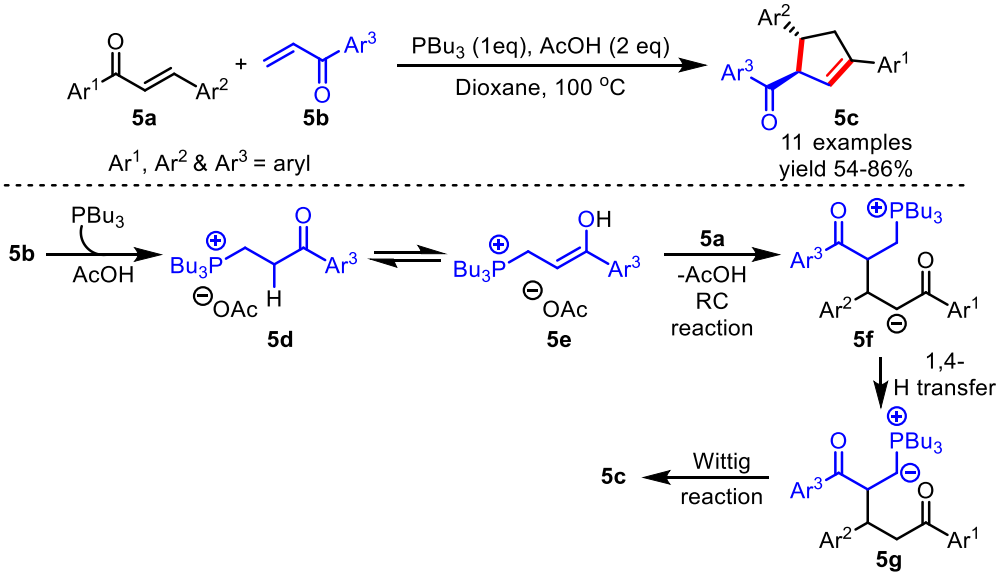
Scheme 3: Malachowski's phosphine-catalyzed intramolecular RC reaction.

In 2012, Shi *et al.*[16] disclosed an intramolecular enantioselective Rauhut-Currier reaction. A multifunctional chiral phosphine **4c** was employed to synthesize the functionalized cyclopentenes and indenes **4b** in moderate yield and excellent enantiopurities from dienones **4a**, Scheme 4. The asymmetric induction in the product **4b** can be accounted for by the indicated stereochemical model, where the formation of transition state I (TS-I) is more favorable compared to the TS-II due to the steric hindrance.



Scheme 4: Shi's work for cyclopentene core synthesis.

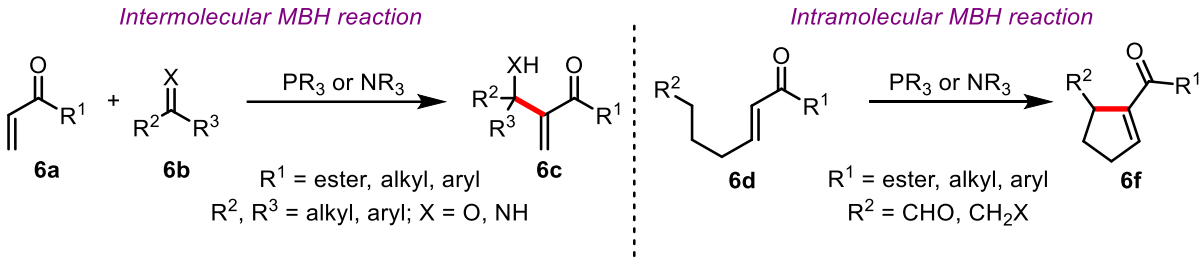
Recently, Huang *et al.*[17] discovered a synthesis of trisubstituted cyclopentene **5c** through a cross Rauhut-Currier/ Wittig domino reaction from two different enone systems in the presence of PBu_3 and acetic acid, Scheme 5. Initially, after the nucleophilic addition of phosphine to **5b**, the zwitterionic species **5e** formed via tautomerization of **5d** undergoes cross RC reaction with another enone **5a** to generate intermediate **5f**, which undergoes 1,4-proton shift to form ylide **5g** followed by intramolecular Wittig reaction to obtain **5c**. The presence of AcOH (protic acid) in this transformation helps to barricade from generating enolic anion of **5b** with PBu_3, hence self-dimerization of **5b** (Rauhut-Currier reaction of **5b**) could be avoided, eventually leading to the moderate to high yield of the product **5c**.



Scheme 5: Huang's work towards the synthesis of trisubstituted cyclopentene **5c**.

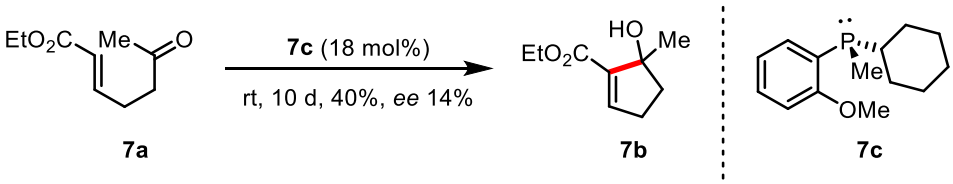
1.2: Morita-Baylis-Hillman (MBH) reaction: a tool for cyclopentane synthesis

The Morita-Baylis-Hillman (MBH) reaction is one of the most powerful C-C bond forming reaction pertaining to the formation of densely functionalized carbon-carbon framework under mild conditions. First reported by Morita [18] in 1968 and later by Baylis and Hillman [19] in 1972, MBH reaction involves coupling of an activated double bond from its α-position and an electrophile (usually aldehyde or imine) in presence of a catalyst (phosphines and amines). To date, such transformation persists as the most advanced body of work enabling α-functionalization of enone. In last few decades, this reaction has gained remarkable attention because of its operational simplicity and atom economic nature. This method also provides access to a large number of natural products and biologically active molecules.[20] MBH reaction remains as one of the important transformations for the synthesis of cyclopentanoids, Scheme 6.[21]



Scheme 6: General representation of MBH reaction.

After Morita and Baylis-Hillman's seminal work, Frater *et al.*[22] in 1992 discovered the first intramolecular version of MBH (IMBH) reaction to access functionalized cyclopentanes **7b** from α,β-unsaturated ester-ketone **7a**. The development of asymmetric induction of the transformation has been done using (–)-CAMP **7c**, albeit in low enantioselectivity, Scheme 7.

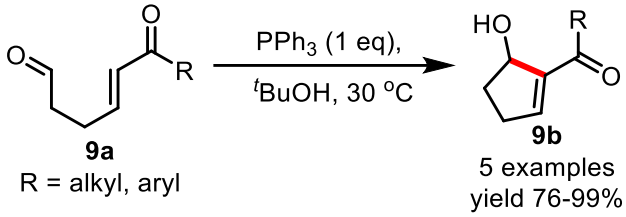


Scheme 7: Frater's work towards the synthesis of cyclopentene core.

Later in 2002, Keck's group reported a trimethylphosphine-mediated IMBH reaction to obtain cyclopentanoate **8b** from α,β-unsaturated thiol ester-aldehyde **8a**, Scheme 8.[23] During the investigation of substrate scope, it was realized that the amount of phosphine required in this study was substrate-dependent.

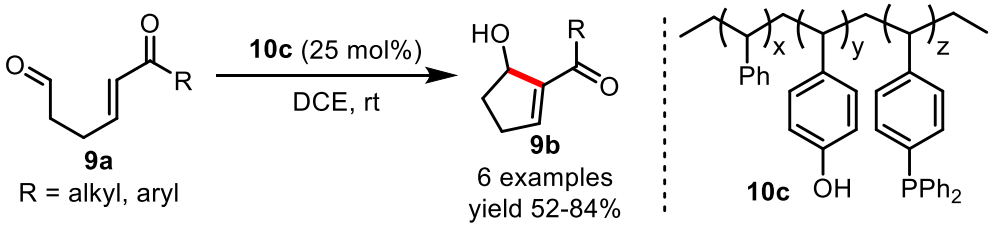
Scheme 8: Keck's work towards the synthesis of five-membered carbocycles.

In 2003, Koo *et al.*[24] devised ω-formyl-α,β-unsaturated carbonyl compounds **9a** and applied IMBH reaction in PPh_3 to synthesize five-membered carbocycles **9b** with good to excellent yield, Scheme 9.



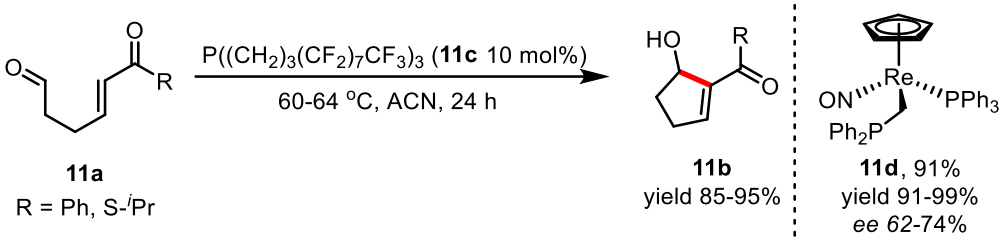
Scheme 9: Koo's work towards the synthesis of cyclopentene.

In 2007, Toy *et al.*[25] synthesized a variety of polystyrene-supported bifunctional phosphines **10c**. The application of these phosphines was further explored by employing Koo's substrate **9a**, to access cyclopentenes **9b**, Scheme 10.



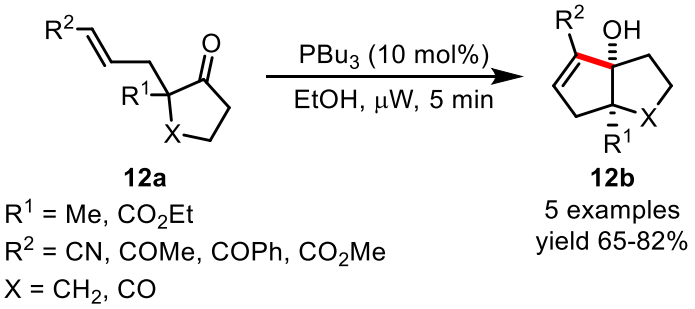
Scheme 10: Toy's work towards the synthesis of cyclopentene.

In 2008, Gladysz *et al.*[26] disclosed thermomorphic fluorous phosphine **11c** for IMBH reaction of **11a**, Scheme 11. The advantage of using this catalyst is easy and feasible recovery of the catalyst by simply precipitation from organic solvents. Later on, an asymmetric version[27] was also developed by the same group in presence of chiral Rhenium-containing phosphine **11d** and synthesized cyclopentenes **11b** in high levels of yield and moderate enantiopurities.



Scheme 11: Gladysz's work for the synthesise of cyclopentenes **11b**.

Later in 2013, Miesch's *et al.*[28] reported a substrate and solvent-controlled organophosphine-catalyzed IMBH reaction under microwave from activated olefines tethered with cycloalkanones **12a**, Scheme 12. A library of polyfunctionalized diquinanes **12b** was synthesized with moderate to good yield and high levels of diastereoselectivity.



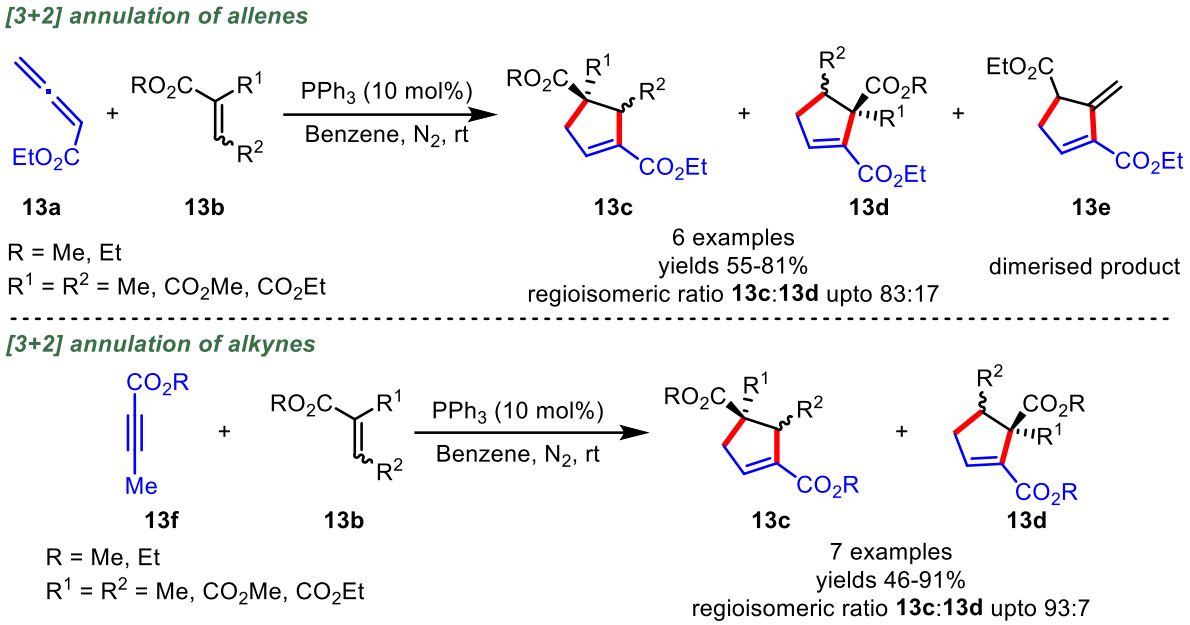
Scheme 12: Miesch's phosphine catalyzed IMBH reaction to synthesize diquinanes **12b**.

1.3: Cycloaddition reaction: a tool for cyclopentane synthesis

During past decades, phosphine-promoted annulation reactions have been a successful strategy for the construction of cyclopentanes. Towards this, several groups have reported phosphine-catalyzed [3+2], [4+1], [2+2+1] cycloaddition reaction.

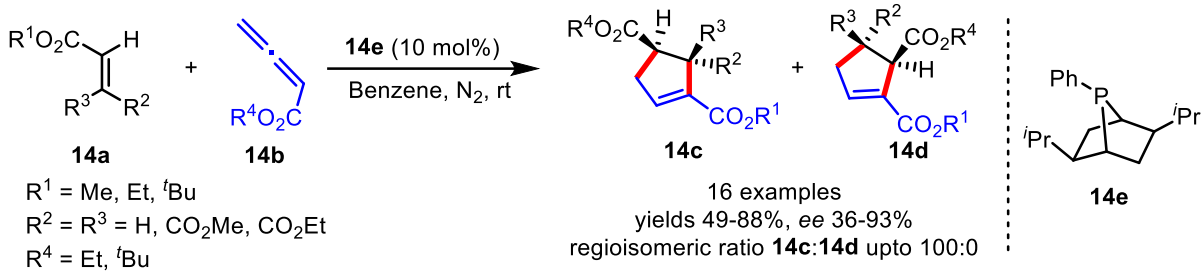
1.3.1: [3+2] annulation-based approaches for cyclopentanes

In 1995, Lu *et al.*[29] documented the first intermolecular phosphine-catalyzed [3+2] cycloaddition reaction of allenes and alkynes. The reaction of 2,3-butadienoates **13a** or 2-butynoates **13f** with activated alkenes **13b** resulted in the formation of highly substituted cyclopentenes **13c** and **13d** in good yields and regioisomeric ratio, albeit small amount of dimerized product of allenoate **13e** also was observed, Scheme 13. This reaction opened a new avenue in the area of nucleophilic phosphine catalysis of allenes with electrophiles to synthesize highly functionalised carbocyclic compounds.



Scheme 13: Lu's [3+2] for cyclopentene synthesis.

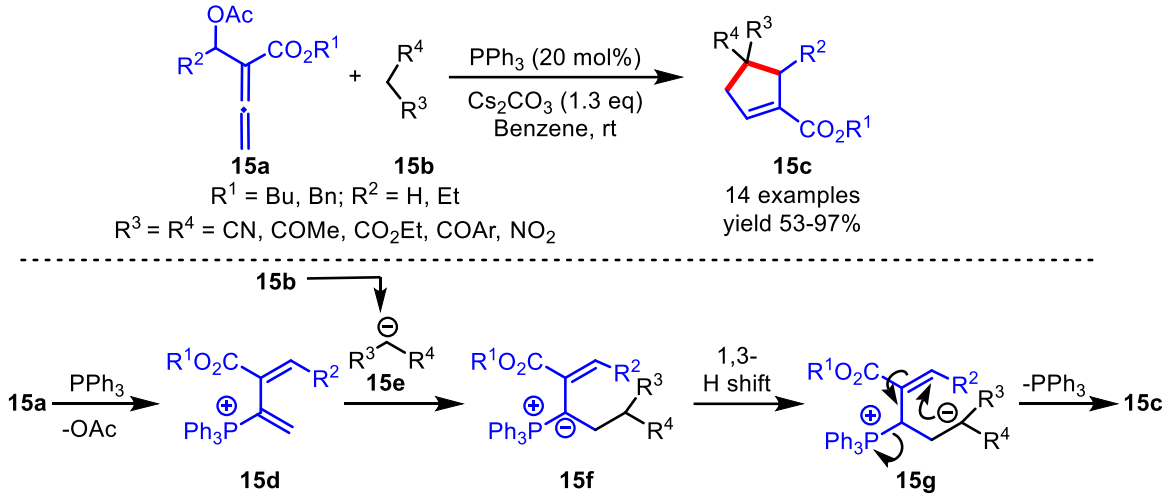
In continuation, the asymmetric version of the Lu's [3+2] annulation protocol was discovered by Zhang's group by employing the rigid-bridged chiral phosphines **14e**, Scheme 14.[30] A wide variety of substituted cyclopentenes **14c** and **14d** were synthesized in good yields and excellent enantio- and regioselectivities. It was observed that sterically hindered alkenes influenced the better enantio-induction in the product.



Scheme 14: Zhang's asymmetric [3+2] annulation for cyclopentene synthesis.

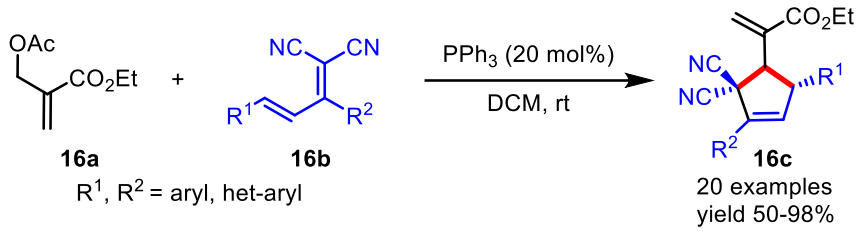
1.3.2: [4+1] annulation-based approaches for cyclopentanes

In 2010, Tong *et al.*[31] disclosed a novel [4+1] cycloaddition reaction for the synthesis of cyclopentenes **15c**, Scheme 15. 2-(Acetoxymethyl)-buta-2,3-dienoate **15a** forms the species **15d** in the presence of triphenylphosphine and serves as a 1,4-biselectrophilic system. The base-mediated generation of **15e** followed by a γ-umpolung addition to the diene **15d** forms **15f**. An intramolecular proton shift of ylide **15g** and subsequent cyclization by the elimination of phosphine lead to desired cyclopentenes **15c**.



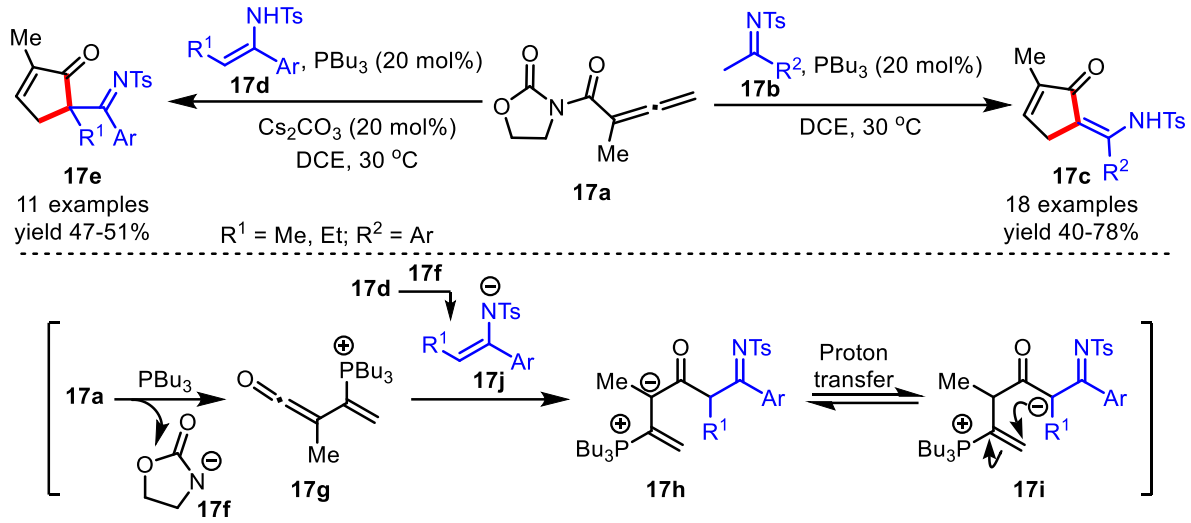
Scheme 15: Tong's [4+1] annulation for cyclopentene synthesis.

In 2013, He *et al.*[32] developed another variant of [4+1] cycloaddition by employing activated diene **16b** as a C4 synthon and Morita-Baylis-Hillman acetate **16a** as a C1 synthon to provide the polysubstituted cyclopentenes **16c** in good yields, Scheme 16.



Scheme 16: He's [4+1] annulation of MBH adducts for cyclopentene synthesis.

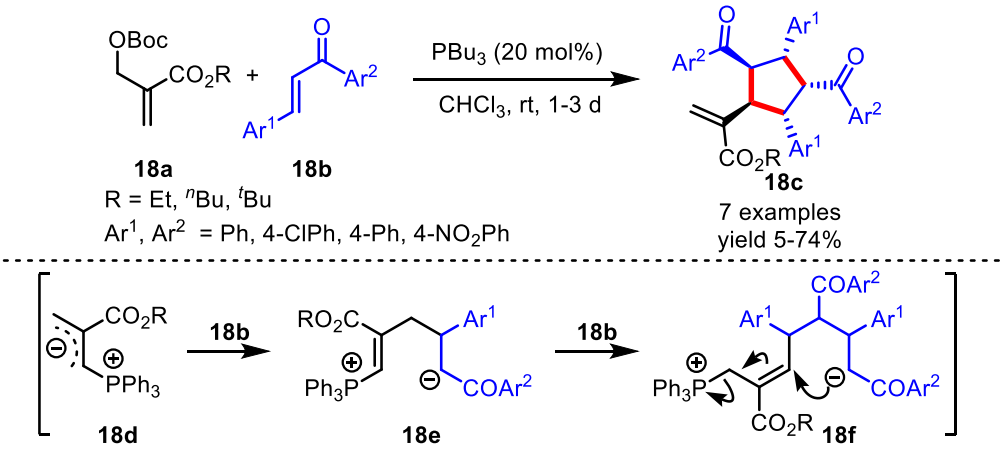
Recently in 2020, Huang's group[33] reported PBu_3-catalyzed [4+1] annulation of allenyl imide **17a** with imines **17b** or enamines **17d** to access cyclopentenes **17c** and **17e** in moderate to good yields, Scheme 17. The detailed mechanistic insights of this transformation show the crucial role of 2-oxazolidinyl group of the allenyl imide **17a** in triggering smooth generation of a α,β-unsaturated ketenyl phosphonium key intermediate **17g**. The intermediate **17j** generated from **17d** attacks to the electrophilic center of **17g** to generate **17h** which undergoes tautomerization to form **17i** and subsequent cyclization leads to the formation of annulated product.



Scheme 17: Huang's [4+1] annulation of allenyl imide for the synthesis of cyclopentene.

1.3.3: [2+2+1] annulation-based approaches for cyclopentanes

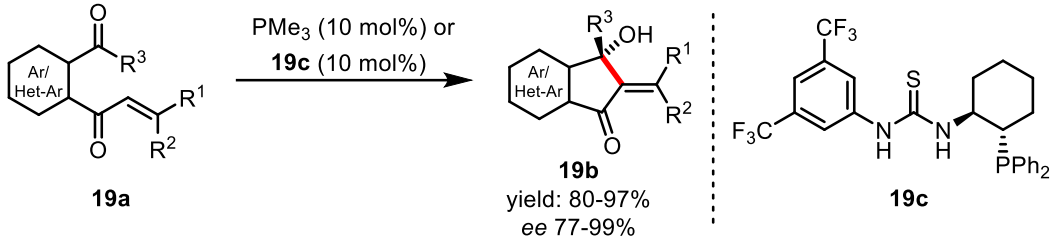
In 2011, He and co-worker documented an unusual dimerization of chalcones **18b** via [2+2+1] cycloaddition reaction, Scheme 18.[34] The initially formed ylide **18d** undergoes sequential Michael addition with two molecules of chalcone **18b** to form **18f**, and cyclizes to furnish fully substituted cyclopentanes **18c**.



Scheme 18: He's [2+2+1] annulation of MBH adducts for cyclopentane synthesis.

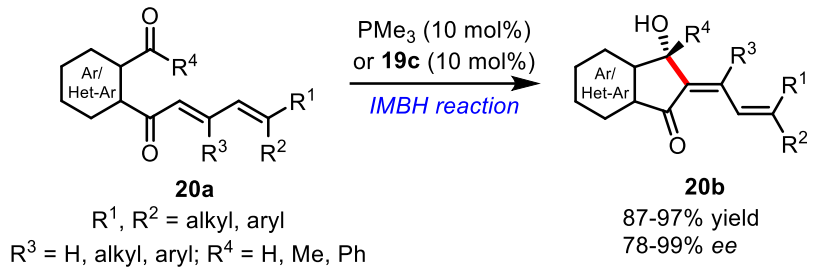
Recently, with the progress on synthesizing cyclopentane core, our research group is also contributing to the advancement of organo-phosphine-mediated construction of various useful scaffolds consisting cyclopentanes.[35] Recently, we have discovered the first example of phosphine-catalyzed IMBH reaction of sterically and electronically highly demanding β-mono- and β,β-disubstituted enones **19a** to access cyclopenta[*b*]annulated arenes and heteroarenes

19b, Scheme 19.[36] The high level of enantioselectivity was attained by using bifunctional catalyst **19c** in combination with 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) as solvent.



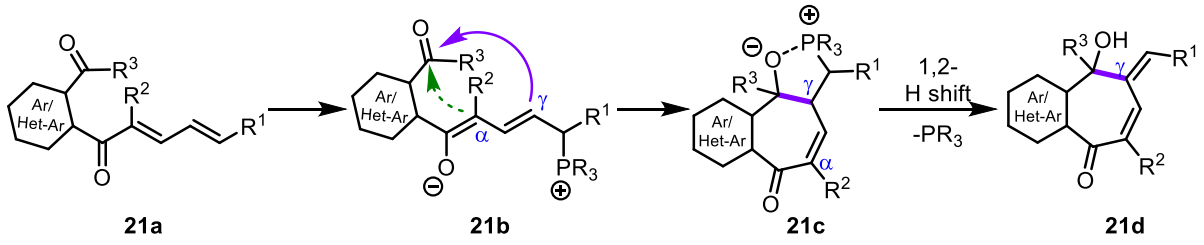
Scheme 19: Phosphine-catalyzed asymmetric IMBH reactions.

In continuation, we have also developed an enantioselective organocatalytic IMBH reaction of dienones **20a**, Scheme 20,[37] where strategically designed dienes for the 1,6-addition of phosphine was applied, which has been seldom acheived in MBH reaction for the synthesis of cyclopenta-fused arenes and heteroarenes **20b**.



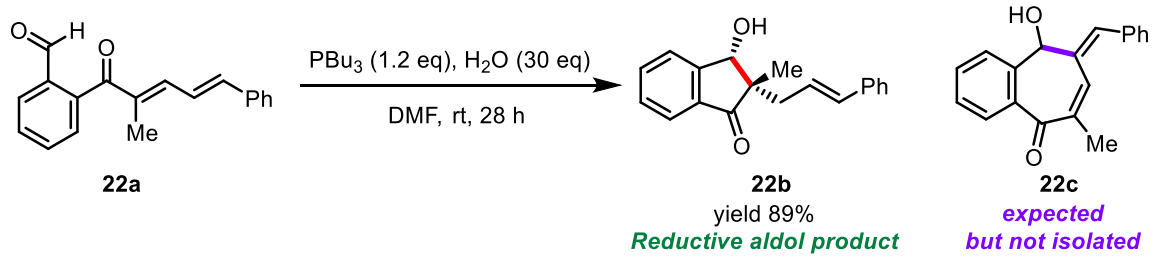
Scheme 20: Phosphine-catalyzed asymmetric IMBH reactions of dienones **20a**.

After successfully establishing IMBH reaction with dienone carbonyl system, we were curious to see the fate of the reaction where α position of diene part of **20a** is blocked deliberately to abort the MBH approach, Scheme 21. Hence, we came up with a new substrate design **21a** with α-substituted dienone-carbonyl system, so that after 1,6-phosphine addition, the zwitterionic species **21b** can possibly undergo cyclization from γ position to provide cycloheptanoids **21d** via **21c**.



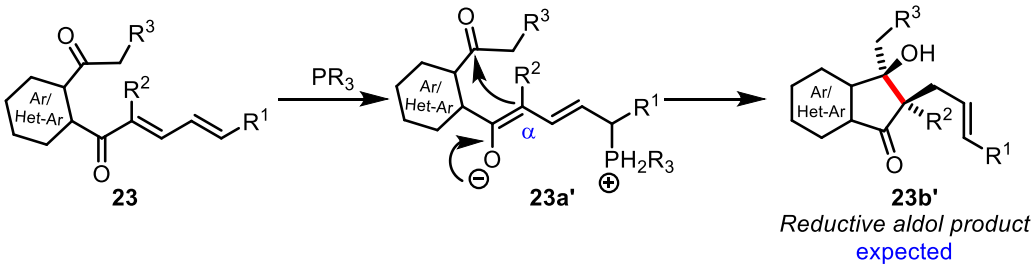
Scheme 21: Substrate design for phosphine-mediated α-substituted dienone-carbonyl system.

Interestingly, when α-substituted dienone-aldehydes **22a** were treated under the optimized condition, cyclopentanoids **22b** was obtained exclusively, which is nothing but the reductive aldol product, Scheme 22.[38] Strikingly, not even a trace amount of cycloheptanoids **22c** was observed. Herein, we have disclosed a phosphine- and water-promoted diastereoselective intramolecular reductive aldol reaction (RAR) of α-substituted dienone-aldehydes **22a** to synthesize a wide range of cyclopenta[*b*]annulated arenes and heteroarenes **22b** bearing two contiguous stereogenic centers, one of them being an all-carbon quaternary center, in good yields and diastereoselectivities, Scheme 22. Interestingly, water acts as a terminal oxidant in this transformation.



Scheme 22: Phosphine-mediated reductive aldol reaction of α-substituted dienone-aldehydes.

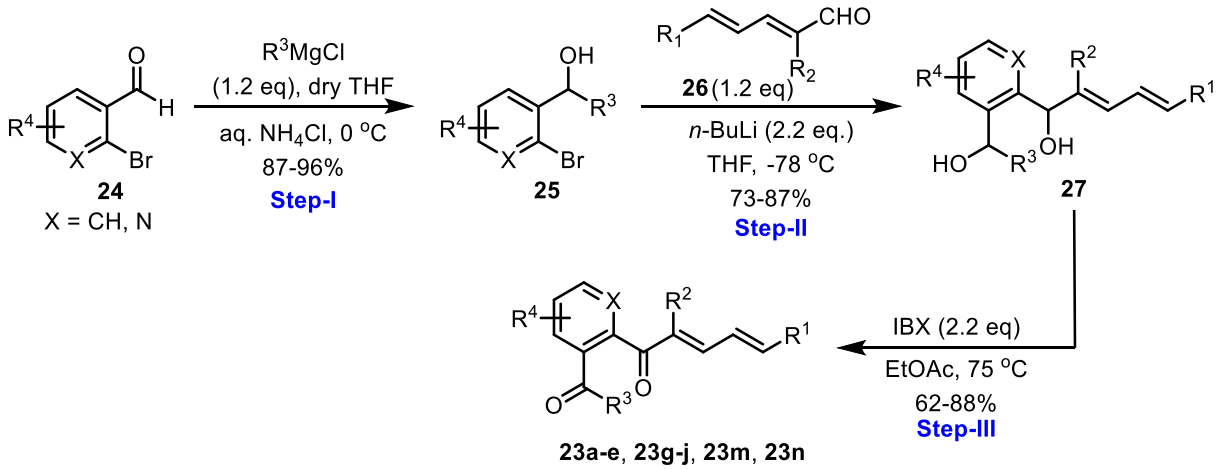
After successfully establishing phosphine- and water-promoted reductive aldol product with α-substituted dienone-aldehydes **22a**, we were curious about the reductive aldol strategy with dienone-ketone substrate **23**. According to the strategy, 1,6-phospha-Michael attack into the substrate **23** generates the zwitterionic species **23a′**, which undergoes reductive aldol strategy to form the product **23b′**, Scheme 23.



Scheme 23: Our hypothesis towards reductive aldol reaction of α-substituted dienone-ketone.

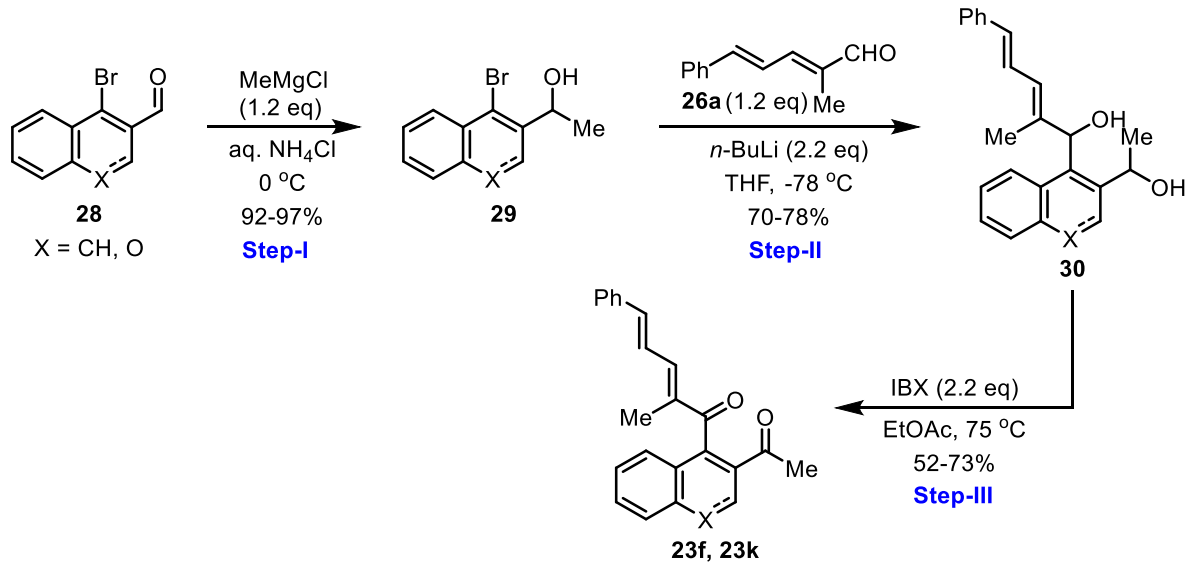
Accordingly, the substrate **23** was synthesized using a three-step protocol starting from commercially available 2-bromo aldehyde **24**, Scheme 24. The respective Grignard reagent was added to bromo aldehyde **24** to afford **25**. After that, direct *n*-butyllithium mediated alkylation of freshly synthesized alcohol **25** with α-substituted dienal **26** provided the

respective diol **27**. Subsequent IBX oxidation of **27** at 75 °C in EtOAc furnished the α-substituted dienone-ketone **23a-e**, **23g-j**, **23m**, **23n**.



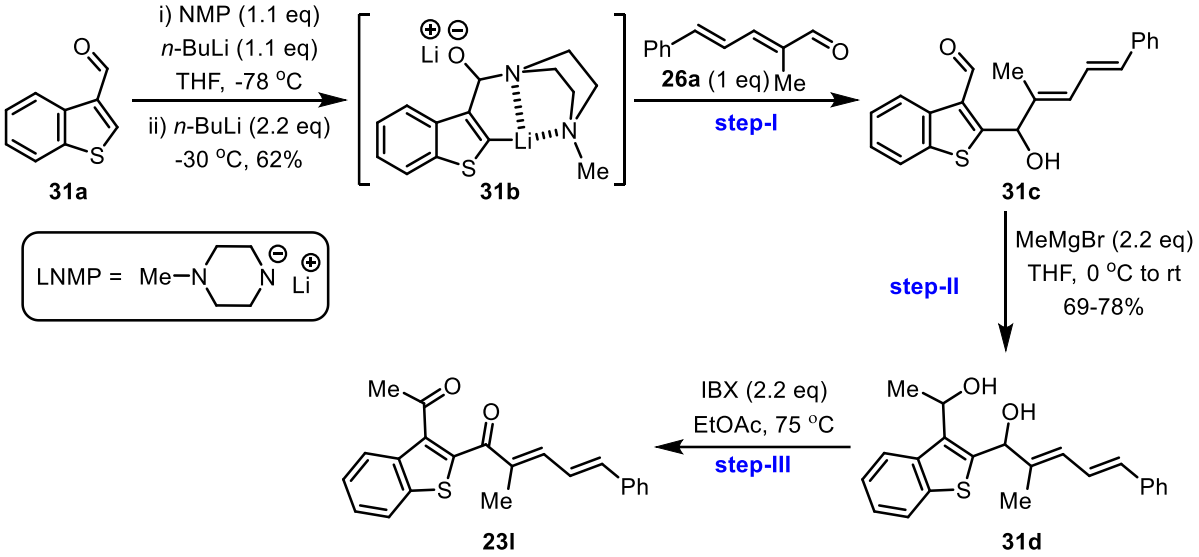
Scheme 24: Synthesis of α-substituted dienone-ketone **23a-e**, **23g-j**, **23m**, **23n**.

Chromene and naphthalene-based substrates were prepared following the same protocol starting from commercially available respective 2-bromo aldehyde **28**, Scheme 25.



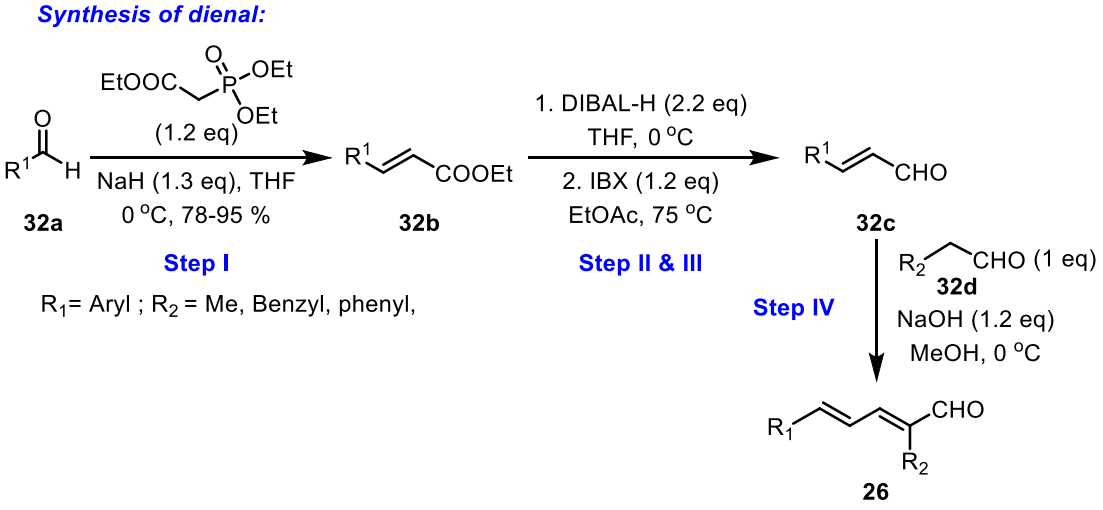
Scheme 25: synthesis of **23f**, **23k**.

For the synthesis of benzothiophene-based substrate **23l**, *in situ* masking of aldehyde functionality by lithium N-methylpiperazide (generated from NMP and *n*-BuLi) in benthiophene-3-carboxaldehyde **31a** followed by directed C-2 *α*-alkylation (α-lithiation) with dienal **26a** led to the formation of **31c**. Then Grignard addition onto the freshly synthesized **31c** and IBX oxidation of the respective diol **31d** furnished the dienone-ketone **23l**, Scheme 26.



Scheme 26: synthesis of **23l**.

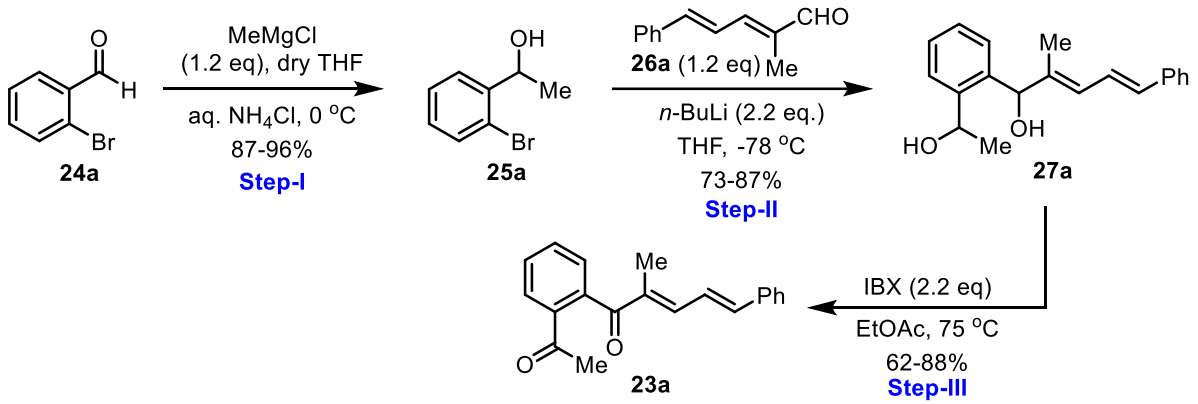
The dienal **26** employed in this study can be accessed from respective aldehyde **32a** by a four-step protocol, Scheme 27. Starting from the Witttg-Horner reaction of the respective aldehyde to furnish the ester **32b**, which was subjected to DIBAL-H mediated reduction followed by IBX oxidation to obtain the enal **32c**. After that, aldol reaction with another aldehyde **32d** in the presence of NaOH to furnish the respective dienal **26**.



Scheme 27: Synthesis of dienal **26**.

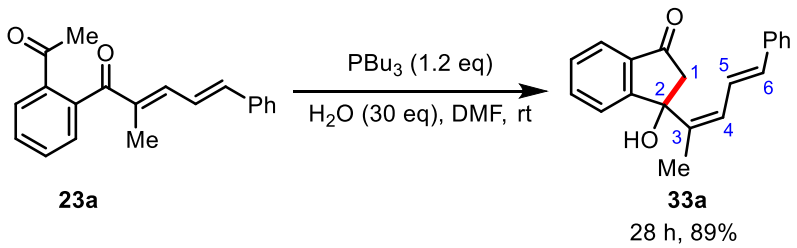
Next, we prepared our model starting material **24a** from *o*-bromo benzaldehyde, Scheme 28. First, methyl Grignard was added to **24a** to obtain the corresponding alcohol **25a**.

Then, *n*-BuLi mediated alkylation with **26a** at -78 °C to access the respective diol **27a**, and IBX oxidation at 75 °C furnishes the desired model starting material **23a**.



Scheme 28: Synthesis of **23a**.

To validate the hypothesis, the model substrate **23a** was treated with our prototypical condition employed for the RAR (see Scheme 22). Strikingly, α-substituted dienone-ketone **23a** delivered **33a**, which is nothing but an intramolecular aldol product.[39] However, even a trace amount of the expected reductive aldol product **23b′** was not observed, Scheme 29. The structure of **33a** was deduced from spectral data. In ^{1}H NMR, the presence of two doublets at 3.02 (J_{AB} = 18.9 Hz) and 2.85 (J_{AB} = 18.9 Hz) is due to the CH_2 (C-1 proton). Peak at 2.85 is for alcoholic proton (C-2 OH). The presence of doublet at 6.55 (J = 11.1 Hz) indicates the presence of double bond (C-4 proton). The doublet of doublet (dd) at 7.00 (J = 15.4 and 11.4 Hz) and a doublet at 6.59 (J = 15.6 Hz) confirm the trans double bonds of C-5 and C-6. In ^{13}C NMR, the presence of a downfielded quaternary benzylic carbon (C-2) at 80.0 and a methylene group (C-1) at 52.0 asserted the formation of 3-hydroxy-3-dienylcyclopentanone-fused arenes **33a**. In the IR spectrum, a broad absorption band at 3418 cm^{-1} due to the tertiary alcohol and a strong band at 1705 cm^{-1} due to the presence of carbonyl further supported the product formation. In the high-resolution mass spectrum (HRMS), the presence of protonated molecular ion peak at *m*/*z* 291.1371 for $(M+H)^+$ confirmed the formation of **33a**.



Scheme 29: Reaction with α-substituted dienoene-ketone **23a** and phosphine.

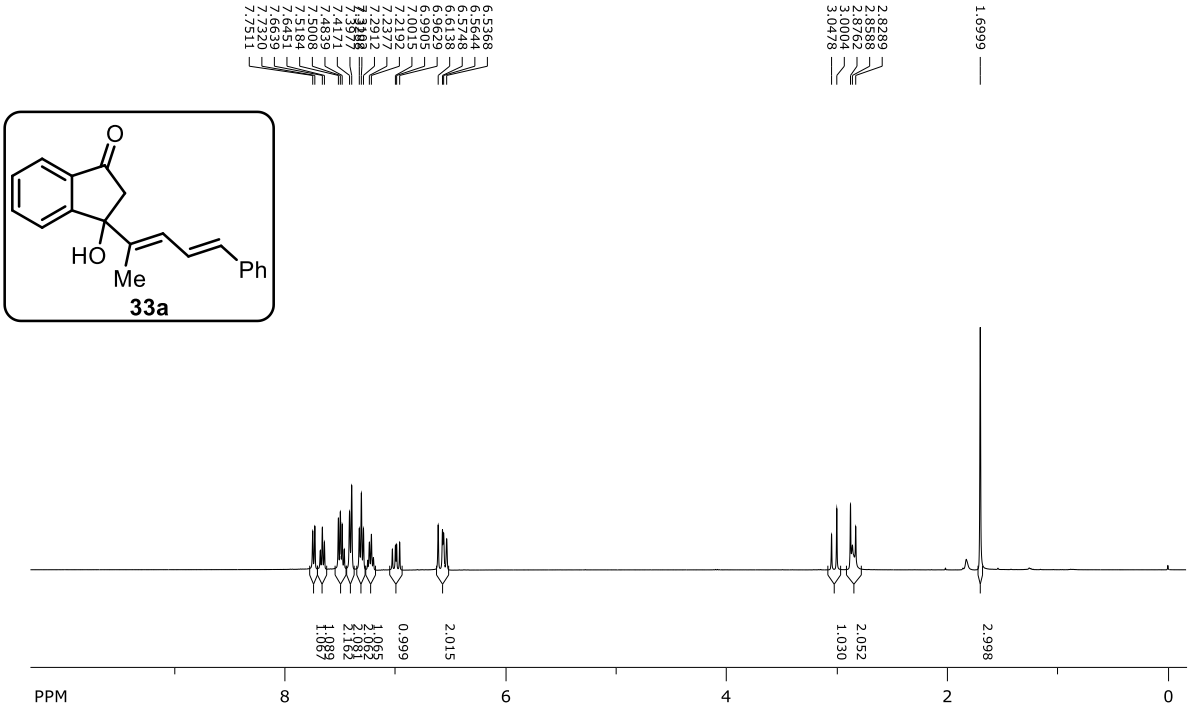


Figure 1: ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of indane **33a**.

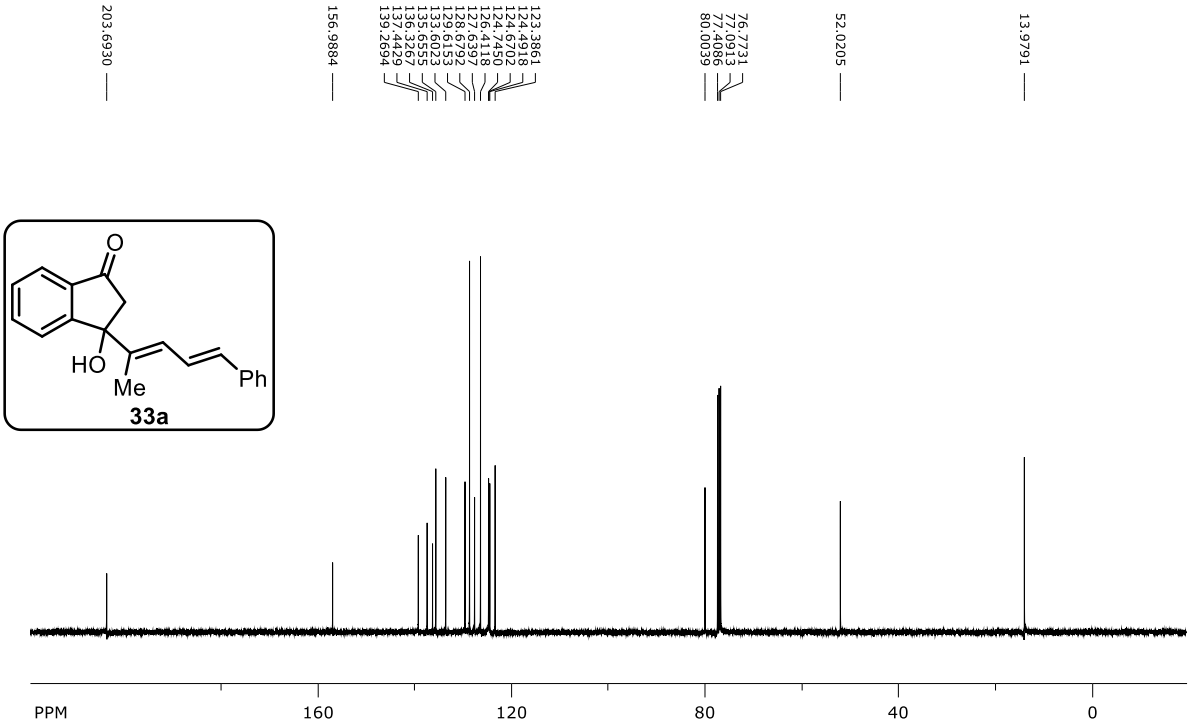
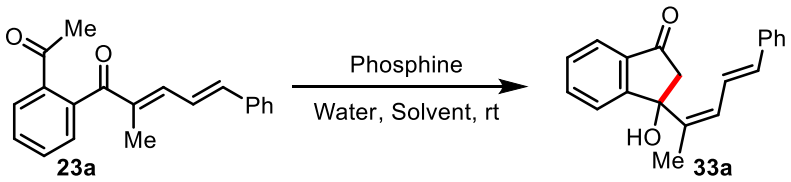


Figure 2: ^{13}C-NMR spectrum (400 MHz, $CDCl_3$) of indane **33a**.

1.4: Results and Discussion

Prompted by our earlier success on intramolecular reductive aldol reaction of α-substituted dienoene-aldehyde **22a**, we have applied the prototypical condition in our initial optimization study to obtain **33a** with 89% yield in 28 h. At this stage, we were curious about the amount of phosphine required and the role of water in this transformation. Hence, we performed the reaction with 20 mol% of PBu_3 in the absence of water in different solvents (protic and aprotic), no product was observed even after 48 h (Table 1, entry 2-6). Sequentially, when phosphine loading was increased to 1 equivalent and 1.2 equivalent, a trace amount of aldol product was isolated (entries 7-8). Interestingly, when water was added as an additive along with phosphine, the yield of the **33a** significantly increased (entries 9-12). Hence, after brief screening, it was realized that 1.2 eq of PBu_3 along with 30 eq of H_2O in DMF at rt is the optimized condition to obtain **33a** in 89% yield.

Table 1: Screening of reaction parameters for the intramolecular aldol reaction with **23a**



Sl. No	Phosphine	Additive	Solvent	Time (h)	Yield (%)[a]
1	**PBu_3 (1.2 eq)**	**H_2O (30 eq)**	**DMF**	**28 h**	**89 %**
2	PBu_3 (20 mol%)	_	DMF	48	NR
3	PBu_3 (20 mol%)	_	CH_3CN	48	NR
4	PBu_3 (20 mol%)	_	IPA	48	NR
5	PBu_3 (20 mol%)	_	DCM	48	NR
6	PBu_3 (20 mol%)	_	Toluene	48	NR
7	PBu_3 (1.0 eq))	_	DMF	48	7
8	PBu_3 (1.2 eq)	_	DMF	48	10
9	PBu_3 (40 mol%)	H_2O (20 eq)	DMF	48	8
10	PBu_3 (60 mol%)	H_2O (30 eq)	DMF	48	37%
11	PBu_3 (80 mol%)	H_2O (30 eq)	DMF	40 h	61%
12	PBu_3 (1.0 eq))	H_2O (30 eq)	DMF	28 h	81%

All reactions were performed on 0.1 mmol scales. [a] Yields were calculated after silica gel column chromatography.

With an interest in expanding the scope of the methodology, a wide variety of α-substituted dienone-ketone **23** was synthesized and subjected to the optimized condition (Table 2). A diverse range of synthetically challenging 3-hydroxy-3-dienylcyclopentanone-fused arenes and heteroarenes **33** having different substitution patterns can be accessed through phosphine and water-promoted intramolecular aldol reaction with 81-96% yield (**33a**-**33n**).[40] Although substrates with electron donating as well as electron withdrawing groups on the backbone were well tolerated under the optimized condition**,** the electron rich substrates (**23g**-**23i**) required longer time to deliver the expected product **33g**-**33i**. Furthermore, substrate with hetero atom backbone takes relatively short time to synthesize the respective indanones (**23k**, **23l**), which are otherwise difficult-to-access. The most interesting feature of this methodology is that the narrow yield range (81-96%) to access a variety of 3-hydroxy-3-dienylcyclopentanone-fused arenes and heteroarenes clearly indicates the robustness of the methodology concerning the steric and electronic contribution of the substitution. In addition, α-branched ketone **23m**, **23n** (when R^3 = Et) under optimized condition furnished the product **33m**, **33n** with two contiguous stereogenic centers, one of them being a quaternary carbon with 81-88% yield in 8:1 diastereomeric ratio.

The molecular structure with relative stereochemistry of **33m** was unambiguously confirmed by X-ray diffraction analysis, Figure 3.

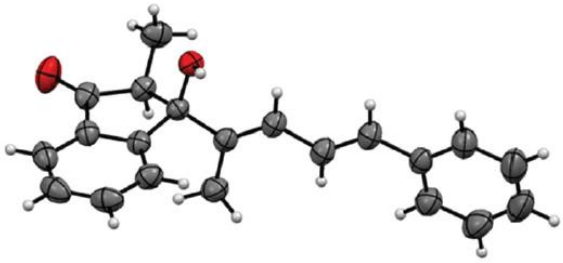
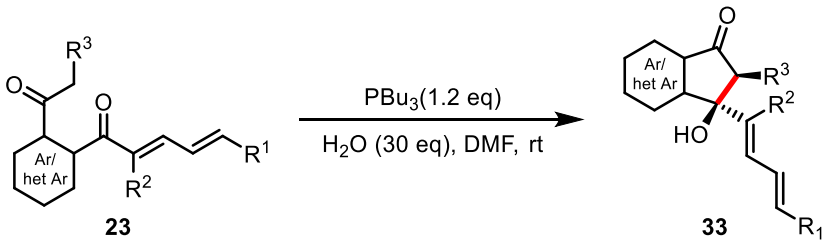
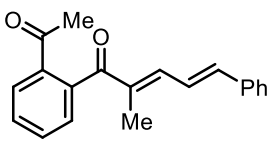
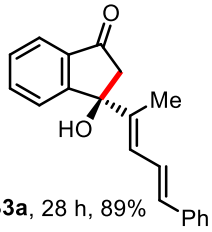
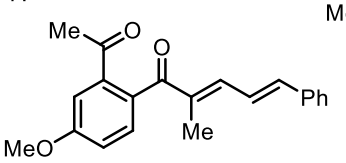
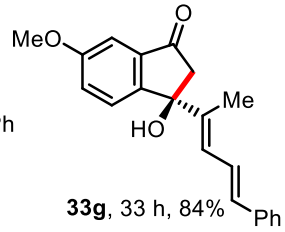
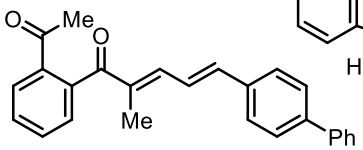
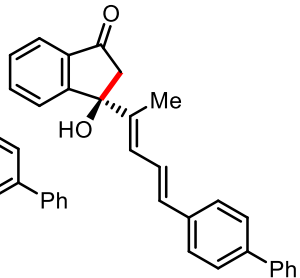
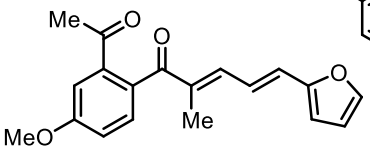
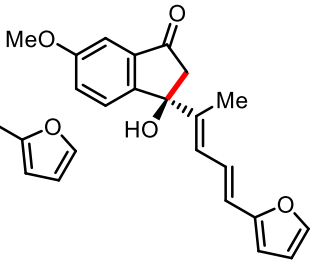
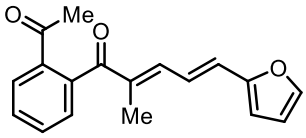
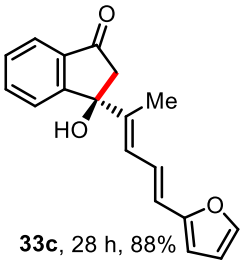
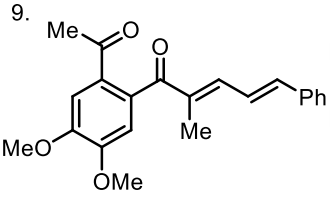
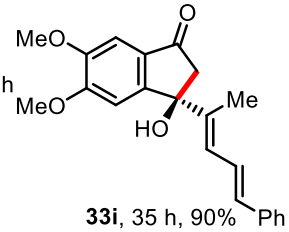
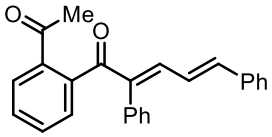
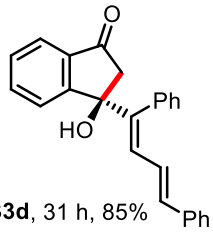
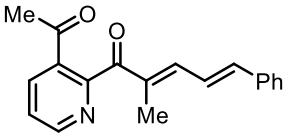
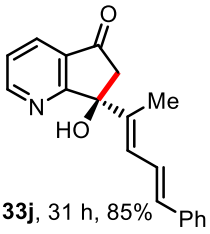
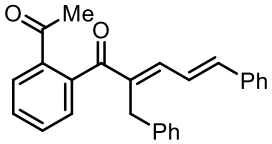
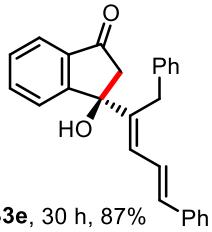
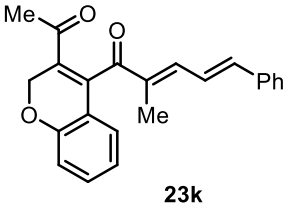
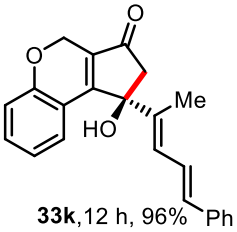
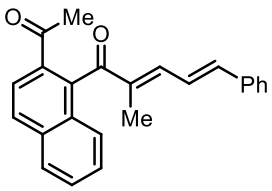
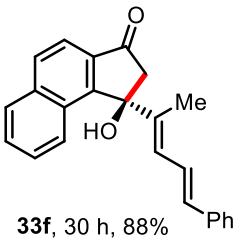
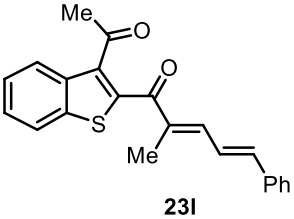
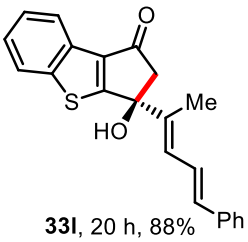
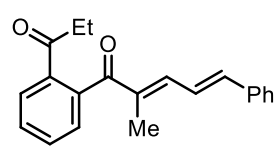
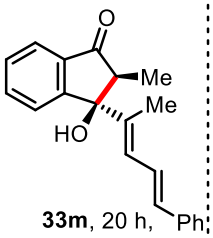
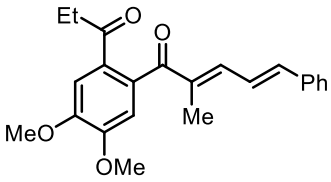
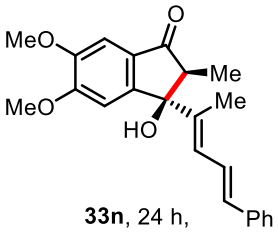


Figure 3: ORTEP diagram of **33m**.

Table 2: Substrate Scope: 3-hydroxy-3-dienyl indanone **33**



Entry	Substrate	Product	Entry	Substrate	Product
1.	 **23a**	 **33a**, 28 h, 89%	7.	 **23g**	 **33g**, 33 h, 84%
2.	 **23b**	 **33b**, 30 h, 81%	8.	 **23h**	 **33h**, 40 h, 86%
3.	 **23c**	 **33c**, 28 h, 88%	9.	 **23i**	 **33i**, 35 h, 90%
4.	 **23d**	 **33d**, 31 h, 85%	10.	 **23j**	 **33j**, 31 h, 85%
5.	 **23e**	 **33e**, 30 h, 87%	11.	 **23k**	 **33k**,12 h, 96%
6.	 **23f**	 **33f**, 30 h, 88%	12.	 **23l**	 **33l**, 20 h, 88%

Entry	Substrate	Product	Entry	Substrate	Product
13.	 **23m**	 **33m**, 20 h, 81% (dr = 2:1)[a]	14.	 **23n**	 **33n**, 24 h, 83% (dr = 3:2)[a]

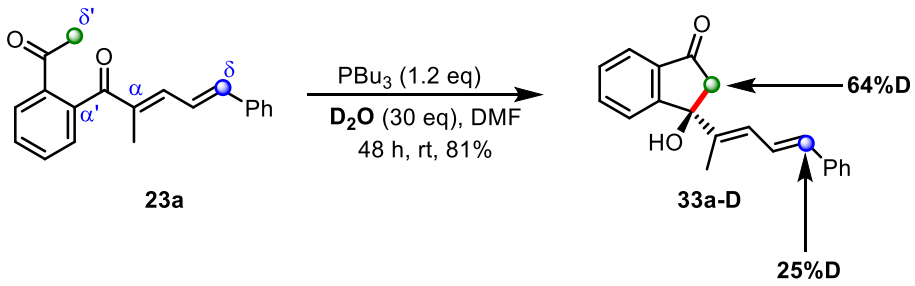
[a] diastereomeric ratio (dr) is obtained from the ^{1}H-NMR data of crude.reaction mixture.

1.5: Mechanistic Aspects:

Based on the optimization result presented in Table 1, it can be perceived that a stoichiometric amount of phosphine and water was needed for this transformation. A few factors were considered to gain mechanistic insights, (i) the role of water, and (ii) the fate of the phosphine after the reaction. To address the above, we have performed a few control experiments as described below.

1.5.1: D_2O experiments on the phosphine-promoted intramolecular aldol reaction

To know mechanistic insight, we performed isotope labeling experiments. The intramolecular aldol reaction of **23a** was conducted in the presence of D_2O, Scheme 30. Dienone-ketone **23a**, dissolved in DMF (1 ml) was treated with PBu_3 (1.2 eq) in presence of 30 eq of deuterium oxide at room temperature and continued stirring for 48 h before commencing the purification. The reaction provided **33a-D** in 81% yield, where D incorporation was realized to be 25% at δ-carbon and 64% at δ'-carbon. This result strongly suggests that the carbon center experienced anionic character at a certain stage during the reaction.



Scheme 30: Intramolecular aldol reaction in presence of D_2O.

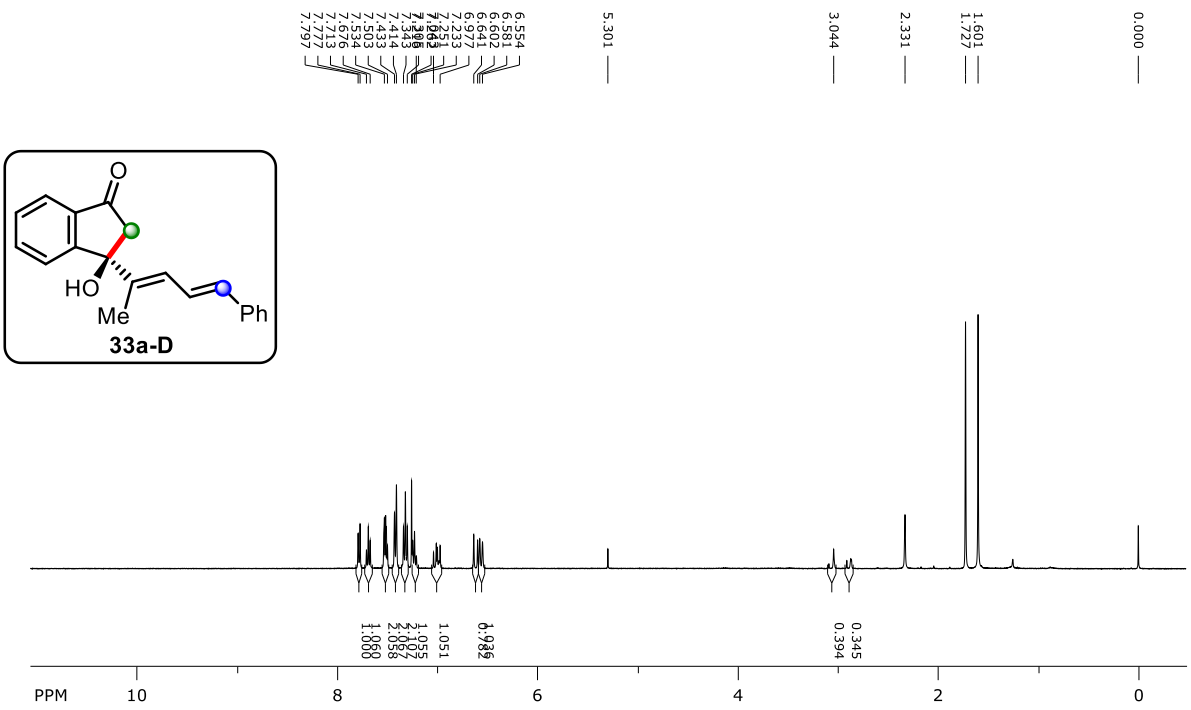


Figure 4: ^{1}H-NMR (400 MHz) of **33a-D** in $CDCl_3$.

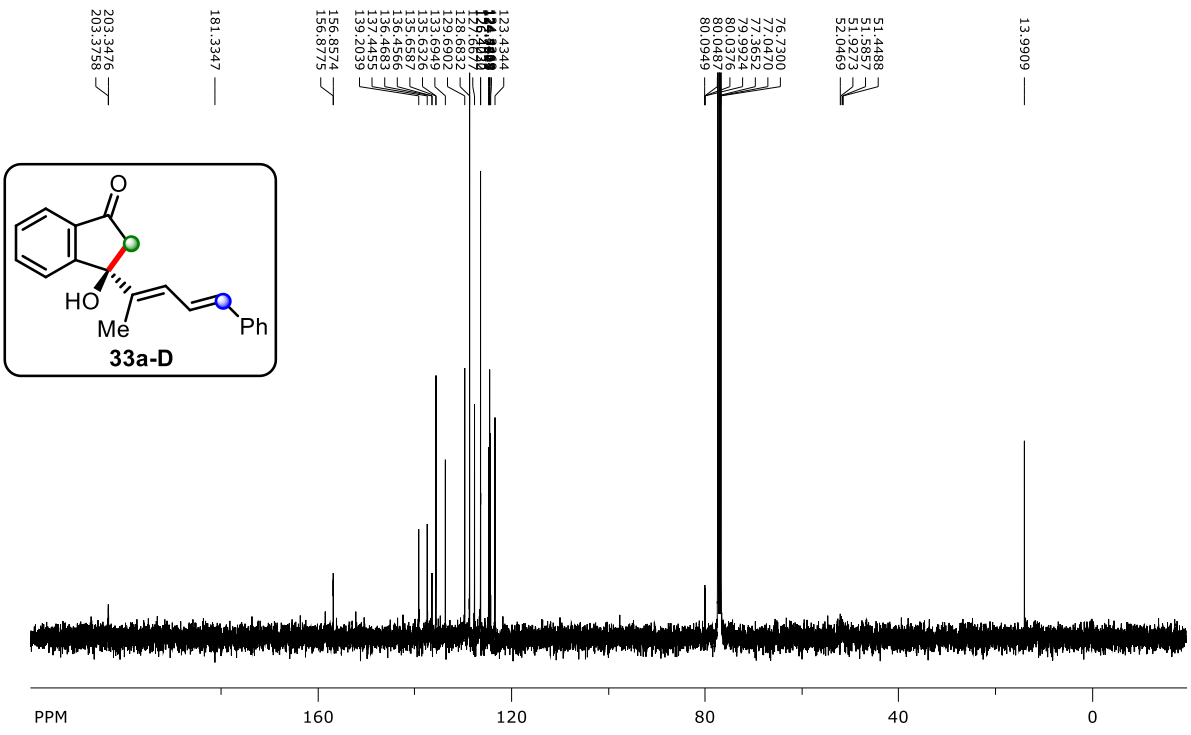


Figure 5: ^{13}C-NMR (100 MHz) of **33a-D** in $CDCl_3$.

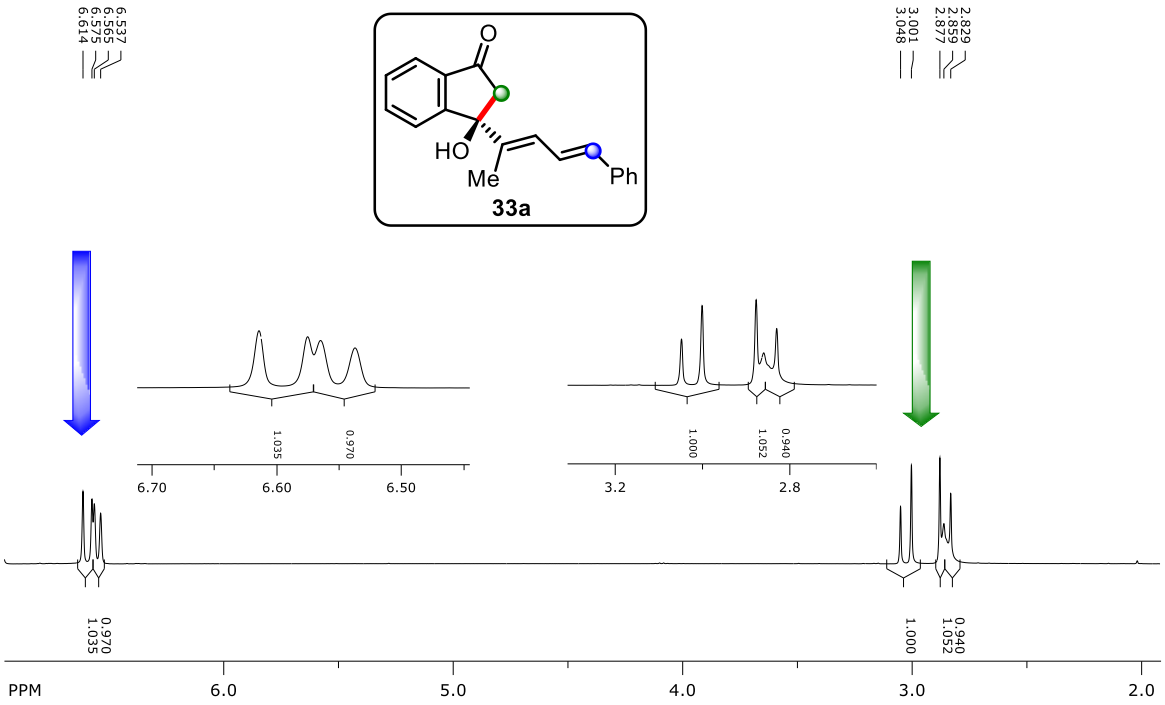


Figure 6: Expanded version of ^{1}H-NMR (400 MHz) of **33a** in $CDCl_3$.

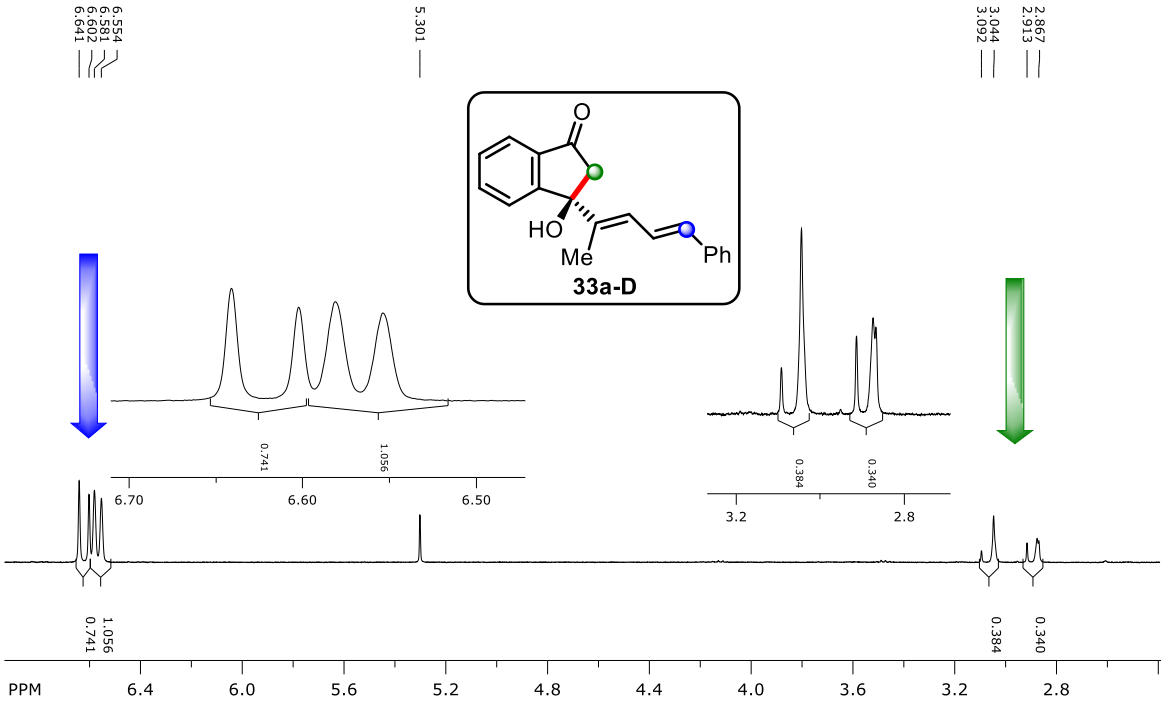
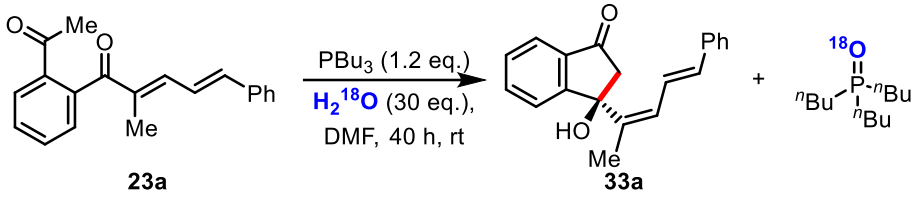


Figure 7: Expanded version of ^{1}H-NMR (400 MHz) of **33a-D** in $CDCl_3$.

1.5.2: Intramolecular aldol reaction of 23a with labeled H_2O^{18}

The role of water in this study was investigated by performing the aldol reaction of **23a** with labelled water, Scheme 31. The reaction was carried out with the model substrate **23a** under our optimized condition in presence of labelled water (H_2O^{18}). Upon completion of the starting material **23a** (monitored by TLC), the crude mixture was subjected to high resolution mass spectrometry (HRMS) analysis. The HRMS spectra revealed that the abundance of peak at 221.1913 for $P(^{18}O)Bu_3$ (calculated $(M+H)^+$: 221.1920) in $H_2{}^{18}O$ reaction was observed to be increased significantly than the respective abundance of $P(^{18}O)Bu_3$ at 221.1910 (calculated $(M+H)^+$: 221.1920) obtained from the water reaction (Fig. 9). This result clearly indicates the nucleophilic addition onto the phosphonium center during the course of the reaction prompts the elimination of tributylphosphine oxide.



Scheme 31: Reaction of **23a** in presence of $H_2{}^{18}O$.

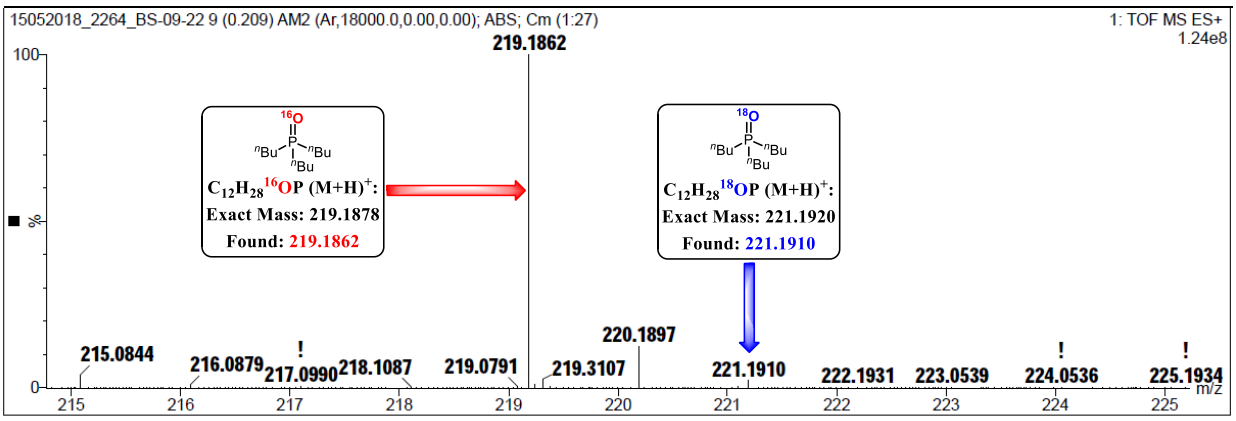


Figure 8: HRMS spectrum of the crude reaction mixture of **23a** with H_2O.

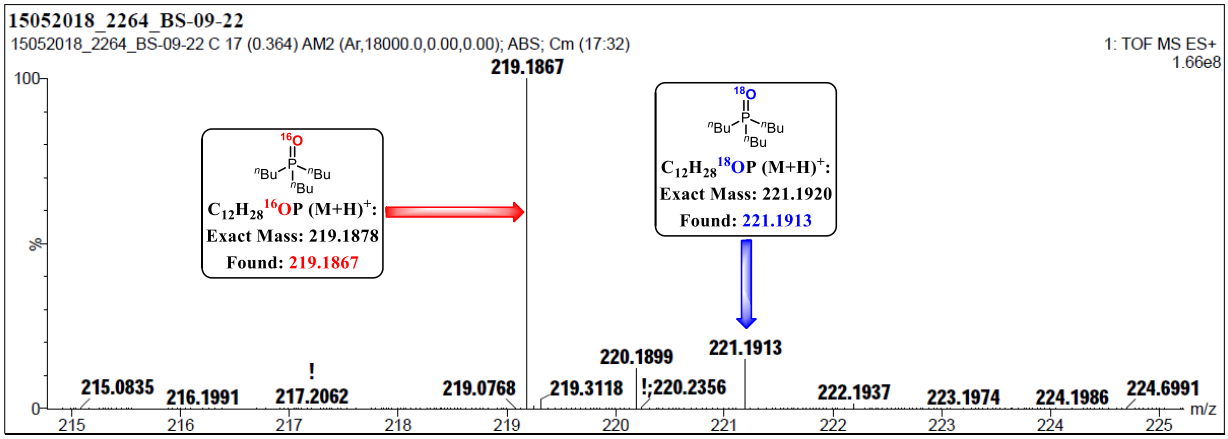
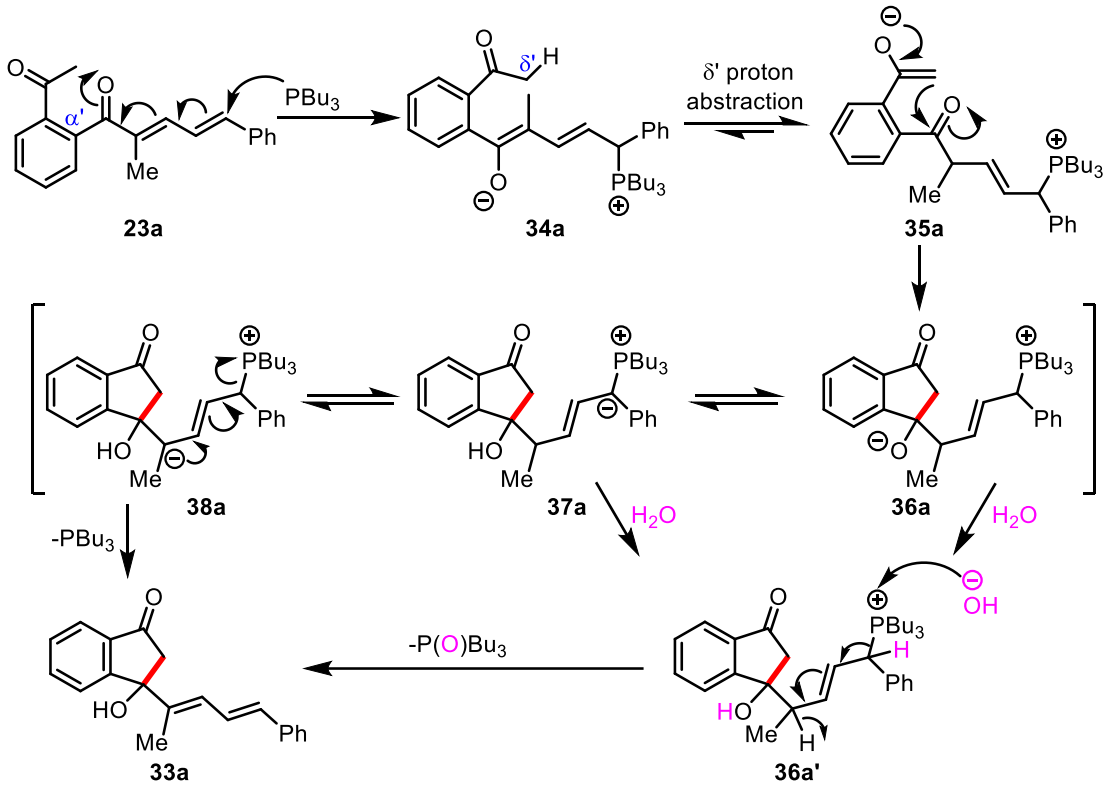


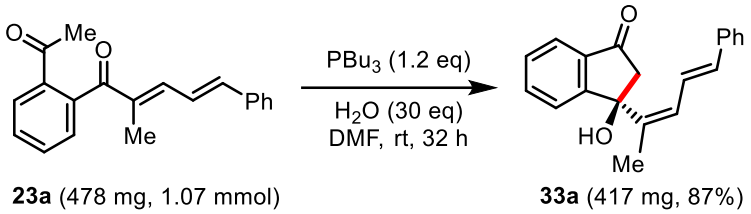
Figure 9: HRMS spectrum of the crude reaction mixture of **23a** with $H_2{}^{18}O$.

Based on the aforementioned experimental evidence and literature reports,[41] a plausible mechanism is depicted in Scheme 32. The initial 1,6-phospha-Michael addition of **23a** produces the zwitterionic species **34a** followed by abstraction of δ' proton to afford **35a**. After that, an intramolecular aldol reaction of **35a** generates zwitterionic species **36a**, which further undergoes an inter- or intramolecular proton transfer to form **37a**. Furthermore, a 1,3-proton shift involving **36a** or a 1,4-proton shift of **37a** leads to the formation of **38a**, which delivers **33a** by expelling phosphine. On the other hand, the protonation of the alkoxide **36a** or the ylide **37a** forms **36a'**, which undergoes hydroxide induced elimination of phosphine oxide to afford **33a**. These mechanistic considerations fit well with the experimental observations. Furthermore, it has to be accounted that the formation of product can be observed even when sub-stoichiometric amount of phosphine is employed (see Table 1); the rate of the reaction is significantly improved with an increase in the amount of PBu_3. Thus, the observation from Scheme 31 does not necessarily reflect the stoichiometric nature of the reaction. In order to accelerate the reaction, a stoichiometric amount of phosphine was required, but the reaction might actually be catalytic.[42]



Scheme 32: Plausible mechanism of the intramolecular aldol reaction.

To verify the practicality and generality of the method, a scale-up batch reaction was done with **23a** on 1.07 mmol scales as depicted in Scheme 33. The respective product **33a** was obtained in 87% in 32 h.



23a (478 mg, 1.07 mmol) **33a** (417 mg, 87%)

Scheme 33: The scale-up batch reaction of **23a**.

In conclusion, we have established a phosphine- and water-assisted cyclopentannulative aldol reaction of α-substituted α,β-unsaturated dienones tethered to ketones. This method renders a convenient approach for the synthesis of a library of 3-hydroxy-3-dienyl-cyclopentanones fused to arenes and heteroarenes, which can potentially serve as benzoabscisic acid analogues.[43] Most interestingly annulated cyclopentannulated cyclopentanones can be synthesized in a diastereoselective manner bearing two contiguous stereogenic centre. However, an effort for the asymmetric induction into our methodology were unsuccessful; mainly due to the stoichiometric amount of the phosphine used.

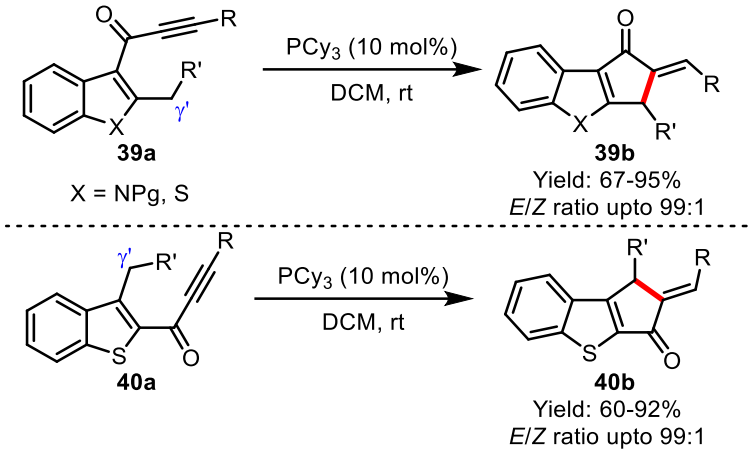
Chapter 2

Phosphine-Mediated Redox Cyclization of 1-(2-Nitroaryl)prop-2-ynones to 3-Hydroxyquinolin-4-ones: Formal Intramolecular Oxyamination of α,β-Ynones

The use of trivalent phosphines as Lewis base has great significance on organic synthesis mainly because of its stronger nucleophilicity and weaker basicity.[44] Based on its non-bonded electron pair, nucleophilic phosphines primarily attack electron-deficient activated carbon−carbon multiple bonds (alkene, alkyne, allene) to form β-phosphonium α-carbanion species which can be trapped by various electrophile or pronucleophile for the outcome of the whole reaction. Another distinctive feature of phosphines is their ability to promote transformations via the P^{III}-P^{V} redox cycle.[45] Parallel phosphine−substrate redox sequences have also been established.[46a]

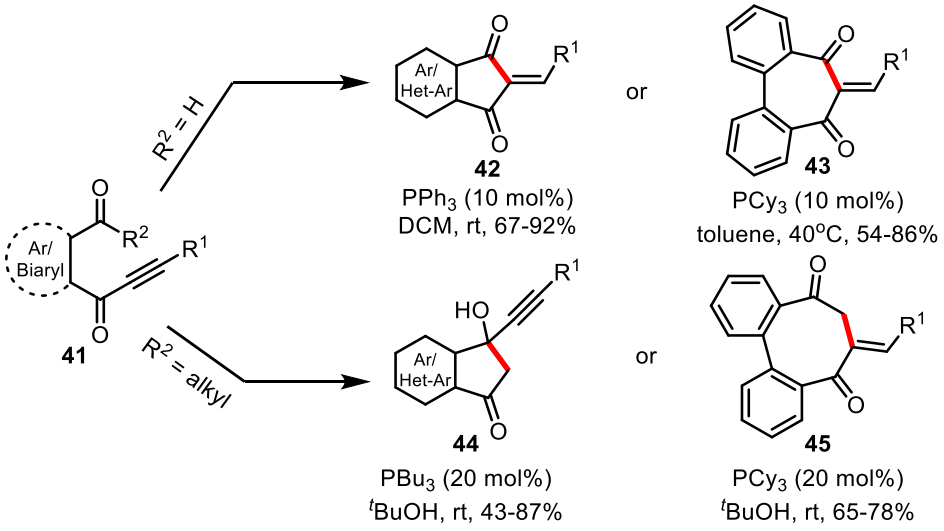
Similar to activated alkenes (e.g., enones), activated alkynes (e.g., ynones) are very reactive towards nucleophile. Though the reactivity of nucleophile towards enones and ynones are similar,[46b] after establishing the phosphine-promoted intramolecular aldol reaction of dienone-ketone system, we moved towards ynone system tethered with different functionalities. Recently, our group studied the outcome of a variety of phosphine-catalyzed

α,β-unsaturated ynone systems. For example, we have developed phosphine-catalyzed γ′[C(sp^3)-*H*]-functionalization/intramolecular hydroalkylation[47] of α,β-unsaturated ynones tethered heteroarenes **39a**, **40a** to access cyclopenta[*b*]annulated heteroarenes **39b** and **40b** in good to excellent yield and high regioselectivity. The excellent levels of efficiency and consistency in terms of yield and stereoselectivity make this methodology superior.



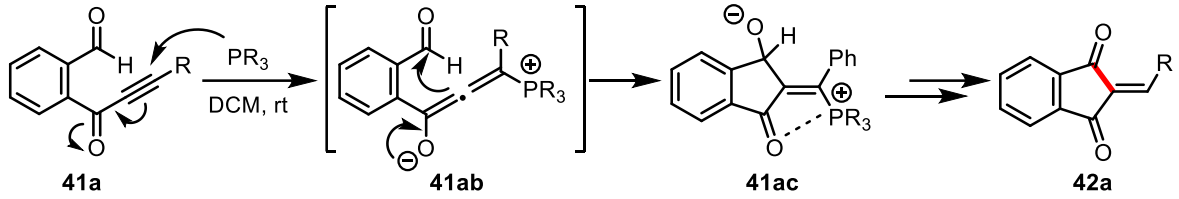
Scheme 34: Phosphine-catalyzed hydroalkylation of α,β-unsaturated ynone.

In continuation, we disclosed phosphine-catalyzed intramolecular hydroacylation of α,β-ynones **41** leading to the formation of 1,3-cyclopenta-, cyclohepta-, and cyclooctadione-fused arenes and heteroarenes **42-45**[41c] in moderate to excellent yield, Scheme 35. Interestingly, the methodology presents a fair access to 3-ethynyl-3-hydroxyindanones through δ′[C(sp^3)-*H*]-functionalization and dibenzo[*a*,*c*]-cyclooctadiones via ω′[C(sp^3)-*H*]-functionalization.



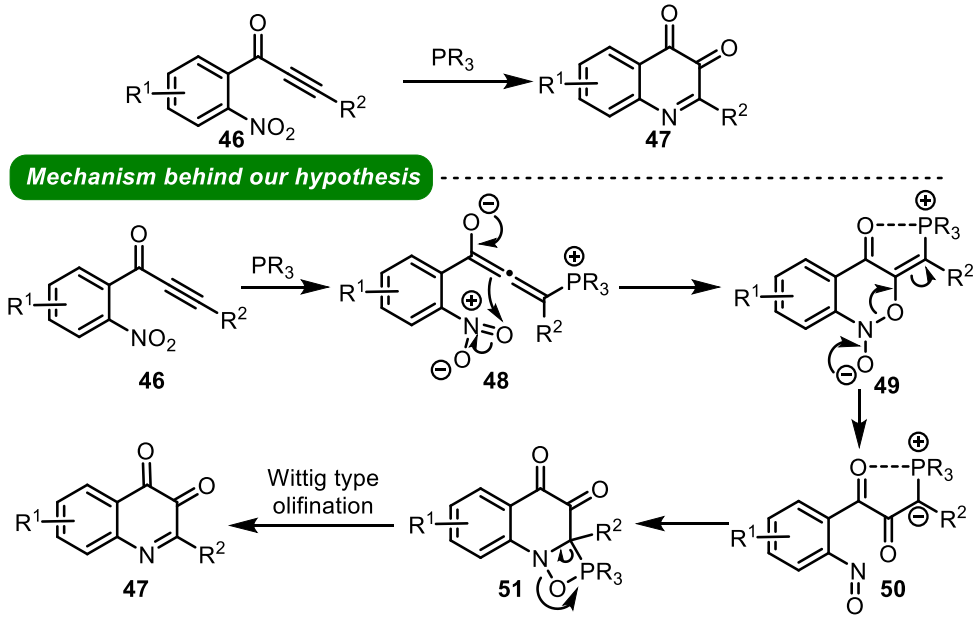
Scheme 35: Phosphine-catalyzed hydroacylation of α,β-ynones **41**.

The mechanism involves a nucleophilic 1,4-addition to the α,β-ynones to generate the corresponding zwitterionic species **41ab** followed by trapping the intermediate with carbonyls to form **41ac**. After that, subsequent proton transfer and elimination of phosphine delivers **42a**.



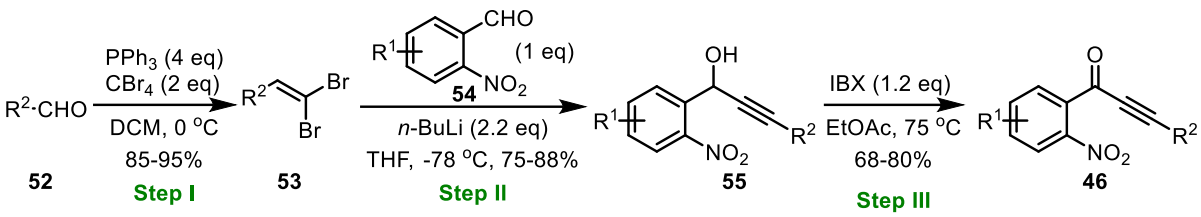
Scheme 36: Phosphine-catalyzed hydroacylation of α,β-ynones **42a**.

After the studies as mentioned above with α,β-ynones tethered with different electrophiles prompted us to design a new substrate: nitro-ynones, where the nitro group as electrophile was infused to trap the zwitterionic species, Scheme37. We envisioned that the 1,4-addition to **46** generates allenolate **48**, which could be trapped by the nitro group to form the corresponding zwitterionic species **49**. **49** can reorganise to **50**[48] embodied with a new carbonyl group and phosphonium ylide, which can undergo an intramolecular Wittig-type deoxygenation to obtain 2-substituted quinoline-3,4-diones **47**.[49]



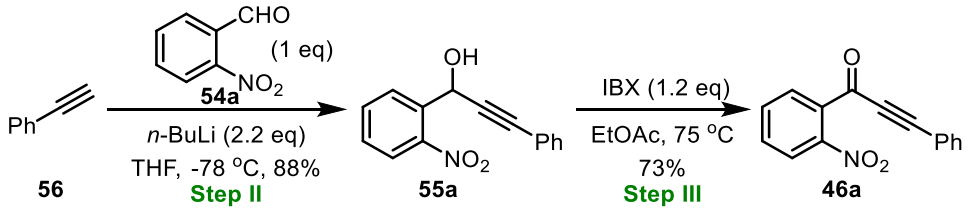
Scheme 37: Our hypothesis towards nitro-ynone **46** with phosphine.

In line with this, we made the required starting material via an easy three-step protocol from the required aldehyde **52**, Scheme 38. The aldehyde was subjected to Corey-Fuchs reaction condition to provide the dibromo product **53**, which upon directed *n*-BuLi mediated reaction with **54** and further IBX oxidation delivers the nitro-ynones **46**.



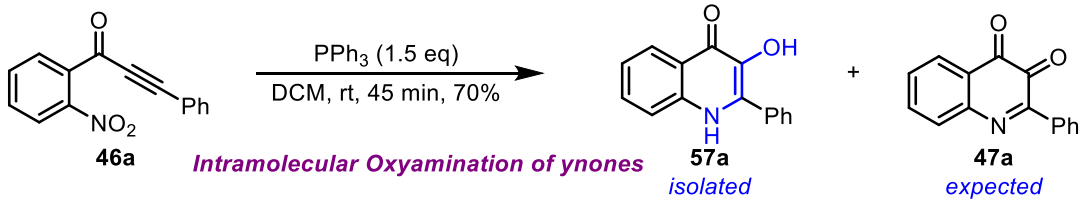
Scheme 38: Synthesis of nitro-ynones **46**.

We initiated our study by synthesizing the model substrate nitro-ynone **46a** by following the procedure shown in Scheme 39, starting from commercially available 2-nitro benzaldehyde **54a** and phenylacetylene **56**.



Scheme 39: Synthesis of **46a**.

To validate the hypothesis, our model substrate **46a** was treated with 1.5 eq of PPh_3 in DCM solvent and it delivered a polar compound in a reasonable yield at room temperature, Scheme 40. To our surprise, a careful analysis of the spectral data revealed the exclusive formation of 3-hydroxyquinolin-4-one (HQ) **57a**. However, the product **47a** was not observed, not even in a trace amount. A careful observation on this transformation results in the first oxyamination of α,β-ynones.[50] Along these lines, it encompasses an unusual redox chemistry encompassing nitro and ynone functionalities and phosphines. Moreover, it stamps a new synthetic approach of 3HQs which holds a great significance in material chemistry and medicinal sciences. In the ^{1}H-NMR spectrum (see Figure 10), the presence of singlet at δ 11.57 ppm is due to the NH proton. In ^{13}C-NMR spectrum (see Figure 11), the peak at δ 170.4 ppm indicates the presence of carbonyl group. In the IR spectrum, absorption band at 3417 cm^{-1} for the tertiary alcohol and a strong band at 1650 cm^{-1} due to the presence of carbonyl further supported the product formation. In the high-resolution mass spectrum, the presence of protonated molecular ion peak at *m*/*z* 238.0857 $(M+H)^{+}$ confirmed the structure of **57a**.



Scheme 40: Reaction of nitro-ynone **46a** with phosphine.

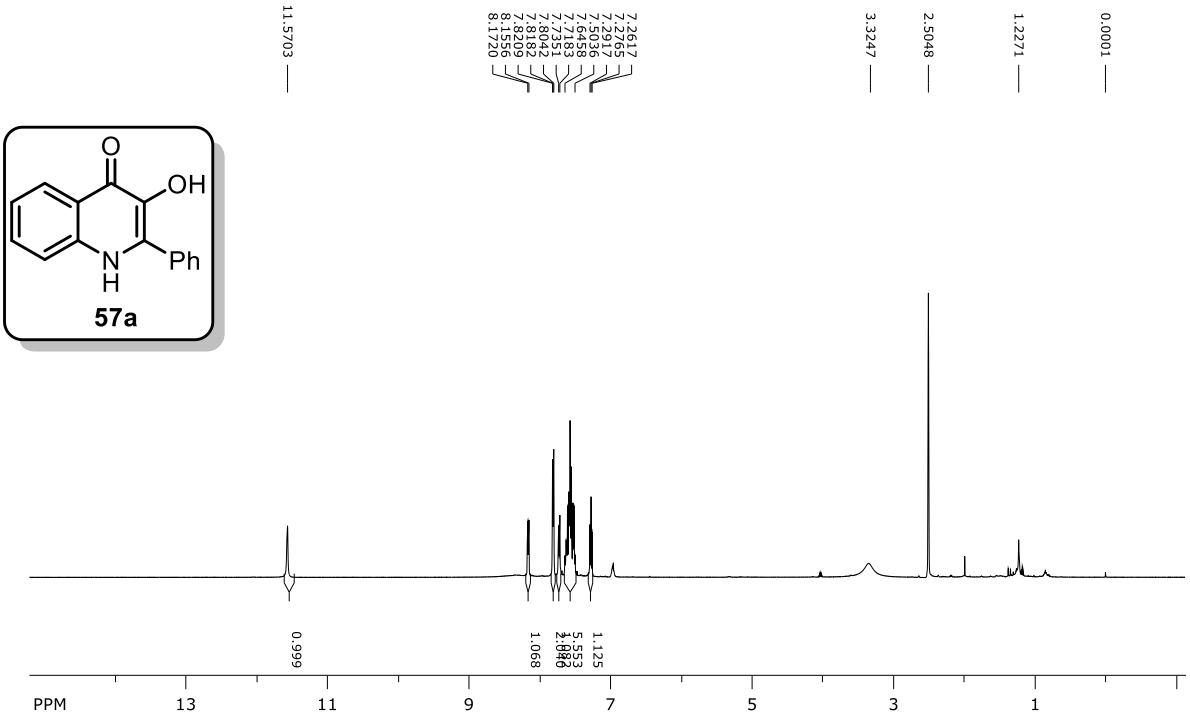


Figure 10: ^{1}H-NMR spectrum (500 MHz, DMSO-d^6) of the **57a**.

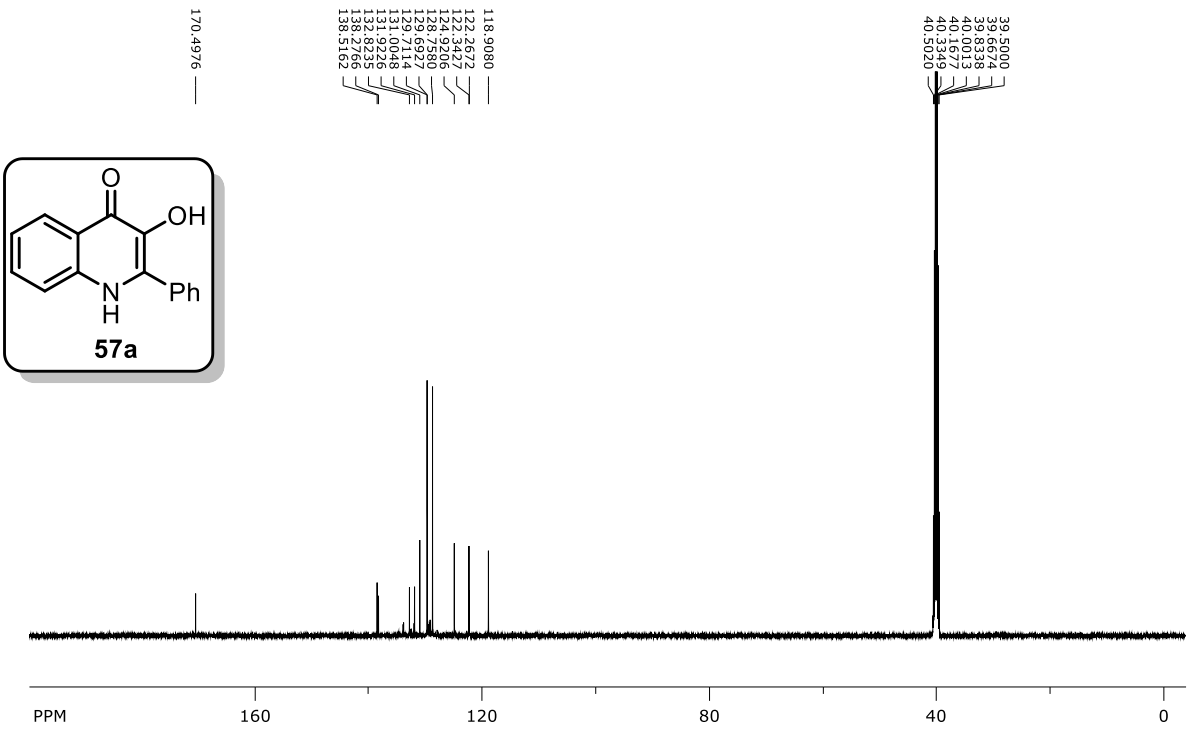
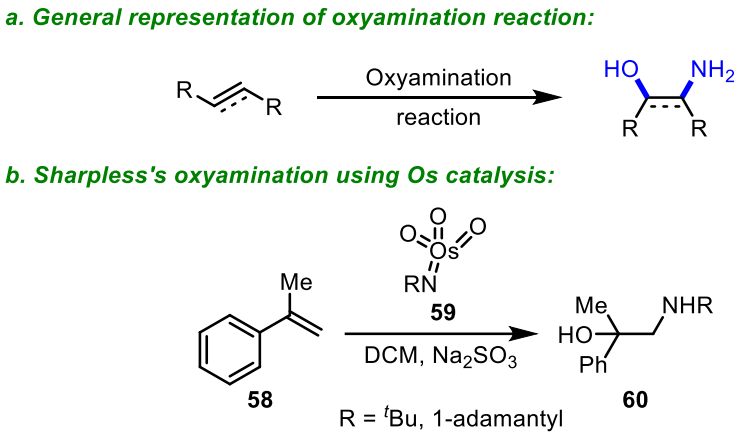


Figure 11: ^{13}C-NMR spectrum (125 MHz, DMSO-d^6) of the **57a**.

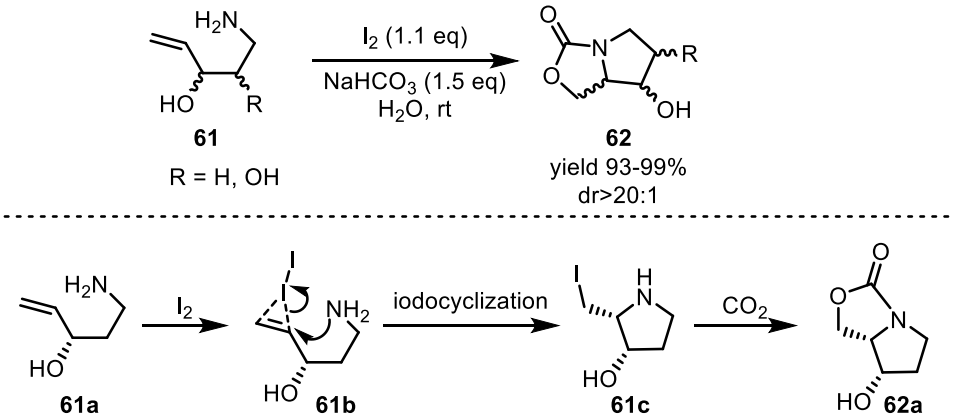
Oxyamination reaction is the deployment of an amino group and a hydroxyl group across the carbon-carbon multiple bond (alkenes, alkynes) and persists as a useful transformation in chemical synthesis.[51] Realizing the importance of 1,2-amino alcohol in synthetic organic chemistry by its occurrence in a wide range of natural products, bioactive compounds and chiral reagents, oxyamination reaction was first discovered by Sharpless[52] in 1975 using a stoichiometric amount of osmium catalyst.



Scheme 41: (a) General representation of oxyamination (b)Sharpless's oxyamination reaction using Os catalysis

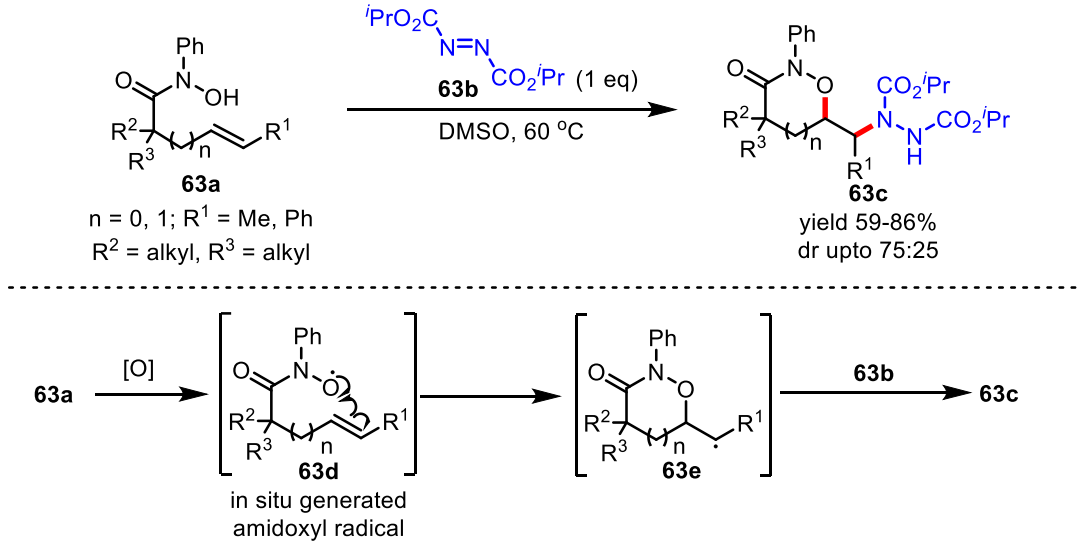
There is enormous transition metal (Rh, Ir, Os, Pd, Pt) catalyzed method reported for oxyamination of olefins. However, the major drawback associated with these transition metals is being expensive, toxic and air sensitive. Moreover, difficulty in removing all the traces of metal from the reaction limited its use in an industrial scale. In response to this, metal-free oxyamination reaction is gaining attention because it is more handful, cheap and reactive under milder conditions.

Towards this, Stocker *et al.*[53] in 2009 reported a metal-free one-pot oxyamination reaction in presence of iodine(0) by using amino alcohol **61** to access hydroxypyrrolidines **62** with high regio- and diastereoselectivity, Scheme 42. The mechanism starts with the attack of the terminal alkene onto iodine, then an intramolecular attack of the amine on the I_2-ethylene complex **61b** via 5-exo-tet cyclization to form **61c**. After that, the nucleophilic substitution of in situ generated CO_2 from $NaHCO_3$ to the haloamine intermediate **61c** provides the oxyaminated product **62**. Further, this strategy was extrapolated to the several naturally occurring imino sugar. However, the stoichiometric use of iodine in this transformation restricts its application in the industrial field.



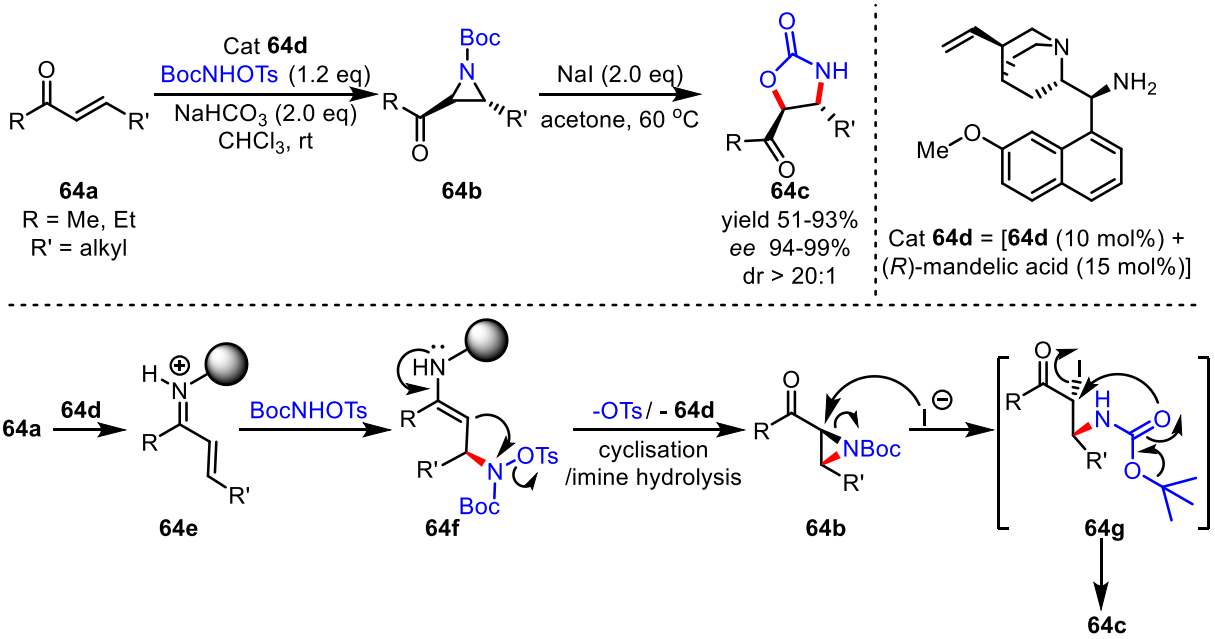
Scheme 42: Stocker's one-pot oxyamination of **61**.

In 2011, Alexanian[54] established a radical-mediated approach for the alkene oxyamination using hydroxamic acid **63a** and azidocarboxylates **63b** in DMSO solvent at 60 °C, Scheme 43. Moreover, the method capitalizes on the intramolecular version to provide regio- and diastereo-induced product with high yield, which otherwise is difficult to access. The mechanism behind this transformation is that the initially, **63a** undergoes a spontaneous radical oxidation to provide amidoxyl radical **63d** which upon intramolecular addition to the tethered alkene gives carbon-centred radical **63e**. The radical **63e** could be trapped by azidocarboxylates **63b** to provide **63c**.



Scheme 43: Alexanian's radical-mediated oxyamination reaction.

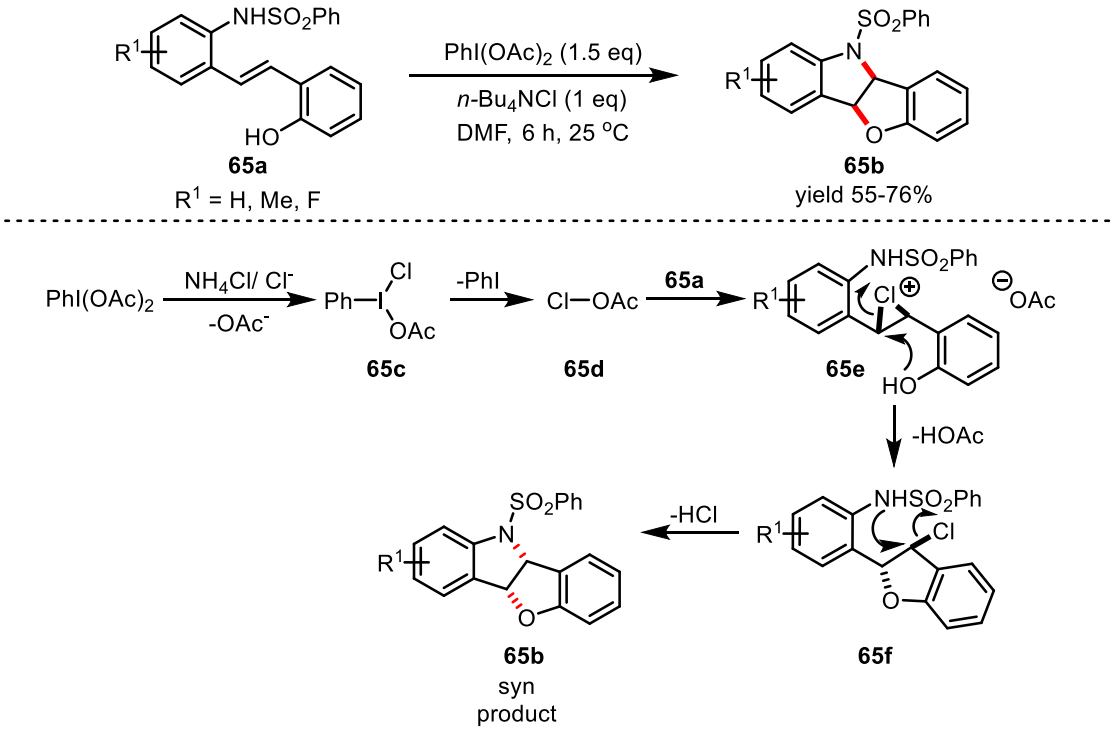
In 2012, Jorgenson *et al.*[55] disclosed an asymmetric oxyamination of enone system **64a** via aziridination using catalyst **64d** and double S_N2 sequence in presence of sodium iodide to access oxazolidinones **64c** in high yield and excellent stereoselectivity, Scheme 44.



Scheme 44: Jorgenson's asymmetric oxyamination of enones.

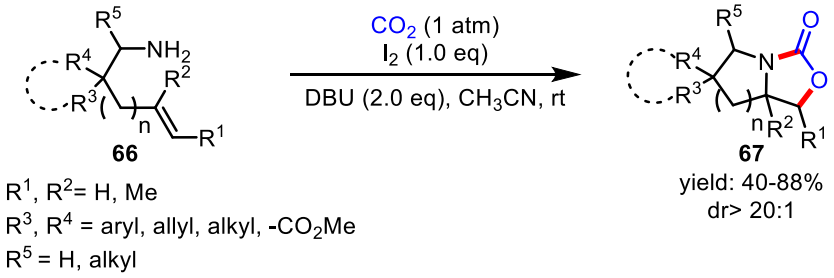
The mechanism commences with the condensation of enone **64a** and catalyst **64d** in presence of (R)-mandelic acid to form an activated iminium species **64e**. After the nucleophilic addition of BocNHOTs onto **64e** from β side generates **64f**. Subsequnety, spontaneous ring cyclization followed by imine hydrolysis and liberation of the catalyst **64d** gives the optically active aziridine **64b**. Afterwards, the three-membered **64b** is regioselectively unfastened by the iodide ion to provide α-iodo-β-amino ketone species **64g**, which undergoes O-alkylation from the Boc group and elimination of iodide gives access to the desired optically active **64c**.

Parallelly in the same year, Chang's group[56] discovered the first example of oxyamination reaction of stilbenes **65a** tethered with a sulfonamide group and hydroxyl group at the *ortho* position using a hypervalent iodine and a halide additive under metal-free conditions. The mechanism involved in this transformation is delineated in Scheme 45. Initially, $PhI(OAc)_2$ undergoes a chloride exchange reaction to furnish the reactive intermediate **65c**, which is further transformed into active hypochlorite species **65d**. The electrophilic addition of **65d** across the olefin generates **65e** followed by an intramolecular attack of the tethered sulfonamido group onto the halonium carbon center yields **65f**. Finally, S_N2 replacement from sulfonamide group gives syn-product **65b**.

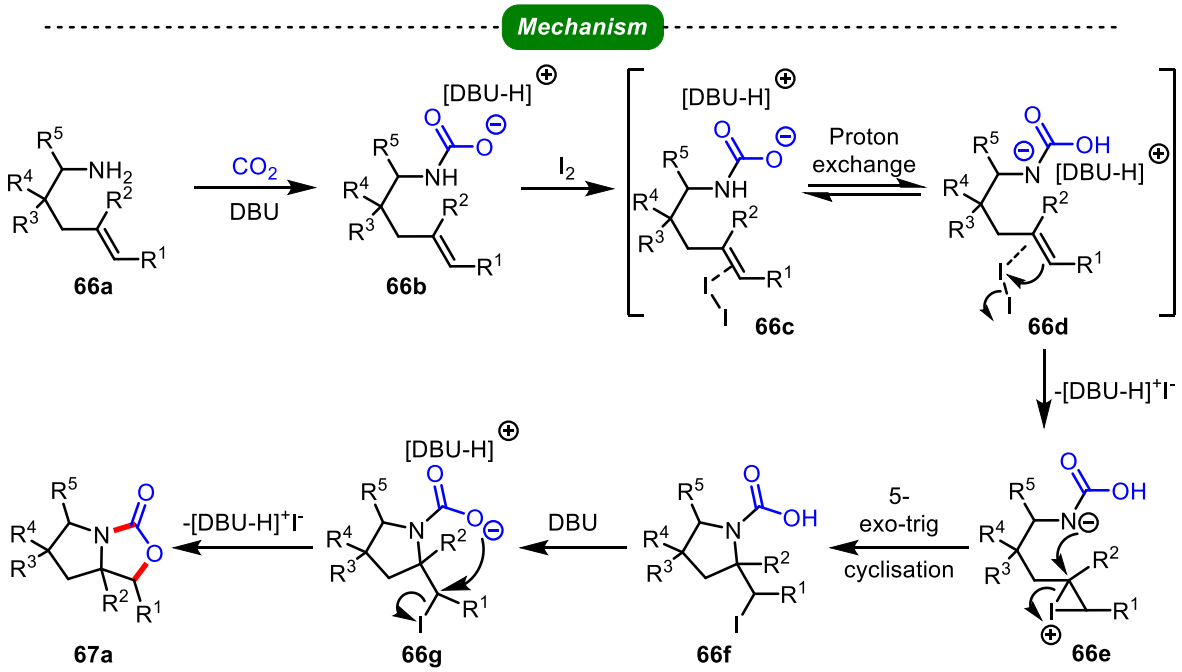


Scheme 45: Cheng's work on intramolecular oxyamination.

In 2017, Xi *et al.*[57] disclosed a metal-free iodine-mediated oxyamination of amine-chained olefin with ambient CO_2 to access prolinol carbamates, Scheme 46. Here, CO_2 plays a vital role as it directly deploys the synthon of prolinol carbamate **67** via in situ generation of protecting group to modulate the nucleophilicity of the amino group and ease the bicyclization of **66** with high chemoselectivity. A detailed mechanistic study revealed that in the beginning amino group of **66a** was trapped by CO_2 group in presence of DBU to form carbamic salt **66b**. After that, I_2 mediated olefin activation to generate **66c** followed by proton exchange forms active intermediate **66d**, which further transforms into iodonium species **66e** and eliminates $[DBUH]^+I$. Subsequently, a 5-exo-trig cyclization from nitrogen centre to form **66f**. Eventually, another molecule of DBU abstracts the acidic proton of carbamic acid **66f** followed by intramolecular substitution of iodide by oxygen atom furnish **67a**.

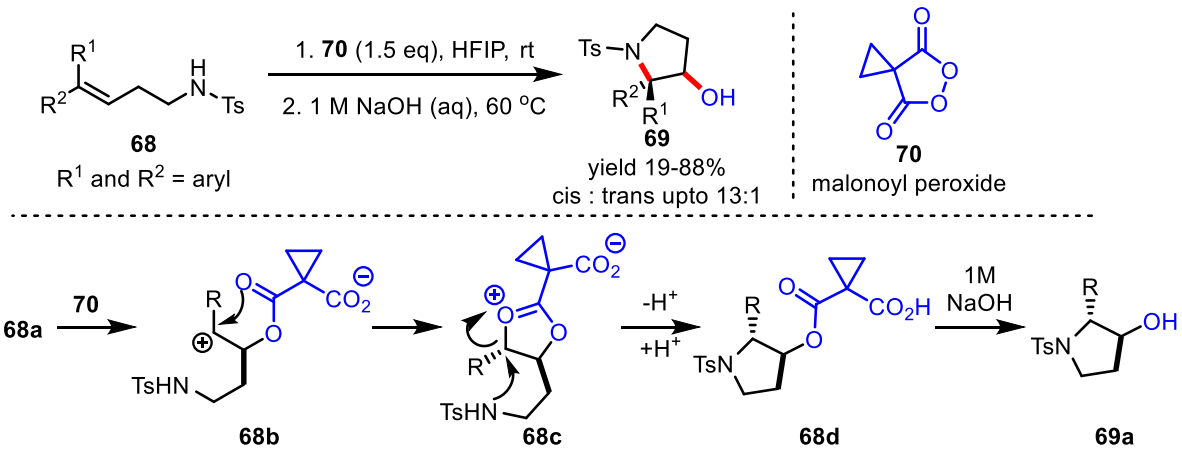


R^1, R^2= H, Me
R^3, R^4 = aryl, allyl, alkyl, -CO_2Me
R^5 = H, alkyl



Scheme 46: Xi's iodine-mediated aminohydroxylation.

In 2018, Tomkinson and co-worker[58] exploited the aminohydroxylation reaction of alkenes **68** using malonoyl peroxide **70** in presence of HFIP solvent to access pyrrolidine **69**, Scheme 47. The mechanism begins with the nucleophilic attack of the substituted alkene **68a** on the peroxide leading to **68b**. After that, a subsequent intramolecular cyclization to ease dioxonium species **68c** further undergoes another cyclization from amino group and followed by base-mediated hydroxylation gives the pyrrolidine **69a** in poor to excellent yield.



Scheme 47: Tomkinson's alkene aminohydroxylation using malonoyl peroxide.

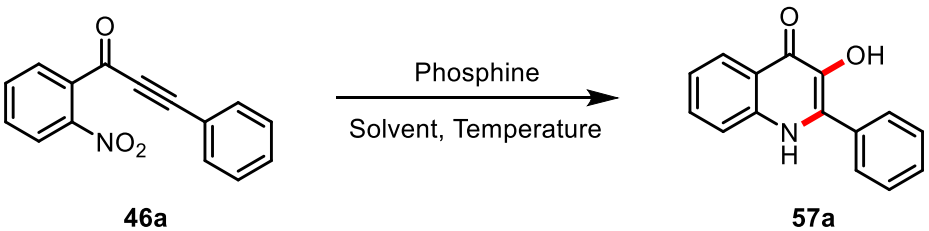
As showcased above, the literature survey disclosed a few important aspects of oxyamination reaction: (i) the phosphine-promoted oxyamination of ynone system is yet to be

achieved, (ii) moreover, ynones possessing α,β- substitutions and tethered with nitro group are not explored, (iii) the mild reaction condition in oxyamination process remains always an encouraging factor.

2.1: Results and Discussion

Interestingly, our observation sketched in Scheme 40 encompasses an metal-free phosphine-promoted formal intramolecular oxyamination of α,β-ynones to synthesise 3-Hydroxyquinoline-4(1*H*)-ones (3HQs). After the initial result with PPh_3 in DCM solvent at room temperature, a variety of phosphine and solvent combinations were screened to further improve the efficiency of the transformation and the results are summarised in Table 3. After the detailed solvent screening, it was realized that the reactions in polar solvents (such as DMSO, DMF, ACN) are not encouraging. When the reaction of **46a** was performed with PPh_3 in DMSO solvent, the product **57a** was obtained in 52% yield (entry 1). In presence of other polar solvents e.g., DMF and ACN, the reaction even performed worse (entries 2-3). Noticeably, in presence of nitromethane as polar solvent, the reaction remained unsuccessful in delivering the product **57a** (entry 4). Whereas the reaction of **46a** with PPh_3 in presence of THF solvent gave poor yield of 3-hydroxyquinolin-4-one **57a** (entry 5). Remarkably, the transformation of **46a** to **57a** fared well in non-polar solvent e.g., DCM and toluene. Next, we investigated the role of the temperature on the conversion of **46a** to **57a**. Reaction of **46a** was found to give **57a** with lower yield in lowering the temperature (entries 6-8). Interestingly, the reaction performed at 100 ^oC obtained **57a** in high yield. Afterwards, to improve the efficiency of the reaction further, we focused on tuning the nucleophilicity of the phosphine. The result attained in trialkyl- and diarylalkylphosphines were not encouraging (entries 10-12). Whereas, in presence of tris(4-methoxyphenyl)phosphine, the product **57a** was isolated in 79% yield (entry 13). Furthermore, subsequent studies of phosphine loading revealed that even 1.2 equivalent of triphenylphosphine could bring about an efficient transformation in about 20 min (entries 14−17).

Table 3: Screening of reaction parameters for the oxyamination reaction with **46a**



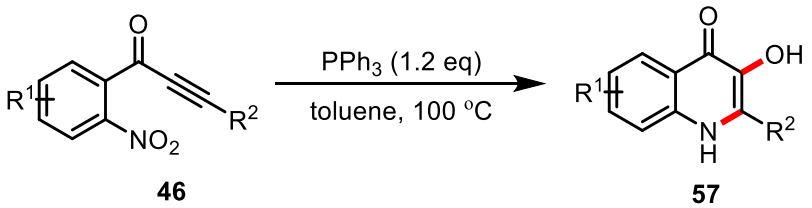
46a **57a**

Sl No.	Phosphine (eq.)	Solvent	Temperature (^oC)	Time (min)	Yield (%)[a]
1	PPh_3 (1.5)	DMSO	rt	180	52
2	PPh_3 (1.5)	DMF	rt	180	40
3	PPh_3 (1.5)	ACN	rt	180	<5%
4	PPh_3 (1.5)	$MeNO_2$	rt	60	-
5	PPh_3 (1.5)	THF	rt	180	26
6	PPh_3 (1.5)	Toluene	rt	120	73
7	PPh_3 (1.5)	Toluene	50	150	59
8	PPh_3 (1.5)	Toluene	70	150	63
9	PPh_3 (1.5)	Toluene	100	15	78
10	PBu_3 (1.5)	Toluene	100	15	-
11	PCy_3 (1.5)	Toluene	100	15	42
12	PPh_2Et (1.5)	Toluene	100	15	64
13	$(p\text{-}CH_3OC_6H_4)_3P$ (1.5)	Toluene	100	15	79
14	PPh_3 (0.5)	Toluene	100	60	37
15	PPh_3 (0.8)	Toluene	100	60	47
16	PPh_3 (1)	Toluene	100	25	70
17	**PPh_3 (1.2)**	**Toluene**	**100**	**20**	**77**

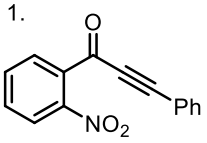
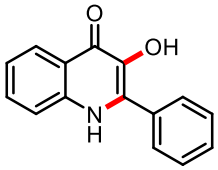
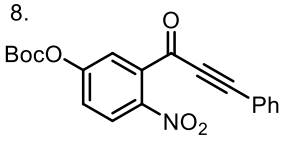
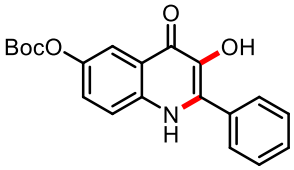
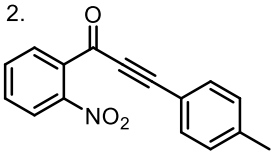
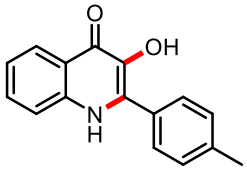
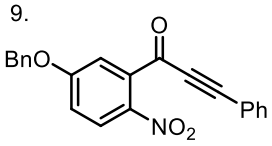
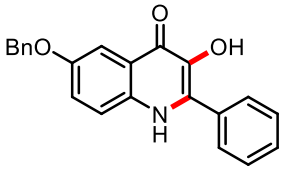
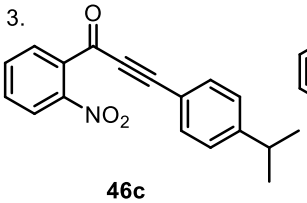
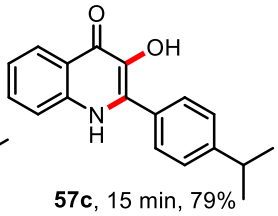
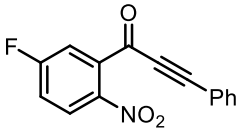
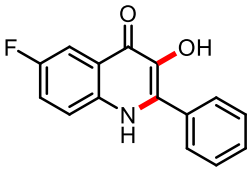
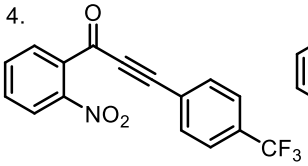
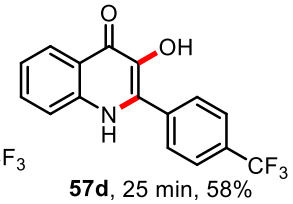
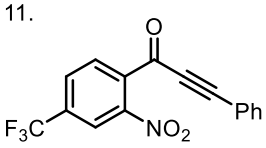
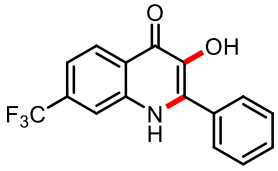
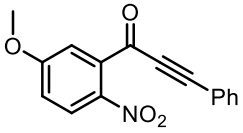
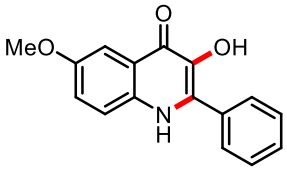
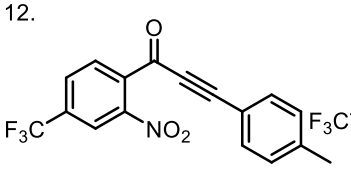
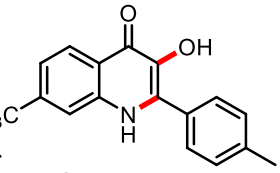
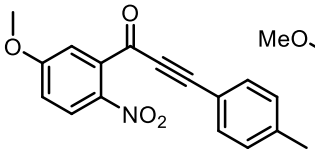
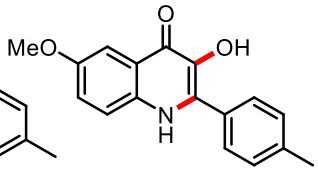
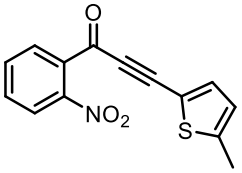
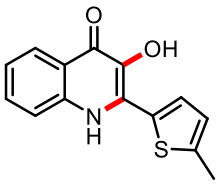
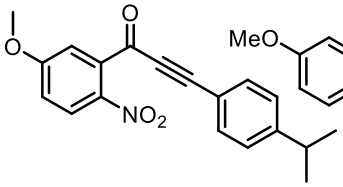
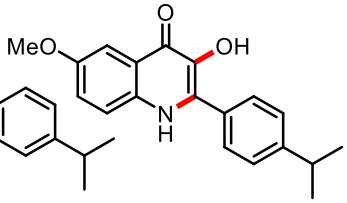
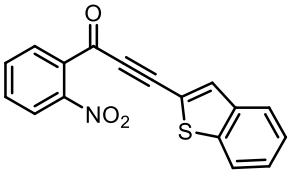
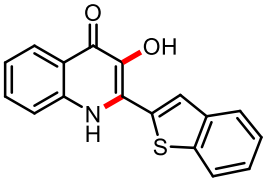
All reactions were performed on 0.1 mmol scales. [a] Yields were calculated after silica gel column chromatography.

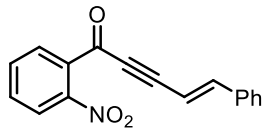
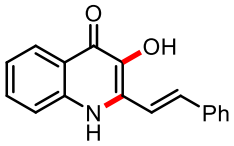
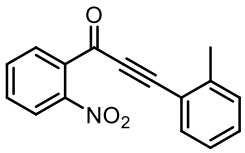
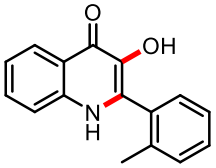
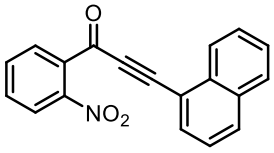
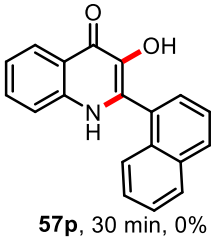
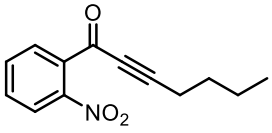
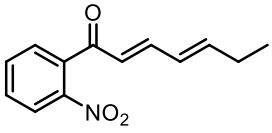
After having the optimized condition in hand, we investigated the substrate scope with various kinds of nitro-ynones bearing different electronic features. The results of the study were presented in Table 4. A diverse range of substituents on the ynone and the arene backbone were evaluated and an array of 3-Hydroxyquinoline-4(1*H*)-ones (3HQs) **57a-q** were rapidly assembled in good to excellent yields. Ynones having electron-donating or withdrawing groups or heteroarenes on the alkyne part **46b-d**, **46m-n** have no significant effect in the yields of the reaction while obtaining respective 3HQs **57b-d**, **57m-n**, Table 4.

Table 4: Substrate Scope: 3-Hydroxyquinoline-4(1*H*)-ones (3HQs) **57a-q**



46 **57**

Entry	Substrate	Product	Entry	Substrate	Product
1.			8.		
	46a	**57a**, 20 min, 77%		**46h**	**57h**, 15 min, 90%
2.			9.		
	46b	**57b**, 20 min, 78%		**46i**	**57i**, 20 min, 75%
3.			10.		
	46c	**57c**, 15 min, 79%		**46j**	**57j**, 30 min, 73%
4.			11.		
	46d	**57d**, 25 min, 58%		**46k**	**57k**, 15 min, 72%
5.			12.		
	46e	**57e**, 15 min, 80%		**46l**	**57l**, 15 min, 74%
6.			13.		
	46f	**57f**, 15 min, 75%		**46m**	**57m**, 25 min, 64%
7.			14.		
	46g	**57g**, 20 min, 78%		**46n**	**57n**, 10 min, 71%

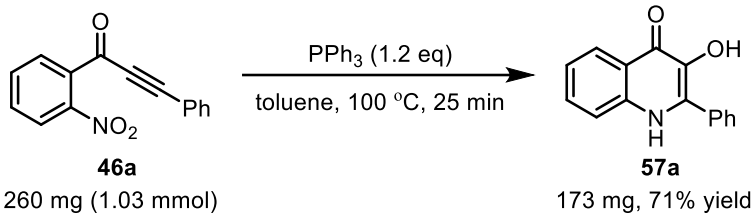
Entry	Substrate	Product	Entry	Substrate	Product
15.			17.		
	46o	**57o**, 5 min, 53%		**46q**	**57q**, 30 min, 21%[a]
16.			18.		
	46p	**57p**, 30 min, 0%		**46r**	**57r**, 10 min, 75%

[a] reaction was performed in PBu_3

Next, we studied the role of the substituents on the arene backbone. Substrates having electron-withdrawing groups (such as -F, -CF_3) in the aryl backbone (**47j-l**) worked nicely under the optimized condition to obtain the hydroxyquinolone **57j-l**, Table 4. Remarkably, substituents bearing the electron-donating group (e.g., OMe, OBn, OBoc) **46e-i** were found to be efficient in this methodology. Even the transformation is amenable with nitro-enynone **46o** to produce 3HQ **57o** with an alkenyl group. Whereas substrate possessing *ortho*-substituted arenes on alkynes was inferior to the reaction condition, Table 4. To specify, the *o*-tolyl adduct **57q** under the optimized reaction condition was not observed. Rather, **57q** was isolated with 21% yield in presence of 1.2 eq of PBu_3 as promoter. Parallelly, naphthyl nitro-ynone **46p** failed to produce the respective 3HQ **57p** despite several attempts. We speculated steric hindrance on the ortho position may be the reason behind these results. During the substrate scope study, we realized that substrate containing aliphatic group attached to ynone remained inefficacious in delivering the desired HQ. For example, when **46r** was subjected to our optimized condition, the dienone **57r** was isolated in 75% yield within 10 mins. This result is in line with Trost's phosphine-catalyzed internal redox transformation of α,β-ynones to 2,4-dienones.[59]

Scale-up batch:

To verify the generality and practicality of the method, a scale-up batch reaction was done with **46a** on 1.03 mmol scales as depicted in Scheme 48. The respective product **57a** was obtained in 71% in 25 min.



46a
260 mg (1.03 mmol)

57a
173 mg, 71% yield

Scheme 48: Scale up reaction of **46a**.

The molecular structure of **57j** was unambiguously confirmed by X-ray diffraction analysis, Figure 12.

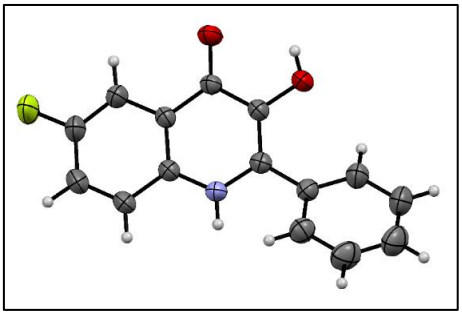


Figure 12: ORTEP diagram of 3HQ **57j**.

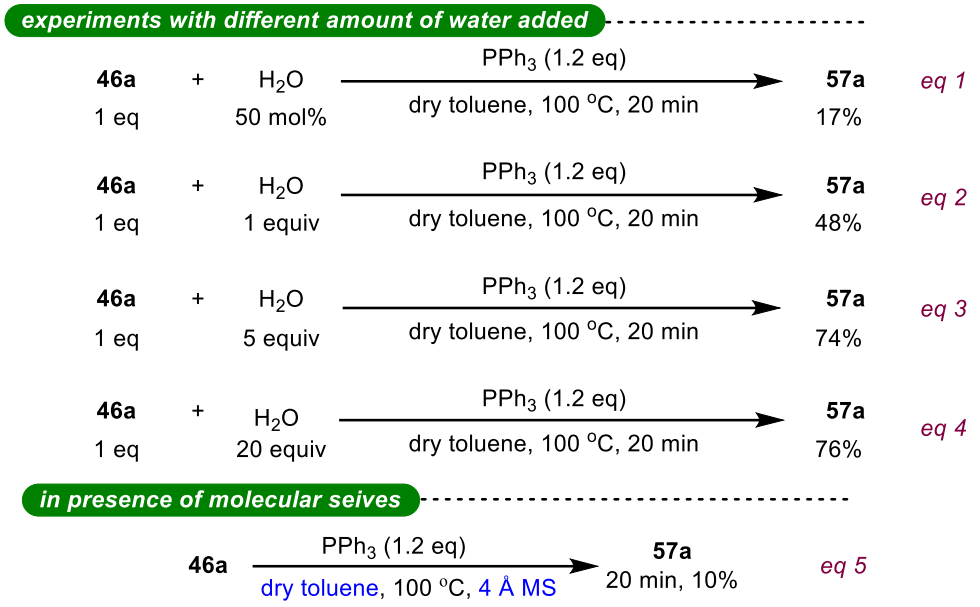
2.2: Mechanistic Insights

Having established novel synthetic approach of 3HQs, we moved to gaining mechanistic insights into the in situ reduction of quinoline diones **47** to β-hydroxyenaminones **57**. To streamline the discussion of mechanism, few factors were considered: (i) the role of water in this transformation and (ii) the amount of phosphine loading. To address the above, few control experiments were performed, which are discuss below.

2.2.1: Investigations to know the role of water:

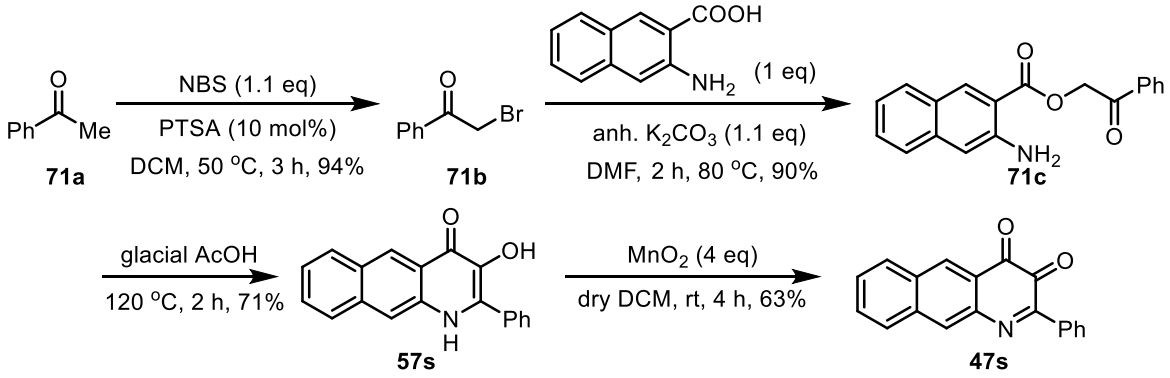
First, we investigated the role of water in this transformation by conducting the reaction of **46a** in dry toluene with different amounts of water as the additive (eq 1-4) and the outcome was condensed in Scheme 49. We performed the reaction with **46a** in freshly dried toluene in presence of 50 mol% water in our optimized condition to obtain **57a** in 17% of yield. Interestingly, when the reaction was done with 1 equivalent of water in optimized condition, we isolated **57a** in 48% yield. Subsequently, we observed good yield of **57a** when the reaction was performed with 5 equivalent or 20 equivalent of added water in our optimized condition. The above control experiments clearly indicate that the water has a decisive role at a certain stage of the transformation. Additionally, when an experiment was performed in dry toluene

and 4 Å molecular sieves (MS) (eq 5), the product isolated in poor yield, further highlighting the crucial role of water.



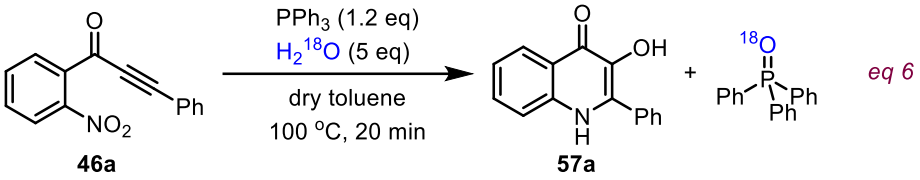
Scheme 49: Oxyamination of **46a** in different amounts of water and 4 Å MS.

Furthermore, to understand the exact function of water, we performed control experiments with $H_2{}^{18}O$. Since, quinoline-3,4-diones **47a** are hypothesized intermediates in the conversion of **46a** to **57a**, Scheme 37, we wanted to synthesize **47a** following known literature procedure,[60] however, despite our several attempts we could not able to prepare the same. Meanwhile, we synthesized **47s**[61] via a four-step protocol starting from commercially available acetophenone **71a**. NBS-mediated bromination of acetophenone in DCM at 50 °C provided phenacyl bromide **71b**. After that, base-mediated esterification of anthranilic acid with **71b** in DMF gave the amino ester **71c**, which underwent cyclization to form **57s**. Finally, manganese dioxide-mediated oxidation furnished the diketo compound **47s**.



Scheme 50: Synthesis of **47s**.

The role of water during the reaction was further elucidated by performing the reaction of **46a** in presence of ^{18}O-labeled water under the optimized condition (eq 6). The crude reaction mixture was analyzed by HRMS, which revealed the abundance of $P(^{18}O)Ph_3$ increased with respect to the abundance of $P(^{18}O)Ph_3$ obtained from the standard reaction.



Scheme 51: Reaction of **46a** in the presence of $H_2{}^{18}O$.

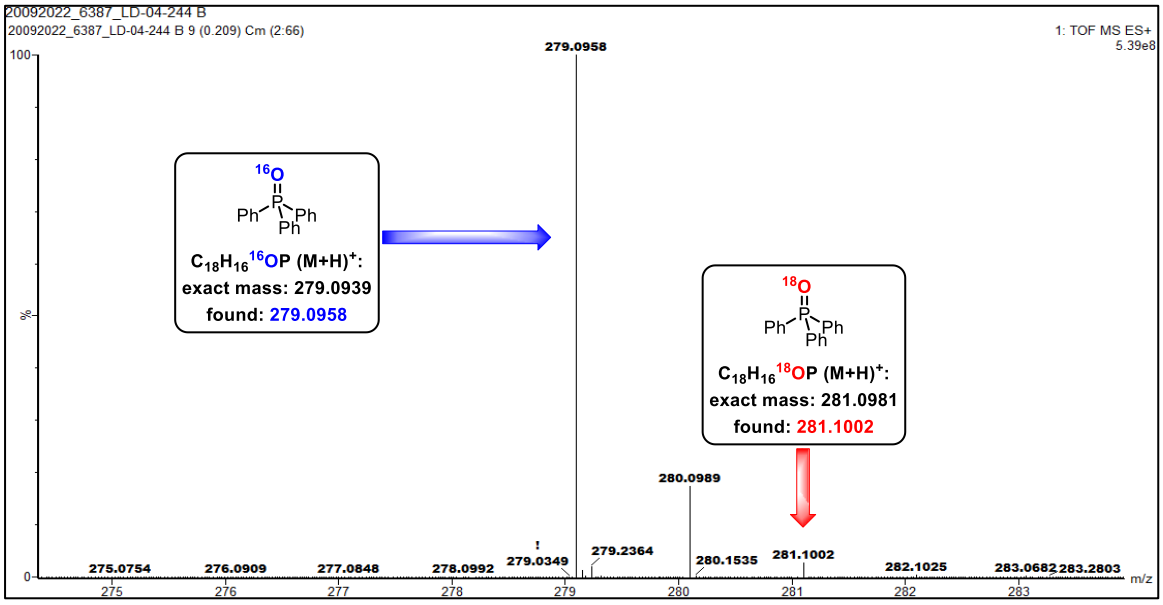


Figure 13: HRMS spectrum of the crude reaction mixture of **46a** under optimized condition.

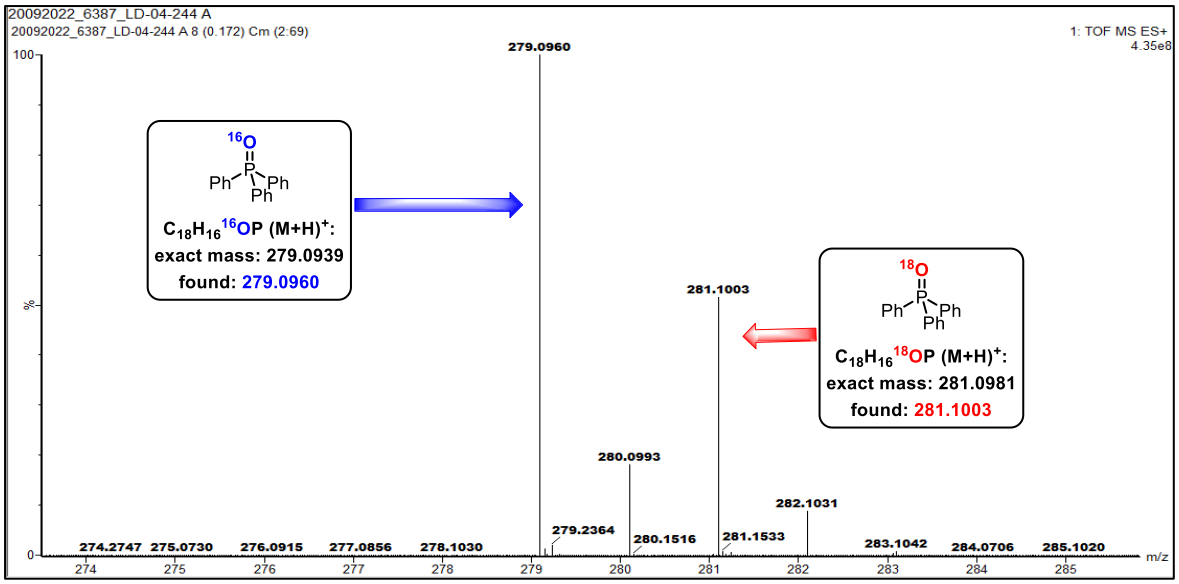
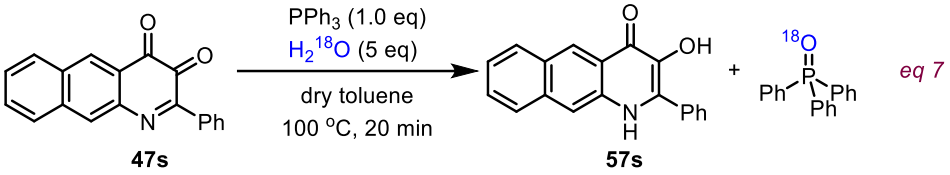


Figure 14: HRMS spectrum of the crude reaction mixture of **46a** in the presence of $H_2{}^{18}O$.

We also performed the reaction of **47s** with ^{18}O-labeled water under the optimized condition (eq 7). The crude reaction mixture was analyzed by HRMS, which revealed the abundance of P(^{18}O)Ph$_3$ increased with respect to the abundance of P(^{18}O)Ph$_3$ obtained from the standard reaction.



Scheme 52: Reaction of **47s** in the presence of $H_2{}^{18}O$.

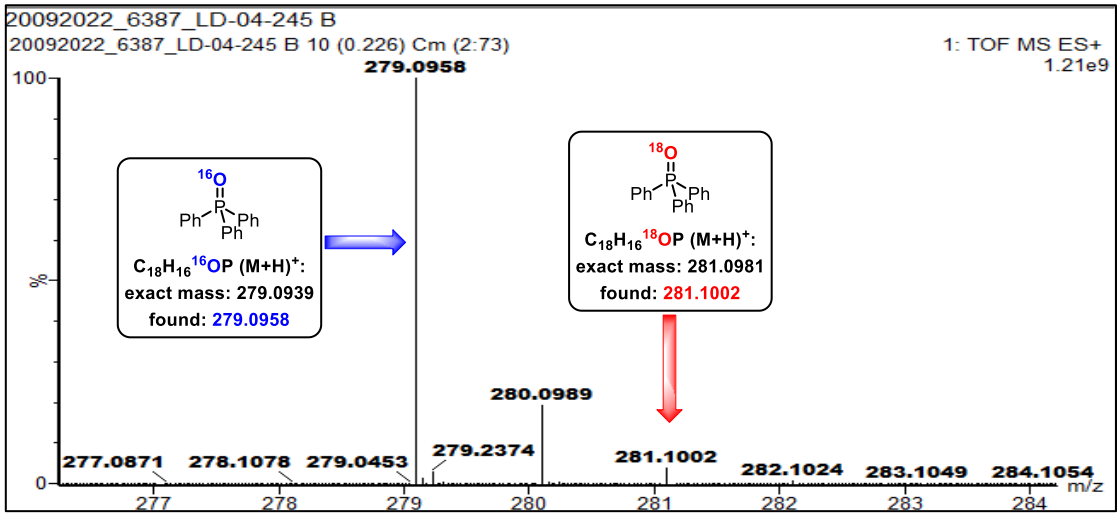


Figure 15: HRMS spectrum of the crude reaction mixture of **47s** without $H_2{}^{18}O$.

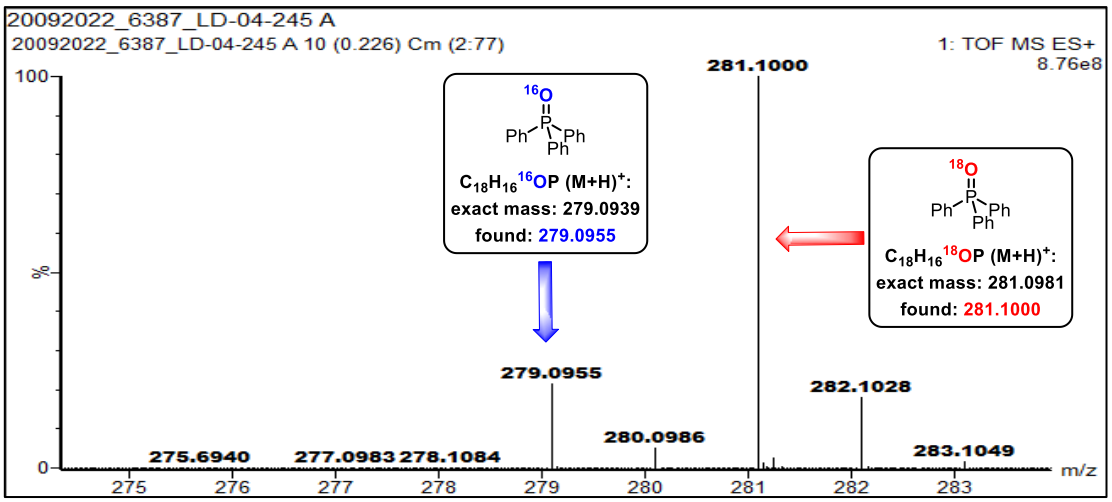
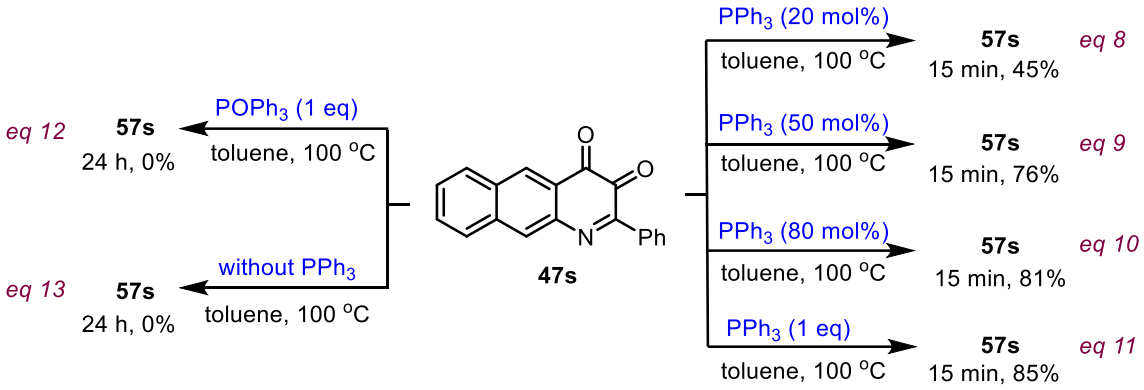


Figure 16: HRMS spectrum of the crude reaction mixture of **47s** in the presence of $H_2{}^{18}O$.

These results confirm the nucleophilic addition of water onto the phosphonium center during the course of the reaction, thereby triggering the elimination of triphenylphosphine oxide (TPPO).

2.2.2: Control experiments for phosphine loading:

For the investigation of amount of phosphine required, we performed a series of reaction with **47s** in presence of different amount of triphenylphosphine (TPP) added. The results are summarised in Scheme 53. When **47s** was treated with 20 mol% PPh_3, we isolated **57s** in 45% yield (eq 8). The yield of product **57s** increased to 76% in presence of 50 mol% TPP (eq 9) and it was realized that with the increase in the amount of PPh_3 from 80 mol% to 1 eq, the product **57s** obtained increased gradually (eq 10-11). So, it can be concluded that a sub-stoichiometric amount of phosphine was required for an efficient transformation of **47s** to **57s**. On the other hand, the reaction of **47s** with triphenylphosphine oxide (TPPO) gives no product (eq 12), ruling out the role of TPPO in this conversion. Parallelly, no product formation was observed in absence of PPh_3 (eq 13), which excludes the possibility of thermal transformation of **47s** to **57s**.



Scheme 53: Reaction of **47s** with different amounts of TPP loading.

The crude reaction mixture of **46a** (to **57a**) was subjected to HRMS analysis. The observation of m/z at 236.0712 [m/z calculated for $(M+H)^+$: 236.0712] in the HRMS data indicated the prevalence of **47a**.

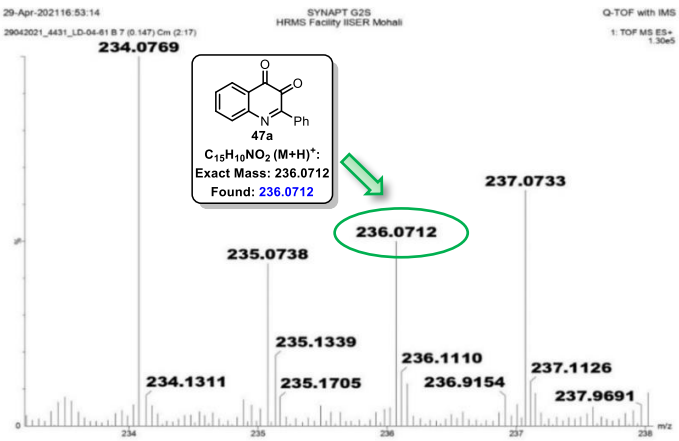
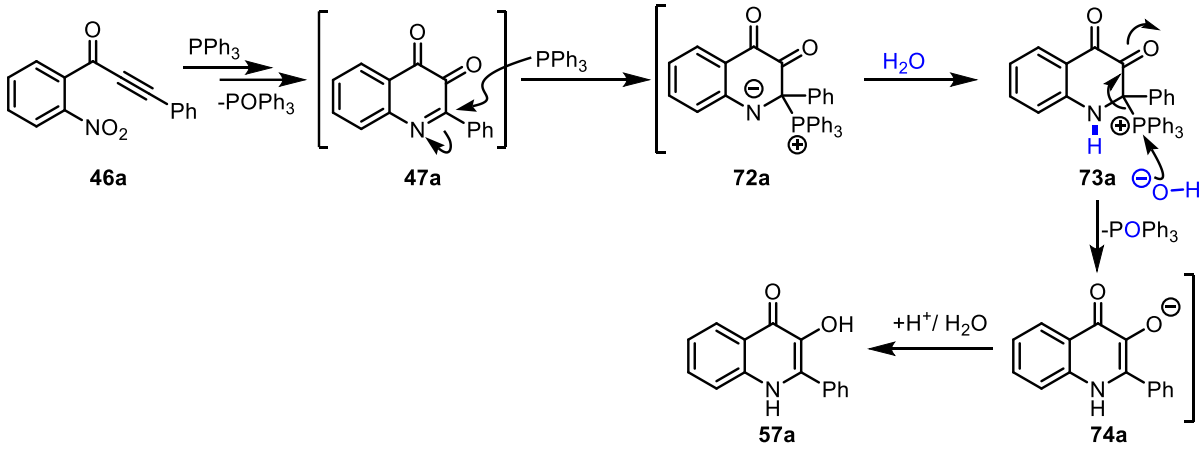


Figure 17: HRMS spectra of crude reaction mixture for **46a** to **57a**.

Based on the above experimental evidence, a plausible mechanism is outlined in Scheme 54. After 1,4-phosphine attack on **46a** followed by trapping of the allenolate and subsequent Wittig-type deoxygenation delivers the diketo intermediate **47a**. Next, TPP attacks in Mannich-type to the imino-ketone **47a** to form the zwitterionic intermediate **72a**, which abstracts proton from adventitious water to furnish intermediate **73a**. Finally, hydroxide-assisted elimination of triphenylphosphine oxide liberates the intermediate **74a**, which eventually transforms into the hydroxy quinolone product **57a**. An alternate catalytic pathway may be prevailing.[39, 42]



Scheme 54: Plausible mechanism for the transformation of **46a** to **57a**.

2.3: Synthetic utility of oxyaminated products

2.3.1: Synthesis of Natural Product Analogs

After successfully establishing the oxyamination of α,β-ynones to synthesize a library of 3-Hydroxyquinoline-4(1*H*)-ones (3HQs), we intended to elaborate the synthetic utility of this methodology to the natural product synthesis. 3-HQ holds a ubiquitous core in several biologically active natural product, Figure B.[62] Waltherione A and B[62b] were isolated from *Waltheria douradinha* S.-Hill. Waltherione A exhibits a broad spectrum of antifungal activity. Waltherione C and D were found in *M. odoratai*. Waltherione C is a cancer chemopreventive agent that inhibits the NF-κB transcription factor (IC50 ~ 50 μM) and is cytoprotective against HIV infection. Leiokinine A[63] was extracted from *Esenbeckia leiocarpa* stems, is an insecticide. Japonine was isolated form the leaves of *Orixa japonica* Thunberg in 1970.[64] It exhibits relaxant activity against the small intestine muscle of rats that is comparable to the activity of the typical muscle relaxant papaverine.

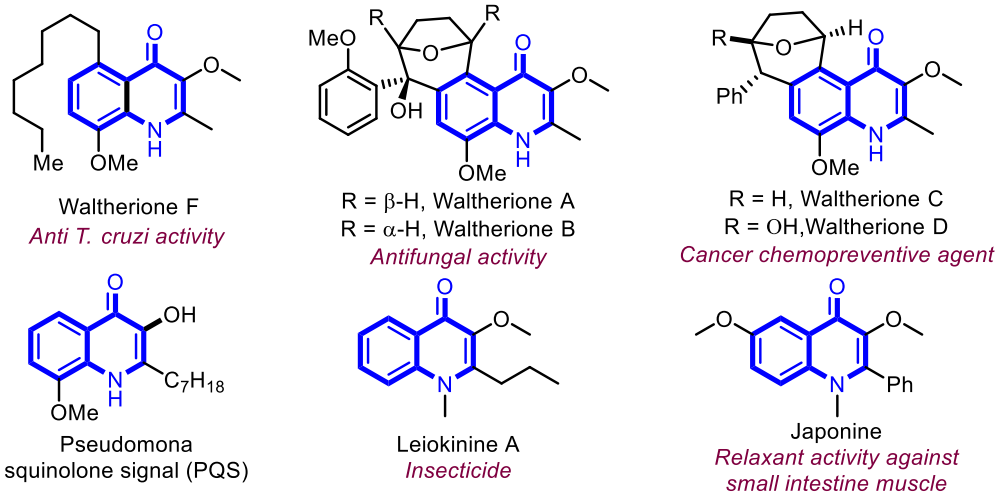
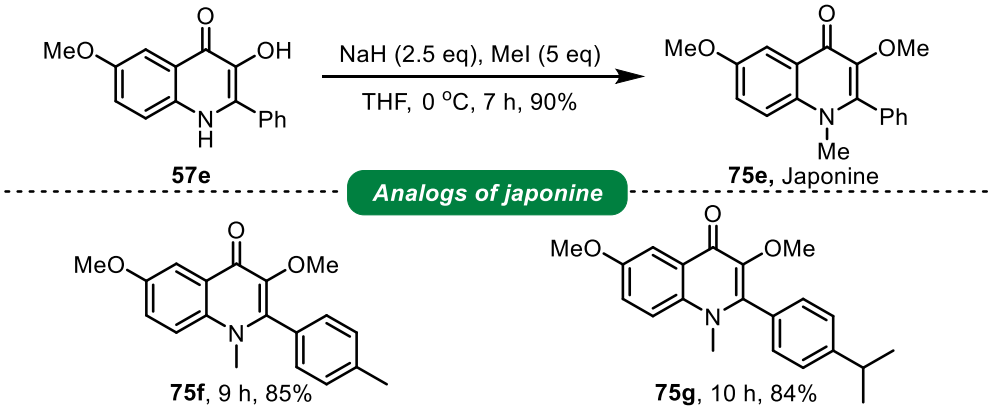


Figure B: Representative natural products bearing 3HQ core.

Realizing its biological importance, we intended to synthesize japonine. Hence, we subjected **57e** for the O and N-methylation in presence of methyl iodide and sodium hydride to achieve japonine **75e** in excellent yield. Similarly, the other japonine analogs **75f** and **75g** were also synthesized, Scheme 55.

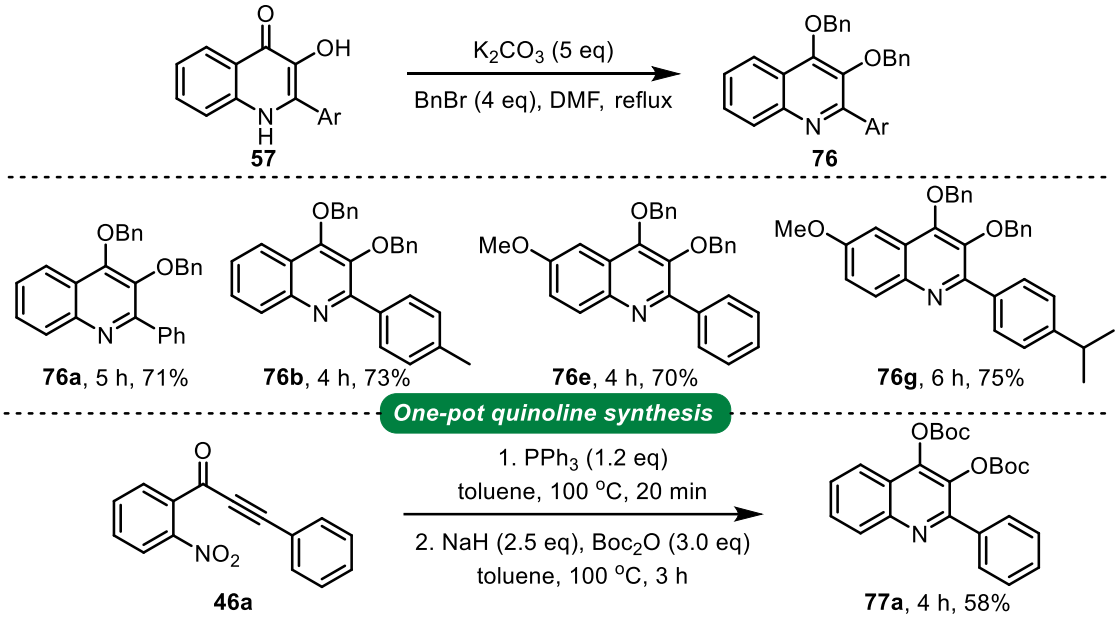


Scheme 55: Total synthesis of Japonine **75e** and its analogs **75f**, **75g**.

2.3.2: Synthesis of 3,4-Dialkoxyquinolines and Their One-Pot Assembly

The synthetic utility of this methodology was also extended to the synthesis of 2-aryl-3,4-dialkoxyquinolines **76**, a less-known class of compounds known to have significant biological properties, Scheme 56.[65] The oxyaminated product **57a-b, 57e, 57g** were subjected in K_2CO_3-mediated alkylation with benzyl bromide to obtain different types of 2-aryl-3,4-dialkoxyquinolines **76a-b, 76e, 76g** in good yields. Furthermore, after realizing the importance of this core, we made a one-pot synthesis of 3,4-di-*tert*-butyloxycarbonyloxy-2-phenylquinolines **77a** directly from nitro-ynone **46a**. We believe that the new one-pot protocol would find immense utility in the synthesis of 3,4-dialkoxyquinolines. Towards this, the

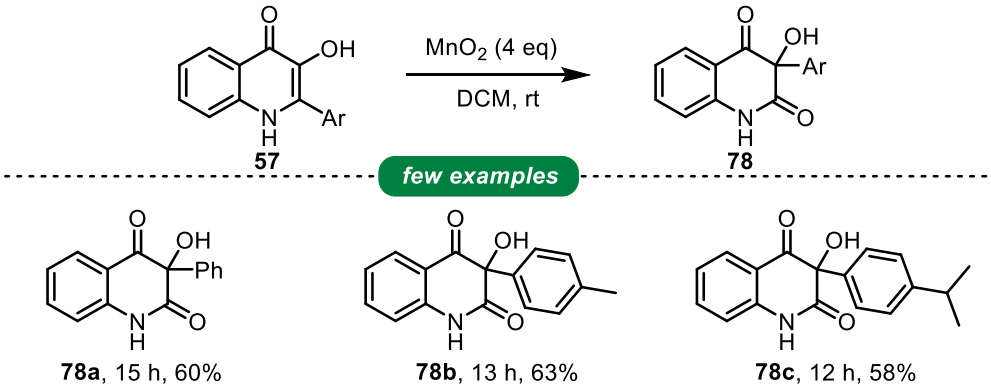
compound **46a** was subjected to our optimized reaction condition until the complete disappearance of **46a** after which it was treated with NaH-mediated O-acylation with Boc anhydride to access **77a**.



Scheme 56: Synthesis of 3,4-dialkoxyquinolines **78** and their one-pot assembly **77**.

2.3.3: A New Strategy for the Synthesis of 3-Hydroxy-3-arylquinoline-2,4-diones

Parallel progress on the synthetic utility of the oxyaminated product, we synthesized 3-hydroxy-3-phenylquinoline-2,4-dione **78**, which is natural metabolites of some *Pseudomonas* species.[66] In an intention to obtain the intermediate **47a** from **57a**, we did MnO_2 oxidation of the same in DCM solvent at room temperature. Surprisingly, we isolated an unusual rearrangement product **78**, Scheme 57. The structure of **78** was compared with known literature data by ^{1}H-NMR and ^{13}C-NMR analysis (see Figure 18 and 19, respectively)[67]. In the same line realizing the structural importance of this compound, we made few examples to establish a new entry to the synthesis of 3-Hydroxy-3-arylquinoline-2,4-diones **78**.[68]



Scheme 57: Synthesis of 3-hydroxy-3-arylquinoline-2,4-diones **78**.

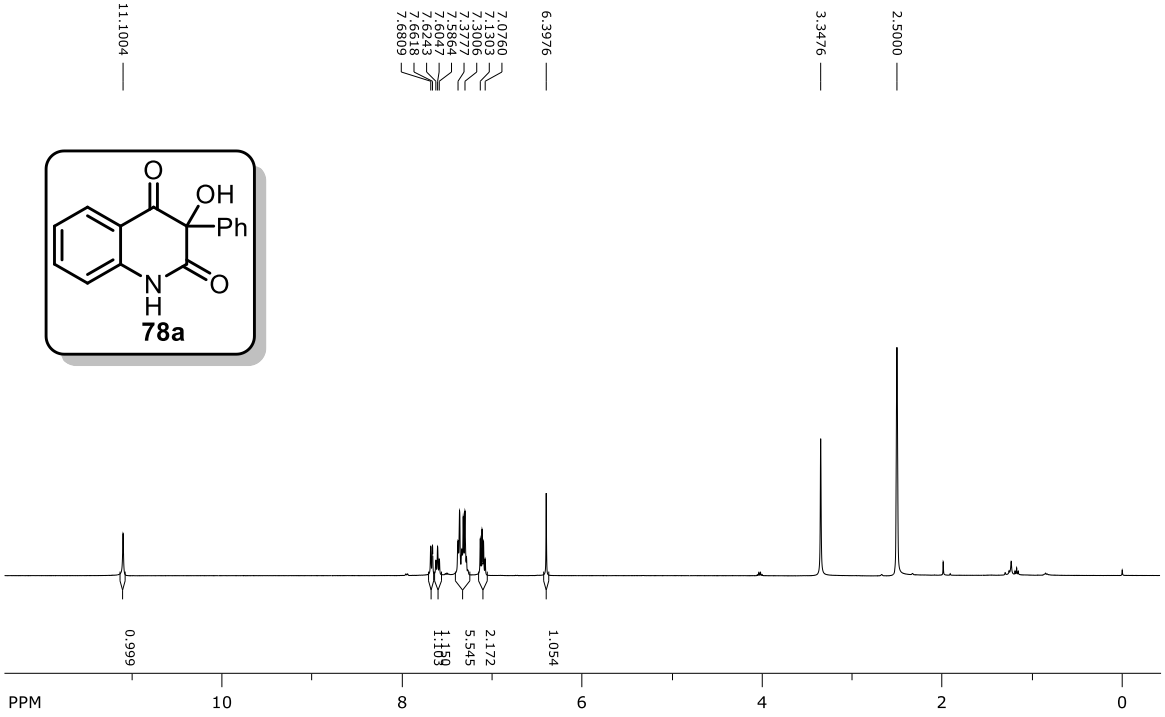


Figure 18: ^{1}H-NMR spectrum (400 MHz, DMSO-d^6) of the **78a**.

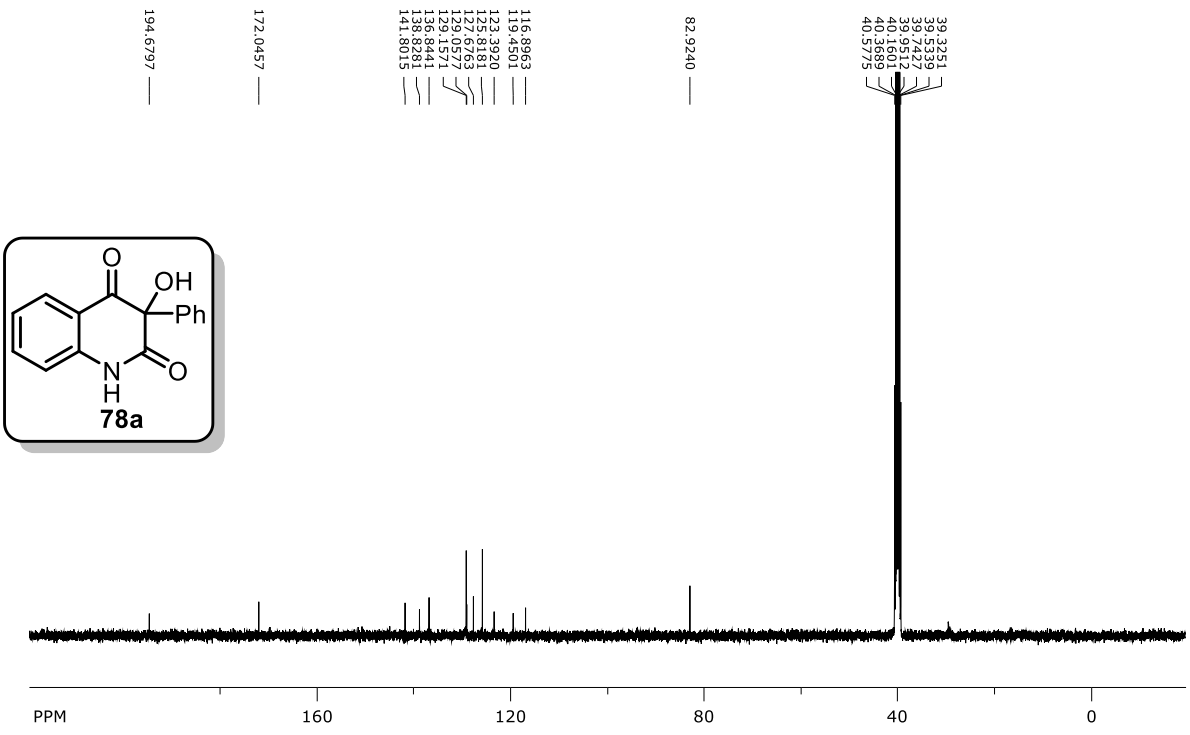
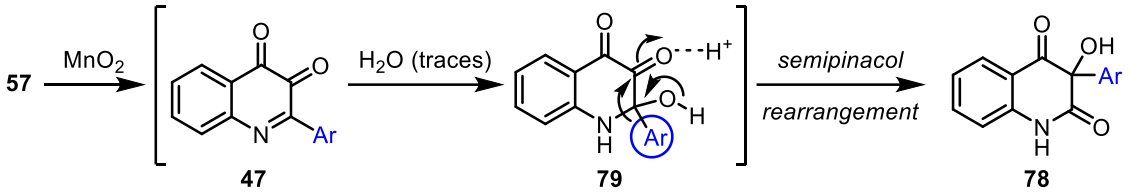


Figure 19: ^{13}C-NMR spectrum (100 MHz, DMSO-d^6) of the **78a**.

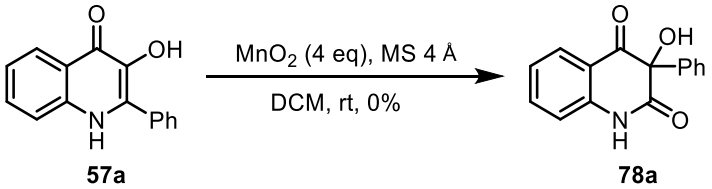
From the mechanistic point of view, we believe that the MnO_2 oxidation of **57** in presence of DCM solvent initially forms the diketo product **47**, which in presence of adventitious water transforms into the hemiaminal **79**. The intermediate **79** undergoes semipinacol rearrangement to furnish **78**, Scheme 58.



Scheme 58: Mechanism for the conversion of **57** to **78**.

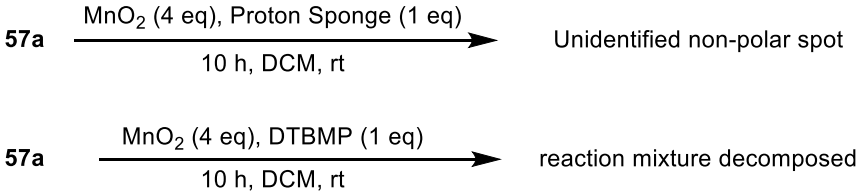
2.3.3.1: Control experiments to gain insights about the conversion of 57a to 78a

To ascertain the influence of moisture on the conversion of **57a** to **78a**, we performed an experiment with **57a** in the presence of 4 Å molecular sieves (MS). The progress of the reaction was monitored by TLC at different time intervals. TLC profiles indicated that **78a** did not form even after 24 h. This observation suggests the importance of moisture for the semipinacol rearrangement step.



Scheme 59: Reaction of MnO_2 oxidation of **57a** in presence of MS.

To ascertain the role of acid (H^+), the reaction of **57a** with MnO_2 was performed in presence of proton scavengers [Proton Sponge and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP)]. The progress of the reactions was monitored by TLC. In the presence of the Proton Sponge, unidentified non-polar spots were observed. While in presence of DTBMP, the reaction mixture decomposed. These results indicated the prevalence of H^+ during the transformation, which could have facilitated the semipinacol rearrangement.



Scheme 60: Reaction of **57a** in presence of DTBMP and proton sponge.

In conclusion, we have established a practical and efficient organophosphine-promoted redox method for transforming 1-(2-nitroaryl)prop-2-ynones into 3-hydroxyquinoline-4(1*H*)-ones. This work encompasses the first intramolecular oxyamination of α,β-ynones to comprise a new entry to the synthesis of 3HQs. Furthermore, the synthetic utility was demonstrated by establishing access to japonine and its analogs. Additionally, the synthetic utility of this methodology was extrapolated to the synthesis of 3,4-dialkoxyquinolines and 3-hydroxy-3-phenylquinoline-2,4-diones. The generality of this strategy was thoroughly verified by applying this methodology on a large scale. A few merits of this transformation include: (i) the neutral reaction condition, (ii) the easily accessible starting compounds, and (iii) the occurrence of numerous bioactive molecules with the kind of molecular architectures accessed herein.

Chapter 3

Phosphine-catalyzed denitrative rearomatizing [3 + 2] annulation of α,β ynones and 3-nitroindoles

The advantage of using small organic molecule as organocatalyst has gained a special attention. Organocatalyst is greener than traditional transition metal catalysis, because (i) It employs mild conditions, consequently saving energy, (ii) it is less toxic, (iii) It prevents the formation of metallic waste and avoids traces of metals in the products, which is an essential feature for applications in medicinal chemistry. Whereas, the use of metals or organometallic compounds presents some related environmental concerns, mostly owing to their toxicity and the generation of polluting metal waste. Among the various organocatalysis, the use of trivalent phosphines as organocatalysts has a significant impact on organic synthesis mainly because of its stronger nucleophilicity and weaker basicity. Some of the interesting features associated with phosphines are (i) the nucleophilicity can be tuned depending upon the group present in trivalent phosphine in the domain of trialkyl phosphine to triarylphosphines. (ii) the presence

of R group on phosphine embedded with different functional group can influence the mechanistic details addressing the stereochemical aspects. (iii) its ability to promote transformations via the P^{III}-P^{V} redox cycle.

α,β ynones are unique synthetic materials that can act as a pool of electrophiles and serve as easily accessed synthons in many chemical transformations (Fig 20).[69] After successfully developing phosphine-mediated oxyamination of ynones tethered to a nitro group,[50] we wanted to explore more on the field of phosphine-promoted ynone chemistry.[7] In this regard, after a detailed literature survey, we took α,β-ynone having α′-hydrogen **80a**. It is well known in the literature that **80a** in presence of phosphine undergoes 1,4-addition to form the allenolate **80b** followed by 1,3-proton shift to generate species **80d**. The species **80d** acts as C3 synthon and can be trapped with any suitable electrophile.

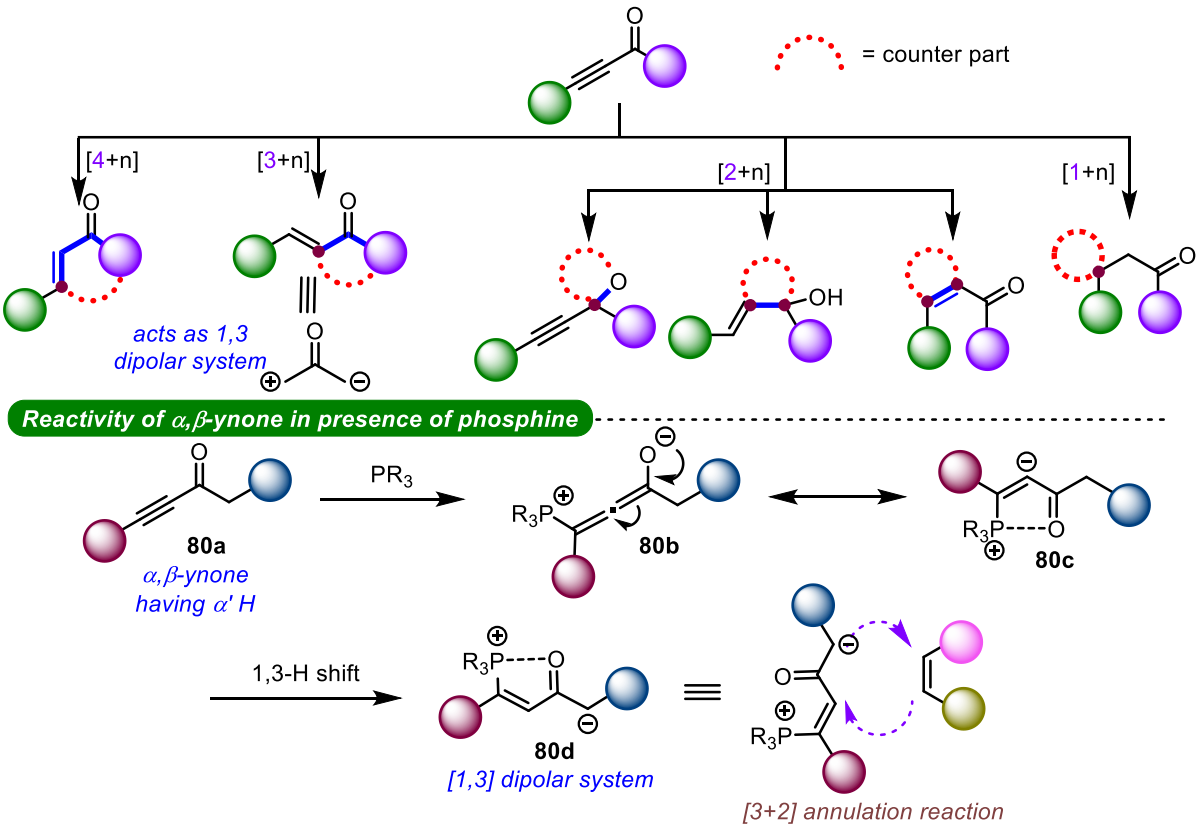
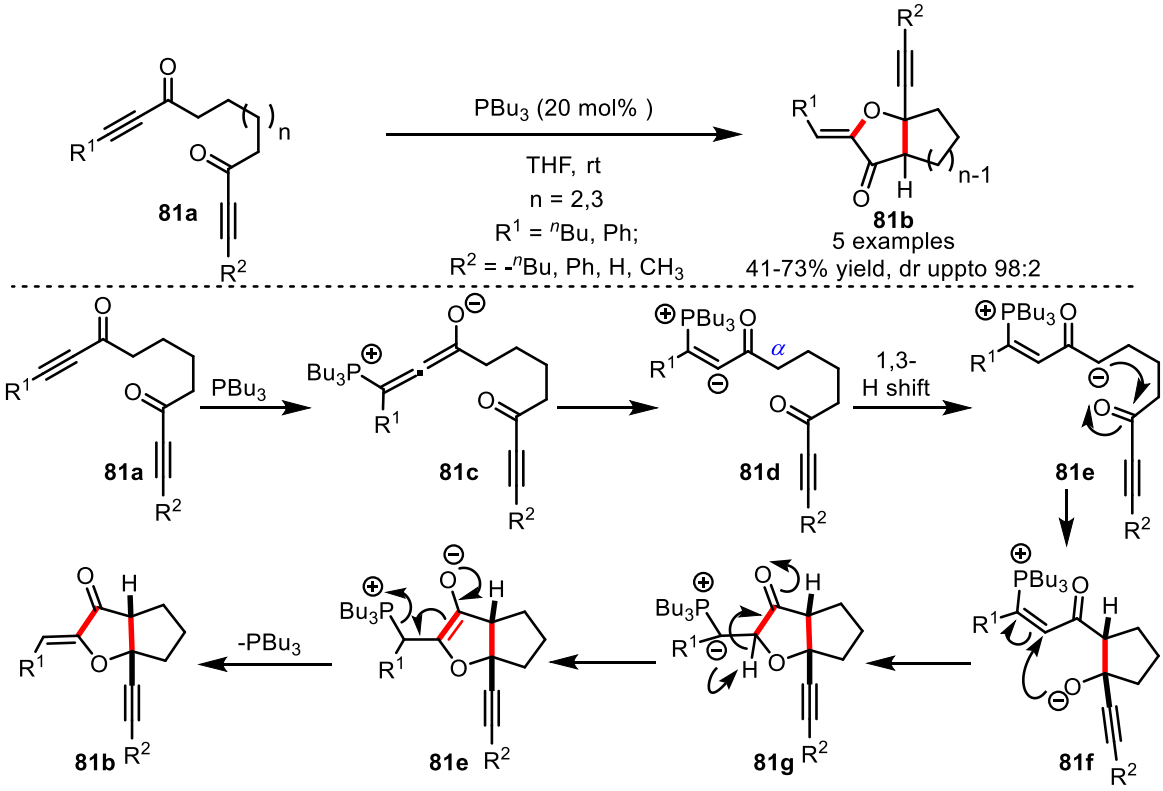


Figure 20: Different modes in α,β-ynones and reactivity in presence of phosphine.

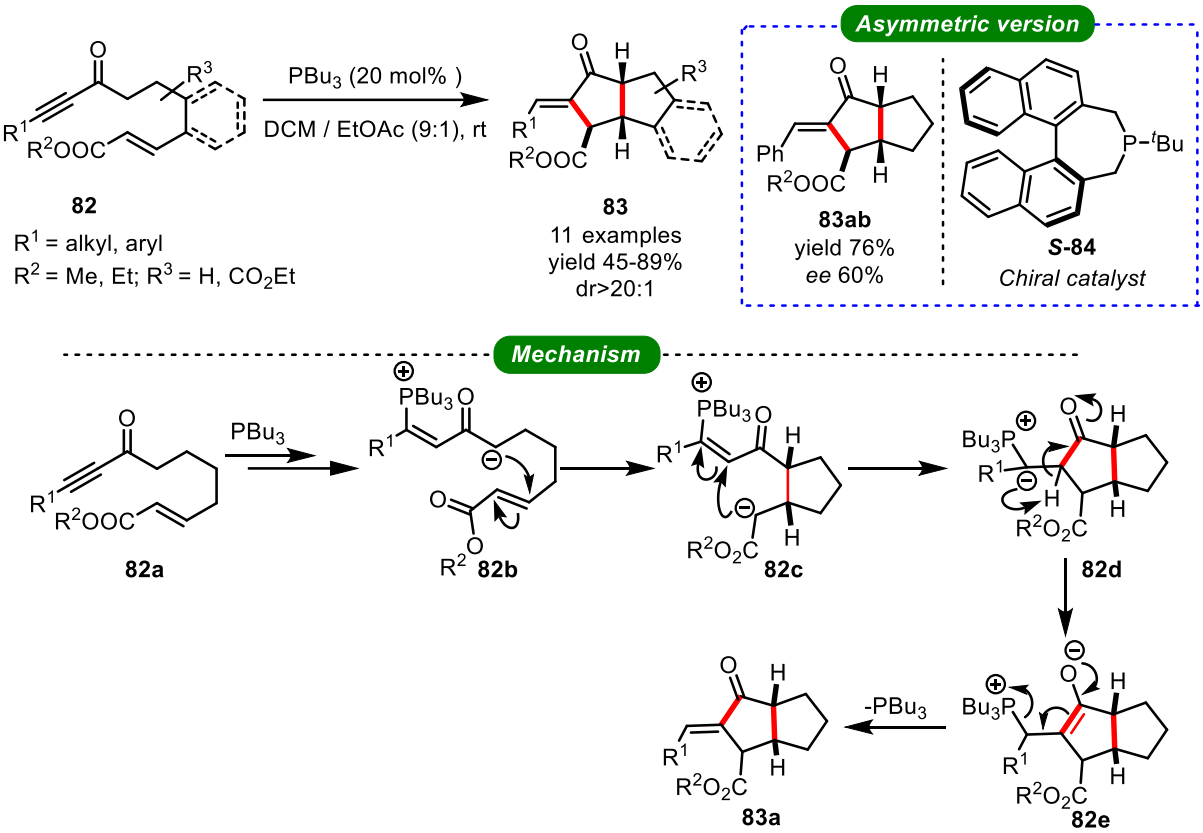
Towards this, Tomita's group in 2003 reported highly diastereoselective tributylphosphine-catalyzed zipper cyclization of bisynone **81a** having tetra and pentamethylene spacer to afford bicyclic ketone fused to five-membered ring, Scheme 61.[70] Noticeably, bisynone with hexamethylene spacer (i.e., n = 4) remains unsuccessful to furnish the corresponding zipper cyclized product. The mechanism starts with the 1,4-addition of PBu_3

to **81a** to form the allenoate **81c** which is further converted into **81d**. **81d** then undergoes 1,3-proton migration from the inner methylene to generate **81e** which attacks the other carbonyl group to form **81f**. Interestingly, through computational study, it has been observed that the cis-**81f** is more stable compared to trans-**81f**. After that, the addition of newly formed alkoxide to olefin in **81f** produces ylide **81g**, which undergoes intramolecular 1,2-proton transfer followed by elimination of PBu_3 affords **81b**.



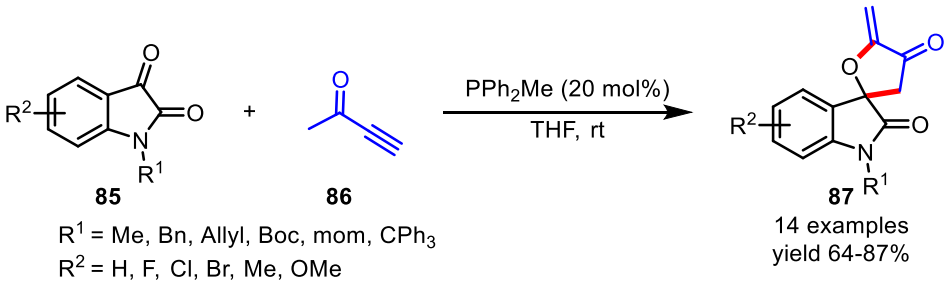
Scheme 61: Tomita's zipper cyclization with **81a**.

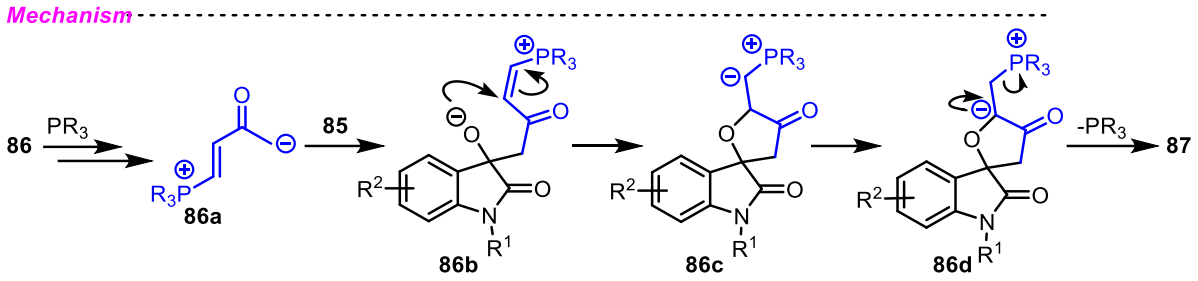
In 2010, Fu *et al*. disclosed PBu_3-catalyzed diastereoselective synthesis of a variety of diquinanes **83** bearing multiple contiguous stereocenters from acyclic precursor **82**, Scheme 62.[71] From the mechanistic point of view, after the 1,4-addition of tributylphosphine to **82a** and 1,3-proton transfer, **82b** attacks to the adjacent olefinic center in a Michael fashion to produce **82c** followed by consecutive intramolecular cyclization to form the phosphonium ylide **82d**. Then, intramolecular proton shift and elimination of PBu_3 deliver the diquinanes **83a**. Furthermore, the enantioselective version of this transformation was demonstrated by applying the catalyst ***S*-84** to obtain **83ab** in 60% *ee* and 60 % yield.



Scheme 62: Fu's work in PBu_3-catalyzed cyclization with ynone **82**.

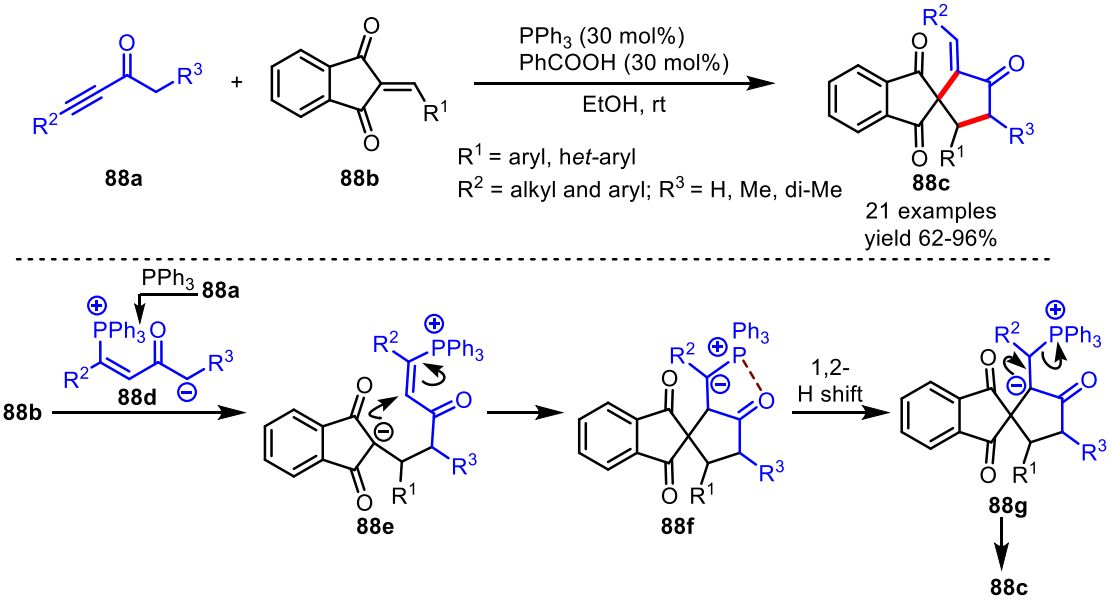
In 2012, Shi's group developed PPh_2Me-catalyzed [3+2] annulation of isatins **85** with ynone **86** to access spiro[furan-2,3′indoline]-2′,4(5*H*)-diones **87** in good to excellent yields, Scheme 63.[72] A plausible mechanism for this transformation is that first, after the treatment of phosphine onto **86** forms the intermediate **86a**, which upon nucleophilic addition to the carbonyl group of isatin **85** delivers **86b**. Then, an intramolecular attack of the alkoxide to the alkenyl group of **86b** to form the ylide **86c** and 1,2-proton shift followed by elimination of PPh_2Me produces **87**.





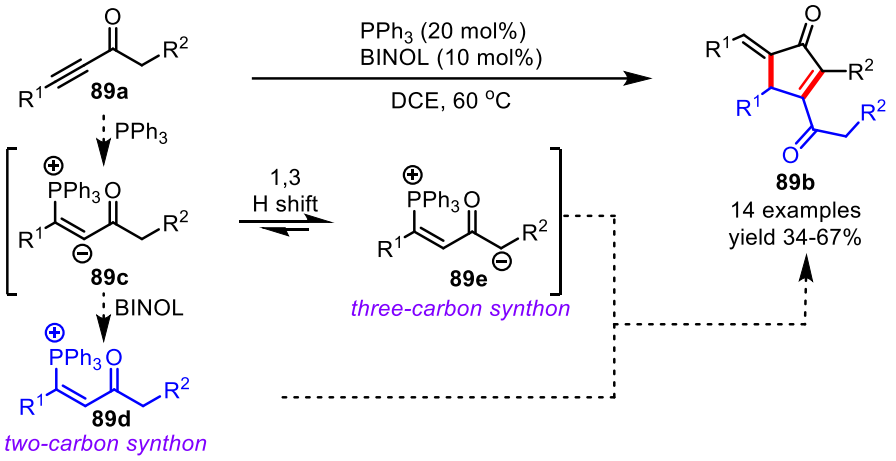
Scheme 63: Shi's [3+2] annulation with isatin **85**.

Similarly, Huang *et al*. in 2014 reported a phosphine-catalyzed [3+2] annulation of **88a** and **88b** to afford highly functionalized spiro-cyclopentanones **88c** in good to excellent yields, Scheme 64.[73] A detailed control experiments for the mechanistic insights behind this transformation reveals that the benzoic acid (as additive) accelerates the generation of the species **88d** formed by the nucleophilic addition of triphenylphosphine onto **88a** and followed by 1,3-proton shift. The intermediate **88d** then attacks **88b** to generate **88e**, which upon further addition to the double bond of vinyl phosphonium part, delivers **88f**. Finally, intramolecular proton shift and expulsion of phosphine produce the [3+2] annulated product **88c**.



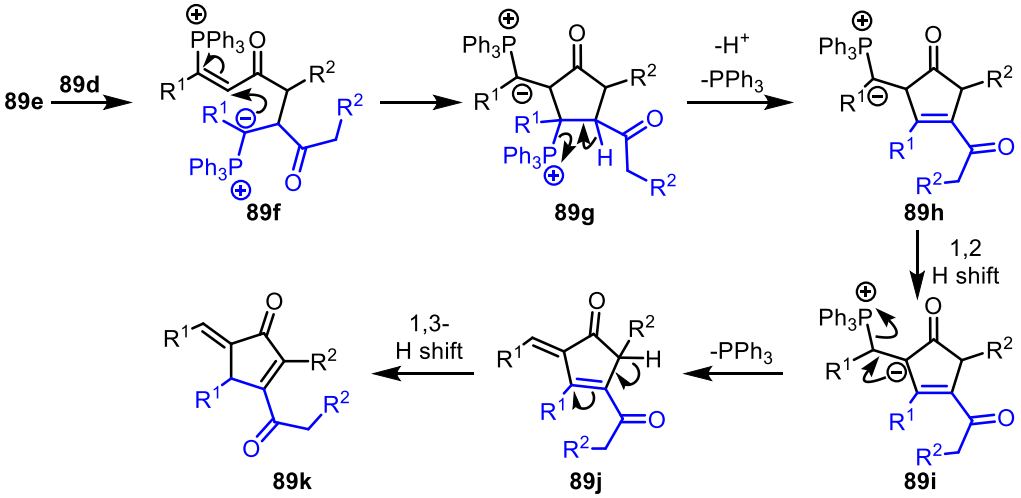
Scheme 64: Huang's work on phosphine-catalyzed [3+2] annulation of **88b** and **88a**.

In 2017, Ramachary's group came up with a novel phosphine-catalyzed umpolung [3+2] annulative dimerization of ynones **89a** to furnish highly functionalized 5-alkylidene-2-cyclopentenones **89b**, Scheme 65.[74] The methodology represents a unique feature of simultaneous generation of three-carbon synthon **89e** and two-carbon synthon **89d** from the same molecule.



Scheme 65: Ramachary's umpolung [3+2] annulative dimerization of **89a**.

A plausible mechanism is outlined in Scheme 66. Initially, 1,4-addition to **89a** and followed by 1,3-proton shift generates intermediate **89e**. At the same time, the newly formed intermediate **89c** can be quenched by BINOL or the residual water present in solvent DCE to produce intermediate **89d**. A nucleophilic addition of the resulting enolate **89e** to **89d** delivers the phosphonium species **89f**, which upon intramolecular cyclization to form **89g** followed by proton abstraction and elimination of phosphine, generates **89h**. After that, 1,2-proton migration from **89h** to form **89i** and then expulsion of phosphine produces **89j**, which undergoes 1,3-proton shift to afford the dimerized product **89k**.



Scheme 66: Mechanism of umpolung [3+2] annulative addition of **89e**.

On the other side, cyclopenta[*b*]indole moiety resides as a part structure of various bioactive natural products and pharmaceutically relevant compounds, Fig. C.[75] For example, Fischer indole L exhibits cytotoxicity against HCl-H460 cell lines,[76] bruceollines are

traditionally used for the treatment of malaria and other parasitic diseases,[77] laropiprant shows cholesterol-lowering effect,[78] and yuehchukene shows anti-fertility and estrogenic activities.[79] Because of the attractive biological properties of cyclopenta[*b*]indoles, the development of several new methods for their preparation, especially under metal-free conditions,[80] has become a major area of investigation for synthetic chemists.[75d]

Due to the resemblance of cyclopenta[*b*]indole moiety in many natural products and pharmaceutically active compounds, indolyl core has gained attention to many chemists over the decades, Figure C. The installment of strong electron-withdrawing nitro group induces electrophilic profile of indole by reversing its innate nucleophilicity.[81] Specifically, 3-nitroindoles are commonly employed substrates engaging C2-C3 π-bond to generate poly(hetero)-cyclic structures.

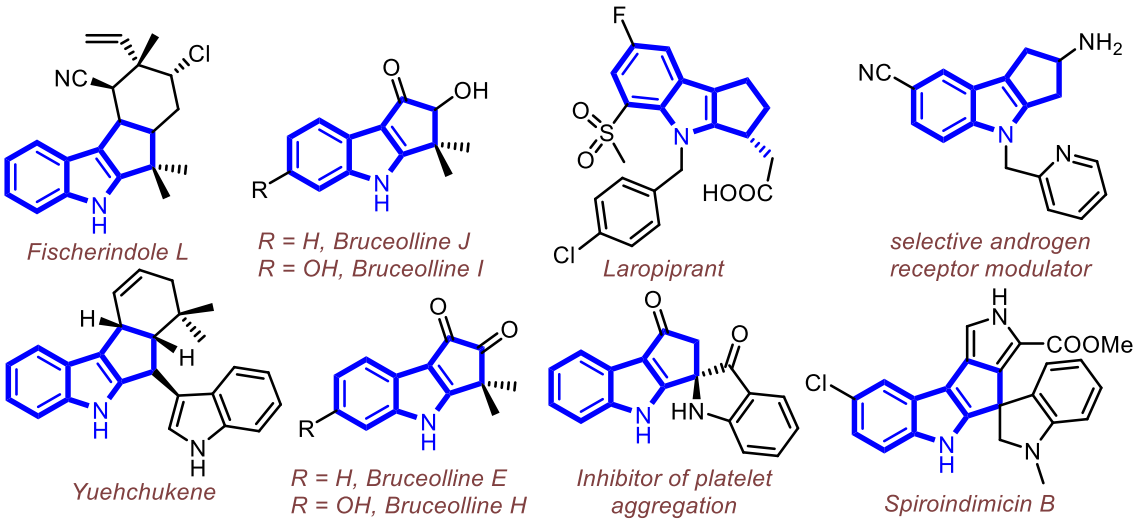
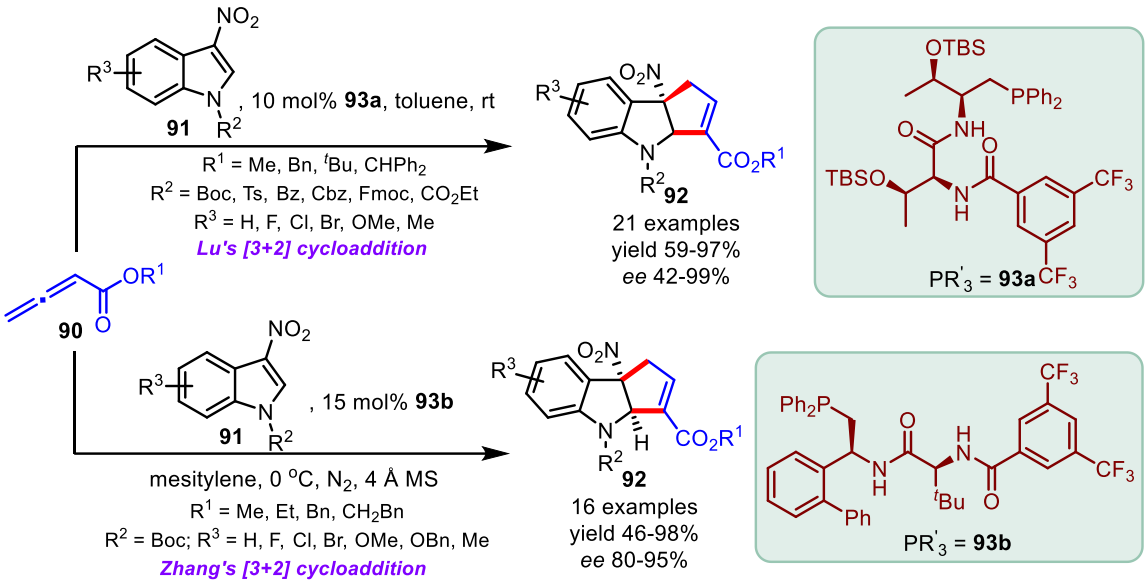


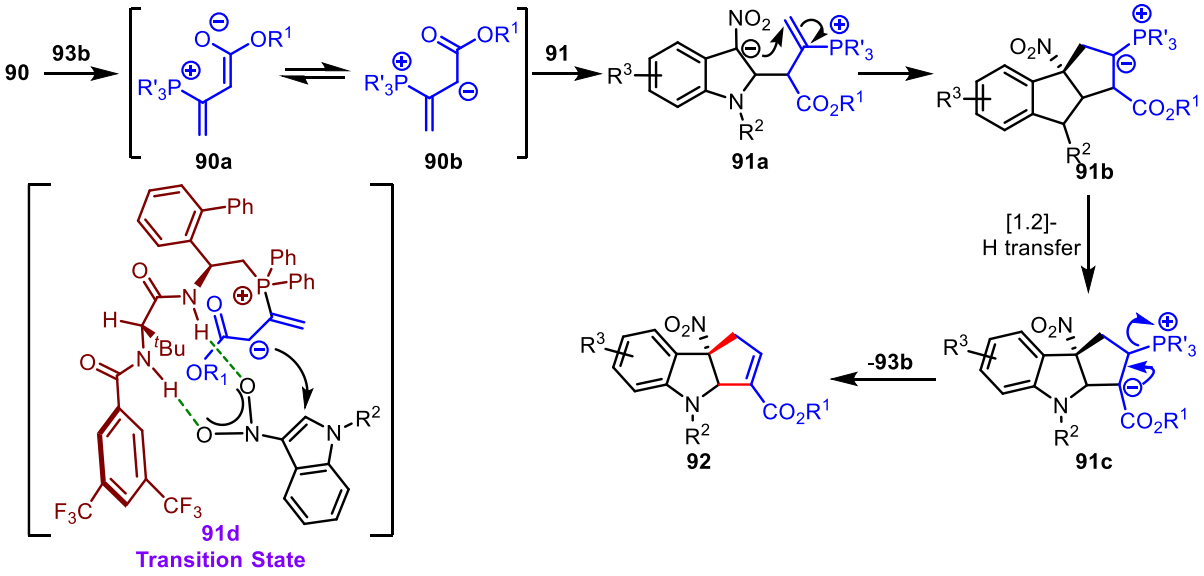
Figure C: Representative natural product containing cyclopenta[*b*]indole moiety.

Towards this, Lu's group's[82a] and Zhang's group[82b] in 2019 developed independently phosphine-catalyzed enantioselective dearomative [3+2] annulation of 3-nitroindole **91** to afford cyclopenta[*b*]indoline **92** in moderate to excellent yields and high enantioselectivity, Scheme 67.



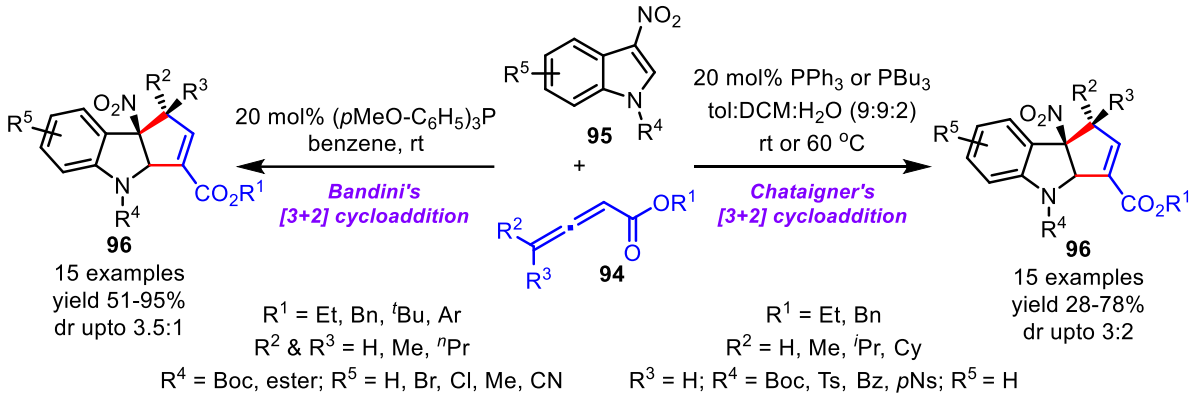
Scheme 67: Lu's and Zhang's asymmetric dearomative [3+2] annulation with **91**.

Plausible mechanism associated with these transformations is outlined in Scheme 68. First, 1,4-addition of **93b** to the allenoate **90** forms **90a** which is further transformed into **90b**. Then, the zwitterionic species **90b** attacks to the C2 center of 3-nitroindole **91** forming **91a** which undergoes an intramolecular cyclization to deliver the intermediate **91b** followed by 1,2-proton migration and elimination of phosphine leads to the formation of the dearomative annulated product **92**. It is believed that the main reason behind the asymmetric induction is the hydrogen bonding between the amide NH and the nitro group of **91** (transition state **91d**) which facilitates a drastically decrease in the LUMO energy of the aromatic partner easing a smooth cycloaddition process.[83]



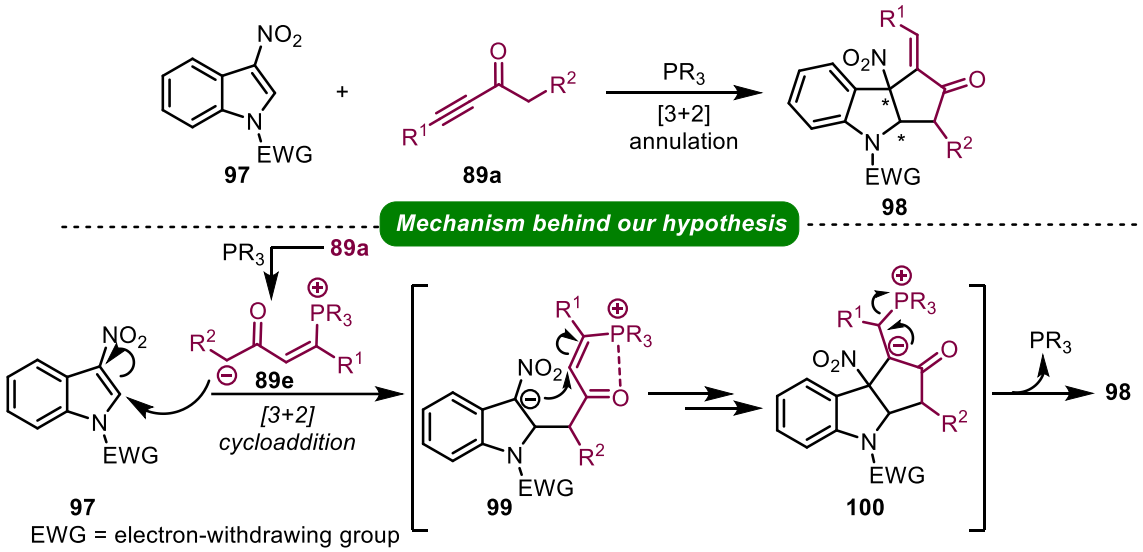
Scheme 68: Mehanism of dearomative [3+2] annulation with 3-nitroindole **91**.

Parallelly in the same year, Bandini's group[82c] and Chataigner's[82d] group also separately reported stereoselective phosphine-catalyzed dearomative [3+2] annulation of 3-nitroindole **95** with **94** to obtain indolines **96** in moderate to good yield, Scheme 69. The mechanism of these transformations is akin to the scheme 68.



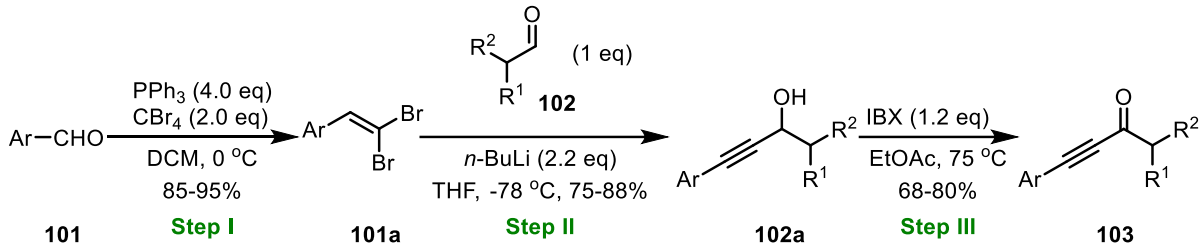
Scheme 69: Bandini's and Chataigner's dearomative [3+2] annulation with 3-nitroindole **95**.

Interestingly, it can be perceived from the literature reports[82] that to synthesize the core of cyclopenta[*b*]indole in [3+2] annulation, nitroindoles were explored only with allenoates. Moreover, Nitroolefins with ynones have not been employed yet to synthesize the same. Hence, we aspired to explore 3-nitroindoles in the [3+2] annulation process involving α,β-ynone having α′-H and phosphines. Our hypothesis is that the designed α,β-ynone in presence of phosphine would form intermediate **89e**, which would undergo [3+2]-cycloaddition reaction with 3-nitroindole **97** in a concerted way via intermediate **99** and **100**, Scheme 70.



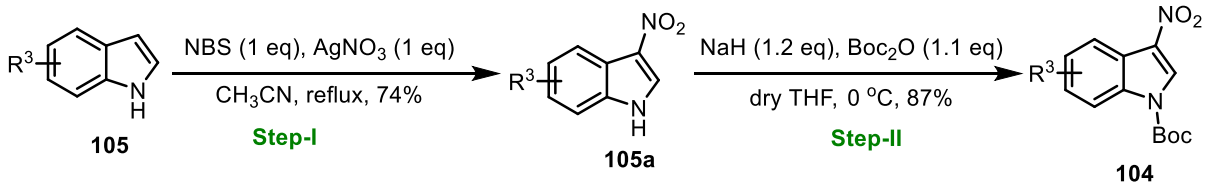
Scheme 70: Our hypothesis.

Accordingly, we synthesized our starting material via a three-step protocol from the required aldehyde **101,** Scheme 71. The aldehyde was subjected to Corey-Fuchs reaction condition to provide the dibromo product **101a**, which upon directed *n*-BuLi mediated reaction with **102** to form **102a** and further IBX oxidation delivers the respective α,β-ynones **103**.



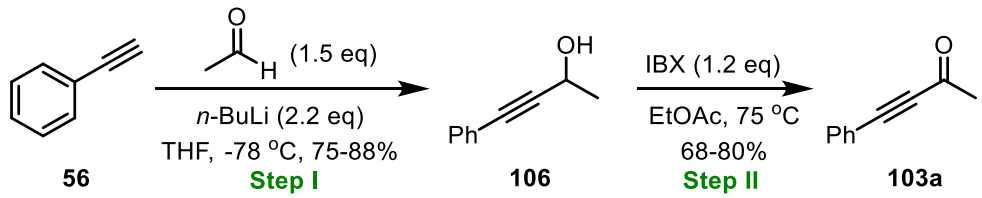
Scheme 71: Synthesis of α,β-ynones **103**.

Another starting material, 3-nitroindole was synthesized using a two-step synthetic procedure starting from commercially available indoles **105**, Scheme 72. The selective nitration of indoles was done with N-bromosuccinimide and silver nitrate system in acetonitrile solvent to access 3-nitroindole **105a**. After that, Boc protection of the respective nitroindole **105a** was performed with NaH and Boc-anhydride under dry THF at 0 °C to deliver **104**.



Scheme 72: Synthesis of Boc-protected nitroindoles **104**.

We initiated our study by synthesizing the model substrate α,β-ynone **103a** by following the procedure shown in Scheme 73, starting from commercially available phenylacetylene and acetaldehyde.

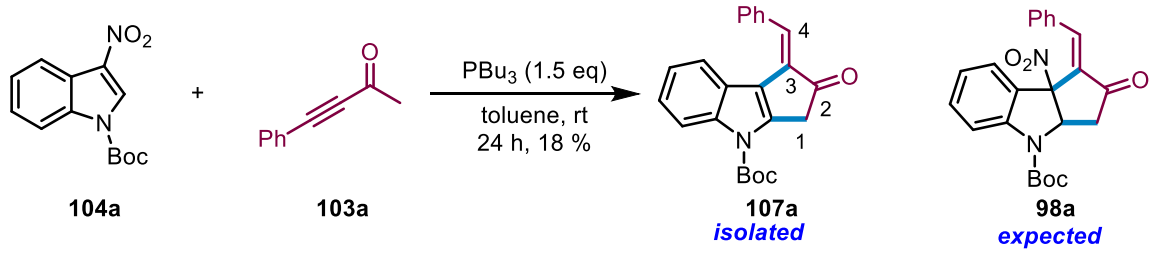


Scheme 73: Synthesis of **103a**.

3.1: Results and Discussion

After synthesizing both the starting materials, we subjected our model substrates 1 eq of **104a** and 2 eq of **103a** with 1.5 equivalent of PBu_3 in toluene at room temperature, Scheme

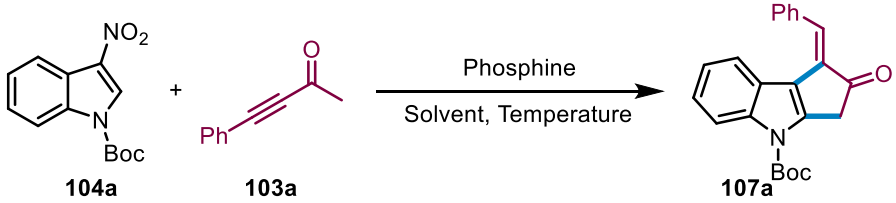
74. It furnished a slightly nonpolar compound to nitroindole **104a** with 18% yield. After careful evaluation of the spectral data of NMR, IR and HRMS revealed the formation of rearomatized [3+2] annulation adduct **107a**, which is nothing but an intramolecular denitrative rearomatizing annulation reaction.[84] However, the expected product **98a** was not isolated even in trace amount. In ^{1}H-NMR spectrum (Figure 21), the presence of singlet at δ 7.11 ppm due to the β proton (C-4), the singlet at δ 3.74 ppm for the CH_2 (C-1) and singlet δ 1.67 ppm for the presence of nine proton of three methyl group in Boc supported the formation of **107a**. ^{13}C-NMR (Figure 22), the peak at δ 201.4 ppm for the carbonyl carbon (C-2), the peak at δ 149.1 ppm due to the carbonyl of Boc group, the peak at δ 84.5 ppm for quaternary carbon of Boc group, peak at δ 41.8 ppm for methylene carbon (C-1)and the peak at δ 28.2 ppm for the methyl group of Boc confirms the formation of rearomatized [3+2] annulation product **107a**. In IR spectra, the sharp peak at 1740 cm^{-1} is for the presence of carbonyl group further asserted the formation **107a**. In the high-resolution mass spectrum, the presence of protonated molecular ion peak at *m*/*z* 360.1599 $(M+H)^+$ corroborated the formation of **107a**.



Scheme 74: [3+2] annulation of **104a** and **103a**.

As the initial result with the stoichiometric amount of PBu_3 was encouraging, we took **104a** and **103a** as our model substrates and performed a detailed screening to improve the yield of the reaction. A wide range of phosphines with various solvent combinations was applied during the course of optimization (entries 1-17, Table 5).

Table 5: Optimization of reaction conditions



Sl No.	Phosphine (eq)	Solvent	Temperature (°C)	Time (h)	Yield (%)[a]
1[c]	PBu_3 (1)	ACN	rt	24	trace
2[b]	PCy_3 (1.5)	toluene	rt	24	26
3[b]	PCy_3 (1.5)	dioxane	rt	24	44
4[b]	PPh_3 (1.5)	toluene	rt	24	22
5[b]	PPh_3 (1.5)	DMF	rt	24	15
6[c]	PPh_3 (1)	ACN	rt	24	37
7[d]	PBu_3 (0.3)	toluene: ACN (1:1)	100	15	40
8[d]	PCy_3 (0.3)	toluene: ACN (1:1)	100	5	–
9[d]	PPh_2Me (0.3)	toluene: ACN (1:1)	100	15	70
10[d]	**PPh_3 (0.3)**	**toluene: ACN (1:1)**	**100**	**17**	**77**
11[c]	PPh_3 (0.3)	toluene: ACN (1:1)	100	36	44
12[b]	PPh_3 (0.3)	toluene: ACN (1:1)	100	17	59
13[d]	PPh_3 (0.3)	toluene: ACN (1:1)	80	24	70
14[d]	PPh_3 (0.3)	toluene: ACN (1:1)	50	36	47
15[d]	PPh_3 (0.3)	toluene: ACN (1:1)	rt	48	29
16[d]	PPh_3 (0.2)	toluene: ACN (1:1)	100	24	63
17[d]	PPh_3 (0.1)	toluene: ACN (1:1)	100	30	48

All reactions were performed on 0.1 mmol scales. [a] Yields were calculated after silica gel column chromatography. [b] 2 eq of **103a** was used. [c] 1.2 eq of **103a** was used. [d] 3 eq of **103a** was used.

We started the screening with highly nucleophilic phosphines such as PBu_3 and PCy_3, the isolated rearomatized product was obtained albeit in poor yields (entries 1-3). Although, the reaction with PPh_3 gave similar results, it indicates the influence of solvent (entries 4-6). Accordingly, we tried reactions with catalytic amount of nucleophilic phosphines (PBu_3 and PCy_3) in a combination of solvent (toluene-acetonitrile) to obtain **107a** in low yields (entry 7-8). Surprisingly, the reaction with catalytic amount of PPh_2Me in toluene-ACN solvent gave excellent result (entry 9). To investigate further, it has been observed that PPh_3 in presence of toluene-ACN solvent was able to produce **107a** in 77% yield (entry 10). In this dual solvent system, we studied other parameters in detail (entries 11-17). For example, we realized that when the amount of ynone loading was decreased from 3 equivalents to 1.2 equivalent, the yield of annulated product **107a** also gradually decreased (entries 11-12). Furthermore, we found that the isolated yield of the **107a** was not encouraging in lowering the temperature as well as catalyst loading (entries 13-17). Hence, after exhaustive optimization we found that 3 equivalents of ynone **103a** and 1 equivalent of 3-nitroindole **104a** with 30 mol% PPh_3 in toluene-ACN dual solvent at 100 °C gave the best result to deliver the rearomatized annulated product **107a**.

With an interest in expanding the scope of the strategy, a diverse range of ynones **103** and 3-nitroindole **104** having different electronic features were treated under optimized condition and the results were compiled in Table 6.

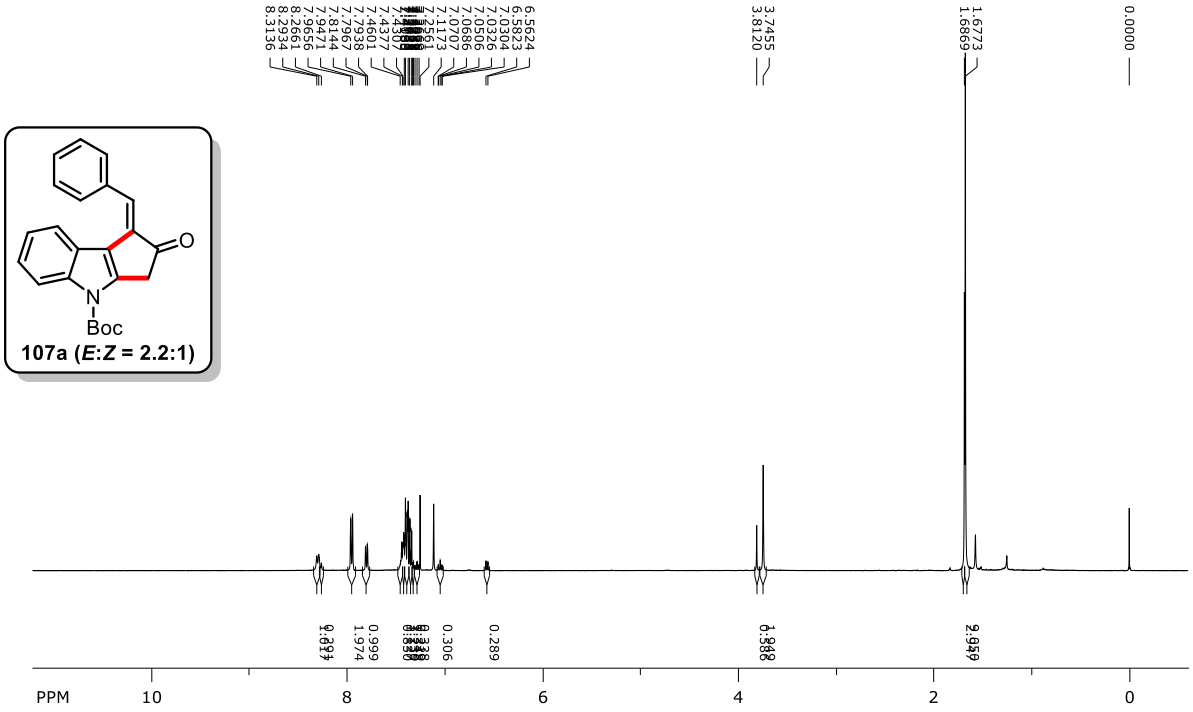


Figure 21: ^{1}H NMR (400 MHz, $CDCl_3$) of **107a**.

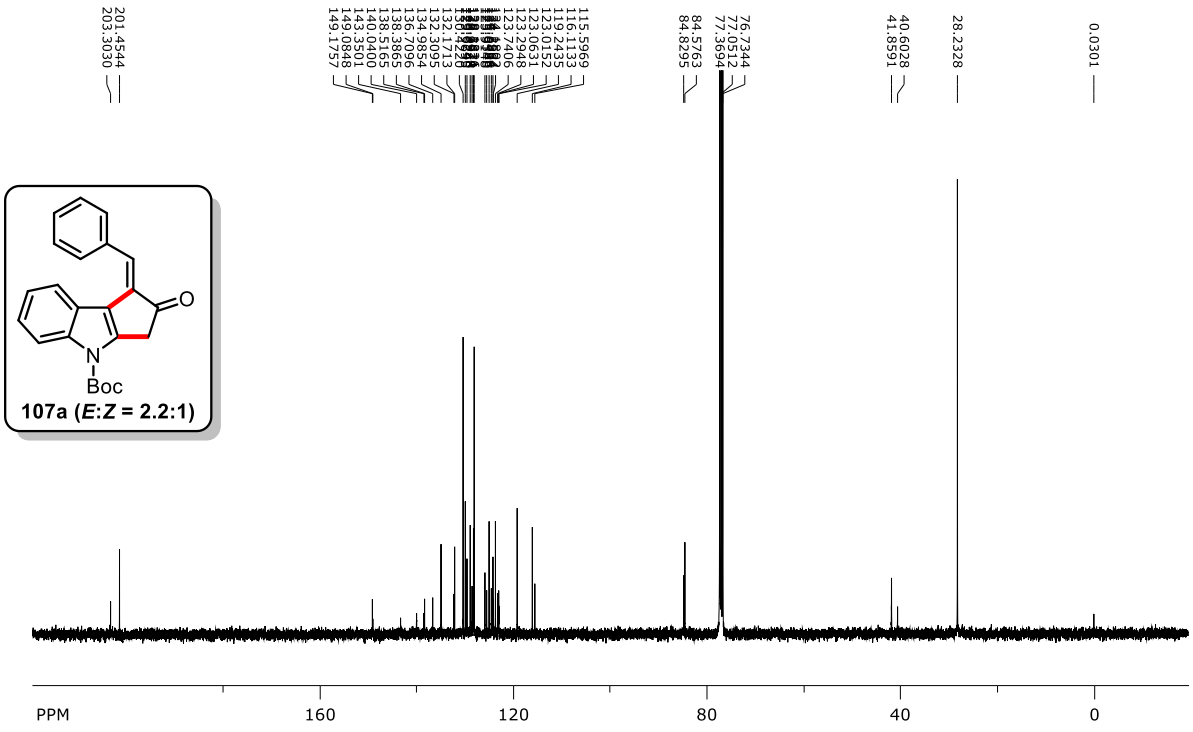
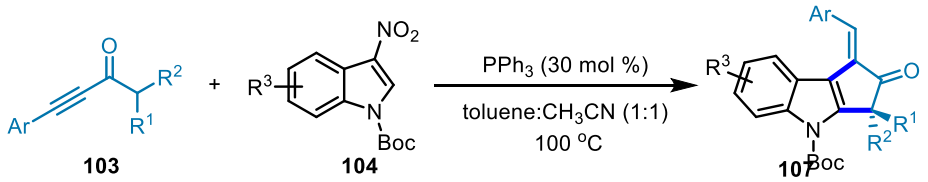
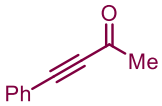
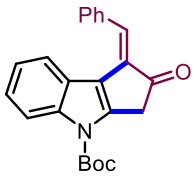
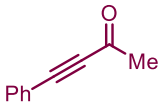
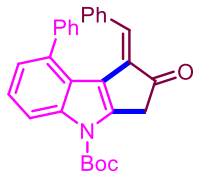
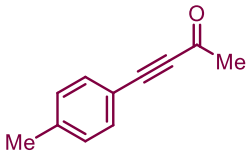
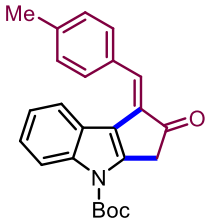
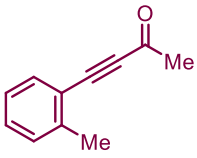
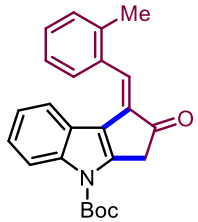
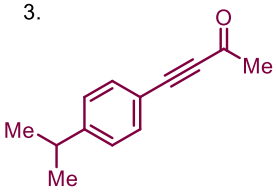
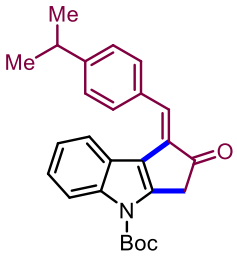
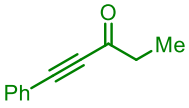
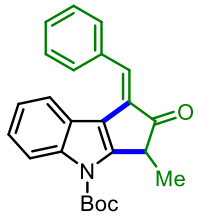
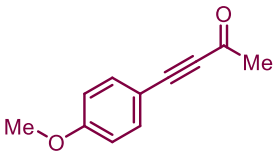
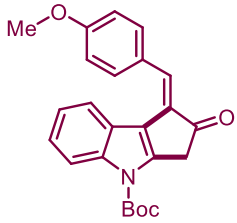
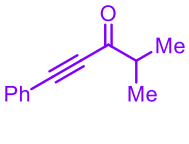
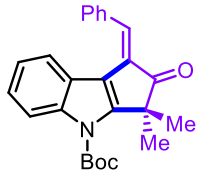
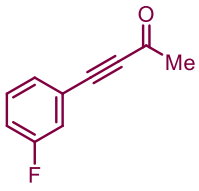
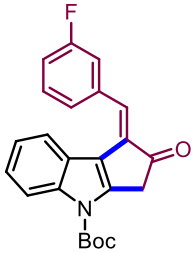
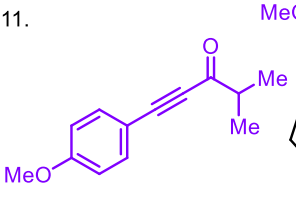
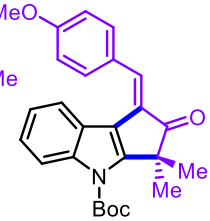
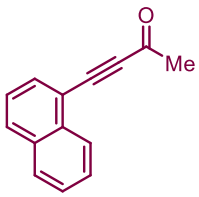
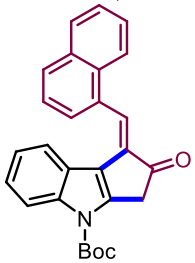
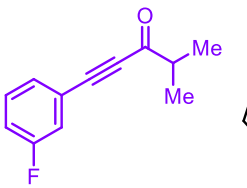
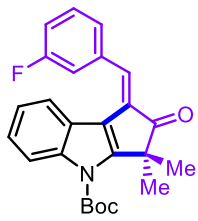
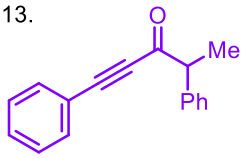
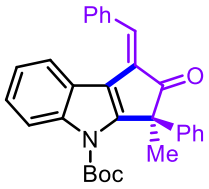
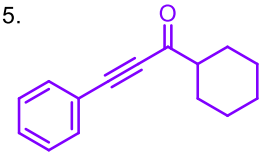
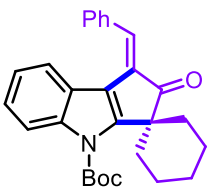
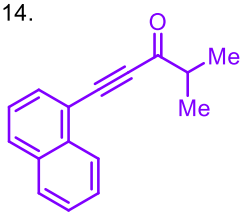
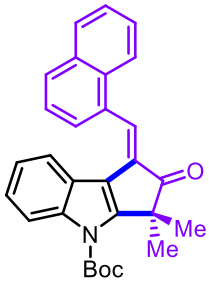
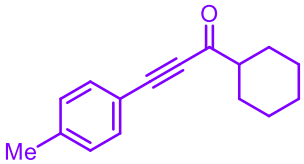
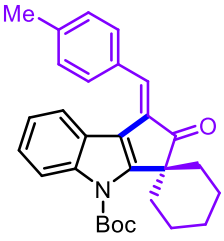


Figure 22: ^{13}C NMR (100 MHz, $CDCl_3$) of **107a**.

Table 6: Substrate Scope: 1-arylidene-cyclopenta[*b*]indol-2-ones[a,b,c]



Entry	Substrate	Product	Entry	Substrate	Product
1.			7.		
	103a	**107a**, 17 h, 77% (*E*/*Z* = 2.2:1)		**103a**	**107g**, 17 h, 77% (*E*/*Z* = 2.2:1)
2.			8.		
	103b	**107b**, 14 h, 75% (*E*/*Z* = 2.5:1)		**103g**	**107h**, 24 h, 0%
3.			9.		
	103c	**107c**, 14 h, 74% (*E*/*Z* = 2:1)		**103h**	**107i**, 24 h, 70% (*E*/*Z* = 2.2:1)
4.			10.		
	103d	**107d**, 15 h, 68% (*E*/*Z* = 2:1)		**103i**	**107j**, 15 h, 69% (*E*/*Z* = 1.6:1)
5.			11.		
	103e	**107e**, 22 h, 63% (*E*/*Z* = 2.3:1)		**103j**	**107k**, 18 h, 71% (*E*/*Z* = 2.7:1)
6.			12.		
	103f	**107f**, 15 h, 74% (*E*/*Z* = 2:1)		**103k**	**107l**, 14 h, 70% (*E*/*Z* = 3.4:1)

Entry	Substrate	Product	Entry	Substrate	Product
13.			15.		
	103l	**107m**, 16 h, 72% (*E*/*Z* = 2:1)		**103n**	**107o**, 15 h, 62% (*E*/*Z* = 2:1)
14.			16.		
	103m	**107n,** 20 h, 11% (*E*/*Z* = 1.5:1)		**103o**	**107p**, 17 h, 65% (*E*/*Z* = 2.5:1)

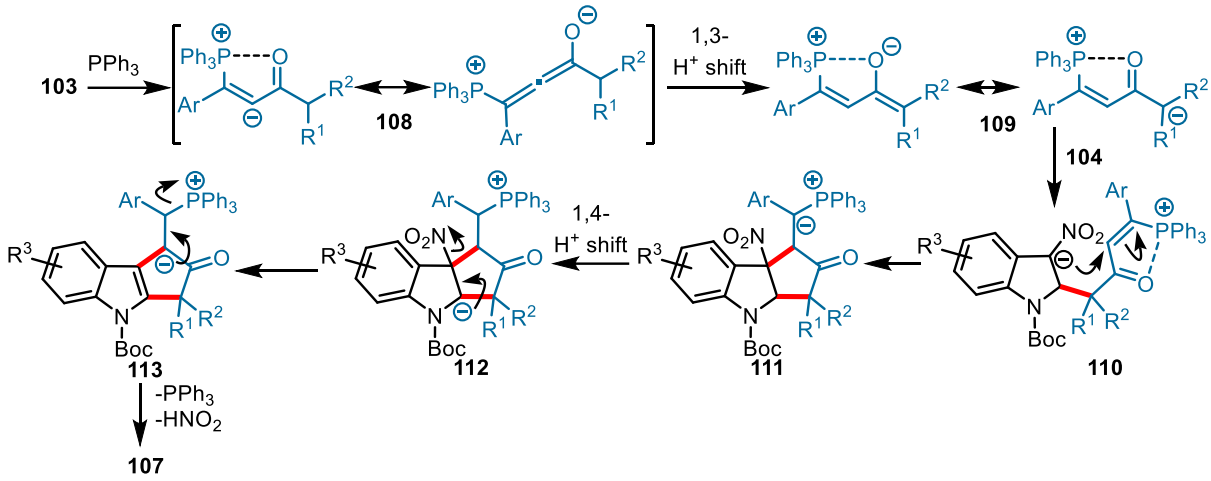
[a] 1 eq of **104** and 3 eq of **103** was used under optimized condition. [b] isolated yields after column chromatography. *E*/*Z* ratio is calculated from ^{1}H-NMR spectra of the crude reaction mixture.

A library of synthetically challenging 1-arylidene-cyclopenta[*b*]indol-2-ones **107** were prepared in good yields. Substrates having electron-donating (**103b-d, 103j**, **103o**) and electron-withdrawing groups (**103e, 103k**) on the ynone moiety showed negligible influence on the yields of the reaction in obtaining the rearomatized product. The reaction fared moderate with substituent (phenyl group) in indole part to generate **107g**. Moreover, the monosubstituted cyclopenta[*b*]indol-2-ones **107i** having tertiary carbon was prepared in good yield by applying this strategy having α′-branched ynone **103h**. In an interest on synthesizing disubstituted rearomatized product **107j-n** which are otherwise difficult to prepare, α′-branched ynone **103i-m** were able to successfully access **107j-n** having an all-carbon quarternary center in moderate to good yields. Furthermore, the protocol was also extended to creating spirocenter in the [3+2] annulated product **107n, 107o** in moderate yields. However, the strategy also has limitation as the reaction of ynones possessing *ortho*-substituted arenes on alkynes **103g** and **103m** did not produce encouraging results even after prolonged reaction time. For instance, the 1-naphthyl adduct **107n** was isolated in poor yield, while the ynone **103g** with the *o*-tolyl group failed to produce the desired product **107h**.

3.2: Plausible mechanism

A plausible mechanism behind this transformation is sketched in Scheme 75. The 1,4-addition to **103** to form **108** which undergo proton shift generating **109**. The zwitterionic species then attacks to the C2 position of 3-nitroindole **104** producing the intermediate **110**

followed by an umpolung addition to the vinyl phosphonium moiety to form ylide **111**. After that, a subsequent 1,4-proton shift in **111** dives into the elimination of nitrite from **112** delivering **113**. Finally, expulsion of phosphine from **113** affords the cyclopenta[*b*]indoles **107**. Alternatively, the rearomatization is also possible under thermal conditions.[85a]

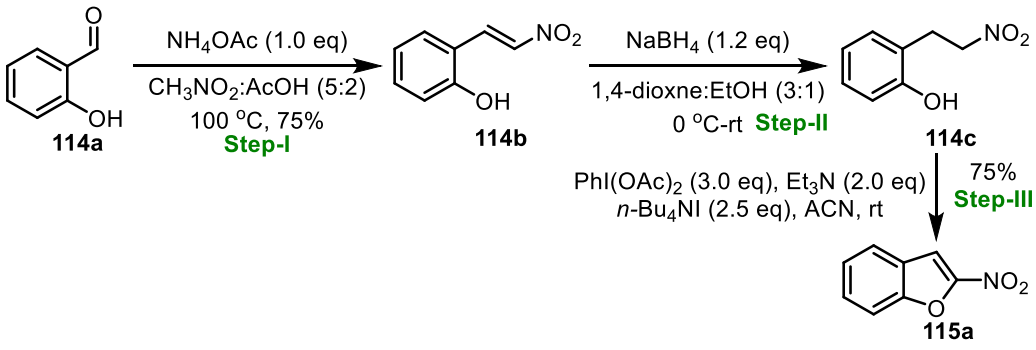


Scheme 75: Plausible mechanism for the formation of **107**.

3.3: [3+2] annulation with 2-nitroheteroarene system and ynone 103a:

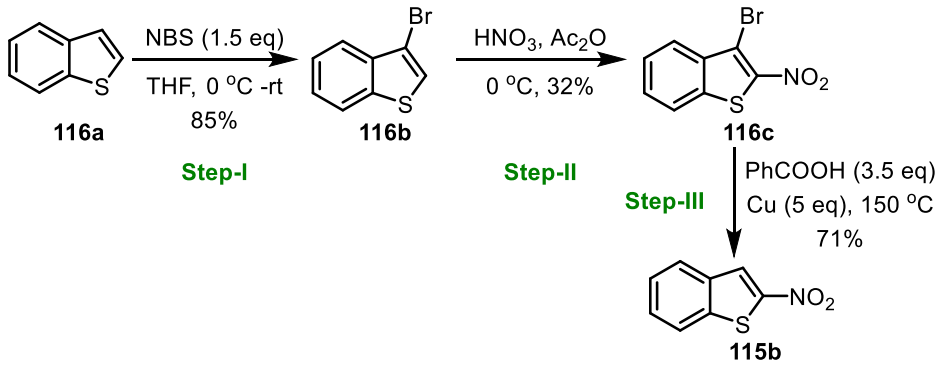
After establishing a general and efficient method for [3+2] annulation of ynones **103** and 3-nitroindole **104**, we wanted to extend this methodology by synthesizing the [3+2] annulated product with benzofuran and benzothiophene core and at the same time we were curious about the fate of reaction with the reactivity of 2-nitroheteroaromatic system. Accordingly, we prepared the starting materials.

2-nitrobenzofuran **115a** was synthesized using a three-step protocol starting from salicylaldehyde **114a**, Scheme 76.[85b,c] At first, **114b** was prepared from **114a** in presence of ammonium acetate in nitromethane and acetic acid mixture (5:2) at 100 °C. Then, **114b** was reduced by $NaBH_4$ in 1,4-dioaxne: EtOH mixture (3:1) at 0 °C to give **114c**. Finally, $PhI(OAc)_2$-mediated cyclization forms **115a** in 75% yield.



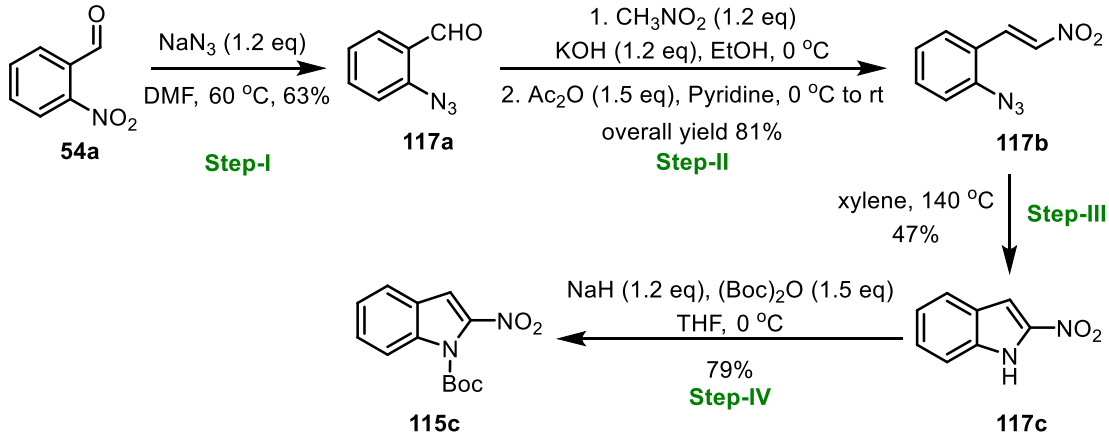
Scheme 76: Synthesis of 2-nitrobenzofuran **115a**.

2-nitrobenzothiophene **115b** was synthesized following a three-step protocol starting form commercially available benzothiophene **116a**, Scheme 77. First, NBS-mediated bromination delivered 3-bromobenzothiophene **116b** which was nitrated by in situ generated acetyl nitrate from HNO_3 in acetic anhydride at 0 °C to form **116c**. Finally, debromination of **116c** using Cu powder and benzoic acid formed **115b**.



Scheme 77: Synthesis of 2-nitrobenzothiophene **115b**.

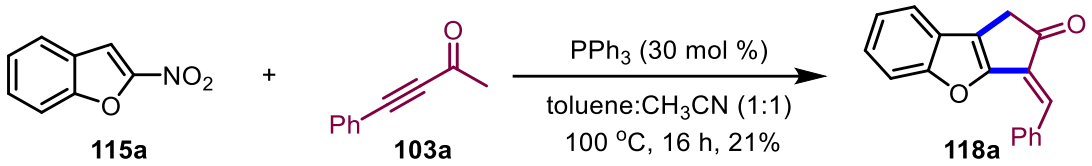
2-nitroindole **115c** was synthesized from commercially available 2-nitrobenzaldehyde **54a** using a four-step protocol, Scheme 78. Formation of 2-azidobenzaldehyde **117a** was performed in presence of sodium azide at 60 °C. Then, Henry reaction of **117a** in presence of nitromethane followed by deacetylation forming **117b** and after thermolysis it gives **117c**. Finally, it was protected with Boc anhydride to form **115c**.



Scheme 78: Synthesis of 2-nitroindole **115c**.

After synthesizing 2-nitroheteroarenes **115**, 1 equivalent of **115a** and 3 equivalent of **103a** were subjected to our prototypical condition and we isolated the [3+2] annulated product **118a** in 21% yield, Scheme 79. Further, the structure of **118a** was confirmed by analyzing the ^{1}H-NMR, ^{13}C-NMR, IR and HRMS spectra of corresponding product (see Figure 23 and 24).

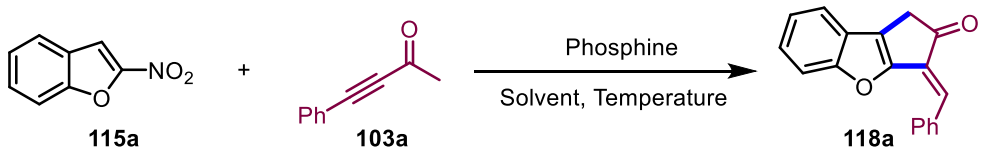
3-Arylidene-cyclopenta[*b*]-fused heteroarenes **118** have found great relevance in medicinal chemistry.[86]



Scheme 79: Initial result of [3+2] annulation reaction with **103a** and **115a**.

As the initial result with PPh_3 was not satisfactory, we performed a brief screening of reaction conditions by considering **115a** as model substrate to improve the yield, Table 7. A wide variety of phosphines in combination with different solvents were screened for the [3+2] annulation (entries 1-7). Among them, 30 mol% of PPh_3 in ACN at 100 °C delivered the desired product with 63% yield and it was realized to be the best condition for this transformation (entry 4).

Table 7: Optimization of reaction parameters



Entry	Phosphine (mol%)	Solvent	Temperature (°C)	Time (h)	Yield (%)[a]
1	PBu_3 (30)	toluene-ACN (1:1)	100	7	10
2	PCy_3 (30)	toluene-ACN (1:1)	100	16	13
3	PPh_3 (30)	toluene	100	24	trace
4	**PPh_3 (30)**	**ACN**	**100**	**18**	**63**
5	PPh_3 (30)	1,4-dioxane	100	24	decomposed
6	PPh_3 (30)	DMF	100	24	decomposed
7	PBu_3 (0.3)	DCM	50	24	trace

All reactions were performed on 0.1 mmol scales. [a] Yields were calculated after silica gel column chromatography. 3 eq of **103a** was used.

With the optimal conditions in hand, we next focused on investigating the substrate scope. Towards this, 3-benzylidene-1,3-dihydro-2*H*-cyclopenta[*b*]benzofuran-2-one **118a** and 3-benzylidene-cyclopenta[*b*]-fused benzothiophene **118b** were synthesized in moderate to good yields. Interestingly, substituents with 2-nitroindole core failed to give the [3+2] annulated product despite our several attempts.

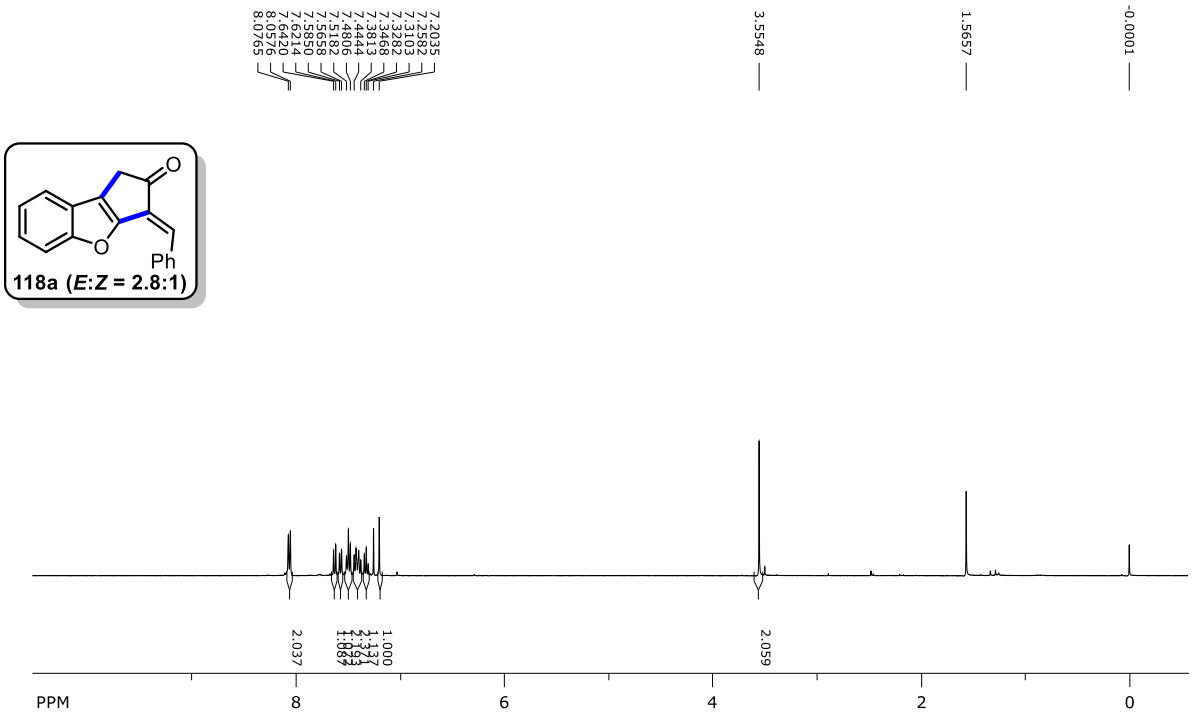


Figure 23: ^{1}H NMR (100 MHz, $CDCl_3$) of **118a**.

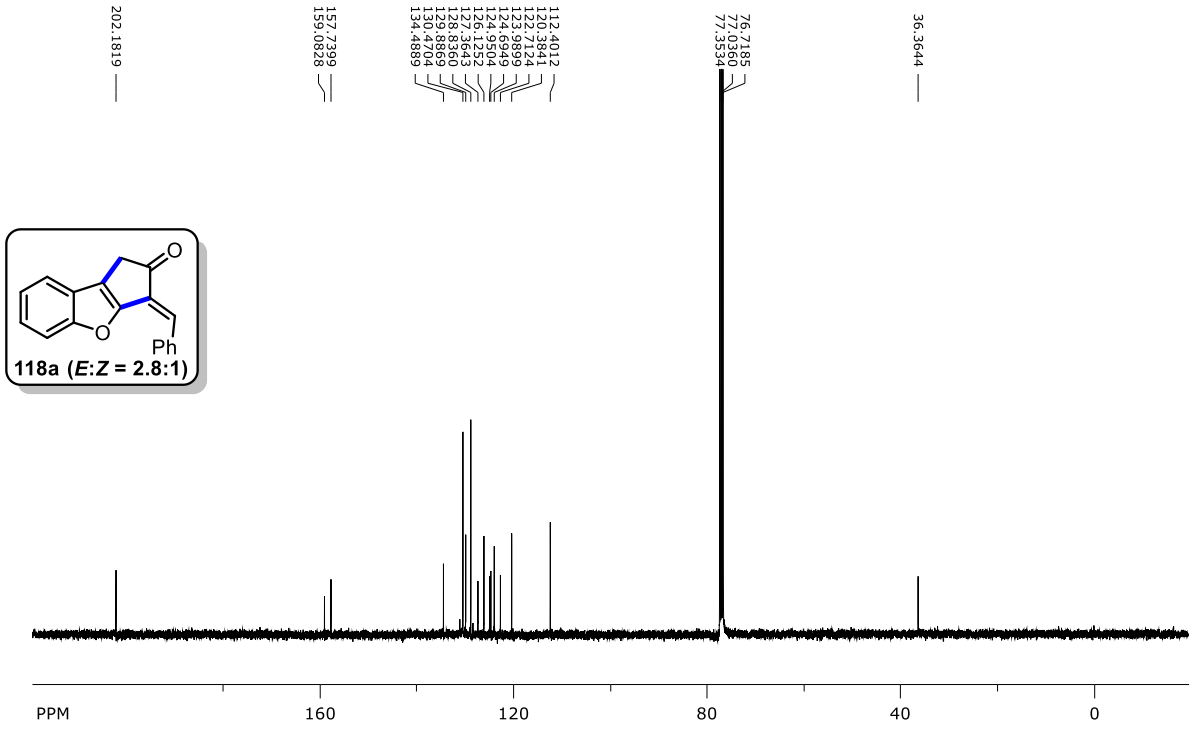
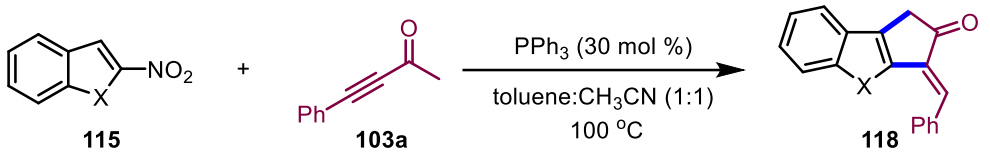
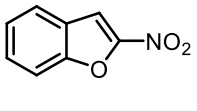
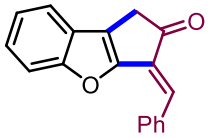
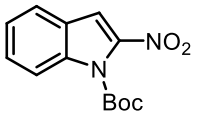
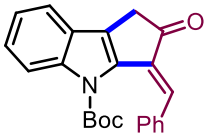
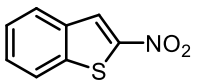
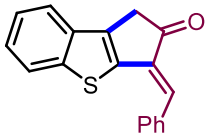
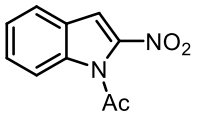
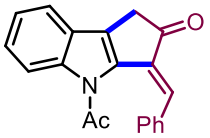


Figure 24: ^{13}C NMR (100 MHz, $CDCl_3$) of **118a**.

Table 8: Substrate Scope: 3-arylidene-cyclopenta[*b*]-fused heteroarenes[a,b,c]



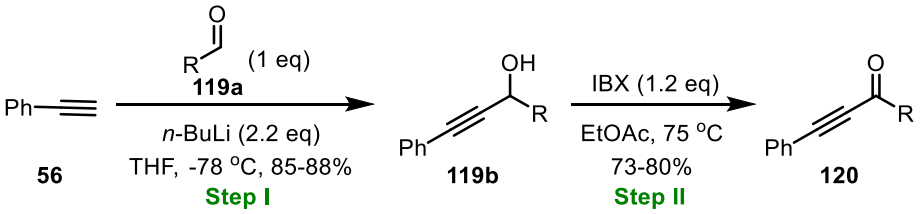
Entry	Substrate	Product	Entry	Substrate	Product
1.			3.		
	115a	**118a**, 10 h, 63% (*E*/*Z* = 2.8:1)		**115c**	**118c**, 7 h, 0%
2.			4.		
	115b	**118b**, 8 h, 43% (*E*/*Z* = 4.7:1)		**115d**	**118d**, 8 h, 0%

[a] 1 eq of **115** and 3 eq of **103a** was used under optimized condition. [b] isolated yields after column chromatography. *E*/*Z* ratio is calculated from ^{1}H-NMR spectra of the crude reaction mixture.

3.4: Reaction with ynones lacking α′-hydrogen and 3-nitroindole:

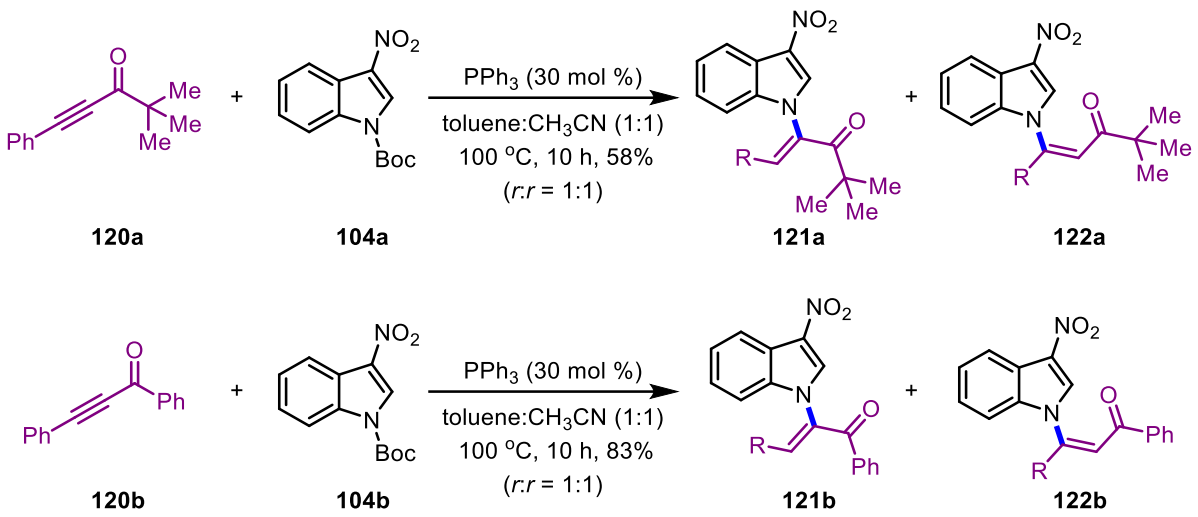
After exhaustive studies with the role of substituent around the ynone part bearing α-hydrogen and nitroheteroarenes **104** and **115**, we were curious about the fate of the reaction with ynones lacking α′-hydrogen and 3-nitroindole **104** under our optimized condition, Scheme 80.

Acoordingly, we prepared the required ynones **120** using a two-step synthetic protocol. The synthetic protocol is same as describes in Scheme 71.



Scheme 80: Synthesis of **120**.

Upon synthesizing ynones **120a** and **120b**, we subjected 3 equivalents of **120a** and **120b** with 1 equivalent of **104a** separately to our prototypical condition. Interestingly, a separable mixture of α- and β-N-indolyl enones (**121** and **122**) were isolated in 1:1 regioisomeric ratio with good yields. The structure of **121** and **122** were unambiguously confirmed by ^{1}H-NMR, ^{13}C NMR, IR, HRMS data respectively, Fig **25-28**. Interestingly, the synthesis of enones **121** and **122** are not known in the literature yet and otherwise difficult to access.



Scheme 81: Reaction of **120a** and **120b** with 3-nitroindole **104a**.

The molecular structure of the **122a** was assigned based on the X-ray diffraction analysis, Figure 29.

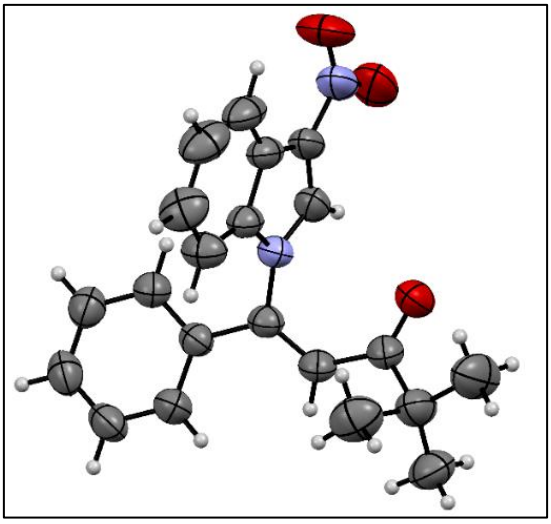


Figure 29: ORTEP diagram of **122a**.

A plausible mechanism associated with this reaction is outlined in Scheme 82. Initially, after 1,4- addition of **120**, the species **123** having no α′-hydrogen abstracts proton from Boc group of 3-nitroindole **104a** to produce intermediate **124** by eliminating carbon dioxide and isobutylene. Then, intermediate **124** undergoes umpolung addition to **125** to generate **126** which after a subsequent proton shift followed by expulsion of phosphine delivers **121**. On the other hand, Michael addition of **124** to **120** produces **122**.

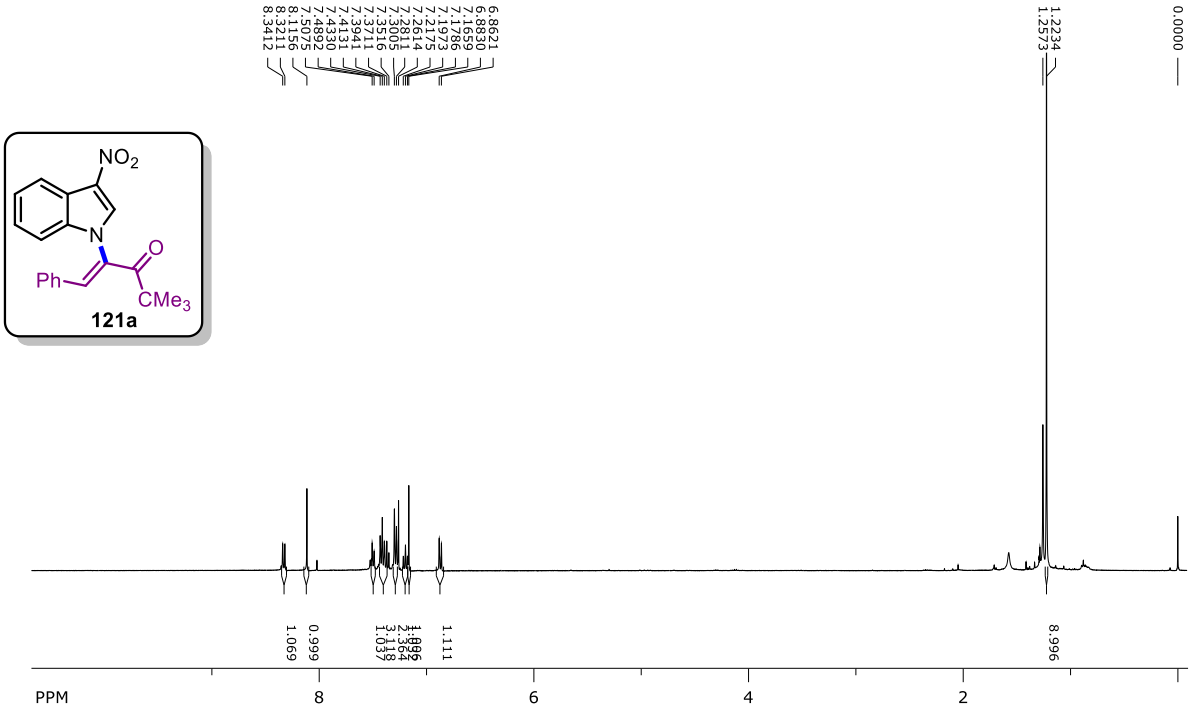


Figure 25: ^{1}H NMR (100 MHz, $CDCl_3$) of **121a**.

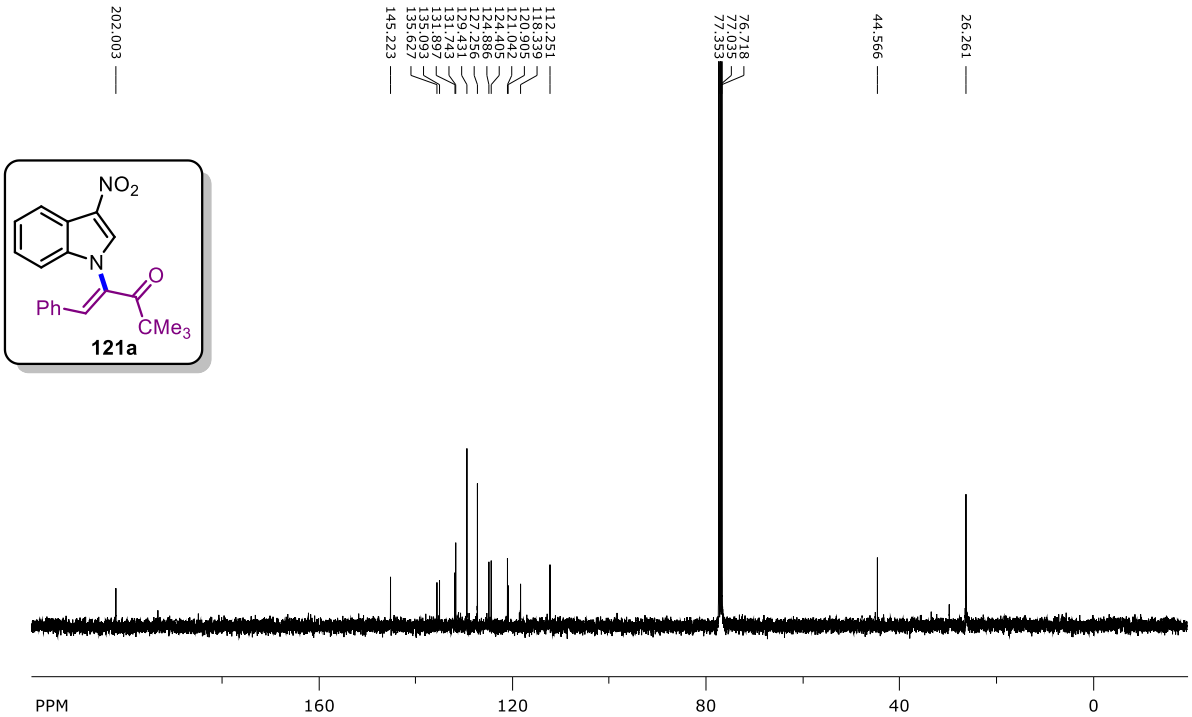


Figure 26: ^{13}C NMR (100 MHz, $CDCl_3$) of **121a**.

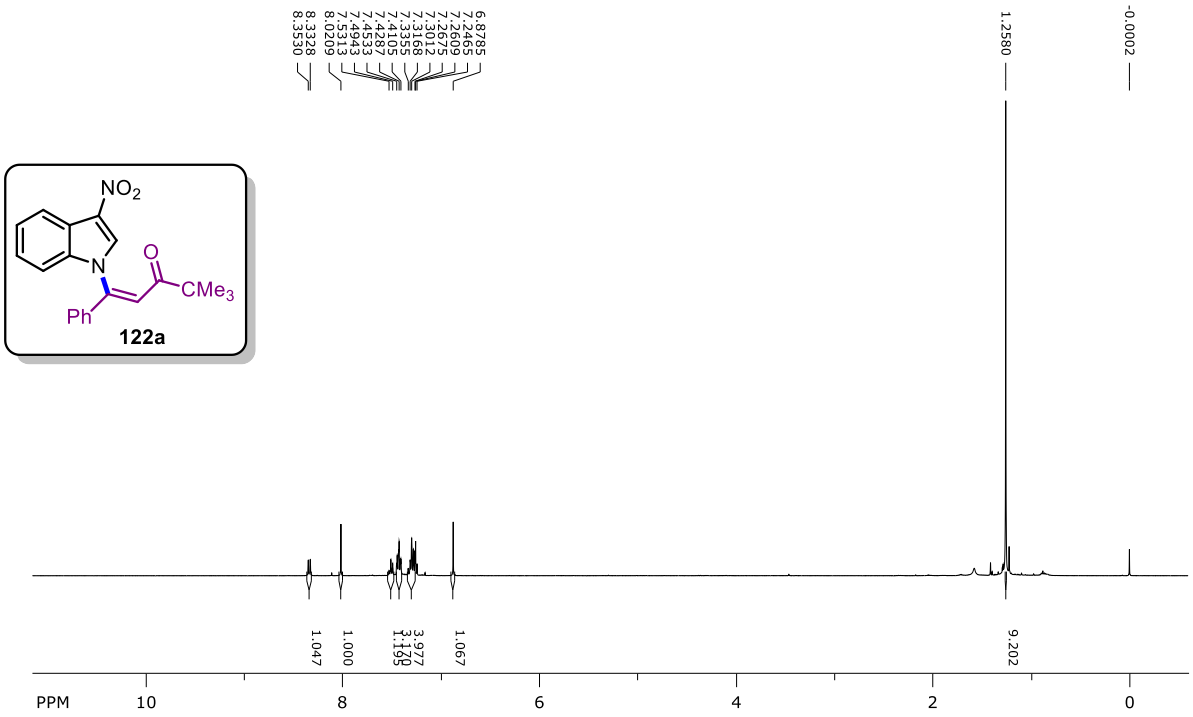


Figure 27: ^{1}H NMR (100 MHz, $CDCl_3$) of **122a**.

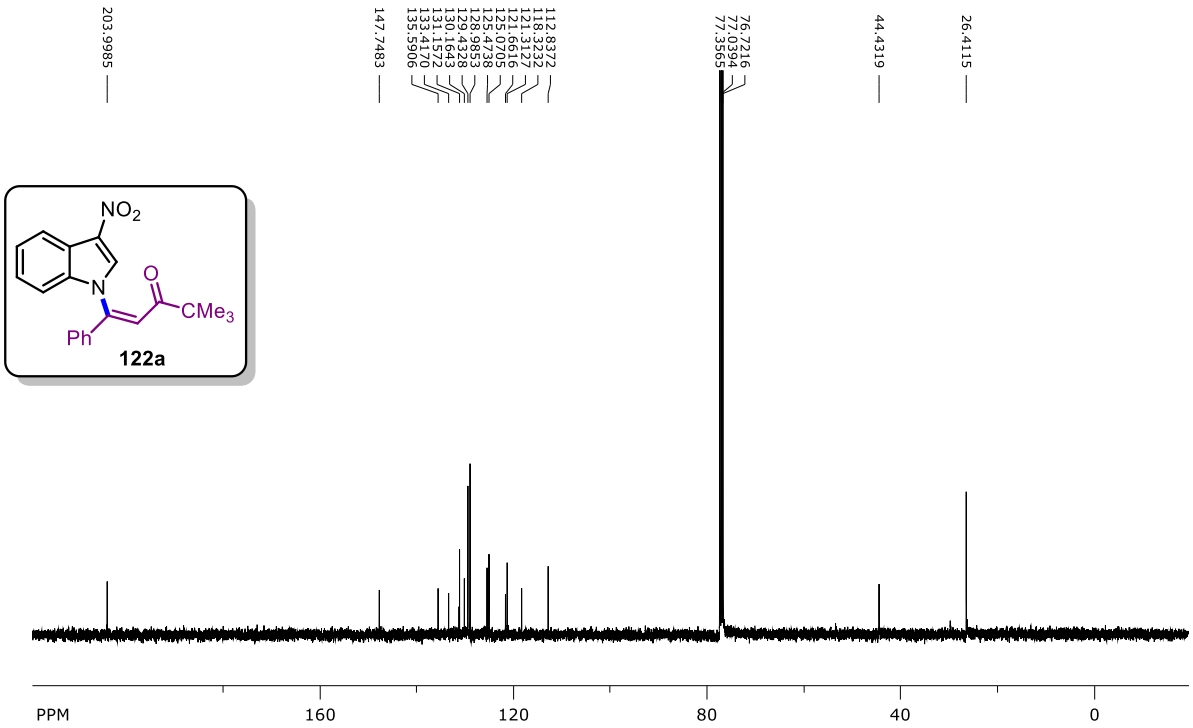
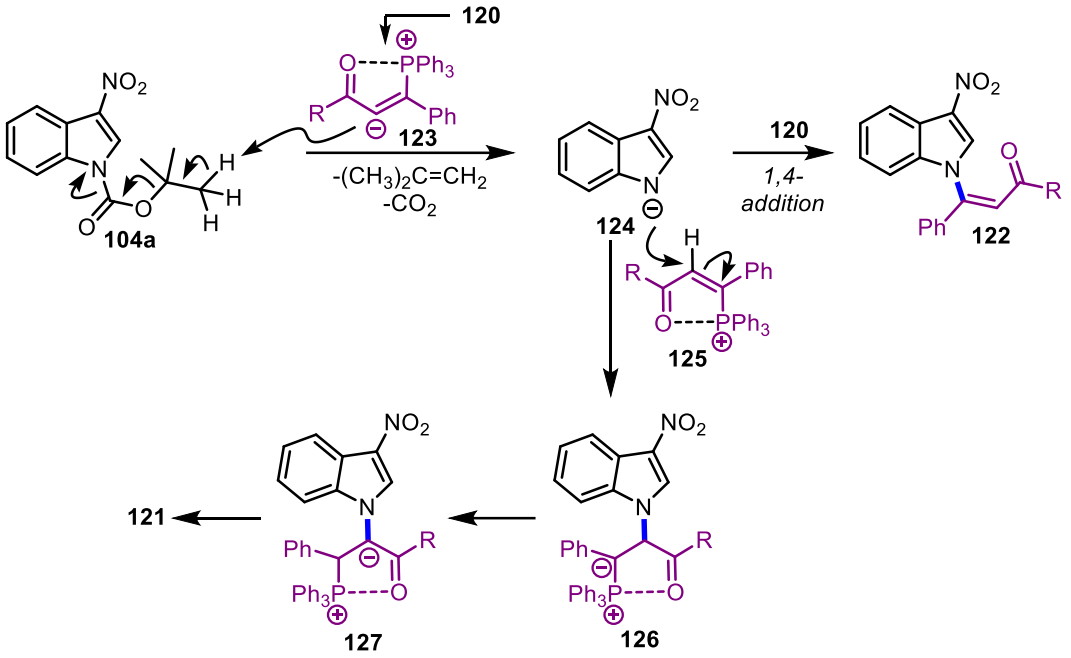


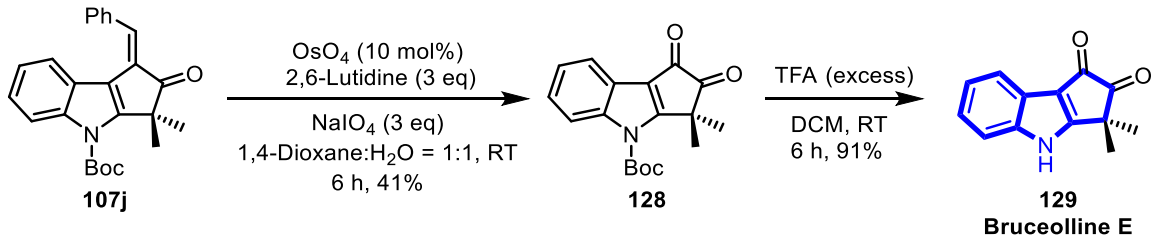
Figure 28: ^{13}C NMR (100 MHz, $CDCl_3$) of **122a**.



Scheme 82: Plausible mechanism behind the reaction of **120** and **104a**.

3.5: Synthesis of Natural Product Bruceolline E:

The synthetic application of the [3+2] annulated adduct was demonstrated by preparing the bioactive natural product, Bruceolline E, isolated by Ohmoto and co-workers in 1994 from the root wood of *Brucea mollis* var. *ronkinensis*.[77a] The genus *B. mollis* is traditionally used as remedy for malaria and other parasitic diseases. Despite their potential medicinal utility, bruceollines have gained much less attention from the synthetic community. To synthesize **129**, we took **107j** and subjected to OsO_4-mediated dihydroxylation followed by $NaIO_4$-mediated oxidative cleavage to form **128**. Finally, Boc deprotection of **128** in presence of TFA furnished the natural product, Bruceolline E, Figure 30, 31.



Scheme 84: Synthesis of Bruceolline E **129**.

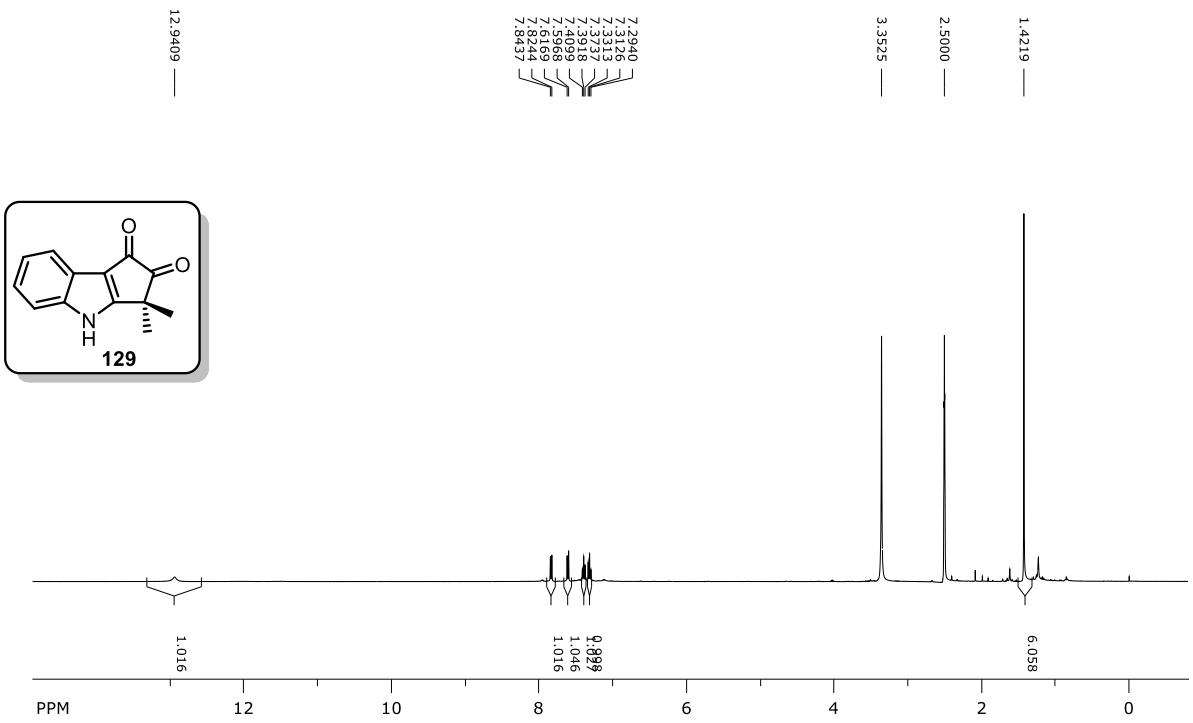


Figure 30: ^{1}H NMR (100 MHz, $CDCl_3$) of **129**.

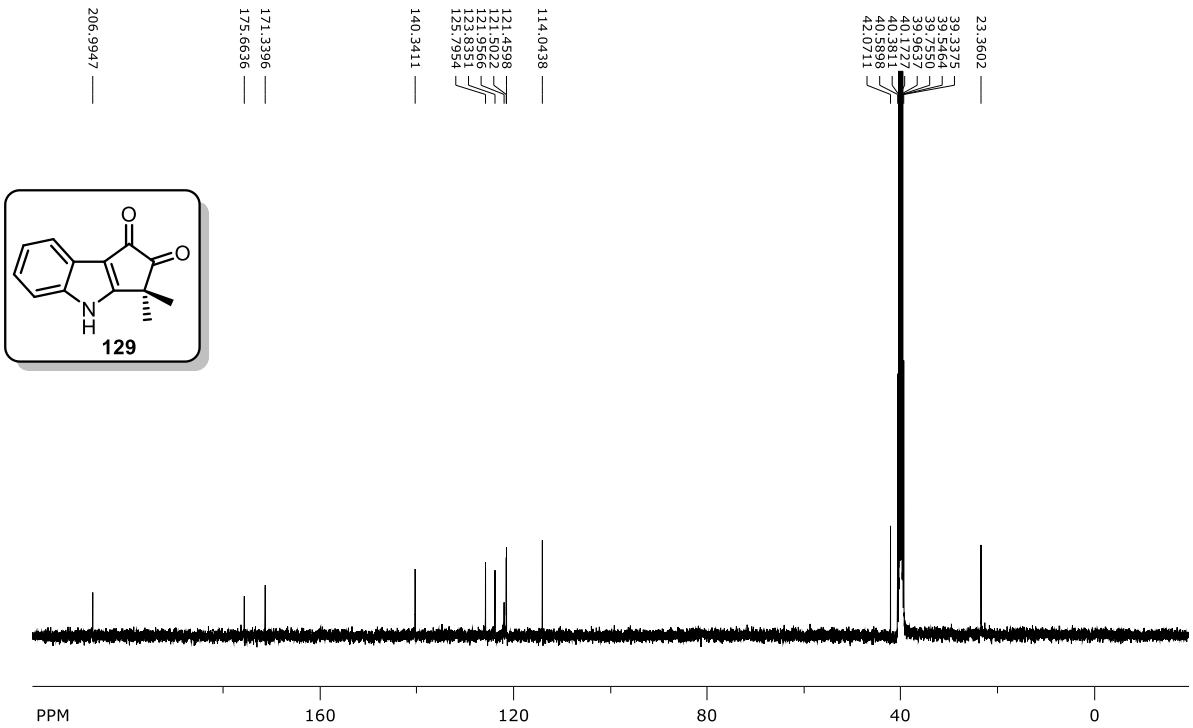
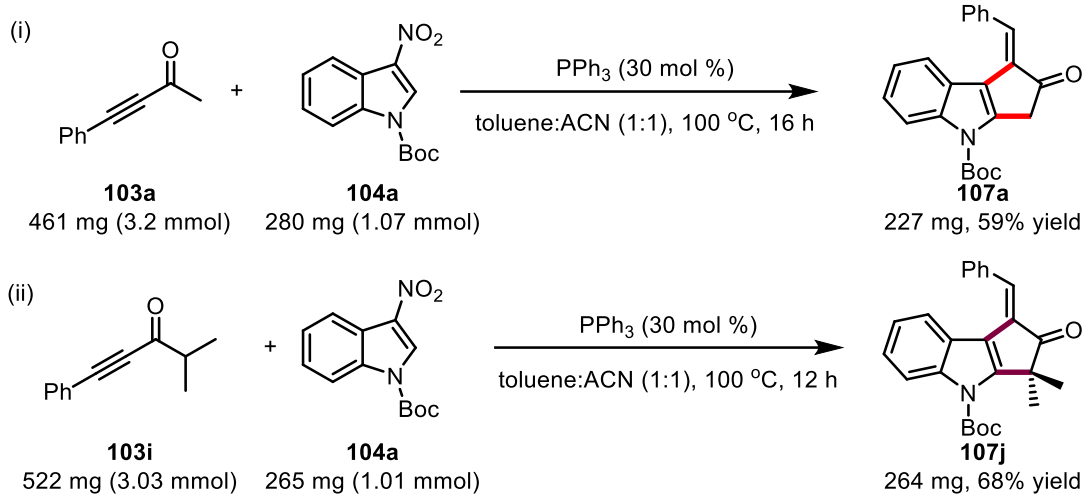


Figure 31: ^{13}C NMR (100 MHz, $CDCl_3$) of **129**.

To verify the generality and practicality of the method, a scale-up batch reaction was done with **103a** and **103i** separately on 1.0 mmol scales as depicted in Scheme 83. The respective product **107a** and **107j** was obtained in 59% and 68% yields, respectively.



Scheme 83: The scale-up batch reaction.

In summary, we have disclosed the first phosphine-catalyzed rearomatizing [3+2] annulation of α,β-ynones with nitroheteroarenes to access an unprecedented α-arylidene cyclopenta[*b*]indoles. The methodology fared well in creating a tertiary center and sterically encumbered all-carbon quaternary- and spiro- centers. The strategy was further extended to synthesise 3-benzylidene-cyclopenta[*b*]benzofuran-2-ones, 3-benzylidene-cyclopenta[*b*]-fused benzothiophenes, α- and β-N-indolyl enones, the synthesis of which is not known yet. Furthermore, the utility of the protocol was elaborated by synthesising the antimalarial natural product, bruceolline E. Most salient feature of this protocol includes: (i) easily accessible starting materials (ii) straightforward mechanism (iii) efficient and practical reaction condition.

Conclusions

In conclusions, we have established phosphine- and water-assisted cyclopentannulative aldol reaction of α-substituted α,β-unsaturated dienones tethered to ketones to access a library of 3-hydroxy-3-dienyl-cyclopentanones fused to arenes and heteroarenes in good to excellent yields, which can potentially serve as benzoabscisic acid analogs. Most interestingly, cyclopentanones can be synthesized in a diastereoselective manner bearing two contiguous stereogenic centres.

Next, we have developed a practical and efficient organophosphine-promoted redox method for transforming 1-(2-nitroaryl)prop-2-ynones into 3-hydroxyquinoline-4(1*H*)-ones (3HQ). This work encompasses the first intramolecular oxyamination of α,β-ynones to comprise a new entry to the synthesis of 3HQs. Furthermore, the synthetic utility was demonstrated by establishing access to japonine and its analogs, 3,4-dialkoxyquinolines and 3-hydroxy-3-phenylquinoline-2,4-diones. The generality of this strategy was thoroughly verified by applying this methodology on a large scale.

We have disclosed the first phosphine-catalyzed denitrative rearomatizing [3+2] annulation of α,β-ynones with 3-nitroindoles to access an unprecedented α-arylidene cyclopenta[*b*]indoles. The methodology fared well in creating a tertiary center and sterically encumbered all-carbon quaternary- and spiro- centers. The strategy was further extended to synthesize 3-benzylidene-cyclopenta[*b*]benzofuran-2-ones, 3-benzylidene-cyclopenta[*b*]-fused benzothiophenes, α- and β-N-indolyl enones, establishing their first synthesis. Furthermore, the utility of the protocol was elaborated by synthesising the antimalarial natural product, bruceolline E.

Experimental Section

General experimental methods: All the starting compounds and catalysts employed in this study were procured from Sigma-Aldrich, Avra Chemicals and were used without further purification. For thin layer chromatography (TLC), silica aluminium foils with fluorescent indicator 254 nm (from Aldrich) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using SD Fine silica gel 60-120 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and stored over sodium wire. IR spectra were recorded on a Perkin–Elmer FT IR spectrometer as thin films or KBr pellet, as indicated, with ν_{max} in inverse centimetres. Melting points were recorded on a digital melting point apparatus Stuart SMP30 and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker Biospin Avance III FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$ (7.26 ppm) or in $(CD_3)_2SO$ (δ 2.50 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm) or in $(CD_3)_2SO$ (δ 39.5 ppm). Single crystal X-ray analysis was carried on a Bruker AXS KAPPA APEX II system. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer.

General procedure-1: Synthesis of *α*-substituted dienone-ketone 23a-e, 23g-j, 23m, 23n.

Step-I: To an oven dried 25 mL RB flask, 2-bromobenzaldehyde **24a** (2.0 mmol) and anhydrous THF (10 mL) were added. Appropriate Grignard reagent (2.4 mmol) at 0 ^oC under nitrogen atmosphere and continued stirring at room temperature until **24a** disappeared (as monitored by TLC). The reaction mixture was quenched with saturated aq. NH_4Cl and extracted with ethyl acetate. Organic extracts were combined and dried over anhydrous sodium sulphate and concentrated to afford 2-bromo alcohol **25a**. The crude reaction mixture was taken forward to the next step without further purification.

Step-II: An oven dried 25 mL long neck RB flask was charged with 2-bromobenzyl alcohol **25a** (1.0 mmol), dry THF (5 mL) and placed at −78 ^oC. *n*-BuLi (1.6 *M* in hexanes, 2.2 mmol) was added drop wise at the same temperature and stirred for an hour. Then, *α*-methyl

trans-cinnamaldehyde (1.3 mmol) dissolved in 1 mL of dry THF was added dropwise over 2 mins and stirred at room temperature for 30 mins. The reaction mixture was quenched with saturated aq. NH_4Cl solution and extracted using ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The product was purified by silica gel column chromatography using hexane/ethyl acetate (10:3) as eluent to afford the diol **27a**.

Step-III: The diol **27a** (1.0 mmol) was dissolved in ethyl acetate (10 mL) and IBX (2.2 mmol) was added. The resulting suspension was immersed in an oil bath set to 75 °C and stirred until diol **27a** disappeared as monitored by TLC. The reaction mixture was cooled to room temperature and filtered through a Buchner funnel. The filter cake was washed with 3×5 mL of ethyl acetate. Organic extracts were combined and washed with saturated sodium bicarbonate solution to remove excess iodobenzoic acid. The extract was dried over anhydrous sodium sulphate and concentrated under vacuum. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford the *α*-substituted dienone-ketone **23a**.

General procedure-2: Synthesis of cromene and naphthalene based *α*-substituted dienone-ketone 23f, 23k.

Reactions were performed by following the general procedure described for step-I, II and III, Scheme 25.

General procedure-3: Synthesis of benzothiophene based *α*-substituted dienone-ketone 23l.

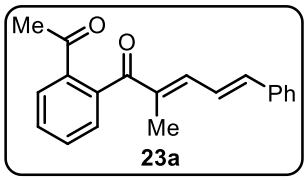
Step-I: To a solution of *N*-methylpiperazine (NMP, 0.18 mL, 1.6 mmol) in THF (5 mL) at −78 °C was added *n*-BuLi (1.6*M* in hexane, 1.0 mL, 1.6 mmol). After 15 min, benzothiophene-3-carboxaldehyde **31a** (200 mg, 1.2 mmol) was added and then the reaction mixture was stirred for an additional 30 min. A hexane solution of *n*-BuLi (2.0 mL, 3.2 mmol) was added and the mixture was stirred for an additional 15 min and then the mixture was warmed to −30 °C in 2 h. The solution was again cooled down to −78 °C and an appropriate dienal (1.5 mmol) dissolved in dry THF (1.0 ml), was added drop wise over 5 min. The mixture was warmed to room temperature over 30 min. The reaction progress was monitored by TLC. Reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium

sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford **31c.**

Step-II: To an oven dried 25 mL RB flask, alcohol **31c** (1.0 mmol) and anhydrous THF (10 mL) were added. Appropriate Grignard reagent (2.2 mmol) at 0 ^{o}C under nitrogen atmosphere and continued stirring at room temperature until **31c** disappeared (as monitored by TLC). The reaction mixture was quenched with saturated *aq*. NH_4Cl and extracted with ethyl acetate. Organic extracts were combined and dried over anhydrous sodium sulphate and concentrated to afford the diol **31d**.

Step-III: The diol **31d** (1.0 mmol) was dissolved in ethyl acetate (10 mL) and IBX (2.2 mmol) was added. The resulting suspension was immersed in an oil bath set to 75 °C and stirred until diol disappeared as monitored by TLC. The reaction mixture was cooled to room temperature and filtered through a Buchner funnel. The filter cake was washed with 3×5 mL of ethyl acetate. Organic extracts were combined and washed with saturated sodium bicarbonate solution to remove excess iodobenzoic acid. The extract was dried over anhydrous sodium sulphate and concentrated under vacuum. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford dienone-ketones **23l**.

(2*E*,4*E*)-1-(2-Acetylphenyl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23a).

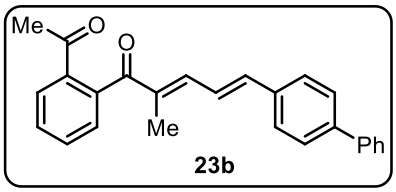


23a

This compound was prepared by following the general procedure-1 and isolated as pale-yellow solid. M.P = 106-107 ^{o}C. R_f = 0.5 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3037, 2924, 1682, 1648, 1617, 1359, 1285, 1012, 756. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.42-7.40 (m, 2H), 7.35-7.26 (m, 4H), 7.13 (dd, *J* = 15.5 and 11.2 Hz, 1H), 6.63 (d, *J* = 15.5 Hz, 1H), 6.55 (d, *J* = 11.2 Hz, 1H), 2.54 (s, 3H), 2.20 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 199.9, 198.4, 141.3, 141.0, 139.5, 137.7, 137.0, 136.4, 132.1, 129.5, 129.2, 128.9, 128.8 (2C), 128.2, 127.1 (2C), 124.3, 27.5, 12.1. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{19}O_2$ $(M+H)^+$: 291.1385. Found: 291.1397.

(2*E*,4*E*)-5-([1,1'-Biphenyl]-4-yl)-1-(2-acetylphenyl)-2-methylpenta-2,4-dien-1-one (23b).

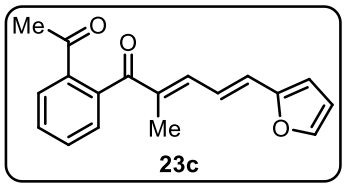
This compound was prepared by following the general procedure-1 and isolated as white solid. M.P = 168-170 ^{o}**C**. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3032, 1683,



23b

1648, 1615, 1484, 1358, 1263, 1009, 762. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 7.88 (dd, *J* = 8.0 and 1.1 Hz, 1H), 7.61-7.53 (m, 6H), 7.52-7.41 (m, 4H), 7.36-7.35 (m, 2H), 7.17 (dd, *J* = 15.2 and 11.2 Hz, 1H), 6.67 (d, *J* = 15.3 Hz, 1H), 6.58 (dd, *J* = 11.2 and 0.9 Hz, 1H), 2.55 (s, 3H), 2.22 (*J* = 1.0 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 199.8, 198.4, 141.5, 141.4, 141.0, 140.3, 139.0, 137.7, 137.1, 135.4, 132.1, 129.4, 129.2, 128.8 (2C), 128.2, 127.6, 127.5 (2C), 127.4 (2C), 126.9 (2C), 124.3, 27.6, 12.2. **HRMS (ESI)**: *m/z* calcd for $C_{26}H_{23}O_2$ $(M+H)^+$: 367.1698. Found: 367.1683.

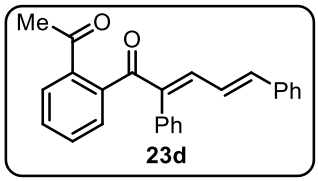
(2*E*,4*E*)-1-(2-Acetylphenyl)-5-(furan-2-yl)-2-methylpenta-2,4-dien-1-one (23c).



23c

This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.5 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2925, 1683, 1645, 1606, 1476, 1358, 1260, 1074, 757. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 7.85 (dd, *J* = 7.6 and 1.2 Hz, 1H), 7.58-7.51 (m, 2H), 7.41 (d, *J* = 1.6 Hz, 1H), 7.33 (dd, *J* = 7.5 and 1.4 Hz, 1H), 7.00 (dd, *J* = 15.2 and 11.3 Hz, 1H), 6.49 (d, *J* = 11.6 Hz, 1H), 6.42 (d, *J* = 15.3 Hz, 1H), 6.40-6.39 (m, 1H), 6.35 (d, *J* = 3.5 Hz, 1H), 2.52 (s, 3H), 2.17 (d, *J* = 1.0 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 199.6, 198.5, 152.5, 143.6, 141.3, 140.7, 137.6, 137.1, 132.0, 129.4, 129.1, 128.2, 126.0, 122.6, 112.1, 111.5, 27.6, 12.1. **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{17}O_3$ $(M+H)^+$: 281.1178. Found: 281.1164.

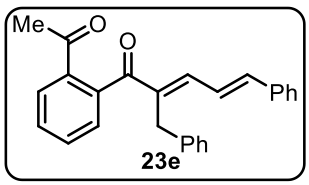
(2*E*,4*E*)-1-(2-Acetylphenyl)-2,5-diphenylpenta-2,4-dien-1-one (23d).



23d

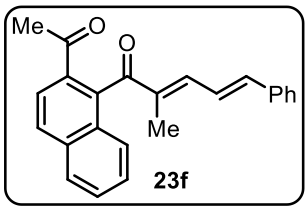
This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.4 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3058, 1680, 1654, 1611, 1491, 1444, 1267, 1240, 1084, 1054, 975, 700. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 7.84 (dd, *J* = 7.9 and 0.8 Hz, 1H), 7.61 (dt, *J* = 7.4 and 1.2 Hz, 1H), 7.53 (dt, *J* = 7.6 and 1.4 Hz, 1H), 7.47-7.43 (m, 5H), 7.38-7.35 (m, 1H), 7.29-7.23 (m, 5H), 6.92-6.83 (m, 2H), 6.76-6.73 (m, 1H), 2.54 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 198.4, 198.1, 141.8, 141.7, 141.6, 140.8, 137.0, 136.2, 135.2, 132.2, 130.6 (2C), 129.4, 129.3, 129.0, 128.7 (2C), 128.4, 128.1 (2C), 127.8, 127.2 (2C), 125.3, 27.4. **HRMS (ESI)**: *m/z* calcd for $C_{25}H_{21}O_2$ $(M+H)^+$: 353.1542. Found: 353.1530.

(2*E*,4*E*)-1-(2-Acetylphenyl)-2-benzyl-5-phenylpenta-2,4-dien-1-one (23e).



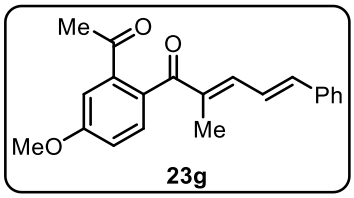
This compound was prepared by following the general procedure-1 and isolated as pale-yellow solid. M.P = 107-109 ^{o}C. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3028, 1613, 1438, 1360, 1261, 740**.** **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.84 (d, *J* = 7.2 Hz, 1H), 7.55-7.53 (m, 2H), 7.37-7.25 (m, 10H), 7.21-7.15 (m, 2H), 6.79 (d, *J* = 11.2 Hz, 1H), 6.70 (d, *J* = 15.4 Hz, 1H), 4.06 (s, 2H), 2.52 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 198.9, 198.7, 143.5, 141.1, 140.9, 140.0, 139.7, 137.6, 136.2, 131.8, 129.3, 129.2, 129.1, 128.8 (2C), 128.5 (4C), 128.2, 127.2 (2C), 126.0, 124.2, 31.8, 27.8. **HRMS (ESI)**: *m/z* calcd for $C_{26}H_{23}O_2$ $(M+H)^+$: 367.1698. Found: 367.1679.

(2*E*,4*E*)-1-(2-Acetylnaphthalen-1-yl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23f).



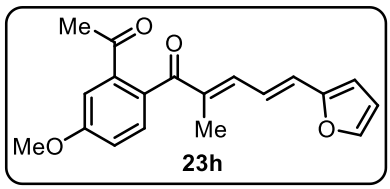
This compound was prepared by following the general procedure-2 and isolated as white solid. M.P = 152-153 ^{o}**C.** R_f = 0.3 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3060, 2921, 1682, 1646, 1616, 1463, 1426, 1382, 1279, 1243, 1074, 736. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.01-7.91 (m, 3H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.60 (dt, *J* = 6.8 and 1.2 Hz, 1H), 7.52 (dt, *J* = 8.1 and 1.3 Hz, 1H), 7.36-7.34 (m, 2H), 7.31-7.24 (m, 3H), 7.13 (dd, *J* = 15.2 and 11.3 Hz, 1H), 6.49-6.45 (m, 2H), 2.65 (s, 3H), 2.33 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 200.6, 198.0, 140.9, 140.2, 139.5, 138.5, 136.3, 135.1, 132.0, 130.8, 129.1, 128.8, 128.7 (2C), 128.6, 127.9, 127.7, 127.4, 127.0 (2C), 125.1, 124.3, 28.0, 12.0. **HRMS (ESI)**: *m/z* calcd for $C_{24}H_{21}O_2$ $(M+H)^+$: 341.1542. Found: 341.1524.

(2*E*,4*E*)-1-(2-Acetyl-4-methoxyphenyl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23g).



This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2933, 2849, 1688, 1604, 1486, 1358, 1284, 1177, 1010, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44-7.42 (m, 2H), 7.36-7.25 (m, 5H), 7.13 (dd, *J* = 15.4 and 11.2 Hz, 1H), 7.09-7.05 (m, 1H), 6.65 (d, *J* = 15.7 Hz, 1H), 6.63 (d, *J* = 11.3 Hz, 1H), 3.91 (s, 3H), 2.49 (s, 3H), 2.17 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 199.5, 199.2, 160.3, 141.0, 140.4, 139.5, 137.9, 136.4, 132.8, 130.3, 128.9 (2C), 127.1 (2C), 124.3, 115.9, 114.9, 55.7, 28.2, 12.4. **HRMS (ESI)**: *m/z* calcd for $C_{21}H_{21}O_3$ $(M+H)^+$: 321.1491. Found: 321.1476.

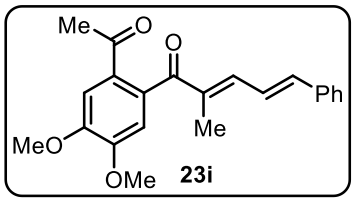
(2*E*,4*E*)-1-(2-Acetyl-4-methoxyphenyl)-5-(furan-2-yl)-2-methylpenta-2,4-dien-1-one



23h

(23h). This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.4 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2938, 2843, 1687, 1642, 1603, 1479, 1358, 1286, 1219, 1010, 740. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.42 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.23 (d, *J* = 1.5 Hz, 1H), 7.05 (dd, *J* = 8.0 and 2.6 Hz, 1H), 7.00 (dd, *J* = 15.3 and 11.5 Hz, 1H), 6.57 (d, *J* = 11.5 Hz, 1H), 6.45 (d, *J* = 15.4 Hz, 1H), 6.41-6.36 (m, 2H), 3.90 (s, 3H), 2.46 (s, 3H), 2.17 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 199.6, 198.9, 160.3, 152.5, 143.5, 140.8, 140.5, 137.9, 132.7, 130.3, 126.0, 122.6, 115.9, 114.8, 112.1, 111.5, 55.6, 28.2, 12.3. **HRMS (ESI)**: *m/z* calcd for $C_{19}H_{19}O_4$ $(M+H)^+$: 311.1283. Found: 311.1267.

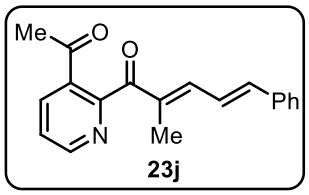
(2*E*,4*E*)-1-(2-Acetyl-4,5-dimethoxyphenyl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23i).



23i

This compound was prepared by following the general procedure-1 and isolated as white solid. M.P = 110-112 ^oC. R_f = 0.2 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2933, 2851, 1672, 1646, 1614, 1448, 1344, 1279, 1206, 1021, 745. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.35-7.26 (m, 4H), 7.12 (dd, *J* = 15.6 and 11.2 Hz, 1H), 6.82 (s, 1H), 6.65 (d, *J* = 15.6 Hz, 1H), 6.54 (d, *J* = 11.2 Hz, 1H), 4.00 (s, 3H), 3.95 (s, 3H), 2.48 (s, 3H), 2.20 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 199.6, 197.0, 152.0, 148.8, 140.5, 139.5, 138.0, 136.3, 135.5, 129.8, 128.9, 128.8 (2C), 127.0 (2C), 124.3, 111.9, 110.8, 56.3, 56.2, 27.6, 12.3. **HRMS (ESI)**: *m/z* calcd for $C_{22}H_{23}O_4$ $(M+H)^+$: 351.1596. Found: 351.1580.

(2*E*,4*E*)-1-(3-Acetylpyridin-2-yl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23j).

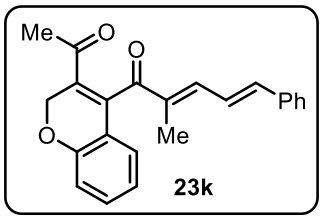


23j

This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.2 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3057, 2926, 1687, 1614, 1565, 1434, 1360, 1277, 1021, 737. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.77 (dd, *J* = 4.8 and 1.6 Hz, 1H), 8.14 (dd, *J* = 8.0 and 1.6 Hz, 1H), 7.50 (dd, 8.0 and 4.8 Hz, 1H), 7.45-7.43 (m, 2H), 7.36-7.29 (m, 3H), 7.19 (dd, *J* = 15.5 and 11.2 Hz, 1H), 6.77-6.70 (m, 2H), 2.56 (s, 3H), 2.22 (d, *J* = 0.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 197.9, 196.4, 158.2, 151.3,

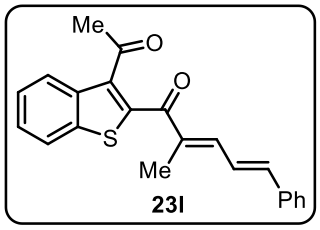
143.6, 140.6, 136.8, 136.3, 135.6, 133.1, 129.0, 128.8 (2C), 127.2 (2C), 124.2, 123.6, 28.0, 11.8. **HRMS (ESI)**: *m/z* calcd for $C_{19}H_{18}NO_2$ $(M+H)^+$: 292.1338. Found: 292.1353.

(2*E*,4*E*)-1-(3-Acetyl-2*H*-chromen-4-yl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23k).



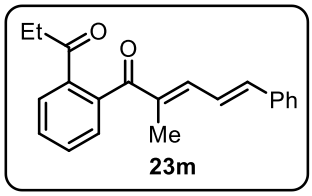
This compound was prepared by following the general procedure-2 and isolated as pale-yellow oil. R_f = 0.6 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3427, 2962, 2927, 1710, 1602, 1461, 1378, 1287, 1060, 767. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.45-7.43 (m, 2H), 7.36-7.27 (m, 5H), 7.13 (dd, *J* = 15.2 and 11.2 Hz, 1H), 7.00-6.89 (m, 4H), 6.80 (d, *J* = 15.2 Hz, 1H), 5.06 (s, 2H), 2.23 (s, 3H), 2.18 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 197.9, 194.8, 154.8, 143.7, 142.8, 141.6, 136.1, 136.0, 132.5, 129.3, 128.8 (2C), 127.3 (2C), 126.2, 123.8, 122.4, 120.8, 116.7, 64.7, 29.0, 11.4. **HRMS (ESI)**: *m/z* calcd for $C_{23}H_{20}O_3$ $(M)^+$: 344.1412. Found: 344.1414.

(2*E*,4*E*)-1-(3-Acetylbenzo[*b*]thiophen-2-yl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23l).



This compound was prepared by following the general procedure-3 and isolated as pale-yellow oil. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3050, 2927, 2854, 1676, 1641, 1608, 1502, 1428, 1282, 1225, 756. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.26-8.24 (m, 1H), 7.88-7.86 (m, 1H), 7.51-7.45 (m, 4H), 7.37-7.31 (m, 3H), 7.21-7.11 (m, 2H), 6.85 (d, *J* = 10.4 Hz, 1H), 2.47 (s, 3H), 2.21 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 196.3, 192.0, 145.2, 145.1, 142.3, 139.5, 137.3, 137.1, 136.6, 135.9, 129.5, 128.9 (2C), 127.5 (2C), 126.5, 126.0, 125.2, 123.5, 122.2, 31.5, 12.3. **HRMS (ESI)**: *m/z* calcd for $C_{22}H_{19}O_2S$ $(M+H)^+$: 347.1106. Found: 347.1123.

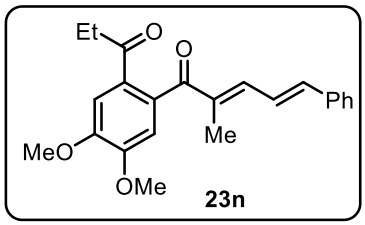
(2*E*,4*E*)-2-Methyl-5-phenyl-1-(2-propionylphenyl)penta-2,4-dien-1-one (23m).



This compound was prepared by following the general procedure-1 and isolated as pale-yellow oil. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3126, 3060, 2848, 2749, 1699, 1642, 1601, 1476, 1360, 1242, 1011, 746. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.85 (dd, *J* = 7.9 and 1.2 Hz, 1H), 7.58-7.50 (m, 2H), 7.43-7.40 (m, 2H), 7.35-7.25 (m, 4H), 7.13 (dd, *J* = 15.4 and 11.2 Hz, 1H), 6.64 (d, *J* = 15.4 Hz, 1H), 6.58 (d, *J* = 11.2 Hz, 1H), 2.91 (q, *J* = 7.2 Hz, 2H), 2.20 (d, *J* = 0.9 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz,**

$CDCl_3$): δ 201.5, 199.8, 141.2, 139.5, 137.6, 137.3, 136.4, 131.7, 129.2, 128.9, 128.8 (2C), 128.7, 128.6, 128.3, 127.1 (2C), 124.3, 33.0, 12.2, 8.1. **HRMS (ESI)**: *m/z* calcd for $C_{21}H_{21}O_2$ $(M+H)^+$: 305.1542. Found: 305.1533.

(2*E*,4*E*)-1-(4,5-Dimethoxy-2-propionylphenyl)-2-methyl-5-phenylpenta-2,4-dien-1-one (23n).



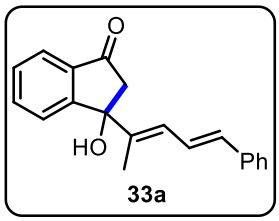
23n

This compound was prepared by following the general procedure-1 and isolated as white solid. R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2937, 1646, 1614, 1355, 1277, 1020, 743. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44-7.42 (m, 2H), 7.35-7.28 (m, 4H), 7.11 (dd, *J* = 15.3 and 11.2 Hz, 1H), 6.83 (s, 1H), 6.65 (d, *J* = 15.3 Hz, 1H), 6.55 (dd, *J* = 11.2 and 1.0 Hz, 1H), 3.99 (s, 3H), 3.94 (s, 3H), 2.84 (q, *J* = 7.2 Hz, 2H), 2.20 (d, *J* = 1.0 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 200.1, 199.5, 151.7, 148.9, 140.6, 139.4, 137.9, 136.4, 135.3, 130.0, 128.9, 128 (2C), 127.0 (2C), 124.2, 111.2, 110.9, 56.2 (2C), 33.0, 12.3, 8.3. **HRMS (ESI)**: *m/z* calcd for $C_{23}H_{25}O_4$ $(M+H)^+$: 365.1753. Found: 365.1741.

General procedure-4: Synthesis of indanones 33a-n via intramolecular aldol reaction of *α*-substituted dienoen-ketone 23a-n.

An oven dried 5 mL glass vial was charged with **23** (30 mg, 0.11 mmol). An appropriate solvent (1 mL), water (3.3 mmol) and PBu_3 (1.3 mmol) were introduced at room temperature (rt) and stirring continued at rt until **23** disappeared as monitored by TLC. The reaction mixture was extracted using ethyl acetate. All the volatiles were removed under reduced pressure. The crude product was directly purified by silica gel chromatography using hexane/ethyl acetate as eluent to afford **33**.

3-Hydroxy-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33a).

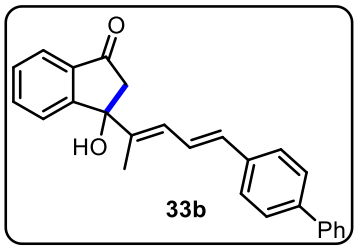


33a

This compound was isolated as pale-yellow solid. Following the general procedure-4, 40 mg of **23a** afforded 35.7 mg of **33a** (89% yield). M.P = 119-120 ^{o}C. R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3418, 3025, 2930, 1695, 1595, 1499, 1286, 738. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.51-7.46 (m, 2H), 7.41-7.39 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.24-7.20 (m, 1H), 7.00 (dd, *J* = 15.4 and

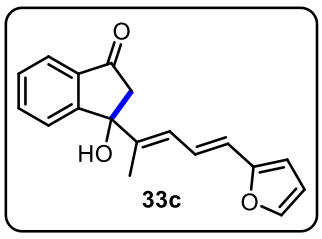
11.4 Hz, 1H), 6.59 (d, *J* = 15.6 Hz, 1H), 6.55 (d, *J* = 11.1 Hz, 1H), 3.02 (d, J_{AB} = 18.9 Hz, 1H), 2.85 (d, J_{AB} = 18.9 Hz, 1H) 2.85 (s, 1H), 1.70 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.6, 156.9, 139.2, 137.4, 136.3, 135.6, 133.6, 129.6, 128.6 (2C), 127.6, 126.4 (2C), 124.7, 124.6, 124.4, 123.3, 80.0, 52.0, 13.9. **HRMS (ESI)**: *m/z* calcd for $C_{20}H_{19}O_2$ $(M+H)^+$: 291.1385. Found: 291.1371.

3-((2*E*,4*E*)-5-([1,1'-biphenyl]-4-yl)penta-2,4-dien-2-yl)-3-hydroxy-2,3-dihydro-1*H*-inden-1-one (33b).



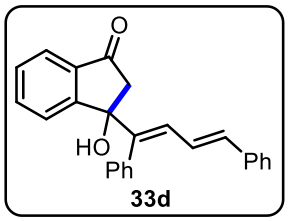
This compound was prepared by following the general procedure-4 and isolated as pale-yellow solid. 40 mg of **23b** afforded 33 mg of **33b** (81% yield). M.P = 201-203 ºC. R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3421, 2917, 2852, 1703, 1597, 1059, 982, 764. **^{1}H NMR (400 MHz, $(CD_3)_2SO$)**: δ 7.76 (dt, *J* = 7.6 and 1.0 Hz, 1H), 7.69-7.60 (m, 6H), 7.57-7.52 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.20 (dd, *J* = 15.6 and 11.2 Hz, 1H), 6.65 (d, *J* = 15.5 Hz, 1H), 6.49 (d, *J* = 11.2 Hz, 1H), 6.05 (s, 1H), 3.01 (d, J_{AB} = 18.8 Hz, 1H), 2.75 (d, J_{AB} = 18.8 Hz, 1H), 1.68 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.8, 158.5, 141.9, 140.1, 139.3, 137.0, 136.2, 135.8, 132.2, 129.5, 129.4 (2C), 127.8, 127.4 (2C), 127.2 (2C), 126.8 (2C), 125.8, 125.7, 124.4, 122.7, 79.1, 52.2, 14.1. **HRMS (ESI)**: *m/z* calcd for $C_{26}H_{22}NaO_2$ $(M+Na)^+$: 389.1517. Found: 389.1512.

3-((2*E*,4*E*)-5-(Furan-2-yl)penta-2,4-dien-2-yl)-3-hydroxy-2,3-dihydro-1*H*-inden-1-one (33c).



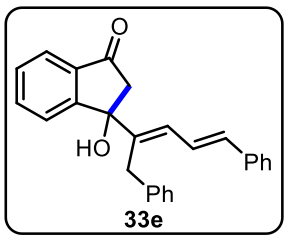
This compound was isolated as pale-yellow oil. Following the general procedure-4, 40 mg of **23c** afforded 36 mg of **33c** (88% yield). R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3427, 2927, 2859, 1697, 1602, 1236, 1059, 737. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.52-7.48 (m, 2H), 7.36 (d, *J* = 1.3 Hz, 1H), 6.89 (dd, *J* = 15.4 and 11.2 Hz, 1H), 6.50 (d, *J* =11.3 Hz, 1H), 6.40-6.37 (m, 2H), 6.27 (d, *J* = 3.2 Hz, 1H), 3.04 (d, J_{AB} = 19.0 Hz, 1H), 2.86 (d, J_{AB} = 19.0 Hz, 1H), 2.61 (s, 1H), 1.69 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.4, 156.9, 153.2, 142.2, 139.4, 136.3, 135.6, 129.6, 124.5, 124.3, 123.3, 123.0, 120.9, 111.6, 108.6, 80.0, 51.9, 13.9. **HRMS (ESI)**: *m/z* calcd for $C_{18}H_{15}O_2$ $(M-OH)^+$: 263.1072. Found: 263.1042.

3-((1*E*,3*E*)-1,4-Diphenylbuta-1,3-dien-1-yl)-3-hydroxy-2,3-dihydro-1*H*-inden-1-one



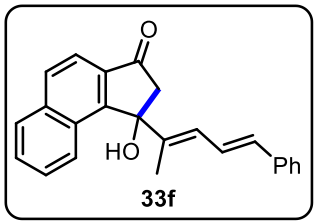
(33d). This compound was isolated as pale-yellow oil. Following the general procedure-4, 40 mg of **23d** afforded 34 mg of **33d** (85% yield). R_f = 0.4 (Hexane/EtOAc = 2/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3418, 3030, 2926, 1711, 753. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.74 (d, J = 3.6 Hz, 2H), 7.69 (d, J = 7.6 Hz, 1H), 7.54-7.50 (m, 1H), 7.27-7.15 (m, 8H), 6.84-6.80 (m, 3H), 6.65 (d, J = 15.6 Hz, 1H), 6.47 (d, J = 10.8 Hz, 1H), 3.12 (d, J_{AB} = 18.8 Hz, 1H), 2.84 (d, J_{AB} = 18.8 Hz, 1H), 2.59 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 202.7, 156.5, 145.5, 137.1, 136.8, 136.6, 135.4, 134.4 (2C), 127.9, 19.7, 128.5 (2C), 128.3 (2C), 127.8, 127.7, 127.3, 126.5 (2C), 125.7, 125.1, 123.2, 79.4, 52.7. **HRMS (ESI)**: *m/z* calcd for $C_{25}H_{21}O_2$ $(M+H)^+$: 353.1542. Found: 353.1534.

3-((2*E*,4*E*)-1,5-Diphenylpenta-2,4-dien-2-yl)-3-hydroxy-2,3-dihydro-1*H*-inden-1-one (33e).



This compound was isolated as pale-yellow oil. Following the general procedure-4, 30 mg of **23e** afforded 26 mg of **33e** (87% yield). R_f = 0.2 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3422, 3059, 3029, 2926, 1709, 1602, 1455, 1285, 1058, 749. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.77 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.51-7.48 (m, 1H), 7.46-7.44 (m, 1H), 7.39-7.36 (m, 2H), 7.33-7.18 (m, 8H), 7.13-7.11 (m. 2H), 7.04 (dd, J = 15.2 and 11.2 Hz, 1H), 6.69 (d, J = 15.2 Hz, 1H), 6.68 (d, J = 11.0 Hz, 1H), 3.77 (d, J_{AB} = 15.7 Hz, 1H), 3.49 (d, J_{AB} =15.7 Hz, 1H), 2.95 (d, J_{AB} = 19.0 Hz, 1H), 2.80 (d, J_{AB} =19.0 Hz, 1H), 2.29 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.2, 156.8, 142.1, 139.3, 137.1, 136.3, 135.3, 134.9, 129.6, 128.7 (2C), 128.6 (2C), 128.5, 128.0 (2C), 127.8, 127.6, 126.5 (2C), 124.9, 124.5, 123.2, 80.3, 52.9, 34.1. **HRMS (ESI)**: *m/z* calcd for $C_{26}H_{23}O_2$ $(M+H)^+$: 367.1698. Found: 367.1671.

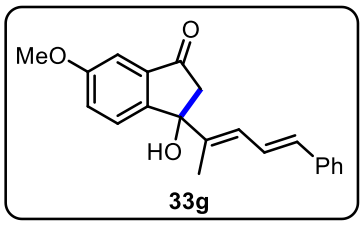
1-Hydroxy-1-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-1*H*-cyclopenta[*a*]naphthalen-3(2*H*)-one (33f).



This compound was isolated as pale-yellow oil. Following the general procedure-4, 40 mg of **23f** afforded 35.2 mg of **33f** (88% yield). R_f = 0.3 (Hexane/EtOAc = 2/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3429, 3055, 2924, 1693, 1453, 1278, 746. **^{1}H NMR (400**

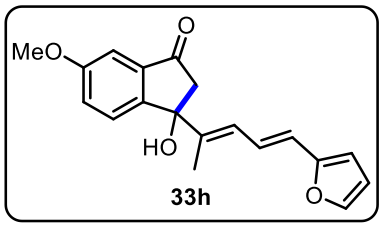
MHz, $CDCl_3$): δ 8.35 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.68-7.61 (m, 2H), 7.57-7.53 (m, 1H), 7.40 (d, J = 3.3 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.24-7.18 (m, 1H), 7.03 (dd, J = 15.4 and 11.0 Hz, 1H), 6.76 (d, J = 11.0 Hz, 1H), 6.61 (d, J = 15.6 Hz, 1H), 3.08 (s, 1H), 3.05 (d, J_{AB} = 19.0 Hz, 1H), 2.92 (d, J_{AB} = 19.0 Hz, 1H), 1.62 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.3, 155.4, 139.7, 137.5, 135.0, 133.3, 131.1, 129.2, 129.14, 129.13, 128.6 (2C), 127.6, 127.5, 126.3 (2C), 126.0, 124.6, 124.5, 118.6, 80.8, 53.5, 13.8. **HRMS (ESI)**: *m/z* calcd for $C_{24}H_{19}O_2$ $(M-H)^+$: 339.1385. Found: 339.1363.

3-Hydroxy-6-methoxy-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33g).



This compound was isolated as white solid. Following the general procedure-4, 40 mg of **23g** afforded 36 mg of **33g** (84% yield). R_f = 0.3 (Hexane/EtOAc = 2/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3058, 2926, 2854, 2749, 1762, 1694, 1643, 1609, 1459, 1386, 1282, 1081, 745. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.43-7.39 (m, 3H), 7.33-7.30 (m, 2H), 7.25-7.22 (m, 2H), 7.18 (d, J = 2.4 Hz, 1H), 7.00 (dd, J = 15.5 and 11.1 Hz, 1H), 6.60 (d, J = 15.5 Hz, 1H), 6.53 (d, J = 11.1 Hz, 1H), 3.86 (s, 3H), 3.06 (d, J_{AB} = 18.9 Hz, 1H), 2.89 (d, J_{AB} = 18.9 Hz, 1H), 2.34(s, 1H), 1.72 (d, J = 0.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.2, 161.0, 149.6, 139.4, 137.9, 137.4, 133.5, 128.6 (2C), 127.6, 126.3 (2C), 125.5, 124.7, 124.6, 124.5, 104.4, 79.6, 55.7, 52.6, 13.9. **HRMS (ESI)**: *m/z* calcd for $C_{21}H_{21}O_3$ $(M+H)^+$: 321.1491. Found: 321.1485.

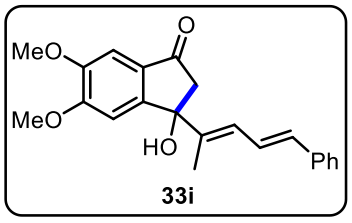
3-((2*E*,4*E*)-5-(Furan-2-yl)penta-2,4-dien-2-yl)-3-hydroxy-6-methoxy-2,3-dihydro-1*H*-inden-1-one (33h).



This compound was isolated as pale-yellow oil. Following the general procedure-4, 30 mg of **23h** afforded 25.8 mg of **33h** (86% yield). R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3422, 2928, 2849, 1708, 1605, 1488, 1282, 1056. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.40 -7.38 (m, 2H), 7.25 (dd, J = 8.4 and 2.6 Hz, 1H), 7.18 (d, J = 2.4 Hz, 1H), 6.92 (dd, J = 15.4 and 11.2 Hz, 1H), 6.48 (d, J = 11.2 Hz, 1H), 6.42-6.38 (m, 2H), 6.28 (d, J = 3.2 Hz, 1H), 3.88 (s, 3H), 3.07 (d, J_{AB} = 19.0 Hz, 1H), 2.90 (d, J_{AB} = 19.0 Hz, 1H), 2.25 (s, 3H), 1.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.2, 161.0, 153.2,

149.6, 142.1, 139.6, 137.8, 125.5, 124.7, 124.2, 123.1, 120.8, 111.6, 108.5, 104.4, 79.6, 55.7, 52.5, 13.9. **HRMS (ESI)**: *m/z* calcd for $C_{19}H_{17}O_3$ $(M\text{-}OH)^+$: 293.1178. Found: 293.1152.

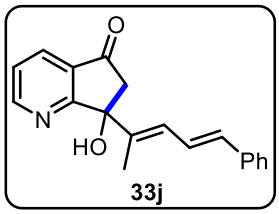
3-Hydroxy-5,6-dimethoxy-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33i).



33i

This compound was isolated as pale-yellow oil. Following the general procedure-4, 40 mg of **23i** afforded 36 mg of **33i** (90% yield). R_f = 0.3 (Hexane/EtOAc = 1/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3414, 2931, 1697, 1594, 1499, 1296, 1062, 735. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.42 (d, J = 7.5 Hz, 2H), 7.32 (t, J = 7.7 Hz, 2H), 7.26-7.23 (m, 1H), 7.16 (s, 1H), 7.02 (dd, J = 15.5 and 11.0 Hz, 1H), 6.86 (s, 1H), 6.62 (J = 15.5 Hz, 1H), 6.59 (d, J = 11.1 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.03 (d, J_{AB} = 18.8 Hz, 1H), 2.83 (d, J_{AB} = 18.8 Hz, 1H), 2.55 (s, 1H), 1.70 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.9, 156.1, 151.9, 151.0, 139.3, 137.4, 133.4, 129.6, 128.6 (2C), 127.6, 126.3 (2C), 124.5, 124.4, 105.1, 103, 56.5, 56.2, 52.3, 13.8. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{23}O_4$ $(M+H)^+$: 351.1596. Found: 277.1575.

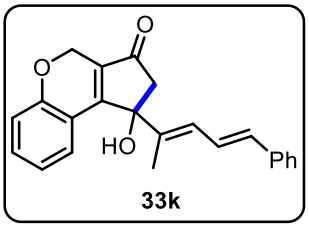
7-Hydroxy-7-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-5-one (33j).



33j

This compound was isolated as colourless oil. Following the general procedure-4, 30 mg of **23j** afforded 25.5 mg of **33j** (85% yield). R_f = 0.2 (Hexane/EtOAc = 1/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3416, 3031, 2927, 1722, 1584, 1422, 1280, 1067, 750. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.87 (dd, J = 8.8 and 1.6 Hz, 1H), 8.09 (dd, J = 7.8 and 2.4 Hz, 1H), 7.46 (dd, J = 7.8 and 4.8 Hz, 1H), 7.38-7.36 (m, 2H), 7.32-7.27 (m, 2H), 7.24-7.20 (m, 1H), 6.98 (dd, J = 15.2 and 11.0 Hz, 1H), 6.56 (d, J = 15.2 Hz, 1H), 6.41 (d, J = 11.0 Hz, 1H), 3.80 (s, 1H), 3.04 (s, 2H), 1.74 (d, J = 0.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.0, 174.4, 156.0, 138.6, 137.4, 133.8, 132.2, 130.0, 128.6 (2C), 127.6, 126.4 (2C), 125.5, 124.3, 124.2, 80.2, 51.2, 13.9. **HRMS (ESI)**: *m/z* calcd for $C_{19}H_{16}NO$ $(M\text{-}OH)^+$: 274.1232. Found: 274.1247.

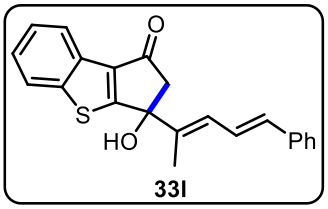
1-Hydroxy-1-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-1,2-dihydrocyclopenta[*c*]chromen-3(4*H*)-one (33k).



33k

This compound was isolated as pale-yellow oil. Following the general procedure-4, 30 mg of **23k** afforded 28.8 mg of **33k** (96% yield). R_f = 0.5 (Hexane/EtOAc = 3/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3419, 3034, 2925, 2859, 1697, 1633, 1483, 1397, 1345, 1041, 753. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.52 (d, J = 7.1 Hz, 1H), 7.43-7.41 (m, 2H), 7.33-7.20 (m, 2H), 7.01 (dd, J = 10.8 Hz, 1H), 6.63 (d, J = 15.4 Hz, 1H), 5.06 (d, J_{AB} = 14.8 Hz, 1H), 5.02 (d, J_{AB} = 14.8 Hz, 1H), 3.07 (s, 1H), 2.79 (d, J_{AB} = 18.6 Hz, 1H), 2.69 (d, J_{AB} = 18.6 Hz, 1H), 1.78 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 201.0, 162.1, 156.2, 137.6, 137.3, 133.6, 133.5, 131.5, 128.6, (2C), 127.7, 126.8, 126.4 (2C), 124.9, 124.4, 121.9, 117.8, 116.9, 80.4, 62.7, 52.1, 13.4. **HRMS (ESI)**: *m/z* calcd for $C_{23}H_{21}O_3$ $(M+H)^+$: 345.1491. Found: 345.1479.

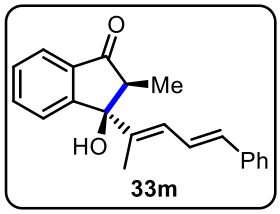
3-Hydroxy-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H* benzo[*b*]cyclopenta[*d*]-thiophen-1-one (33l).



33l

This compound was isolated white solid. Following the general procedure-4, 30 mg of **23l** afforded 26.5 mg of **33l** (88% yield). M.P =126-129 ^{o}C. R_f = 0.3 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3410, 3057, 2927, 1695, 1466, 1385, 966, 736. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.18-8.16 (m, 1H), 7.79-7.77 (m, 1H), 7.46-7.38 (m, 4H), 7.32-7.29 (m, 2H), 7.24-7.20 (m, 1H), 6.98 (dd, J = 15.7 and 10.7 Hz, 1H), 6.60 (d, J = 15.2 Hz, 1H), 6.59 (d, J = 10.6 Hz, 1H), 3.29 (d, J_{AB} = 18.3 Hz, 1H), 3.25 (s, 1H), 3.16 (d, J_{AB} = 18.3 Hz, 1H), 1.84 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.0, 175.8, 145.2, 140.5, 137.8, 137.3, 134.3, 130.7, 128.7 (2C), 127.8, 126.5 (2C), 126.4, 126.2, 125.3, 124.2, 123.9, 123.5, 79.1, 56.7, 13.6. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{18}OS$ $(M-OH)^+$: 329.1000. Found: 329.1017.

3-Hydroxy-2-methyl-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33m).

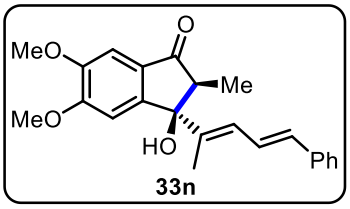


33m

This compound was isolated as white solid. Following the general procedure-4, 30 mg of **23m** afforded 24.3 mg of **33m** (81% yield). M.P = 153-155 ^{o}C. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3419, 2927, 2855, 1708, 1600, 1455, 1265, 752. **^{1}H**

NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.67 (dt, *J* = 7.5 and 1.2 Hz, 1H), 7.52-7.43 (m, 4H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 11.1 Hz, 1H), 6.66 (d, *J* = 15.6 Hz, 1H), 2.87 (q, *J* = 7.3 Hz, 2H), 1.98 (s, 1H), 1.76 (d, *J* = 0.8 Hz, 3H), 1.26 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 206.4, 155.8, 138.3, 137.5, 135.7, 135.3, 133.4, 129.7, 128.6 (2C), 127.6, 126.4 (2C), 125.6, 124.5, 123.7, 81.3, 52.1, 14.3, 9.0. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{19}O$ $(M\text{-}OH)^+$: 287.1436. Found: 287.1429.

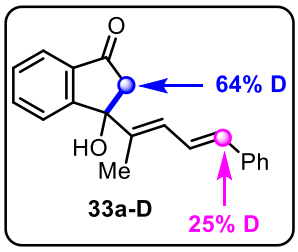
3-Hydroxy-5,6-dimethoxy-2-methyl-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33n).



33n

This compound was isolated as pale-yellow oil. Following the general procedure-4, 30 mg of **23n** afforded 25.0 mg of **33n** (83% yield). R_f = 0.3 (Hexane/EtOAc = 2/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3444, 2971, 2936, 1697, 1595, 1499, 1293, 1111, 749. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.44-7.40 (m, 2H), 7.34-7.29 (m, 2H), 7.18 (s, 1H), 7.00 (dd, *J* = 15.4 and 11.0 Hz, 1H), 6.92 (s, 1H), 6.63 (d, *J* = 11.1 Hz, 1H), 6.59 (d, *J* = 15.4 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 2.87 (q, *J* = 7.3 Hz, 2H), 1.68 (s, 1H), 1.47 (s, 3H), 1.17 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 203.0, 155.8, 150.7, 138.5, 137.4, 133.2, 129.0, 128.6 (2C), 127.6, 126.3 (2C), 126.0, 125.2, 124.6, 105.1, 103.3, 83.4, 57.4, 56.4, 56.2, 15.1, 9.9. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{23}O_3$ $(M\text{-}OH)^+$: 347.1647. Found: 347.1634.

3-Hydroxy-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-2,3-dihydro-1*H*-inden-1-one (33a-D). This compound was isolated as white solid. Following the general procedure-4, 50 mg of **23a** afforded 40.4 mg of **33a-D** (81% yield). M.P = 133-135 °C. R_f = 0.3 (Hexane/EtOAc = 3/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3420, 2926, 1710, 1600, 1459, 1285, 1047, 753. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.53-7.50 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.01 (dd, *J* = 15.5 and 11.0 Hz, 2H), 6.62 (d, *J* = 15.5 Hz, 1H), 6.56 (d, *J* = 11.0 Hz, 1H), 3.07 (d, J_{AB} = 19.2 Hz, 0.37H), 2.89 (d, J_{AB} = 19.2 Hz, 0.33H), 1.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 203.4-203.3 (m, C=O), 156.8 (d, *J* = 2.2 Hz), 139.1, 137.4, 136.4 (d, *J* = 1.3 Hz), 135.6, 133.6, 129.6, 128.6 (2C), 127.6, 126.4 (2C), 124.7, 124.5, 124.4, 123.4, 80.0 (t, *J* = 5.5 Hz), 52.0-51.5 (m, CD_2), 13.9. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{15}D_3O_2$ $(M)^+$: 293.1495. Found: 293.1488.



33a-D

General procedure-5: Synthesis of nitro-ynones 46a-r.

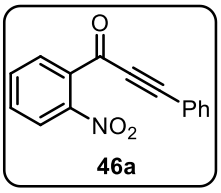
Step-1: To an oven-dried flask was added aldehydes **52b** (R^1 = *p*-tolyl; 1.0 eq, 4.16 mmol), CBr_4 (2.0 eq, 8.33 mmol) in DCM. The flask was cooled to 0 °C and then a solution of PPh_3 (4.0 eq, 16.64 mmol) in DCM was dropwise added at inert atmosphere. The reaction mixture was allowed to stir for 2 h under N_2 atmosphere. After completion, reaction was quenched with water and extracted with DCM (2 x 10 mL). The combined organic phase was washed with brine (2 x 10 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography with 10% ethyl acetate/hexane as an eluent to afford **53b** in 95% yield.

Step-2: The dibromo olefins **53b** (R^2 = *p*-tolyl; 1.0 eq, 3.66 mmol) were dissolved in THF (10 mL) in a flask under N_2 atmosphere. The solution was cooled to -78 °C and *n*-BuLi (1.6 M in hexane, 2.2 eq, 8.05 mmol) was added dropwise. The reaction mixture was stirred at the same temperature and then **54a** (R^1 = H; 1.0 eq, 3.66 mmol) in THF was dropwise added into it maintaining inert atmosphere. After 30 min, the mixture was warmed to room temperature. The reaction was monitored by TLC and quenched with water and extracted with EtOAc (2 x 10 mL). The combined organic phase was washed with brine (2 x 10 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture product was purified by silica gel column chromatography with 20% ethyl acetate/hexane as an eluent to afford **55b** in 87% yield.

Step-3: Alcohols **55b** (R^2 = *p*-tolyl, R^1 = H; 1 eq, 3.18 mmol) were dissolved in EtOAc (10 mL) in RB flask and IBX (1.2 eq, 3.82 mmol) was added to it. After that the reaction mixture was refluxed at 75 °C (using oil bath). The reaction was continued to stir at the same temperature until the full consumption of starting material (monitored by TLC). Upon completion, the reaction was filtered through celite pad and filtrate was extracted with EtOAc (2 x 10 mL). The combined organic phase was washed with brine (2 x 10 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture product was purified by silica gel column chromatography with 20% ethyl acetate/hexane as an eluent to afford **46b** in 74% yield.

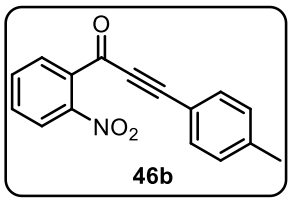
1-(2-Nitrophenyl)-3-phenylprop-2-yn-1one (46a).

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 144-146 °C. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2901, 2198, 1650, 1573, 1536, 1360, 1292, 1209, 961, 759. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.91-



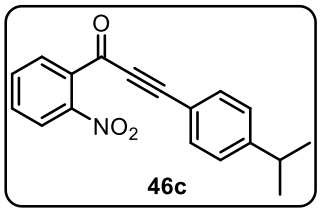
7.89 (m, 2H), 7.76-7.67 (m, 2H), 7.60-7.58 (m, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.41-7.37 (m, 2H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 175.7, 148.3, 133.8, 133.3 (2C), 133.0, 132.5, 131.3, 130.1, 128.7 (2C), 124.1, 119.3, 94.9, 86.7. **HRMS (ESI)**: m/z calcd for $C_{15}H_9NNaO_3$ $(M+Na)^+$: 274.0480, found: 274.0478.

1-(2-Nitrophenyl)-3-(*p*-tolyl)prop-2-yn-1-one (46b).



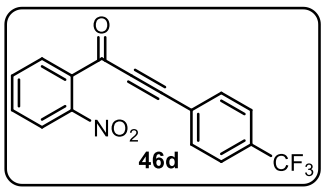
This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 68-70 ^{o}C. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3033. 2922, 2194, 1649, 1574, 1536, 1349, 1207, 1180, 961, 785. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 7.90 (d, *J* = 7.68 Hz, 2H), 7.75-7.66 (m, 2H), 7.48 (d, *J* = 8 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 2.38 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 175.7, 148.3, 142.2, 133.9, 133.4 (2C), 132.9, 132.4, 130.1, 129.5 (2C), 124.1, 116.2, 95.8, 86.7, 21.8. **HRMS (ESI)**: m/z calcd for $C_{16}H_{11}NNaO_3$ $(M+Na)^+$: 288.0637, found: 288.0635.

3-(4-Isopropylphenyl)-1(-2-nitrophenyl)prop-2-yn-1-one (46c).



This compound was prepared by following the general procedure-5 and isolated as pale-yellow liquid. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2962, 2929, 2191, 1650, 1574, 1537, 1349, 1183, 960, 785. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 7.92 (d, *J* = 7.52 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.75-7.66 (m, 2H), 7.51 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 8 Hz, 2H), 2.94-2.87 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 175.6, 153.0, 148.3, 133.6, (2C), 133.5, 133.0, 132.7, 130.2, 127.0 (2C), 124.0, 116.4, 95.8, 86.7, 34.3, 23.5 (2C). **HRMS (ESI)**: m/z calcd for $C_{18}H_{16}NO_3$ $(M+H)^+$: 294.1130, found: 294.1123.

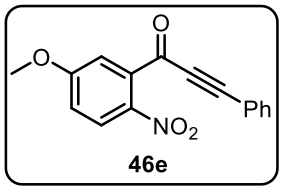
1-(2-Nitrophenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (46d).



This compound was prepared by following the general procedure-5 and isolated as pale-yellow liquid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2206, 1658, 1536, 1324, 1014, 846, 709. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 7.93 (dd, *J* = 7.4 and 1.3 Hz, 2H), 7.79 (dt, *J* = 7.3 and 1.4 Hz, 1H), 7.75 (dd, *J* = 7.7 and 1.6 Hz, 1H), 7.72-7.64 (m,

4H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 175.4, 148.2, 133.4 (2C), 133.28, 133.24, 133.0, 132.5 (d, J = 32.7, 1C), 130.1, 125.6 (q, J = 3.6 Hz, 1C), 124.2 (2C), 123.4 (q, J = 270.8 Hz, 1C), 123.1 (d, J = 0.9 Hz, 1C), 91.9, 87.6. **^{19}F NMR (376.5 MHz, CDCl$_3$)**: δ –63.19. **HRMS (ESI)**: m/z calcd for $C_{16}H_8F_3NNaO_3$ $(M+Na)^+$: 342.0354, found: 342.0336.

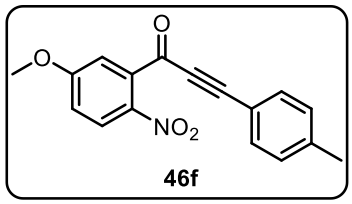
1-(5-Methoxy-2-nitrophenyl)-3-phenylprop-2-yn-1-one (46e).



46e

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 77-79 ^{o}C. R_f = 0.4 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2924, 2924, 2195, 1655, 1580, 1513, 1333, 1171, 996, 782. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 8.04 (d, J = 9.0 Hz, 1H), 7.55-7.53 (m, 2H), 7.47-7.44 (m, 1H), 7.38-7.35 (m, 2H), 7.12 (d, J = 2.7 Hz, 1H), 7.06 (dd, J = 9.0 Hz and 2.7 Hz, 1H), 3.93 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 176.5, 163.6, 140.1, 137.8, 133.2 (3C), 131.2, 128.7 (3C), 126.9, 119.3, 116.0, 114.2, 56.3. **HRMS (ESI)**: m/z calcd for $C_{16}H_{12}NO_4$ $(M+H)^+$: 282.0766, found: 282.0781.

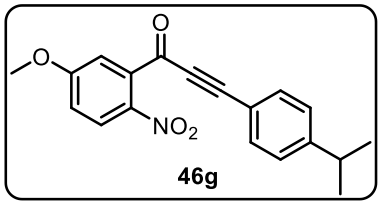
1-(5-Methoxy-2-nitrophenyl)-3-(*p*-tolyl)prop-2-yn-1-one (46f).



46f

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 83-85 ^{o}C. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2943, 2189, 1656, 1582, 1517, 1338, 1194, 1021, 760. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 8.04 (d, J = 9.0 Hz, 1H), 7.45 (d, J = 7.5 Hz, 2H), 7.17 (d, J = 7.7 Hz, 2H), 7.13-7.12 (m, 1H), 7.05 (d, J = 9.0 Hz, 1H), 3.94 (s, 3H), 2.37 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: δ 176.5, 163.6, 142.1, 140.2, 138.0, 133.3 (2C), 129.4 (2C), 126.8, 116.2, 116.1, 114.0, 95.5, 86.8, 56.3, 21.8. **HRMS (ESI)**: m/z calcd for $C_{17}H_{13}NNaO_4$ $(M+Na)^+$: 318.0742, found: 318.0738.

3-(4-Isopropylphenyl)-1-(5-methoxy-2-nitrophenyl)prop-2-yn-1-one (46g).

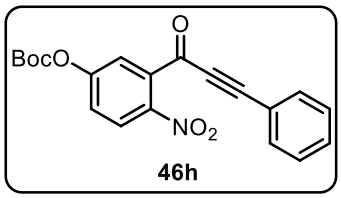


46g

This compound was prepared by following the general procedure-5 and isolated as pale-yellow semi-solid. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2962, 2189, 1654, 1582, 1516, 1296, 1172, 1100, 836. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ 8.04 (d, J = 9.0 Hz, 1H), 7.50-7.47 (m, 2H), 7.24-7.22 (m, 2H), 7.13 (d, J = 2.72 Hz, 1H), 7.05 (dd, J = 9.0 and 2.76 Hz, 1H), 3,94 (s, 3H), 2.92 (sept, J = 6.9 Hz, 1H), 1.24

(d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 176.5, 163.6, 152.8, 140.2, 138.0, 133.5 (2C), 126.9 (2C), 126.8, 116.6, 116.1, 114.0, 95.6, 86.7, 56.3, 34.3, 23.6 (2C). **HRMS (ESI)**: m/z calcd for $C_{19}H_{17}NNaO_4$ $(M+Na)^+$: 346.1055, found: 346.1050.

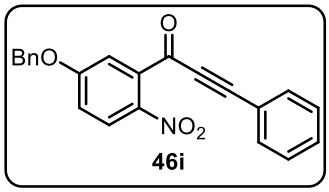
tert-Butyl (4-nitro-3-(3-phenylpropioloy)phenyl)carbonate (46h).



46h

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 83-85 °C. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2934, 2197, 1658, 1586, 1532, 1371, 1173, 1028, 759. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 8.00 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.52-7.47 (m, 2H), 7.41-7.37 (m, 2H), 1.58 (s, 9H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 174.7, 154.2, 150.2, 144.7, 136.0, 133.4, 131.4, 128.7 (2C), 125.9, 124.5, 122.5, 119.1 (2C), 95.4, 86.6, 85.3, 27.6 (3C). **HRMS (ESI)**: m/z calcd for $C_{20}H_{17}NO_6$ $(M+Na)^+$: 390.0954, found: 390.0947.

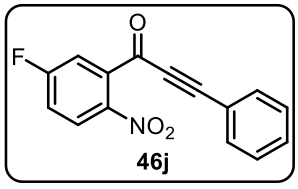
1-(5-(Benzyloxy)-2-nitrophenyl)-3-phenylprop-2-yn-1-one (46i).



46i

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 110-112 °C. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2926, 2197, 1657, 1580, 1518, 1336, 1175, 1012, 757. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 8.03 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.48-7.35 (m, 8H), 7.22 (s, 1H), 7.12 (dd, *J* = 8.9 and 7.5 Hz, 1H), 5.18 (s, 2H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 176.4, 162.6, 140.3, 137.8, 135.0, 133.3 (2C), 131.2, 128.9 (2C), 128.7, 128.6 (2C), 127.6 (2C), 126.9, 119.3, 116.8, 115.0, 94.7, 86.8, 71.0. **HRMS (ESI)**: m/z calcd for $C_{22}H_{15}NNaO_4$ $(M+Na)^+$: 380.0899, found: 380.0906.

1-(5-Fluoro-2-nitrophenyl)-3-phenylprop-2-yn-1-one (46j).

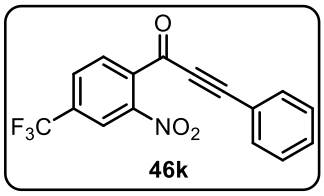


46j

This compound was prepared by following general procedure-5 and isolated as white semi-solid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3079, 2193, 1653, 1532, 1443, 1070, 758. **^{1}H NMR (400 MHz, CDCl$_3$)**: *δ* 8.02 (dd, *J* = 8.9 and 4.5 Hz, 1H), 7.58-7.56 (m, 2H), 7.50-7.46 (m, 2H), 7.41-7.32 (m, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)**: *δ* 174.4 (d, *J* = 1.21 Hz, 1C), 164.5 (d, *J* = 257.6 Hz, 1C), 143.8 (d, *J* = 2.42 Hz, 1C), 137.1(d, *J*

= 7.47 Hz, 1C), 133.3 (2C), 131.6, 128.8 (2C), 127.1 (d, *J* = 9.4 Hz, 1C), 119.1, 118.9 (d, *J* = 9.4 Hz, 1C), 116.9 (d, *J* = 25.1 Hz, 1C), 95.7, 86.4. **^{19}F NMR (376.5 MHz, $CDCl_3$)**: δ –101.74. **HRMS (ESI)**: m/z calcd for $C_{15}H_8FNNaO_3$ $(M+Na)^+$: 292.0386, found: 292.0364.

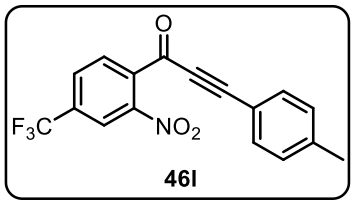
1-(2-Nitro-4-(trifluoromethyl)phenyl)-3-phenylprop-2-yn-1-one (46k).



46k

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 79-81 °C. R_f = 0.6 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2926, 2198, 1658, 1544, 1356, 1181, 1027, 996, 759. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.24 (s, 1H), 8.02-7.97 (m, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.52-7.49 (m, 1H), 7.43-7.39 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 174.5, 147.9, 137.2, 134.3 (d, *J* = 34.48 Hz, 1C), 133.4 (2C), 131.7, 130.6, 130.0 (q, *J* = 3.4 Hz, 1C), 128.8 (2C), 122.6 (q, *J* = 271.6 Hz, 1C), 121.4 (q, *J* = 3.78 Hz, 1C), 118.9, 96.4, 86.4. **^{19}F NMR (376.5 MHz, $CDCl_3$)**: δ –61.51. **HRMS (ESI)**: m/z calcd for $C_{16}H_9F_3NO_3$ $(M+H)^+$: 320.0535, found: 320.0536.

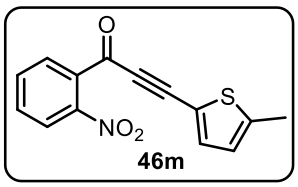
1-(2-Nitro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)prop-2-yn-1-one (46l).



46l

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 79-81 °C. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2925, 2194, 1656, 1545, 1355, 1181, 1013, 760. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.21 (s, 1H), 7.99 (s, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 2.39 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 174.5, 147.9, 142.7, 137.2, 134.7 (q, *J* = 34.2 Hz, 1C), 133.5 (2C), 130.6, 129.9 (q, *J* = 3.43 Hz, 1C), 129.6 (2C), 121.3 (q, *J* = 3.6 Hz, 1C), 122.3 (q, *J* = 271.7 Hz, 1C), 115.7, 97.3, 86.5, 21.8. **^{19}F NMR (376.5 MHz, $CDCl_3$)**: δ –63.10. **HRMS (ESI)**: m/z calcd for $C_{17}H_{11}F_3NO_3$ $(M+H)^+$: 334.0691, found: 334.0690.

3-(5-Methylthiophen-2-yl)-1-(2-nitrophenyl)prop-2-yn-1-one (46m).

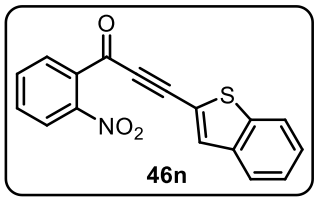


46m

This compound was prepared by following the general procedure-5 and isolated as pale-yellow semi-solid. R_f = 0.8 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2921, 2173, 1642, 1535, 1039. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.89-7.86 (m, 2H), 7.75-7.66 (m, 2H), 7.35 (d, *J* = 3.7 Hz, 1H), 6.75-6.74 (m, 1H), 2.51 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**:

δ 175.1, 148.8, 148.2, 138.5, 133.6, 132.9, 132.4, 130.0, 126.6, 124.1, 116.4, 91.7, 90.3, 15.7. **HRMS (ESI)**: m/z calcd for $C_{14}H_9NNaO_3S$ $(M+Na)^+$: 294.0201, found: 294.0201.

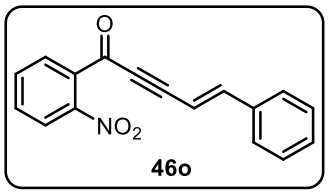
3-(Benzo[*b*]thiophen-2-yl)-1-(2-nitrophenyl)prop-2-yn-1-one (46n).



46n

This compound was prepared by following the general procedure-5 and isolated as pale yellow semi-solid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2958, 2180, 1646, 1532, 1310, 984, 750. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.93-7.88 (m, 2H), 7.82-7.67 (m, 5H), 7.47-7.38 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.1, 148.1, 142.0, 138.4, 134.9, 133.5, 133.1, 132.7, 130.1, 127.2, 125.3, 124.9, 124.2, 122.2, 118.8, 91.9, 88.6. **HRMS (ESI)**: m/z calcd for $C_{17}H_9NNaO_3S$ $(M+Na)^+$: 330.0201, found: 330.0175.

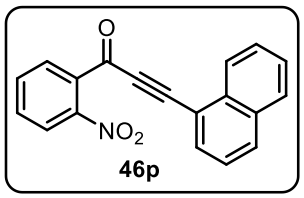
(*E*)-1-(2-Nitrophenyl)-5-phenylpent-4-en-2-yn-1-one (46o).



46o

This compound was prepared by following the general procedure-5 and isolated as pale-yellow liquid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2934, 2197, 1658, 1586, 1532, 1371, 1173, 1028, 759. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.88-7.85 (m, 2H), 7.74-7.64 (m, 2H), 7.43-7.41 (m, 2H), 7.37-7.35 (m, 3H), 7.27 (d, J = 16.0 Hz, 1H), 6.27 (d, J = 16.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.6, 149.3, 148.1, 134.8, 133.8, 133.0, 132.5, 130.5, 130.2, 129.0 (2C), 127.2 (2C), 124.1, 104.6, 95.0, 88.8. **HRMS (ESI)**: m/z calcd for $C_{17}H_{11}NNaO_3$ $(M+Na)^+$: 300.0637, found: 300.0650.

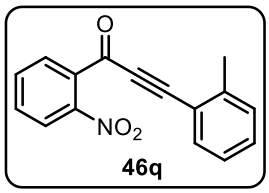
3-(Naphthalen-1-yl)-1-(2-nitrophenyl)prop-2-yn-1-one (46p).



46p

This compound was prepared by following the general procedure-5 and isolated as pale-yellow semi-solid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3062, 2353, 1698, 1530, 1443, 1082, 771. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.24 (d, J = 8.2 Hz, 1H), 7.99-7.95 (m, 3H), 7.89-7.85 (m, 2H), 7.77 (dt, J = 7.5 and 1.3 Hz, 1H), 7.72-7.68 (m, 1H), 7.63-7.60 (m, 1H), 7.58-7.54 (m, 1H), 7.50-7.46 (m, 1H) **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.7, 148.2, 134.2, 133.8, 133.5, 133.1, 133.0, 132.5, 132.1, 130.1, 128.6, 127.9, 127.0, 125.6, 125.2, 124.3, 116.8, 93.4, 91.5. **HRMS (ESI)**: m/z calcd for $C_{19}H_{11}NNaO_3$ $(M+Na)^+$: 324.0637, found: 324.0653.

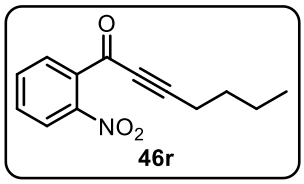
1-(2-Nitrophenyl)-3-(*o*-tolyl)prop-2-yn-1-one (46q).



46q

This compound was prepared by following the general procedure-5 and isolated as pale-yellow solid. M.P- 103-105 °C. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2923, 2190, 1641, 1573, 1532, 1349, 1163, 1011, 759. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.91 (t, *J* = 8.5 Hz, 2H), 7.77-7.66 (m, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.25-7.18 (m, 2H), 2.45 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.8, 148.1, 142.5, 134.2, 133.8, 133.0, 132.4, 131.3, 130.0, 129.9, 125.9, 124.2, 119.2, 94.1, 90.6, 20.6. **HRMS (ESI)**: m/z calcd for $C_{16}H_{11}NNaO_3$ $(M+Na)^+$: 288.0637, found: 288.0645.

1-(2-Nitrophenyl)hept-2-yn-1-one (46r).



46r

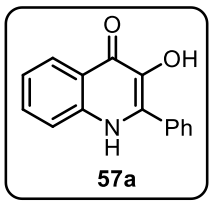
This compound was prepared by following the general procedure-5 and isolated as pale-yellow liquid. R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2960, 2214, 1655, 1533, 1351, 1260, 752. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.86 (d, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 7.4 Hz, 1H), 7.73-7.65 (m, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.59 (quint, *J* = 7.0 Hz, 2H), 1.43 (sext, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 176.0, 148.0, 134.0, 132.9, 132.3, 130.0, 124.0, 99.2, 79.7, 29.5, 21.9, 18.9, 13.4. **HRMS (ESI)**: m/z calcd for $C_{13}H_{13}NNaO_3$ $(M+Na)^+$: 254.0793, found: 254.0775.

General procedure-6: Synthesis of 3HQ 57a-o, 57q via intramolecular oxyamination reaction of 46a-o.

An oven-dried 5 mL glass vial was charged with **46** (1.0 eq). Toluene (1 mL) and triphenylphosphine (1.2 eq) were introduced. The reaction mixture was stirred at 100 °C (in heating block) until **46** disappeared (as detected by TLC). The reaction was quenched with water and extracted with EtOAc (2 x 2 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate as eluent (3:2), to afford **57** in 21-90% yield.

3-Hydroxy-2-phenylquinolin-4-(1*H*)-one (57a).

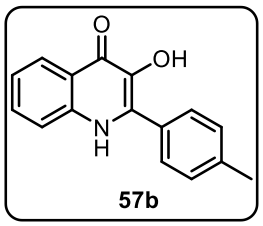
This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46a** afforded 17 mg of **57a** (77% yield). M.P- 273-275 °C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1650, 1262, 1048, 998, 765. **^{1}H NMR**



57a

(500 MHz, $CDCl_3$): δ 11.57 (s, 1H), 8.17-8.15 (m, 1H), 7.82-7.80 (m, 2H), 7.73-7.71 (m, 1H), 7.64-7.50 (m, 5H), 7.27 (t, *J* = 7.4 Hz, 1H). **^{13}C NMR (125 MHz, DMSO-*d*^{6})**: δ 170.4, 138.5, 138.2, 132.8, 131.9, 131.0, 129.7 (2C), 129.7, 128.7 (2C), 124.9, 122.3, 122.2, 118.9. **HRMS (ESI)**: m/z calcd for $C_{15}H_{12}NO_2$ $(M+H)^+$: 238.0868, found: 238.0857.

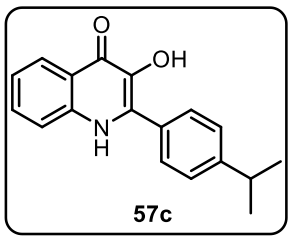
3-Hydroxy-2-(*p*-tolyl)quinolin-4-(1*H*)-one (57b).



57b

This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46b** afforded 18 mg of **57b** (78% yield). M.P- 270-272 ^{o}C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1657, 1050, 1026, 825, 764. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.51 (s, 1H), 8.14 (d, *J* = 8.1 Hz, 1H) 7.73-7.70 (m, 3H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 2.40 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.3, 139.3, 138.4, 138.2, 131.9, 130.9, 129.9, 129.5 (2C), 129.2 (2C), 124.8, 122.2, 122.1, 118.8, 21.4. **HRMS (ESI)**: m/z calcd for $C_{16}H_{14}NO_2$ $(M+H)^+$: 252.1025, found: 252.1013.

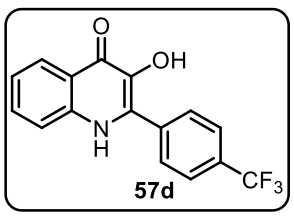
3-Hydroxy-2-(4-isopropylphenyl)quinolin-4(1*H*)-one (57c).



57c

This compound was prepared by following general procedure-6 and isolated as yellow solid. 25 mg of **46c** afforded 19 mg of **57c** (79% yield). M.P- 243-245 ^{o}C. R_f = 0.5 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1660, 1050, 1026, 825, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.55 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.72-7.69 (m, 3H), 7.59-7.56 (m, 1H), 7.42 (d, *J* = 7.9 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 3.00-2.93 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.3, 150.2, 138.4, 138.1, 132.1, 130.9, 130.3, 129.7 (2C), 126.7 (2C), 124.9, 122.29, 122.26, 118.8, 33.8, 24.2 (2C). **HRMS (ESI)**: m/z calcd for $C_{18}H_{18}NO_2$ $(M+H)^+$: 280.1338, found: 280.1345.

3-Hydroxy-2-(4-(trifluoromethyl)phenyl)quinolin-4(1*H*)-one (57d).

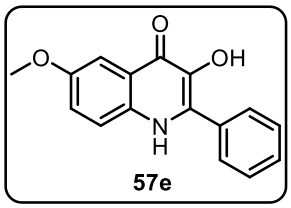


57d

This compound was prepared by following the general procedure-6 and isolated as white solid. 25 mg of **46d** afforded 14 mg of **57d** (58% yield). M.P- 318-320 ^{o}C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3461, 1660, 1024, 822, 756. **^{1}H NMR (400**

MHz, DMSO-*d*^{6}): δ 11.66 (s, 1H), 8.15 (d, J = 9.1 Hz, 1H), 8.02-8.00 (m, 2H), 7.94-7.92 (m, 2H), 7.70-7.68 (m, 1H), 7.62-7.58 (m, 1H), 7.29-7.25 (m, 1H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.7, 138.6 (d, J = 6.0 Hz, 1C), 136.8, 131.3, 130.6 (4C), 130.2, 129.8, 129.5, 125.6 (q, J = 3.1 Hz, 1C), 124.9, 124.2 (d, J = 270.6 Hz, 1C), 122.4 (d, J = 9.2 Hz, 1C), 118.9. **^{19}F NMR (376.5 MHz, DMSO-*d*^{6})**: δ –61.16. **HRMS (ESI)**: m/z calcd for $C_{16}H_{11}F_3NO_2$ $(M+H)^+$: 306.0742, found: 306.0768.

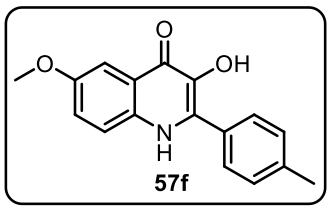
3-Hydroxy-6-methoxy-2-phenylquinolin-4(1*H*)-one (57e).



57e

This compound was prepared by following the general procedure-6 and isolated as white solid. 25 mg of **46e** afforded 19 mg of **57e** (80% yield). M.P- 282-284 ^{o}C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3401, 2990, 1649, 1555, 1484, 1184, 1071, 995, 753. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.60 (s, 1H), 7.81-7.79 (m, 2H), 7.68 (d, J = 9.1 Hz, 1H), 7.58-7.48 (m, 5H), 7.26 (dd, J = 9.16 Hz and 2.92 Hz, 1H), 3.85 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.4, 155.1, 137.7, 133.5, 132.8, 131.3, 129.66 (2C), 129.66, 128.7 (2C), 123.0, 122.5, 120.7, 103.0, 55.7. **HRMS (ESI)**: m/z calcd for $C_{16}H_{14}NO_3$ $(M+H)^+$: 268.0974, found: 268.0977.

3-Hydroxy-6-methoxy-2-(*p*-tolyl)quinolin-4(1*H*)-one (57f).

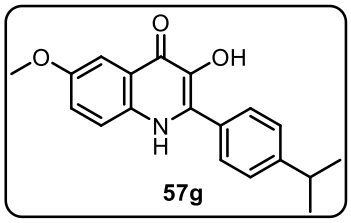


57f

This compound was prepared by following the general procedure-6 and isolated as white semi-solid. 25 mg of **46f** afforded 18 mg of **57f** (75% yield). R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3410, 2255, 1660, 1023, 998, 824, 761. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.52 (s, 1H), 7.71-7.66 (m, 3H), 7.48 (d, J = 2.84 Hz, 1H), 7.37 (d, J = 8.1 Hz, 2H), 7.25 (dd, J = 9.1 and 2.8 Hz, 1H), 3.85 (s, 3H), 2.40 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.3, 155.0, 139.2, 137.7, 133.5, 131.3, 129.9, 129.5 (2C), 129.2 (2C), 122.9, 122.4, 120.7, 103.0, 55.7, 21.4. **HRMS (ESI)**: m/z calcd for $C_{17}H_{16}NO_3$ $(M+H)^+$: 282.1130, found: 282.1140.

3-Hydroxy-2-(4-isopropylphenyl)-6-methoxyquinolin-4(1*H*)-one (57g).

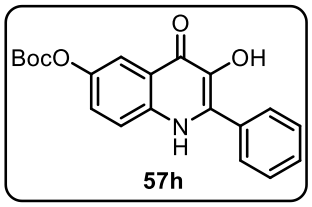
This compound was prepared by following the general procedure-6 and isolated as white solid. 25 mg of **46g** afforded 19 mg of **57g** (78% yield). M.P- 268-270 ^{o}C. R_f = 0.4 (EtOAc/ Hexane



57g

= 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3448, 2921, 1614, 1569, 1481, 1171, 1026, 764. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.56 (s, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.51 (d, J = 2.7 Hz, 1H), 7.41 (d, J = 8.1 Hz, 2H), 7.25 (dd, J = 9.0 and 2.7 Hz, 1H), 3.85 (s, 3H), 2.96 (sept, J = 6.8 Hz, 1H), 1.24 (d, J = 6.8 Hz, 6H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.4, 155.0, 150.1, 137.7, 133.4, 131.6, 130.4, 129.6 (2C), 126.6 (2C), 123.0, 122.4, 120.7, 103.0, 55.7, 33.8, 24.2 (2C). **HRMS (ESI)**: m/z calcd for $C_{19}H_{20}NO_3$ $(M+H)^+$: 310.1443, found: 310.1442.

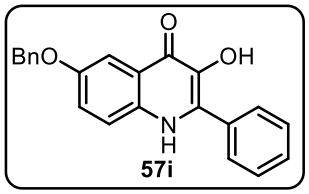
tert-Butyl (3-hydroxy-4-oxo-2-phenyl-1,4-dihydroquinolin-6-yl) carbonate (57h).



57h

This compound was prepared by following the general procedure-6 and isolated as white solid. 25 mg of **46h** afforded 22 mg of **57h** (90% yield). M.P- 270-272 ^{o}C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1660, 1050, 1005, 764. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.73 (s, 1H), 7.85 (d, J = 4.8 Hz, 1H), 7.81-7.79 (m, 2H), 7.76 (d, J = 9.1 Hz, 1H), 7.59-7.50 (m, 3H), 7.45 (dd, J = 9.0 and 2.7 Hz, 1H), 1.51 (s, 9H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.9, 151.9, 145.8, 138.1, 136.2, 132.6, 132.4, 129.8, 129.7 (2C), 128.7 (2C), 125.6, 122.6, 120.6, 115.7, 83.8, 27.7 (3C). **HRMS (ESI)**: m/z calcd for $C_{20}H_{20}NO_5$ $(M+H)^+$: 354.1341, found: 354.1363.

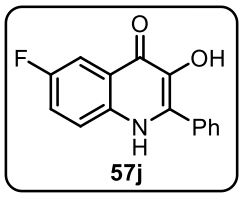
6-(Benzyloxy)-3-hydroxy-2-phenylquinolin-4(1*H*)-one (57i).



57i

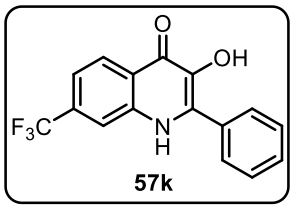
This compound was prepared by following the general procedure-6 and isolated as white solid. 25 mg of **46i** afforded 18 mg of **57i** (75% yield). M.P- 302-304 ^{o}C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3410, 1659, 1023, 1005, 761. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.60 (s, 1H), 7.79 (d, J = 7.7 Hz, 2H), 7.70 (d, J = 9.1 Hz, 1H), 7.62-7.57 (m, 3H), 7.52-7.50 (m, 3H), 7.41 (t, J = 7.0 Hz, 3H), 7.36-7.33 (m, 2H), 5.21 (s, 2H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.4, 154.1, 137.7, 137.4, 133.6, 132.8, 131.4, 129.6 (2C), 128.9, 128.8 (2C), 128.7 (2C), 128.3, 128.2 (2C), 123.0, 122.9, 120.8, 104.5, 69.9. **HRMS (ESI)**: m/z calcd for $C_{22}H_{18}NO_3$ $(M+H)^+$: 344.1287, found: 344.1296.

6-Fluoro-3-hydroxy-2-phenylquinolin-4(1*H*)-one (57j).



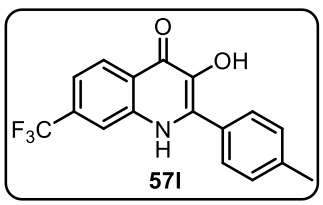
This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46j** afforded 17 mg of **57j** (73% yield). M.P- 233-235 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3418, 1659, 1050, 1004, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.74 (s, 1H), 7.80-7.78 (m, 4H), 7.63-7.50 (m, 5H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.6 (d, *J* = 2.9 Hz, 1C), 157.9 (d, *J* = 239.1 Hz, 1C), 138.0, 135.2, 133.9 (d, *J* = 9.3 Hz, 1C), 132.6 (d, *J* = 8.6 Hz, 1C), 129.7 (2C), 129.4 (d, *J* = 12.16 Hz, 1C), 128.7 (2C), 123.0 (d, *J* = 7.2 Hz, 1C), 121.7 (d, *J* = 8.1 Hz, 1C), 120.3 (d, *J* = 25.9 Hz, 1C), 108.2 (d, *J* = 21.8 Hz, 1C). **^{19}F NMR (376.5 MHz, DMSO-*d*^{6})**: δ –119.40. **HRMS (ESI)**: m/z calcd for $C_{15}H_{11}FNO_2$ $(M+H)^+$: 256.0774, found: 256.0784.

3-Hydroxy-2-phenyl-7-(trifluoromethyl)quinolin-4(1*H*)-one (57k).



This compound was prepared by following general procedure-6 and isolated as yellow semi-solid. 25 mg of **46k** afforded 17.2 mg of **57k** (72% yield). R_f = 0.6 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3418, 1660, 1051, 1026, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.91 (s, 1H), 8.35 (d, *J* = 8.5 Hz, 1H), 8.12 (s, 1H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.61-7.51 (m, 4H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.0, 139.5, 137.4, 133.1, 132.4, 130.8 (q, *J* = 31.6 Hz, 1C), 130.0, 129.6 (2C), 128.8 (2C), 126.9, 124.4 (q, *J* = 271.0 Hz, 1C), 124.1, 117.6 (q, *J* = 2.74 Hz, 1C), 116.7 (q, *J* = 2.27 Hz, 1C). **^{19}F NMR (376.5 MHz, DMSO-*d*^{6})**: δ –61.51. **HRMS (ESI)**: m/z calcd for $C_{16}H_{11}F_3NO_2$ $(M+H)^+$: 306.0742, found: 306.0748.

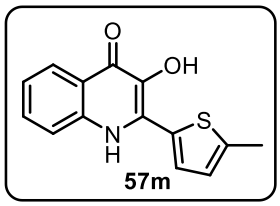
3-Hydroxy-2-(*p*-tolyl)-7-(trifluoromethyl)quinolin-4(1*H*)-one (57l).



This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46l** afforded 18 mg of **57l** (74% yield). M.P- 257-259 °C. R_f = 0.6 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1658, 1050, 1170, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.83 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 8.14 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 2H), 2.41 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 169.8, 139.7, 139.5, 137.4, 131.1, 130.6 (q, *J* = 31.6 Hz, 1C), 129.54 (2C), 129.51, 129.4 (2C), 126.9, 124.2 (q, *J* = 270.9Hz, 1C), 124.0, 117.5(q, *J* = 2.72 Hz, 1C), 116.7

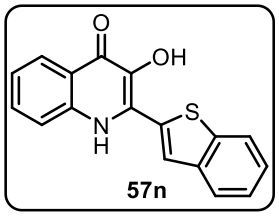
(q, *J* = 4.2Hz, 1C), 21.4. **^{19}F NMR (376.5 MHz, $CDCl_3$)**: δ –61.52. **HRMS (ESI)**: m/z calcd for $C_{17}H_{13}F_3NO_2$ $(M+H)^+$: 320.0898, found: 320.0922.

3-Hydroxy-2-(5-methylthiophen-2-yl)quinolin-4(1*H*)-one (57m).



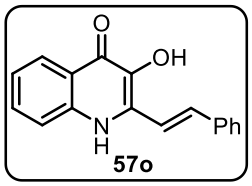
This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46m** afforded 15.1 mg of **57m** (64% yield). M.P- 247-249 °C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1659, 1050, 1026, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.17 (s, 1H), 8.10 (d, *J* = 7.4 Hz, 1H), 7.84 (d, *J* = 3.7 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.61-7.57 (m, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 2.53 (s, 3H) **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.2, 144.4, 138.5, 137.0, 131.2, 130.7, 129.1, 127.8, 126.7, 125.7, 124.8, 122.1, 118.5, 15.2. **HRMS (ESI)**: m/z calcd for $C_{14}H_{12}NO_2S$ $(M+H)^+$: 258.0589, found: 258.0586.

2-(Benzo[*b*]thiophen-2-yl)-3-hydroxyquinolin-4(1*H*)-one (57n).



This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46n** afforded 17 mg of **57n** (71% yield). M.P- 282-284 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3439, 1660, 1023, 1003, 759. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.42 (s, 1H), 8.32 (s, 1H), 8.14 (d, *J* = 9.0 Hz, 1H), 8.08-8.06 (m, 1H), 8.01-7.99 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.47-7.45 (m, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.66-7.62 (m, 1H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.7, 141.3, 138.8, 138.7, 138.5, 134.0, 131.6, 125.9, 125.8, 125.2, 124.9, 124.4, 124.2, 122.7, 122.3, 122.2, 118.7. **HRMS (ESI)**: m/z calcd for $C_{17}H_{12}NO_2S$ $(M+H)^+$: 294.0589, found: 294.0599.

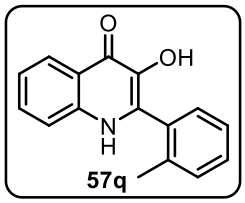
(*E*)-3-Hydroxy-2-styrylquinolin-4-(1*H*)-one (57o).



This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46o** afforded 13 mg of **57o** (53% yield). M.P- 282-284 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1659, 1052, 764. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.29 (s, 1H), 8.11 (dd, *J* = 8.1 and 7.1 Hz, 1H), 7.68 (t, *J* = 8.4 Hz, 1H), 7.66-7.59 (m, 4H), 7.57-7.54 (m, 1H), 7.47-7.37 (m, 4H), 7.23 (t, *J* = 7.6 Hz, 1H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.2, 139.4, 138.4, 136.6, 133.5, 132.0, 131.3, 129.5 (2C), 129.3 (2C), 127.3 (2C),

124.9, 122.3, 122.0, 118.4. **HRMS (ESI)**: m/z calcd for $C_{17}H_{14}NO_2$ $(M+H)^+$: 264.1025, found: 264.1037.

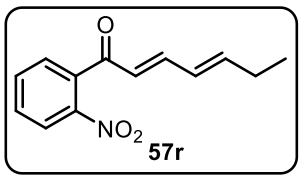
3-Hydroxy-2-(*o*-tolyl)quinolin-4(1*H*)-one (57q).



57q

This compound was prepared by following the general procedure-6 and isolated as yellow solid. 25 mg of **46q** afforded 5 mg of **57q** (21% yield). M.P- 239-241 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 1658, 1650, 1050, 763. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.66 (s, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.60-7.57 (m, 2H), 7.43-7.33 (m, 4H), 7.28-7.25 (m, 1H), 2.22 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 170.1, 138.4, 138.2, 137.2, 132.87, 132.80, 130.8, 130.4, 130.2, 129.7, 126.1, 124.9, 122.6, 122.2, 118.6, 19.6. **HRMS (ESI)**: m/z calcd for $C_{16}H_{14}NO_2$ $(M+H)^+$: 252.1025, found: 252.1028.

(2*E*,4*E*)-1-(2-Nitrophenyl)hepta-2,4-dien-1-one (57r).



57r

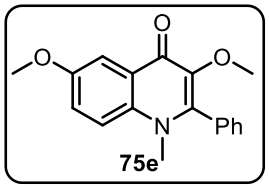
This compound was prepared by following the general procedure-6 and isolated as pale-yellow liquid. 20 mg of **46r** afforded 15 mg of **57r** (75% yield). R_f = 0.7 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2969, 1659, 1631, 1529, 1294, 1001, 789. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.14 (dd, *J* = 8.2 and 0.8 Hz, 1H), 7.29 (dt, *J* = 7.4 and 1.1 Hz, 1H), 7.64-7.60 (m, 1H), 7.44 (dd, *J* = 7.5 and 1.3 Hz, 1H), 6.82 (dd, *J* = 10.2 and 5.3 Hz, 1H), 6.36 (d, *J* = 15.6 Hz, 1H), 6.28-6.12 (m, 2H), 2.19 (quint, *J* = 6.9 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 193.3, 148.8, 147.1, 146.7, 136.4, 133.9, 130.3, 128.7, 127.78, 127.75, 124.4, 26.2, 12.7. **HRMS (ESI)**: m/z calcd for $C_{13}H_{13}NNaO_3$ $(M+Na)^+$: 254.0793, found: 254.0778.

General procedure-7: Synthesis of japonine and its analogs 75e-g.

In an oven-dried RB flask was charged with NaH (60% oil suspension, 2.5 eq, 0.27 mmol) in dry THF (5 mL) and placed at 0 °C under N_2 atmosphere. Compound **57** (1.0 eq, 0.11 mmol) was added dropwise in THF into it. The reaction was allowed to stir at the same temperature for 30 minutes. After 30 minutes, MeI (5.0 eq, 0.55 mmol) was added to the reaction mixture at same temperature, and stirring was continued for the next 6 h. After complete consumption of starting material (monitored by TLC), the reaction was quenched with water and extracted with EtOAc (2 x 5 mL). The combined organic phase was washed

with brine (2 x 5 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture product was purified by silica gel column chromatography with 40% ethyl acetate/hexane as an eluent to afford **75** in 90% yield.

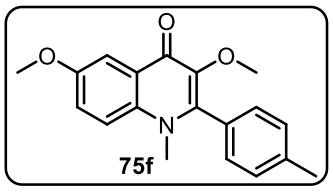
3,6-Dimethoxy-1-methyl-2-phenylquinolin-4(1*H*)-one (75e).



75e

This compound was prepared by following the general procedure-7 and isolated as white solid. 25 mg of **57e** afforded 25 mg of **75e** (90% yield). M.P- 144-146 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2926, 1623, 1543, 1376, 1167, 1051, 741. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.97 (d, *J* = 3.0 Hz, 1H), 7.55-7.51 (m, 4H), 7.39-3.33 (m, 3H), 3.97 (s, 3H), 3.64 (s, 3H), 3.56 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 171.6, 156.0, 147.0, 140.3, 134.8, 132.8, 129.4, 129.0 (2C), 128.8 (2C), 128.0, 123.3, 117.6, 105.2, 60.0, 55.8, 37.5. **HRMS (ESI)**: m/z calcd for $C_{18}H_{18}NO_3$ $(M+H)^+$: 296.1287, found: 296.1287.

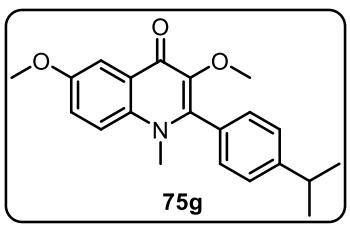
3,6-Dimethoxy-1-methyl-2-(*p*-tolyl)quinolin-4(1*H*)-one (75f).



75f

This compound was prepared by following the general procedure-7 and isolated as pale-yellow solid. 25 mg of **57f** afforded 23 mg of **75f** (85% yield). M.P- 163-165 °C. R_f = 0.5 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2958, 2839, 1592, 1499, 1307, 1052, 759. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.96 (d, *J* = 3.0 Hz, 1H), 7.47 (d, *J* = 9.3 Hz, 1H), 7.35-7.33 (m, 3H), 7.26-7.24 (m, 2H), 3.96 (s, 3H), 3.65 (s, 3H), 3.52 (s, 3H), 2.46 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 172.0, 155.7, 146.8, 140.5, 139.3, 134.9, 129.5, 129.4 (2C), 128.9 (2C), 128.2, 122.9, 117.4, 105.3, 59.9, 55.8, 37.2, 21.4. **HRMS (ESI)**: m/z calcd for $C_{19}H_{19}NNaO_3$ $(M+Na)^+$: 332.1263, found: 332.1293.

2-(4-Isopropylphenyl)-3,6-dimethoxy-1-methylquinolin-4(1*H*)-one (75g).



75g

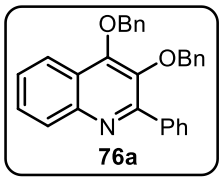
This compound was prepared by following the general procedure-7 and isolated as white solid. 23 mg of **57g** afforded 21 mg of **75g** (84% yield). M.P- 148-151 °C. R_f = 0.6 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2960, 1592, 1498, 1054, 792. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.96 (d, *J* = 3.0 Hz, 1H), 7.47 (d, *J* = 9.3 Hz, 1H), 7.39-7.37 (m, 2H), 7.32-7.26 (m, 3H), 3.96 (s, 3H), 3.67 (s, 3H), 3.51 (s, 3H), 3.00 (sept, *J* = 6.9 Hz, 1H), 1.32 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz,**

$CDCl_3$): δ 172.1, 155.7, 150.6, 146.8, 140.5, 134.9, 129.8, 128.9 (2C), 128.3, 126.8, 122.8, 117.5, 105.2, 59.9, 55.8, 37.2, 34.0 (2C), 23.9 (2C). **HRMS (ESI)**: m/z calcd for $C_{21}H_{24}NO_3$ $(M+H)^+$: 338.1756, found: 338.1786.

General procedure-8: One step elaboration to synthesize 3,4-Dialkoxyquinolines 76a, 76b, 76e, 76g.

In an oven-dried 25 mL RB flask was charged with compound **57** (1.0 eq, 0.12 mmol) in anhydrous DMF (5 mL) at room temperature and K_2CO_3 (5.0 eq, 0.63 mmol) was added under the nitrogen atmosphere. The reaction was allowed to stir for 5 min. After 5 min, benzyl bromide (4.0 eq, 0.48 mmol) was added. Then the reaction mixture was heated at 100 ^oC (using oil bath) for 5 h. After full consumption of the starting material the reaction was quenched with water and extracted with EtOAc (2 x 5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography with 20% ethyl acetate/hexane as an eluent to afford **76** in 71% yield.

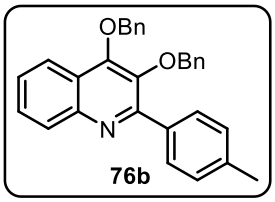
3,4-Bis(benzyloxy)-2-phenylquinoline (76a).



76a

This compound was prepared by following the general procedure-8 and isolated as pale-yellow liquid. 20 mg of **57a** afforded 25 mg of **76a** (71% yield). R_f = 0.7 (EtOAc/ Hexane = 1/9). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3062, 2926, 1359, 1078, 769. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.14 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.66-7.62 (m, 1H), 7.97-7.95 (m, 2H), 7.51-7.46 (m, 5H), 7.41-7.35 (m, 4H), 7.28-7.24 (m, 3H), 7.12-7.10 (m, 2H), 5.47 (s, 2H), 4.77 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 157.0, 153.8, 146.2, 141.4, 138.0, 136.8, 136.2, 129.7 (2C), 129.2, 128.9, 128.8, 128.7 (2C), 128.6 (2C), 128.46, 128.42 (2C), 128.40 (2C), 128.3, 128.2 (2C), 126.1, 124.4, 121.9, 75.8, 75.6. **HRMS (ESI)**: m/z calcd for $C_{29}H_{24}NO_2$ $(M+H)^+$: 418.1807, found: 418.1807.

3,4-Bis(benzyloxy)-2-(*p*-tolyl)quinoline (76b).

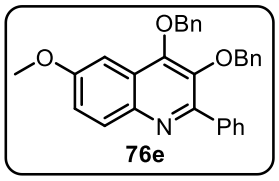


76b

This compound was prepared by following the general procedure-8 and isolated as white solid. 20 mg of **57b** afforded 25 mg of **76b** (73% yield). M.P- 108-110 ^oC. R_f = 0.7 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3063, 2919, 1585, 1454, 1358, 1139, 1079, 765. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.10 (dd, J = 15.2 and 7.68 Hz, 2H), 7.90 (d, J = 8.0 Hz, 2H),

7.65-7.61 (m, 1H), 7.48-7.44 (m, 3H), 7.40-7.34 (m, 3H), 7.31-7.27 (m, 5H), 7.18-7.15 (m, 2H), 5.45 (s, 2H), 4.77 (s, 2H), 2.44 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 156.9, 153.7, 146.2, 141.5, 138.8, 136.9, 136.3, 135.2, 129.6 (2C), 129.2, 128.9 (2C), 128.7, 128.68 (2C), 128.62 (2C), 128.4 (5C), 128.2, 125.9, 124.3, 121.9, 75.7, 75.6, 21.4. **HRMS (ESI)**: m/z calcd for $C_{30}H_{26}NO_2$ $(M+H)^+$: 432.1964, found: 432.1965.

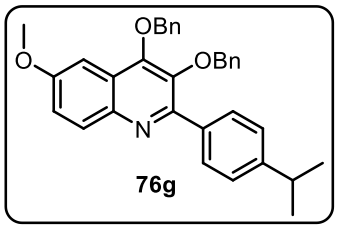
3,4-Bis(benzyloxy)-6-methoxy-2-phenylquinoline (76e).



76e

This compound was prepared by following the general procedure-8 and isolated as white solid. 20 mg of **57e** afforded 23 mg of **76e** (70% yield) M.P- 82-84 ^oC. R_f = 0.7 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3062, 2928, 1586, 1469, 1430, 1359, 1169, 1079, 768. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.99-7.93 (m, 3H), 7.48-7.44 (m, 5H), 7.38- 7.36 (m, 3H), 7.31-7.25 (m, 5H), 7.15-7.13 (m, 2H), 5.43 (s, 2H), 4.79 (s, 2H), 3.86 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 157.8, 154.1, 153.0, 142.3, 142.2, 138.1, 136.9, 136.3, 130.8, 129.6 (2C), 128.69 (2C), 128.64 (3C), 128.5 (2C), 128.4, 128.3 (2C), 128.2, 128.1 (2C), 125.4, 121.4, 99.5, 75.79, 75.75, 55.4. **HRMS (ESI)**: m/z calcd for $C_{30}H_{26}NO_3$ $(M+H)^+$: 448.1913, found: 448.1912.

3,4-Bis(benzyloxy)-2-(4-isopropylphenyl)-6-methoxyquinoline (76g).



76g

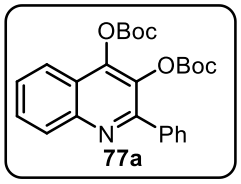
This compound was prepared by following the general procedure-8 and isolated as pale-yellow liquid. 20 mg of **57g** afforded 24 mg of **76g** (75% yield). R_f = 0.7 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3031, 2959, 1585, 1468, 1430, 1360, 1169, 1079, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.96 (d, J = 9.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.48-7.46 (m, 2H), 7.38-7.25 (m, 10), 7.13-7.11 (m, 2H), 5.43 (s, 2H), 4.80 (s, 2H), 3.85 (s, 3H), 2.99 (sept, J = 6.8 Hz, 1H), 1.32 (d, J = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 157.6, 154.3, 152.8, 149.5, 142.3, 142.2, 137.0, 136.4, 135.6, 130.8, 129.5 (2C), 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.4, 128.3 (2C), 128.2, 126.2 (2C), 125.3, 121.3, 99.6, 75.7 (2C), 55.4, 34.1, 24.1 (2C). **HRMS (ESI)**: m/z calcd for $C_{33}H_{32}NO_3$ $(M+H)^+$: 490.2382, found: 490.2361.

General procedure-9: One-pot synthesis of 77a.

An oven-dried 5 mL glass vial was charged with **57a** (1.0 eq, 0.1 mmol). Toluene (1 mL) and triphenylphosphine (1.2 eq, 0.12 mmol) were introduced. The reaction mixture was

stirred at 100 °C (in heating block) until **57a** disappeared (as detected by TLC). After 20 min, NaH (60% oil suspension, 1.5 eq, 0.15 mmol) was added into it. After 5 min, Boc_2O (1.2 eq, 0.12 mmol) was added. It was stirred for 3 h at 100 °C (in heating block). The reaction was quenched with water and extracted with EtOAc. The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate as eluent (3:2), to afford **77a** in 58% yield.

Di-*tert*-butyl (2-phenylquinoline-3,4-diyl) bis(carbonate) (77a).



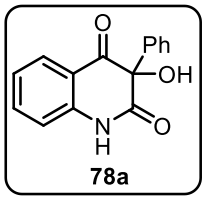
77a

This compound was prepared by following the general procedure-9 and isolated as white semi-solid. 20 mg of **57a** afforded 20 mg of **77a** (58% yield). R_f = 0.7 (EtOAc/ Hexane = 9/1). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2981, 1774, 1254, 1141, 1132, 1054, 768. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.17 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 9.1 Hz, 1H), 7.88-7.85 (m, 2H), 7.75-7.71 (m, 1H), 7.61-7.57 (m, 1H), 7.50-7.44 (m 3H), 1.59 (s, 9H), 1.29 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 155.1, 149.5, 149.3, 147.0, 145.3, 137.1, 134.6, 129.8, 129.6, 129.1, 128.9 (2C), 128.5 (2C), 127.2, 122.6, 121.3, 85.0, 84.3, 27.6 (3C), 27.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{25}H_{28}NO_6$ $(M+H)^+$: 438.1917, found: 438.1912.

General procedure-10: synthesis of 3-Hydroxy-3-arylquinoline-2,4-dione 78a-c.

An oven dried RB flask was charged with **57** (1 eq, 0.08 mmol) at room temperature and dissolved in DCM. Activated MnO_2 (4.0 eq, 0.32 mmol) was then added to the reaction mixture and stirred for 15 h. After complete consumption of the starting material (monitored by TLC), reaction was quenched with water and extracted with DCM. The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate as eluent (3:2), to afford **78** in 60% yield.

2-Hydroxy-2-phenyl-1,2-dihydroquinoline-3,4-dione (78a).

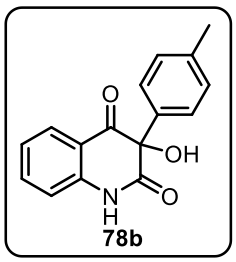


78a

This compound was prepared by following the general procedure-10 and isolated as white solid. 40 mg of **57a** afforded 26 mg of **78a** (60% yield). M.P- 218-220 °C. R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3417, 2522, 1659, 1050, 1026, 763. **^{1}H NMR (400 MHz, DMSO-d^6)**: δ 11.10 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.37-7.30 (m, 5H), 7.13-7.07 (m, 2H), 6.39 (s, 1H). **^{13}C NMR (100 MHz, DMSO-d^6)**: δ 194.6, 172.0, 141.8, 138.8,

136.8, 129.1 (2C), 129.0, 127.6, 125.8 (2C), 123.3, 119.4, 116.8, 82.9. **HRMS (ESI)**: m/z calcd for $C_{15}H_{11}NNaO_3$ $(M+Na)^+$: 276.0637, found: 276.0632.

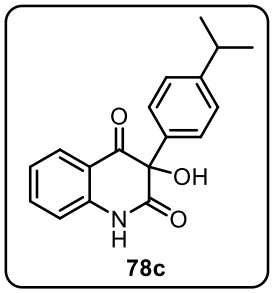
3-Hydroxy-3-(*p*-tolyl)quinoline-2,4(1*H*,3*H*)-dione (78b).



78b

This compound was prepared by following the general procedure-10 and isolated as pale-yellow solid. 40 mg of **57b** afforded 27 mg of **78b** (63% yield). M.P- 208-210 °C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3269, 2360, 1678, 1614, 1162, 1107, 1040, 752. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.05 (s, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.60-7.56 (m, 1H), 7.24-7.22 (m, 2H), 7.12-7.06 (m, 4H), 6.30 (s, 1H), 2.22 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 194.7, 172.1, 141.7, 138.5, 136.6, 135.8, 129.6 (2C), 127.6, 125.8 (2C), 123.2, 119.5, 116.8, 83.0, 21.0. **HRMS (ESI)**: m/z calcd for $C_{16}H_{13}NNaO_3$ $(M+Na)^+$: 290.0793, found: 290.0799.

3-Hydroxy-3-(4-isopropylphenyl)quinoline-2,4(1*H*,3*H*)-dione (78c).



78c

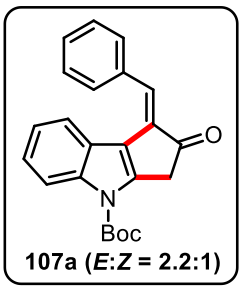
This compound was prepared by following the general procedure-10 and isolated as white solid. 35 mg of **57c** afforded 22 mg of **78c** (59% yield). M.P- 246-248 °C. R_f = 0.3 (EtOAc/ Hexane = 2/3). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3459, 2960, 2361, 1704, 1669, 1611, 1162, 1017, 761. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 11.07 (s, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.28-7.26 (m, 2H), 7.19-7.17 (m, 2H), 7.11-7.06 (m, 2H), 6.31 (s, 1H), 2.79 (sept, J = 6.8 Hz, 1H), 1.11 (d, J = 6.8 Hz, 6H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 194.6, 172.1, 149.3, 141.7, 136.7, 136.2, 127.6, 127.0 (2C), 125.9 (2C), 123.3, 119.5, 116.8, 82.9, 33.5, 24.1 (2C). **HRMS (ESI)**: m/z calcd for $C_{18}H_{17}NNaO_3$ $(M+Na)^+$: 318.1106, found: 318.1112.

General procedure-11: synthesis of *α*-arylidene cyclopenta[*b*]indoles 107a-p.

An oven-dried 10 mL glass vial was charged with **104** (1.0 eq) and **103** (3 eq). Toluene (0.5 mL) and acetonitrile (0.5 mL) were introduced. Then, triphenylphosphine (30 mol%) was added into the reaction mixture. The reaction mixture was stirred at 100 °C (in a heating block) until **104** disappeared (as detected by TLC). The reaction was quenched with water and extracted with EtOAc (2 x 2 mL). The organic extracts were combined, dried over Na_2SO_4, and

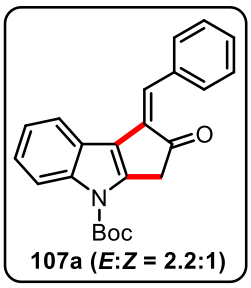
concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as an eluent (49:1), to afford **107** in 43-77% yield.

tert-Butyl (_E_)-1-benzylidene-2-oxo-2,3-dihydrocyclopenta[_b_]indole-4(1_H_)-carboxylate (major isomer) (107a):



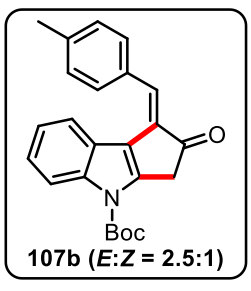
This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 35 mg of **104a** afforded 37 mg of **107a** (77% yield). R_f = 0.5 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2984, 1740, 1373, 1242, 1046, 787. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.30 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 7.4 Hz, 2H), 7.80 (d, J = 8.2 Hz, 1H), 7.43-7.41 (m, 1H), 7.40-7.37 (m, 3H), 7.36-7.34 (m, 1H), 7.11 (s, 1H), 3.74 (s, 2H), 1.67 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.4, 149.1, 140.0, 138.3, 134.9, 132.1, 130.4 (2C), 128.2, 128.1 (2C), 125.9, 125.0, 124.5, 123.7, 123.06, 119.2, 116.1, 84.5, 41.8, 28.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{23}H_{22}NO_3$ $(M+H)^+$: 360.1600, found: 360.1599.

tert-Butyl (_Z_)-1-benzylidene-2-oxo-2,3-dihydrocyclopenta[_b_]indole-4(1_H_)-carboxylate (minor isomer) (107a):



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29-8.26 (m, 1H), 7.57 (d, J = 7.96 Hz, 1H), 7.46-7.33 (m, 3H), 7.40-7.37 (m, 1H), 7.36-7.34 (m, 1H), 7.33-7.32 (m, 1H), 7.30-7.26 (m, 1H), 7.05 (dt, J = 8.08 and 0.88 Hz, 1H), 3.81 (s, 2H), 1.68 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.3, 149.0, 143.3, 138.5, 136.7, 132.3, 129.9 (2C), 129.6, 128.9 (2C), 128.5, 125.5, 124.2, 124.1, 123.2, 123.01, 115.9, 84.8, 40.6, 28.2 (3C).

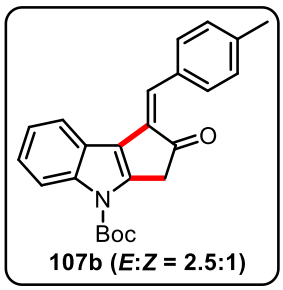
tert-Butyl (_E_)-1-(4-methylbenzylidene)-2-oxo-2,3-dihydrocyclopenta[_b_]indole-4(1_H_)-carboxylate (major isomer) (107b):



This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 30 mg of **104a** afforded 32 mg of **107b** (75% yield). R_f = 0.5 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2978, 1716, 1454, 1366, 1156, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.29 (t, J = 6.6 Hz, 1H), 8.89 (d, J = 8.1 Hz, 2H), 7.41-7.34 (m, 4H), 7.33- 7.27 (m, 1H), 7.11 (s, 1H), 3.75 (s, 2H), 2.39 (s, 3H), 1.67 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.5, 149.2, 143.04, 139.3, 138.7, 132.2, 131.4, 130.5 (2C),

128.90 (2C), 126.0, 124.9, 124.3, 123.6, 123.0, 119.2, 116.0, 84.5, 41.9, 28.2 (3C), 21.5. **HRMS (ESI)**: m/z calcd for $C_{24}H_{23}NNaO_3$ $(M+Na)^+$: 396.1576, found: 396.1569.

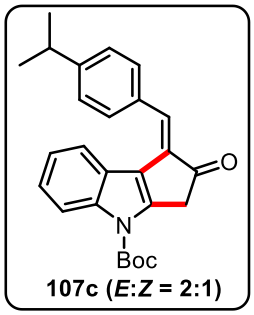
***tert*-Butyl (*Z*)-1-(4-methylbenzylidene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107b):**



107b (*E*:*Z* = 2.5:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.5 Hz, 2H), 7.24-7.20 (m, 6H), 6.73 (d, J = 7.9 Hz, 1H), 3.80 (s, 2H), 2.44 (s, 3H), 1.68 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.4, 149.1, 143.07, 138.5, 138.3, 133.6, 131.5, 130.0 (2C), 129.9, 128.99 (2C), 125.9, 124.5, 124.2, 123.4, 123.1, 115.9, 84.7, 40.6, 28.2 (3C), 21.57.

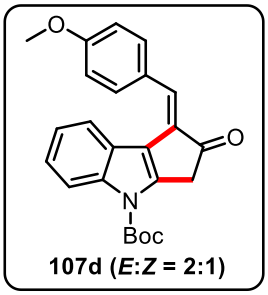
***tert*-Butyl (*E*)-1-(4-isopropylbenzylidene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107c):**



107c (*E*:*Z* = 2:1)

This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 34 mg of **107c** (74% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **M.P** = 148-150 ^{o}C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2962, 1730, 1365, 1321, 1117, 746. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.31-8.29 (m, 1H), 7.93 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.4 Hz, 1H), 7.37 (dt, J = 7.1 and 1.6 Hz, 2H), 7.30-7.26 (m, 2H), 7.11 (s, 1H), 3.75 (s, 2H), 2.99-2.89 (m, 1H), 1.67 (s, 9H), 1.28 (d, J = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.5, 150.1, 149.2, 139.5, 138.3, 132.6, 131.5, 130.6 (2C), 129.9, 126.3 (2C), 126.0, 124.9, 124.3, 123.6, 119.2, 116.1, 84.4, 41.9, 34.1, 28.2 (3C), 23.8 (2C). **HRMS (ESI)**: m/z calcd for $C_{26}H_{28}NO_3$ $(M+H)^+$: 402.2069, found: 402.2061.

***tert*-Butyl (*E*)-1-(4-methoxybenzylidene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107d):**

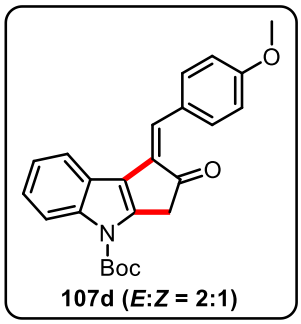


107d (*E*:*Z* = 2:1)

This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 30 mg of **104a** afforded 30 mg of **107d** (68% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3049, 2939, 1735, 1321, 1254, 1113, 736. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.02 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.44-7.42 (m, 2H), 7.38-7.34 (m, 2H), 7.10 (dt, J = 7.1, 0.88 Hz, 1H), 7.07 (s, 1H), 3.88 (s, 3H), 3.79 (s, 2H), 1.68 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.4,

160.3, 149.1, 142.8, 138.5, 131.6 (2C), 130.7, 128.9, 125.7, 124.4, 124.30, 123.6, 123.0, 119.1, 115.6, 113.7 (2C), 84.7, 55.4, 40.7, 28.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{24}H_{24}NO_4$ $(M+H)^+$: 390.1705, found: 390.1690.

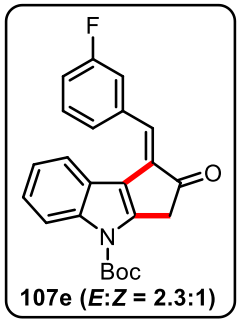
***tert*-Butyl (*Z*)-1-(4-methoxybenzylidene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107d):**



107d (*E*:*Z* = 2:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.28 (m, 2H), 7.32-7.30 (m, 2H), 6.97-6.92 (m, 4H), 6.82 (d, *J* = 7.9 Hz, 1H), 3.86 (s, 3H), 3.74 (s, 2H), 1.67 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.8, 160.0, 149.2, 139.0, 138.3, 132.4 (2C), 130.4, 129.9, 128.0, 126.1, 124.8, 123.4, 124.33, 123.1, 116.0, 113.5 (2C), 84.4, 55.3, 41.9, 28.2 (3C).

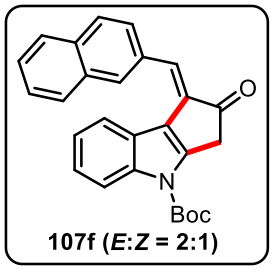
***tert*-Butyl (*E*)-1-(3-fluorobenzylidene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107e):**



107e (*E*:*Z* = 2.3:1)

This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 30 mg of **104a** afforded 27 mg of **107e** (63% yield). R_f = 0.5 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2978, 1736, 1369, 1322, 1138, 760. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.30 (d, *J* = 7.8 Hz, 1H), 7.84-7.81 (m, 1H), 7.79-7.77 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.42-7.32 (m, 3H), 7.06-7.01 (m, 2H), 3.75 (s, 2H), 1.68 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.3, 162.4 (d, *J* = 243.2 Hz, 1C), 149.1, 140.6, 138.4, 137.0 (d, *J* = 8.5 Hz, 1C), 133.0, 129.4 (d, *J* = 8.2 Hz, 1C), 127.8, 126.4 (d, *J* = 2.7 Hz, 1C), 125.7, 125.2, 124.1, 123.8, 119.2, 116.7 (d, *J* = 22.8 Hz, 1C), 116.1, 115.7 (d, *J* = 21.3 Hz, 1C), 84.7, 41.7, 28.2 (3C). **^{19}F NMR (376.4 MHz, $CDCl_3$)**: δ -113.34. **HRMS (ESI)**: m/z calcd for $C_{18}H_{11}FNO$ $(M\text{-}Boc)^+$: 276.0825, found: 276.0818.

***tert*-Butyl (*E*)-1-(naphthalen-2-ylmethylene)-2-oxo-2,3 dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107f):**

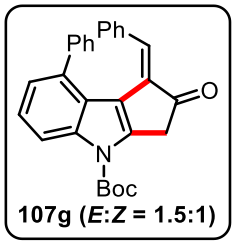


107f (*E*:*Z* = 2:1)

This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 35 mg of **107f** (74% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **M.P** = 168-170 ^{o}C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 3055, 2978, 1731, 1369, 1352, 1111, 762. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.23 (d, *J* = 8.3 Hz, 1H), 8.08-8.06 (m, 1H), 7.96-7.94 (m, 2H), 7.86 (s, 1H), 7.55-7.50 (m, 4H), 7.21 (t, *J* = 8.3

Hz, 1H), 6.87 (t, *J* = 8.1 HZ, 1H), 6.07 (d, *J* = 7.9 HZ, 1H), 3.88 (s, 2H), 1.69 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.1, 149.1, 143.1, 138.4, 134.1, 133.9, 133.3, 132.2, 129.1, 128.6, 127.7, 126.9, 126.3, 125.3, 125.1, 124.5, 124.0, 123.18, 123.16, 123.07, 123.01, 115.5, 84.8, 40.5, 28.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{27}H_{23}NNaO_3$ $(M+Na)^+$: 432.1585, found: 432.1576.

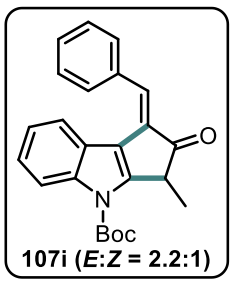
***tert*-Butyl (*E*)-1-benzylidene-2-oxo-8-phenyl-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107g):**



107g (*E*:*Z* = 1.5:1)

This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 20 mg of **104h** afforded 11 mg of **107g** (43% yield). R_f = 0.6 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2977, 1732, 1344, 1252, 1123, 754. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.39 (d, *J* = 8.3 Hz, 1H), 7.45-7.41 (m, 6H), 7.34-7.32 (m, 2H), 7.29 (dd, *J* = 7.4 and 0.9 Hz, 1H), 7.24-7.20 (m, 3H), 5.14 (s, 1H), 3.76 (s, 2H), 1.69 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 201.7, 149.2, 142.0, 140.6, 138.6, 135.4, 134.9, 133.6, 131.0, 130.2 (2C), 129.9 (2C), 128.4, 128.2 (2C), 127.7, 127.5 (2C), 125.6, 125.4, 124.6, 123.2, 114.7, 84.7, 41.6, 28.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{29}H_{26}NO_3$ $(M+H)^+$: 436.1913, found: 436.1904.

***tert*-Butyl (*E*)-1-benzylidene-3-methyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107i):**

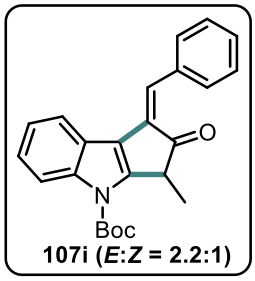


107i (*E*:*Z* = 2.2:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 30 mg of **107i** (70% yield). R_f = 0.45 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2978, 1727, 1354, 1316, 1154, 1116, 736. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.20 (d, *J* = 8.3 Hz, 1H), 7.89-7.87 (m, 2H), 7.36-7.33 (m, 3H), 7.31-7.29 (m, 3H), 7.06 (s, 1H), 3.63 (q, *J* = 7.2 Hz, 1H), 1.61 (s, 9H), 1.44 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 205.0, 149.1, 145.5, 138.7, 135.0, 130.9, 130.4 (2C), 128.9, 128.5, 128.1 (2C), 125.1, 124.1, 123.7, 123.0, 119.4, 116.2, 84.7, 46.2, 28.16 (3C), 17.0. **HRMS (ESI)**: m/z calcd for $C_{24}H_{24}NO_3$ $(M+H)^+$: 374.1756, found: 374.1787.

***tert*-Butyl (*Z*)-1-benzylidene-3-methyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107i):**

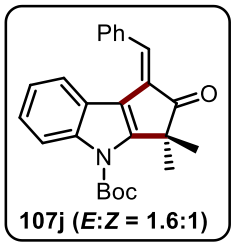
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.4 Hz, 1H), 7.74-7.72 (m, 2H), 7.28-7.16 (m, 5H), 6.95 (t, *J* = 8.1 Hz, 1H), 6.48 (d, *J* = 7.9 HZ, 1H), 3.73 (q, *J* = 7.4 Hz, 1H), 1.62 (s, 9H),



107i (*E*:*Z* = 2.2:1)

1.47 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: *δ* 206.8, 149.06, 148.9, 138.8, 136.8, 131.0, 129.9 (2C), 129.7, 128.2 (2C), 125.8, 125.0, 124.6, 124.0, 123.5, 122.2, 115.7, 84.9, 44.9, 28.14 (3C), 17.1.

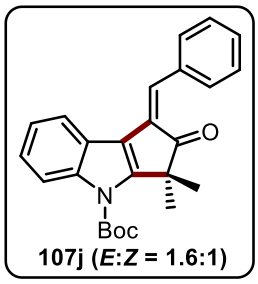
***tert*-Butyl (*E*)-1-benzylidene-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107j):**



107j (*E*:*Z* = 1.6:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 31 mg of **107j** (69% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2974, 1737, 1363, 1155, 1107, 760. **^{1}H NMR (400 MHz, $CDCl_3$)**: *δ* 8.23-8.20 (m, 1H), 8.00-7.98 (d, *J* = 7.5 Hz, 2H), 7.88-7.85 (m, 1H), 7.42-7.39 (m, 5H), 7.216 (s, 1H), 1.74 (s, 9H), 1.55 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: *δ* 209.6, 152.7, 149.2, 138.8, 136.9, 130.5 (2C), 130.0 (2C), 129.76, 128.4, 125.0, 124.5, 123.8, 123.7, 122.9, 119.4, 116.0, 85.2, 48.8, 28.30 (3C), 22.73 (2C). **HRMS (ESI)**: m/z calcd for $C_{25}H_{26}NO_3$ $(M+H)^+$: 388.1893, found: 388.1913.

***tert*-Butyl (*Z*)-1-benzylidene-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107j):**

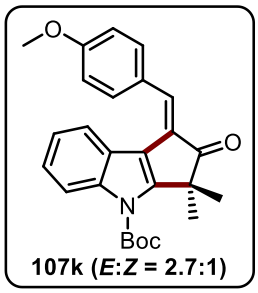


107j (*E*:*Z* = 1.6:1)

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.15 (d, *J* = 8.4 Hz, 1H), 7.45-7.44 (m, 2H), 7.38-7.33 (m, 4H), 7.29-7.24 (m, 1H), 7.02 (dt, *J* = 8.0 and 0.8 Hz, 1H), 6.52 (d, *J* = 7.8 Hz, 1H), 1.74 (s, 9H), 1.59 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: *δ* 207.8, 149.5, 149.3, 138.7, 135.1, 129.8, 129.74, 128.8, 128.2 (2C), 128.0 (2C), 126.1, 124.0, 123.9, 123.5, 121.5, 126.6, 85.2, 49.7, 28.34 (3C), 22.78 (2C).

***tert*-Butyl (*E*)-1-(4-methoxybenzylidene)-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107k):**

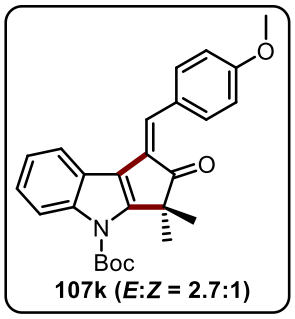
This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 34 mg of **107k** (71% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **M.P** = 150-



107k (*E*:*Z* = 2.7:1)

152 °C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2970, 1730, 1300, 1251, 1151, 1104, 742. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.23-8.20 (m, 1H), 8.06 (d, *J* = 8.7 Hz, 2H), 7.44-7.42 (m, 1H), 7.38-7.35 (m, 2H), 7.17 (s, 1H), 6.99-6.94 (m, 2H), 3.86 (s, 3H), 1.74 (s, 9H), 1.54 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 208.1, 160.2, 149.3, 148.5, 138.7, 132.5 (2C), 130.0, 128.19, 128.0, 124.9, 124.13, 123.9, 123.5, 119.3, 116.0, 113.5 (2C), 84.9, 55.38, 49.7, 28.33 (3C), 22.78 (2C). **HRMS (ESI)**: m/z calcd for $C_{26}H_{28}NO_4$ $(M+H)^+$: 418.2018, found: 418.2018.

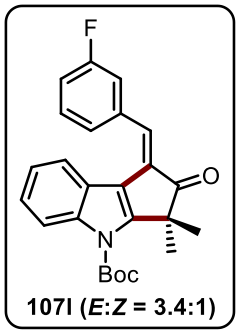
tert-Butyl (*Z*)-1-(4-methoxybenzylidene)-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107k):



107k (*E*:*Z* = 2.7:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.4 Hz, 1H), 7.87-7.85 (m, 2H), 7.32 (s, 1H), 7.30-7.26 (m, 1H), 7.08 (dt, *J* = 8.0 and 0.8 Hz, 1H), 6.93-6.92 (m, 2H), 6.78 (d, *J* = 7.8 Hz, 1H), 3.88 (s, 3H), 1.75 (s, 9H), 1.58 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 209.8, 159.9, 152.2, 149.2, 138.8, 131.6 (2C), 129.2, 128.14, 126.3, 124.4, 124.10, 123.7, 122.8, 121.6, 116.5 (2C), 113.6, 85.1, 55.34, 48.8, 28.30 (3C), 22.71 (2C).

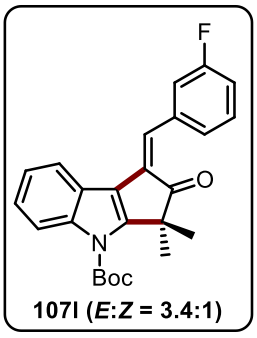
tert-Butyl (*E*)-1-(3-fluorobenzylidene)-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107l):



107l (*E*:*Z* = 3.4:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 32 mg of **107l** (70% yield). R_f = 0.35 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} [1] 2975, 1736, 1358, 1303, 1153, 1109, 747. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.21 (d, *J* = 8.9 Hz, 1H), 7.89-7.83 (m, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.40-7.34 (m, 4H), 7.14 (s, 1H), 7.03 (dt, *J* = 8.3 Hz and 7.4 Hz, 1H), 1.74 (s, 9H), 1.55 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 207.8, 162.5 (d, *J* = 242.8 Hz, 1C), 150.1, 149.2, 138.7, 137.20 (d, *J* = 8.1 Hz, 1C), 130.7, 129.36 (d, *J* = 8.1 Hz, 1C), 126.50 (d, *J* = 2.8 Hz, 1C), 125.2, 123.7, 123.1 (d, *J* = 13.5 Hz, 1C), 121.6, 119.4, 115.9 (d, *J* = 34.4 Hz, 1C), 116.6, 115.5, 106.6, 85.2, 49.7, 28.3 (3C), 22.74 (2C). **^{19}F NMR (376.4 MHz, $CDCl_3$)**: δ -113.44. **HRMS (ESI)**: m/z calcd for $C_{25}H_{24}FNNaO_3$ $(M+Na)^+$: 428.1638, found: 428.1623.

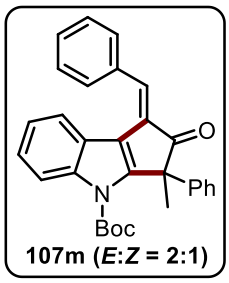
***tert*-Butyl (*Z*)-1-(3-fluorobenzylidene)-3,3-dimethyl-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107l):**



107l (*E*:*Z* = 3.4:1)

^{1}H NMR (400 MHz, $CDCl_3$): Peaks corresponding to the minor isomer are not clearly distinguishable. **^{13}C NMR (100 MHz, $CDCl_3$):** δ 209.4, 162.5 (d, J = 245.6 Hz, 1C), 153.3, 149.1, 139.1 (d, J = 7.8 Hz, 1C), 138.8, 130.4, 129.74 (d, J = 8.3 Hz, 1C), 127.95 (d, J = 2.3 Hz, 1C), 125.7, 124.7, 124.3, 123.9, 123.73, 123.67, 121.1, 116.8 (d, J = 23.1Hz, 1C), 115.4 (d, J = 15.8 Hz, 1C), 85.4, 48.8, 28.2 (3C), 22.70 (2C). **^{19}F NMR (376.4 MHz, $CDCl_3$):** δ -111.78.

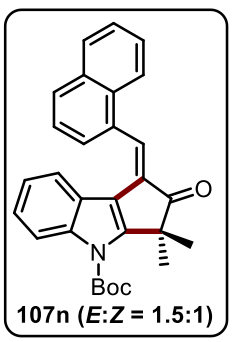
***tert*-Butyl (*E*)-1-benzylidene-3-methyl-2-oxo-3-phenyl-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107m):**



107m (*E*:*Z* = 2:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 37 mg of **107m** (72% yield). R_f = 0.45 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat):** ν_{max}/cm^{-1} 2978, 1730, 1351, 1311, 1142, 745. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.47 (dd, J = 7.6 and 1.7 Hz, 1H), 7.96-7.94 (m, 1H), 7.92-7.90 (m, 2H), 7.48-7.42 (m, 3H), 7.35-7.33 (m, 2H), 7.31-7.28 (m, 3H), 7.27 (s, 1H), 7.22-7.20 (m, 2H), 1.99 (s, 3H), 1.26 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 203.7, 149.0, 145.8, 140.5, 139.5, 134.8, 131.2, 130.6 (2C), 129.4, 129.0, 128.3 (2C), 128.0 (2C), 126.9, 126.8 (2C), 125.9, 125.6, 123.9, 123.8, 119.5, 116.9, 85.0, 57.7, 27.7 (3C), 22.1. **HRMS (ESI):** m/z calcd for $C_{30}H_{28}NO_3$ $(M+H)^+$: 450.2069, found: 450.2093.

***tert*-Butyl (*E*)-3,3-dimethyl-1-(naphthalen-1-ylmethylene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (major isomer) (107n):**

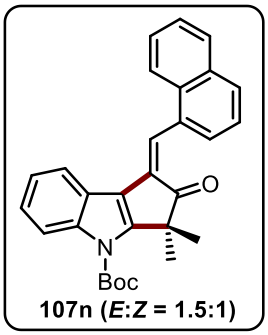


107n (*E*:*Z* = 1.5:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 5 mg of **107n** (11% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat):** ν_{max}/cm^{-1} 2972, 1737, 1369, 1312, 1165, 1109. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.26-8.23 (m, 1H), 8.11-8.07 (m, 3H), 7.84 (s, 1H), 7.54-7.51 (m, 4H), 7.19 (t, J = 8.4 Hz, 1H), 6.83 (t, J = 7.9 Hz, 1H), 6.04 (d, J = 7.9 Hz, 1H), 1.74 (s, 9H), 1.64 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 209.5, 152.9, 149.2, 138.78, 134.4, 133.3, 132.3, 131.3, 129.0, 128.5, 127.7, 126.5, 126.30, 125.9, 125.4, 125.13, 124.5,

124.1, 123.71, 123.3, 121.5, 115.9, 85.2, 49.71, 28.2 (3C), 22.7 (2C). **HRMS (ESI)**: m/z calcd for $C_{29}H_{27}NNaO_3$ $(M+Na)^+$: 460.1889, found: 460.1906.

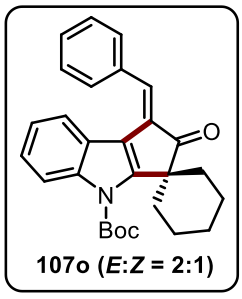
***tert*-Butyl (*Z*)-3,3-dimethyl-1-(naphthalen-1-ylmethylene)-2-oxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (minor isomer) (107n):**



107n (*E*:*Z* = 1.5:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-7.91 (m, 4H), 7.90-7.85 (m, 2H), 7.80 (s, 1H), 7.49-7.48 (m, 3H), 7.43-7.40 (m, 2H), 1.75 (s, 9H), 1.53 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 207.5, 150.0, 138.73, 134.5, 133.3, 131.7, 131.4, 130.8, 128.7, 128.2, 127.8, 126.6, 126.34, 126.27, 125.9, 125.7, 125.17, 125.0, 124.2, 123.73, 119.6, 116.6, 85.1, 49.73, 28.3 (3C), 22.6 (2C).

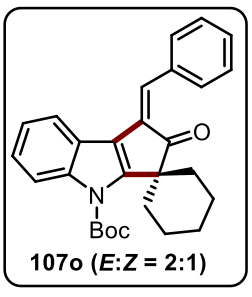
***tert*-Butyl (*E*)-1'-benzylidene-2'-oxo-1',2'-dihydro-4'*H*-spiro[cyclohexane-1,3'-cyclopenta[*b*]indole]-4'-carboxylate (major isomer) (107o):**



107o (*E*:*Z* = 2:1)

This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 30 mg of **107o** (62% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **M.P** = 158-161 ^{o}C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2931, 1732, 1359, 1301, 1152, 742. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.15-8.12 (m, 1H), 7.95 (d, J = 7.6 Hz, 2H), 7.42-7.379 (m, 4H), 7.373-7.343 (m, 2H), 7.16 (s, 1H), 2.58-2.53 (m, 2H), 2.17-2.10 (m, 2H), 1.83-1.79 (m, 2H), 1.75 (s, 9H), 1.64-1.63 (m, 2H), 1.51-1.44 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 206.9, 149.3, 138.7, 135.2, 133.0, 130.4 (2C), 129.9, 128.6, 128.0 (2C), 126.7, 125.3, 124.47, 123.9, 123.60, 119.4, 116.6, 84.9, 51.6, 29.4, 28.33 (3C), 24.3 (2C), 21.2 (2C). **HRMS (ESI)**: m/z calcd for $C_{28}H_{29}NNaO_3$ $(M+Na)^+$: 450.2045, found: 450.2045.

***tert*-Butyl (*Z*)-1'-benzylidene-2'-oxo-1',2'-dihydro-4'*H*-spiro[cyclohexane-1,3'-cyclopenta[*b*]indole]-4'-carboxylate (minor isomer) (107o):**

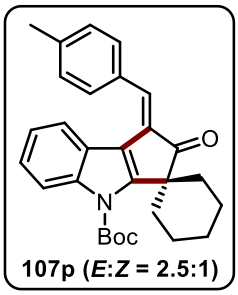


107o (*E*:*Z* = 2:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08-8.06 (m, 1H), 7.86-7.84 (m, 3H), 7.59-7.57 (m, 1H), 7.32-7.30 (m, 3H), 6.99 (t, J = 7.7 Hz, 1H), 6.47 (d, J = 8.0 Hz, 1H), 2.51-2.50 (m, 2H), 2.09-2.07 (m, 2H), 1.86-1.85 (m, 2H), 1.75 (s, 9H), 1.639-1.633 (m, 2H), 1.33-1.30 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 208.2, 149.9, 138.8, 137.1, 130.58, 130.51 (2C),

130.34, 128.8, 128.2, 128.1 (2C), 124.9, 124.43, 123.68, 123.5, 122.8, 115.9, 85.9, 51.6, 29.5, 28.35 (3C), 25.6 (2C), 21.4 (2C).

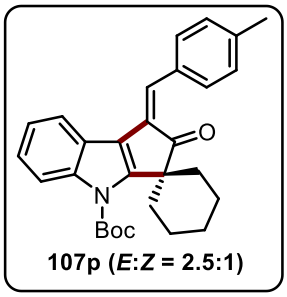
tert-Butyl (_E_)-1'-(4-methylbenzylidene)-2'-oxo-1',2'-dihydro-4'_H_-spiro[cyclohexane-1,3'-cyclopenta[_b_]indole]-4'-carboxylate (major isomer) (107p):



107p (*E*:*Z* = 2.5:1)

This compound was isolated as pale-yellow liquid. Following the general procedure-11, 30 mg of **104a** afforded 33 mg of **107p** (65% yield). R_f = 0.4 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2978, 1731, 1352, 1142, 745. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.14-8.12 (m, 1H), 7.87-7.85 (m, 2H), 7.37-7.34 (m, 2H), 7.22-7.19 (m, 3H), 7.14 (s, 1H), 2.54-2.49 (m, 2H), 2.38 (s, 3H), 2.12-2.07 (m, 2H), 1.82-1.79 (m, 2H), 1.66-1.63 (m, 2H), 1.53-1.46 (m, 2H), 1.74 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 206.9, 149.4, 138.89, 138.7, 132.5, 130.4 (2C), 129.8, 128.1, 128.80 (2C), 125.6, 124.8, 123.9, 123.5, 122.7, 119.4, 116.6, 84.9, 51.6, 29.4, 28.36 (3C), 25.7, 24.4 (2C), 21.2 (2C). **HRMS (ESI)**: m/z calcd for $C_{29}H_{32}NO_3$ $(M+H)^+$: 442.2382, found: 442.2382.

tert-Butyl (_Z_)-1'-(4-methylbenzylidene)-2'-oxo-1',2'-dihydro-4'_H_-spiro[cyclohexane-1,3'-cyclopenta[_b_]indole]-4'-carboxylate (minor isomer) (107p):



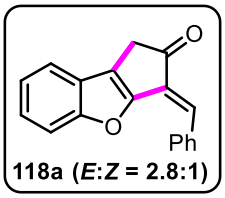
107p (*E*:*Z* = 2.5:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 1H), 7.85-7.84 (m 2H), 7.342-7.33 (m, 2H), 7.28-7.27 (m, 2H), 7.03 (dt, J = 7.1 and 0.8 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 2.60-2.56 (m, 2H), 2.42 (s, 3H), 2.17-2.13 (m, 2H), 1.90-1.84 (m, 2H), 1.74 (s, 9H), 1.66-1.63 (m, 2H), 1.45-1.41 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 208.4, 149.5, 138.88, 138.3, 134.0, 132.5, 130.0, 129.5, 128.87 (2C), 126.4, 124.5, 124.3 (2C), 123.7, 123.6, 122.2, 115.9, 85.0, 51.1, 29.5, 28.33 (3C), 25.8, 24.5 (2C), 21.4 (2C).

General procedure-12: synthesis of 118a and 118b.

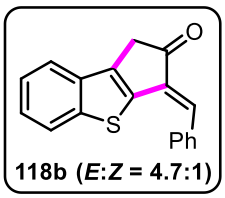
An oven-dried 10 mL glass vial was charged with **115** (1.0 eq), ynone **103a** (3.0 eq) and ACN (1.0 mL). Then, PPh_3 (30 mol%) was introduced. The progress of the reaction was detected by TLC. Upon completion, the reaction was quenched with water and extracted with EtOAc (2 x 2 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as an eluent (49:1) to afford **118**.

(*E*)-3-Benzylidene-1,3-dihydro-2*H*-cyclopenta[*b*]benzofuran-2-one (major isomer) (118a):



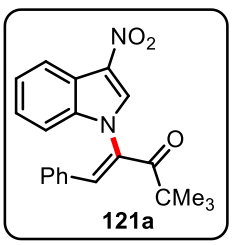
This compound was isolated as pale-yellow solid. Following the general procedure-12, 30 mg of **115a** afforded 30 mg of **118a** (63% yield). R_f = 0.45 (EtOAc/ Hexane = 0.5/9.5). **M.P** = 108-110 °C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2929, 1731, 1515, 1372, 1111, 750. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.63 (d, *J* = 8.2 Hz,1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.51-7.48 (m, 2H), 7.44-7.38 (m, 2H), 7.34-7.31 (m, 1H), 7.20 (s, 1H), 3.55 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 202.1, 159.0, 157.7, 134.4, 130.4 (2C), 129.8, 128.8 (2C), 127.3, 126.1, 124.9, 124.6, 123.9, 122.7, 120.3, 112.4, 36.3. **HRMS (ESI)**: m/z calcd for $C_{18}H_{13}O_2$ $(M+H)^+$: 261.0916, found: 261.0912.

(*Z*)-3-Benzylidene-1,3-dihydro-2*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-one (major isomer) (118b):



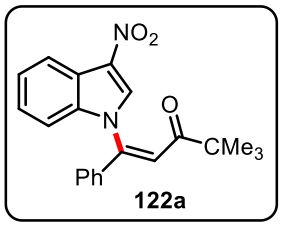
This compound was isolated as pale-yellow semi-solid. Following the general procedure-12, 30 mg of **115b** afforded 20 mg of **118b** (43% yield). R_f = 0.45 (EtOAc/ Hexane = 0.5/9.5). **IR (thin film, neat)**: ν_{max}/cm^{-1} 3058, 2926, 1732, 1617, 1190, 755. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.82-7.79 (m, 1H), 7.75-7.73 (m, 2H), 7.70-7.68 (m, 1H), 7.51-7.47 (m, 2H), 7.45-7.43 (m, 1H), 7.42-7.38 (m, 2H), 7.38 (s, 1H), 3.63 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.0, 141.7, 140.1, 140.0, 135.1, 134.7, 133.0, 129.5, 128.9 (2C), 128.8 (2C), 128.2, 126.2, 125.1, 123.0, 122.3, 38.4. **HRMS (ESI)**: m/z calcd for $C_{18}H_{13}OS$ $(M+H)^+$: 277.0687, found: 277.0685.

(*Z*)-4,4-Dimethyl-2-(3-nitro-1*H*-indol-1-yl)-1-phenylpent-1-en-3-one (121a):



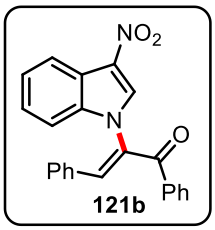
This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 12 mg of **121a** (30% yield). R_f = 0.45 (EtOAc/ Hexane = 1/4). **M.P** = 164-166 °C. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2968, 1689, 1602, 1533, 1482, 1453, 1305, 1228, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.33 (d, *J* = 8.0 Hz, 1H), 8.11 (s, 1H), 7.50-7.49 (m, 1H), 7.43-7.37 (m, 3H), 7.30-7.28 (m, 2H), 7.21-7.17 (m, 1H), 7.16 (s, 1H), 6.88-6.86 (m, 1H), 1.22 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 202.0, 145.2, 135.6, 135.0, 131.8, 131.7, 129.4 (3C), 127.2 (2C), 124.8, 124.4, 121.0, 120.9, 118.3, 112.2, 44.5, 26.2 (3C). **HRMS (ESI)**: m/z calcd for $C_{21}H_{21}N_2O_3$ $(M+H)^+$: 349.1552, found: 349.1554.

(*Z*)-4,4-Dimethyl-1-(3-nitro-1*H*-indol-1-yl)-1-phenylpent-1-en-3-one (122a):



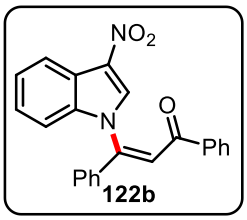
This compound was isolated as pale-yellow solid. Following the general procedure-11, 30 mg of **104a** afforded 11 mg of **122a** (27% yield). R_f = 0.45 (EtOAc/ Hexane = 1/4). **M.P** = 135-137 ºC. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2968, 1689, 1600, 1536, 1482, 1450, 1228, 750. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.34 (d, *J* = 8.0 Hz, 1H), 8.02 (s, 1H), 7.53-7.49 (m, 1H), 7.45-7.41 (m, 3H), 7.33-7.26 (m, 4H), 6.87 (s, 1H), 1.25 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 203.9, 147.7, 135.5, 133.4, 131.1, 130.1, 129.4 (2C), 128.9 (3C), 125.4, 125.0, 121.6, 121.3, 118.3, 112.8, 44.3, 26.4 (3C). **HRMS (ESI)**: m/z calcd for $C_{21}H_{21}N_2O_3$ $(M+H)^+$: 349.1552, found: 349.1546.

(*Z*)-2-(3-Nitro-1*H*-indol-1-yl)-1,3-diphenylprop-2-en-1-one (121b):



This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 30 mg of **104a** afforded 16 mg of **121b** (38% yield). R_f = 0.45 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2927, 1664, 1600, 1577, 1451, 1226, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.24 (d, *J* = 8.0 Hz, 1H), 8.08 (s, 1H), 7.81-7.78 (m, 2H), 7.55-7.53 (m, 1H), 7.49-7.44 (m, 3H), 7.41-7.40 (m, 1H), 7.37 (s, 1H), 7.36-7.32 (m, 3H), 7.24-7.17 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 189.2, 145.6, 137.1, 135.7, 134.7, 133.5, 131.9, 131.4, 129.5 (2C), 129.3, 128.6 (2C), 128.1 (2C), 127.4 (2C), 125.0, 124.5, 120.9, 120.8, 120.3, 112.4. **HRMS (ESI)**: m/z calcd for $C_{23}H_{17}N_2O_3$ $(M+H)^+$: 369.1239, found: 369.1249.

(*Z*)-3-(3-Nitro-1*H*-indol-1-yl)-1,3-diphenylprop-2-en-1-one (122b):



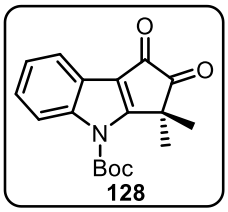
This compound was isolated as pale-yellow semi-solid. Following the general procedure-11, 30 mg of **104a** afforded 17 mg of **122b** (40% yield). R_f = 0.5 (EtOAc/ Hexane = 1/4). **IR (thin film, neat)**: ν_{max}/cm^{-1} 2928, 1667, 1599, 1534, 1482, 1304, 1228, 751. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.36 (d, *J* = 8.0 Hz, 1H), 8.12(s, 1H), 7.95-7.92 (m, 2H), 7.58-7.54 (m, 1H), 7.46-7.43 (m, 3H), 7.37-7.33 (m, 4H), 7.32-7.28 (m, 3H), 7.13 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 190.6, 147.5, 137.2, 135.6, 133.6, 133.3, 131.3, 130.1, 129.6 (2C), 129.1 (2C), 128.79 (3C), 128.76 (2C), 125.5, 125.1, 121.6, 121.3, 120.7, 112.9. **HRMS (ESI)**: m/z calcd for $C_{23}H_{17}N_2O_3$ $(M+H)^+$: 369.1239, found: 369.1237.

General procedure-13: synthesis of Bruceolline E 129.

Step 1: To a solution of **107j** (1 eq, 0.25 mmol) in 1,4-dioxane-water (1:1, 4 mL) were added 2,6-lutidine (3 eq, 0.77 mmol), OsO_4 (0.1 eq, 0.025 mmol) and $NaIO_4$ (3 eq, 0.77 mmol) sequentially. The reaction mixture was stirred at room temperature and monitored by TLC. Upon completion, reaction was quenched with water and extracted with DCM (2 x 5 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as an eluent (3:2) to afford **128** in 41% yield.

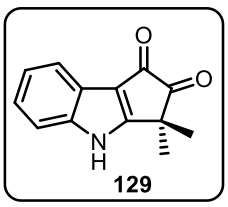
Step 2: To a solution of **128** (1 eq, 0.09 mmol) in DCM (3 mL), TFA (0.1 mL) was added and the reaction mixture was stirred at room temperature until the complete consumption of the starting material. After 6 h, the solution was quenched with $NaHCO_3$ and extracted with DCM (2 x 2 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as an eluent (3:2) to afford **129** in 91% yield.

tert-Butyl 3,3-dimethyl-1,2-dioxo-2,3-dihydrocyclopenta[*b*]indole-4(1*H*)-carboxylate (128):



This compound was isolated as pale-yellow solid. Following the general procedure-13, 30 mg of **107j** afforded 10 mg of **128** (41% yield). R_f = 0.5 (EtOAc/ Hexane = 1/4). **M.P** = 295-297 ºC. **IR (thin film, neat)**: ν_{max}/cm^{-1} 2977, 1746, 1706, 1423, 1360, 1142, 765. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.10 (d, *J* = 8.3 Hz, 1H), 8.07-8.05 (m, 1H), 7.47 (dt, *J* = 8.5 and 1.0 Hz, 1H), 7.44-7.40 (m, 1H), 1.77 (s, 9H), 1.63 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 205.2, 177.9, 170.7, 148.1, 138.7, 127.2, 126.7, 125.4, 122.0,4, 122.01, 116.4, 87.3, 45.8, 28.1 (3C), 22.2 (2C). **HRMS (ESI)**: m/z calcd for $C_{18}H_{19}NNaO_4$ $(M+Na)^+$: 336.1212, found: 336.1215.

3,3-Dimethyl-3,4-dihydrocyclopenta[*b*]indole-1,2-dione (129):

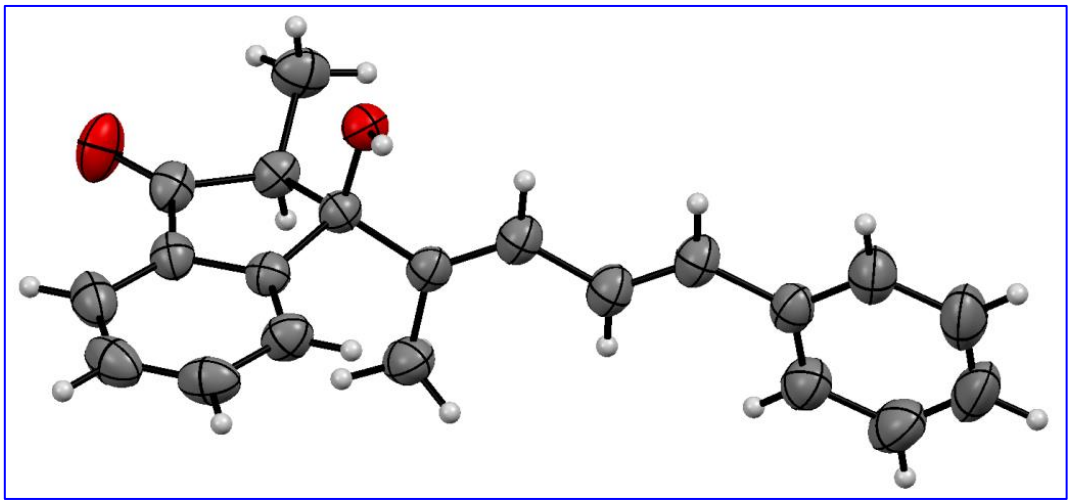


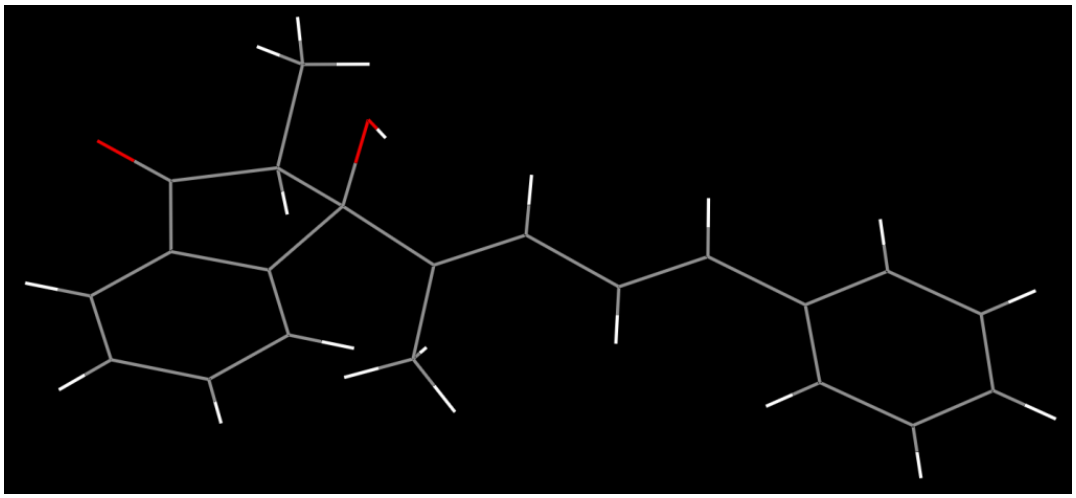
This compound was isolated as pale-yellow solid. Following the general procedure-13, 50 mg of **128** afforded 31 mg of **129** (91% yield). R_f = 0.3 (EtOAc/ Hexane = 2/3). **M.P** = 288-290 ºC. **IR (thin film, neat)**: ν_{max}/cm^{-1} 3393, 1735, 1661, 1023, 996, 761. **^{1}H NMR (400 MHz, DMSO-*d*^{6})**: δ 12.94 (s, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.33-7.29 (m, 1H), 1.42 (s, 6H). **^{13}C NMR (100 MHz, DMSO-*d*^{6})**: δ 206.9, 175.6, 171.3, 140.3,

125.7, 123.8, 121.9, 121.5, 121.4, 114.0, 42.0, 23.3 (2C). **HRMS (ESI)**: m/z calcd for $C_{13}H_{11}NNaO_2$ $(M+Na)^+$: 236.0687, found: 236.0693.

Crystal structure of 33m (CCDC 1865325):

Structure of the **33m** was confirmed by single crystal X-ray diffraction analysis.





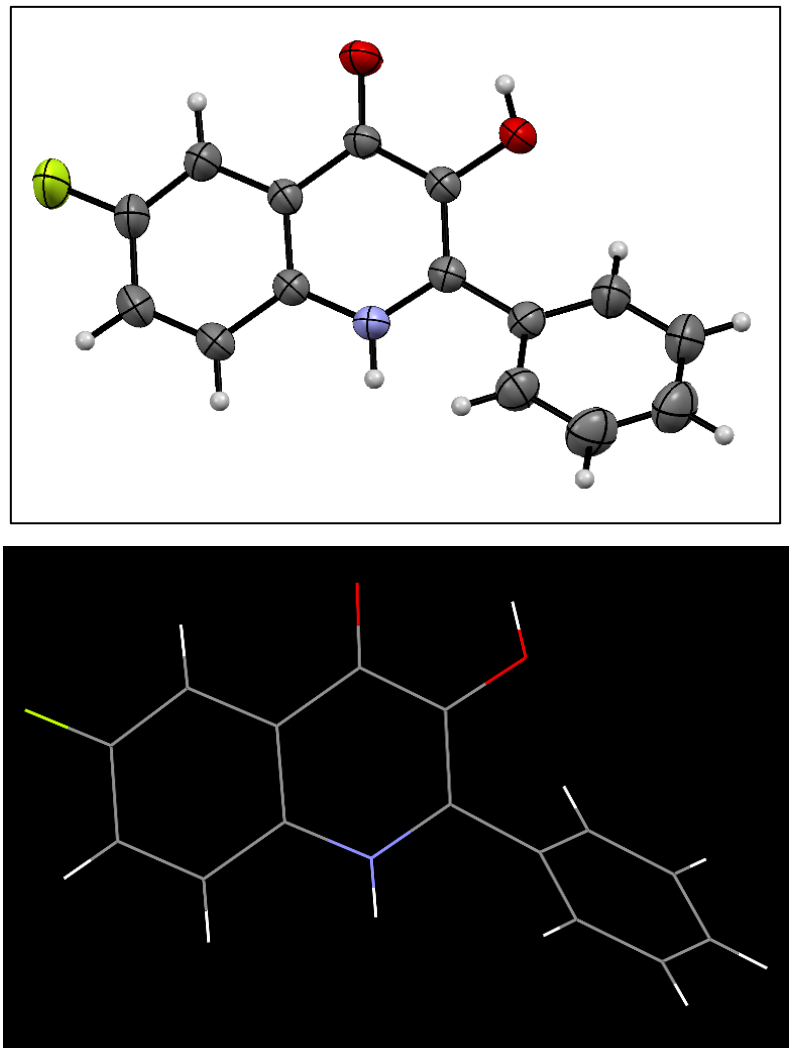
Crystal Data for $C_{21}H_{20}O_2$ (M =304.39 g/mol): triclinic, space group P-1 (no. 2), a = 6.299(4) Å, b = 11.213(7) Å, c = 12.297(8) Å, α = 92.294(8)°, β = 92.253(9)°, γ = 96.879(8)°, V = 860.7(9) Å^3, Z = 2, T = 296.15 K, μ(Mo Kα) = 0.074 mm^{-1}, *Dcalc* = 1.1744 g/cm^3, 10039 reflections measured (3.32° ≤ 2Θ ≤ 49.78°), 3003 unique (R_{int} = 0.0263, R_{sigma} = 0.0240) which were used in all calculations. The final R_1 was 0.0391 (I>=2u(I)) and wR_2 was 0.1119 (all data).

Table 9: Crystal data and structure refinement for 33m

Identification code	33m
Empirical formula	$C_{21}H_{20}O_2$
Formula weight	304.39
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	6.299(4)
b/Å	11.213(7)
c/Å	12.297(8)
α/°	92.294(8)
β/°	92.253(9)
γ/°	96.879(8)
Volume/Å^3	860.7(9)
Z	2
ρ_{calc}g/cm^3	1.1744
μ/mm^{-1}	0.074
F(000)	324.2
Crystal size/mm^3	0.2 × 0.15 × 0.15
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	3.32 to 49.78
Index ranges	$-7 \leq h \leq 7$, $-13 \leq k \leq 13$, $-14 \leq l \leq 14$
Reflections collected	10039
Independent reflections	3003 [R_{int} = 0.0263, R_{sigma} = 0.0240]
Data/restraints/parameters	3003/0/212
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.1025
Final R indexes [all data]	R_1 = 0.0497, wR_2 = 0.1119
Largest diff. peak/hole / e Å^{-3}	0.17/-0.19

Crystal structure of 57j (CCDC 2058628):

The structure of **57j** was confirmed by single-crystal X-ray diffraction analysis.



ORTEP diagram of **57j** with 50% ellipsoidal probability.

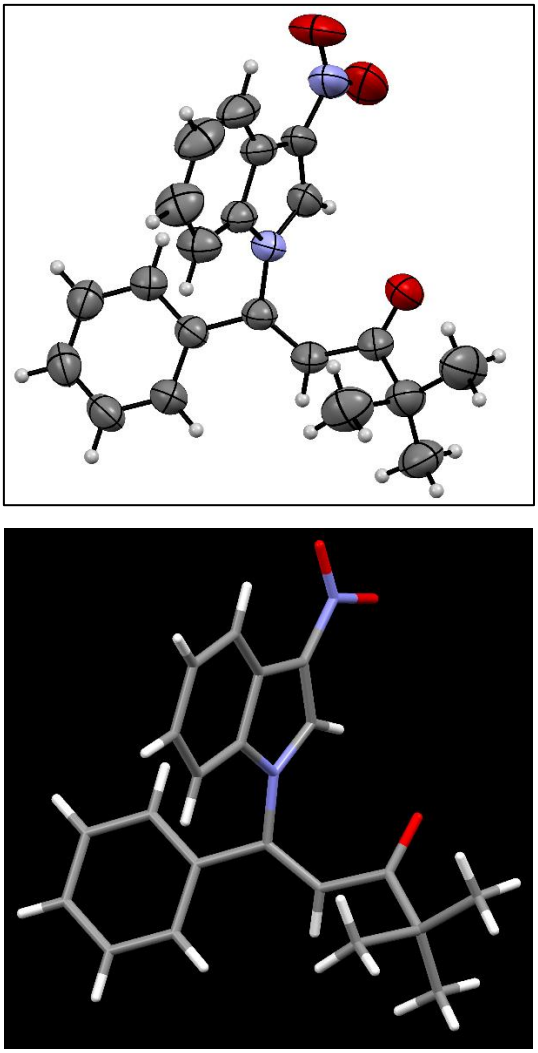
Crystal Data for $C_{30}H_{20}F_2N_2O_4$ (M = 510.501g/mol): monoclinic, space group Cc, *a* = 18.8275(6) Å, *b* = 13.1791(5) Å, *c* = 9.7264(3) Å, α = 90°, β = 97.555(3)°, γ = 90°, *V* = 2392.46(14) Å3, *Z* = 4, T = 298 K, μ(Mo Kα) = 0.105 mm-1, *Dcalc* = 1.417 g/cm3, 13567 reflections measured (5.46° ≤ 2Θ ≤ 65.5°), 7218 unique (R_{int} = 0.0163, R_{sigma} = 0.0243) which were used in all calculations. The final R1 was 0.0437 (I > 2σ(I)) and wR2 was 0.1447 (all data).

Table 10: Crystal data and structure refinement for 57j.

Identification code	57j
Empirical formula	$C_{30}H_{20}F_2N_2O_4$
Formula weight	510.501
Temperature/K	298
Crystal system	monoclinic
Space group	Cc
a/Å	18.8275(6)
b/Å	13.1791(5)
c/Å	9.7264(3)
α/°	90
β/°	97.555(3)
γ/°	90
Volume/Å^3	2392.46(14)
Z	4
ρ_{calc}g/cm^3	1.417
μ/mm^{-1}	0.105
F(000)	1056.6
Crystal size/mm^3	0.3 × 0.3 × 0.3
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.46 to 65.5
Index ranges	-27 ≤ h ≤ 28, -18 ≤ k ≤ 17, -14 ≤ l ≤ 14
Reflections collected	13567
Independent reflections	7218 [R_{int} = 0.0163, R_{sigma} = 0.0243]
Data/restraints/parameters	7218/2/345
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0437, wR_2 = 0.1307
Final R indexes [all data]	R_1 = 0.0533, wR_2 = 0.1447
Largest diff. peak/hole / e Å^{-3}	0.30/-0.19
Flack parameter	0.4(5)

Crystal structure of 122a (CCDC- 2214774):

The structure of **122a** was confirmed by single-crystal X-ray diffraction analysis.



ORTEP diagram of **122a** with 50% ellipsoidal probability.

Crystal Data for $C_{21}H_{20}N_2O_3$ (*M* =348.39 g/mol): triclinic, space group P-1 (no. 2), *a* = 9.9977(7) Å, *b* = 10.0721(7) Å, *c* = 10.6301(8) Å, *α* = 73.343(7)°, *β* = 82.375(6)°, *γ* = 63.636(7)°, *V* = 918.83(11) Å^3, *Z* = 2, *T* = 293.0(10) K, μ(Mo Kα) = 0.085 mm^{-1}, *Dcalc* = 1.259 g/cm^3, 7049 reflections measured (5.32° ≤ 2Θ ≤ 65.48°), 5725 unique (R_{int} = 0.0197, R_{sigma} = 0.0459) which were used in all calculations. The final R_1 was 0.0648 (>2sigma(I)) and wR_2 was 0.2074

Table 11: Crystal data and structure refinement for 122a.

Identification code	122a
Empirical formula	$C_{21}H_{20}N_2O_3$
Formula weight	348.39
Temperature/K	293.0(10)
Crystal system	triclinic
Space group	P-1
a/Å	9.9977(7)
b/Å	10.0721(7)
c/Å	10.6301(8)
α/°	73.343(7)
β/°	82.375(6)
γ/°	63.636(7)
Volume/Å^3	918.83(11)
Z	2
ρ_{calc}g/cm^3	1.259
μ/mm^{-1}	0.085
F(000)	368.0
Crystal size/mm^3	0.2 × 0.2 × 0.2
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.32 to 65.48
Index ranges	$-14 \leq h \leq 14$, $-9 \leq k \leq 13$, $-16 \leq l \leq 15$
Reflections collected	7049
Independent reflections	5725 [R_{int} = 0.0197, R_{sigma} = 0.0459]
Data/restraints/parameters	5725/36/268
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0648, wR_2 = 0.1642
Final R indexes [all data]	R_1 = 0.1100, wR_2 = 0.2074
Largest diff. peak/hole / e Å^{-3}	0.27/-0.18

References

(1) (a) Kane, R. *Ann*. *Phys*. **1838**, *120*, 473. (b) Kane, R. *J. Prakt. Chem.* **1838**, *15*, 129.

(2) Borodin, A. *Ber*. *Dtsch. Chem. Ges.* **1873**, *6*, 982.

(3) (a) Würtz, C. A. *Bull. Soc. Chim. Fr*. **1872**, *17*, 436. (b) Würtz, C. A. *J. Prakt. Chem.* **1872**, *5*, 457.

(4) (a) Palomo, C.; Oiarbide, M.; Garcia, J. M. *Chem. Soc. Rev.* **2004**, *33*, 65. (b) Trost, B. M.; Brindle, C. S. *Chem. Soc. Rev.* **2010**, *39*, 1600. (c) Dias, L. C.; de Lucca, E. C., Jr.; Ferreira, M. A. B.; Polo, E. C. *J. Braz. Chem. Soc.* **2012**, *23*, 2137.

(5) For representative articles on natural product having β-hydroxy carbonyl motifs, see: (a) Paterson, I.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569. (b) Tatsuta, K.; Ishiyama, T.; Tajima, S.; Koguchi, Y.; Gunji, H. *Tetrahedron Lett.* **1990**, *31*, 709. (c) Paterson, I.; Perkins, M. V. *Tetrahedron Lett.* **1992**, *33*, 801. (d) Nerenberg, J. B.; Hung, D. T.; Somers, P. K.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 12621. (e) I. Paterson, I.; Hulme, A. N. *J. Org. Chem.* **1995**, *60*, 3288. (f) Murakami, N.; Wang, W.; Aoki, M.; Tsutsui, Y.; Sugimoto, M.; Kobayashi, M. *Tetrahedron Lett.* **1998**, *39*, 2349. (g) Masse, C. E.; A. J. Morgan, A. J.; Adams, J.; Panek, J. S. *Eur. J. Org. Chem.* **2000**, 2513. (h) Ehrlich, G.; Hassfeld, J.; Eggert, U.; Kalesse, M. J. Am. Chem. Soc. 2006, 128, 14038. (i) Brodmann, T.; Lorenz, M.; Schäckel, R.; Simsek, S.; Kalesse, M. *Synlett* **2009**, *2*, 174. (j) Chandra, B.; Fu, D.; Nelson, S. G. *Angew*. *Chem. Int. Ed.* **2010**, *49*, 2591; *Angew. Chem.* **2010**, *122*, 2645. (k) Anderl, T.; Nicolas, L.; Munkemer, J.; Baro, A.; Sasse, F.; Steinmetz, H.; Jansen, R.; Hçfle, G.; Taylor, R. E.; Laschat, S. *Angew*. *Chem. Int. Ed.* **2011**, *50*, 942; *Angew*. *Chem.* **2011**, *123*, 972.

(6) For representative articles on natural product having cyclopentanoid cores, see: (a) Ramaiah, M. *Synthesis* **1984**, 529. (b) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671. (c) Heasley, B. *Curr. Org. Chem.* **2014**, *18*, 641. (d) Ferreira, A. J.; Beaudry, C. M.; *Tetrahedron* **2017**, *73*, 965. For Standishinal, see (e) Minami, T.; Iwamoto, M.; Ohtsu, H.; Ohishi, H.; Tanaka, R.; Yoshitake, A. *Planta Med.* **2002**, *68*, 742. For Chromodorolide B, see (f) Tao, D. J.; Slutskyy, Y.; Overman. L. E. *J. Am. Chem. Soc.* **2016**, *138*, 2186. For CR-31-B, see (g) Schulz, G.; Victoria, C.; Kirschning, A.; Steinmann, E. Nat. Prod. Rep., 2021, 38, 18. For Subergoic acid, see (h) Iwata, C.; Takemoto, Y.; Doi, M.; Imanishi, T. *J. Org. Chem*. **1988**, *53*, 1623. For Brazilin, see (i) Nirmal, N. P.; Rajput, M. S.; Prasad, R. G. S. V.; Ahmad, M. *Asian Pac. J. Trop. Med.* **2015**, *8*, 421.

(7) Satpathi, B.; Mondal, A.; Ramasastry, S. S. V. *Chem. Asian. J.* **2018**, *13*, 1642.

(8) (a) Dhiman, S.; Ramasastry, S. S. V. *Chem. Commun.* **2015**, *51*, 557. (b) Dhiman, S.; Ramasastry, S. S. V. *Org. Lett.* **2015**, *17*, 5116. (c) Petrovic, M.; Occhiato, E. G. *Chem. - Asian J.* **2016**, *11*, 642.

(9) (a) Henderson, W. A.; Buckler, S. A. *J. Am. Chem. Soc.* **1960**, *82*, 5794. (b) Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319. (c) for a comprehensive table of phosphine pKa values and cone angles, see: Rahman, M. M.; Liu, H.-Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1989**, *8*, 3. (d) Methot, J. L.; Roush, W. R. *Adv. Synth. Catal.* **2004**, *346*, 1035. (e) Ye, L.-W.; Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2008**, *37*, 1140. (f) Wang, Z.; Xub, X.; Kwon, O. *Chem. Soc. Rev.* **2014**, *43*, 2927. (g) Bharadwaj, K. C. *RSC Adv.* **2015**, *5*, 75923. (h) Borie, C.; Ackermann, L.; Nechab, M. *Chem. Soc. Rev*. **2016**, *45*, 1368. (i) Basavaiah, D.; Reddy G. C. *ARKIVOC* **2016**, 172.

(10) Rauhut, M. M.; Currier, H. U.S. Patent 3074999, **1963**; *Chem. Abstr*. **1963**, *58*, 66109.

(11) For selected review on RC reaction, see (a) Kaur, K.; Namboothiri, I. N. N. *Chimia* **2012**, *66*, 913−920. (b) Xie, P.; Huang, Y. *Eur. J. Org. Chem*. **2013**, *2013*, 6213.

(12) Aroyan, C. E.; Dermenci, A.; Miller, S. J. *Tetrahedron* **2009**, *65*, 4069.

(13) Wang, L.-C.; Luis, A. L.; Agapiou, K.; Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2402.

(14) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404.

(15) Qiao, Y.; Kumar, S.; Malachowski, W. P. *Tetrahedron Lett.* **2010**, *51*, 2636.

(16) Zhang, X.-N.; Shi, M. *Eur. J. Org. Chem.* **2012**, *2012*, 6271.

(17) Li, Y.-Q.; Xu, G.-D.; Huang, Z.-Z. *Org. Biomol. Chem.* **2021**, *19*, 2487.

(18) (a) Morita, K. Japan Patent 6803364, **1968**; *Chem. Abstr*. **1968**, *69*, 58828s. (b) Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn*. **1968**, *41*, 2815.

(19) Baylis, A. B.; Hillman, M. E. D. German Patent 2155113, **1972**; *Chem. Abstr*. **1972**, *77*, 34174q.

(20) Bhowmik, S.; Batra, S. *Curr. Org. Chem.* **2014**, *18*, 3078.

(21) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003,** *103*, 811.

(22) Roth, F.; Gygax, P.; Frater, G. *Tetrahedron Lett.* **1992**, *33*, 1045.

(23) Keck, G. E.; Welch, D. S. *Org. Lett*. **2002**, *4*, 3687-3690.

(24) Yeo, J. E.; Yang, X.; Kim, H. J.; Koo, S. *Chem. Commun.* **2004**, 236.

(25) Kwong, C. K. -W.; Huang, R.; Zhang, M.; Shi, M.; Toy, P. H. *Chem. - Eur. J.* **2007**, *13*, 2369.

(26) Seidel, F. O.; Gladysz, J. A. *Adv. Synth. Catal.* **2008**, *350*, 2443.

(27) Seidel, F.; Gladysz, J. A. *Synlett* **2007**, 986.

(28) Wang, Y.; Jaunet, A.; Geoffroy, P.; Miesch, M. *Org. Lett.* **2013**, *15*, 6198.

(29) Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 2906.

(30) Zhu, G.; Chen, Z.; Jiang, Q.; Xiao, D.; Cao, P.; Zhang, X. J. Am. Chem. Soc. 1997, 119, 3836.

(31) Zhang, Q.; Yang, L.; Tong, X. *J. Am. Chem. Soc.* **2010**, *132*, 2550.

(32) Tian, J.; Sun, H.; Zhou, R.; He, Z. *Chin. J. Chem*. **2013**, *31*, 1348.

(33) Cao, Z. -H.; Wang, Y. -H.; Kalita, S. J.; Schneider, U.; Huang, Y. -Y. *Angew. Chem., Int. Ed.* **2020**, *59*, 1884.

(34) Zhou, R.; Wang, J.; Song, H.; He, Z. *Org. Lett.* **2011**, *13*, 580.

(35) Few selected reports: (a) Dhiman, S.; Ramasastry, S. S. V. *Ind. J. Chem.* **2013**, *52A*, 1103. (b) Shirke, R. P.; Ramasastry, S. S. V. *J. Org. Chem.* **2015**, *80*, 4893. (c) Mishra, U. K.; Yadav, S.; Ramasastry, S. S. V. *J. Org. Chem.* **2017**, *82*, 6729. (d) Bankar, S. K.; Singh, B.; Tung, P.; Ramasastry, S. S. V. *Angew. Chem. Int. Ed.* **2018**, *57*, 1678. (e) Satpathi, B.; Dutta, L.; Ramasastry, S. S. V. *Org. Lett*. **2019**, *21*, 170. (f) Maurya, J. P.; Ramasastry, S. S. V. *J. Org. Chem.* **2021**, *86*, 525.

(36) Satpathi, B.; Ramasastry, S. S. V. *Angew. Chem. Int. Ed.* **2016**, *55*, 1777.

(37) Satpathi, B.; Wagulde, S. V.; Ramasastry, S. S. V. *Chem. Commun.* **2017**, *53*, 8042.

(38) Satpathi, B.; Dutta, L.; Ramasastry, S. S. V. *Org. Lett*. **2019**, *21*, 170.

(39) Satpathi, B.; Dutta, L.; Ramasastry, S. S. V. *Org. Biomol. Chem.*, **2019**, *17*, 1547.

(40) For the synthesis of structures similar to 33, see: T. Chanda, T.; Chowdhury, S.; Anand, N.; Koley, S.; Gupta, A.; Singh, M. S. *Tetrahedron Lett.*, **2015**, *56*, 981.

(41) a) Kuroda, H.; Tomita, I.; Endo, T. *Org. Lett*., **2003**, *5*, 129. (b) Lian, Z.; Shi, M. Eur. J. Org. Chem., 2012, 581. (c) Mondal, A.; Hazra, R.; Grover, J.; Raghu, M.; Ramasastry, S. S. V. *ACS Catal*. **2018**, *8*, 2748.

(42) Guo, H.; Xu, Q.; Kwon, O. *J. Am. Chem. Soc.*, **2009**, *131*, 6318.

(43) Han, X.; Wan, C.; Li, X.; Li, H.; Yang, D.; Du, S.; Xiao, Y.; Qin, Z. *Bioorg. Med. Chem. Lett*., **2015**, *25*, 2438.

(44) (a) Guo, H.; Fan, Y. C; Sun, Z.; Wu, Y.; Kwon, O. *Chem. Rev.* **2018**, *118*, 10049. (b) Marinetti, A.; Voituriez, A. *Synlett* **2010**, *2*, 174.

(45) (a) Kosal, A. D.; Wilson, E. E.; Ashfeld, B. L. Angew. Chem., Int. Ed. 2012, 51, 12036. (b) Zhao, W.; Yan, P. K.; Radosevich, A. T. A. J. Am. Chem. Soc. 2015, 137, 616. (c) Lorton, C.; Castanheiro, T.; Voituriez, A. J. Am. Chem. Soc. 2019, 141, 10142.

(46) (a) Xie, C.; Smaligo, A. J.; Song, X.-R.; Kwon, O. ACS Cent. Sci. 2021, 7, 536−558. (b) Morita, K.; Ohta, R.; Watanabe, K.; Fujioka, H. *Asian. J. Org. Chem.*, **2018**, *7*, 829.

(47) (a)Raghu, M.; Grover, J.; Ramasastry, S. S. V. *Chem. Eur. J.* **2016**, *22*, 18316. (b) Grover, J.; Raghu, M.; Hazra, R.; Mondal, A.; Ramasastry, S. S. V. *Synthesis* **2018**, *50*, 1462.

(48) Shimizu, H.; Yoshinaga, K.; Yokoshima, S. *Org. Lett.* **2021**, *23*, 2704.

(49) Meng, H.; Xu, Z.; Qu, Z.; Huang, H.; Deng, G.-J. Org. Lett. 2020, 22, 6117.

(50) Dutta, L.; Ramasastry, S. S. V. *Org. Lett.* **2022**, *24*, 7665.

(51) a) Christie, S.; Warrington, A. *Synthesis* **2008**, *2008*, 1325. (b) Gasser, V. C. M.; Makai, S.; Morandi, B. *Chem. Commun.* **2022**, *58*, 9991. (c) Donohoe, T. J.; Callens, C. K. A.; Lacy, A. R.; Winter, C. *European J. Org. Chem.* **2012**, *2012*, 655. (d) Donohoe, T. J.; Callens, C. K. A.; Flores, A.; Lacy, A. R.; Rathi, A. H. *Chem. -Eur. J.* **2011**, *17*, 58.

(52) Sharpless, K. B.; Patrick, D. W.; Truesdale, L. K.; Biller, S. A. *J. Am. Chem. Soc.* **1975**, *97*, 2305.

(53) (a) Dangerfield, E. M.; Timmer, M. S. M.; Stocker, B. L. *Org. Lett.* **2009**, *11*, 535. (b) Dangerfield, E. M.; Plunkett, C. H.; Stocker, B. L.; Timmer, M. S. M. *Molecules* **2009**, *14*, 5298.

(54) Schmidt, V. A.; Alexanian, E. J. *J. Am. Chem. Soc.* **2011**, *133*, 11402.

(55) Cruz, D. C.; Sánchez-Murcia, P. A.; Jørgensen, K. A. *Chem. Commun.*, 2012, **48**, 6112.

(56) Kim, H. J.; Cho, S. H.; Chang, S. *Org. Lett.* **2012**, *14*, 1424.

(57) Wang, S.; Zhang, X.; Cao, C.; Chen, C.; Xi, C. *Green Chem.* **2017**, *19*, 4515.

(58) Alamillo-Ferrer, C.; Curle, J. M.; Davidson, S. C.; Lucas, S. C. C.; Atkinson, S. J.; Campbell, M.; Kennedy, A. R.; Tomkinson, N. C. O. *J. Org. Chem.* **2018**, *83*, 6728.

(59) Trost, B. M.; Kazmaier, U. *J. Am. Chem. Soc.* **1992**, *114*, 7933.

(60) Spence, T. W. M.; Tennant, G. *J. Chem. Soc., C* **1971**, 3712.

(61) (a) Popova, M.; Lazarus, L. S.; Ayad, S.; Benninghoff, A. D.; Berreau, L. M. *J. Am. Chem. Soc.* **2018**, *140*, 9721. (b) Bilokin, M. D.; Shvadchak, V. V.; Yushchenko, D. A.; Klymchenko, A. S.; Duportail, G.; Mely, Y.; Pivovarenko, V. G. Tetrahedron Lett. 2009, 50, 4714.

(62) (a) Hradil, P.; Hlavac, J.; Soural, M.; Hajduch, M.; Kolar, M.; Vecerova, R. *Mini Rev. Med. Chem.* **2009**, *9*, 696. (b) Aguilar, A. A. A.; Avila, S. J. B.; Kaufman, T. S.; Larghi, E. L. *Org. Lett.* **2018**, *20*, 5058. (c) Popova, M.; Lazarus, L. S.; Ayad, S.; Benninghoff, A. D.; Berreau, L. M. *J. Am. Chem. Soc.* **2018**, *140*, 9721. (d) Aguilar, A. A. A.; Ledesma, G. N.; Tirloni, B.; Kaufman, T. S.; Larghi, E. L. *Synthesis* **2019**, *51*, 4253.

(63) Cardoso-Lopes, E. M.; Maier, J. A.; da Silva, M. R.; Regasini, L. O.; Simote, S. Y.; Lopes, N. P.; Pirani, J. R.; Bolzani, V. da S.; Young, M. C. M. *Molecules* **2010**, *15*, 9205.

(64) Hā-Huy-Kê; Luckner, M.; Reisch, J. *Phytochemistry* **1970**, *9*, 2199.

(65) (a) Wang, W.; Cencic, R.; Whitesell, L.; Pelletier, J.; Porco, J. A. Jr. *Chem. -Eur. J.* **2016**, *22*, 12006. (b) Hodgkinson, J. T.; Gross, J.; Baker, Y. R.; Spring, D. R.; Welch, M. *Chem. Sci*. **2016**, *7*, 2553. (c) Horák, R.; Kořistek, K.; Šamšulová, V.; Slaninová, L.; Grepl, M.; Kvapil, L.; Funk, P.; Hradil, P.; Soural, M. *J. Heterocycl. Chem.* **2020**, *57*, 1605.

(66) Klásek, A.; Kořistek, K.; Polis, J.; Košmrlj, J. *Tetrahedron* **2000**, *56*, 1551.

(67) Stadlbauer, W.; Lutschounig, H.; Schindler, G.; Witoszynskyj, T.; Kappe, T. *J. Heterocycl. Chem.* **1992**, *29*, 1535.

(68) (a) Kafka, S.; Klasek, A.; Kosmrlj, J. *J. Org. Chem*. **2001**, *66*, 6394. (b) Chen, Y. L.; Chung, C. H.; Chen, I. L.; Chen, P. H.; Jeng, H. Y. *Bioorg. Med. Chem*. **2002**, *10*, 2705. (c) Kafka, S.; Proisl, K.; Kasparkova, V.; Urankar, D.; Kimmel, R.; Kosmrlj, J. *Tetrahedron* **2013**, *69*, 10826.

(69) Wang, L.; Zhu, H.; Peng, T.; Yang, D. *Org. Biomol. Chem*. **2021**, *19*, 2110.

(70) Kuroda, H.; Tomita, I.; Endo, T. *Org. Lett*. **2003**, *5*, 129.

(71) Wilson, J. E.; Sun, J.; Fu, G. C. . *Angew*. *Chem*., *Int*. *Ed*. **2010**, *122*, 165.

(72) Lian, Z.; Shi, M. *Eur. J. Org. Chem.* **2012**, *2012*, 581.

(73) Liang, L.; Li, E.; Xie, P.; Huang, Y. *Chem. -Asian J.* **2014**, *9*, 1270.

(74) Ramachary, D. B.; Reddy, P. T.; Kumar, S. A. *Org*. *Biomol*. *Chem*. **2017**, *15*, 9785.

(75) (a) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. *Nat. Prod. Rep*. **2013**, *30*, 694. (b) Marcos, I. S.; Moro, R. F.; Costales, I.; Basabe, P.; Díez, D. *Nat. Prod. Rep*. **2013**, *30*, 1509. (c) Petrović, M.; Occhiato, E. G. *Chem. Asian J.* **2016**, *11*, 642. (d) Vivekanand, T.; Satpathi, B.; Bankar, S. K.; Ramasastry, S. S. V. *RSC Adv.* **2018**, *8*, 18576.

(76) Richter, J. M.; Ishihara, Y.; Masuda, T.; Whitefield, B. W.; Llamas, T.; Pohjakallio, A.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 17938.

(77) (a) Ouyang Kazuo Koike, Y.; Ohmoto, T. *Phytochemistry* **1994**, *37*, 575. (b) Scarpi, D.; Faggi, C.; Occhiato, E. G. *J. Nat. Prod.* **2017**, *80*, 2384.

(78) Lai, E.; De Lepeleire, I.; Crumley, T. M.; Liu, F.; Wenning, L. A.; Michiels, N.; Vets, E.; O'Neill, G.; Wagner, J. A.; Gottesdiener, K.. *Clin. Pharmacol. Ther.* **2007**, *81*, 849.

(79) Kong, Y. C.; Ng, K. H.; Wat, K. H.; Wong, A.; Saxena, I. F.; Cheng, K. F.; But, P. P.; Chang, H. T. *Planta Med.* **1985**, *51*, 304.

(80) (a) Zhang, Y.-C.; Jiang, F.; Shi, F. *Acc. Chem. Res.* **2020**, *53*, 425. (b) Tu, M.-S.; Chen, K.-W.; Wu, P.; Zhang, Y.-C.; Liu, X.-Q.; Shi, F. *Org. Chem. Front.* **2021**, *8*, 2643.

(81) For some selected articles on 3-nitroindoles as electrophiles, see: (a) Cerveri, A.; Bandini, M. *Chin. J. Chem.* **2020**, *38*, 287. (b) Rkein, B.; Bigot, A.; Birbaum, L.; Manneveau, M.; De Paolis, M.; Legros, J.; Chataigner, I. *Chem. Commun.* **2021**, *57*, 27. (c) Rkein, B.;

Manneveau, M.; Noël-Duchesneau, L.; Pasturaud, K.; Durandetti, M.; Legros, J.; Lakhdar, S.; Chataigner, I. *Chem. Commun.* **2021**, *57*, 10071. (d) Li, Y.-L.; Wang, K.-K.; He, X.-L. *Adv. Synth. Catal*. **2022**, *364*, 3630.

(82) (a) Li, K.; Goncalves, T. P.; Huang, K.-W.; Lu, Y. *Angew*. *Chem*., *Int*. *Ed*. **2019**, *58*, 5427. (b) Wang, H.; Zhang, J.; Tu, Y.; Zhang, J. *Angew*. *Chem*., *Int*. *Ed*. **2019**, *58*, 5422. (c) Cerveri, A.; Faza, O. N.; López, C. S.; Grilli, S.; Monari, M.; Bandini, M. *J. Org. Chem*. **2019**, *84*, 6347. (d) Birbaum, L.; Gillard, L.; Gerard, H.; Oulyadi, H.; Vincent, G.; Moreau, X.; De Paolis, M.; Chataigner, I. *Chem.- Eur. J.* **2019**, *25*, 13688. (e) Jin, L.-W.; Jiang, F.; Chen, K.-W.; Du, B.-X.; Mei, G.-J.; Shi, F. *Org. Biomol. Chem.* **2019**, *17*, 3894.

(83) (a) Andreini, M.; De Paolis, M.; Chataigner, I. *Catal. Commun.* **2015**, *63*, 15. (b) Li, Y.; Tur, F.; Nielsen, R. P.; Jiang, H.; Jensen, F.; Jørgensen, K. A. *Angew. Chem. Int. Ed*. **2016**, *55*, 1020.

(84) Dutta, L.; Chattopadhyay, A.; Yadav, N.; Ramasastry, S. S. V. *Org. Biomol. Chem*., **2023**, *21*, 738.

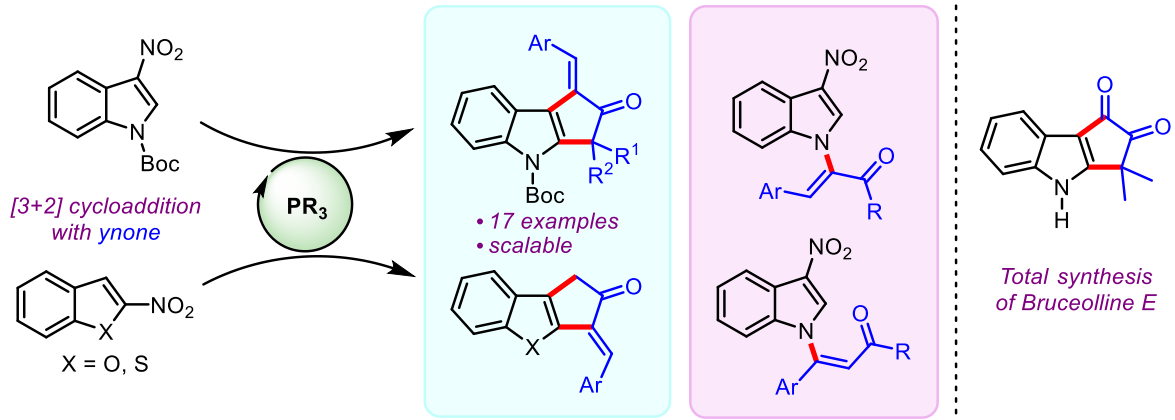
(85) (a) Wales, S. M.; Rivinoja, D. J.; Gardiner, M. G.; Bird, M. J.; Meyer, A. G.; Ryan, J. H.; Hyland, C. J. T. *Org. Lett.* **2019**, *21*, 4703. (b) Laviós, A.; Sanz-Marco, A.; Vila, C.; Munoz, M. C.; Pedro, J. R.; Blay, G. *Org. Lett*. **2022**, *24*, 2149. (c) Lu, S.-C.; Zheng, P.-R.; Liu, G. *J. Org. Chem*. **2012**, *77*, 7711.

(86) (a) Ekebergh, A.; Börje, A.; Mårtensson, J. *Org. Lett.* **2012**, *14*, 6274. (b) Ekebergh, A.; Mårtensson, J.; Ekebergh, C. L. *ACS Omega* **2020**, *5*, 33455.

List of publications

(1) *"Phosphine-catalysed denitrative rearomatising [3 + 2] annulation of α,β-ynones and 3-nitroindoles"*

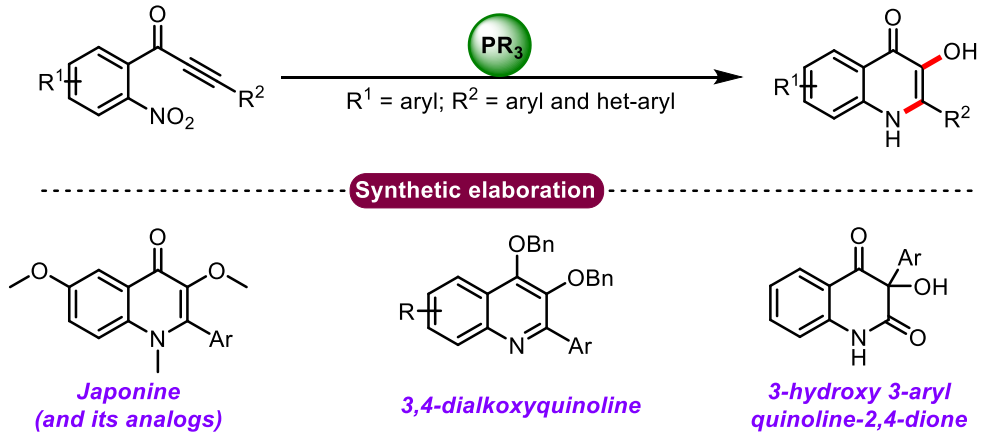
Dutta, L.; Chattopadhyay, A.; Yadav, N; Ramasastry, S. S. V. *Org. Biomol. Chem.*, **2023**, *21*, 738-742. *[Invited for the 20th anniversary themed collection of OBC]*



* *First denitrative rearomatising [3+2] annulation of 3-nitroindole and α,β-ynone*
* *Rapid synthesis of a variety of α-arylidene cyclopenta[b]indoles*
* *Unusual class of α and β-N-indolylenone*

(2) *"Phosphine-Mediated Redox Cyclization of 1-(2-Nitroaryl)prop-2-ynones to 3-Hydroxyquinolin-4-ones: Formal Intramolecular Oxyamination of α,β-Ynones"*

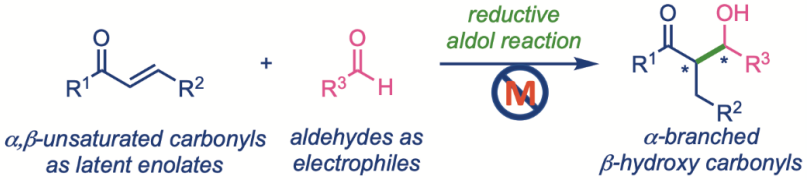
Dutta, L.; Ramasastry, S. S. V. *Org. Lett.* **2022**, *24*, 7665–7670.



* *First intramolecular oxyamination reaction of α,β-ynones*
* *Synthesis of 3HQ under neutral condition*

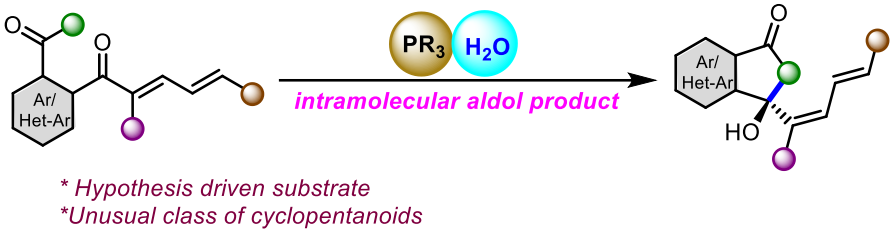
(3) *"Metal-Free Reductive Aldol Reactions"*

Dutta, L.; Mondal, A.; Ramasastry, S. S. V. *Asian J. Org. Chem.* **2021**, *10*, 680-691. *[Invited for a special issue on 'Organocatalysis']*



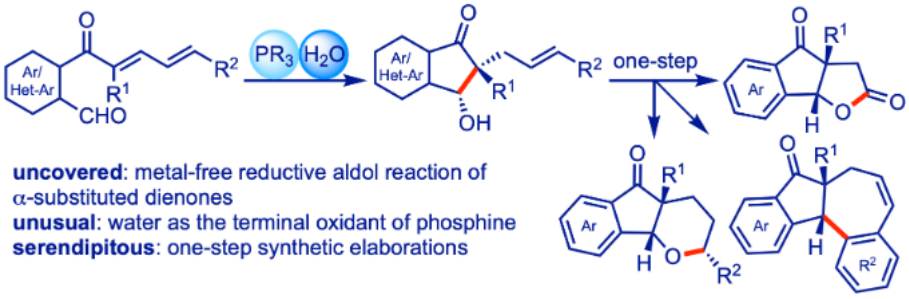
(4) "Phosphine- and Water-Promoted Pentannulative Aldol Reaction"

Satpathi, B.; **Dutta, L**.; Ramasastry, S. S. V. *Org. Biomol. Chem.*, **2019**, *17*, 1547-1551.



(5) "Metal- and Hydride-Free Pentannulative Reductive Aldol Reaction"

Satpathi, B.; **Dutta, L**.; Ramasastry, S. S. V. *Org. Lett.* **2019**, *21*, 170–174.



(6) "Conceptual advances in nucleophilic organophosphine-promoted synthetic transformations."

Dutta, L.[#]; Mondal, A.[#]; Maurya, J; Mukhopadhyay, D; Ramasastry, S. S. V. (communicated) *[Invited feature article]*

Lona Dutta

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Gender: Female
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Academic Summary:

Aug 2017 – till date	**Ph.D. Scholar** at Indian Institute of Science Education and Research (IISER) Mohali, India. *Thesis title: "**Phosphine-mediated Annulations of Designed Enones and Ynones**."* Supervisor: Dr. S. S. V. Ramasastry.
Aug 2014 – May 2016	**M.Sc. in Organic Chemistry** from Scottish Church College, University of Calcutta, West Bengal, India. Marks obtained: 78.8%, First Class.
July 2011 – June 2014	**B.Sc. in Chemistry (Honours)** from Scottish Church College, University of Calcutta, India. Marks obtained: 71.2%, First Class.
May 2009 – June 2011	**Higher Secondary (W.B.C.H.S.E) in Science**, West Bengal, India. Marks obtained: 84.8%, First Class.
April 2009	**Secondary (W.B.B.S.E)**, West Bengal, India. Marks obtained: 80.4%, First Class.

Academic Achievements:

- Qualified **Graduate Aptitude Test in Engineering (GATE 2017)** (All India Rank 1013).
- Qualified **Joint Admission for M.Sc. (JAM 2014)** (All India Rank 299).
- Recipient of **INSPIRE Scholarship (2011-2016)** by the Department of Science and Technology (DST) of India. (For being among the top 1% in the state board and pursuing science at undergraduate and post graduate level with first-class).

Research Interests:

- Organic synthesis and its direct application in biological systems and bio-catalysis.
- Photoredox catalysis, Metal catalysis and organo-catalysis.
- Asymmetric methodology development.
- Total synthesis of natural products.

Research Experiences:

Aug 2017 – till date	**Senior Research Fellow** at IISER Mohali, India. ***Thesis title:*** *Phosphine-mediated Annulations of Designed Enones*

	and Ynones. Supervisor: Dr. S. S. V. Ramasastry.
March 2016 – May 2016	**M. Sc. project work** at Bhabha Atomic Research Centre (BARC), India. **Project title:** Organocatalyzed synthetic studies on Stereo-defined 1,3-disilyl compounds. Supervisor: Dr. Sunil. Kumar Ghosh, Scientific Officer-H (+).
Oct 2015 – Nov 2015	**Winter Project** at Bhabha Atomic Research Centre (BARC), India **Project title:** Synthetic studies on Stereo-defined 1,3-disilyl Compounds with Embedded Functional Groups. Supervisor: Dr. Sunil. Kumar Ghosh, Scientific Officer-H (+).

Teaching Experiences:

Aug 2018 – Nov 2018	Teaching Assistant in CHM111 Laboratory Course for BS-MS.
Jan 2019 – Apr 2019	Teaching Assistant in CHM112 Laboratory Course for BS-MS.
Jan 2019 – Apr 2019	Teaching Assistant in CHM112 Laboratory Course for BS-MS.
Aug 2017 – till date	Trained Three Masters Students and Three Summer Interns.
Feb 2016 – May 2016	Guest Lecturer at Narula Institute of Technology, affiliated with the WBUT and the AICTE.

Expertise and Skill:

- First-hand experience in multi-step organic synthesis by handling air/moisture sensitive reagents/reactions and gram/milligram scale reactions.
- Well versed with various computer packages viz. Microsoft Office, Paint, ChemDraw, SciFinder and X-Ray crystallographic packages viz. Olex2 and Mercury.
- Trained and expertise in handling instruments like IR (Perkin–Elmer FT-IR), NMR (Bruker Biospin Avance III FT-NMR, 400 MHz), HPLC (Waters 502), GC-MS (Agilent), Polarimeter (Anton-Par), and Ozonolysis apparatus (Oz-Air).
- Good communication skill, self-motivated, creative, well organized and a good team worker with leadership qualities.

Publications:

1. Conceptual advances in nucleophilic organophosphine-promoted synthetic transformations.

Dutta, L.[#]; Mondal, A.[#]; Maurya, J; Mukhopadhyay, D; Ramasastry, S. S. V. (communicated) *Invited feature article*

2. Phosphine-catalysed denitrative rearomatising [3 + 2] annulation of α,β-ynones and 3-nitroindoles.

Dutta, L.; Chattopadhyay, A.; Yadav, N; Ramasastry, S. S. V. *Org. Biomol. Chem.*, **2023**, *21*, 738. *[Invited for the 20th anniversary themed collection of OBC]*

3. Phosphine-Mediated Redox Cyclization of 1 (2-Nitroaryl)prop-2-ynones to 3 Hydroxyquinolin-4-ones: Formal Intramolecular Oxyamination of α,β-Ynones.

Dutta, L.; Ramasastry, S. S. V. *Org. Lett.* **2022**, *24*, 7665.

4. Metal-Free Reductive Aldol Reactions.
Dutta, L.; Mondal, A.; Ramasastry, S. S. V. *Asian J. Org. Chem.* **2021**, *10*, 680.
[*Invited for a special issue on 'Organocatalysis'*]

5. Phosphine- and Water-Promoted Pentannulative Aldol Reaction.
Satpathi, B.; **Dutta, L.**; Ramasastry, S. S. V. *Org. Biomol. Chem.*, **2019**, *17*, 1547.

6. Metal- and Hydride-Free Pentannulative Reductive Aldol Reaction.
Satpathi, B.; **Dutta, L.**; Ramasastry, S. S. V. *Org. Lett.* **2019**, *21*, 170.

Conference Presentations:

- Presented a poster in the ***RSC Twitter Conference 2023*** (28th Feb, 2023).
- Presented a poster in the ***Recent Advances in Bioorganic and Medicinal Chemistry (RABMC)*** at the National Institute of Pharmaceutical Education and Research (NIPER), Mohali, India (19th November, 2022).
- Presented a poster in the ***CRSI National Symposium in Chemistry (NSC-29)*** at the Indian Institute of Science Education and Research (IISER) Mohali, India (8th-10th July 2022).
- Presented a poster in the ***First Virtual 16th Junior National Organic Conference (J-NOST)*** at the CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad, India. (31st October-1st November, 2020).
- Participated in the ***1st CRIKC Chemistry Symposium (CCS-2019)*** at the Indian Institute of Science Education and Research (IISER) Mohali, India (2nd-3rd November 2019).
- Participated in a symposium on ***Recent Advances in Bioorganic and Medicinal Chemistry (RABMC)*** at the National Institute of Pharmaceutical Education and Research (NIPER), Mohali, India (30th August 2019).
- Participated in the ***Recent Advances in Organic and Bio-organic Chemistry (RAOBC)*** at the Indian Institute of Science Education and Research (IISER) Mohali, India (22nd-24th March 2019).