New Strategies to Synthesize Small and Medium Sized Rings Bearing a Stereogenic Center

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the degree of Doctor of Philosophy

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Dedicated to
My Beloved Grandmother and My Mother

Late Mrs. Jaswant Kaur

and Mrs. Karamjit Kaur

Declaration

I do hereby declare that the work presented in this thesis titled "***New Strategies to Synthesize Small and Medium Sized Rings Bearing a Stereogenic Center***" has been carried out by me under the supervision of **Dr. S. S. V. Ramasastry** 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 fellowship to any other university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly with due acknowledgements 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.

Bara Singh

Date:

Place: IISER Mohali

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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Carbo- and heterocyclic compounds consisting of small and medium-sized rings with a stereogenic center are pertinent in organic chemistry. The importance of scaffolds containing tertiary, all-carbon quaternary/spiro centers in synthetic chemistry, organic functional materials and pharmaceuticals necessitates the development of innovative methodologies to access them in an efficient and atom-economic manner.

The thesis entitled "*New Strategies to Synthesize Small and Medium Sized Rings Bearing a Stereogenic Center*" describes the efforts towards the development of novel approach to construct small and medium ring-sized carbocycles bearing 3^o, all-carbon quaternary/spiro center as well as assembly of at least two vicinal stereogenic centers (one being an all-carbon spiro center). The content of the thesis has been divided into three chapters. A brief introduction is provided in all the chapters, the compounds are sequentially numbered (bold), and references are marked sequentially as superscripts and listed at the end of the thesis.

Five-membered carbocycles are privileged structures found in various natural products, either as a prominent component of a molecular framework or as a less apparent, embedded substructure within a more sophisticated polycyclic network. Among the different classes of cyclopentanoids, cyclopentannulated arenes and heteroarenes are the primary structural motifs of many bioactive natural compounds and are relevant in pharmaceutical chemistry and material science. The first chapter of the thesis describes the neutral $PdCl_2$-catalyzed Nazarov-type cyclization of designed allyl acetates to synthesize various indenes possessing a tertiary stereocenter and a diverse range of cyclopenta[*b*]annulated heteroarenes in good to excellent yields. Several other complex polycyclic cyclopentanoids such as analogues of brazilin, pestalachloride D, BMS-593214, and highly substituted indacenes were also obtained in excellent yields under this acid-free cyclization condition. Throughout the study, the methodology's generality and practicability were carefully evaluated. After successfully establishing an acid-free Pd-catalyzed Nazarov-type cyclization, this method was utilitzed for the first total synthesis of (±) *β*-diasarone using suitable synthetic transformations on indene, obtained through the $PdCl_2$-catalyzed cyclization of substituted allylic pivalate.

The importance of scaffolds with an all-carbon quaternary/spiro center in a wide range of natural products, synthetic chemistry, organic functional materials, and pharmaceuticals necessitates the development of innovative methodologies to access them. The second chapter of the thesis describes an unprecedented Pd(II)-promoted *5-endo-trig* carbocyclization similar to acid-free Nazarov-type cyclization to synthesize fused cyclopentenes with an all-carbon

quaternary/spiro center. The reaction demonstrated remarkable functional group tolerance with electronically varied substituents, allowing good to excellent yields of spirocyclopentene oxindoles, cyclopentene-fused arenes and heteroarenes. Furthermore, several bioactive compounds, for example, those representing the spiroindimicin and polyveoline families of natural products were efficiently synthesized under these acid-free reaction conditions. The first acid-free total synthesis of taiwaniaquinone H and dichroanone further demonstrated the synthetic utility of this method. In this case, desired substituted indene was synthesized from suitable acetate and oxidized by CAN to generate taiwaniaquinone H. Following that, taiwaniaquinone H was treated with methanolic KOH, resulting in the formation of dichroanone. Natural products and pharmaceutically relevant compounds were synthesized efficiently without any external oxidant, base, addition, or ligand, demonstrating the method's generality and practicability.

We have presented a hybrid strategy that combines the nucleophilic features of sulfur ylides with the electrophilic properties of azaarenium salts to create new classes of spirocarbocyclic-piperidines/quinolones bearing contiguous stereogenic centers in good to excellent yields. In the case of pyridinium salts, three unique rings and three contiguous stereocenters (two of which are all-carbon vicinal spiro centers) are generated through a single-pot synthetic operation. While in the case of enone tethered quinolinium salts, the formation of three novel rings with an unusual *6-3-7* fusion, four new C-C bonds, five contiguous stereogenic centers, and a fully functionalized quinoline core combined with a methylene sulfoxide moiety was observed in a highly diastereoselective manner in a single step. These hybrid structures and their analogs containing indanes, beznocyclohaptanes, cyclopropanes, and piperidines/ (tetrahydro)quinolones could be used as lead compounds in drug development.

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
COD	cyclooctadiene
d	day(s)
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of a doublet
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	electrospray ionization
FT-IR	fourier-transform infrared spectroscopy
THF	tetrahydrofuran
TMS	trimethylsilyl
TMS	tetramethylsilane
TLC	thin layer chromatography
h	hour(s)
HRMS	high resolution mass spectrometry
Hz	Hertz
ppm	parts per million
IBX	2-iodoxybenzoic acid
J	coupling constant

m	multiplet
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mmol	milli mole(s)
m.p.	melting point
MS	molecular sieves
m/z	mass/charge
NBS	*N*-bromosuccinimide
p-TSA	*p*-toluenesulfonic acid
q	quartet
qd	quartet of doublet
RT	room temperature
s	singlet
t	triplet

Chapter 1

Palladium-catalyzed Nazarov-type cyclization of allylic acetates to cyclopentanoids

Five-membered carbocycles are privileged structures in various natural products, either as a prominent component of a molecular framework or as a less apparent, embedded substructure within a more sophisticated polycyclic framework. In particular, cyclopentanes have been bestowed with diverse range of functionalities which has led to bewildering array of natural products. In this context, synthetic chemists have become more focused towards developing and testing new synthetic procedures for synthesis of cyclopentanes containing complex targets. (Figure **1**).[1] For instance, Flupsostenol, a commercialized drug is a potent and highly selective prostaglandin F2-alpha (FP) receptor agonist. Sordaricin is an antifungal agent with promising results.[2] Peramivir with a highly functionalized cylcopantane moiety has antiviral efficacy *via* inhibiting influenza neuraminidase.[3]

Similarly, cyclopentane fused arenes and heteroarenes are essential intermediates in producing biologically relevant compounds such as pharmaceutical components and natural products. In particular, pentanulated arenes, such as indanes (benzocyclopentanes), indenes (benzocyclopentadienes), and their derivatives hold importance

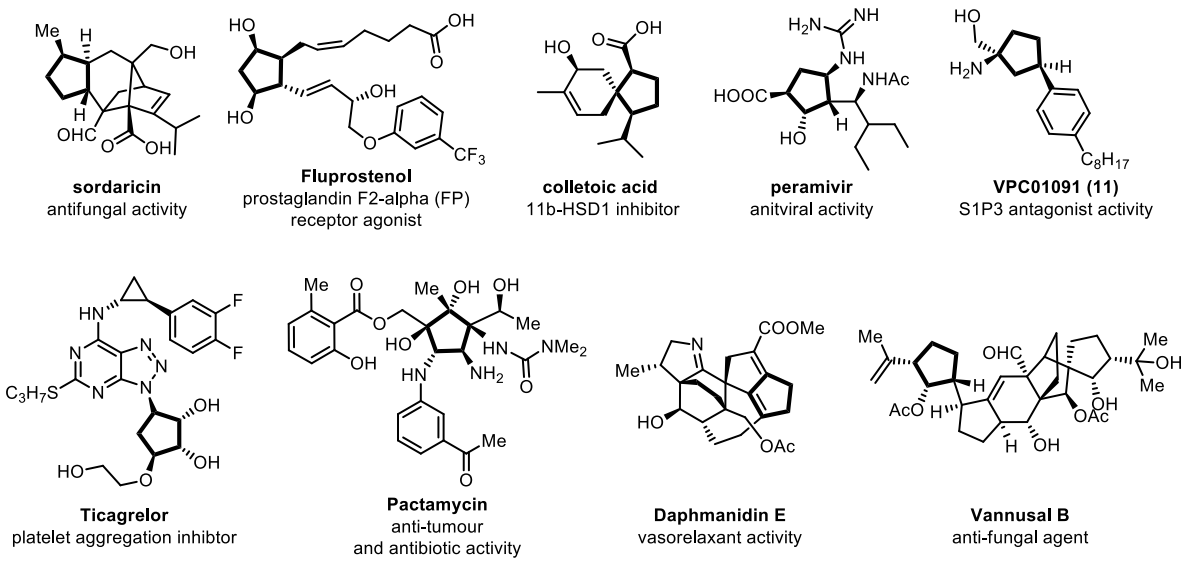


Figure 1: Natural products and pharmaceutically important molecules possessing cyclopentanes.

in the field of material science and can be used as chiral ligands, organocatalysts in organic synthesis. Also, these scaffolds possess diverse range of biological activities such as antitumor, antihypercholesterolemic, antiallergic, anticonvulsant, herbicidal, fungicidal, and antimicrobial *etc*. (Figure **2**). For example, Indinavir is a protease inhibitor used for treatment of human immunodeficiency virus infections (HIV).[4] Paucifloral F is a resveratrol-like polyphenolic natural product with cytotoxic, antibacterial, and anti-HIV activities.[5] Tripartin indanone-based natural molecule identified from the culture broth of *Streptomyces sp.* with a larva of the dung beetle *Copris tripartitus* is one of the putative KDM4 inhibitors.[6] Tetrapetalone A, a substance produced from the *Streptomyces sp.* USF-4727 strain is a soybean lipoxygenase inhibitor.[7] Ileabethin and Ilebethoxazole diterpenes, isolated from *Pseudopterogorgia elisabetha* exhibited significant antimycobacterial efficacy against *Mycobacterium tuberculosis*.[8]

Similarly, various pentannulated heteroarenes consisting indole, pyrrole, benzothiophene, and chromenes are also popular among organic chemists (Figure **2**). Roseophilin is a cyclopenta-fused pyrrole macrocycle, an antibiotic and anti-cancer drug derived from *Streptomyces griscovirides*.[9a] BMS-593214, a direct FVIIa inhibitor with a 2,3-dihydro-1*H*-indane structure and a chemically *cis*-fused tetrahydroquinoline structure, showed antithrombotic bioactivity.[9b] Brazilin and related natural products, isolated from *Caesalpinia sappan* L heartwood alcoholic extracts are important tetracyclic homoisoflavanoid with chromane skeleton structurally *cis*-fused to a 2,3-dihydro-1*H*-indene moiety. These have

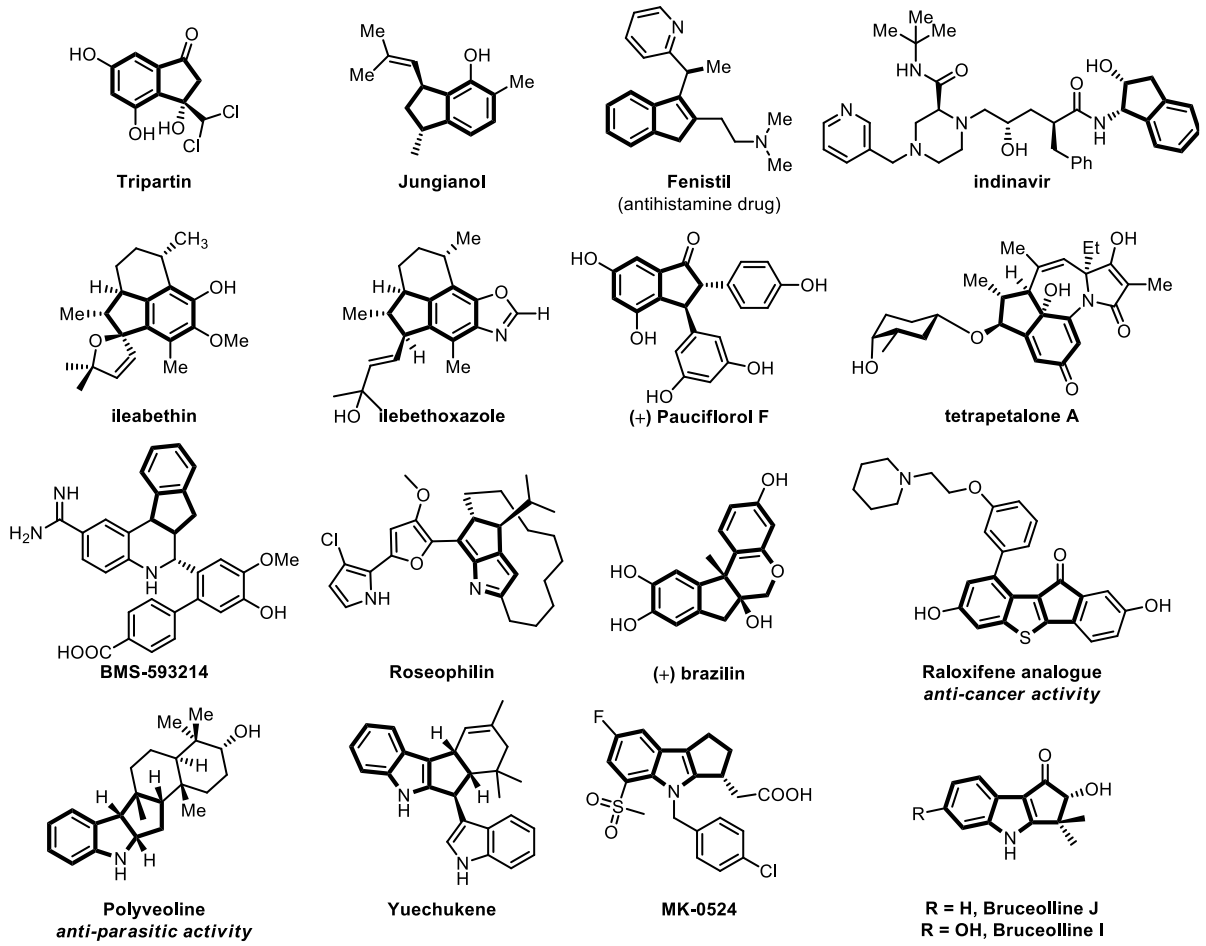


Figure 2: Representative examples of bioactive cyclopenta-fused arenes and heteroarenes.

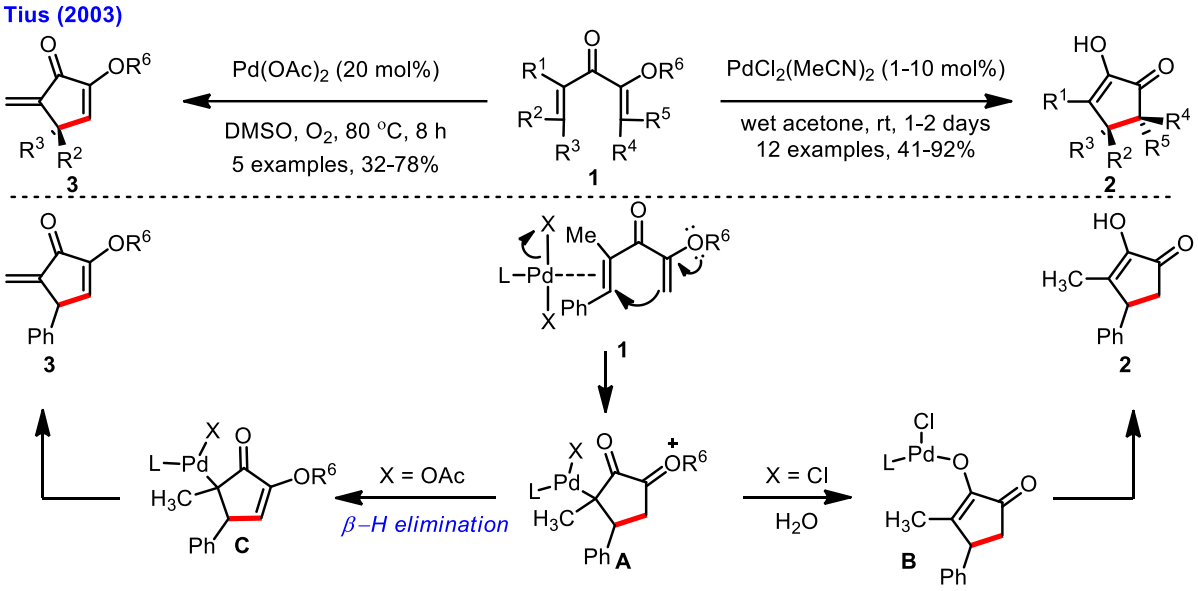
potent anti-inflammatory, hepatoprotective, vasorelaxant, antibacterial, anticancer, and antitumor properties.[9c] Due to the significant electrical properties of organic semiconductors, cyclopenta[*b*]annulated benzothiophenes may also be employed in these materials.[10] Many alkaloids and medicinally relevant substances also have the cyclopenta[*b*]indole core. Polyveoline is a cyclopenta[*b*] indole-based sesquiterpene isolated from *Polyalthia suaveolens* with antiparasitic properties.[11a] Another example of cyclopenta[*b*]annulated indole yuehchukene is known to exhibit a wide range of biological activities, such as anti-fertility and estrogenic activity, extracted from *Murraya paniculata*.[11b]

Thus, due to the various benefits and importance of cyclopentannulated arenes and heteroarenes, there is a need to develop generic and efficient techniques for synthesis of cyclopentanoids. Till date, organic chemists have developed multiple procedures for synthesis of (hetero)arene-fused cyclopentanes. The Nazarov cyclization is known as a reliable and effective method for producing extremely chemo-, regio-, and stereoselective fused cyclopentanes.[12] The traditional Nazarov variation uses aryl vinyl ketones as the reactants;

however, recent advances have provided numerous unique precursors for the *in situ* formation of a 4π-electron system, and subsequent Nazarov-type cyclization thus delivering cyclopentenone derivatives. However, the majority of these substrates necessitate the use of Brønsted or Lewis acidic reagents, typically in stoichiometric concentrations.[13] This aspect severely restricts the method's adaptation for systems with sensitive functionality. Therefore, a potential substitute for acid-promoted Nazarov-type reactions needs to be considered.

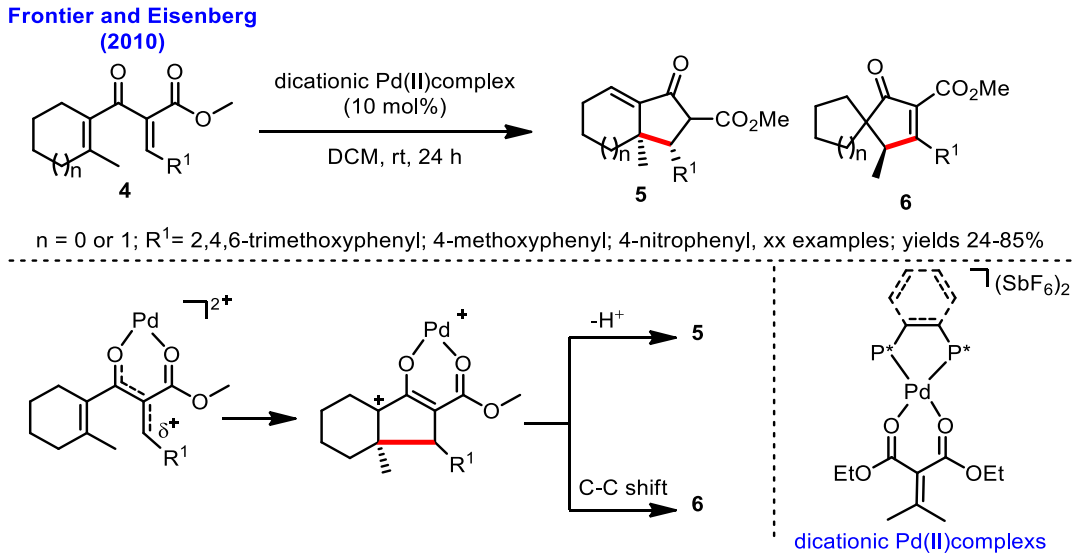
In the late 20th century, the efficient strategies were developed by introducing the transition metals to make carbon-carbon bonds (C-C bonds), which opened a new vista towards natural product synthesis, pharmaceutical chemistry, and materials chemistry. Among all the transition metals, palladium-catalyzed C-C bond formation techniques have gone a long way and are now an important aspect of organic synthesis.[14] Palladium (Pd) has attracted a lot of attention in transition metal catalyzed processes. Despite its high cost compared to many other transition metals, it is very efficient for the reasons listed below: 1) Pd can help to couple less reactive substrates such as aryl chlorides. 2) Pd enables reactions to take place at lower temperatures. 3) Pd has an unusually high turnover number (TON) for large-scale industrial processes.[15] The need for innovative methodologies for synthesising five-membered carbocycles has prompted a surge in Nazarov cyclization research. This newfound interest in the reaction has resulted in the development of numerous novel Pd-catalyzed Nazarov reactions for producing the pentadienyl cation intermediates required for cyclization.

In 2003, Tius *et al.* discovered the first Pd-catalyzed Nazarov cyclization of divinyl ketones **1** (Scheme **1**).[16] Activation of the electron-poor olefin by palladium complexation seems to be a more likely first step. According to the nature of the catalyst, this reaction occurred under mild conditions and produced two types of products. Though an oxidative process, the $PdCl_2$-catalyzed cyclization of α-alkoxy dienones **1** provided 2-hydroxycyclopentenones **2**, which proceed through a palladium enolate intermediate **B** *via* rapid protonation of **A** through *in situ* formed HCl upon hydrolysis. At the same time, the $Pd(OAc)_2$-catalyzed reaction yielded cross-conjugated cyclopentenones **3** by allowing β-hydride elimination to compete with the protonation of **C**.



Scheme 1: Pd(II) catalyzed Tius-Nazarov cyclization of α-alkoxy dienones **1**.

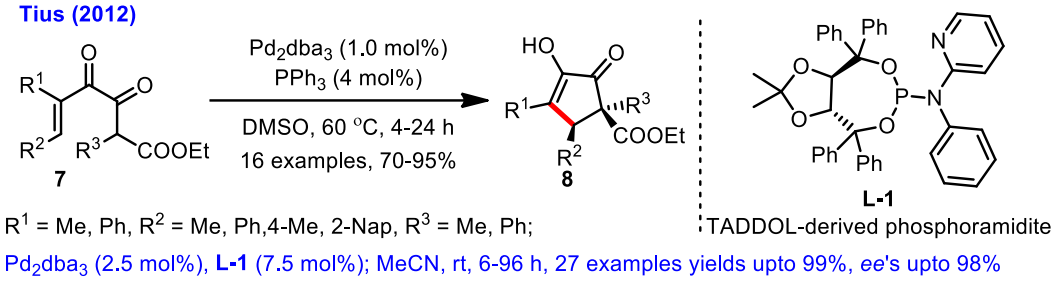
In 2010, Frontier and Eisenberg demonstrated the application of dicationic Pd(II) complex as an active Lewis acid for Nazarov cyclization of electronically polarized substrates **4**.[17] Competing formation of a spirocyclic product **6** over **5** was observed for substrates in which a quaternary center was generated upon the C-C shift. It was also observed that the addition of NaBAr^f affects product distribution (Scheme **2**).



Scheme 2: Frontier and Eisenberg dicationic's Pd(II)-catalyzed Nazarov cyclization.

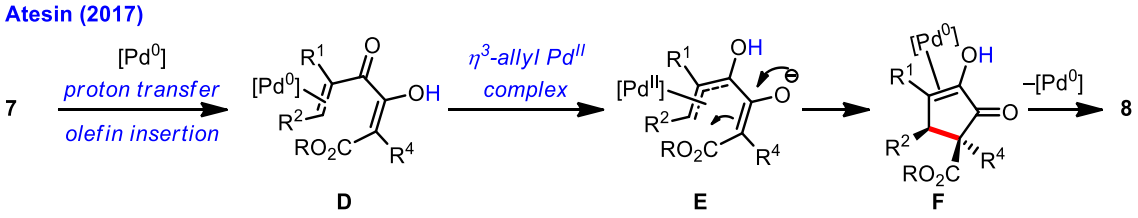
In 2012, the Tius group explored diketoesters **7** under neutral reaction conditions to synthesize various 2-hydroxycyclopentenones **8** *via* Pd-catalyzed Nazarov-type cyclization.[18a] It was the first Pd^0-catalyzed Nazarov-type cyclization of diketoesters **7** (Scheme **3**). Under absolutely neutral *p*H conditions such as Pd_2dba_3 as catalyst and PPh_3 as a basic ligand, the

reaction proceeds in good to excellent yields for a range of substrates showing significantly broader scope. The asymmetric reaction version was produced in 2015 by the same group using the TADDOL-derived phosphoramidite ligand **L-1,** Pd_2dba_3, and acetonitrile as the solvent. Surprisingly, under optimal reaction conditions, the reaction of diketoesters **7** produced a broad range of 2-hydroxycyclopentenones **8** with excellent yields and enantioselectivities (Scheme **3**).[18b]



Scheme 3: Pd(0) catalyzed Tius-Nazarov cyclization of diketoesters **7**.

In 2017, Atesin investigated the mechanistic aspects of Pd^0-catalyzed Nazarov cyclization of **7** using DFT calculations.[19] By comparing the free energies for the concerted and stepwise proton transfer and cyclization phases, this neutral Pd^0 catalyzed Nazarov-type cyclization was concluded to be an intramolecular allylic alkylation reaction (Scheme **4**). In both processes, the proton transfer followed by cyclization has the lowest free energy of activation. The critical involvement of the Pd^0 catalyst was identified by comparing cyclization processes with and without a Pd^0 catalyst. The enol tautomerization of the ketoester **7** follows a catalytic cycle that begins with the first coordination of Pd^0 to the alkene group of the diketoesters **7**. This catalyst-to-Nazarov substrate binding mode is unusual and specific to the soft Pd^0 metal center. The crucial intermediate η^3-allyl Pd^{II} complex **E** development proceeds from proton transfer from the enol to the ketone. The relatively stable intermediate η^3-allyl Pd^{II} complex **E** was critical for the outcome of high induction of chirality due to steric interactions

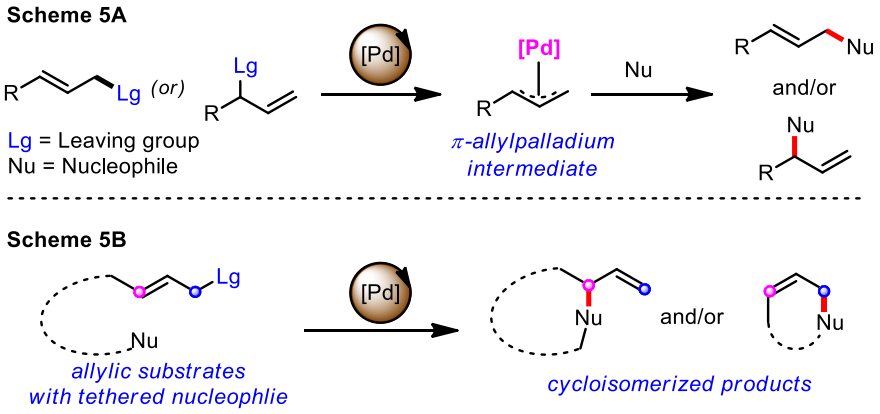


Scheme 4: Atesin's proposed mechanism based on DFT studies.

between the TADDOL phosphoramidite ligand **L-1**, metal and **E**. An intramolecular nucleophilic attack forms a C-C on bond from the C2 to the C6 terminus. The proton transfers

and the cyclization stages synchronized with the Pd migration. Nazarov substrates nevertheless gave the same Nazarov products in the presence of a palladium (0) catalyst, albeit by a different mechanism.

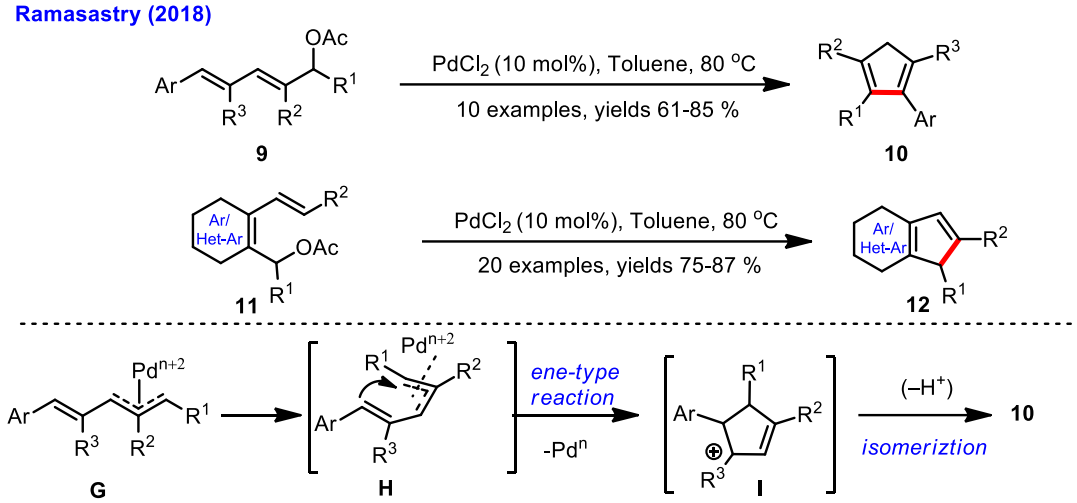
Another powerful synthetic method of constructing new C-C/C-X bonds is Tsuji-Trost palladium-catalyzed allylic C(sp^3)–H functionalization. Tsuji and Trost's seminal contributions to the allylic alkylation of π-allylpalladium complexes paved the path for producing a wide range of carbon-carbon and carbon-heteroatom linkages. The Tsuji-Trost reaction is mechanistically extremely distinct from usual Pd-catalyzed carbon/heteroatom bond formation; proceeds *via* a π-allyl palladium intermediate. As shown in Scheme **5A**, an allylic C(sp^3)–H functionalization *via* the η^3-allylpalladium species is involved in the Tsuji-Trost reaction. The Tsuji-Trost allylic alkylation process forms C-C bonds between C(sp^3)-H and depending on the nature of the nucleophile. In the case of stable or soft pronucleophile a direct attack on the π-allylic termini occurred without any coordination to the Pd complex, whereas Pd(II) species, coordinate with hard nucleophiles or unstabilized nucleophiles to form intermediate *via* reductive elimination. Using different leaving groups and diverse phosphorus, nitrogen, and sulfur-based ligands, the scope of this reaction has been expanded to accommodate different carbon, nitrogen, and oxygen-based nucleophiles. The electrophilic π-allylpalladium species can be nucleophilically trapped either intermolecularly or intramolecularly. Scheme **5B** shows intramolecular Pd-catalyzed Tsuji-Trost type transformations that lead to the formation of a variety of complex molecular scaffolds and natural products.[20]



Scheme 5: General depiction of the Tsuji-Trost type reactions.

Our research group has recently devised a broad and practical approach for synthesizing a wide range of cyclopentadienes.[21] The linear dienylic substrates **9** generate (vinyl) π-allylpalladium complexes **G** in the presence of $PdCl_2$, which isomerizes to **H** and

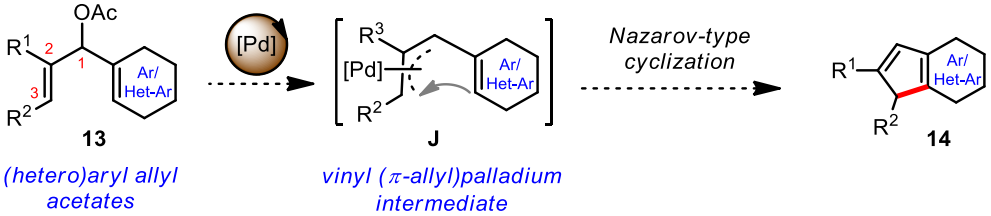
undergo the Trost-Oppolzer type Alder-ene reaction to yield the cyclopentenyl cationic intermediate **I**, which led to the formation of tetrasubstituted cyclopentadienes **10** upon deprotonation of **I**. This approach was utilized to synthesize a diverse range of cyclopentene-



Scheme 6: Pd-catalyzed intramolecular Alder-Ene reaction for the synthesis of cyclopentadienes, and cyclopentene-fused arenes and heteroarenes.

fused arenes and heteroarenes **10** and Paucifloral F by suitably modulating the substituents across the dienylic substrates and fusing the diene system with aromatic or heteroaromatic groups (Scheme **6**).

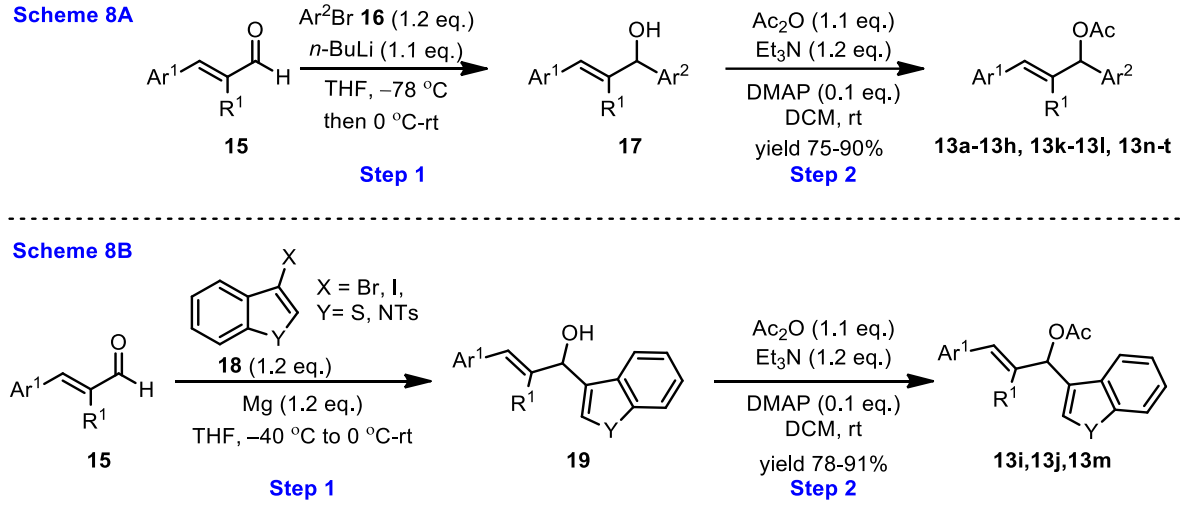
The investigations mentioned above such as Tius-Atesin's work (scheme **4**) and our recent work (Scheme **6**) for synthesizing multifunctional cyclopentanoids encouraged us to develop a novel substrate **13**, which would lead to a completely different strategy, such as Nazarov-type cyclization, to synthesize (hetero)arene-fused cyclopentanes using palladium catalysts (Scheme **7**). We hypothesized that allylic substrates with tethered nucleophile **13** might undergo oxidative addition to palladium catalyst, resulting in (π-allyl)palladium species **J**, which is a 4π -electron system in principle, leading to fused cyclopentanoids **14** by subsequent Nazarov-type cyclization.



Scheme 7: Our hypothesis towards the Pd-catalyzed Nazarov-type cyclization.

1.1: Results and Discussion

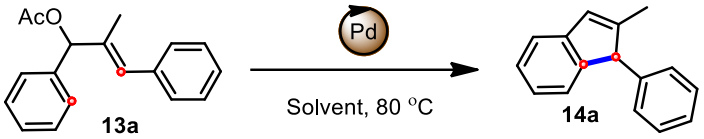
With the desire to access the cyclopentanoids **14** *via* Pd-catalyzed Nazarov-type cyclization, we have initiated the studies to synthesize the proposed allylic acetates **13a-13t**, Scheme **8**. The allyl acetate **13** can be easily synthesized by an efficient two-step protocol starting from substituted *trans*-cinnamaldehyde **15**. The *n*-BuLi mediated alkylation of (hetero)aryl bromides **16** with appropriate enals **15** at −78 °C generated the corresponding allylic alcohols **17**. Subsequently, the acylation of **17** furnished the allylic acetates **13a-13h**, **13k-13l**, **13n-13t** (Scheme **8A**). By applying similar synthetic transformations, allylic acetates **13i**, **13j**, **13m** can be easily obtained from **15** (freshly prepared) (Scheme **8B**). At –40 °C, the 1,2-addition of *in situ* generated Grignard of **18** afforded the corresponding allylic alcohols **19** which further subjected to acylation to produce **13i**, **13j**, **13m**.



Scheme 8: General schematic representation for the synthesis of allylic acetates **13a-13t**.

We have commenced the optimization study by choosing (*E*)-2-methyl-1,3-diphenylallyl acetate **13a** as a model substrate. A wide variety of catalysts and solvents combinations were tested, and the results are compiled in Table **1**. Initial screening using Pd(0) catalysts yielded inconclusive results. For example, $Pd(PPh_3)_4$ catalyzed no conversion, whereas $Pd_2(dba)_3$ promoted the production of the desired product **14a**, produced a non-polar spot isolated as **14a** in moderate yield. (Table **1**, entries 1 and 2, respectively). ^{1}H NMR, ^{13}C NMR spectroscopy, and mass spectrometry were used to comprehensively characterize the isolated molecule **14a**. In ^{1}H-NMR (see Figure **3**), the presence of a singlet at δ 6.47 ppm due to olefinic proton and singlet at δ 4.22 ppm due to the C-1 methine proton, a singlet at δ 1.84 ppm due to the methyl group supported the structure of 2-methyl-1-phenyl-1*H*-indene **14a** and in ^{13}C-NMR spectrum (see Figure **4**), presence of a peak at δ 59.5 ppm due

Table 1: Optimization of reaction parameters



Entry	[Pd] (x mol%)	Solvent	Time (h)	Yield (%)[a]
1	$Pd(PPh_3)_4$ (5)	1,2-DCE	52	NR
2[b]	$Pd_2(dba)_3$ (5)	1,2-DCE	48	42
3	$Pd(OAc)_2$ (5)	1,2-DCE	48	48
4	$Pd(PPh_3)_2Cl_2$ (5)	1,2-DCE	52	NR
5	$PdCl_2(dppf)$ (5)	1,2-DCE	48	Trace
6	$PdCl_2$ (5)	1,2-DCE	48	67
7[b]	$PdCl_2$ (10)	1,2-DCE	19	76
8	$Ni(cod)_2$ (10)	1,2-DCE	48	NR
9	$[Ir(cod)Cl]_2$ (10)	1,2-DCE	48	NR
10[c]	**$PdCl_2$ (10)**	**1,2-DCE**	**12**	**82**
11[c]	$PdCl_2$ (10)	MeCN	32	63
12[c]	$PdCl_2$ (10)	Toluene	48	40
13[c]	$PdCl_2$ (10)	DMF	48	Trace
14[c]	$PdCl_2$ (10)	1,4-Dioxane	36	72
15[c]	$PdCl_2$ (10)	1,2-DME	48	47
16[c]	$PdCl_2$ (10)	$MeNO_2$	16	75
17[c]	No Catalyst	1,2-DCE	120	NR

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yield after column chromatography. [b]At room temperature **13a** was as such, and at 60 °C the reaction was sluggish. [c]At 100 °C. NR = no reaction.

to methine carbon (C-1), and a peak at δ 15.3 ppm confirmed the formation of **14a**. The presence of a molecular ion peak at *m/z* 207.1162 $(M+H)^+$ further supported the product formation. The structure of **14a** was also validated by comparing the NMR results to the reported data. We used Pd(II) catalysts to increase the efficiency of the transformation. $Pd(OAc)_2$ produced **14a** in a low yield even after a prolonged reaction time, but the $PdCl_2$-catalyzed reaction produced **14a** in a fair yield (Table **1**, entry 3-6). Furthermore, we tried Ni and Ir-based catalysts to improve the efficiency of this strategy, but no product was observed in the presence of both catalysts (Table **1**, entry 8-9). Surprisingly, on increasing the catalyst

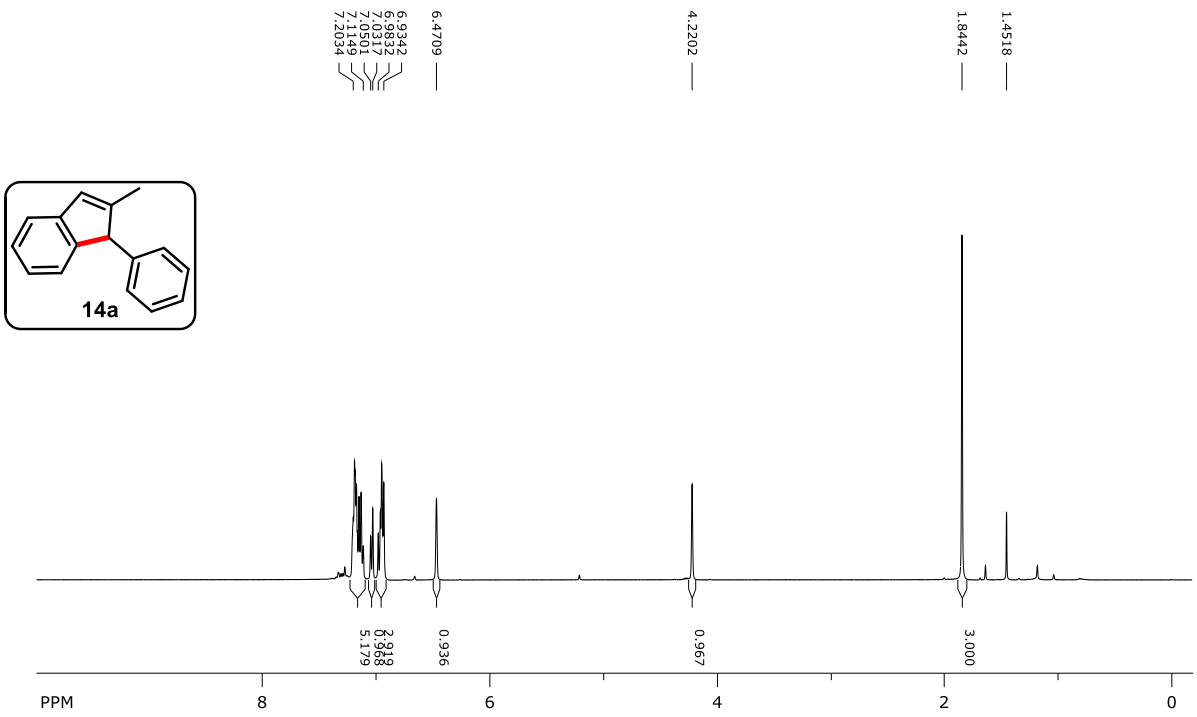


Figure 3: ^{1}H-NMR spectrum of indene **14a**

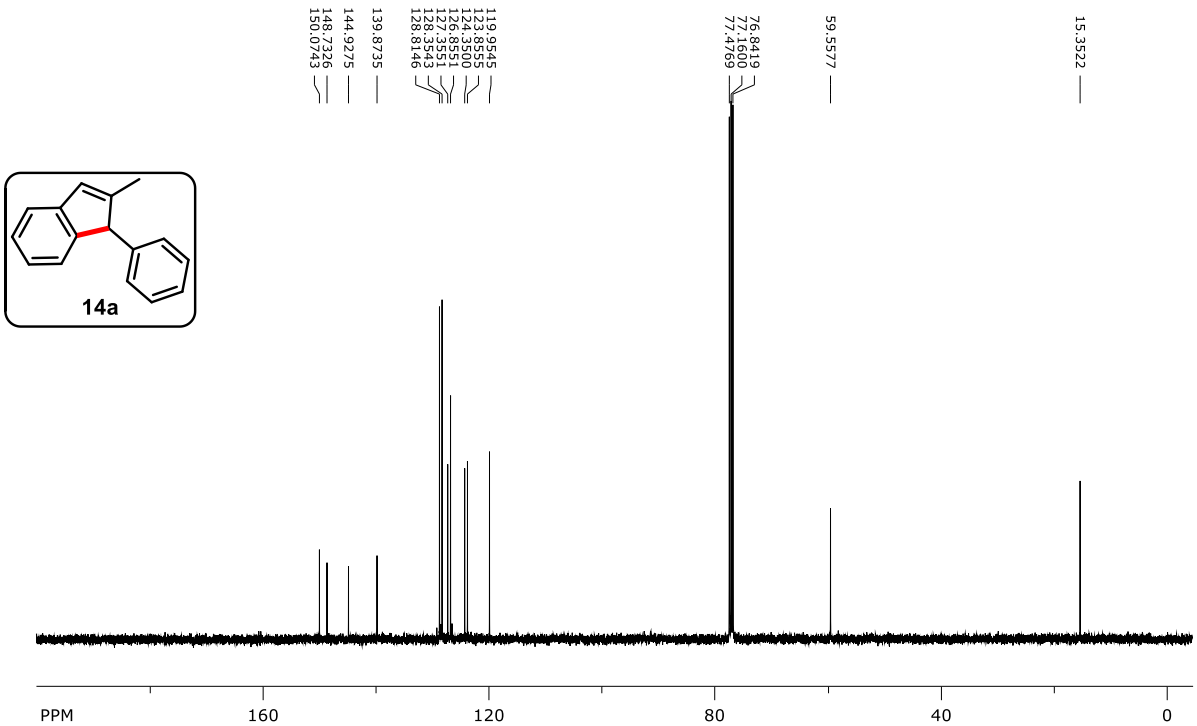


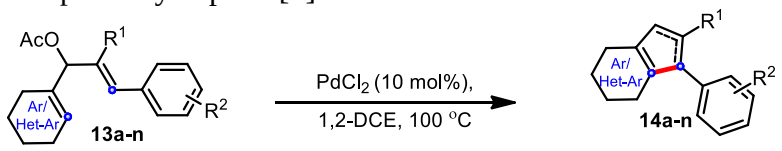
Figure 4: ^{13}C-NMR spectrum of indene **14a**

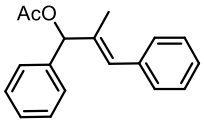
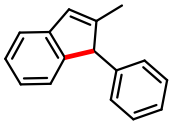
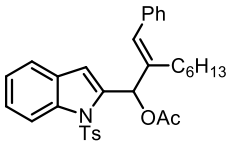
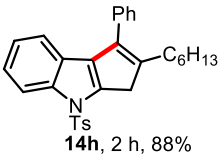
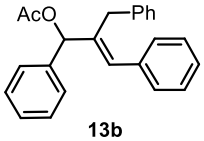
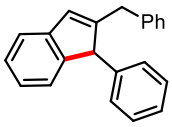
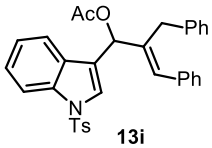
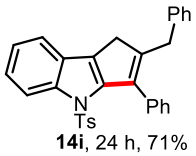
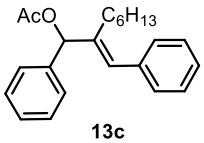
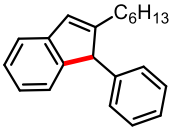
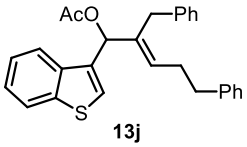
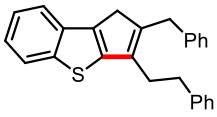
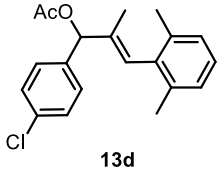
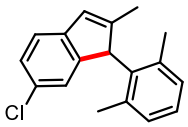
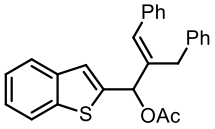
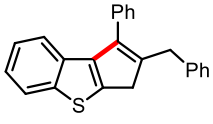
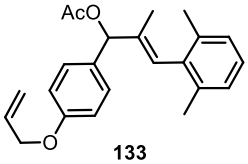
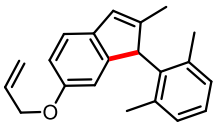
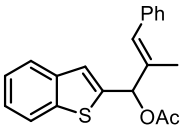
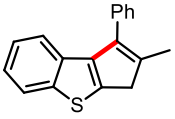
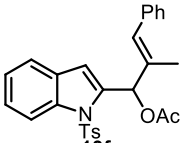
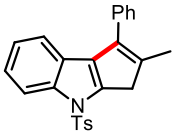
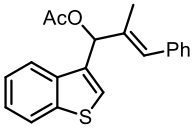
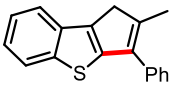
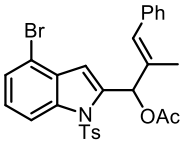
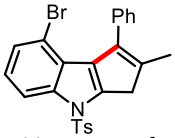
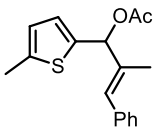
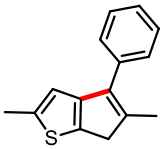
loading the isolated yield was also increased upto 76% (Table **1**, entry 7). When the reaction was carried out at 100 °C, it delivered the expected product **14a** in a short reaction time with excellent yield (Table **1**, entry 10). Following that, a quick solvent screening was performed, but we were unable to acquire a better result (Table **1**, entry 11-16). Even after an extended reaction period, no product was generated in the absence of the catalyst (Table **1**, entry 17). Thus, the best reaction conditions for this Nazarov-type reaction was identified as 10 mol% $PdCl_2$ in 1,2-dichloroethane as solvent at 100 ^oC.

With this promising result, we started exploring the substrate scope with varying electronic and steric features. Towards this, numerous types of allyl acetates **13a-13n** appended to aryl and heteroaryl backbones were synthesized. Table **2** summarises the study's findings. The intramolecular Pd-catalyzed Nazarov-type reaction was found to be general and efficient, granting access to a wide range of cyclopenta[*b*]annulated arenes and heteroarenes in excellent yields with consistent reaction times. An intriguing regioisomeric complementarity among indenes and cyclopenta[*b*]annulated heteroarenes was noticed concerning the internal doublebond. For instance, **14a-14e** has a tri-substituted double bond with a tertiary carbon center, but **14f-14n** were isolated with a fully substituted double bond. Under optimal conditions, the substrates having electron-donating (-Me) and mild electron-withdrawing substituents (-Cl) (Table **2**, entry 1-4) on either of the aromatic backbones were also well tolerated. Remarkably, the indene **14e** with the sensitive functionality such as the O-allyl group was synthesized in high yield. To further extend our strategy, substituted cyclopenta[*b*]annulated indole **14f-14i**, benzothiophene **14j-14m**, and thiophene-based derivatives **14n** were also assembled successfully in excellent yields, Table **2**. It is worth noting the efficient reaction from both C-2 and C-3 of indoles (**13f-13h** vs. **13i**) and benzothiophenes (**13j,13m** vs. **13k-13l)**, inferring that the reaction does not involve a C–H activation pathway. However, heteroarenes respond differently (from C-2 and C-3) under C–H activation conditions.[22] The flexibility of this strategy was illustrated further by synthesizing cyclopenta[*b*]indole with a bromo group **13g**, which can be utilized as a handle for further synthetic transformations. All of these observations emphasize the mild and selective nature of reaction conditions. The reaction of **13a** on a 1.95 mmol scale generated **14a** in a 77% yield, demonstrating the method's practicality.

Encouraged by the results in Table **3s**, we investigated of the reaction's broader scope and generality, intending to synthesize natural product-like polycyclic cyclopentenes with

Table 2: Substrate scope for cyclopenta[*b*]annulated arenes and heteroarenes[a]



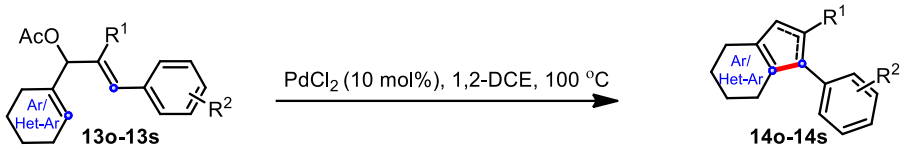
Entry	Substrate	Product	Entry	Substrate	Product
1.	 **13a**	 **14a**, 12 h, 82%	8.	 **13h**	 **14h**, 2 h, 88%
2.	 **13b**	 **14b**, 14 h, 78%	9.	 **13i**	 **14i**, 24 h, 71%
3.	 **13c**	 **14c**, 10 h, 83%	10.	 **13j**	 **14j**, 13 h, 87%
4.	 **13d**	 **14d**, 32 h, 83%[b]	11.	 **13k**	 **14k**, 24 h, 68%
5.	 **133**	 **14e**, 12 h, 66%	12.	 **13l** *E/Z* = 6:1	 **14l**, 8 h, 78%
6.	 **13f**	 **14f**, 5 h, 80%	13.	 **13m**	 **14m**, 5 h, 91%
7.	 **13g**	 **14g**, 4 h, 90%[c]	14.	 **13n**	 **14n**, 10 h, 53%

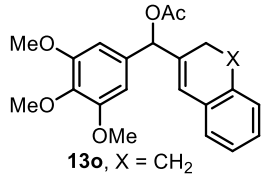
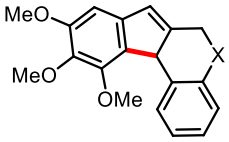
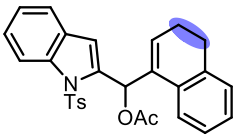
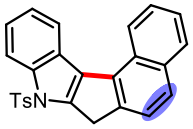
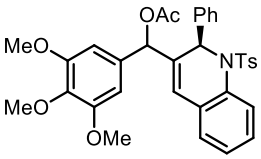
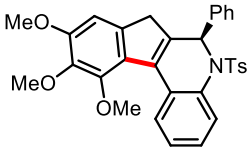
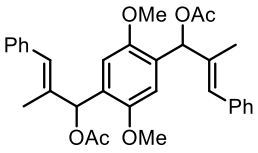
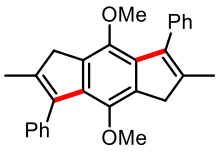
[a]Isolated yields after column chromatography. [b]Major isomer;obtained in 10:1 ratio of regioisomers. [c]Minor isomer; obtained in 8:1 ratio of regioisomers

medicinal chemistry and materials science applications. Towards that, the substrates **13o-13s** were subjected to optimized conditions. In a usual manner, the reaction generated the tri,-tetra, and pentacyclic complex scaffolds in excellent yields (Table **3**). **14o** represents the tetracyclic [6,6,5,6] decahydrobenzofluorene skeleton of the sesquiterpenes such as quinol dasyscyphin E[23], which are known to have a variety of biological activities, and **14p** with an

indene-fused chromene carbon framework could be used as bioactive natural compounds like brazilin[9c] and pestalachloride D.[24] An optically active indeno-fused quinoline-based derivative **14q** synthesized from **13q** could potentially act as an analogue of BMS-593214, a potent and selective FVIIa inhibitor. Interestingly, the pentacyclic indeno-fused indole **14r,** which was isolated by treating indole-based allyl acetate **13r** of tetralone under optimum conditions *via* Nazarov-type cyclization and subsequent aromatization sequence, is known to possess promising implications in medicinal chemistry and materials science.[25] Another intriguing aspect of the approach is that the one-pot double annulation of diacetate **13s** offered an easy access to highly substituted indacenes **14s**, which shows interesting photophysical properties.[26]

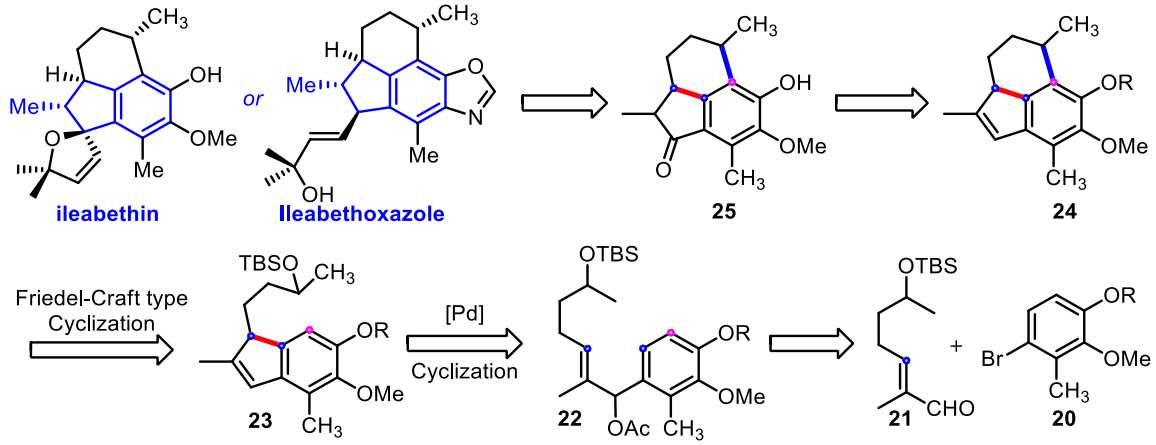
Table 3: Synthesis of polycyclic cyclopentenes[a]



Entry	Substrate	Product	Entry	Substrate	Product
1.	 **13o**, X = CH_2 **13p**, X = O	 **14o**, X = CH_2, 8 h, 87% **14p**, X = O, 12 h, 83%	3.	 **13r**	 **14r**, 24 h, 79%
2.	 **(-)-13q** (*dr* ~ 1.5:1)	 **14q**, 8 h, 79%	4.	 **13s**	 **14s**, 30 h, 70%

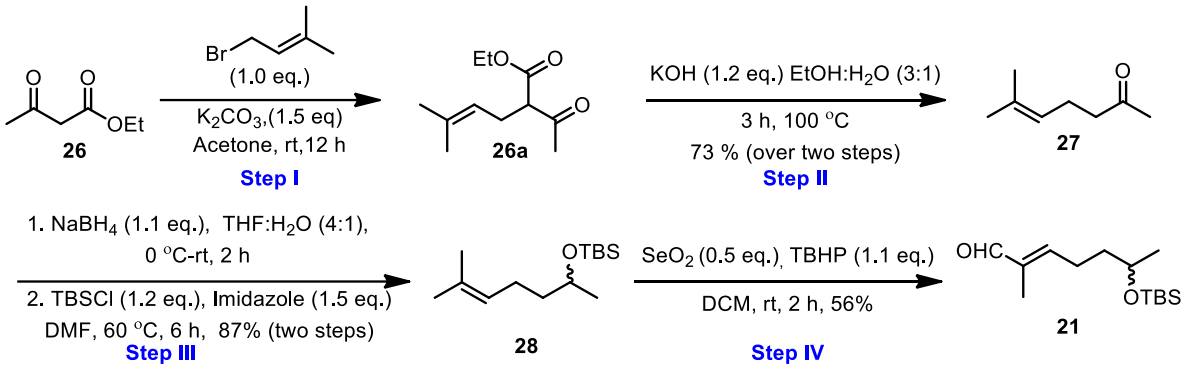
[a]Isolated yields after column chromatography.

Next, we intended to use this approach to build tricyclic carbon architectures for diterpene natural products such as ileabethin or ileabethoxazole by following a suitable retrosynthetic plan demonstrated in the Scheme **9**. Both diterpenoids were extracted from a hexane extract of *Pseudopterogorgia elisabethae* (Bayer) from Colombia. Ileabethoxazole has good antimycobacterial activity against *Mycobacterium tuberculosis* (H37Rv) and anti-inflammatory, analgesic, and antitumor properties. As per scheme **9**, we envisioned that allylic acetate **22**, which can be freshly prepared by coupling **21** and **20** employing BuLi mediated alkylation and acylation, can undergo a Pd-catalyzed Nazarov type reaction. The resulting indene **23** may undergo Friedel craft type cyclization to form **24**, which may oxidize to **25**.



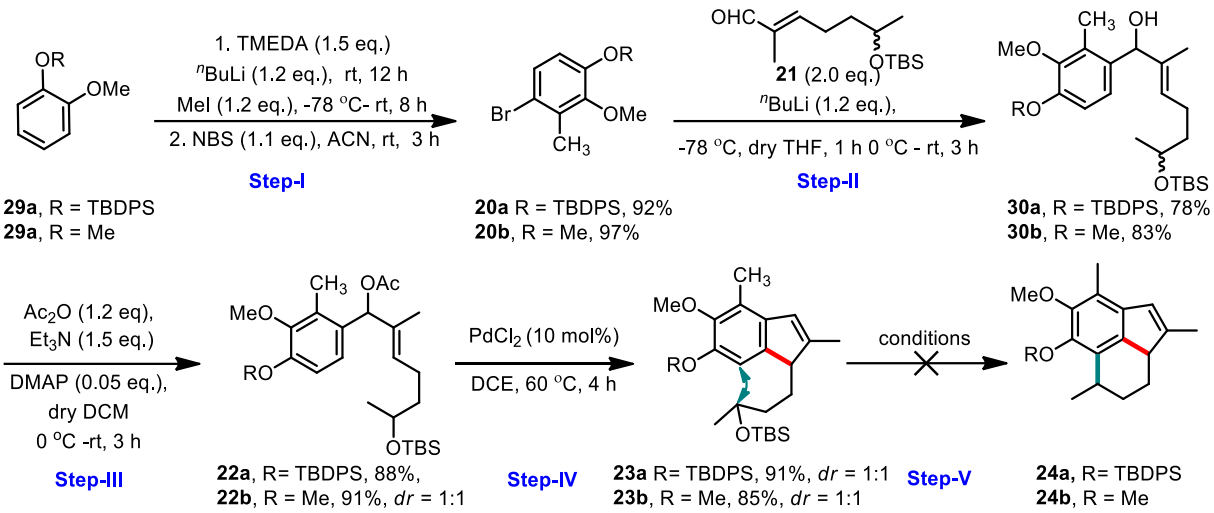
Scheme 9: Retrosynthetic route for the tricyclic carbon skelton of ileabethin.

In this regard, desired (*E*)-6-((tert-butyldimethylsilyl)oxy)-2-methylhept-2-enal **21** was prepared by following the procedure outlined in Scheme **10**, starting from commercially available ethyl acetoacetate **26** and prenyl bromide.



Scheme 10: General representation for the synthesis of **21**

Further**,** the corresponding allylic alcohols **30a** or **30b** were synthesized *via* *n*-BuLi-mediated alkylation of freshly prepared aryl bromides **20a** or **20b** with appropriate enal **21** at –78 °C. The acylation of **30a** or 3**0b** produced allylic acetates **22a** or **22b** (Scheme **11**). The desired acetates were treated to standard reaction conditions; intramolecular $PdCl_2$-catalyzed Nazarov-type cyclization of **22a** or **22b** produced expected indene **23a** or **23b**, respectively, in good yields despite the poor diastereomeric ratio. We attempted to synthesize the tricyclic carbon framework of ileabethin by employing several acid-mediated reaction conditions to indenes **23a** or **23b** as reported in the literature. However, **23a** or **23b** failed to cyclize intramolecularly *via* Friedel-Craft type reaction to provide **24a** or **24b**.[27]



Scheme 11: General representation for the synthesis of **22a-b** and **23a-b**

The following conditions were tried, but the desired product **24a** or **24b** was not obtained.

1. TFA (1.0 eq.), DCE, rt, 6 h
2. TFA (neat), rt-80 °C, 2 h
3. *p*-TSA (1.0 eq.), DCE, rt-80 °C, 8 h
4. dil HCl, THF, rt, 4 h
5. $MeSO_3H$ (1.2 eq.), rt-80 °C, 6 h
6. dil H_2SO_4, THF, rt, 2 h

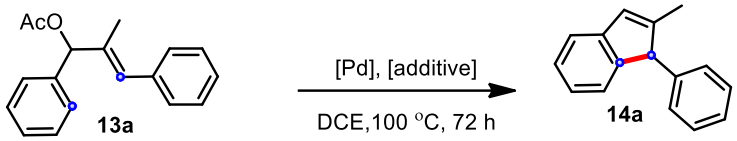
1.2: Mechanistic Insights

Several mechanistic and control experiments were carried out to investigate the plausible reaction mechanism of palladium-catalyzed Nazarov-type cyclization in detail, and the results are summarised below.

1.2.1: Experiments indicating the neutral reaction conditions

To eliminate the possibility of any trace amount of adventitious HCl promoting the reaction i.e. hidden Brønsted acid, we performed the reaction with proton scavenger additive 2,6-di-tert-butyl-4-methylpyridine (DTBMP)[28a-b] and DMAP. Fortunately, the desired product **14a** was isolated in good yields (see Table **4**), indicating that the Pd-catalyzed Nazarov-type cyclization reaction proceeds under strictly neutral pH conditions.

Table 4: Screening with bases additives as proton scavengers

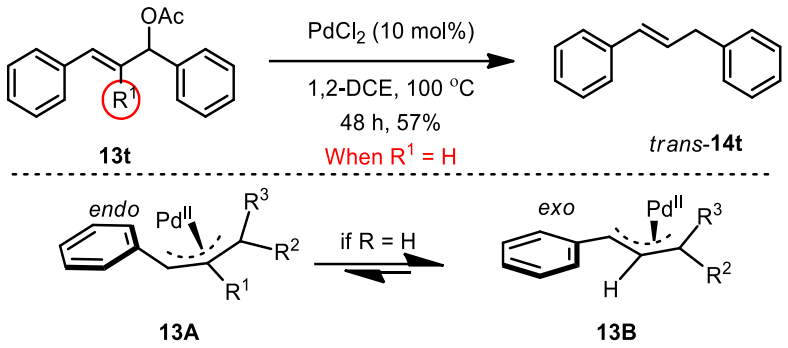


Sr. No.	Catalyst (x eq.)	Additives (1.0 eq.)	Yield (%)[a]
1.	$PdCl_2$ (0.1)	DTBMP	51
2.	$PdCl_2$ (0.1)	DTBMP	67
3.	$PdCl_2$ (0.1)	DMAP	58
4.	$PdCl_2$ (0.1)	DMAP	71

[a]Isolated yields after column chromatography

1.2.2: Study the effect of substituent (R^1)

The necessity of the substituent (R^1) for the outcome of the reaction (Scheme **11**) was identified while studying the substrate scope. The reaction of **13t** with 10 mol% $PdCl_2$ in DCE solvent at 100 °C delivered the deacylated product *trans*-**14t** with yield 57%. As shown in below scheme 11, If R^1 = H, the phenyl group will be in the *exo* position and cyclization cannot occur. If $R^1 \neq$ H, due to steric considerations in the presence of substituent R^1, the intermediate **13A** reorganizes to **13B**, then cyclisation can occur via the one with an *endo*-phenyl group. The formation of *trans*-**14t** inferring the involvement of the π-allyl palladium complex during the reaction mechanism, implied that the R^1 (both electronically and sterically) plays a critical role in the formation of cyclized products.

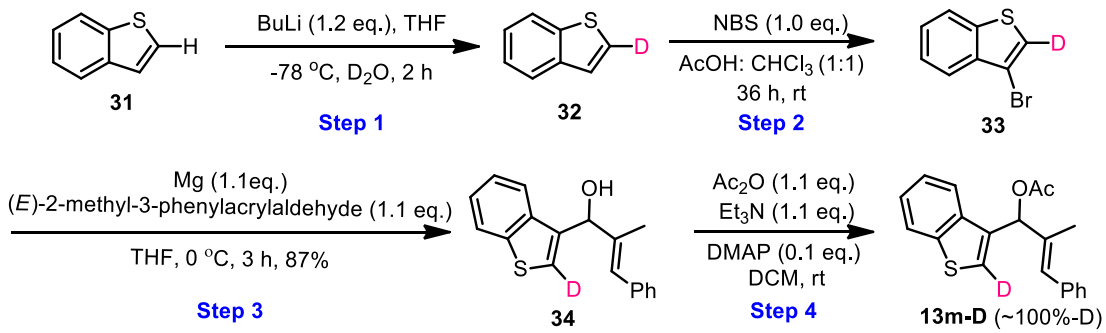


Scheme 11: Pd-catalyzed reaction of substrate **13t**

1.2.3: Kinetic Isotope Effect Experiment (KIE)

Palladium-catalyzed Nazarov type reaction of (hetero)aryl allyl acetates could proceed *via* either pathway, such as the C–H activation pathway, which would include the formation of a six-membered palladacycle, or the non C–H activation pathway**.** Measuring the effect of deuterium substitution on the rate constant or equilibrium constant is considerably more useful for understanding and gaining clear mechanistic information concerning Pd-catalyzed reactions because it involves the C-H/C-D bond formation/breakdown processes. We devised an isotope leveling experiment to measure KIE in order to establish a non-C-H activation pathway, and the results were thoroughly examined.[28c-e]

Towards this, **13m-D** was synthesized by using a four-step protocol starting from commercially available benzothiophene **31** (Scheme **12**). *n*-BuLi mediated proton exchange in the presence of D_2O generated the corresponding deuterated compound **32,** upon treatment of **32** with *N*-bromosuccinimide delivered **33** in 89%. At 0 °C, the 1,2-addition of *in situ* generated Grignard of **33** afford the corresponding allylic alcohols **34** which further subjected to acylation to produce **13m-D** with ~100% "D"-incorporation.



Scheme 12: General schematic representation for the synthesis of allylic acetate **13m-D.**

To determine KIE, we subjected **13m** and **13m-D** to the optimized reaction conditions. An oven dried 5 mL glass vial was charged with **13m** or **13m-D** (10 mg, 0.03 mmol, 1 eq.), $PdCl_2$ (0.5 mg, 0.003 mmol, 10 mol%), and DCE (0.5 mL). The reaction mixture was stirred in a preheated aluminum block at 100 °C. After the indicated time, the reaction mixture was cooled. A stock solution of carbazole (0.400 mL, 0.014µM, 1 mg, 1 equiv.) in EtOAc was added to the 100 µL crude mass and was transferred to 1.5 mL GC vial. The samples were subjected to GC-MS analysis for quantification using carbazole as an internal standard. A plot was drawn between the percentage yield of the product and time. In Figure **5**, Graph **A** indicates the faster reaction rate for **13m-D** as compared to **13m**. From graph **B,** the k_H/k_D ratio was 0.436 (as $k_H/k_D < 1$), indication of a new C-C bond-forming cyclization event

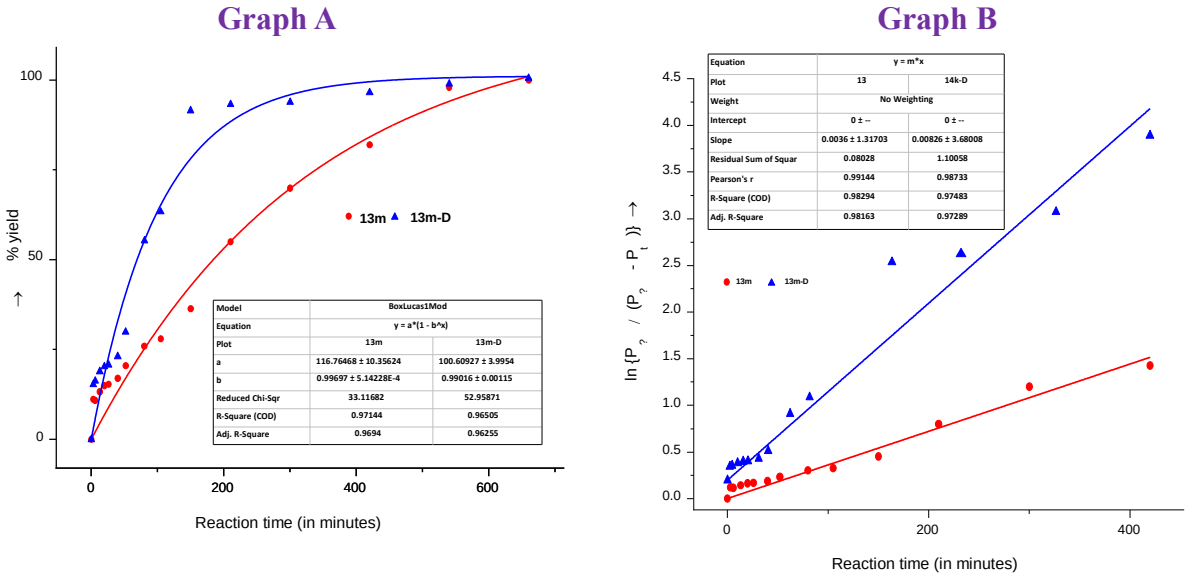
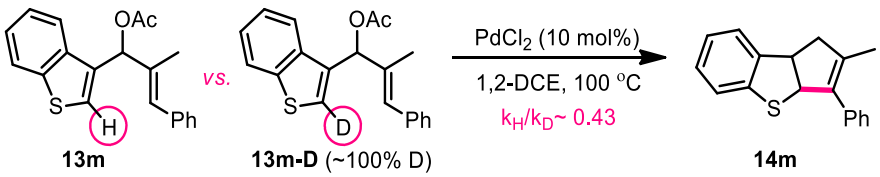


Figure 5: Determination of KIE in the Pd-catalyzed Nazarov-type cyclization

featuring a Nazarov-type step rather than a C-H activation pathway. Otherwise, the rate-determining step in conventional metal-catalyzed C-H functionalization processes is C-H bond cleavage.[28f-g] Furthermore, with comparable efficiency to arene and heteroarenes, the reaction can be regarded as a Nazarov-type cyclization.



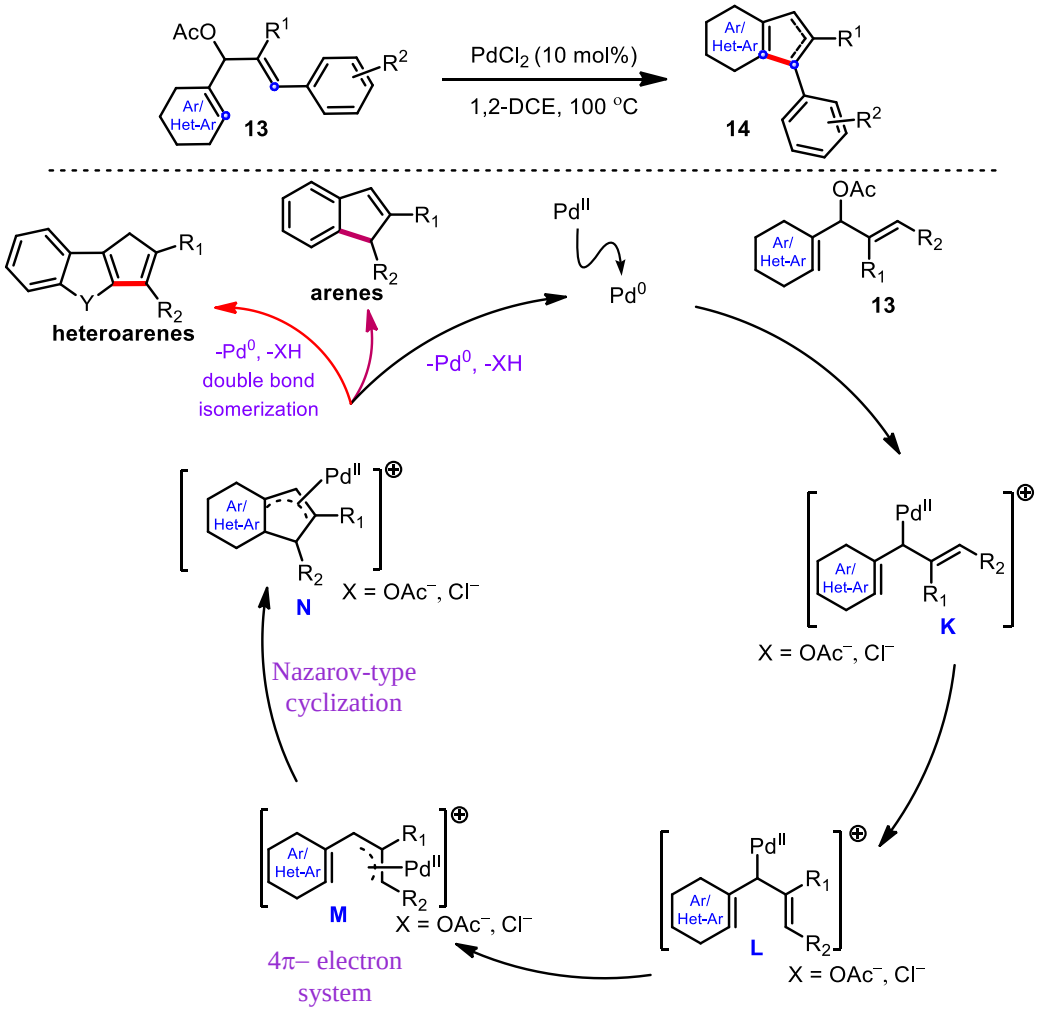
Scheme 13: Measurement of the kinetic isotope effect (KIE) between **13m** and **13m-D**

The formation of Pd black in our reactions is indicative of *in situ* generation of Pd(0), which could be owing to the substrate itself reducing Pd(II) to Pd(0) during the reaction analogous to

the Wacker-type process. As a result, the *in situ* generated Pd(0) acts as an active metal centre, promoting the subsequent allylation reaction.[29]

1.2.4: Plausible mechanism

Based on the above experiments and relevant literature reports, Scheme **14** represents a likely reaction mechanism. Initially, oxidative addition of Pd(0) to substrate **13** generates the σ–palladium complex **K**. Due to steric considerations in the presence of substituent R^1, the intermediate **K** reorganizes to **L**. The so formed π-allylpalladium species **M** undergoes C-C bond formation, similar to Nazarov-type cyclization, to produce the second-allylpalladium species **N**, which upon reductive elimination gave arenes and regenerates the active catalyst. It is also conceivable that double bond isomerization of substrates with heteroarene backbones led to the formation of **N** on substrates with heteroarene backbones.



Scheme 14: Plausible mechanism for the formation of **14**.

1.3: Development of the first total synthesis of (±)β-diasarone

Lignans and neolignans are a large family of secondary metabolites conjured up of dimers of phenylpropanoid units (C6–C3) that exist in nature with a wide range of structural diversity. The anticancer, antioxidant, antibacterial, anti-inflammatory, and immunosuppressive effects of lignans and neolignans and data from over 100 peer-reviewed research papers imply that bioactive lignans could be a first step towards generating drug candidates.[30a-b] This category includes diasarone **35**, diisoeugenol **36**, diisohomogenol **37**, and diisosafrolel **38**, which are polyfunctionalized 2,3-dihydro-1H-indenes with the four possible

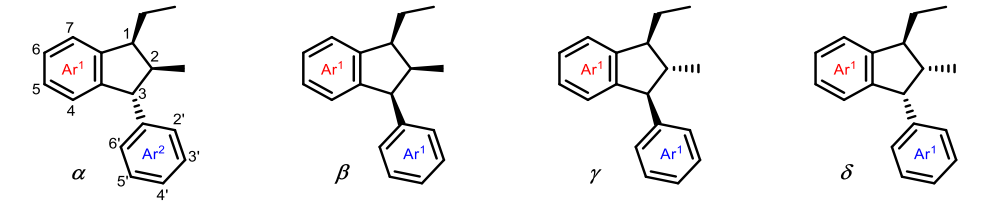
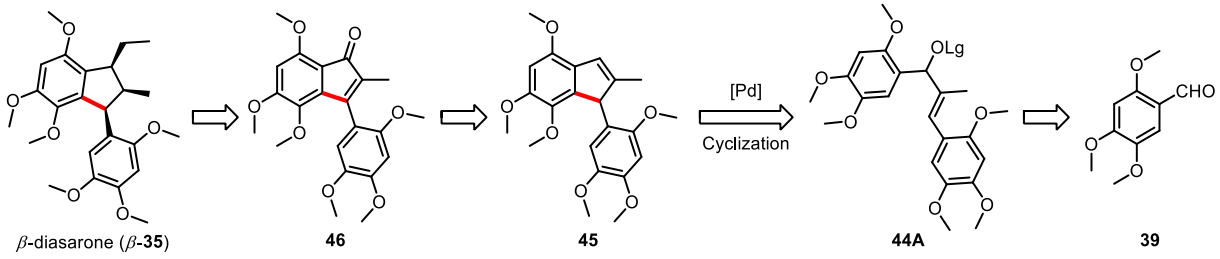


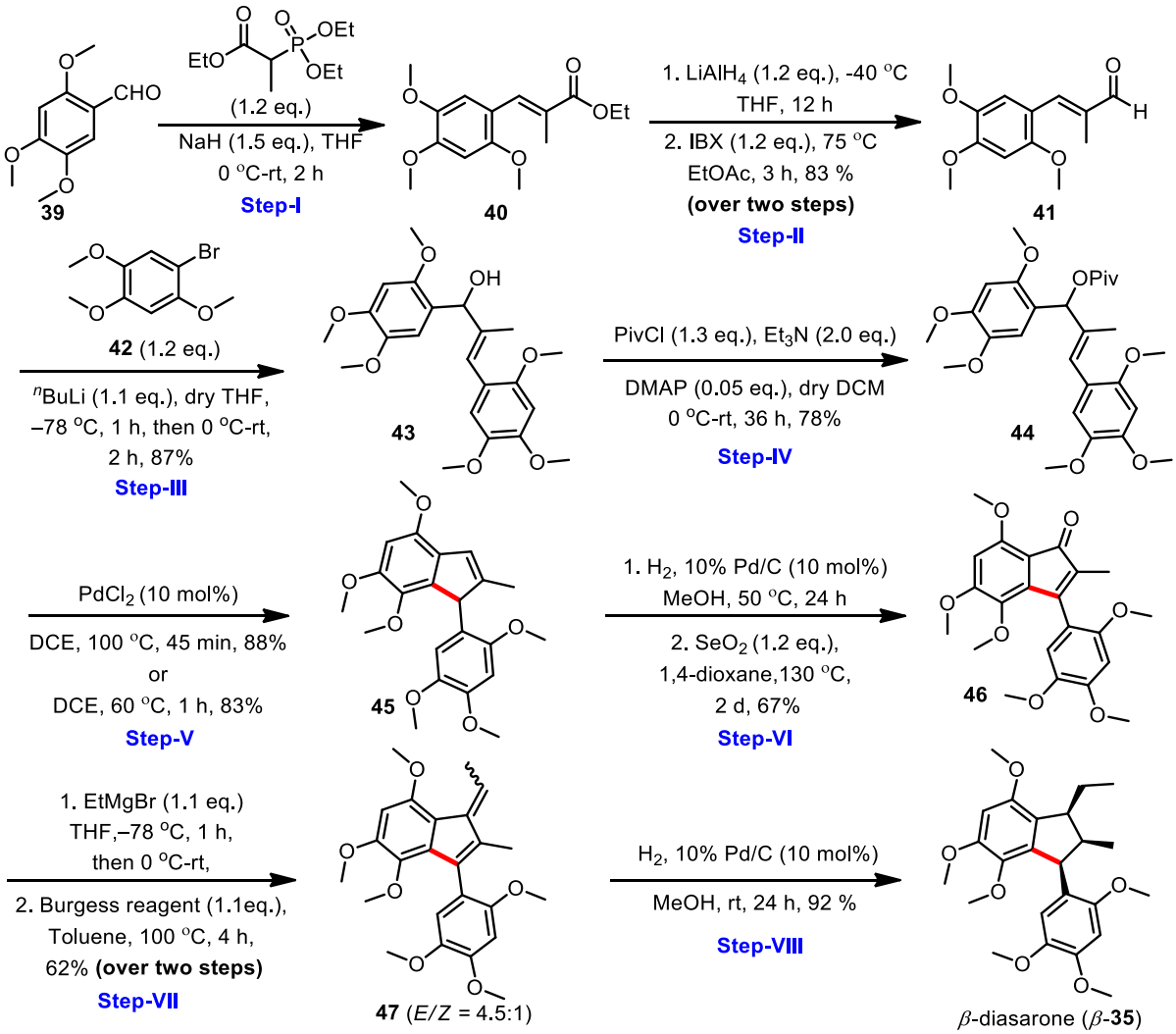
Figure 6: Four stereoisomers of 1,2,3-trisubstituted 2,3-dihydro-1H-indenes

diastereomers such as *α*-(1,2-*cis*-2,3-*trans*), *β*-(1,2-*cis*-2,3-*cis*), *γ*-(1,2-*trans*-2,3-*trans*), and *δ*-(1,2-*trans*-2,3-*cis*); see Figure **6.**[30] In 1982, Saxena isolated fully substituted indane as *γ*-diasarone γ-**35** from the rhizomes of *Acorus calamus.* NMR and X-ray studies allowed this natural diasarone to the *γ*-configuration despite using different synthetic approaches.[31] We sought to show that our current methodology might be used in the total synthesis of (±) *β*-diasarone *β*-**35**, a C-2 epimer of the natural product *γ*-diasarone by following a suitable retrosynthetic plan demonstrated in the Scheme **15A**. We predicted that the Pd-catalyzed Nazarov type cyclization of **44A** acetate would yield the desired indene **45**, which could then be manipulated to yield enone **46**.



Scheme 15A: Retrosynthetic route for (±) *β*-diasarone *β*-**35**.

Accordingly, we commenced our synthetic efforts. The allyl alcohol **43** was synthesized by adding the lithiated form of **42** to freshly generated enal **41**, which was prepared in a three-step protocol starting from **39** *via* Horner-Wadsworth-Emmons (HWE) reaction, $LiAlH_4$ reduction, and IBX oxidation sequence. Later, allylic alcohol **43** was subjected to several acylation conditions, but none yielded the allyl acetate. Fortunately, we obtained an allyl ester of **44** by treating it with freshly distilled pivaloyl chloride, triethylamine, and a catalytic amount of DMAP in dichloromethane as a solvent. $PdCl_2$ promoted the acid-free Nazarov-type cyclization of **44** in DCE at 60 °C or 100 °C and delivered substituted indene



Scheme 15: Our approach towards the first total synthesis of (±) *β*-diasarone (*β*-**35**)

such as **45** in excellent yields. Next, Pd/C based hydrogenation and SeO_2-mediated benzylic oxidation of **45** furnished the enone **46** in 67% yield. At –78 °C, the selective 1,2-addition of EtMgBr to enone **46** produced *tert*-alcohol, which was subsequently dehydrated with the Burgess reagent to yield the diene **47** in a 4.5:1 geometrical isomer ratio. Finally, (±) *β*-

diasarone *β*–**35** was obtained as a single isomer *via* stereoselective hydrogenation of **47** using a catalytic quantity of 10% Pd/C in methanol as solvent. The structure of (±) *β*-diasarone elucidated by ^{1}H-NMR and ^{13}C-NMR analysis, the relative stereochemistry of the three contiguous stereocenters assigned by using 2-D NMR such as COSY, HSQC and NOESY correlations (see Figure **9** - Figure **13**) and single-crystal X-ray diffraction analysis confirmed (±) *β*-diasarone's structure (see Figure **8**).

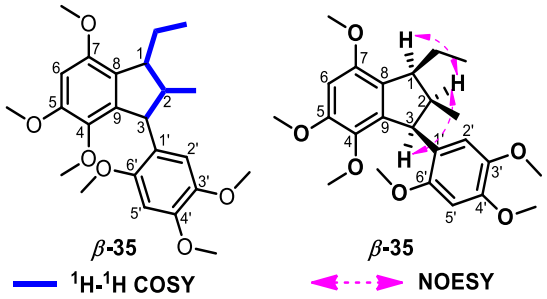


Figure 7: Key NMR correlations of *β*-**35** [blue bold lines for ^{1}H–^{1}H COSY, pink dashed two-way arrows for NOESY.

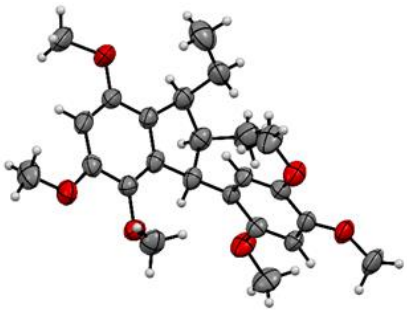


Figure 8: ORTEP diagram of (±) *β*-diasarone

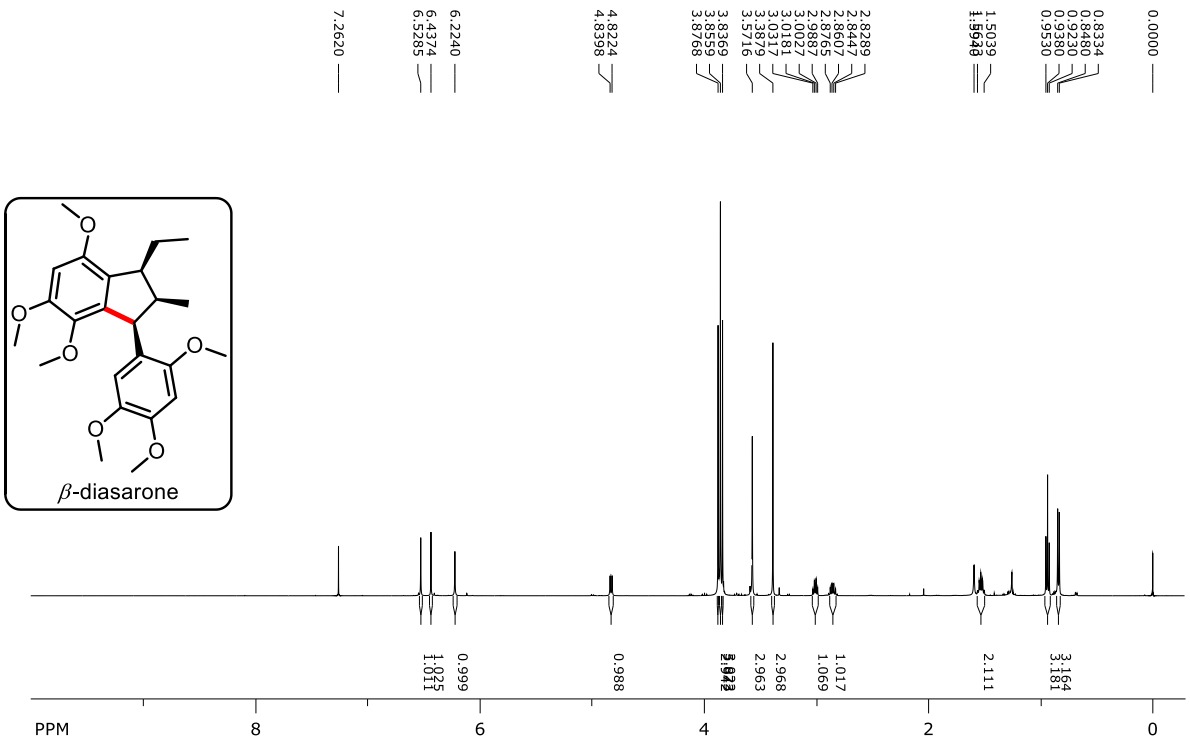


Figure 9: ^{1}H-NMR spectrum of (±) *β*-diasarone

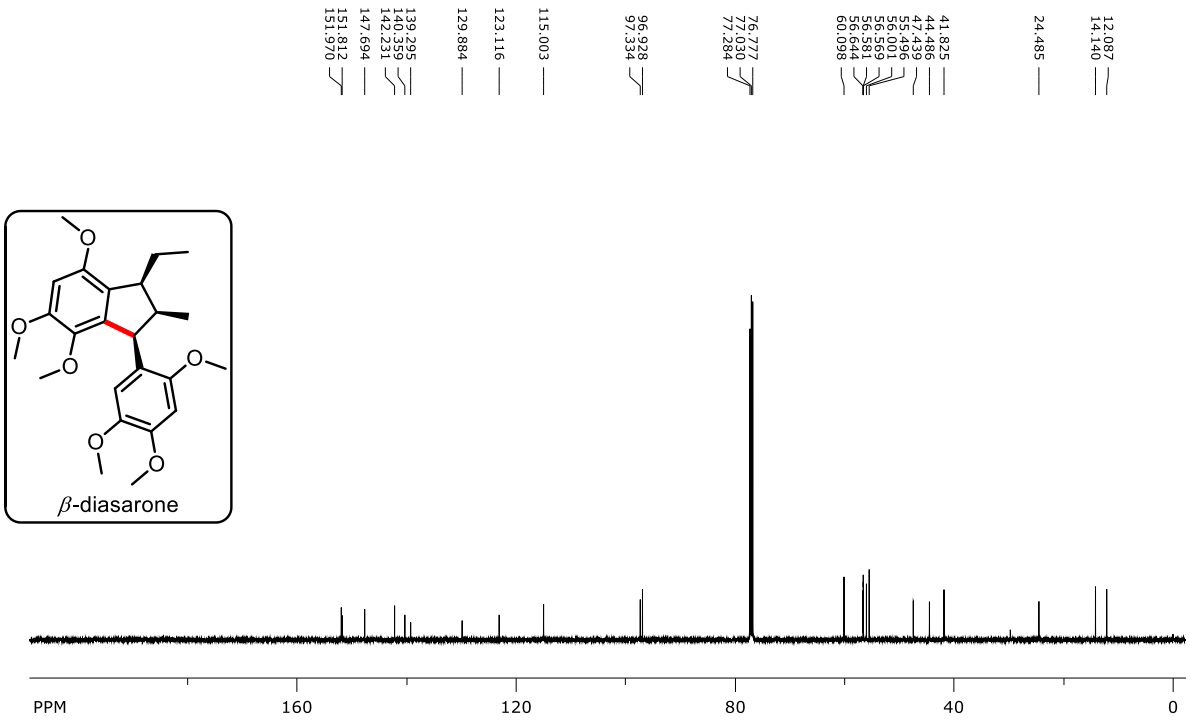


Figure 10: ^{13}C-NMR spectrum of (±) *β*-diasarone

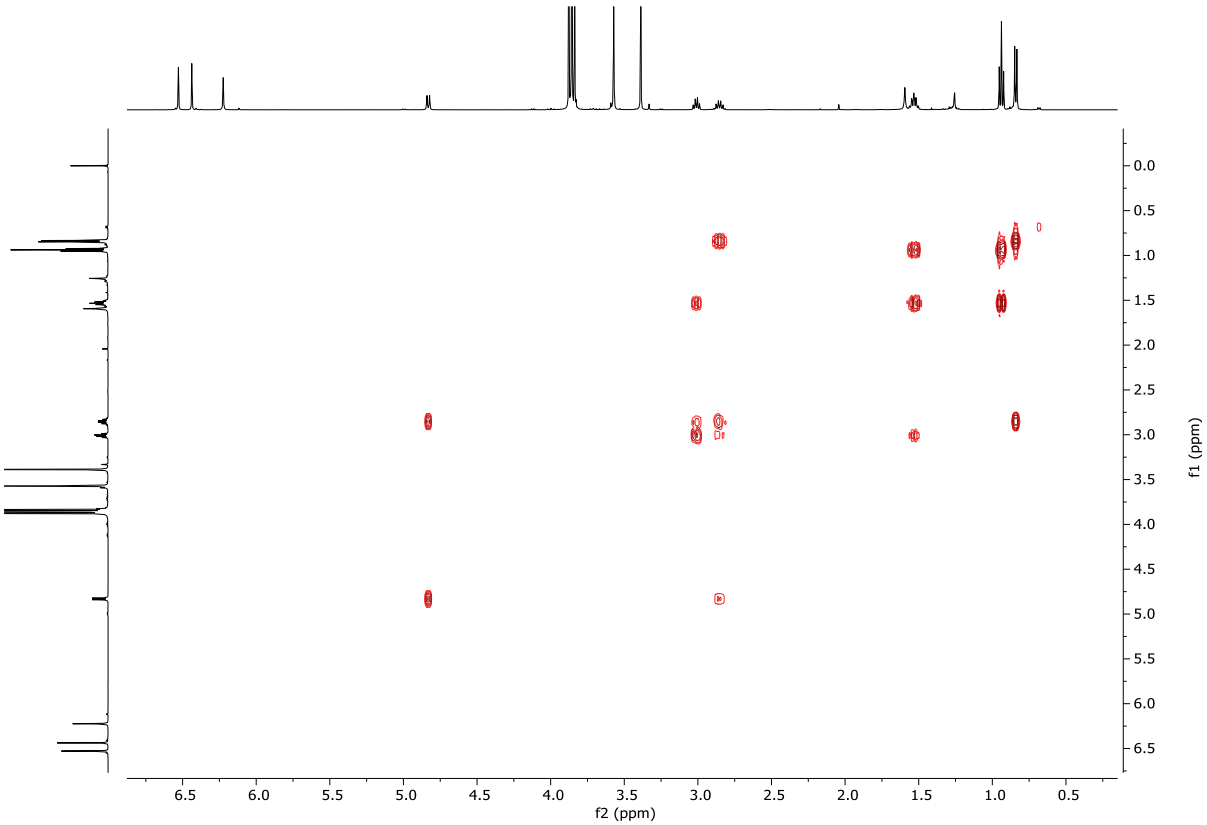


Figure 11: ^{1}H-^{1}H COSY NMR spectrum of (±) *β*-diasarone

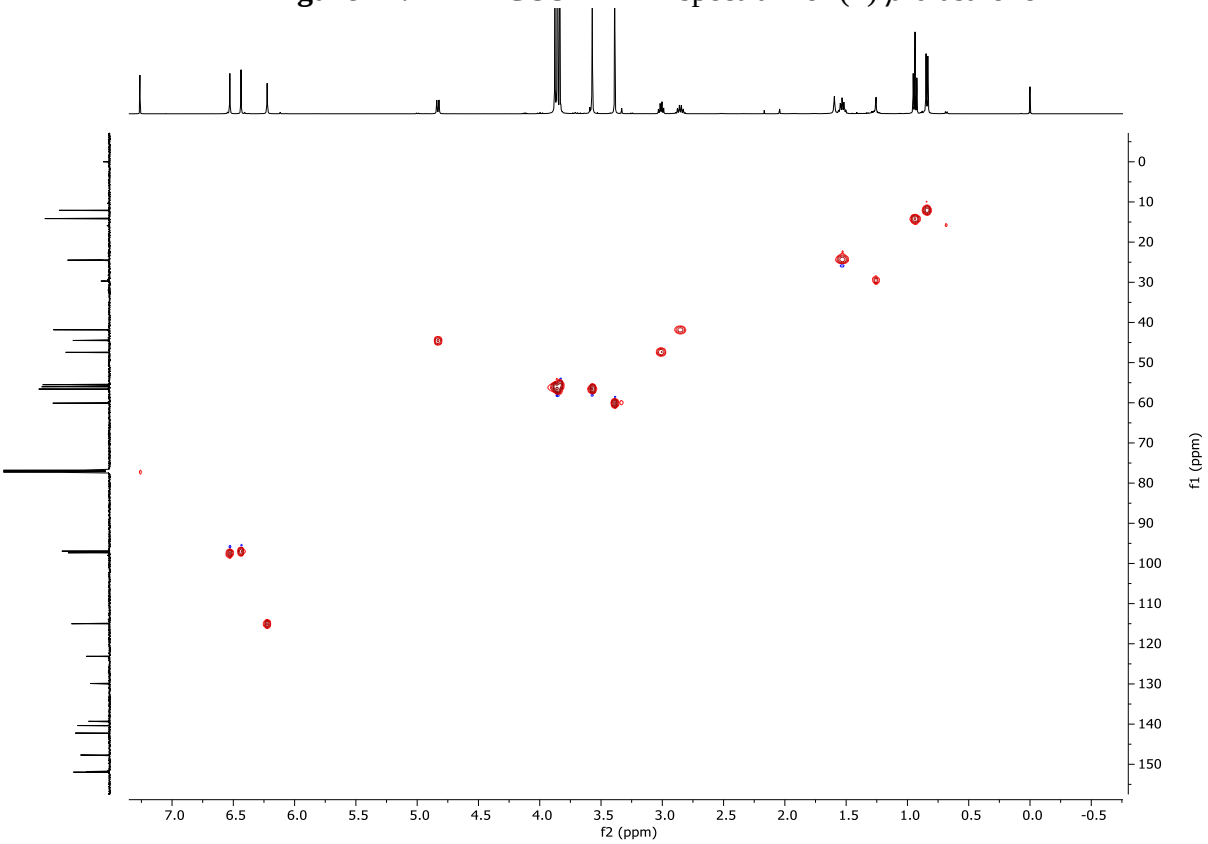


Figure 12: HSQC NMR spectrum of (±) *β*-diasarone

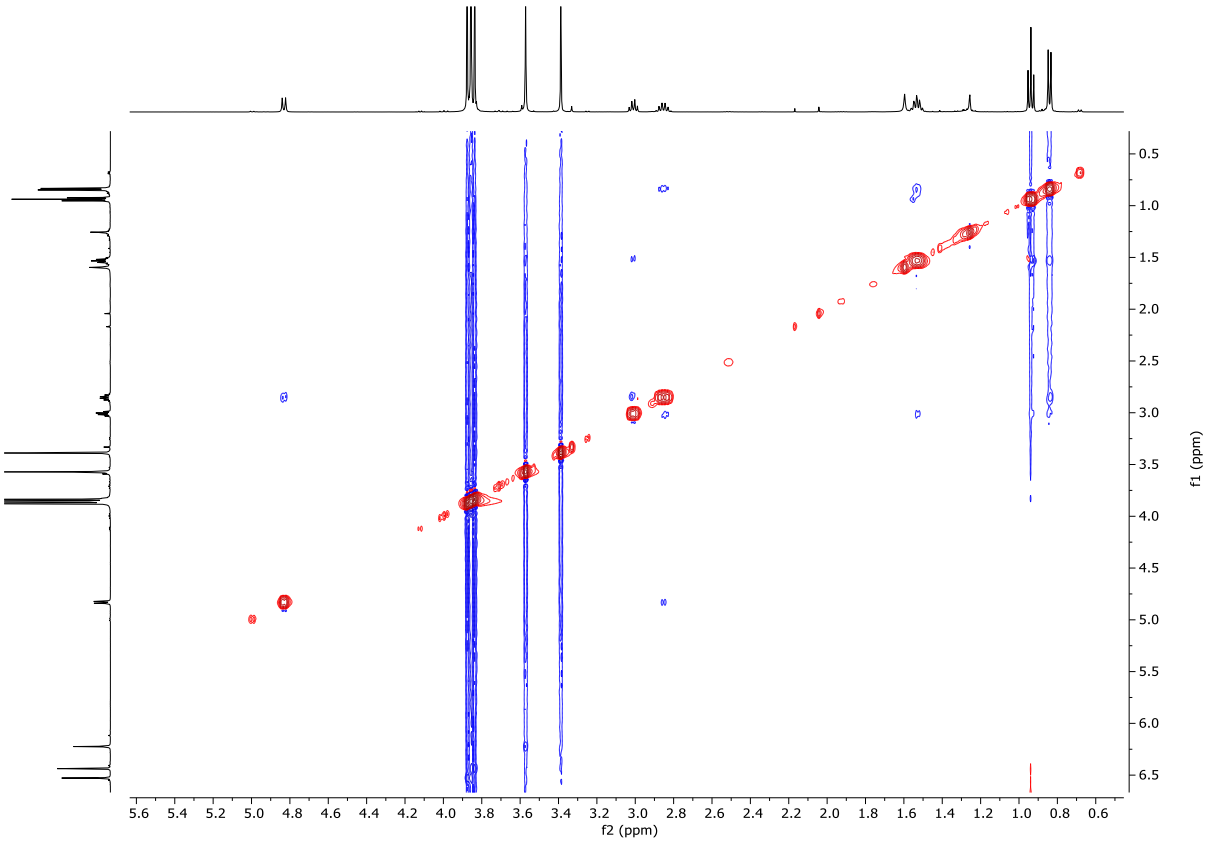


Figure 13: NOESY NMR spectrum of (±) *β*-diasarone

In conclusion, we have established the neutral Pd-catalyzed Nazarov-type cyclization of allyl acetates to synthesize various indanes possessing a tertiary stereocenter and a diverse range of cyclopenta[*b*]annulated heteroarenes. Several other complex cyclopentanoids were obtained in excellent yields under these acid-free cyclization conditions. Unlike typical Pd-catalyzed transformations, we identified that this reaction does not require any external additives, oxidants, or bases. Furthermore, the molecular architectures exposed here possess substructures of numerous bioactive compounds. Throughout the study, the methodology's generality and practicability were carefully evaluated. The important role of substitution (R^1) and the kinetic isotopic effect was investigated for the reaction mechanism. Further, to illustrate the synthetic utility of this method, we have successfully developed the first total synthesis of (±) *β*-diasarone.

Chapter 2

Palladium-catalyzed allylic (hetero)arylation to synthesize cyclopentanoids bearing an all-carbon quaternary/spiro center

For many years, medicinal chemists developed successful drugs mainly based on achiral aromatic and heteroaromatic flat molecules due to the relative ease of preparation by applying cross-coupling chemistries or other parallel syntheses. Due to the absence of sp^3 carbon, these ‘planer’ or 'flat' molecules limit their interaction with target proteins, low solubility (except few marketed drugs such as paracetamol, asipiri, etc.) and poor bioavailability due to strong π-stacking. The solution to such a problem attracts the attention of medicinal chemists toward molecules having quaternary stereocenters.[32a-b] The scaffolds with quaternary carbon occupy a significant fraction of the chemical space and better interact with the target proteins due to their enhanced conformational constraints. The wide range of

natural products, and pharmaceutically active molecules are recognized based on small or medium-sized carbocycles having an sp^3-carbon for instance an all-carbon quaternary center having four other carbon substituents. Many commercially available medications derived from naturally occurring substances such as steroids, opioids, taxanes, and diterpenoids have at least an all-carbon quaternary center. [32c-d]

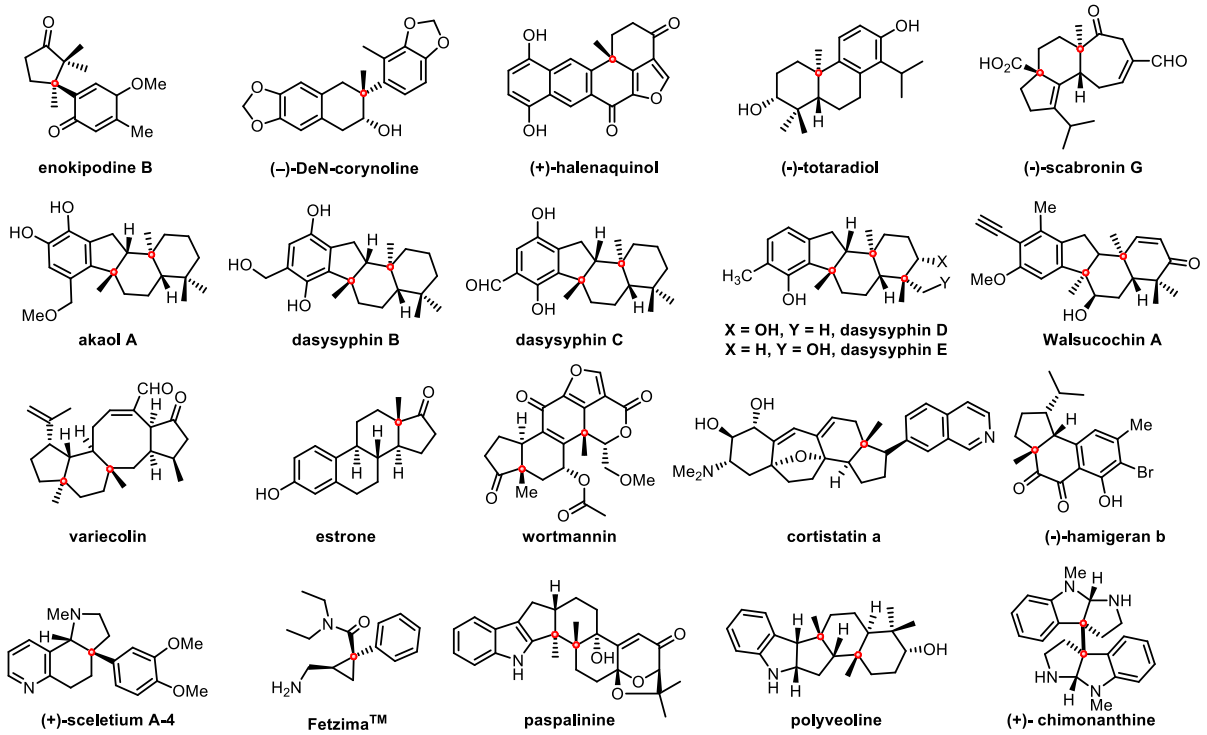


Figure 14: Natural products and pharmaceutically important molecules possessing an all-carbon quaternary center.

For instance, (+)-halenaquinol, which has antibiotic, cardiotonic, and protein tyrosine kinase inhibitory activities, is a naphthoquinol fused with a furan ring that contains a benzylic quaternary carbon center. Dasyscyphin B, a merosesquiterpenoid tricyclic carbon framework with a fused indane ring and a benzylic quaternary carbon centre isolated from marine sponges and terrestrial fungus, possess anticancer activity against many human cell lines.[33b] Another example of a compound having an all-carbon quaternary center is Cortistatin A, a marine 9-(10,19)-*abeo*-androstane steroid, which shows promising antiproliferative activity against human umbilical vein endothelial cells. Paspalinine is a tremorgenic mycotoxin identified from the ergot fungus *Clavicepts paspali*. It is a cyclopenta[*b*]annulated indole-based hexacyclic diterpenoid with two continuous quaternary carbons. Polyveoline, indolosesqiterpene, is a molecule with an all-carbon quaternary core isolated from *Polyalthia suaveolens* and exhibits antiparasitic activity. (+)-Chimonanthine is a dimeric hexahydropyrroloindole-based alkaloid

containing vicinal all-carbon quaternary stereogenic carbon centres that has been discovered to be highly cytotoxic against NUGC3 gastric carcinoma and SNU739 hepatocarcinoma cancer cells. Levomilnacipran is an antidepressant drug marketed under the name Fetima™.[33a-g]

Spirocyclic compounds, first introduced by Baeyer in the early 1900s, are bicyclic organic compounds with two rings united through only one atom, *i.e.*, an all-quaternary spiro carbon.[34] Due to the presence of 3-D spiro carbon, the rigidity and the complex structural diversity of such scaffolds offer several advantages to modern drug development processes.

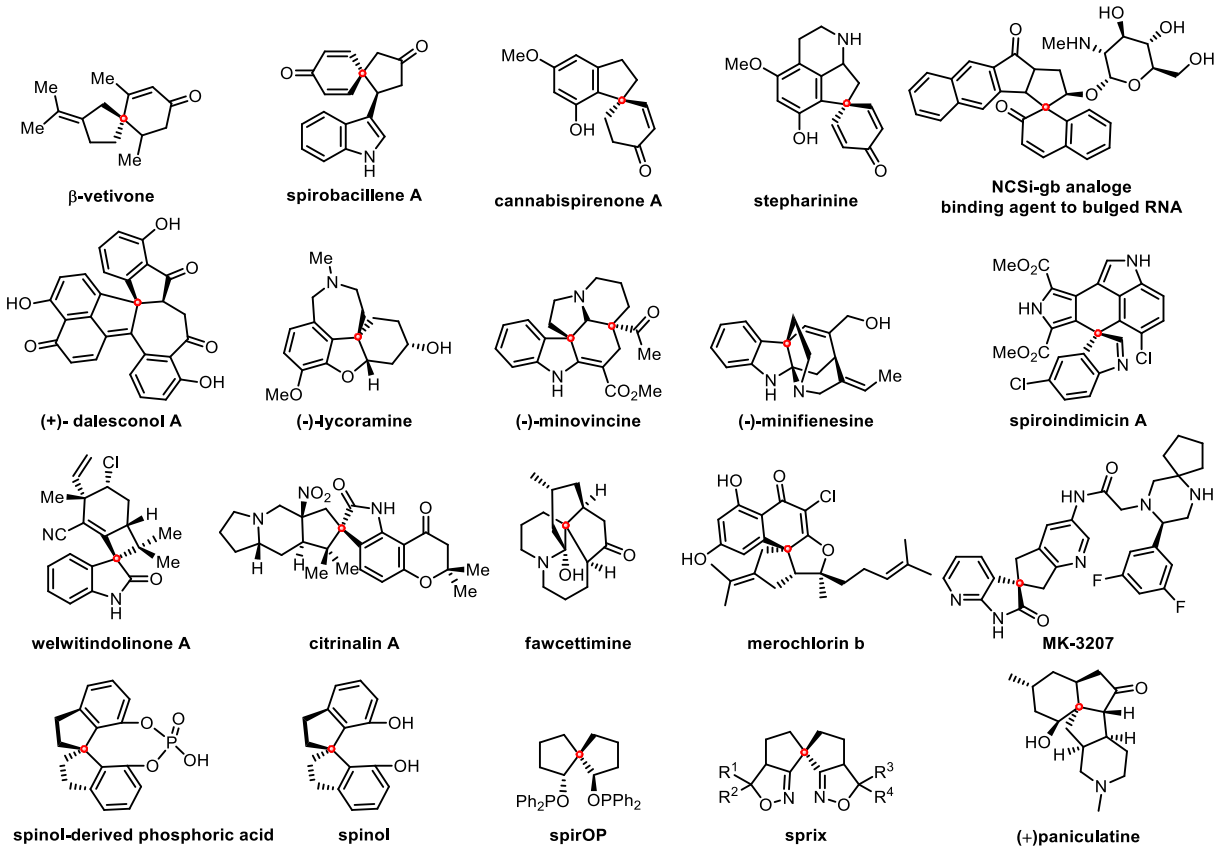


Figure 15: Natural products and pharmaceutically important molecules possessing an all-carbon spirocenter.

Similarly, many naturally occurring compounds possessing all-carbon quaternary spiro centers exhibit excellent biological activities and are essential building blocks for constructing complicated targets. Spirobacillenes A, a spiro-cyclopentenone-containing compound isolated from a broth culture of *Lysinibacillus fusiformis*, reduces nitric oxide generation and reactive oxygen species in LPS-induced RAW264 cells.[35a] Lycoramine, a galanthamine-type opioid alkaloid with a polyfused tetracyclic ring skeleton and an all-carbon spiro quaternary stereocenter, is believed to have a high therapeutic potential for Alzheimer's disease.[35b] Dalesconol A, discovered from the mantis-associated fungus *Daldinia eschscholzii*, has seven

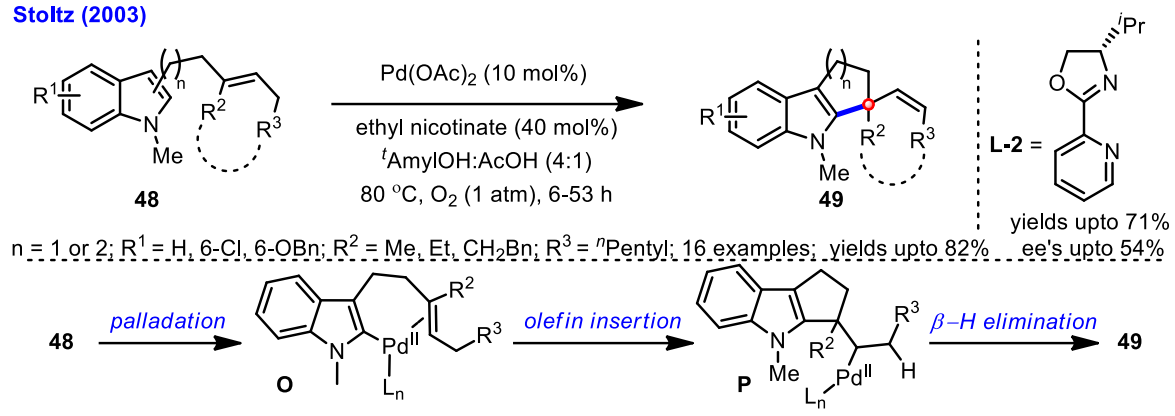
fused rings of various sizes and two stereogenic centers, one of which is a sterically congested all-carbon spiro-quaternary center with more strong immunosuppressive properties. Spirobicycle-based ligands and catalysts, such as diphosphine SpirOP, Spinol, and spirobis(oxazoline) SpriX, are versatile chemical structures that have applications in asymmetric synthesis and catalysis.[35d-e]

The importance of scaffolds with all-carbon quaternary and spiro centres in synthetic chemistry, organic functional materials, and pharmaceuticals necessitates the development of innovative methodologies to access them. Due to its abundance in natural products and medicinal compounds, the development of novel molecules derived from such complex scaffolds is a vibrant area of research. Due to steric repulsion between the carbon substituents frequently found in bond formation, assembling a benzylic quaternary carbon in spiro and non-spirocyclic systems becomes one of the most difficult challenging for an organic chemist.[36]

The generation of all-carbon quaternary and spiro centers using palladium-catalysis can be introduced by C-H activation, α-arylation of carbonyls, intramolecular Domino Heck reactions, intramolecular rearrangements, intramolecular dearomatization of arenes and heteroarenes, Ene-yne cycloisomerisations, Michael additions, Cycloaddition reactions, Tsuji-Trost type allylic alkylations. In the following subsections, a couple of reactions from a few important methods based on palladium catalysts for the construction of all-carbon quaternary and spiro centers are described.

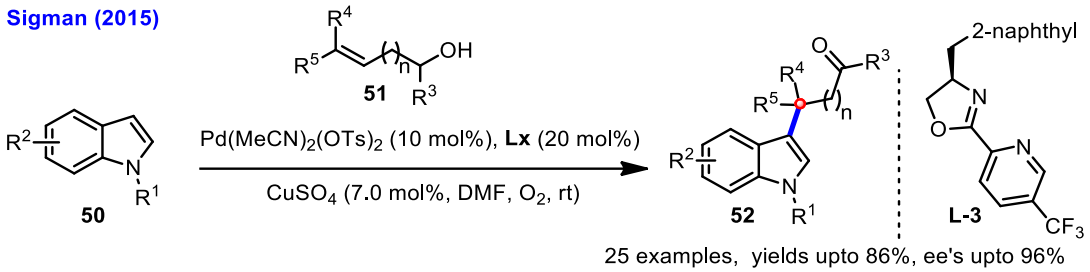
2.1: C-H activation-based approaches

In 2003, Stoltz *et al*. demonstrated unprecedented palladium-catalyzed intramolecular oxidative indole annulation to construct an all-carbon quaternary center/spiro centers *via* intramolecular C-H activation. The treatment of **48** with $Pd(OAc)_2$ and nicotinate ligand under mild oxidative conditions utilizing molecular oxygen led to the formation of cyclopenta[*b*]annulated indoles **49** having all-carbon quaternary center/spiro centers in good yields (Scheme **16**). In 2008, the Oestreich group developed the asymmetric variant of this intramolecular Fujiwara–Moritani annulation. However, only moderate enantioselectivity was attained by employing chiral oxazoline ligand **L-2**. [37]



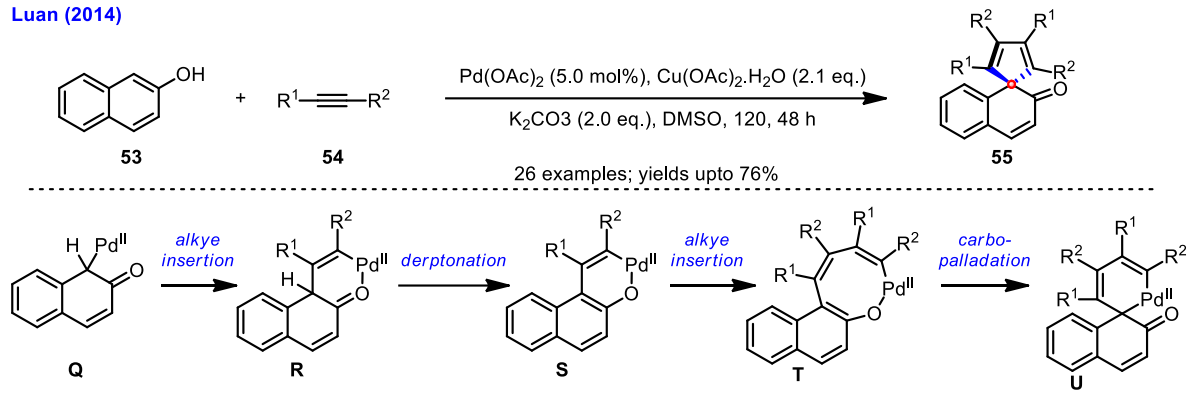
Scheme 16: Stoltz and Oestreich's intramolecular aerobic oxidative annulation of indoles **48.**

In 2015, Sigman and co-workers employed a redox relay strategy to construct an all-carbon quaternary center *via* a palladium-catalyzed asymmetric C-H addition of indoles to trisubstituted alkenols **51** by utilizing PyrOx **L-3** as a chiral ligand (Scheme **17**).[38] A wide variety of indoles and alkenols **51** were well tolerated under mild conditions to deliver the desired products **52** with a pendant ketone containing an all-carbon quaternary center in excellent enantioselectivities and yields.



Scheme 17: Pd-catalyzed asymmetric C-H addition of indoles to trisubstituted alkenes.

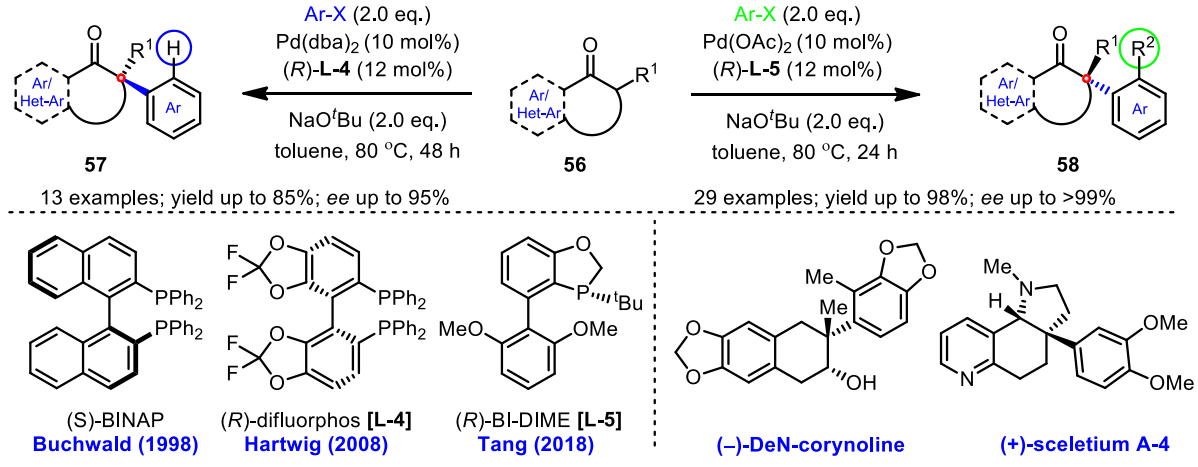
In 2014, the Luan group documented Pd-catalyzed spiroannulation of simple 2-naphthols **53** to the one-step synthesis of spirocyclic compounds **55**.[39] Initially, C-H activation occurs *via* the tautomeric form of phenoxide species **Q**, and subsequent alkyne insertion isomerizes to a more stable six-membered palladacycle **R**. Deprotonation of **R** yields **S**, and migratory insertion of the second alkyne molecule generates strained eight-membered palladacycle **T**, which upon a ring contraction process delivers the dearomatized intermediate **U** due to steric repulsion, resulting in the formation of spirocyclic products **55** after reductive elimination. This method combines arene C-H activation/dearomatization with two molecules of alkynes **54** to provide spirocyclic compounds **55** in good yields (Scheme **18**).



Scheme 18: Pd-catalyzed spiroannulation of 2-naphthols with alkynes *via* C-H activation.

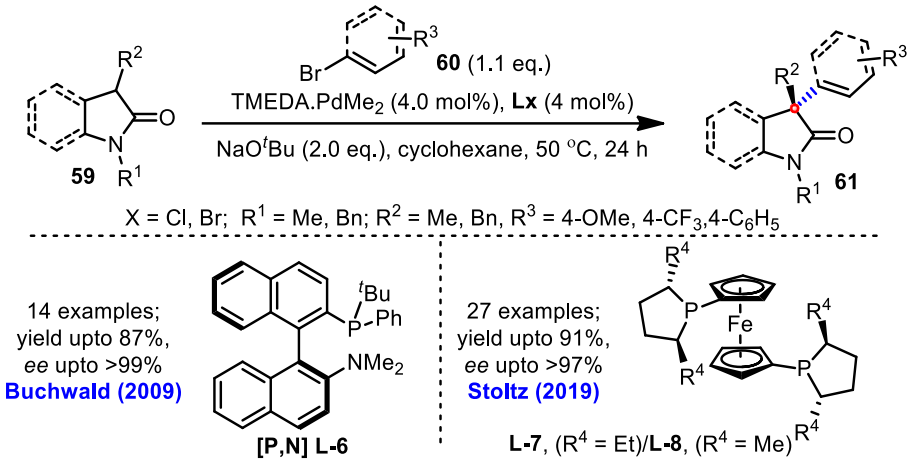
2.2: α-arylation of carbonyl-based approaches

In 1997, the Buchwald group introduced Pd-catalyzed intermolecular coupling of aryl halides with ketones to synthesize α-aryl ketones with a tertiary carbon.[40a] For having an all-carbon quaternary center, the same group in the subsequent next year developed an asymmetric version of this reaction by exploiting α-substituted ketones **56** with aryl bromides in the presence of Pd/BINAP complexes, Scheme **19**. Later, in 2008, Hartwig utilized aryl triflates as electrophilic coupling partners in this reaction.[40b] The reactions of electron-rich aryl triflate electrophiles, using Pd_2dba_3, and the ligand (*R*)-difluorphos **L-4** resulted in a diverse range of ketones such as indanones, tetralones, cyclohexanones, and cyclopentanones with good enantioselectivities. Tang's group utilized sterically hindered substrates (Ar-X) for this reaction in 2018.[40c] Various benzylic quaternary carbon stereocenters with excellent enantioselectivities and functional group compatibility were synthesized using the bulky phosphorus ligand (*R*)-BI-DIME **L-5**. They have also used this method to synthesize natural compounds (+)-sceletium A-4 and (–)-DeN-corynoline.



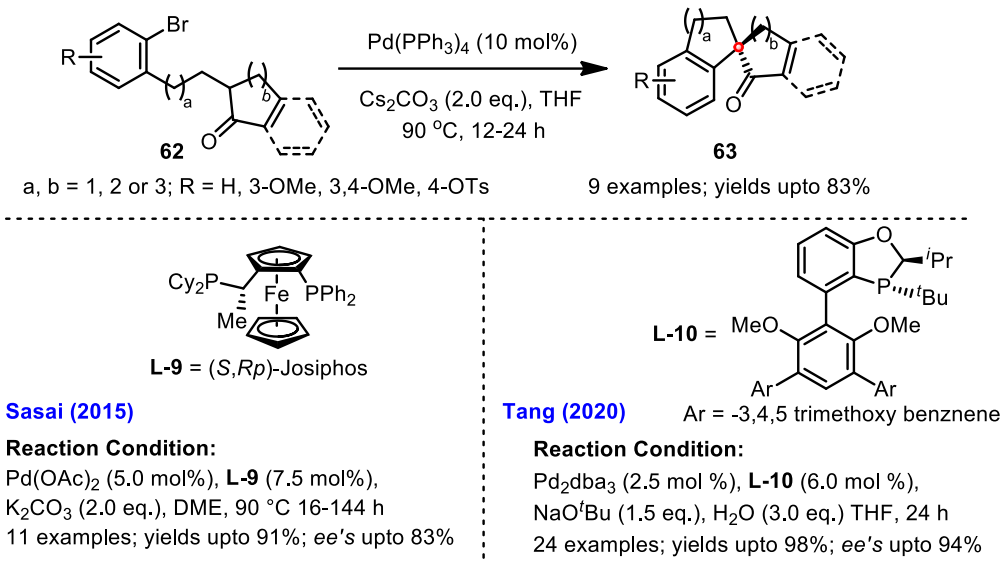
Scheme 19: Pd-catalyzed intramolecular α-arylation of α-substituted cyclic ketones.

In 2009, Buchwald and co-workers described a Pd-catalyzed direct coupling of various aryl bromides **60** and C-3 mono-substituted oxindoles **59** to synthesize chiral 3,3-disubstituted oxindoles, Scheme **20**.[41a] By employing the chiral [P, N] ligand **L-6** with TMEDA.$PdMe_2$, an array of densely substituted oxindoles containing a quaternary carbon **61,** were synthesized in excellent yields and enantioselectivities. In 2019, Stoltz and co-workers reported a similar Pd-catalyzed α-arylation reaction of γ-lactams with aryl chlorides/bromides.[41b] A combination of **L-7** and $Pd(OAc)_2$ in the reaction of aryl chlorides or **L-8** and $Pd(OAc)_2$ in the case of aryl bromides produced the excellent enantioinduction in the related products.



Scheme 20: Pd-catalyzed intramolecular α-arylation of α-substituted cyclic ketones.

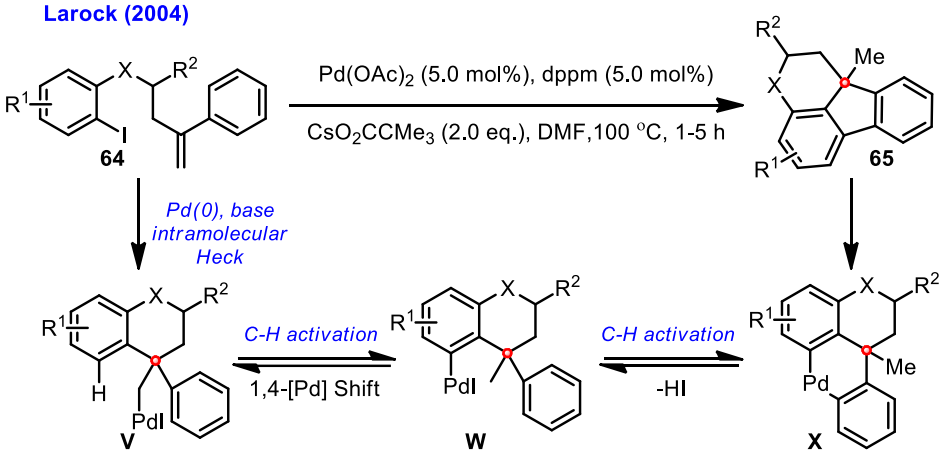
In 1997, Muratake and Natsume developed Pd-catalyzed intramolecular α-arylation of α-substituted cyclic ketones **62** tethered to a bromobenzene moiety at the α-position.[42a] Various α-substituted ketones **62** undergo intramolecular cyclization smoothly in the presence of catalytic amount $Pd(PPh_3)_4$, leading to diverse spiro-bicycle rings **63**. In 2015, Later, Sasai developed the enantioselective version for the construction of α-substituted spiro-cyclic ketones by employing the combination of $Pd(OAc)_2$, (*S*, *Rp*)-Josiphos ligand.[42b] Consistent yields and moderate to good enantioselectivities were realized across various substrates possessing spiro[4,4] as compared to spiro[5,5] and spiro[4,6] alkanones. In 2020, Tang and co-workers introduced new reaction conditions to generate chiral benzylic quaternary carbons with excellent yields and enantioselectivities.[42c] The authors have demonstrated the pronounced effect of water as an additive under strongly basic conditions in combination with the **Pd/L-10** complex in achieving higher enantiomeric excess (Scheme **21**).



Scheme 21: Pd-catalyzed intramolecular α-arylation of α-substituted cyclic ketones.

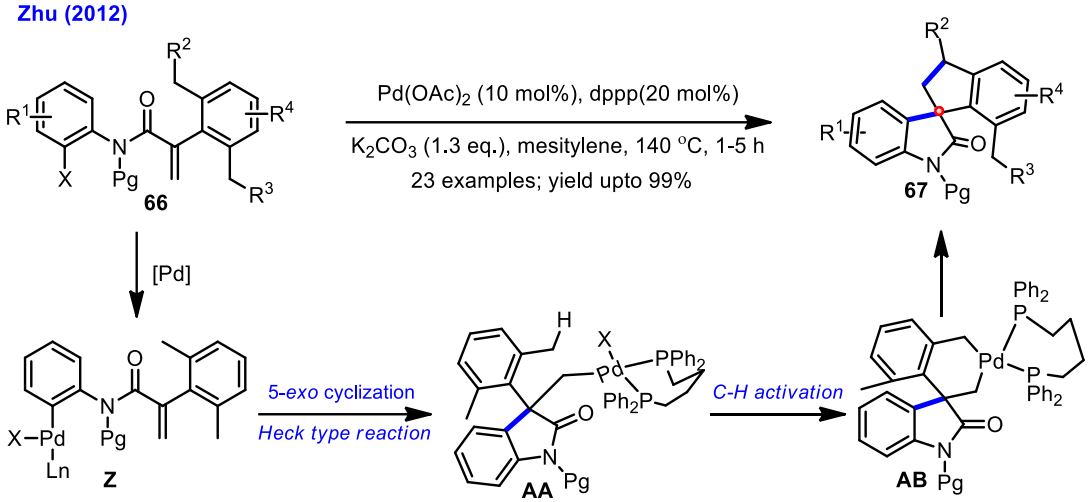
2.3: Domino Heck reactions-based approaches

Tandem C-H functionalization and intramolecular Heck reaction are efficient for constructing complex scaffolds with quaternary or spiro centers. In 2004, the Larock group developed a novel palladium-catalyzed domino heck process of substrate **64** to produce a variety of polycyclic compound **65** bearing all-carbon quaternary centers in moderate to excellent yields (Scheme **22**).[43] Initially, the Heck-type reaction of **V** generates an σ-alkylpalladium intermediate, followed by the 1,4-Pd shift to furnish an aryl palladium intermediate **W**. Thus, the polycyclic products **65** were produced after two Pd-mediated C-H activations and final reductive elimination. The intermolecular trapping of arylpalladium intermediate **W** through Heck, Suzuki, cyanation, and tandem reactions produce the corresponding fused cyclic structures with an all-carbon quaternary center.



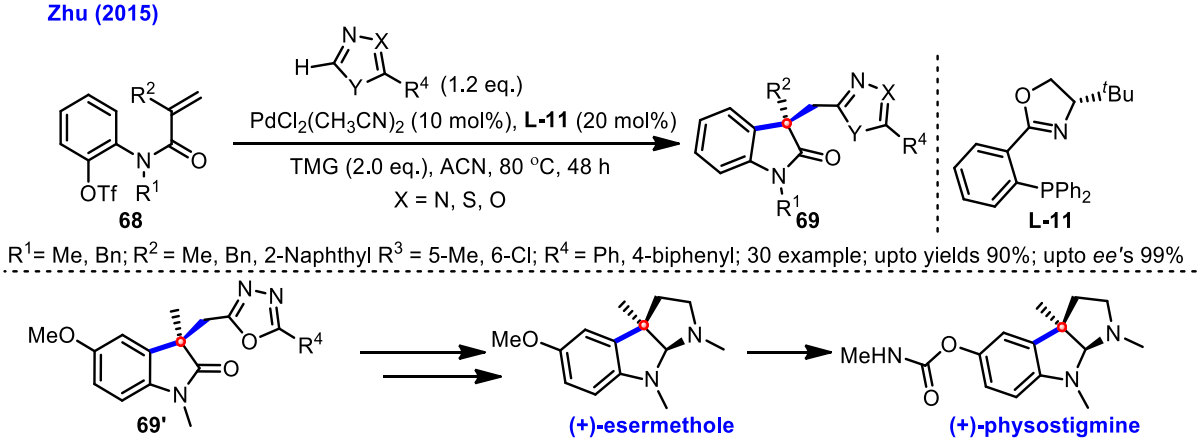
Scheme 22: Larock's intramolecular Pd-catalyzed cyclization *via* Heck/C-H activation

In 2012, Zhu developed a Pd-catalyzed intramolecular domino Heck and C(sp^3)- C(sp^3) bond-forming protocol to synthesize a diverse range of spiro-oxindoles **67**.[44] Intermediate **Z** undergoes 5-*exo* cyclization, neopentyl-type σ-alkyl Pd(II) complex **AA** is formed, which is ideally poised to activate the nearby C(sp^3)-H bond to form indane-fused spriooxindoles **67**.



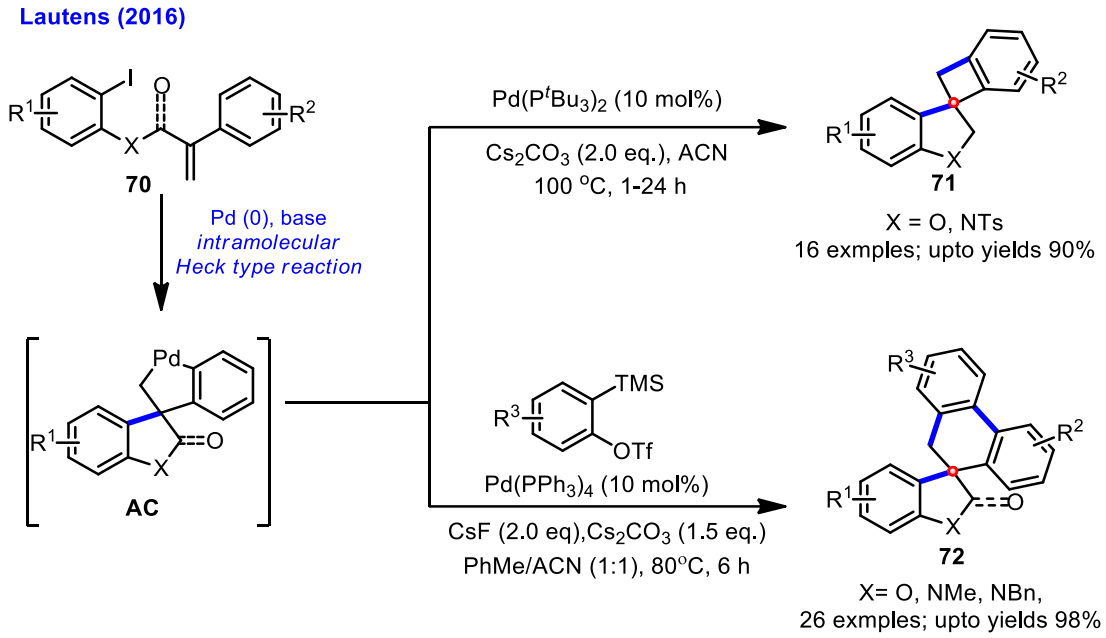
Scheme 23: Zhu's intramolecular domino carbopalladation/C(sp^3)-C(sp^3) bond formation.

In 2015, Zhu and co-workers presented an intermolecular palladium-catalyzed enantioselective Heck/C-H functionalization of *N*-aryl acrylamides **68** and heteroarenes, Scheme **24**.[45] Various functionalized oxindole products **69** with an all-carbon quaternary center were obtained with good yields and high enantioselectivities in the presence of $PdCl_2(CH_3CN)_2$ with a PHOX-type ligand **L-11**. They have also exploited this strategy for the total synthesis of natural products such as (+)-esermethole and (+)-physostigmine by subjecting *N*-aryl acrylamide to this domino process to deliver advanced intermediate **69'**; subsequent synthetic maneuvers led to the (+)-esermethole which was further elaborated to the total synthesis of physostigmine.



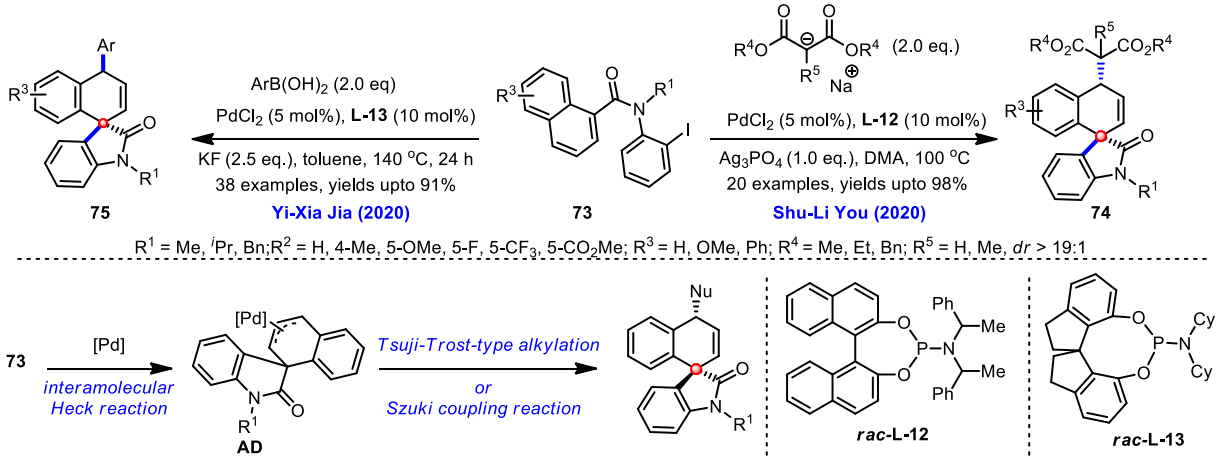
Scheme 24: Zhu's intramolecular Pd-catalyzed asymmetric Heck/C-H functionalization.

In 2016, Lautens and coworkers reported a facile synthesis of a wide range of spirooxindoles and spiro-dihydro benzofuran **72** by utilizing sequential carbopalladation, C–H activation, and benzyne insertion, Scheme **25**.[46] In the subsequent year, the same group observed different reactivity of **70** under Pd-catalysts *via* a common intermediate **AC** without any external coupling partners. In the presence of $Pd(P^tBu_3)_2$, the cyclization of **70** delivers spiro(benzo)cyclobutene derivatives **71** in good yields.



Scheme 25: Pd-catalyzed spiroannulation of **70.**

In 2020, the You and Yi-Xia Jia groups, reported dearomative 1,4-difunctionalization of naphthalenes *via* Pd-catalyzed tandem Heck/anionic-capture sequence.[47a] The research group of You developed a library of 1,4-dihydronaphthalene-based spirooxindoles **74** in excellent yields by treating **73** with $PdCl_2$ (5 mol%), **L-12** (10 mol%), Ag_3PO_4 (1.0 eq.), and

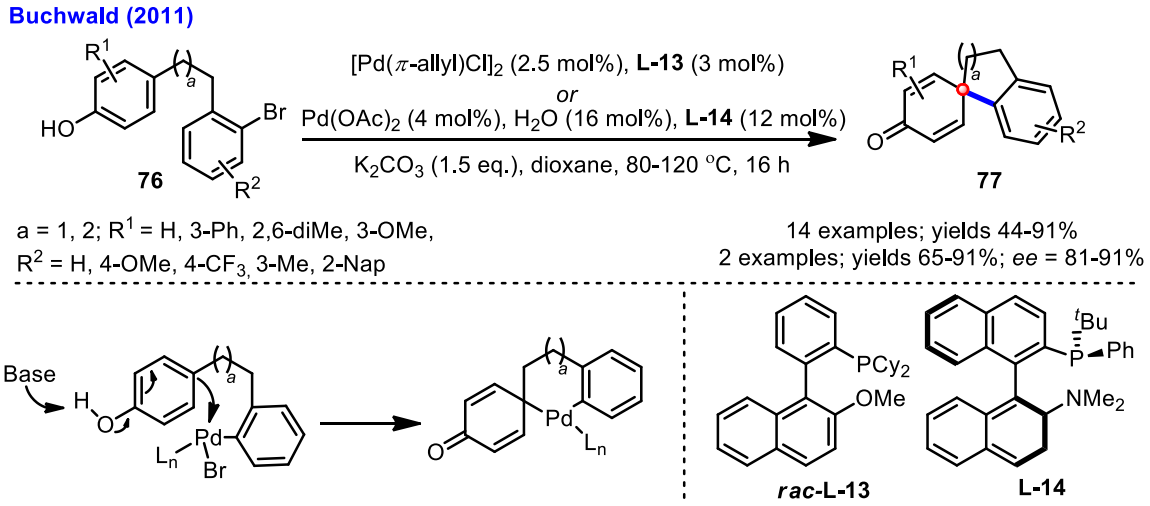


Scheme 26: Palladium-catalyzed dearomative 1,4-difunctionalization of naphthalenes.

malonates (as nucleophilic source) in DMA solvent at 100 °C. Later, the Jia group synthesized diversified spirooxindoles **75** by utilizing tandem Heck/Suzuki coupling reaction of naphthamides **73** with aryl boronic acids using Pd/**L-13** complex in toluene at 140 °C.[47b]

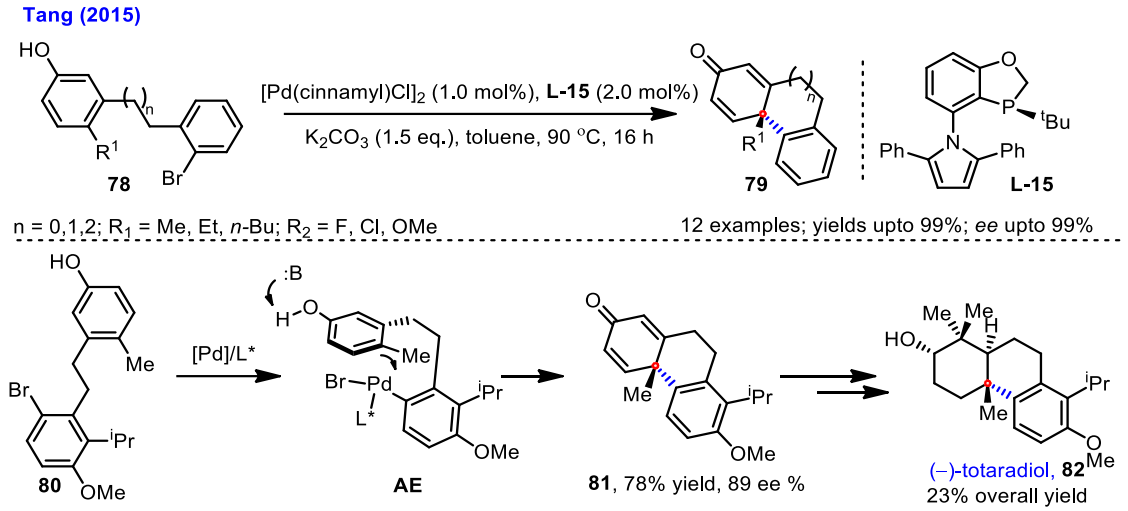
2.4: Dearomatization of arenes and heteroarenes-based approaches

In 2011, the Buchwald group developed an efficient intramolecular arylation of 1,4 substituted phenols **76** *via* the dearomatization process.[48] In the presence of a suitable Pd-phosphine complex, intramolecular cyclization provided spirocyclohexadienones **77** in excellent yields. An exclusive solvent, base, and catalyst-dependent reactivity of phenols **76** were also observed in this study. In the presence of chiral bidentate P, N ligand **L-14** delivered the highly substituted spiro-indanes **77** in good yields and enantioselectivities, Scheme **27**.



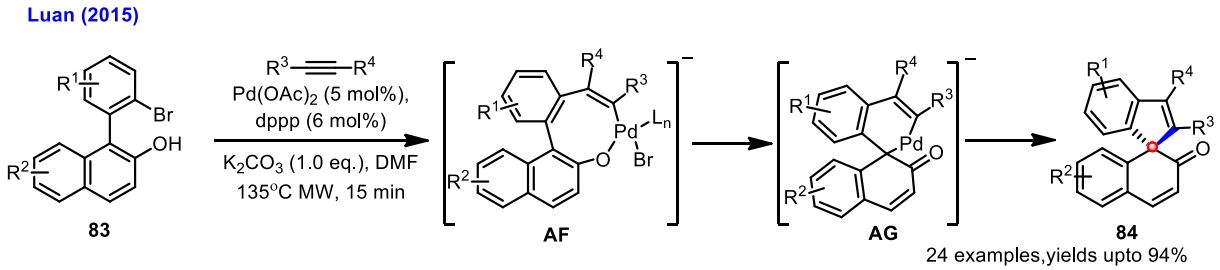
Scheme 27: Buchwald's intermolecular Pd-catalyzed arylative dearomatization of phenols.

In 2015, the Tang group developed a novel strategy to synthesize chiral phenanthrenones **79** having an all-carbon quaternary center by utilizing C3 substituted phenols **78**.[49] An enantioselective Pd-catalyzed dearomative cyclization to **80** using **L-15** as chiral ligand afforded the enantiomerically pure cyclohexadienone **81** (Scheme **28**). After a few synthetic transformations, the total synthesis of natural product (–)-totaradiol **82** was completed with an overall yield of 22% and excellent enantioselectivity**.**



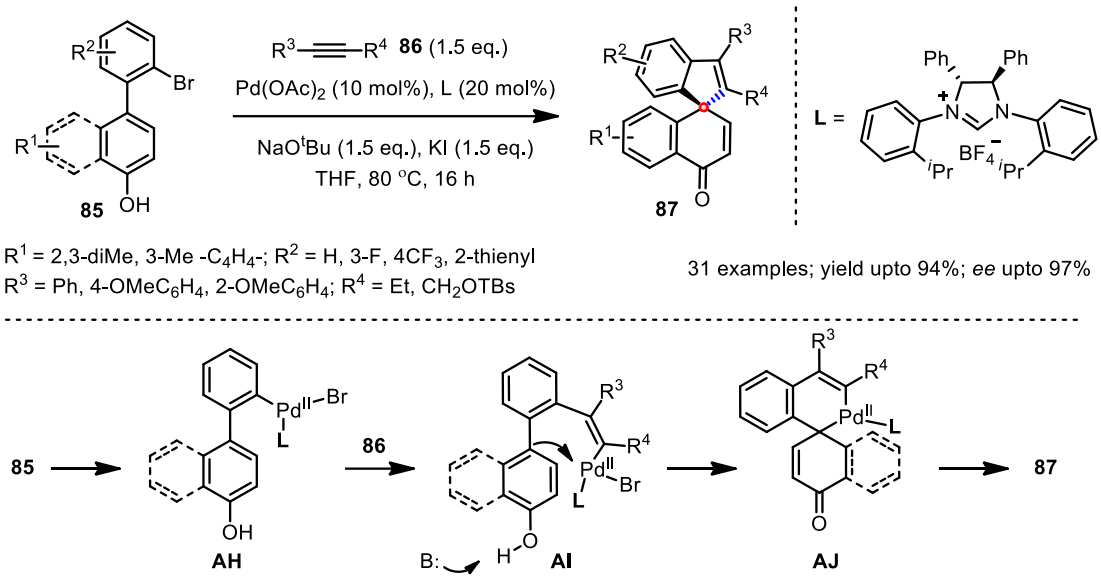
Scheme 28: Tang's asymmetric Pd-catalyzed dearomative cyclization of **78**

In 2015, Luan described a microwave-assisted Pd(0)-catalyzed strategy for the synthesis of spiro[indene-1,1'-naphthalen]-2'-ones (Scheme **29**).[50] It involved the formation of a six-membered palladacycle by initial oxidative addition of Pd(0) to aryl bromide **83**, followed by deprotonation of 2-naphthol. Subsequently, alkyne migratory insertion and *β*-naphthol dearomatization cascade process afforded spirocyclic intermediate **AG** through unstable eight-membered oxapalladacycle **AF**, which upon reductive elimination gave **84** in high yields with excellent chemoselectivities.



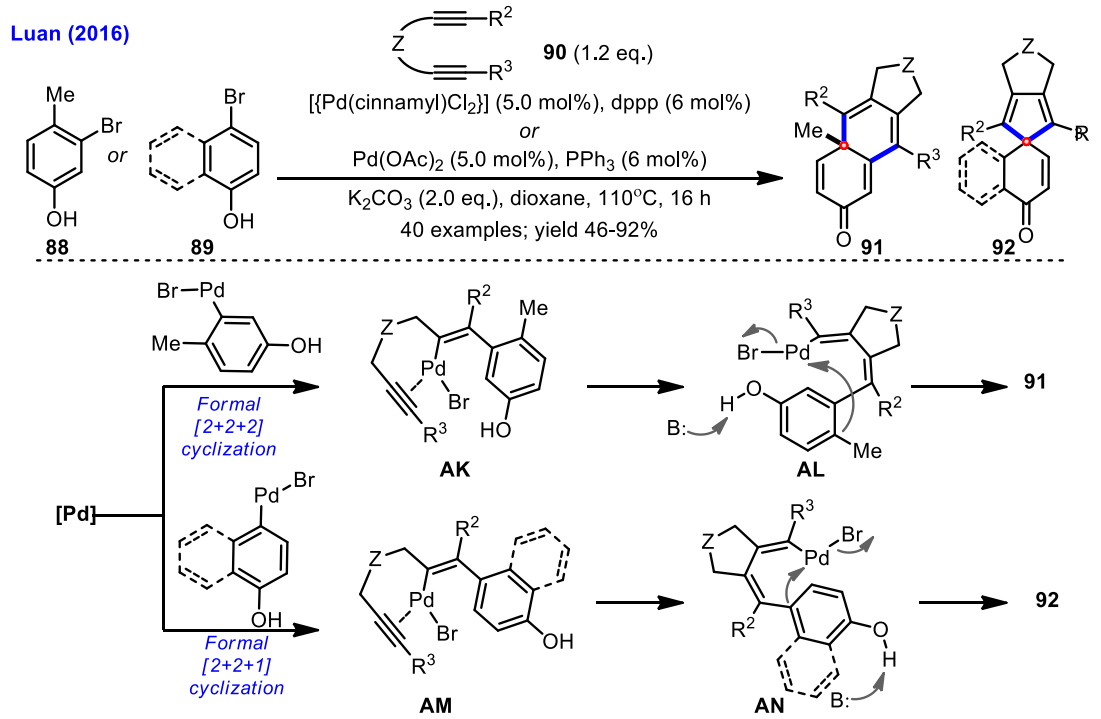
Scheme 29: Luan's intermolecular Pd-catalyzed spiroannulation of *β*-naphthols.

The same group established asymmetric synthesis of 4'H-spiro[indene-1,1'-naphthalen]-4'-ones **87** *via* dearomatization of 4-naphthol derivatives **85** with alkynes **86** using chiral Pd-NHC complex as active catalyst.[51] It was the first report on Pd-catalyzed dynamic kinetic asymmetric transformation of racemic biaryls to enantioenriched spirocyclic compounds bearing an all-carbon quaternary stereocenter *via* axial-to-central chirality transfer (Scheme **30**).



Scheme 30: Pd-catalyzed asymmetric spiroannulation of *β*-naphthols *via* dearomatization

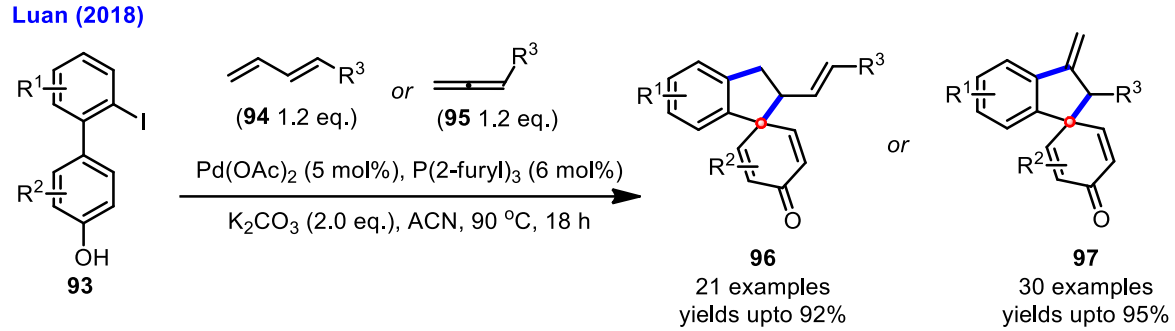
In 2016, the Luan group disclosed an efficient protocol for synthesizing new polycyclic compounds **91** and **92** with an all-carbon quaternary or spiro center.[52] The dearomative process involved the Pd-catalyzed unusual carbopalladation reaction of tethered diynes with bromophenols **88** and **89**. Under standard reaction conditions, *p*-bromo-phenols **89** upon



Scheme 31: Laun's intermolecular carbocyclization of (1,n)- diynes and bromophenols

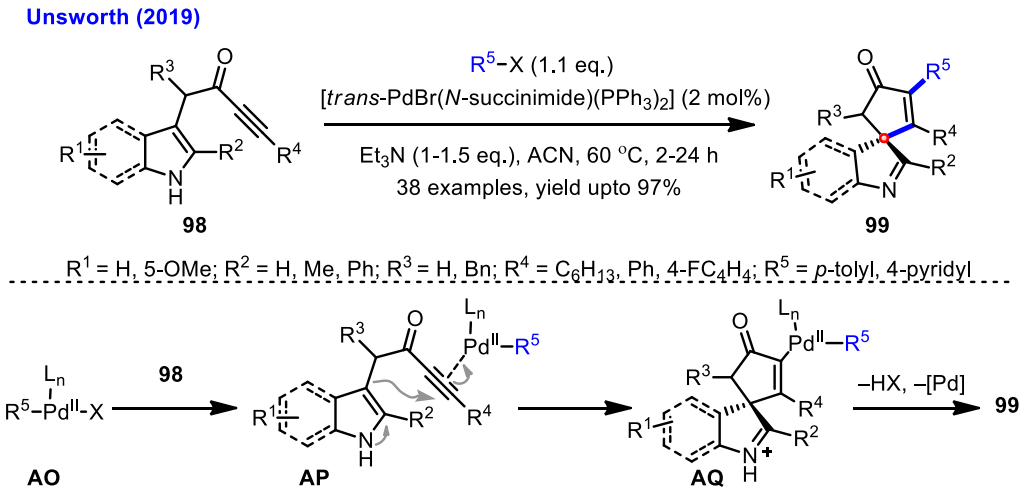
treatment with diynes **90** as coupling partners, delivered spiro fused polycyclic compounds *via* a formal [2+2+1] spiroannulation; whereas *m*-bromophenols **88** favored [2+2+2] cyclization pathway, Scheme **31**.

The construction of spiro-indane fused cyclohexadienones **96** and **97** using Pd-catalyzed dearomatization of halogenated biaryl phenol with 1,3-dienes **94** or allenes **95** has been reported by the same group in 2018, (Scheme **32**).[53] This strategy led to the formation of two contiguous tertiary/quaternary carbon centers *via* formal [3 + 2] spiroannulation process, instead of forming Heck-type byproducts through *β*-hydride elimination.



Scheme **32**: Laun's intermolecular carbocyclization of biraryl phenols

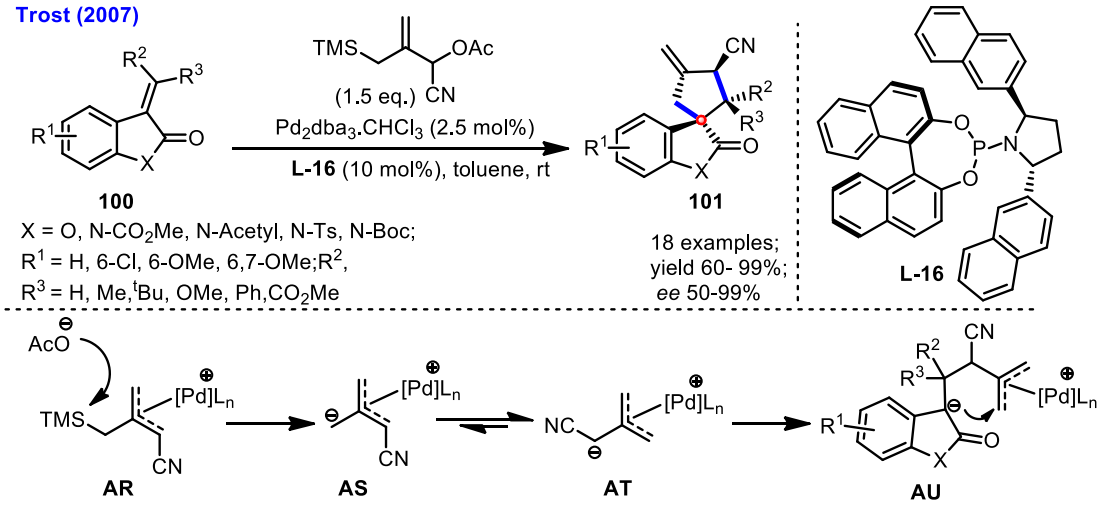
In 2019, Unsworth explored a one-pot protocol to generate functionalized spiroindolines **99** having tetrasubstituted alkenes from indole/pyrrole-tethered ynones **98**, Scheme **33**.[54] The activation of the alkyne by Pd(II) intermediate **AP** encouraged the attack of C3 position of indole to furnish spirocyclic Pd(II)-complex intermediate **AQ**, which upon deprotonation and reductive elimination gave cross-coupling products **99** in high yields.



Scheme 33: Unsworth's one-pot dearomatizing spirocyclization/ cross-coupling cascade

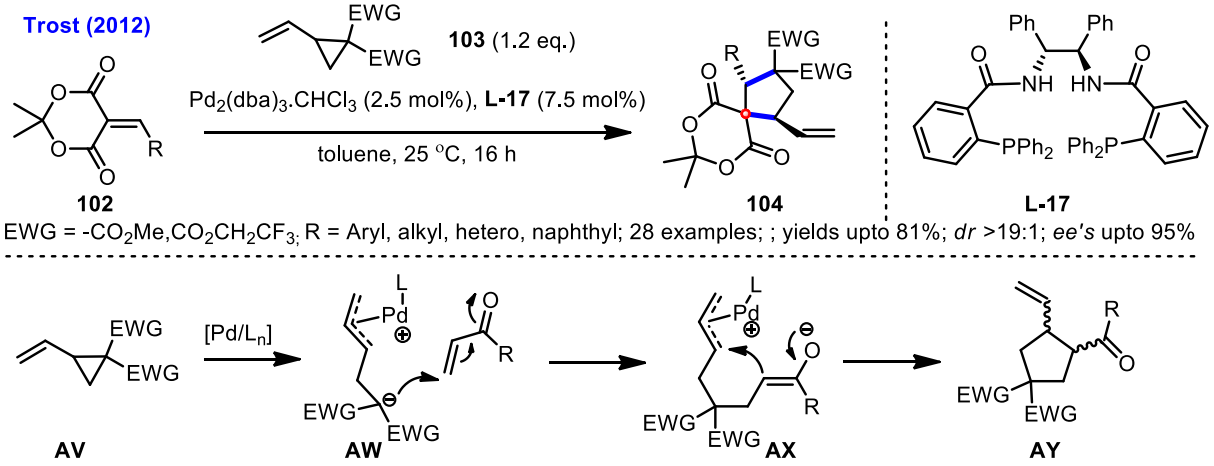
2.5: [3+2] Cycloadditions based approaches

In 2007, the Trost group reported the first enantioselective synthesis of spiro-cyclopentane fused oxindoles **101** using the Pd-catalyzed trimethylenemethane (TMMs) [3+2] cycloaddition strategy (Scheme **34**).[55] It involves the initial formation of a π-allyl intermediate **AR**, followed by the generation of Pd-TMM zwitterionic intermediate **AT** *via* desilylation of cyanosubstituted trimethylenemethane (CN-TMM) **AR** to form the 1,3-dipole. Further, one of the carbon termini carries more negative charge 1,4 conjugate addition on oxindole **100** giving species **AU**, which led to the formation of product **101** *via* intramolecular attack of the α-carbon onto the π-allylpalladium. In the presence of ligand **L-16**, *cis*-**101** formed upto 6:1 *dr* and 50-99% *ee*.



Scheme 34: Trost's asymmetric [3+2] for spirooxindoles **101**

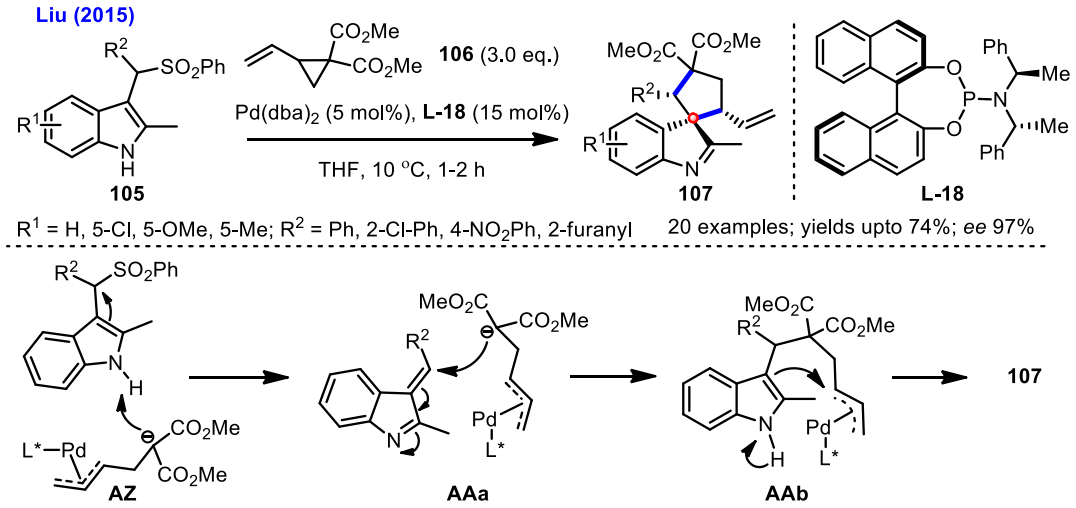
In 2012, the Trost group described the synthesis of a diverse range of enantioenriched spiro-cyclopentane fused adducts **104** *via* palladium-catalyzed [3+2] cycloaddition strategy.[56]



Scheme 35: Trost's asymmetric [3+2] of vinylcyclopropanes **103** and enones **102**

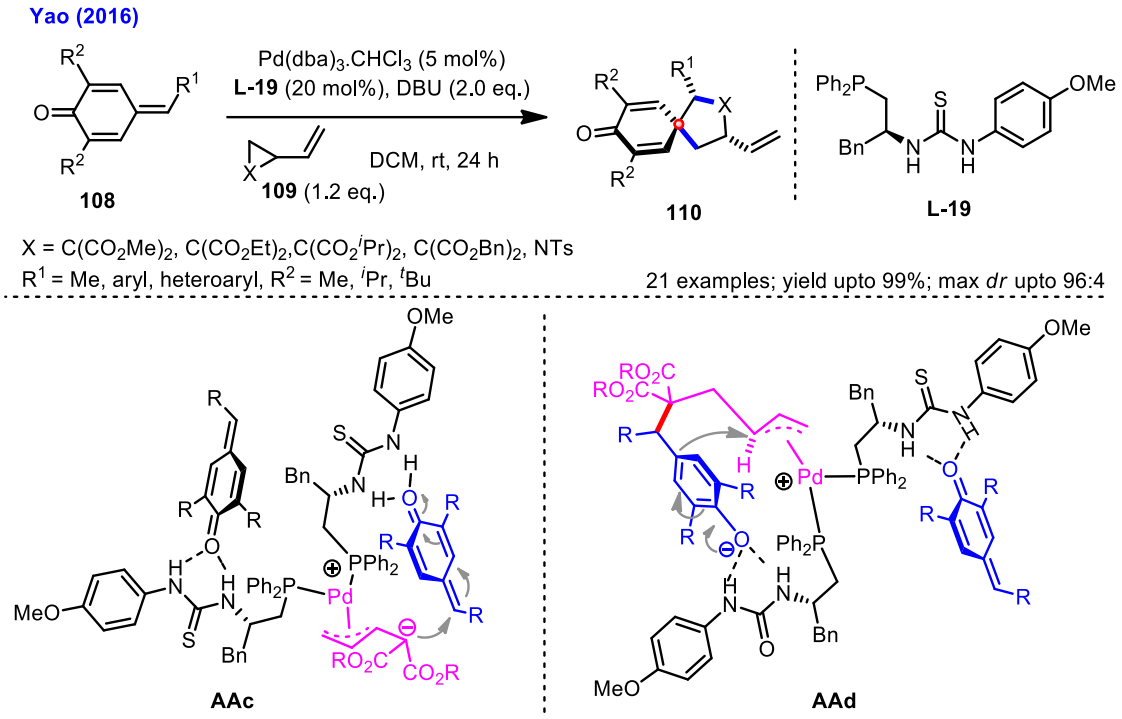
The treatment of substituted vinylcyclopropanes **103** with $Pd_2(dba)_3.CHCl_3$ and **L-17** generate zwitterionic intermediate **AW** which undergoes Michael addition on Meldrum's acid alkylidenes **AX** as (electron-deficient olefins), Scheme **35**. The subsequent palladium-catalyzed intramolecular allylation of **AX** led to the formation of **AY** or **104** in excellent yields and enantioselectivities.

In 2015, Liu and co-workers disclosed palladium-catalyzed enantioselective [3 + 2] reaction to synthesize structurally diverse spiroindolenines **107** from vinylcyclopropanes and *in situ* generated unsaturated imines.[57] the reaction proceeded by deprotonation of sulfonyl indoles by zwitterionic *π*-allylpalladium complex **AZ** to furnishes the conjugate imine. Then 1,4 addition of amphiphilic ions to imine afford **AAb** which upon cyclization deliver spiroindolenines **107**, Scheme **36**. Highly diastereo- and enantioselective spirocyclic products **107** were obtained in good yields in the presence of $Pd(dba)_2$, **L-18** as ligand (Scheme **36**).



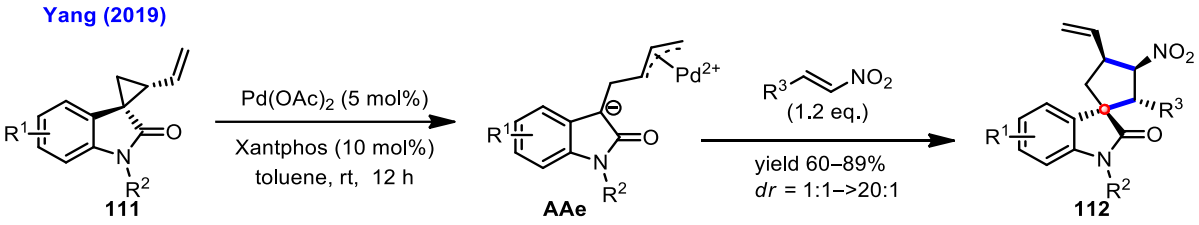
Scheme 36: Liu's enantioselective [3 + 2] for spiroindolenines **107**

In 2016, Yao and coworkers showed palladium and phosphine−thiourea cooperative catalysis for diastereoselective synthesis of spiro[4.5]deca-6,9-diene-8-ones **110**, Scheme **37**.[58] The authors utilized *para*-quinone methides (*p*-QMs) **108** as electron-deficient olefins, which undergo [3+2] spiro annulations with vinylcyclopropanes **109**. The intermolecular hydrogen-bond interaction of bifunctional organocatalyst **L-19** activates *p*-QMs, and subsequently, 1,6-conjugate addition of a carbon anion of zwitterionic *π*-allylpalladium complex generates **AAc-AAd**. The exclusive formation of spiro-cyclized products **110** obtained by Pd- catalyzed intramolecular allylation (Scheme **37**).



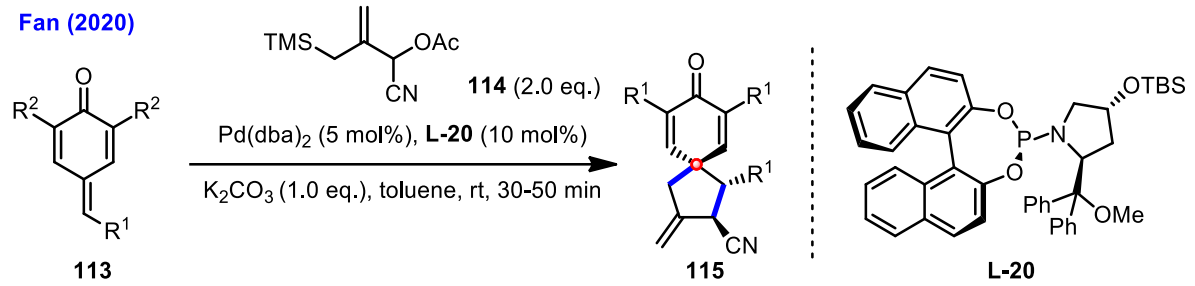
Scheme 37: Yao's asymmetric [3+2] spiro-annulations of *p*-QMs **108** with **109**.

In 2019, Yang group also explored the donor-acceptor cyclopropanes **111** under palladium conditions to synthesize spirocyclopentyl-oxindoles **112** with high diastereoselectivity. Spirovinylcyclopropyl oxindole **111** introduced as a latent zwitterionic π-allylpalladium complex **AAe** and β-nitrostyrene as electron-deficient olefins were exploited in Pd-catalyzed [3+2] reaction, Scheme **38**.[59]



Scheme 38: Yang's [3+2] for spirooxindoles from **111** and β-nitrostyrenes.

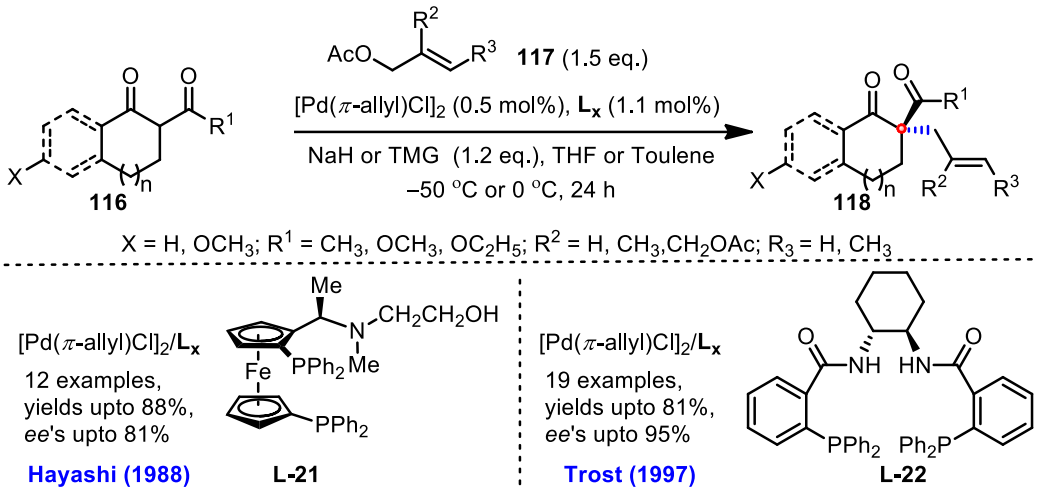
In 2020, Fan and co-workers reported a facile asymmetric synthesis of spirocyclopentyl *p*-dienones **115** bearing three contiguous chiral centers by utilizing the chiral phosphoramidite **L-20** *via* [3+2] cycloaddition, Scheme **39**.[60] A wide variety *p*-QMs **113** and CN-TMMs **114** were well tolerated under the mild conditions to deliver the desired products **115** in excellent enantioselectivities and yields.



Scheme 39: Fan's asymmetric [3+2] of *p*-QMs **113** and CN-TMMs.

2.6: Tsuji-Trost type allylic alkylations based-approaches

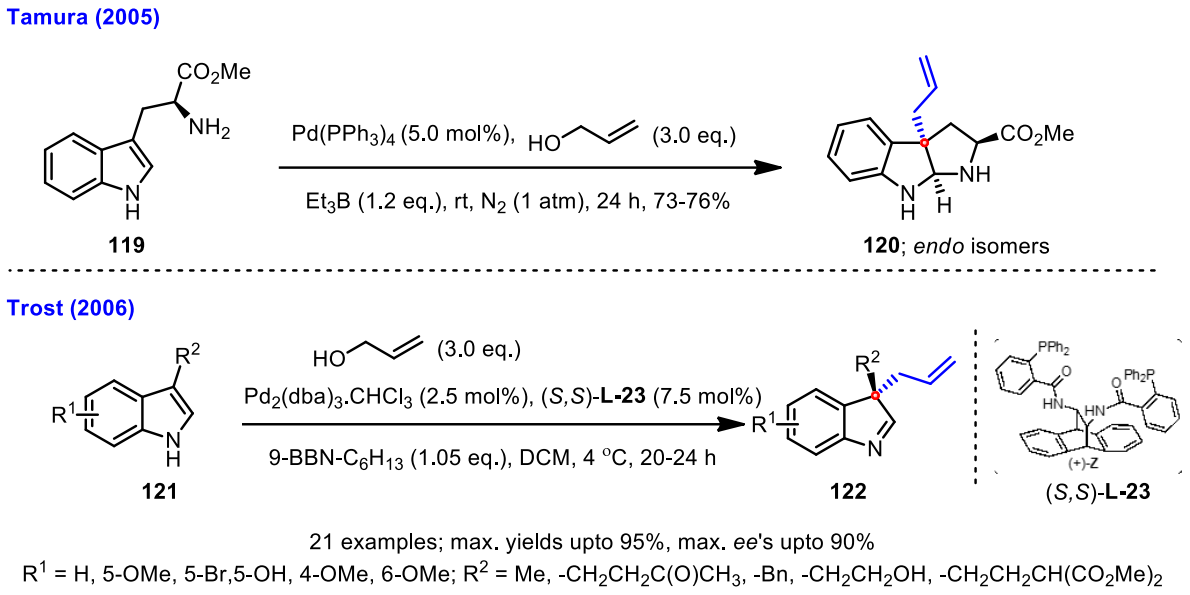
In 1988, Hayashi and co-workers reported the first Pd-catalyzed allylation of active methine compounds **116** to construct an all-carbon quaternary center using a chiral ferrocene diphosphine ligand **L-21**.[61] The sodium enolate of *β*-diketones undergoes a facile allylation with *in situ* chiral η^3-allylpalladium species generated from allyl acetate and a catalytic Pd^0 complex with **L-21** delivered products in high yields with excellent enantioselectivities (Scheme 40). On the other hand, Trost (1997) employed the (R, R)-DACH Phenyl **L-22** to generate the enantioenriched products **118** from a diverse range of *β*-diketones and *β*-diesters and highly substituted allyl acetates **117**.[98] Further, this strategy was also employed in the total synthesis of (-)-Nitramine.



Scheme 40: Enantioselective allylic alkylation of a 1,3-dicarbonyls.

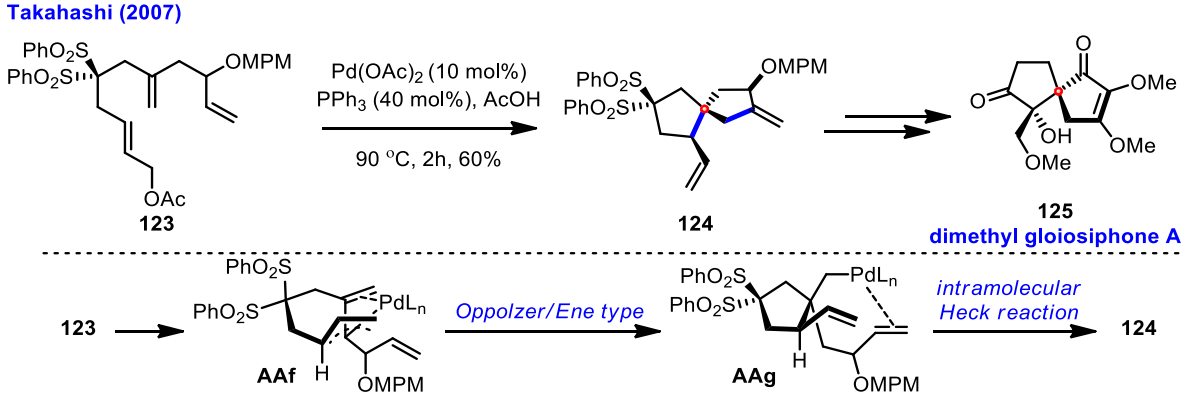
In 2005, Tamaru and co-workers disclosed the first example of Pd-catalyzed C3-selective allylation of indoles to furnish an all-carbon quaternary center.[63a] The treatment of **119** with allylic alcohols in the presence of Et_3B (as the promoter) and a catalytic amount of $Pd(PPh_3)_4$ led to the formation of □-allylpalladium complexes, which direct the exclusive *endo* selectivity of the products **120** *via* dearomatization of indoles **119**. Soon after Tamaru's work,

Trost developed the catalytic asymmetric version of this reaction by utilizing a chiral bisphosphine ligand **L-23** and 9-BBN-C_6H_{13} (Scheme **41**).[63b]



Scheme 41: Pd-catalyzed allylic alkylation of 3-substituted indoles.

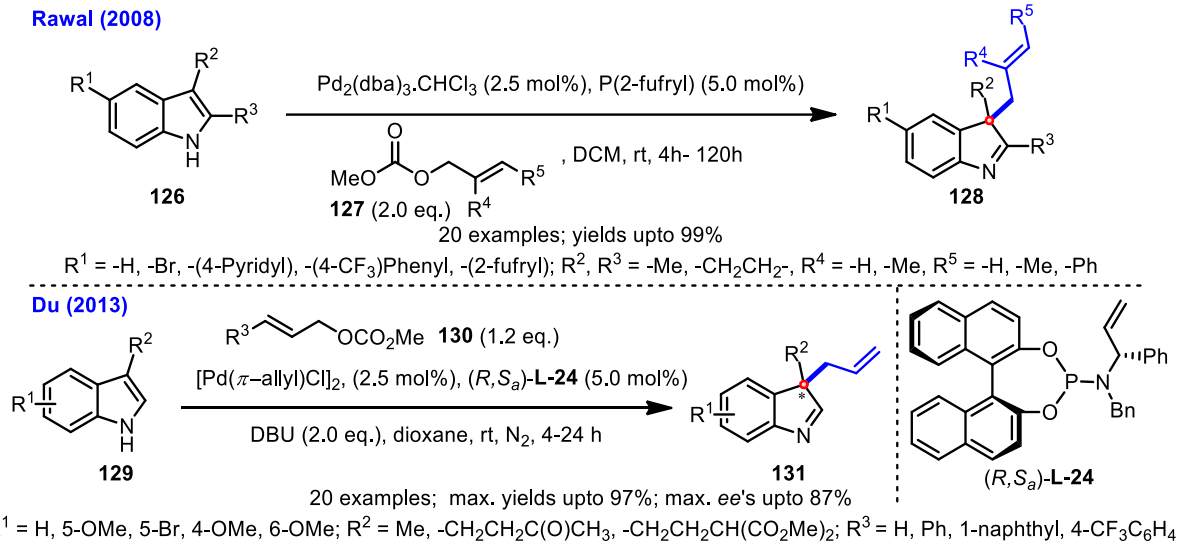
In 2007, Takahashi came up with a new design of dienyl acetates to synthesize spiro[4.4]nonane skeleton *via* palladium-catalyzed domino cyclization. Linear 7-methylene-2,10-undecadienyl acetate **123** underwent intramolecular Ene-type/Trost-Oppolzer type cycloisomerization with high intra-annular diastereoselectivity and led to formation of a σ-alkylpalladium intermediate **AAf**.[64] The authors accomplished the total synthesis of dimethyl glololsphone A **125** by employing **124** to appropriate synthetic transformations (Scheme **42**).



Scheme 42: Intramolecular Ene-type/Trost-Oppolzer type cycloisomerization of **123**

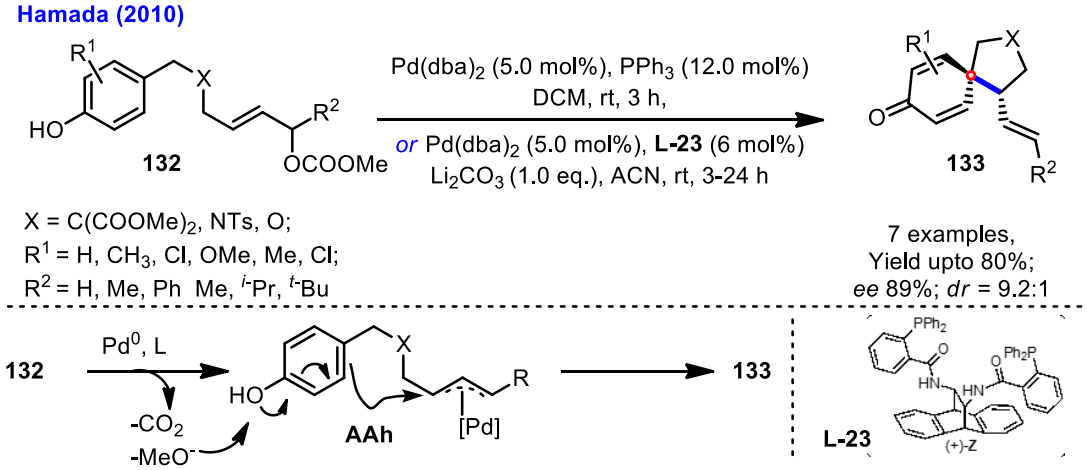
Later, in 2008, Rawal and coworkers explored allylic carbonates instead of allylic alcohols in Pd-catalyzed allylic substitution reactions of 2,3-disubstituted indoles **126** to generate a diverse range of the corresponding indolenine products **128** having an all-carbon quaternary (Scheme **43a**).[65a] Du (2013) disclosed the application of the asymmetric Tsuji-Trost

reaction to synthesize a library of chiral indolenines **128** using the chiral Pd/**L-24** complex.[65b] A wide range of allyl acetates **130** and indoles **129** were well-tolerated under mild conditions to produce the highly substituted indolenines **131** in excellent yields and enantioselectivities (Scheme **43b**).



Scheme 43: Rawal's and Du's work on Pd-catalyzed allylic alkylation reactions of indoles

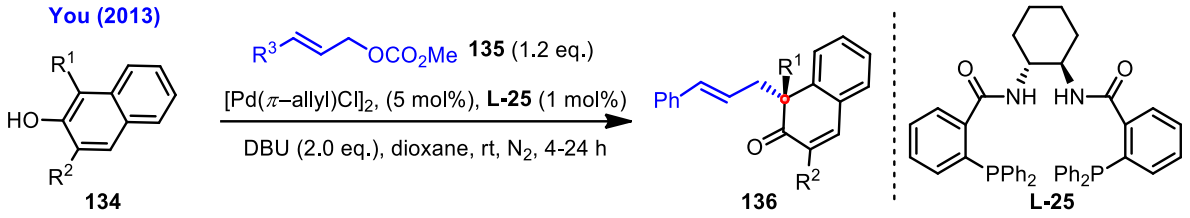
In 2010, Hamada and co-workers disclosed the intramolecular dearomative process to achieve spiro[4.5]cyclohexadienones **133** from *para*-substituted phenols **132** *via* Pd-catalyzed intramolecular *ipso*-Friedel-Crafts allylic alkylation of Scheme **44**.[66a] Initially, the oxidative addition of Pd(0) to allylic carbonates led to the formation of the respective π-allylpalladium



Scheme 44: Hamada's work for the synthesis of spiro[4.5]cyclohexadienones

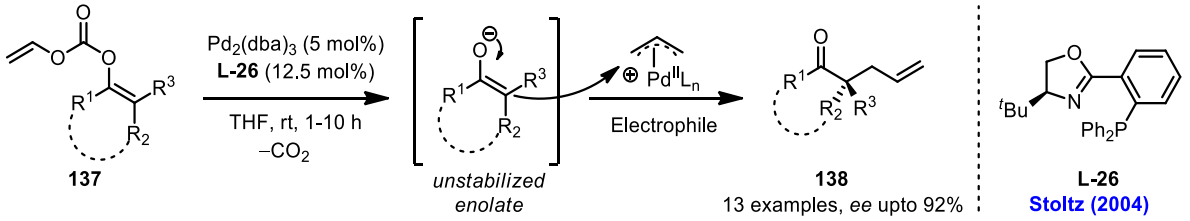
species **AAh**. The deprotonation of **AAh** by methoxide anion furnished the phenoxide intermediates, which underwent the *ipso*-attack onto the π-allylpalladium to deliver the spiro-fused indanes. Later in 2012, authors also developed the asymmetric variant of this reaction by employing a chiral bisphosphine ligand **L-23** and best levels of yields and enantioselectivities were achieved.[66b]

In 2013, You and co-workers reported an asymmetric catalytic method to generate *β*-naphthalenones **136** bearing all-carbon quaternary stereogenic centers from easily accessible aromatic naphthol derivatives **134** (Scheme **45**).[67] An elaborate optimization study identified **Pd/L-25** as the suitable chiral ligand metal complex to produce **136** in good to excellent yields and excellent levels of chemo- and enantioselectivity. A prominent influence of the γ-positions of β-naphthols on the high-chemo and enantioinduction was also demonstrated.



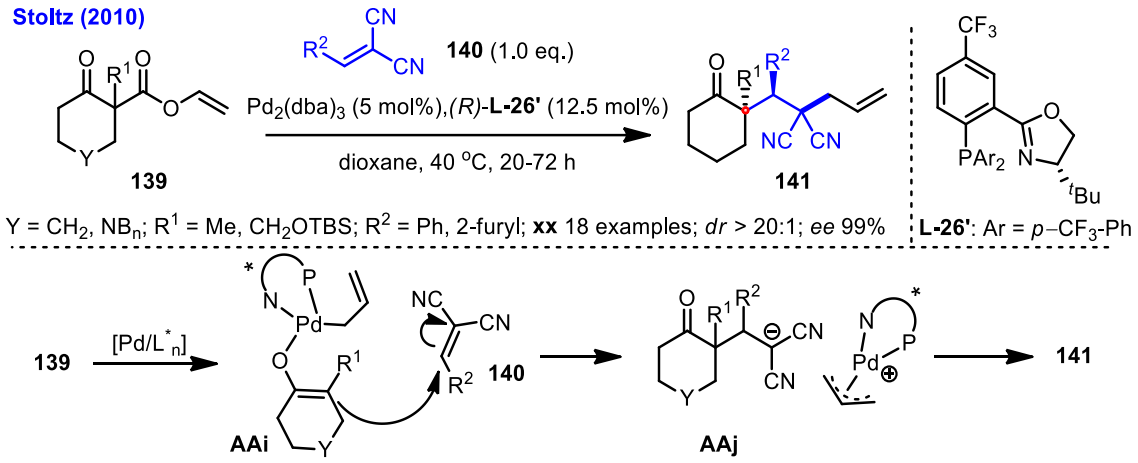
Scheme 45: You's asymmetric intermolecular Pd-catalyzed allylation

Pd-catalyzed decarboxylative allylic alkylation (PDAAA) is widely used method for forming acyclic/cyclic quaternary carbon stereocenters *via* enolate alkylation of prochiral enolates. In 2004, Stoltzintroduced the first PDAAA strategy to construct *α*- ketones **133** having an all-carbon quaternary center.[68a] In the presence of the Pd/**L-26** complex (Scheme **46**), cyclic allyl enol carbonates **137** produced **138** with high yields and excellent enantioselectivities. The Trost group also disclosed a similar technique to synthesize enantioenriched *α*, *α*- disubstituted ketones by utilizing the Pd/**L-23** complex.[68b] This area has received significant attention, especially in developing new efficient methods for assembling complex all-carbon quaternary stereocenters.



Scheme 46: Stoltz's work on decarboxylative asymmetric allylic alkylation of cyclic enol carbonates.

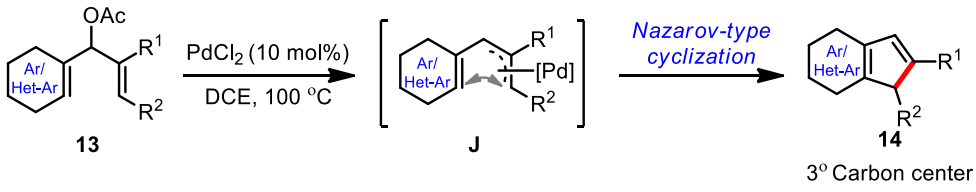
In 2010, Stoltz demonstrated that Pd-complexes modified by **L-26** catalyze enolate alkylation of **139** to form adjacent quaternary and tertiary stereocentres with excellent control of diastereo- and enantioselectivities.[69] In the presence of chiral **Pd-L26'** complex, η^1-allylpalladium enolate **AAi** underwent 1,4-addition to **140** generate stabilized intermediate **AAj**, which upon reductive alkylation delivered **141** in high yields, Scheme **47**.



Scheme 47: Stoltz's enantioselective decarboxylative enolate alkylation cascade.

Despite significant progress, there are still a few challenges associated with π-allyl palladium chemistry, such as a) the need for harsh reaction conditions, which can lead to a variety of side reactions; b) the requirement of additives such as bases, acids, or oxidants; c) the steric and electronic characteristics of the reactants have an impact on reactivity; d) quenching of the reaction by the deactivated catalyst; e) the products' isomerization, leading to a reduction in reaction selectivity. However, further advancement of this intramolecular strategy to construct medium-sized rings having an all-carbon quaternary/spiro center has been dramatically limited.

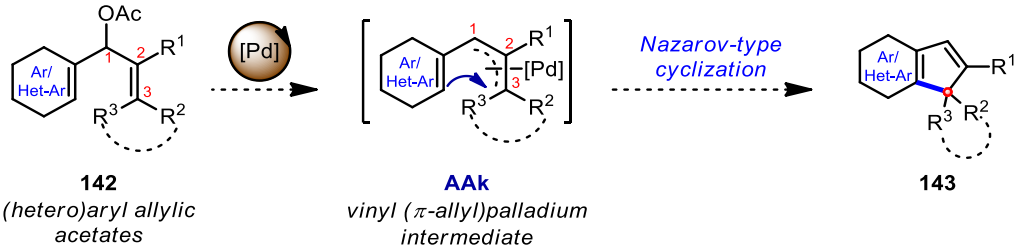
Within the polycyclic framework of complex natural products, the synthesis of highly substituted five-membered carbocycles containing all-carbon quaternary and spiro centers usually demands advanced synthetic planning. As a result of examining a novel reactivity trend in the dienylic substrates, our research group has recently devised a broad and practical approach for synthesizing a wide range of cyclopentanoids having a tertiary carbon. The allylic substrates **13** generate vinyl-π-allylpalladium complexes **J** in the presence of $PdCl_2$,



Scheme 48: Pd-catalyzed Nazarov-type cyclization of allylic acetates to cyclopentanoids.

undergo the Nazarov-type cyclization to yield cyclopentanoids **14** (Scheme **48**). This approach was utilized to synthesize a diverse range of cyclopentene-fused and heteroarenes and first total synthesis of (±) β-diasarone.

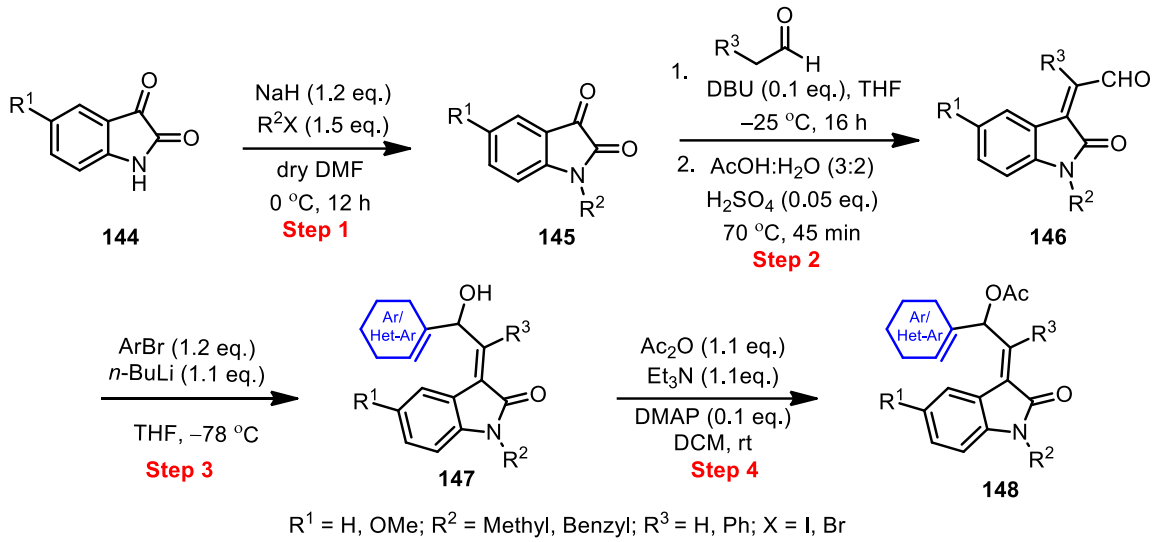
Based on our recent work, we designed an adequately substituted (hetero) aryl acetate **142** to produce a variety of cyclopentanoids **143** incorporated with an all-carbon quaternary or a spiro center, resulting in a novel annulation method using π-allylpalladium chemistry (Scheme **49**). We hypothesized that the dienyl acetate **142** might be subjected to oxidative palladium addition, resulting in the vinyl(π-allyl) palladium complex **AAk**. The vinyl(π-allyl)palladium complex **AAk** has the ability to convert to fused cyclopentenes **143** *via* Pd-catalyzed Nazarov type cyclization.



Scheme 49: Our hypothesis towards the Pd-catalyzed reaction with allylic acetates to construct all-carbon quaternary spiro centers.

2.7: Results and Discussion

We aim to obtain (hetero)arene fused cyclopentene **143** containing all-carbon quaternary/spiro centers *via* Pd-catalyzed intramolecular cyclization, we began our studies by synthesizing the model substrate oxindole-based dienyl acetate **148** to construct an all-carbon spiro center, Scheme **50**. By applying four relevant synthetic transformations, modular access to dienyl acetate could be easily obtained from commercially accessible isatins **144**. *N*-alkylation of **144** produced *N*-protected isatins **145** with alkyl halides under base-mediated reaction conditions. The aldol reaction of **145** with aldehydes under the base mediated reaction conditions generated enal **146**. Further, the *n*-BuLi mediated alkylation of (hetero)aryl bromides with appropriate enals **146** at −78 ^{o}C generated the corresponding allylic alcohols **147**. Subsequently, the acylation of **147** furnished the allylic acetates **148**.



Scheme 50: General schematic representation for the synthesis of allylic acetates **148**

We have started the optimization study by choosing **148a** as the model substrate. Table **5** summarises the results of various optimization studies on a wide range of palladium catalyst and solvent combinations. At the beginning of our studies, we chose (*E*)-1-(benzo[*b*]thiophen-2-yl)-2-(1-benzyl-2 oxindole-3-ylidene)propyl acetate **148a** as substrate, and 10 mol % of $Pd(PPh_3)_4$ as a catalyst, and 1,2-dichloroethane (1,2-DCE) as a solvent. This combination was reacted at 60 °C, but no product was formed. The reaction of **148a** with $Pd_2(dba)_3$ at the same temperature (Table **5** entries 1 and 2) produced a non-polar spot, which was isolated as **149a** in moderate yield. IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy were used to characterize the isolated molecule **149a** comprehensively. In the IR spectrum, the absence of a broad absorption band of ester carbonyl at 1746 cm^{-1} of **148a** (starting material) and the strong band at 1716 cm^{-1} due to the presence of carbonyl of cyclic amide (5-membered lactam) indicated the **149a** product formation. In ^{1}H NMR (DMSO-***d*$_6$**) (see Figure **17**), the absence of acetate proton peak and presence of a quartet in the range of δ 4.98-5.09 ppm due to –CH_2– of cyclic amide, singlet at δ 1.81 ppm due to olefinic methyl confirmed the structure **149a**. The ^{13}C NMR (DMSO-***d*$_6$**) spectrum showed 22 signals (see Figure **18**); a signal at δ 173.91 was assigned to the carbonyl carbon. The presence of an all-carbon quaternary at δ 66.08 and two intense peaks at δ 44.54 and 14.02 ppm were due to nitrogen-connected benzylic carbon and methyl carbon, respectively, affirming the formation of benzothiophene-fused spirocyclopentene oxindole **149a**. In the high-resolution mass spectrum, the presence of [M+Na] molecular ion peak at *m*/*z* 416.1094 $(M+Na)^+$ confirmed the structure of **149a**. Futher, the structure was further confirmed by X-ray diffraction analysis, Figure **16**.

After obtaining the inconsistent results with Pd(0) catalysts provided, we performed the reaction in the presence of Pd(II) catalysts to achive desired product **149a** is good yields. In the presence of $Pd(PPh_3)_2Cl_2$, no desired product was observed even after a prolonged reaction time. In contrast, when the reaction was carried out with $Pd(OAc)_2$ in 1,2-DCE, expected product was obtained in poor yields (Table **5**, entry 3 and 4). The reaction of **148a** with 10 mol % $PdCl_2$ in 1,2-DCE delivered the expected spirocyclopentene oxindole **149a** in a short reaction time with excellent yield (Table **5**, en**t**ry 6). To further improve the efficiency of the reaction, Ni and Ir-based catalysts were investigated, but no product formation was observed (Table **5**, entries 7 and 8). After, a brief solvent screening was carried out, however, no substantial improvement was found (Table **5**, entries 9-14). Furthermore, by lowering the loading of catalyst, *i.e.*, 5 mol% Pd-catalyst has significantly lowered the yield of **149a** (Table **5**, entry 15). In the absence of the catalyst, no product was generated (Table **5**, entry 16). To rule out the possibility of any trace amount of HCl, which can also catalyze the reaction, the reaction was also performed in the presence of 1.0 eq. of *N*, *N*-dimethyl aminopyridine (DMAP) 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP). Fortunately, the furnished product **149a** was isolated in good yields (Table **5**, entries **17**and **16**). Interestingly**,** unlike other Pd-catalyzed reactions, it does not require any bases, additives, or re-oxidants.

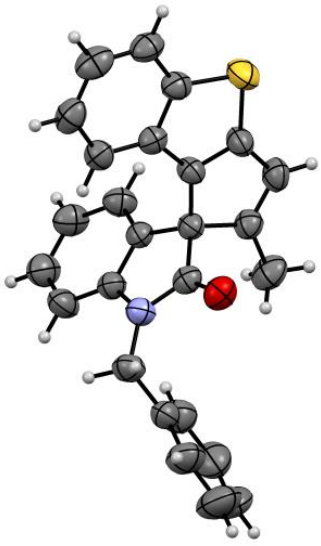
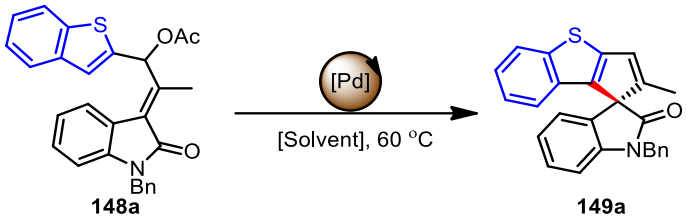


Figure 16: ORTEP diagram of spirocyclopentene oxindole **149a**

Table 5: Optimization of the reaction parameters



Entry	Catalyst (xx mol%)	Solvent	Time (h)	Yield of **149a** [%][a]
1	$Pd(PPh_3)_4$ (10)	1,2-DCE	48	NR
2	$Pd_2(dba)_3$ (10)	1,2-DCE	48	48
3	$Pd(PPh_3)_2Cl_2$ (10)	1,2-DCE	48	NR
4	$Pd(OAc)_2$ (10)	1,2-DCE	48	30
5	$Pd(dppf)_2Cl_2$ (10)	1,2-DCE	48	NR
6	**$PdCl_2$ (10)**	**1,2-DCE**	**8**	**82**
7	Ni $(cod)_2$ (10)	1,2-DCE	48	NR
8	[Ir (cod) Cl]$_2$ (10)	1,2-DCE	48	NR
9	$PdCl_2$ (10)	Toluene	30	43
10[b]	$PdCl_2$ (10)	DMF	10	NR
12	$PdCl_2$ (10)	MeCN	48	35
13	$PdCl_2$ (10)	$MeNO_2$	6	73
14	$PdCl_2$	1,4-Dioxane	36	63
15	$PdCl_2$(5)	1,2-DCE	18	75
16	No catalyst	1,2-DCE	120	NR
17[c]	$PdCl_2$ (10)	1,2-DCE	22	76
16[d]	$PdCl_2$ (10)	1,2-DCE	16	74

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [an] Isolated yield after column chromatography. At room temperature **148a** was as such, and the yield of the reaction at 30 °C (for 36 h) is 53%; the yield at 45 °C (for 12 h) is 62%. [b] **148a** decomposed. [c] In the presence of 1.0 eq. of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP). [d] In the presence of 1.0 eq. of *N*, *N*-dimethylamino pyridine (DMAP). NR = no reaction.

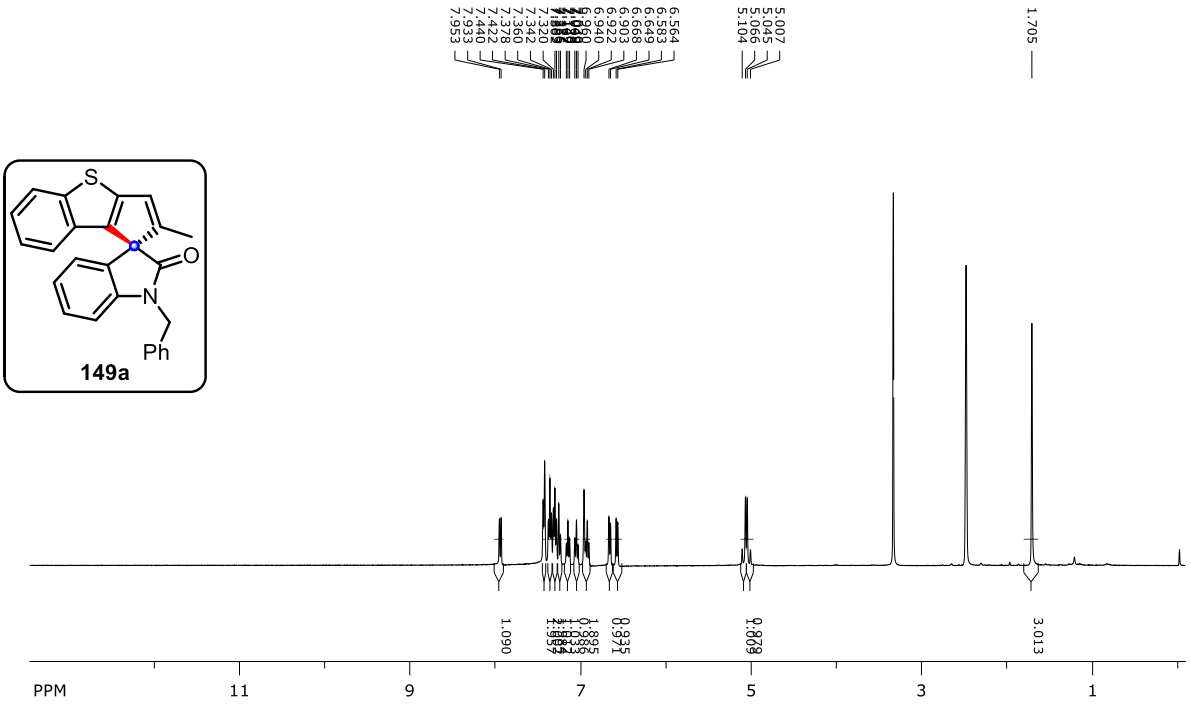


Figure 17: ^{1}H-NMR spectrum of the spirocyclopentene oxindole **149a**

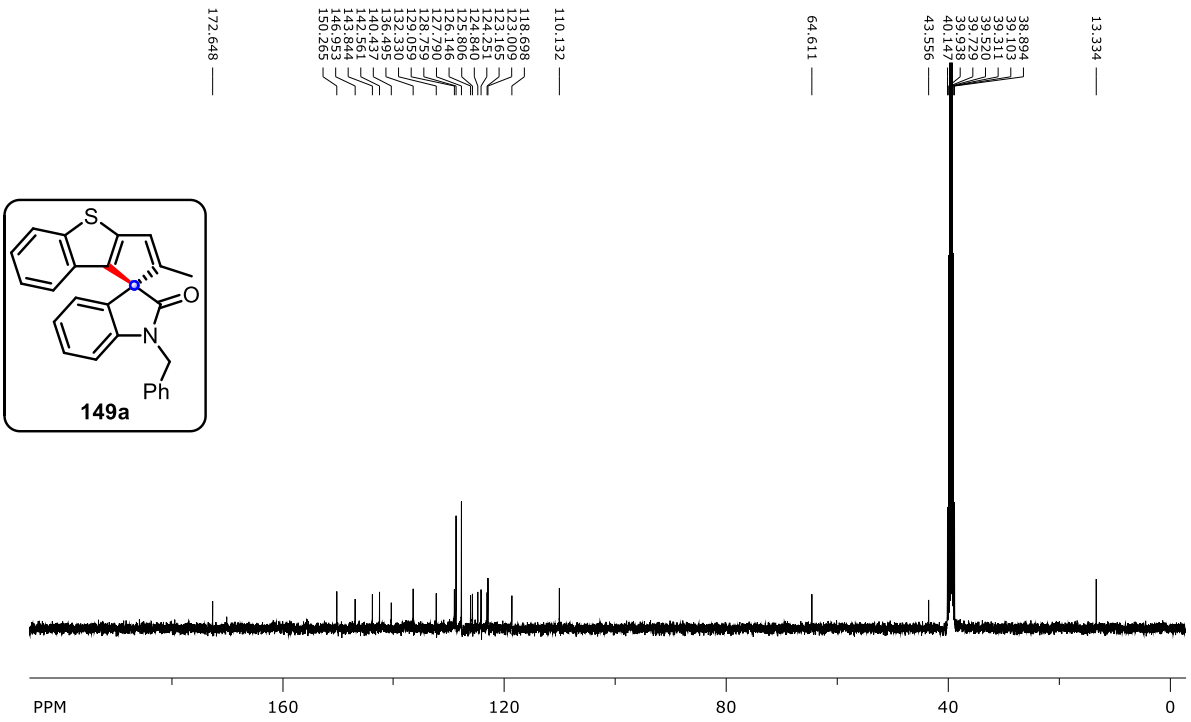


Figure 18: ^{13}C-NMR spectrum of the spirocyclopentene oxindole **149a**

Spiro-cyclopentyl-3-oxindoles are oxindoles with an extensively substituted pentacyclic core and a preferred structural framework with a spirocycle at the oxindole core's C-3 position.[70a-c] These three-dimensional structural motifs are often encountered as favored substructures in various natural products with biological and pharmacological functions (Figure **19**). Marcfortine A, for example, is a fungal metabolite of *Penicillium roqueforti* with significant antiparasitic action.[71] Citrinadin A, a marine-derived alkaloid isolated from the fungus *Penicillium citrinum*, is the most complex member of a family of spirooxindoles with a substantially substituted pentacyclic core that has cytotoxic nature against murine leukemia L1210 and human epidermoid carcinoma KB cells.[72]

Notoamide B was isolated from *Aspergillus species*, which have been extensively studied due to its remarkable anticancer efficacy.[73] Cyclopiamine B is a fungal alkaloid derived from *Penicillium cyclopium* that has a structural framework similar to spirocyclopentane fused

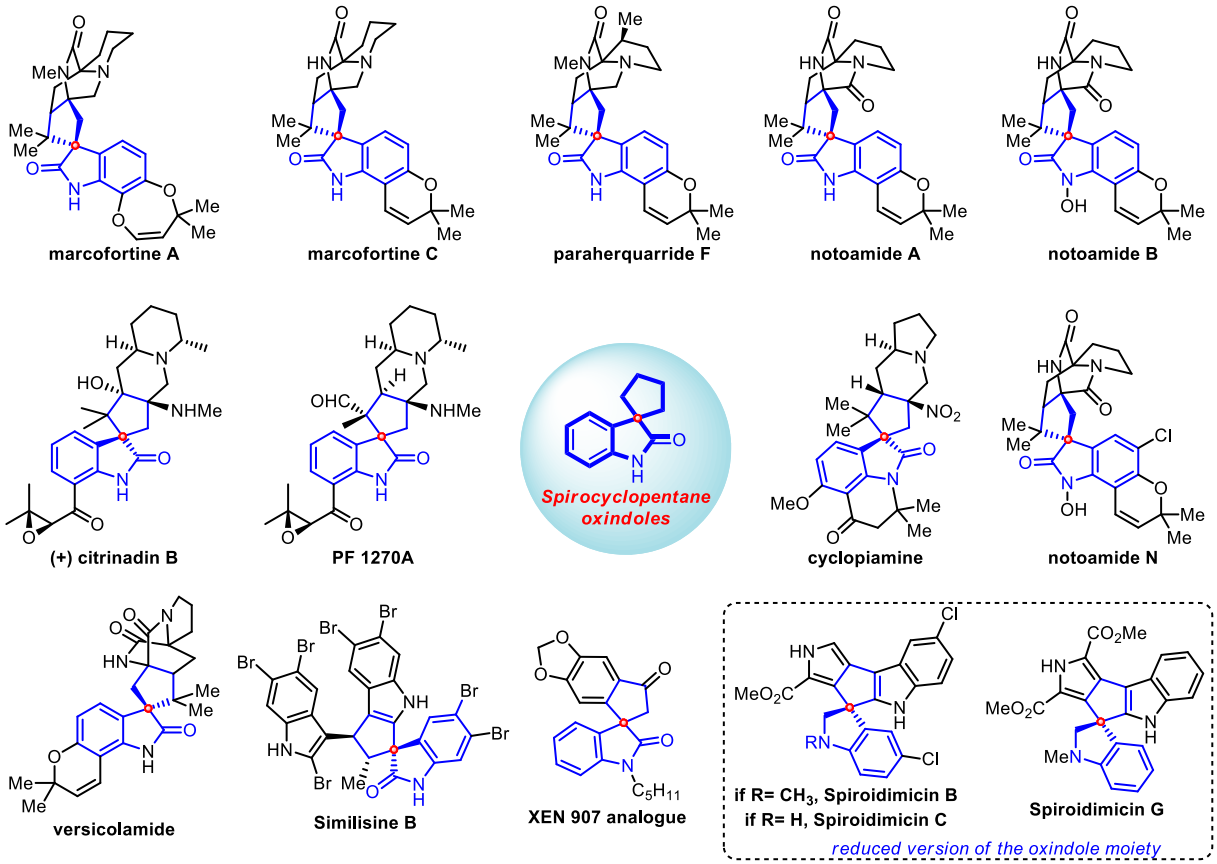
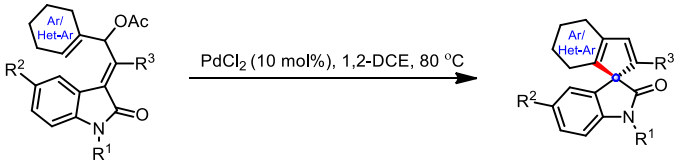
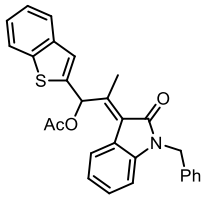
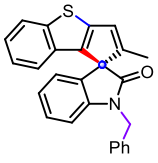
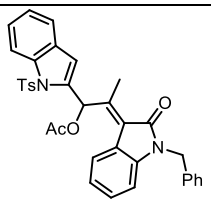
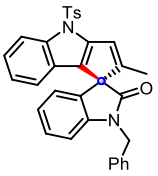
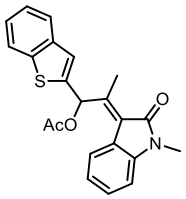
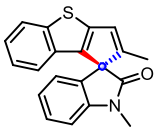
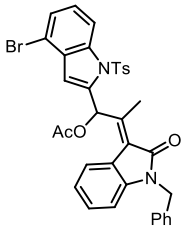
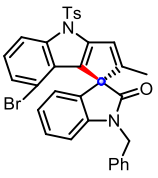
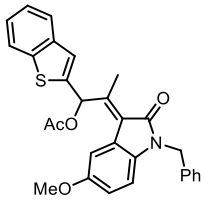
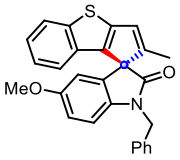
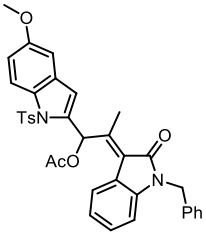
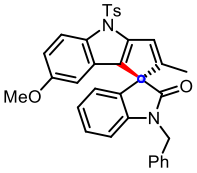
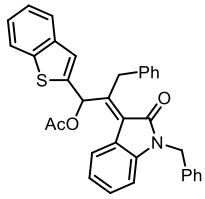
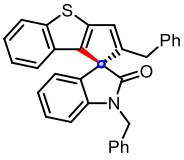
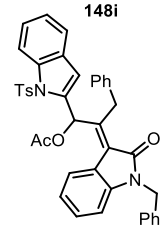
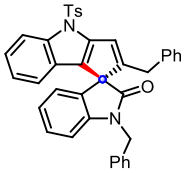
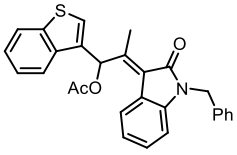
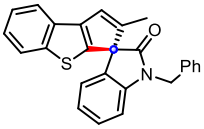
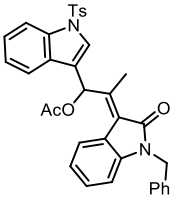
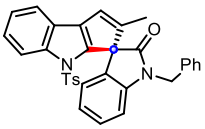
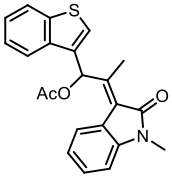
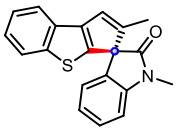
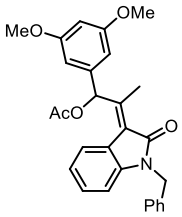
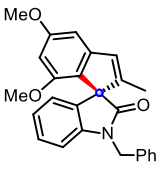


Figure 19: Representative biologically active molecules containing spriocyclopentane oxindoles

oxindole.[74] Similisine B, a polybrominated spiro-trisindole alkaloid isolated from *Laurencia similis*, is cytotoxic and inhibits NO generation. Spiroindimicins are complex scaffolds that contain spiroindoline rings, which are a reduced version of the oxindole moiety.

Table 6: Substrate Scope: spirocyclopentene oxindoles **149a-149l**[a]



Entry	Substrate	Product	Entry	Substrate	Product
1	 **148a**	 **149a**, 8 h, 82%	7	 **148g**	 **149g**, 7 h, 83%
2	 **148b**	 **149b**, 8 h, 82%	8	 **148h**	 **149h**, 8 h, 88%
3	 **148c**	 **149c**, 8 h, 77%	9	 **148i**	 **149i**, 10 h 83%
4	 **148d**	 **149d**, 10 h, 78%	10	 **148j**	 **149j**, 8 h, 73%
5	 **148e**	 **149e**, 10 h 73%	11	 **148k**	 **149k,** 8 h, 79%
6	 **148f**	 **149f**, 9 h, 83%	12	 **148l**	 **149l**, 6 h, 89%,

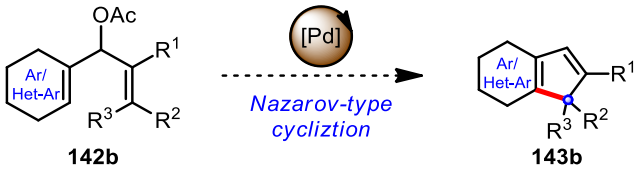
[a]Isolated yield after column chromatography

Spiroindimicin B-C bisindole alkaloids discovered from deep-sea *Streptomyces sp.* SCSIO 03032, with a [5,5] spiro system, exhibits promising cytotoxicity against multiple cancer cell lines.[75,76]

After confirming the **149a** structure by analyzing spectral data and having optimized reaction conditions in hand, we initiated the evaluation of substrate scope to validate the generality of this method. This method was found to be general and proceeded smoothly to afford a wide range of (hetero)arene-fused spirocyclopentene oxindoles in excellent yields with consistent reaction times. Under the optimized reaction environment, a wide range of allyl acetates **149a-149l** bearing different steric and electronic features were well tolerated. To better comprehend the reactivity trends of C-2 and C-3 positions of heteroarenes, respective allylic acetates were exploited to prototypical reaction conditions. It is worth highlighting that the reaction worked very efficiently from both C-2 and C-3 of benzothiophenes (**149a-149d** vs. **149e-149f**), indoles (**149g-149h** vs. **149m**); indicating that the reaction may not be involving a C–H activation pathway as it is well- established that heteroarenes respond differently (from C-2 and C-3) under C–H activation conditions. Table **6** shows that the inclusion of an electron-donating group (such as -OMe) on the backbone of the oxindole moiety **149l** has no effect on reaction efficiency. The versatility of this method was further demonstrated by synthesizing the substrates bearing a functional group Br in **149h**, which can offer a handle for subsequent synthetic transformation.

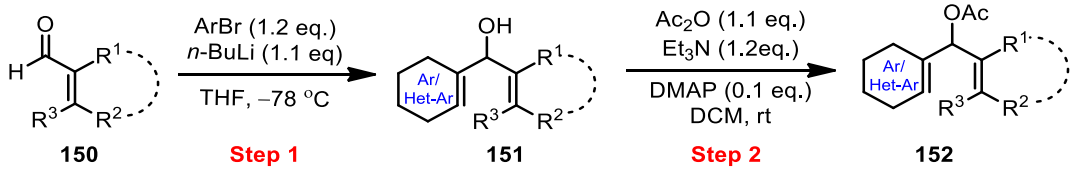
Under mild and selective reaction conditions, a diverse range of synthetically challenging benzothiophene-fused spirocyclopentene oxindoles (**149a-149f**), indole-fused spirocyclopentene oxindoles (**149g-149m**), and spiro-[indene] oxindole (**149l**) bearing an all-carbon spiro carbon were efficiently produced in excellent yields.

Following the successful development of an efficient and practical method for synthesizing oxindoles with a spiro center, we anticipated constructing an all-carbon quaternary centre, Scheme **51**. We designed an appropriate substrate **142b** and envisaged that Pd-catalyzed intramolecular allylic (hetero)arylation of **142b** would produce a new class of functionally rich complex (hetero)arene-fused cyclopentanoids **143b**.



Scheme 51: Our hypothesis towards the Pd-catalyzed reaction with allylic acetates to construct an all-carbon quaternary center

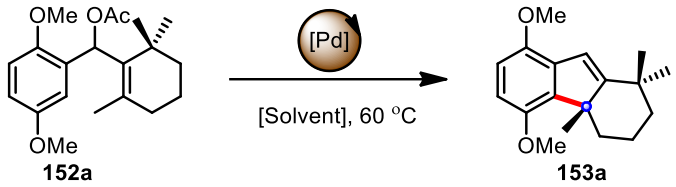
To test this hypothesis stated in Scheme **51**, we commenced synthesizing the substrate **152** using a two-step process that began with commercially available enals **150** (Scheme **52**). Direct *n*-BuLi mediated alkylation of aryl bromides with freshly prepared enals **150** yielded the expected allylic alcohols **151**, acylation yielded the expected allylic acetates **152**.



Scheme 52: General representation for the synthesis of allylic acetates

Accordingly, we have initiated the optimization study with allylic acetate **152a** as the model substrate. Prompted by our earlier success and the aforementioned design considerations, acetate **152a** was subjected under optimized conditions. The desired product **153a** was isolated in low yield under earlier optimized reaction conditions (Table **7**, entry 1). The title compound **153a** was fully characterized by ^{1}H and ^{13}C-NMR spectroscopy (see Figures **20** and **21**) and mass spectrometry data. In order to briefly optimized the reaction condition, we explored **152a** with 10 mol% of $PdCl_2$ in different solvents and temperatures. The use of toluene as solvent showed a dramatical effect on the reaction and was found to be the best choice for the reaction to produce **153a** with 80% of the yield in a shorter reaction time at 80 °C (Table **7**, entry 4). Other solvents such as MeCN, $MeNO_2$, DMF, and 1,4-dioxane did not offer any promising results. Other Ni and Ir-based catalysts failed to produce even a trace of the desired product (Table **7**, entry 12-13). The structure of **153a** was deduced from the spectral data. In the ^{1}H-NMR spectrum, the presence of two doublets at δ 6.70 ppm and δ 6.61 ppm (J = 8.40 Hz) due to the two *ortho*-aromatic protons, a singlet at δ 6.48 ppm due to an olefin proton of indene (C-1) was observed. The presence of three aliphatic methyl groups at δ 1.47 ppm, δ 1.31 ppm and δ 1.26 ppm confirmed the formation of **153a**. The ^{13}C NMR

Table 7: Optimization of the reaction parameters



Entry	Catalyst (xx mol%)	Solvent	Time (h)	Temperature (°C)	Yield of 153a [%][a]
1	$PdCl_2$ (10)	1,2-DCE	48	60	45
2[b]	$PdCl_2$ (10)	1,2-DCE	48	80	60
3	$PdCl_2$ (10)	DMF	48	80	20
4	**$PdCl_2$ (10)**	**Toluene**	**10**	**80**	**80**
5	$PdCl_2$ (10)	$MeNO_2$	60	80	43
6	$PdCl_2$ (10)	1,4-Dioxane	60	80	63
7	$PdCl_2$(10)	DMF	60	80	20
8	$Pd(PPh_3)_4$ (10)	Toluene	48	80	NR
9	$Pd_2(dba)_3$ (10)	Toluene	48	80	39
10	$Pd(PPh_3)_2Cl_2$ (10)	Toluene	48	80	Traces
11	$Pd(OAc)_2$ (10)	Toluene	48	80	54
12	$Ni(cod)_2$ (10)	Toluene	48	80	NR
13	$[Ir(cod)Cl]_2$ (10)	Toluene	48	80	NR
14	No catalyst	Toluene	120	80	NR
15[c]	$PdCl_2$ (10)	Toluene	16	80	70
16[d]	$PdCl_2$ (10)	Toluene	20	80	67

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yield after column chromatography. [b]At room temperature **152a** was as such and at 60 °C reaction was sluggish. [c] In the presence of 1.0 eq. of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP). [d] In the presence of 1.0 eq. of *N*, *N*-dimethylamino pyridine (DMAP). NR = no reaction.

spectrum showed 18 signals, two carbon signals at δ 55.97 ppm, 55.62 ppm due to two -OMe groups, an aliphatic quaternary signal (C-3) at δ 52.6 ppm further established the structure **153a**. In the high-resolution mass spectrum presence of a molecular ion peak at *m*/*z* 273.1844 $(M+H)^+$ further supported the product formation. The X-ray diffraction analysis of **153a** confirmed the product formation, Figure **22**.

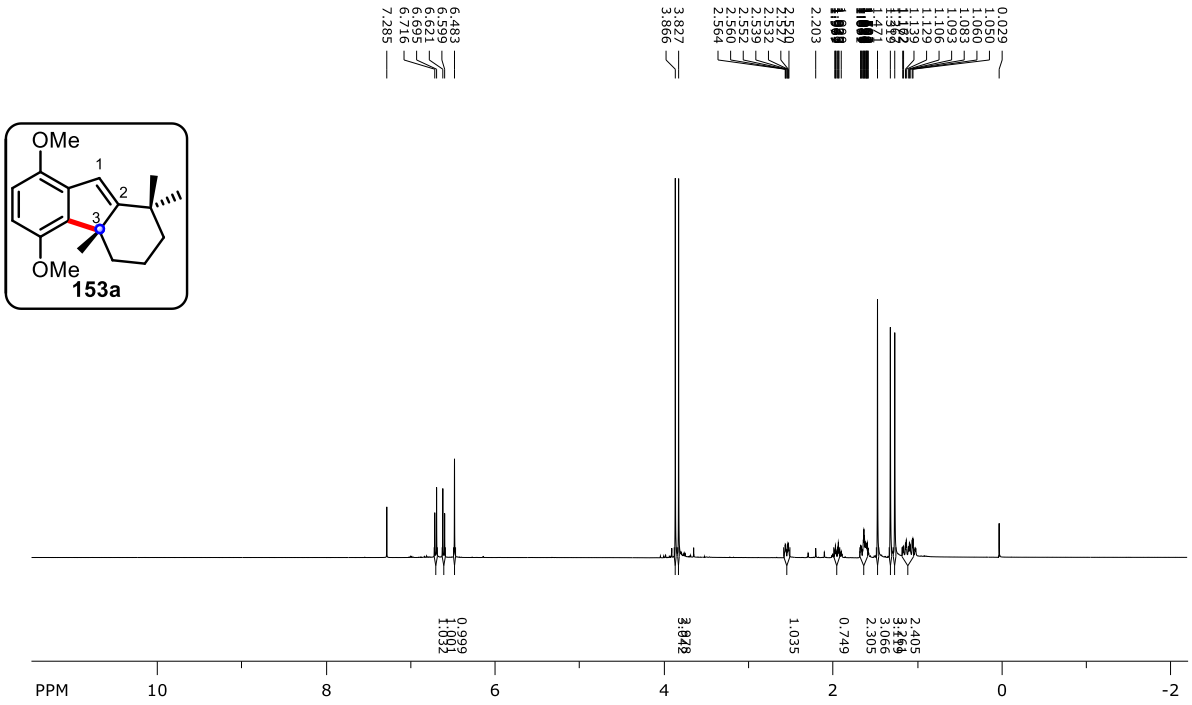


Figure 20: ^{1}H-NMR spectrum of the **153a**

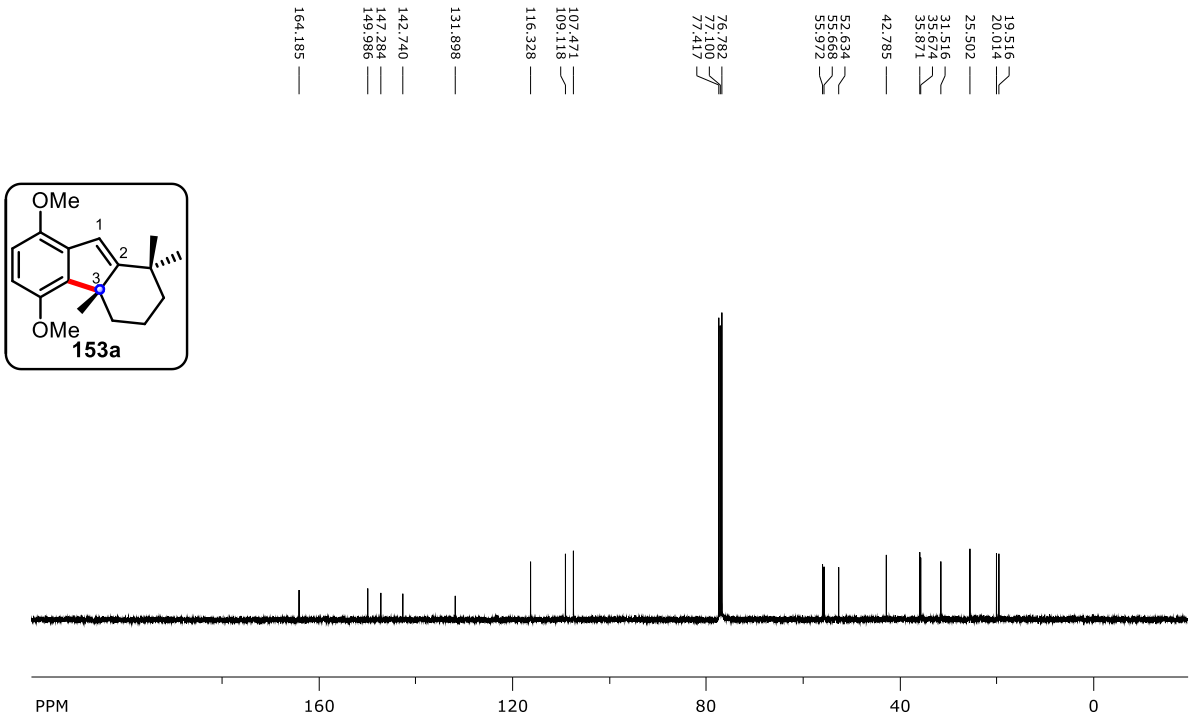
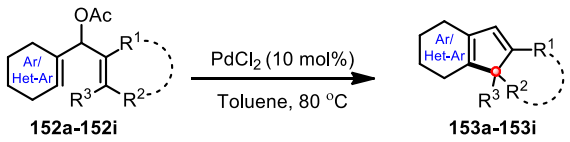


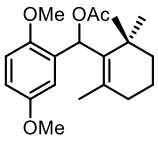
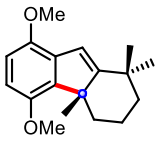
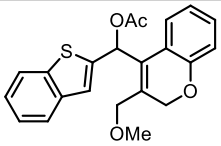
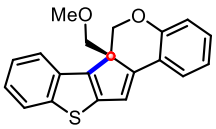
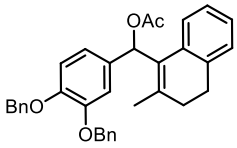
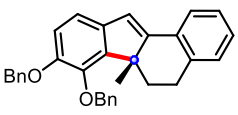
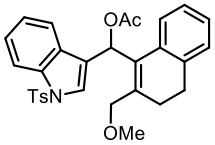
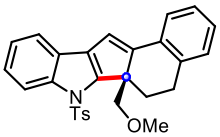
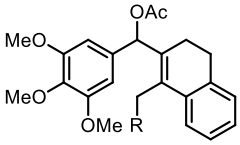
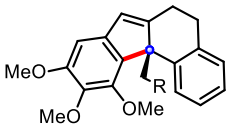
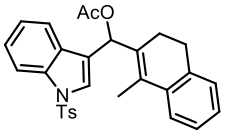
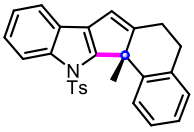
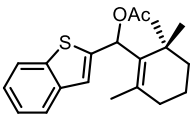
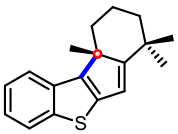
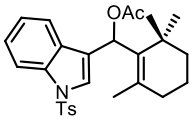
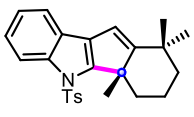
Figure 21: ^{13}C-NMR spectrum of the **153a**

To broaden the protocol's applicability, a variety of allyl acetates with varying electronic features were treated under optimum conditions, and the results were compiled in Table **8**. Interestingly arenes, benzothiophenes, and indole-based substrates efficiently generated the cyclopenta[*b*]annulated products with an all-carbon quaternary sp^3 carbon. **153a-153i** obtained in excellent yields from corresponding acetates represents the 6,5,6-*abeo*-abietane type carbotricyclic structure bearing tetra-hydrofluorene skeleton with an all-carbon quaternary stereocenter. This approach could also provide easily access to natural product-like, tetra- and pentacyclic indenes (**153b-153d**) and cyclopentannulated heteroarenes such as *β*-cyclocitral and chromene based cyclopenta[*b*]annulated benzothiophene (**153e-153f**). Similarly, *β*-cyclocitral or naphthalene-based indolyl acetates delivered respective cyclopenta[*b*]annulated indoles **153g-153i** in good to excellent yields.

Table 8: Substrate Scope: Cyclopentene-fused arenes and heteroarenes[a,]



152a-152i **153a-153i**

Entry	Substrate	Product	Entry	Substrate	Product
1	 **152a**	 **153a**, 10 h, 88%	5	 **152f**	 **153f**, 10 h, 78%
2	 **152b**	 **153b**, 10 h, 81%	6	 **152g**	 **153g**, 20 h, 86%
3	 **152c**, R = H **152d**, R = OMe	 **153c**, R = H, 10 h, 78% **153d**, R = OMe, 10 h, 78%	7	 **152h**	 **153h**, 18 h, 79%
4	 **152e**	 **153e**, 5 h, 92%	8	 **152i**	 **153i**, 15 h, 78%

[a]Isolated yield after column chromatography

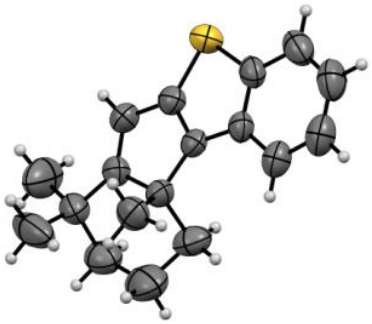
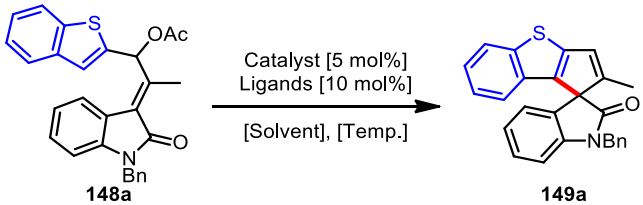


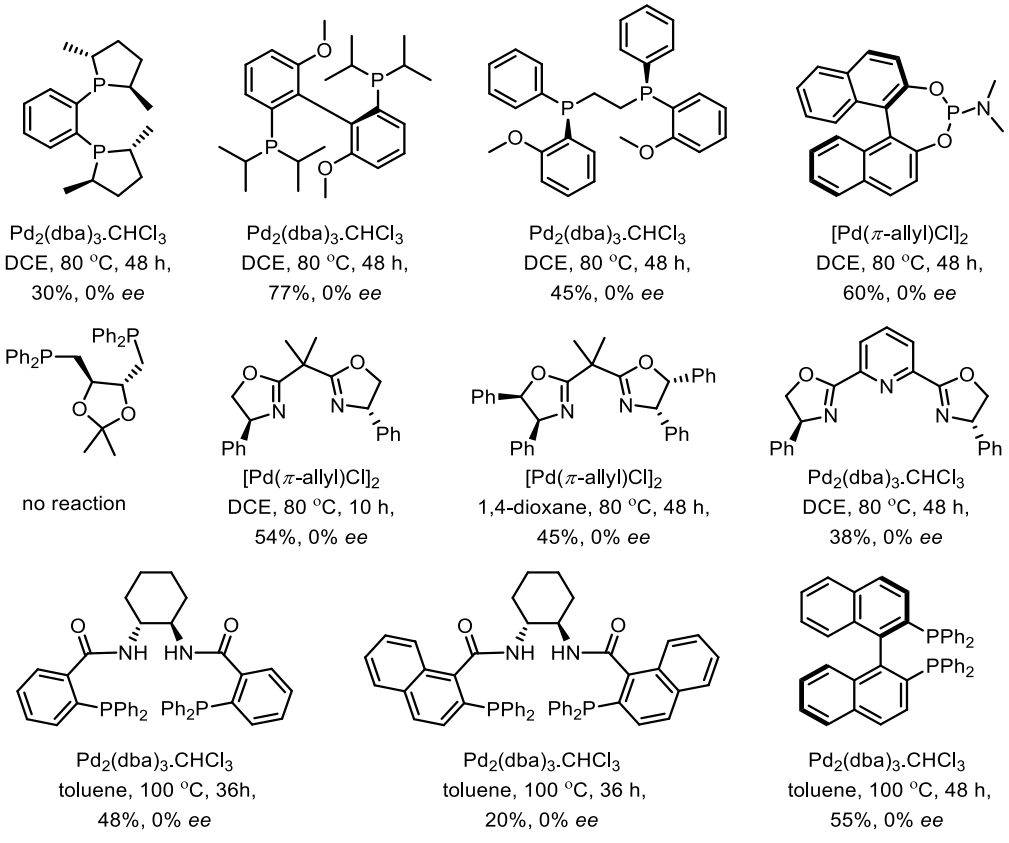
Figure 22: ORTEP diagram of cyclopentannulated heteroarene **153e**

2.8: Efforts towards an enantioselective Nazarov-type reaction

Next, we focused on the development of an enantioselective reaction. Towards that, we initiated the study by investigating chiral phosphines in various solvent combinations with acetate **148a** as a model substrate, (**Table 8A**). But, *ee* did not observe in any case.

Table 8A: Screening of reaction parameters for chiral induction





2.9: Mechanistic Insights

Several mechanistic and control experiments, such as a) Experiments to rule out the Lewis acidic nature of $PdCl_2$, b) Study the effect of substituent (R^3), and c) Kinetic Isotope Effect experiments, were performed to investigate the plausible reaction mechanism of palladium-catalyzed allylic (hetero)arylation or acid-free Nazarov-type reaction in detail, and the results are summarised below.

2.9.1 Experiments to rule out the Lewis acidic nature of $PdCl_2$

We performed the reaction of **148a** with 10 mol% Lewis acids such as $PdCl_2$, $MgBr_2$, $InCl_3$, and $ZnCl_2$ to better understand the role of $PdCl_2$ in the reaction. Based on TLC analysis (Figure **22A**), we observed that, in the case of $PdCl_2$, xx was totally consumed after 8 hours, but none of the other reactions gave any desirable product xx even after 24 hours, ruling out the probability of the $PdCl_2$ being acidic.

TLC monitoring of the reaction between xx and xx with 10% EtOAc/Hexane

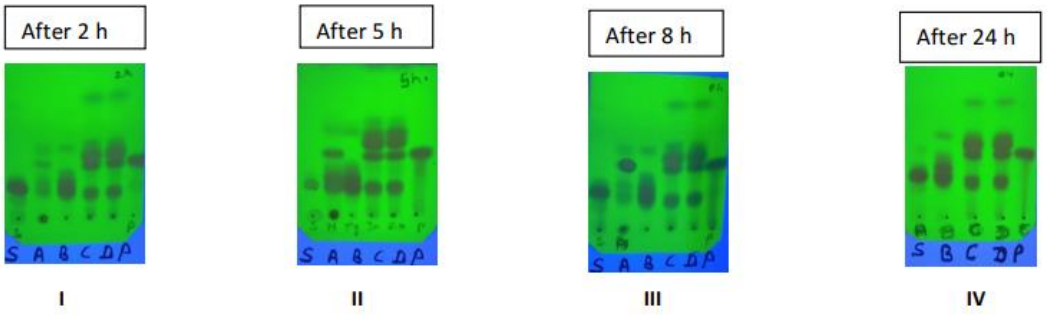


Figure 22A: Experimental observation of compound **148a** with different Lewis acids.

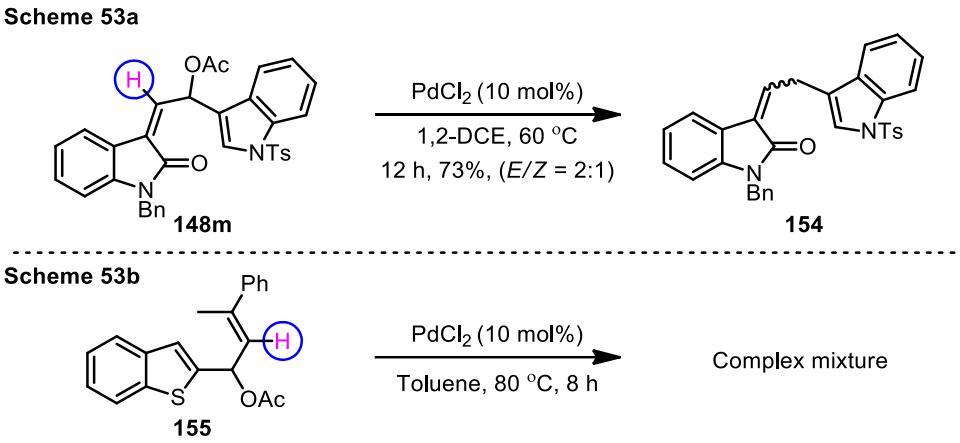
S - Starting compound (**148a**) **A** - $PdCl_2$, **B** - $MgBr_2$

C - $InCl_3$, **D** - $ZnCl_2$ **P** - cycliczed product (**149a**)

2.9.2: Study the effect of substituent (R^3)

While evaluating the substrate scope we realized the critical role of the substituent (R^3) for the outcome of the reaction, Scheme **53a**. For example, the reaction of **148m** with10 mol% of $PdCl_2$ in DCE solvent at 60 ^oC delivered the deacylated product **154** in 2:1 (E/Z) ratio, Scheme **53a**. The formation of **154** was confirmed by closely analyzing the ^{1}H-NMR and ^{13}C-NMR (see Figure **23** and Figure **24**) spectral data of the corresponding product. Expected cyclized product was not found from the mass analysis of the crude reaction mixture (see Figure **25**.) The formation of the deacylated product also supports the formation of the π-allyl palladium complex during the reaction mechanism. On the other hand, we obtained a complex

mixture on treating **155** under optimized reaction conditions. Once the starting material **155** disappeared (as monitored by TLC), the crude reaction mixture was subjected to high-resolution mass spectrometry (HRMS) analysis. These results signify the role of R^3 (both electronically and sterically) in the formation of cyclized products.



Scheme 53: Pd-catalyzed reaction of substrates **148m** and **155**

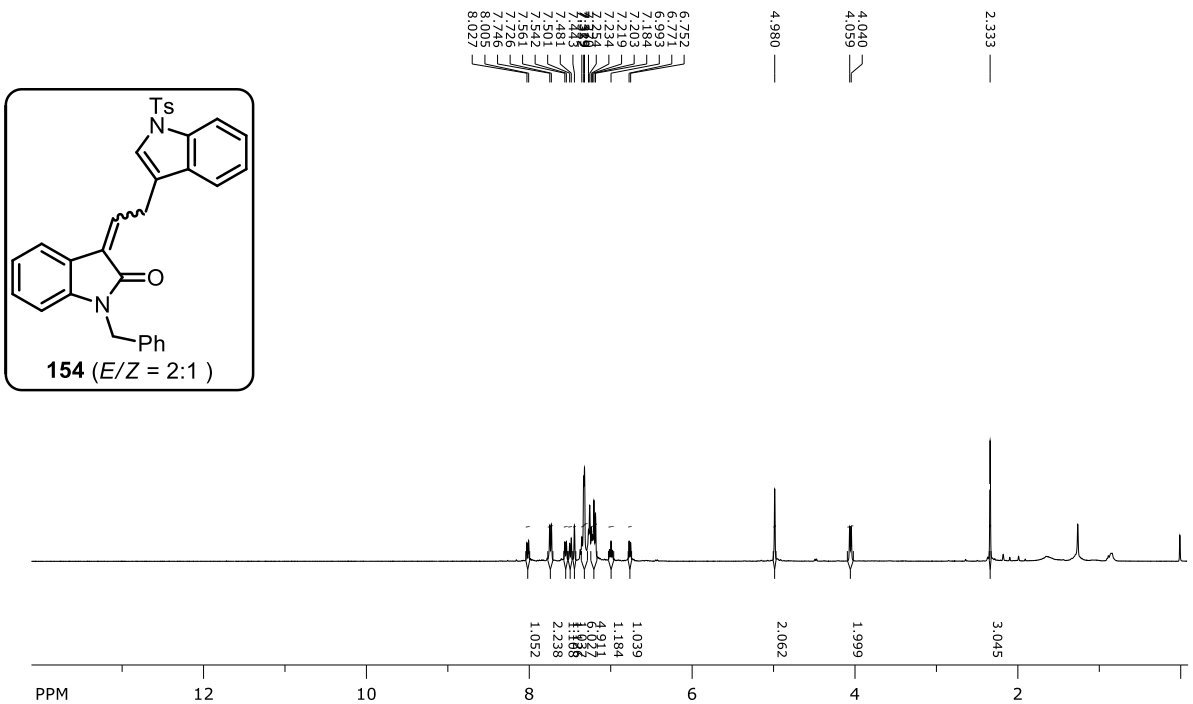


Figure 23: ^{1}H-NMR spectrum of the deacylated product **154.**

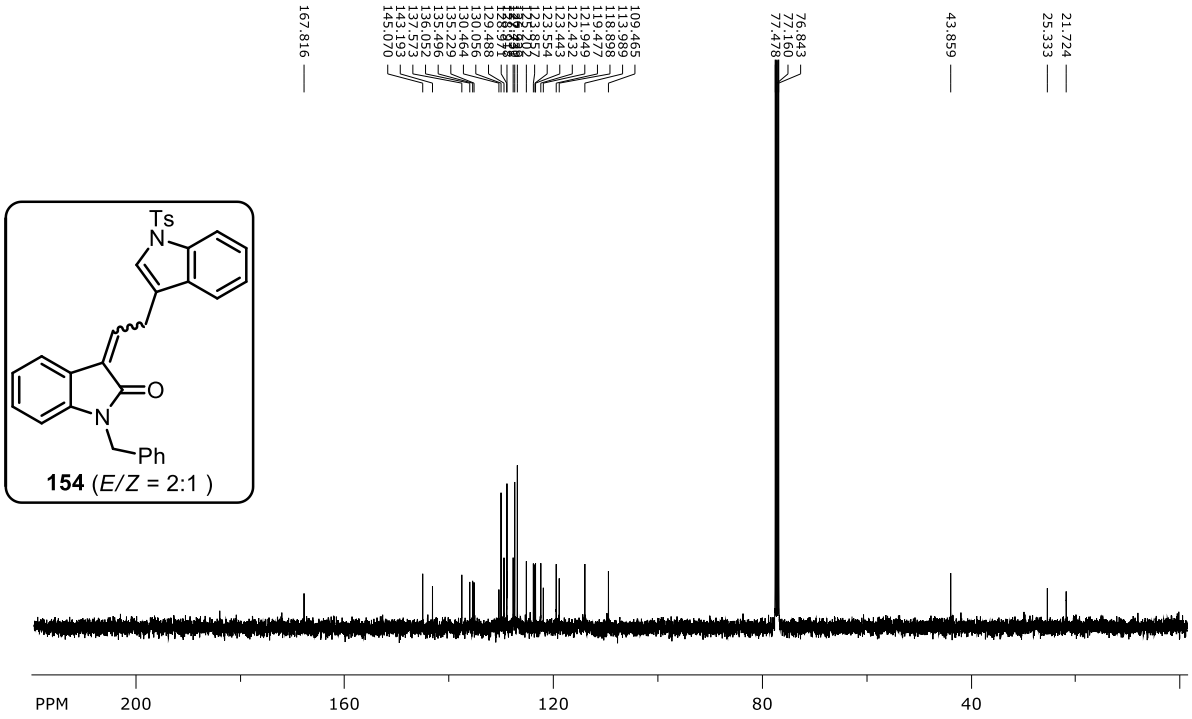


Figure 24: ^{13}C-NMR spectrum of the deacylated product **154**

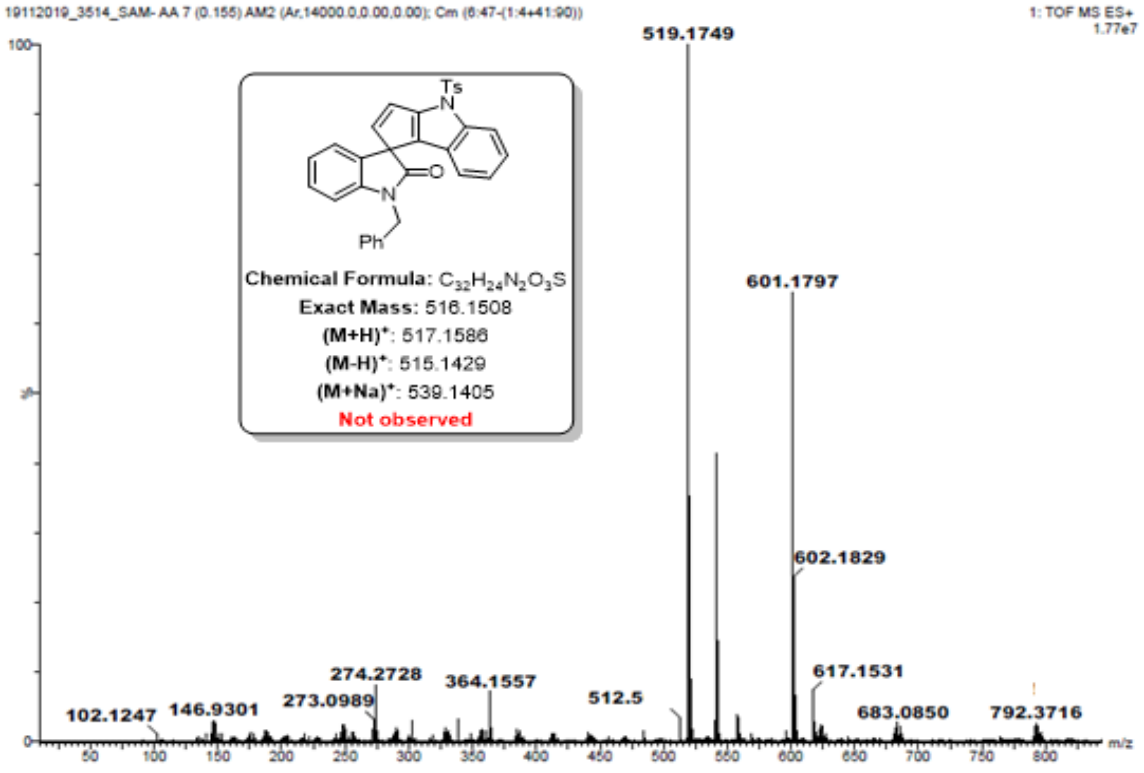
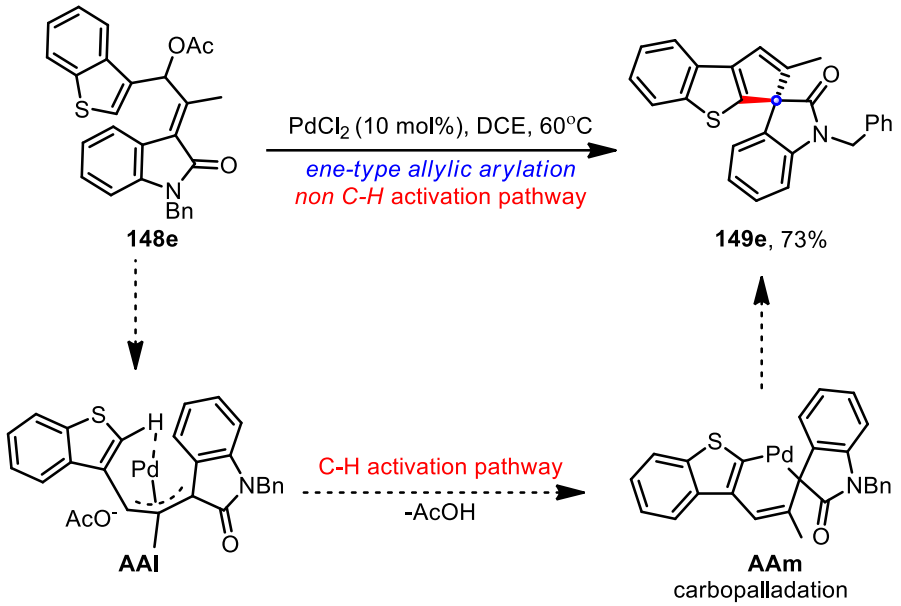


Figure 25: HRMS spectrum of the crude reaction mixture of **144m**

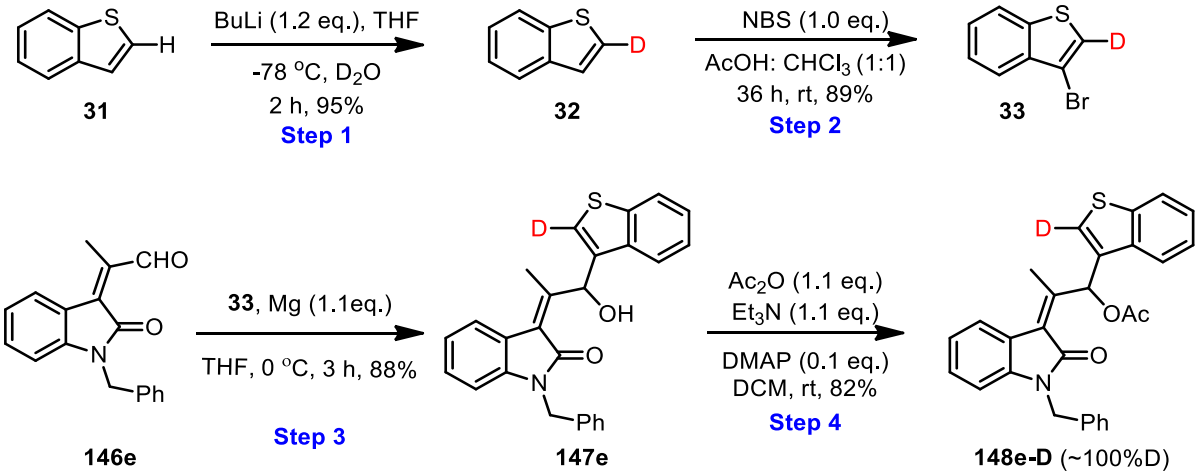
2.9.3: Kinetic Isotope Effect Experiment (KIE)

Palladium-catalyzed allylic(hetero)arylation of (hetero)aryl allyl acetates could proceed either *via* C–H activation pathway, which would include the formation of a six-membered palladacycle, or the non C–H activation pathway, for the formation of all-carbon quaternary and spiro centres, Scheme **54**.



Scheme 54: C-H activation pathway vs a non-C-H activation pathway

We devised an isotope leveling experiment to measure KIE to establish a non-C-H activation pathway, and the results were thoroughly examined. Towards this, **148e-D** was synthesized by using a four-step protocol starting from commercially available benzothiophene



Scheme 55: Synthesis of allyl acetate **148e-D**.

31 (Scheme **55**). *n*-BuLi mediated proton exchange in the presence of D_2O generated the corresponding deuterated compound **32,** upon treatment of **32** with *N*-bromosuccinimide and delivered **33** in 89%. At 0 °C, the 1,2-addition of *in situ* generated Grignard of **33** afford the

corresponding allylic alcohols **147e** which further subjected to acylation to produce **148e-D** with ~100% "D"-incorporation.

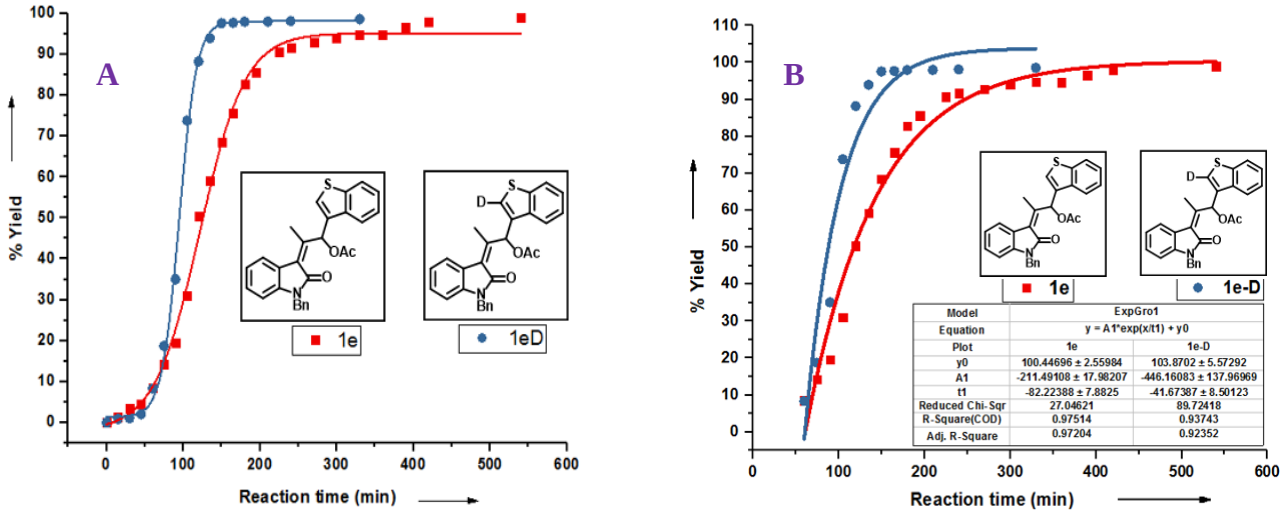


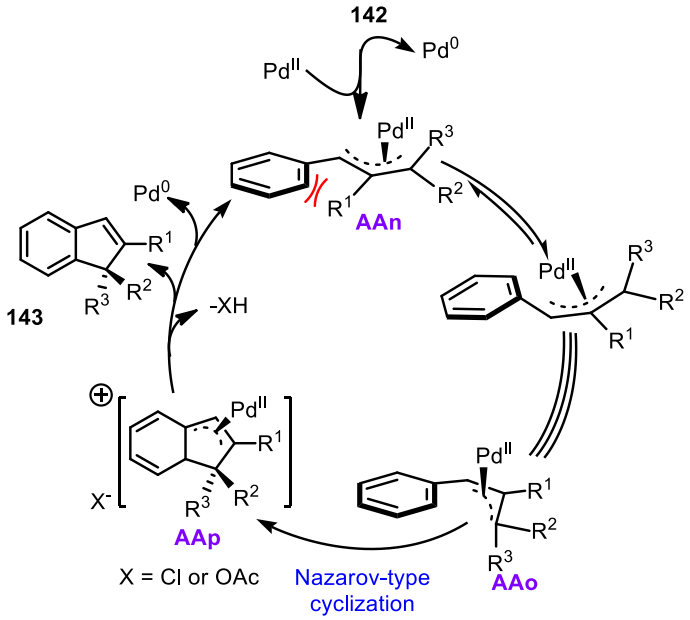
Figure 26: Kinetic isotope effect determined for the reactions of **148e** (red) and **148e-D** (blue)

148e and **148e-D** were subjected to optimal reaction conditions to determine kinetic isotope effects in the Pd-catalyzed allylic arylation reaction. The reaction process was observed by HPLC analysis using a Daicel Chiralpak IB Column (90:10 n-Hexane/2-Propanol, 1 mL/min, 254 nm), and the yield of the product was used to plot the graph. Figure **26A** shows that **148e**-D has a faster reaction rate than **148e**. Initially, the reaction rate in both cases was similar, which can be referred to as the induction period. After then, it grew exponentially. The k_H/k_D ratio was found to be 0.51, indicating that the new C-C bond-forming cyclization event most likely involves Nazarov-type cyclization rather than a C-H activation pathway. Otherwise, the rate-determining step in conventional metal-catalyzed C-H functionalization processes is C-H bond cleavage.

2.9.4: Plausible mechanism

Based on the evidence obtained from the above experiments and related literature reports, a plausible mechanism of the transformation is showcased in Scheme **56**. The reaction commences with the oxidative addition of *in situ* generated Pd(0) with substrate **142** to generate the (π-allyl)palladium complex **AAn**. Due to steric reasons pertaining to the presence of substituent R^1, the intermediate **AAn** reorganizes to **AAo** and undergoes Nazarov-type cyclization**.** R^1 Also plays an electronic role in the stabilisation of both cationic (π-allyl)palladium intermediates such as **AAn** and **AAo.** The carbon connected to R^1 has a formal

positive charge in **AAp**, a stabilized tertiary carbocation. Further, cyclopentanoids with an all-carbon quaternary center **143** are generated *via* rearomatization of **AAp.**



Scheme 56: Plausible mechanism for the formation of **143**.

2.10: The total synthesis of taiwaniaquinone H and dichroanone

Naturally occurring diterpenoids and their derivatives have been widely employed for human welfare as perfumes, agrochemicals, pharmaceutical active ingredients, and organic materials. The taiwaniaquinoids are a group of 18 rearranged *abeo*-abietane diterpenoids that share a 4a-methyl-tetrahydrofluorene skeleton with an all-carbon quaternary stereocenter at the pseudobenzylic position and a 4a-methyl-tetrahydrofluorene skeleton (Figure **27**). In 1995, Cheng and co-workers isolated most of the taiwaniaquinoids from different parts of the endangered species *Taiwania cryptomerioides.* Many taiwaniaquinoids display promising anticancer activity against KB epidermoid carcinoma cancer cells, according to the literature, and a few of these terpenoids are being evaluated as therapeutic leads in the treatment of estrogen-dependent tumors. Due to the sheer importance of biological importance and complex structural properties, various research groups devised a variety of synthetic techniques, the most of which relied on acid-promoted cyclization to construct the cyclopentane ring.[77]

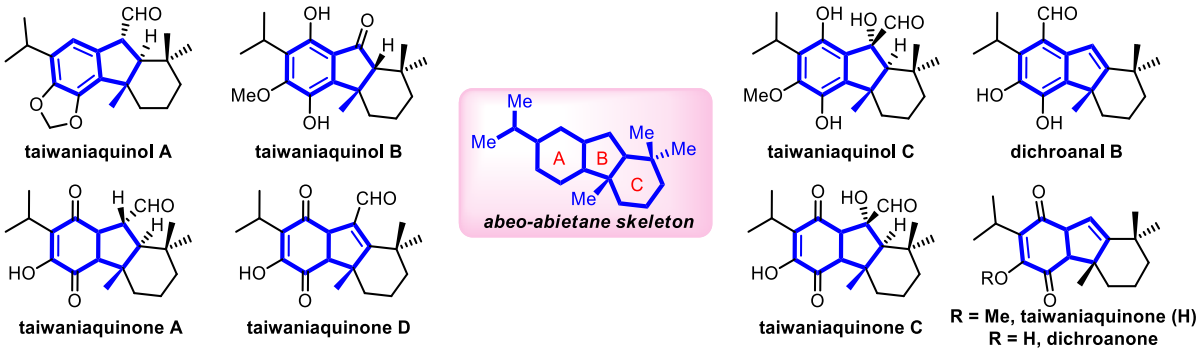
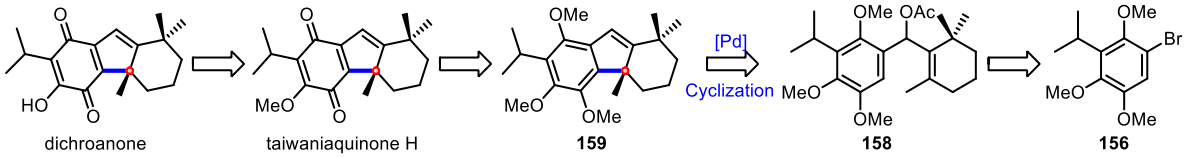


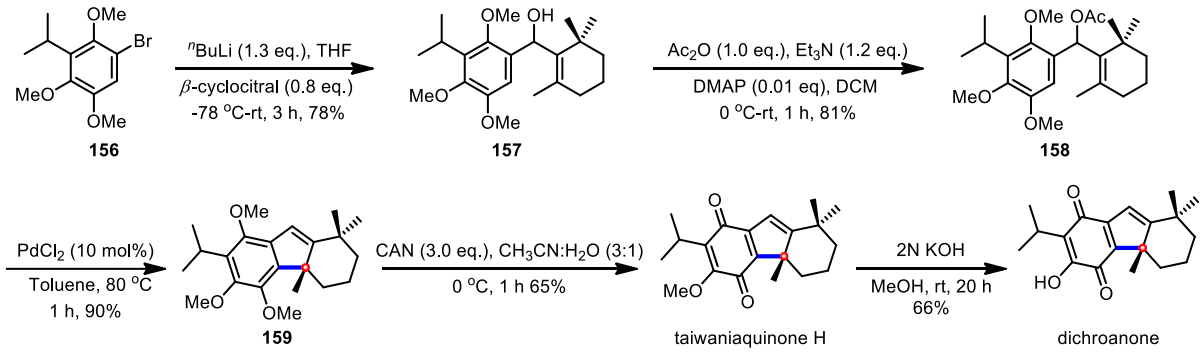
Figure 27: Representative examples of natural products from taiwaniaquinoid's family

Next, we intended to use our strategy in the total synthesis of taiwaniaquinone H and dichroanone by following a suitable retrosynthetic plan demonstrated in the Scheme **56A**.



Scheme 56A: Retrosynthetic route for taiwaniaquinone H and dichroanone.

Accordingly, we initiated our synthetic efforts, and the desired acetate **158** was synthesized by adding the lithiated form of **156** to *β*-cyclocitral followed by acylation of respective alcohol **157** (scheme **57**). $PdCl_2$ promoted the acid-free cyclization of **158** in toluene 80 ^oC and delivered a [6,5,6]-ring system such as **159** in excellent yield. The structure of indene **159** was confirmed by ^1H-NMR and ^{13}C-NMR analysis (see Figure **28** and Figure **29**).



Scheme 57: Acid-free synthesis of taiwaniaquinoid natural products.

Subsequent CAN-mediated oxidation of **159** produced taiwaniaquinone H. Next, upon treatment of methanolic KOH conditions to taiwaniaquinone H led to the formation of

dichroanone. The structure of these taiwaniaquinoid natural products was confirmed by ^{1}H-NMR and ^{13}C-NMR analysis (see Figure **30-31** and Figure **32-33**).

In conclusion, we established an Pd(II)-prompted carbocyclization similar to acid-free Nazarov-type cyclization to synthesize fused cyclopentenes with all-carbon quaternary and spiro centers. The reaction believes to involve a kinetically unfavorable 5-*endo*-trig carbocyclization of the tethered (π-allyl)palladium system (aided by the LUMO umpolung). The reaction demonstrated remarkable functional group tolerance with electronically varied substituents, allowing good to excellent yields of spirocyclopentene oxindoles, cyclopentene-fused arenes, and heteroarenes. Furthermore, several bioactive compounds, for example, those representing the spiroindimicin and polyveoline families of natural products, were efficiently synthesized under these acid-free reaction conditions. The critical role of substitution (R^1) and the kinetic isotopic effect were investigated to establish the reaction mechanism. The total synthesis of taiwaniaquinone H and dichroanone further demonstrated the synthetic utility of this method. Natural products, pharmaceutically relevant compounds, and materials were synthesized efficiently without using any external oxidant, base, addition, or ligand, demonstrating the method's generality and practicability.

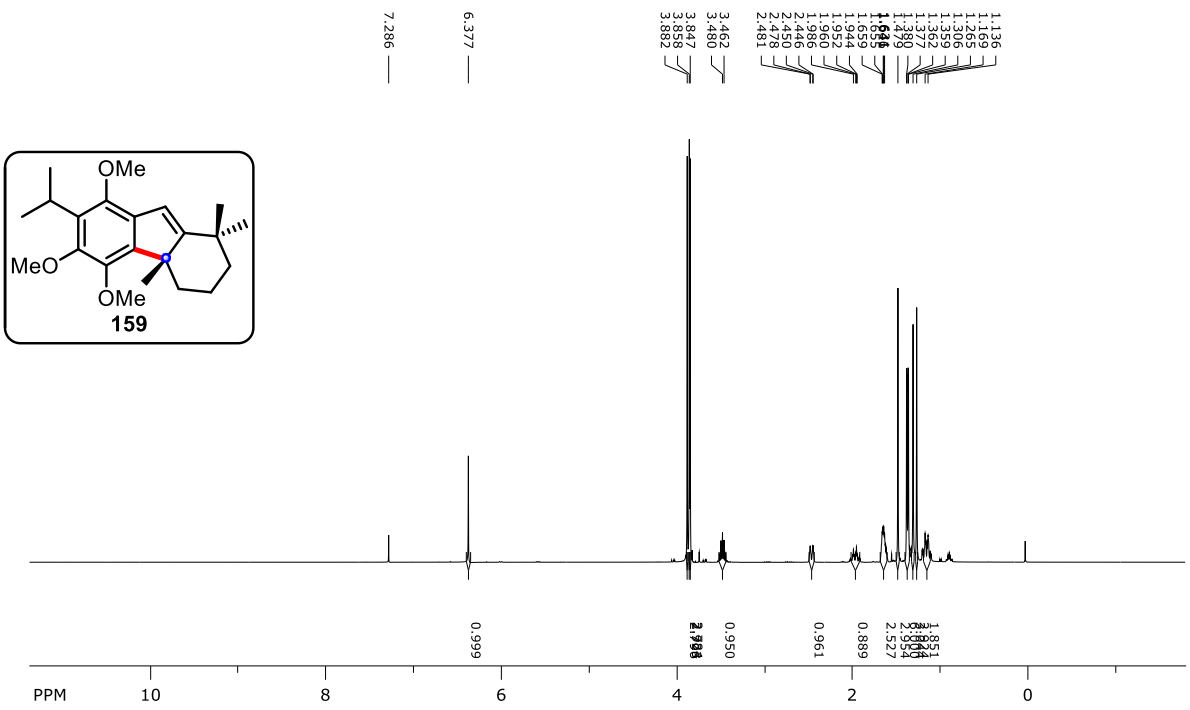


Figure 28: ^{1}H-NMR spectrum of the indene **159**

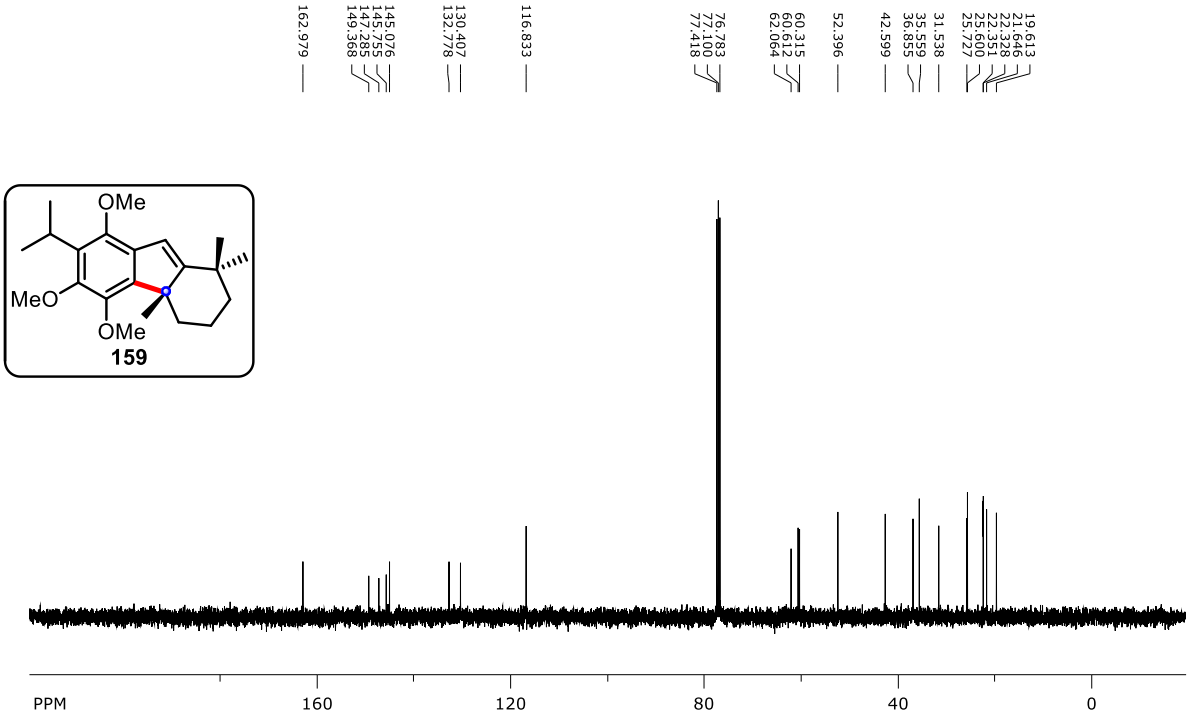


Figure 29: ^{13}C-NMR spectrum of the indene **159**

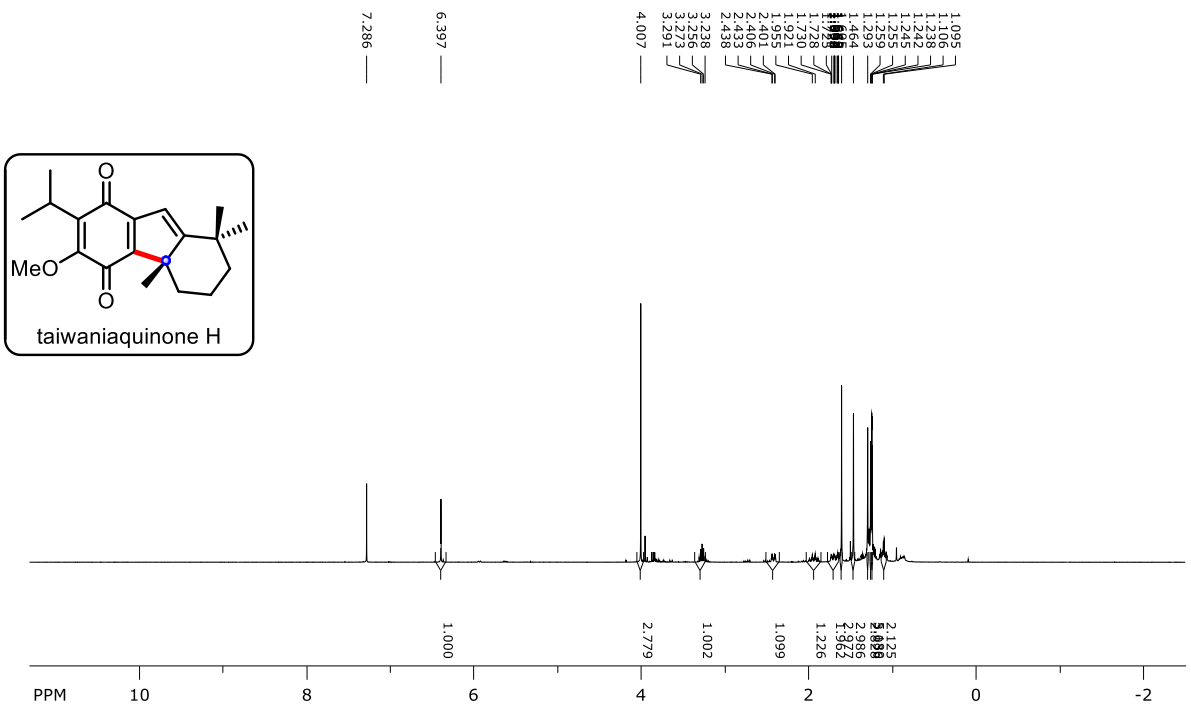


Figure 30: ^{1}H-NMR spectrum of taiwaniaquinone H

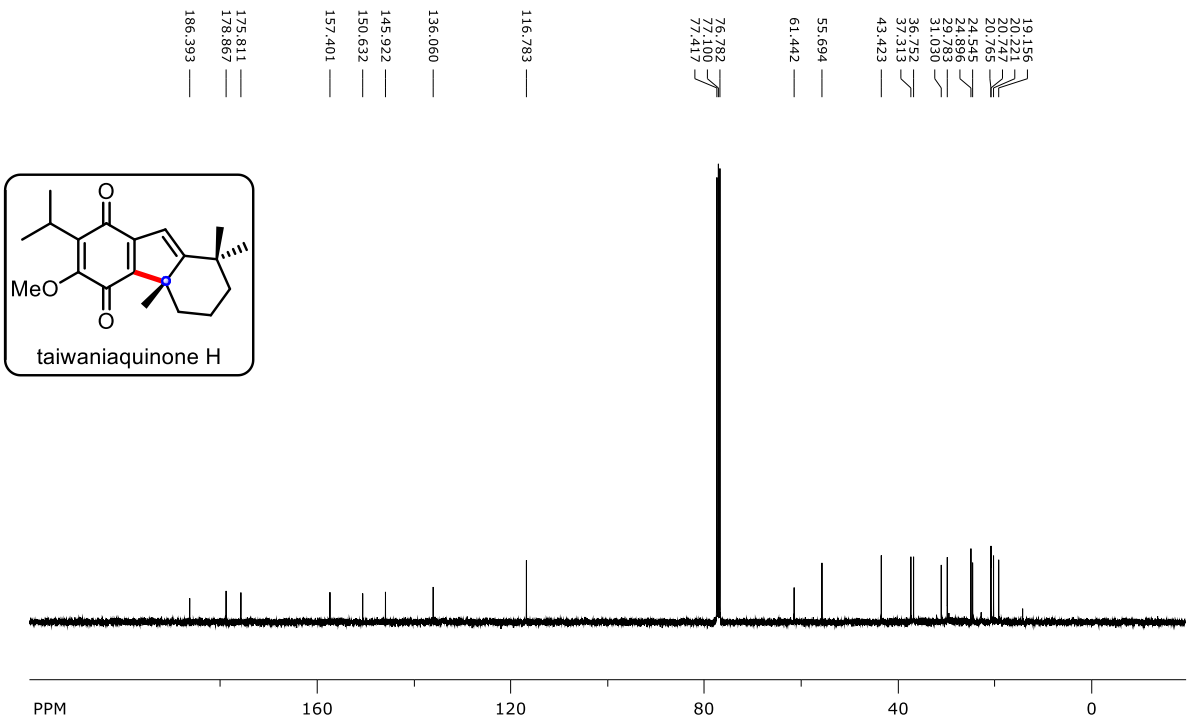


Figure 31: ^{13}C-NMR spectrum of taiwaniaquinone H

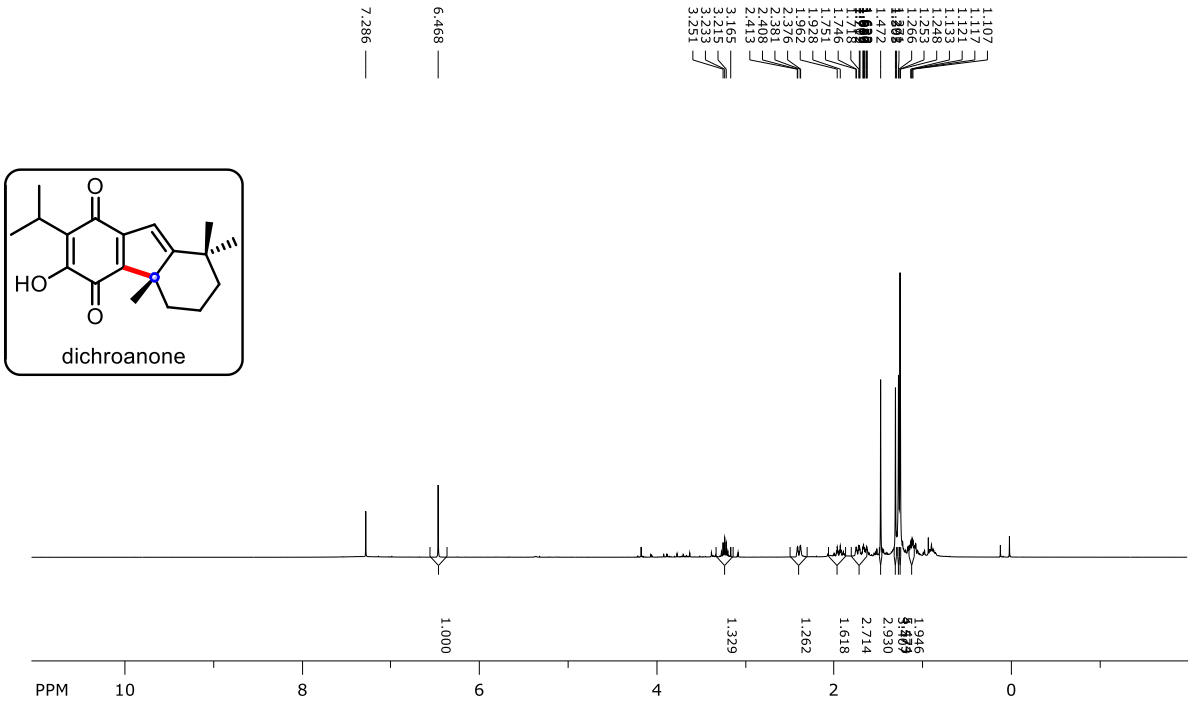


Figure 32: ^{1}H-NMR spectrum of dichroanone

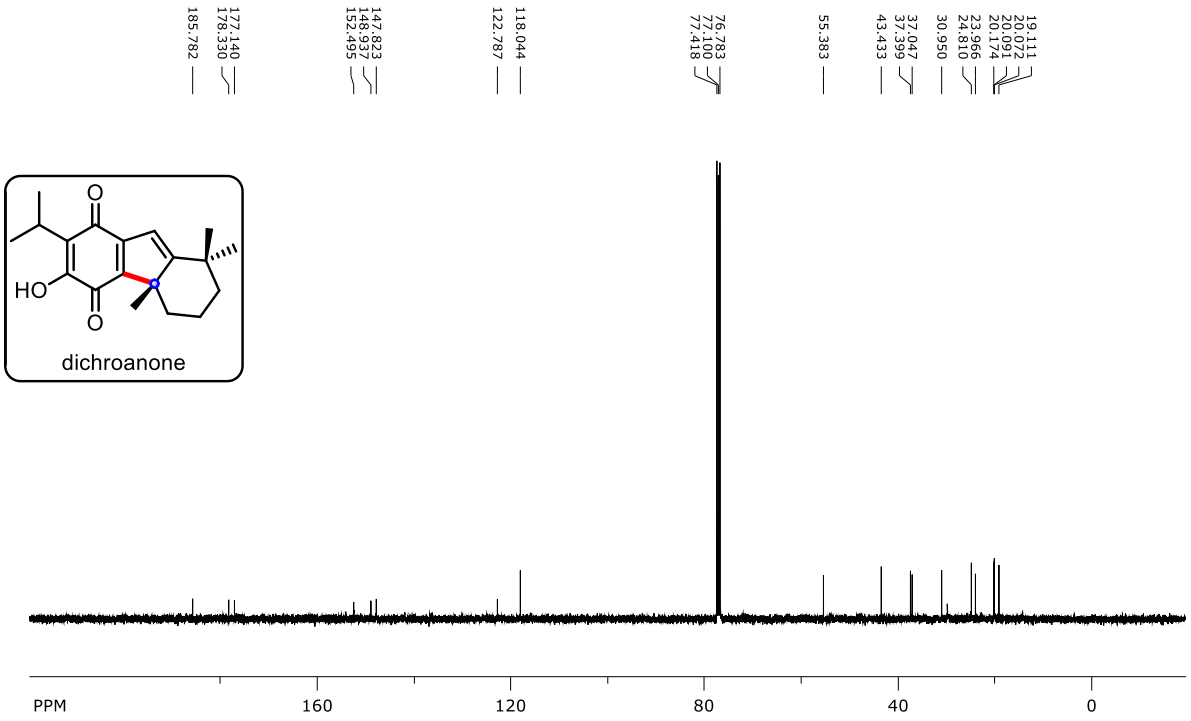


Figure 33: ^{13}C-NMR spectrum of dichroanone

Chapter 3

Sulfur ylide mediated synthesis of complex scaffolds bearing vicinal stereogenic centers via dearomative annulation of azaarenium salts

Organic synthesis has been long focused on the chemical production of complex compounds with stereogenic centers and three-dimensional skeletons. For small-molecule drug development, academic and pharmaceutical scientists seek chemical structure innovation, ranging from classic achiral molecules to preferential three-dimensional architectures.[78a-c] The enormous promise of lead compounds with sp^3-hybridized stereogenic centers is dependent on (1) heightened structural diversity, (2) appropriate pharmacophores to target the necessary proteins selectively, and (3) easily modifiable physical properties to meet *in vivo* metabolic stability. As a result, pharmaceutical discovery will significantly broaden the chemical space of drug-like compounds, making pharmaceutical discovery easier.

Various complex natural products and pharmaceutically active molecules are frequently encountered with contiguous carbon centers. The three-dimensional shape of many structurally intricate frameworks is impacted by the orientation of substituents at carbon

centers, contributing to organic molecules' complexity and diversity by including a wide range of substructures depending on the types of carbons involved. The three most fundamental types are vicinal tertiary carbon stereocenters (I), vicinal tertiary-fully substituted carbon centers (II

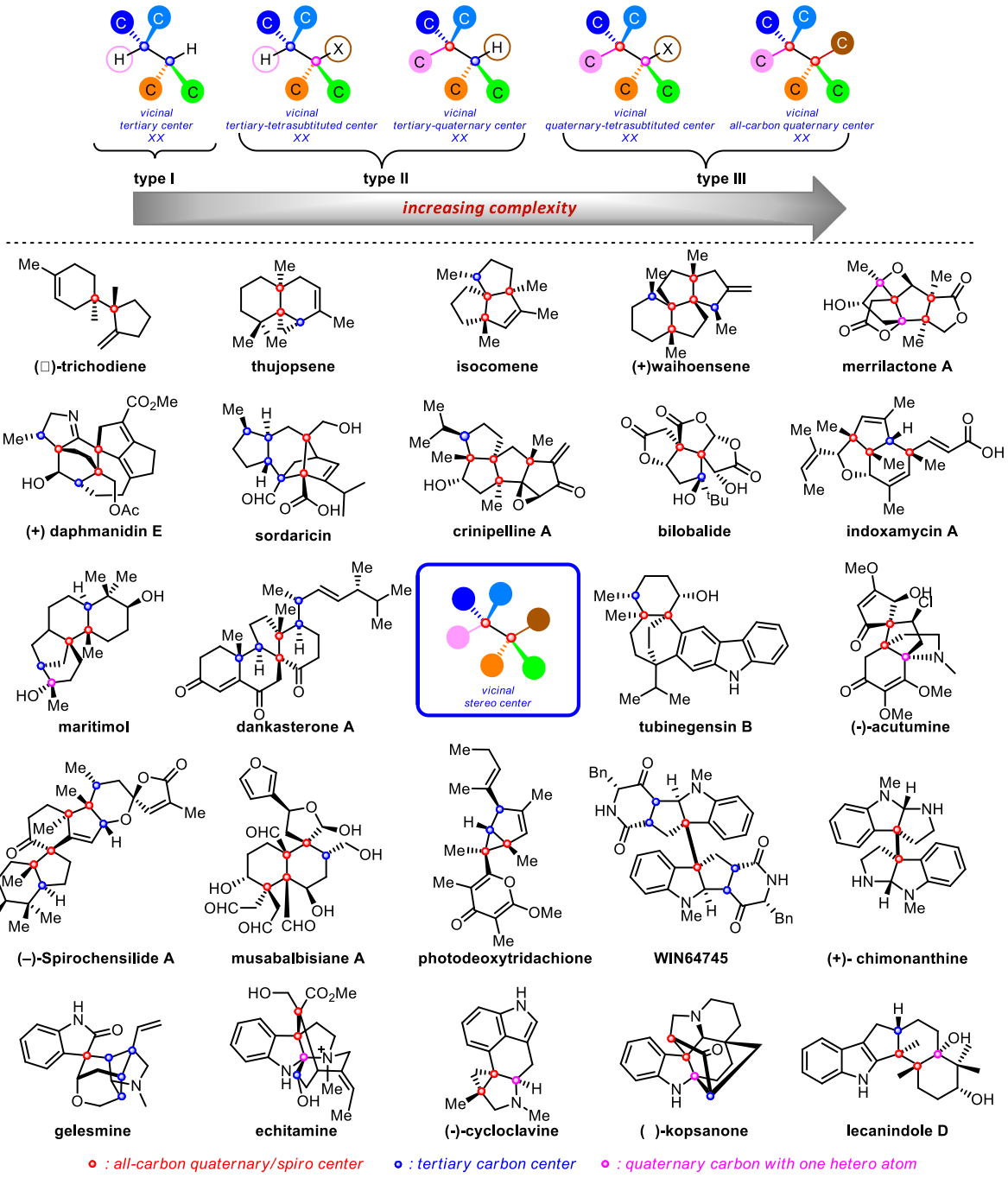
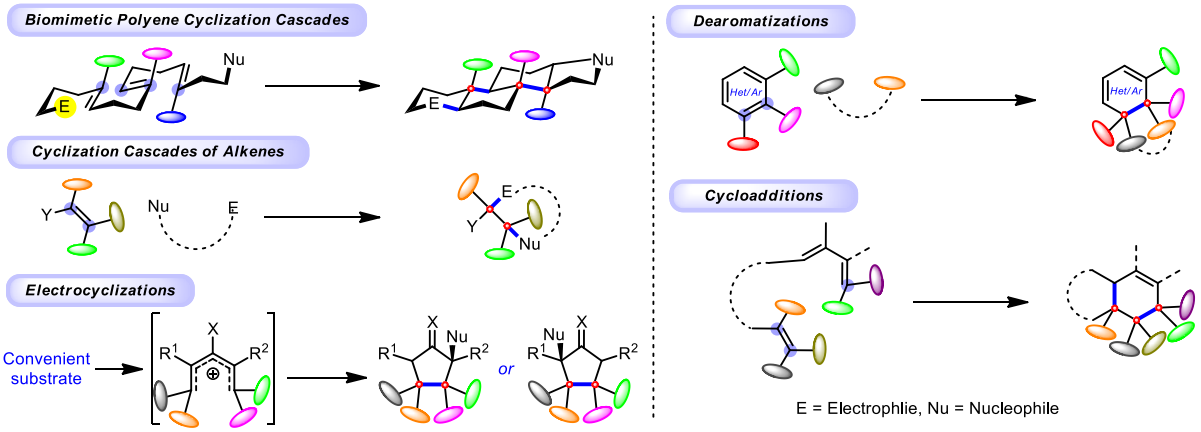


Figure 34: Typical natural products containing vicinal stereogenic centers

and III), and vicinal fully substituted carbons (IV, V). The steric hindrance increases significantly as neighbouring centers evolve from tertiary carbons to tetrasubstituted ones with at least one heteroatom substituent and then to quaternary carbons, posing significant synthesis

challenges. The existence of contiguous all-carbon quaternary centers (V) in the target molecule is one structural factor that inevitably raises the difficulty of chemical synthesis. Figure **34** depicts various biologically active complex natural products and medicinally active compounds with vicinal carbon centers such as vicinal tertiary and quaternary centers or vicinal all-carbon quaternary centers in fused-ring, spirocyclic, and bridge ring skeletons.[78d-e]

The construction of quaternary centers is of great interest due to their prevalence in natural products and bioactive molecule scaffolds. While tremendous work has been achieved in this subject over the previous two decades, most of it has been focused on the challenges of constructing a single all-carbon quaternary carbon. Due to increased degrees of rotational freedom and kinetically prohibitive and poor substrate reactivities due to steric congestion during C-C bond formation, creating two vicinal all-carbon quaternary centres remains a daunting challenge.[79] As a result, general access to contiguous quaternary carbons remains a difficult task that has sparked creative solutions such as biomimetic polyene cyclization cascades; cyclization cascades of olefins; cycloadditions; dearomatizations; electrocyclizations, cyclopropanations, transition, metal-catalyzed, and radical reactions *etc* (Scheme **58**).[80]



Scheme 58: General representation of few strategies for creating contiguous carbon centers.

Following the development of a mild and efficient protocol for the synthesis of a diverse range of cyclopentannulated arenes containing a tertiary carbon (as described in Chapter 1) and (hetero)arene fused cyclopentanoids incorporating an all-carbon quaternary/spiro center (as defined in Chapter 2), we sought to develop a method for the construction of vicinal carbon centers.

One of the most key strategies for the step- and pot-efficient synthesis of intricate

structural motifs have been shown to be sulphur ylide chemistry. Ingold and Jessop reported the first sulfur ylide isolation in 1930. However, the genuinely progressive development of sulfur ylides for synthesizing compact carbo- and heterocycles began in the 1960s. The ylides of these ylides could be produced by treating them with a suitable base at room temperature. They are characterized structurally as zwitterions that have neighbouring opposite charges. The type of substituents attached to the sulfur atom and the delocalization of negative charge induced by the carbon atom over the sulfur atom dictate the stability of these ylides (Figure **35**). Most relevant organic transformations have utilized zwitterionic ylides as nucleophilic one-carbon synthons. The Corey-Chaykovsky cyclopropanation reaction is a metal-free cyclopropanation method involving sulfur ylides. [81] The Michael addition of sulfur ylides to α,β–unsaturated systems followed by 1,3-elimination of the leaving group to form cyclopropanes is known as the Corey-Chaykovsky cyclopropanation reaction. Further, sulfur ylides have a wide range of applications as metal carbenoids and nucleophiles in transition metal catalysis and organic transformation.

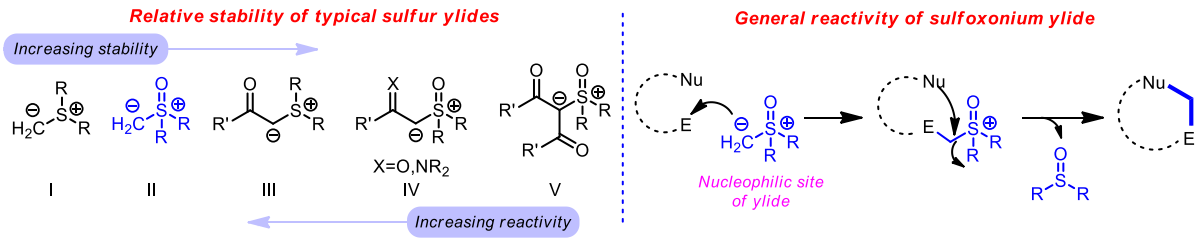


Figure 35: Relative stability of typical sulfur ylides and general reactivity of sulfoxonium ylide.

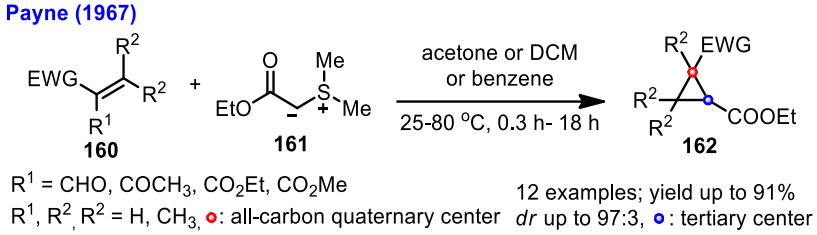
Sulfonium ylides and their applications in many chemical transformations have received much attention, but sulfoxonium ylides need to be thoroughly investigated. In comparison to sulfoxonium ylides, one of the primary contributing reasons to sulfonium salts may be the ease of synthesis with a large structural diversity. Some unexpected reactions triggered by these nucleophilic ylides to construct vicinal carbon centers are discussed in the following few subsections.

3.1 Contruction of stereogenic centers through sulfur ylides

3.1.1. Synthesis of cyclopropanes by sulfonium ylides

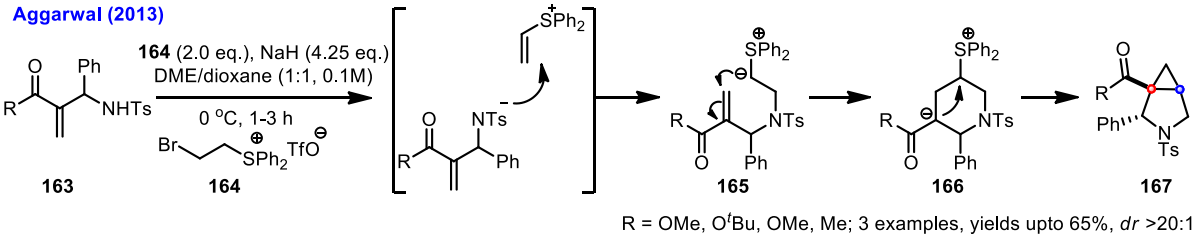
In 1967, Payne *et al*. demonstrated the stable sulfonium ylide **161** application in the cyclopropanation reaction with α, β-unsaturated compounds **160**, Scheme **59**.[82] This protocol produced a wide range of cyclopropyl derivatives **162** in high yields with good

diastereoselectivity. Stereoisomers containing the groups electron withdrawing groups and COOEt in *trans* to each other were predominant over other stereoisomers.



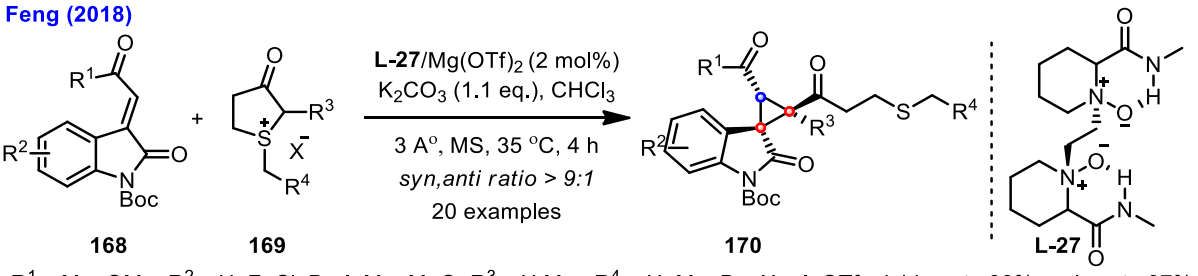
Scheme 59: Payne's synthesis of cyclopropanes.

In 2013, Aggarwal *et al*. described the synthesis of fused cyclopropanes using sulfonium salt **164**, Scheme **60**.[83] Under base-mediated reaction conditions, the reaction of **163** with the sulfonium salt **164** generated cyclopropane fused pyrrolidines having contiguous quaternary and tertiary centers in moderate yields with high diastereoselectivity.



Scheme 60: Aggarwal's synthesis of cyclopropyl fused pyrrolidines.

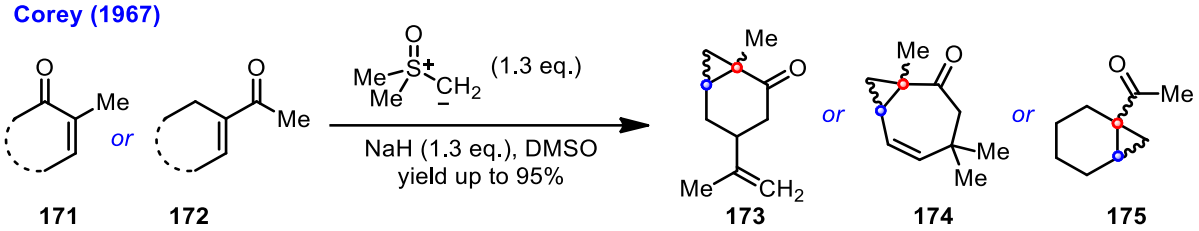
In 2018, Feng *et al*. established a technique to synthesize enantiomeric spiro-cyclopropyloxindoles **170** from **168** by employing chiral ligand **L-27** in combination with Lewis acid (Scheme **61**).[84] The process involves the ring-opening of sulfur ylides **169**, resulting in a broad spectrum of sulfur-containing *syn*, *anti*-spiro-cyclopropyl oxindoles with three contiguous stereocenters in high yields and enantioselectivity.



Scheme 61: Feng's asymmetric synthesis of spiro-cyclopropyloxindoles with contiguous quaternary center.

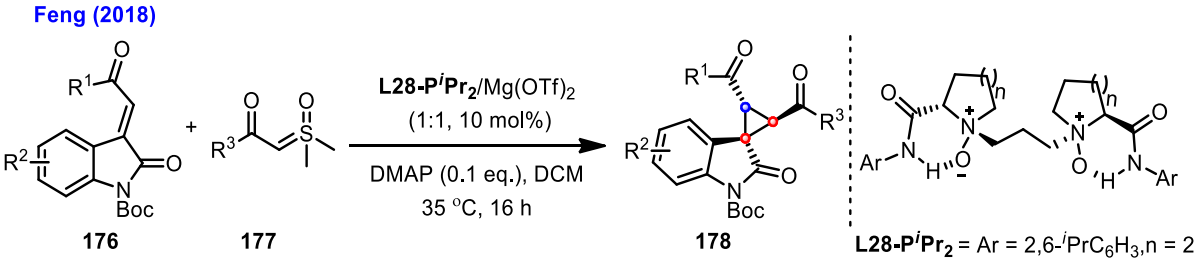
3.1.2. Synthesis of cyclopropanes by sulfoxonium ylides

In 1964, Corey and Chaykovsky, for the first time, introduced dimethyloxosulfonium methylide (DOSM) as a methylene transfer agent to effectuate cyclopropanation at the α,β-unsaturated site of carvone, eucarvone, and 1-acetylcyclohexene, resulting in the corresponding products **173-175** with vicinal stereogenic centers and Scheme **62**.[82a] The DOSM regioselectively transferred the methylene group to the Michael acceptor system's α,β-unsaturated site, avoiding addition to the carbonyl group or, γ,δ-unsaturation in the case of eucarvone **174**.



Scheme 62: Corey and Chaykovsky's pioneering cyclopropanation reaction

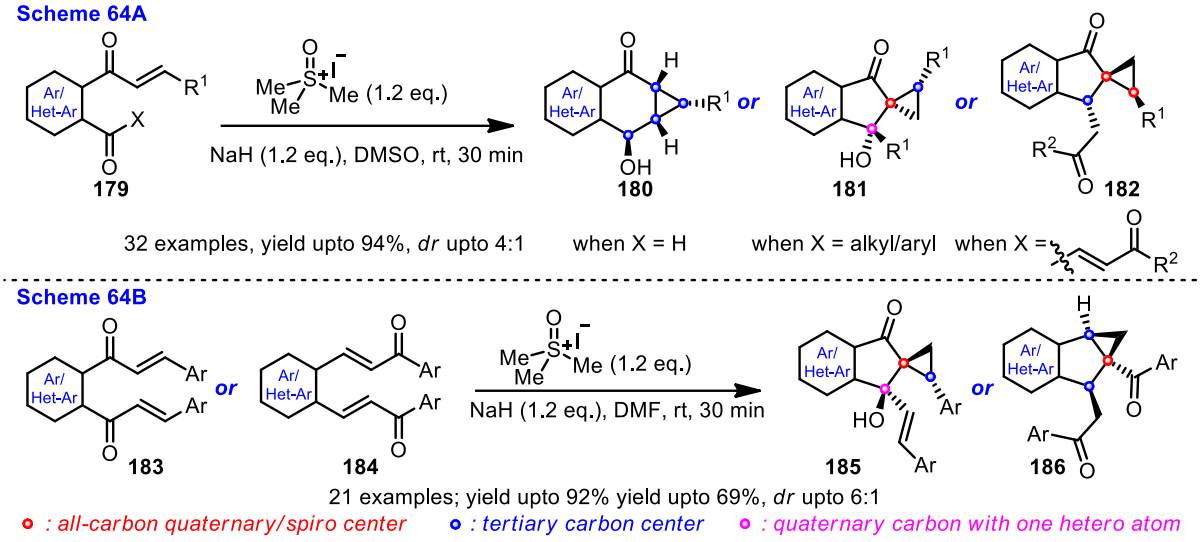
In 2018, Cao and Feng developed the asymmetric synthesis of spiro-cyclopropyl oxindoles **178** bearing three contiguous stereogenic centers by using the chiral complex catalyst **L-28**P^{i}Pr$_2$/Mg(OTf)$_2$ in the reaction of sulfoxonium ylides **177** with oxindoles **176**, Scheme **63**.[85] Under the reaction conditions, a range of oxindoles **178** and sulfoxonium ylides **177** were well tolerated, resulting in excellent yields of spirocyclopropyl oxindoles **178** with high diastereo- and enantioselectivities.



Scheme 63: Feng's asymmetric synthesis of spiro-cyclopropyloxindoles.

Recently, our research group reported the unprecedented diastereoselective synthesis of cyclopropanoids *via* unusual cyclization pathways triggered by the DOSM, Scheme **64**.[86] By positioning the electron-withdrawing enone and carbonyl *ortho* to each other (enone-aldehyde and enone-ketones) provide access to a variety of cyclopropa-fused tetralones **180** and indeno-spirocyclopropanes **181** and **182** with three contiguous stereocenters, respectively (Scheme **64A**). Under the same reaction conditions, numerous functionalized indeno-

spirocyclopropanes **185** and cyclopropa-fused indanes **186** containing VTQCs were synthesized in excellent yields with moderate diastereoselectivity using the first sulfur ylide mediated desymmetrization strategy on symmetric bis-enones **183** or **184** (Scheme **64B**).



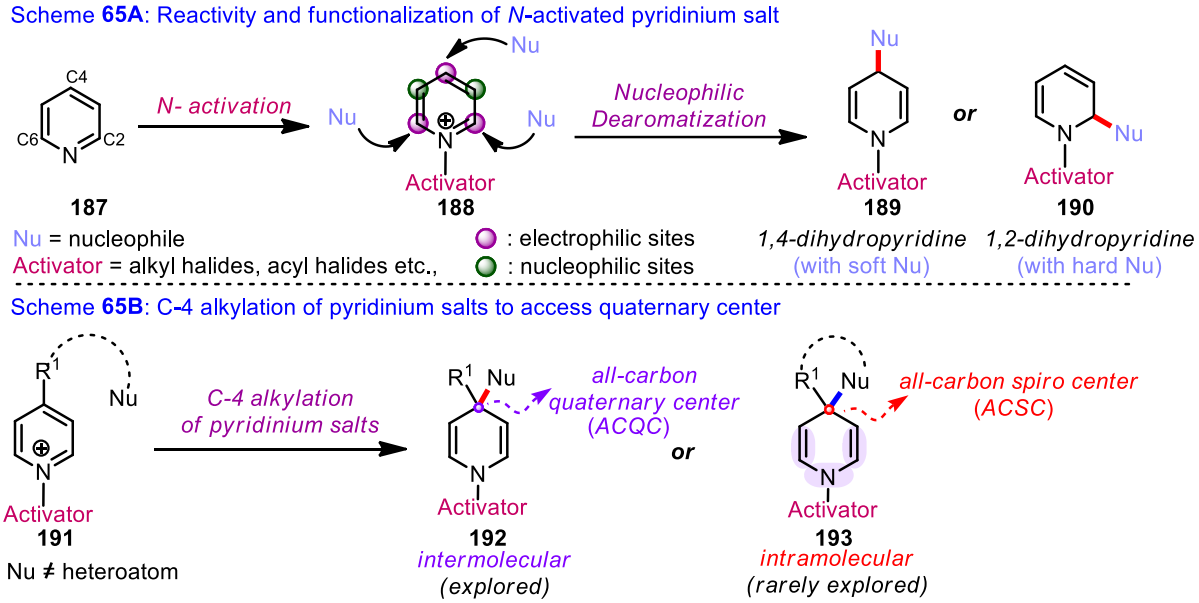
Scheme 64: Synthesis of cyclopropa-fused tetralones and indeno-spirocyclopropanes with three contiguous stereocenters**.**

Azaarenium salts are the salts of nitrogen-containing aromatic rings derived from parent azaarenes such as pyridinium quinolinium, isoquinolinium, acridinium salts, etc. Azaarenium salts, like sulfur ylides, offer a wide range of synthetic implications in natural product chemistry, pharmaceuticals, and material science. Azaarenium cationic salts are extremely reactive species as compared to azaarenes, which led to discovery of various functionalized dihydro, tetrahydropyridines, and piperidines, as well as dihydro- and tetrahydroquinolines through multiple synthetic transformations. These azaheterocyclic structures have gained huge research interst as intermediates in alkaloid synthesis, NADH models, and as various biologically active components. Azaarenium salts being electrophiles and 1,3-dipoles, can undergo a variety of reactions, including condensation, Michael addition, nucleophilic dearomatization, 1,3-dipolar addition, nuclear substitution, and arrangement reactions.[87]

Dearomatizations, transformations capable of disrupting the aromatic system and yielding unsaturated and often functionalized compounds, are of great interest to synthetic organic chemists. The nucleophilic dearomatization of azaarenium salts is a well known synthetic methodology to generate 3D scaffolds. The complicated bridging rings with sophisticated and rigid architectures, synthezied from readily accessible planar aromatic azaarene compounds. However, there are two significant impediments to this synthetic strategy: (1) breaking aromaticity, which is a thermodynamically unfavourable process; and

(2) chemo-, regio-, and stereo-selectivity issues in constructing 3D scaffolds from planar molecules, which notably challenging in the case of bridged rings due to their structural rigidity and complexity.[129]

Dearomatization of readily assembled pyridinium salts is one of the most straightforward synthetic approaches to polysubstituted dihydropyridine (DHP) derivatives. Pyridium salts' (**188**) inherent electrophilicity allows nucleophilic additions at the C-2/C-6 and C-4 positions, leading to the formation of 1,2- or 1,4-DHPs (**189** or **190**) *via* nucleophilic dearomatization depending on the nature of nucleophiles. (Scheme **65A**). Scheme **65B** represents the generation of an all-carbon quaternary center containing DHP **192** at C-4 throughout this strategy is feasible, albeit intermittently explored. 1,4-DHP **193** with an all-carbon spiro center can be anticipated as a result of an *ipso*-nucleophilic addition of tethered nucleophiles at C-4. Despite the fact that the C-4 position in pyridinium salts is soft, the synthesis of spirocarbocyclic piperidines *via* intramolecular nucleophilic dearomatization of pyridinium salts is rare.[88]

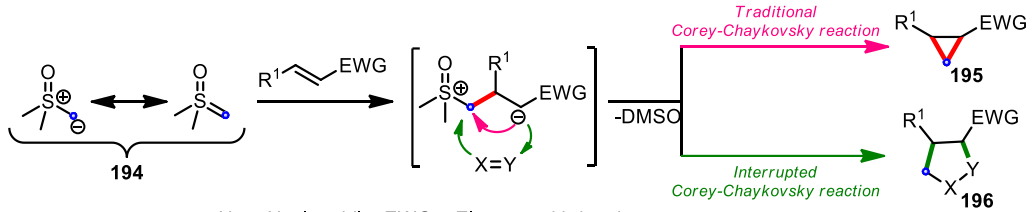


Scheme 65: General reactivity and C-4 alkylation of pyridinium salts to access all-carbon quaternary/spiro center.

To synthesize medium-sized ring carbocycles bearing vicinal stereogenic centers, we sought to develop a hybrid approach that utilizes both sulfur ylides chemistry and pyridinium chemistry. As we know, the traditional Corey-Chaykovsky (CC) reaction involves dimethyloxosulfonium methylide (DOSM) to cyclopropanate the electron-deficient olefins

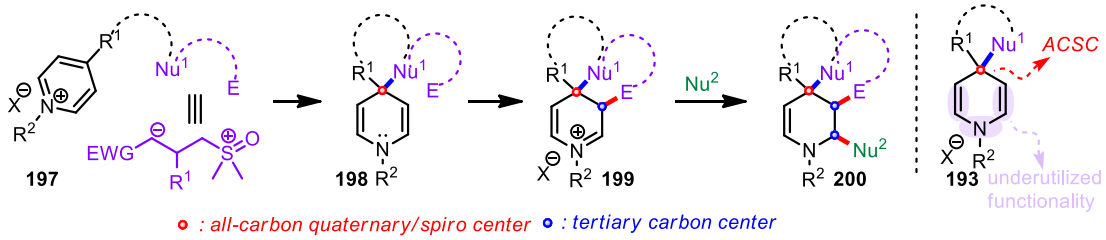
(Scheme **66A**). The dimethyl sulfoxide (DMSO) group is displaced from the zwitterionic intermediate A (path-a) to generate cyclopropanes **195**. So, in principle, a suitable functionality (X=Y) can trap intermediate, resulting in various carbo- and heterocycles **196**, which we call the interrupted CC reaction (path-b). With this backdrop, we postulated an outline of substrate design **197** (Scheme **66B**). The pragmatic anchoring of a Nu^1-E tether (with dual electronic characteristics such as **197**) onto the pyridinium ring is expected to cause C-4 spirannulation.

Scheme **66A**: Traditional Corey-Chaykovsky reaction and realization of a potential opportunity for its possible interrupted version



Nu = Nucleophile, EWG = Electron-withdrawing group

Scheme **66B**: Substrate design for a hybrid method that rationally combines the reactivities of sulfur ylides and pyridinium salts



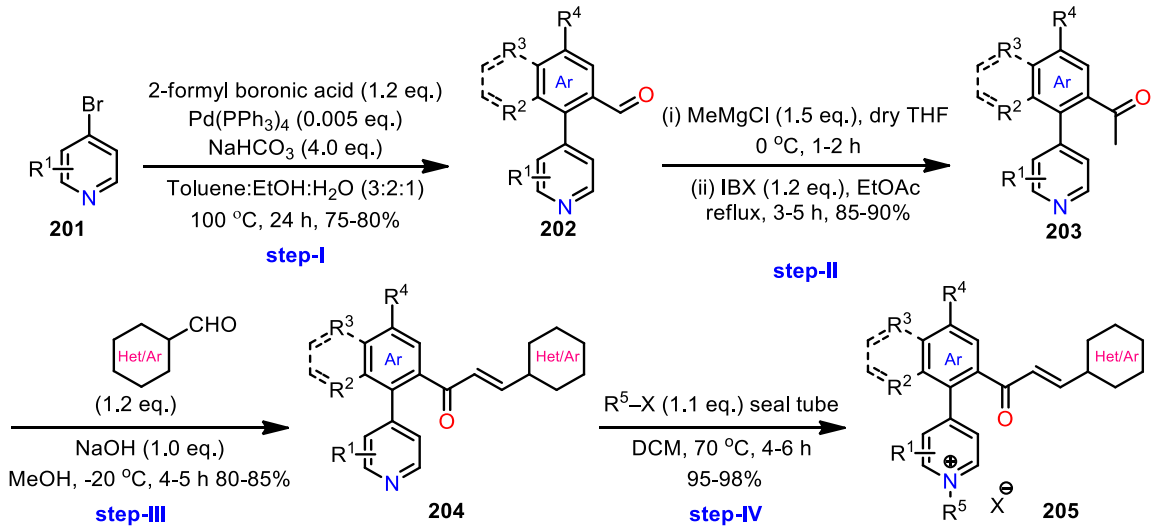
Scheme 66: Our hypothesis to construct vicinal stereogenic centers involving sulfur ylides with pyridinium chemistry.

The enamine-mediated alkylation of the resultant dienamine **198** might provide the iminium species **199**. After that, the synthetic utility of the resulting dihydropyridines' bis-enamine functionality can be utilized by entrapment of another suitable nucleophile (Nu^2) to generate spiro-fused tetrahydropiperidines **200**. In brief, we hypothesized simultaneous dearomatizing spiro-annulation of designed pyridinium salts **197** through an interrupted Corey-Chaykovsky (iC-C) reaction would allow access to unique and architecturally fascinating molecular structures. This fusion method combines the nucleophilic features of sulfur ylides **194** with the electrophilic properties of pyridinium salts **197** to create new classes of spirocarbocyclic-piperidines **200** with at least three new bonds and three new vicinal stereogenic centers. As a result, the suggested design makes efficient use of atleast three of the five reactive sites of pyridinium salts.

3.2: Results and Discussion

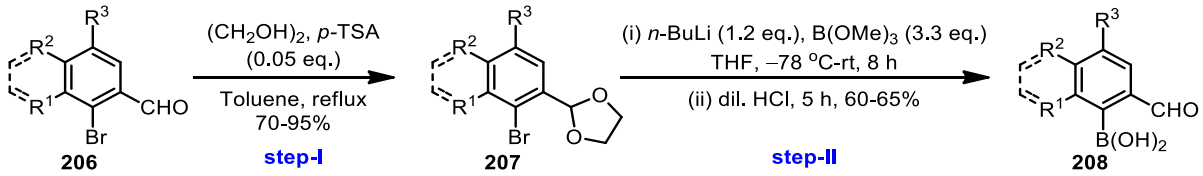
To substantiate our hypothesis presented in Scheme **67**, prepared by tethering the enone and pyridinium moieties *ortho* to each other on the arene backbone, we started synthesizing

the designed substrates **205** using a four-step protocol, Scheme **67**. 2-(pyridin-4-yl)aryl-aldehydes **202** can be accessed through the Suzuki coupling reaction between 2-formyl boronic acids and 4-bromo-pyridines **201** with different functionality. Methyl Grignard reagent addition to the 2-(pyridin-4-yl)aryl-aldehyde **202** and followed by IBX oxidation, generated the required 2-(pyridin-4-yl)aryl-ketone **203**. 2-(pyridin-4-yl)aryl-enones **204** employed in this study can be accessed from diverse aldehydes by using classical aldol reaction. Enone-tethered pyridinium salts **205** were obtained in excellent yields by heating alkyl halides and **204** in DCM at 70 ^{o}C in a sealed tube.



Scheme 67: Synthesis of enone-tethered pyridinium salts **205a-205h, 205k-205o and 205r-t.**

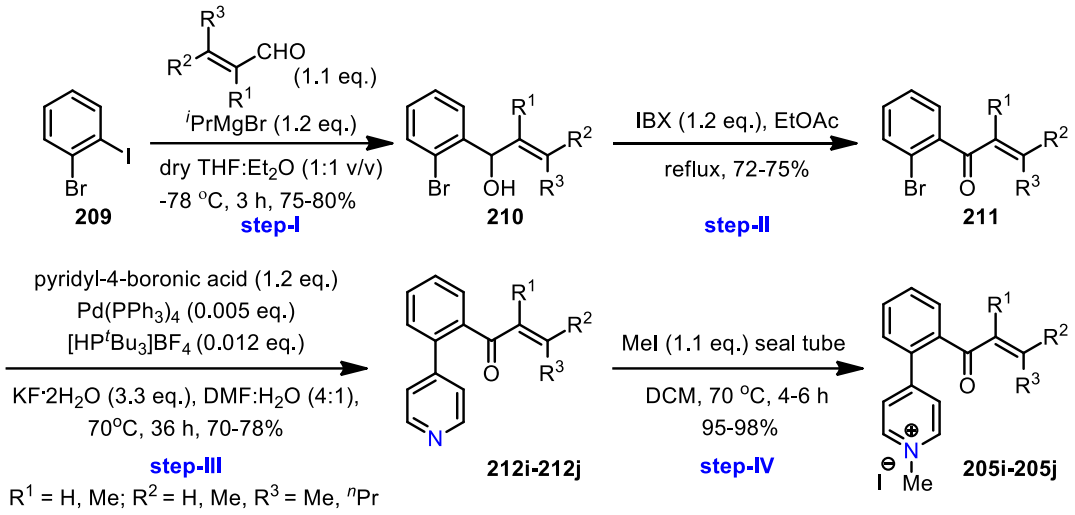
2-formyl boronic acids **208** were synthesized by following a two-step protocol starting from commercially available 2-bromo-aryl-aldehyde. Initially, **206** was protected with ethylene glycol under an acidic medium and subjected to *n*-BuLi mediated borylation to obtain the required 2-formyl boronic acids **208**, Scheme **68**.



Scheme 68: Synthesis of 2-formyl boronic acids **208.**

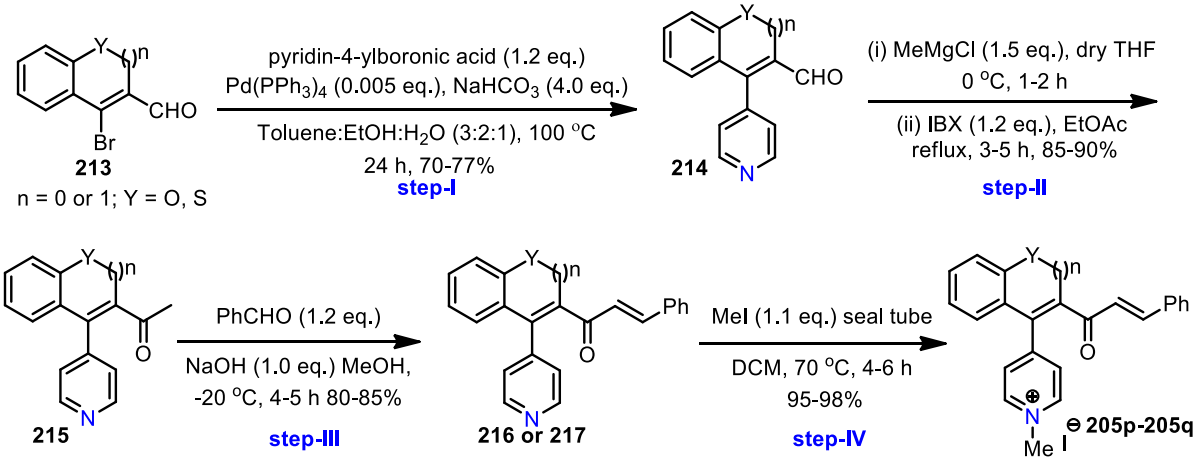
In order to corroborate our intention toward the synthesis of **205i-205j**, model substrates were synthesized by using a four-step protocol starting from commercially available 2-bromo iodobenzene **209** (Scheme **69**). Direct ^{i}PrMgBr mediated alkylation of **209** with aliphatical enals generated the corresponding 2-bromo-alcohol **210**. Subsequent IBX oxidation of **210**

furnished the 2-bromo enone **211**. Later, a modified Suzuki coupling between 2-bromo enone **211** and pyridin-4-ylboronic acid delivered the expected 2-(pyridin-4-yl)aryl-enone **212**. Enone-tethered pyridinium salts **205i-205j** were obtained in excellent yields by heating methyl iodide and **212** in DCM at 70 °C in a sealed tube.



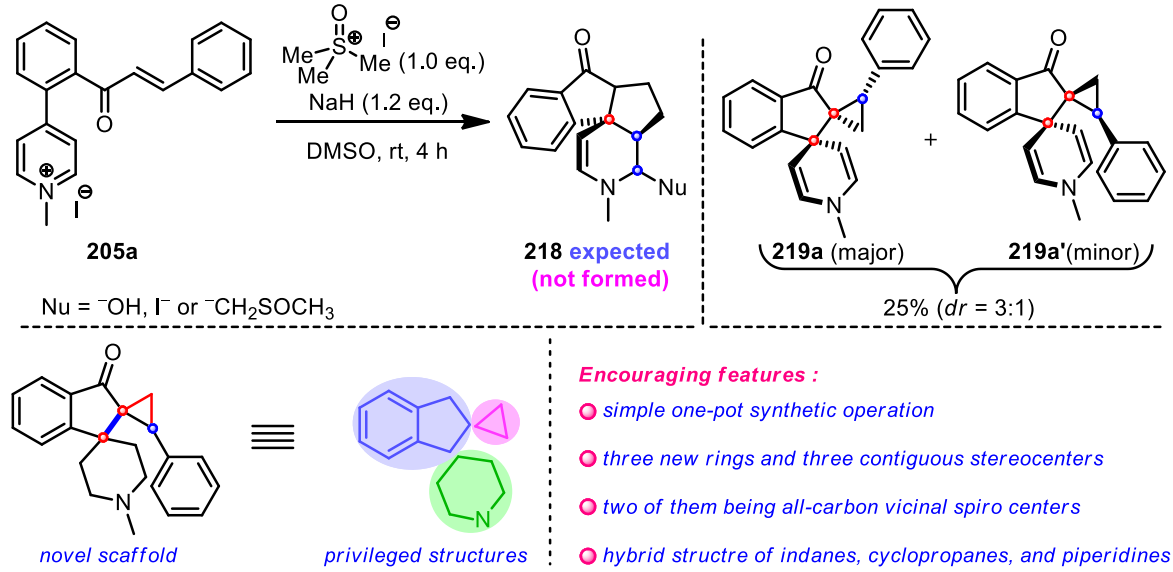
Scheme 69: Synthesis of enone-tethered pyridinium salts **205i-205j**.

. Benzothiophene and chromene-based substrates can be accessed easily in a four-step protocol (Scheme **70**). A Suzuki coupling between **213** and pyridin-4-ylboronic acid delivered the expected 2-(pyridin-4-yl)hetro-aryl-aldehyde **214**. Methyl Grignard reagent addition to the 2-(pyridin-4-yl)hetro-aryl-aldehyde **214** followed by IBX oxidation generated the required 2-(pyridin-4-yl)hetro-aryl-ketone **215**. 2-(pyridin-4-yl)hetro aryl-enones **216** or **217** employed in this study can be accessed from aldehydes **215** by employing classical aldol reaction. Enone-tethered pyridinium salts **205p-q** were obtained in excellent yields by heating methyl iodide and **216-217** in DCM at 70 °C in a sealed tube.



Scheme 70: Synthesis of enone-tethered pyridinium salts **205p** and **205q**.

After successfully synthesizing the enone-tethered pyridinium salt **205a**, we performed the cyclopropanation reaction in DMSO, Scheme **71**. Gratifyingly, unexpected products **219a** and **219a'** were isolated as a separable mixture of diastereomers with *dr* = 3:1 instead of delivering the expected product **218**, although in poor yield. The structure of **219a** and **219a'** were carefully deduced from the IR, NMR, and HRMS data.



Scheme 71: Corey-Chaykovsky reaction with the substrate **205a**

The sharp band at 1697 cm^{-1} is the depicted the presence of a carbonyl group in the IR spectrum, which indicates the formation of the product **219a** for major diastereomer. In the ^{1}H-NMR spectrum (see Figure **36**), the presence of a singlet at δ 3.10 ppm indicates C-1 nitrogen connected methyl group, a triplet at δ 2.99 ppm indicates C-2 methine proton, a dd at δ 2.10 ppm (*J* = 8.2, 4.3 Hz) and a dd at δ 1.71 ppm indicates C-3 methine protons. The presence of downfield pair of two dd at δ 6.20 ppm (*J* = 7.8, 1.7 Hz), 6.09 (*J* = 7.8, 1.8 Hz), and the upfield pair of two dds at δ 4.32 ppm (*J* = 7.8, 2.9 Hz), δ 4.09 ppm (*J* = 7.9, 2.9 Hz) confirms the dihydropyridines' bis-enamine functionality. In ^{13}C-NMR spectrum (see Figure **37**), the presence of a peak at δ 202.9 ppm indicates the presence of ketone (C-6), a peak at δ 40.5 ppm indicates *N*-Methyl carbon (C-1) and the peaks at δ 52.9 ppm and δ 46.1 ppm are due to spiro carbons (at C7 and C8 respectively), peaks at δ 33.6, 18.7 ppm indicate the rest are due to cyclopropane carbons (C-2, C-3). Thus the ^{1}H- and ^{13}C-NMR data confirmed the formation of the product **219a**. In the high-resolution mass spectrum, the presence of deprotonated molecular ion peak at *m*/*z* 312.1395 $(M-H)^{+}$ confirmed the structure of **219a**.

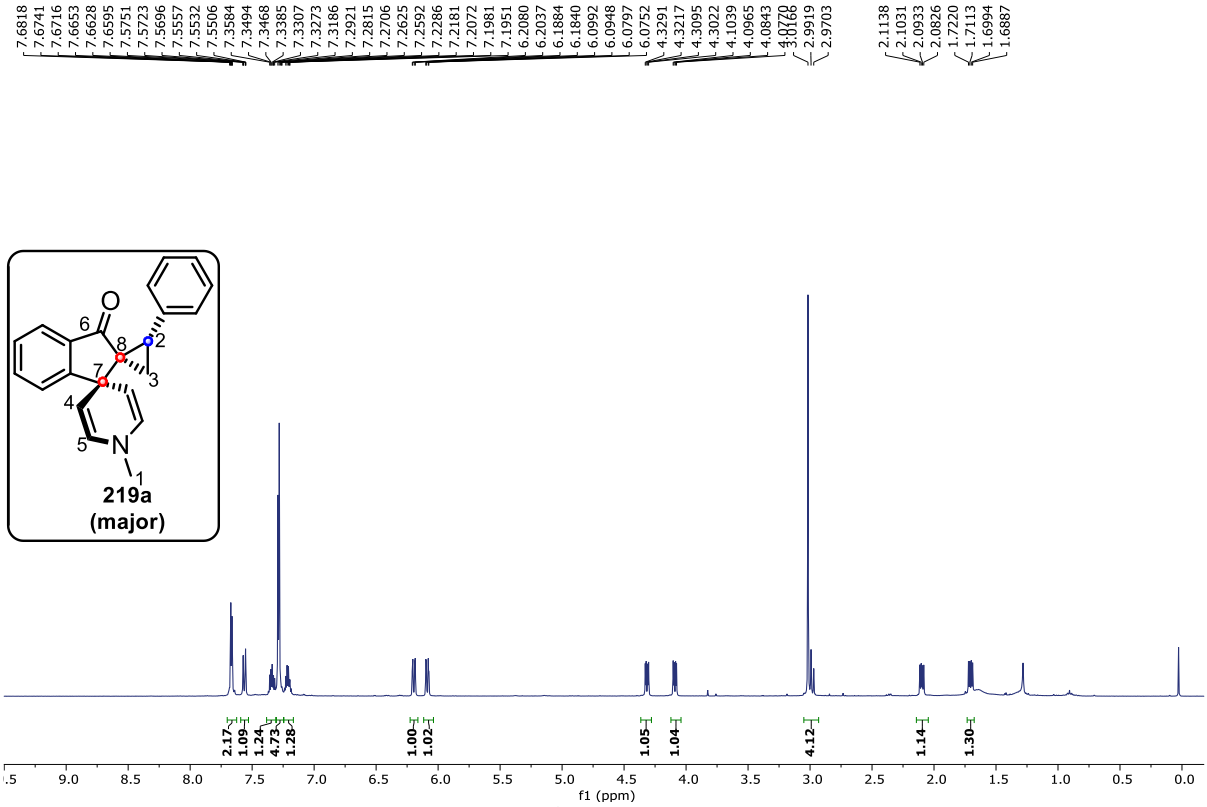


Figure 36: ^{1}H-NMR spectrum of **219a**

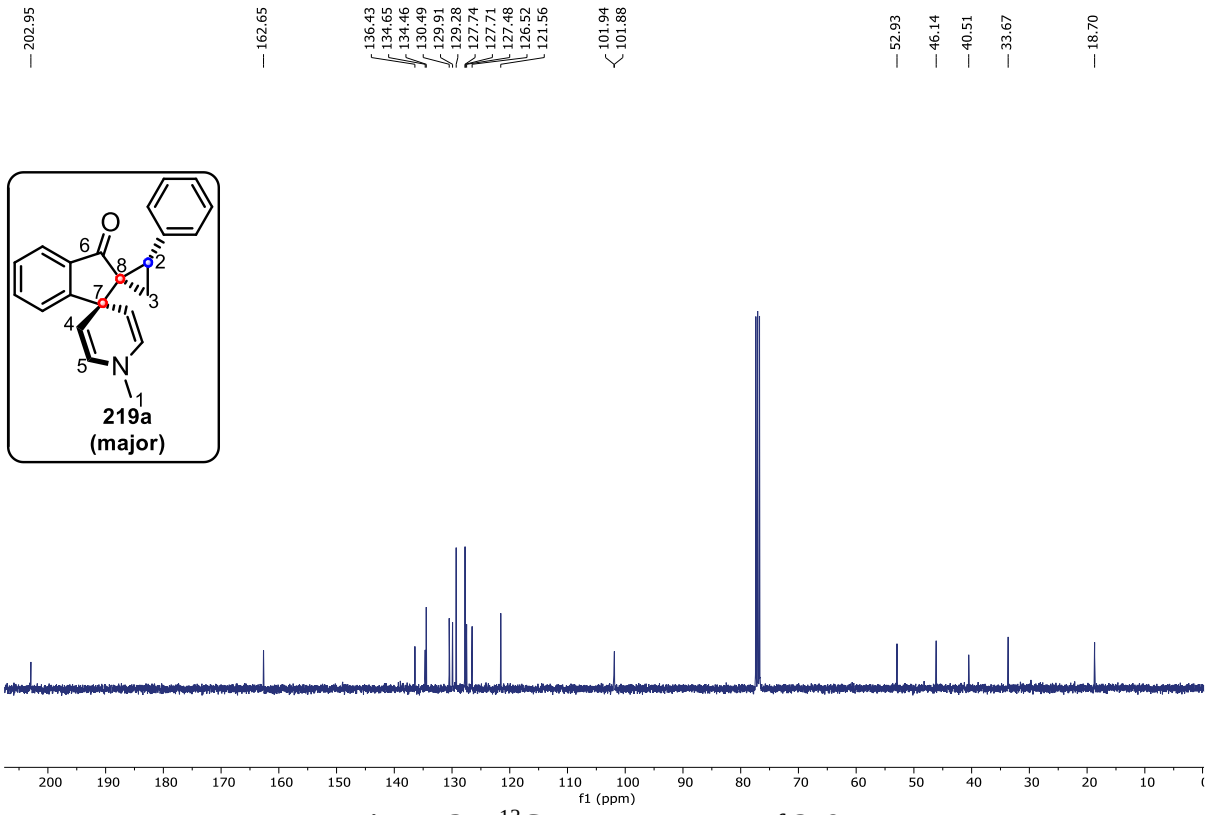


Figure 37: ^{13}C-NMR spectrum of **219a**

The other diastereomer **219a'** was also confirmed by the IR, NMR, and HRMS data. The presence of a sharp band at 1698 cm^{-1} is the indication of a carbonyl group in the IR spectrum, which indicates the formation of product **219a**'. In the ^{1}H-NMR spectrum (see Figure **39**), the presence of a singlet at δ 2.71 ppm indicates C-1'' nitrogen connected to methyl group, a triplet at δ 2.99 ppm indicates C-2' methine proton, a dd at δ 2.02 ppm (*J* = 7.9, 4.2 Hz) and a dd δ 1.57 ppm (*J* = 9.3, 4.1 Hz) indicates C-3' methine protons. The presence of downfield pair of two dd at δ 5.96 ppm (*J* = 7.8, 1.8 Hz), 4.90 (*J* = 7.9, 1.8 Hz), and the upfield pair of two dd at δ 4.12 ppm (*J* = 7.8, 2.9 Hz), δ 3.52 ppm (*J* = 7.8, 3.0 Hz) confirms the dihydropyridines' bis-enamine functionality. In ^{13}C-NMR spectrum (see Figure **40**), presence of a peak at δ 204.9 ppm indicates the presence of ketone (C-6'), a peak at δ 40.1 ppm indicates *N*-Methyl carbon (C-1') and the peaks at δ 53.2 ppm and δ 45.2 ppm are due to spiro-carbons (at C7' and C8' respectively), signals at δ 32.7, 18.8 ppm indicates the rest of cyclopropane carbons (C-2', C-3'). Thus the ^{1}H- and ^{13}C-NMR data and also the HRMS data indicated the formation of product **219a'.** The structures of both major and minor diastereomers and the relative stereochemistry was confirmed from the X-ray diffraction analysis of **219a** and **219a**' assigned to other products in analogy, Figure **38**.

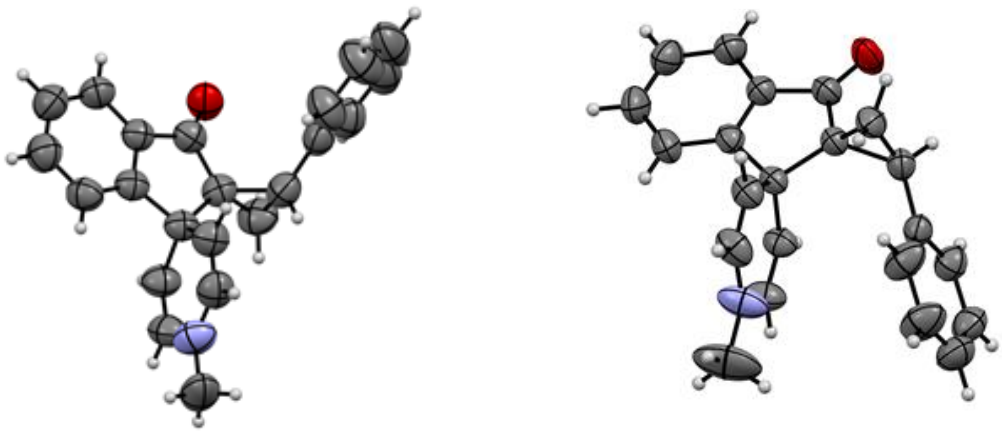


Figure 40: ORTEP diagram of **219a** and **219a'**, ellipsoid probability (50%)

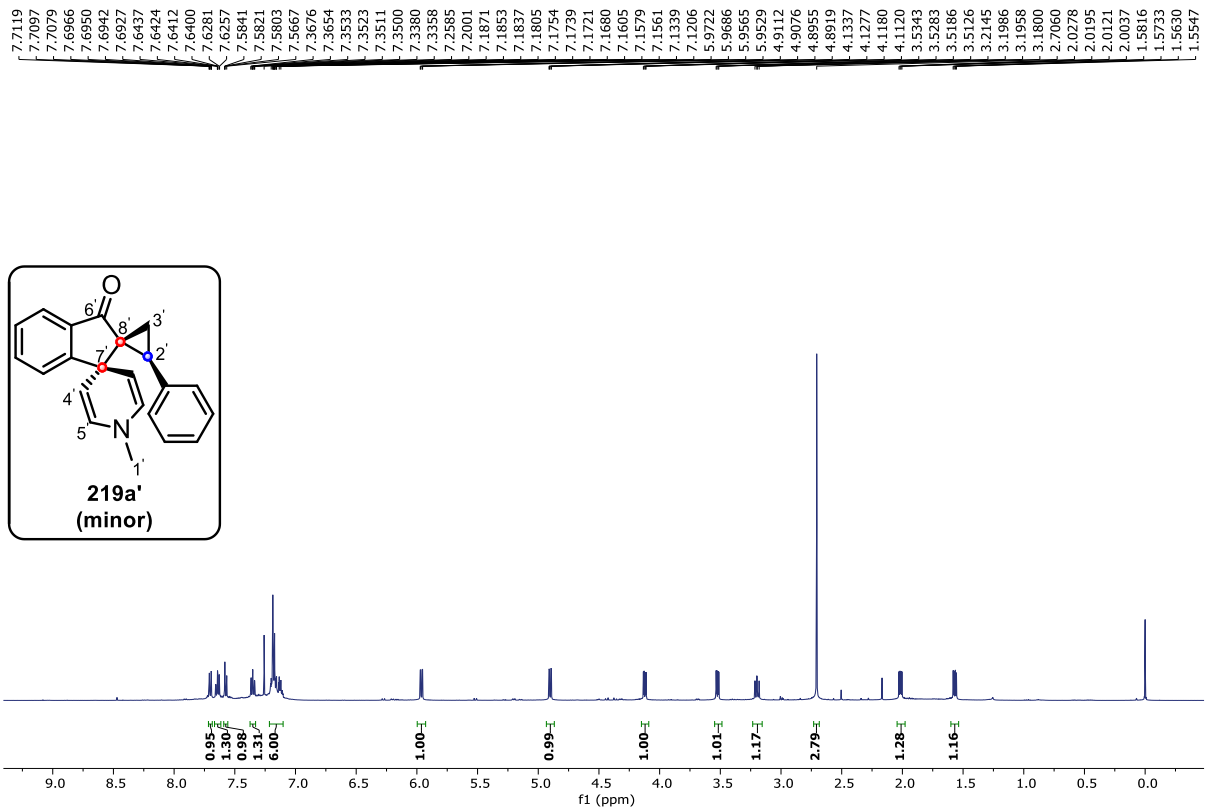


Figure 39: ^{1}H-NMR spectrum of **219a'**

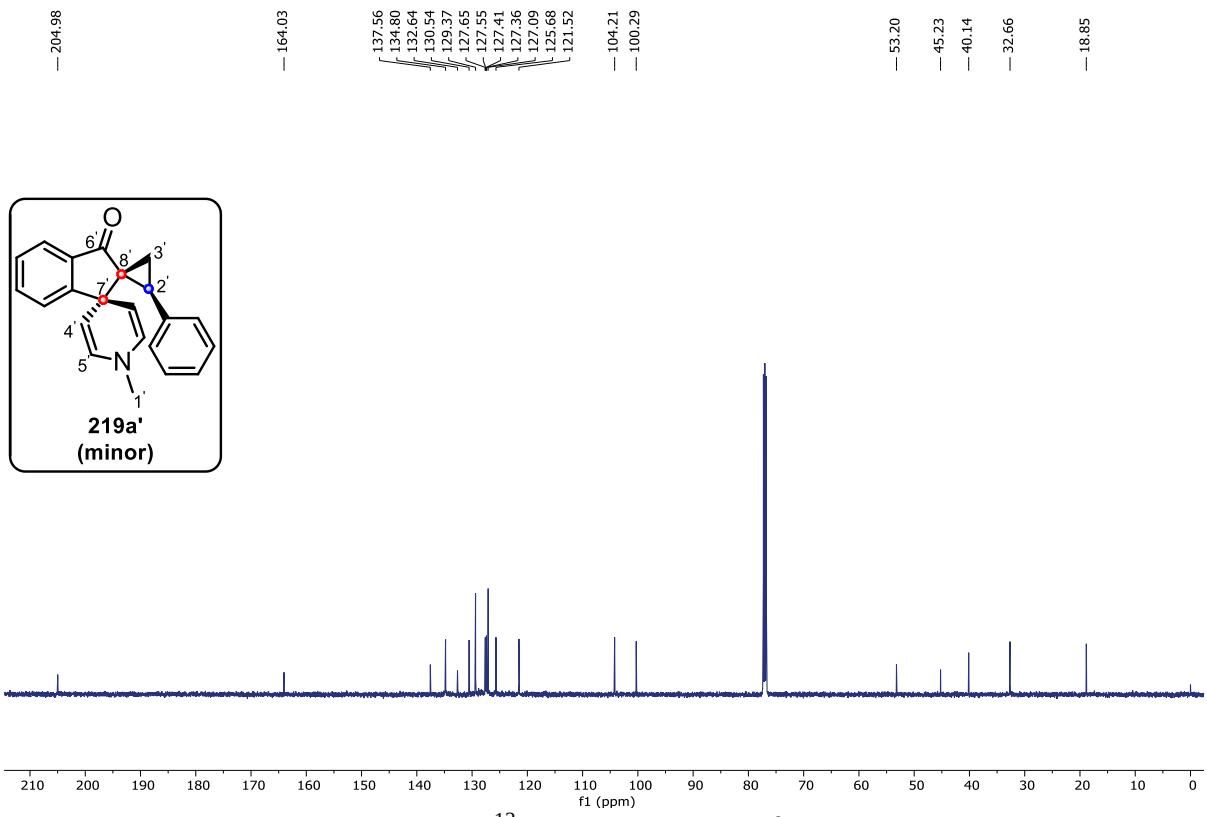
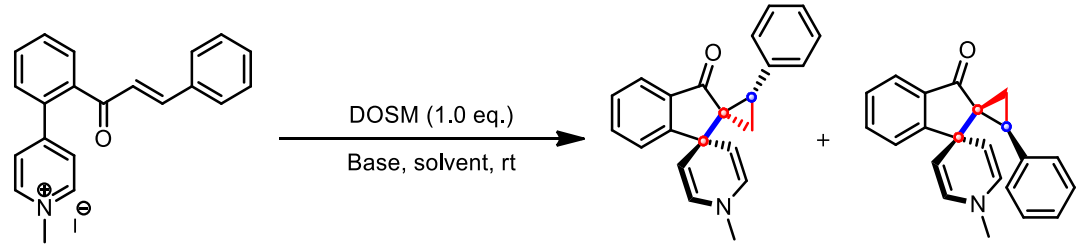


Figure 40: ^{13}C-NMR spectrum of **219a'**

We were highly fascinated that a single-pot synthetic operation generates three new rings and three contiguous stereocenters, two of which are all-carbon vicinal spiro centers. As a result, even in modern organic synthesis, constructing a spiro structure is challenging, and building the vicinal spirocyclic systems is even more daunting. Emphasizing the importance of indanes, cyclopropanes, and piperidines in drug development, the hybrid structure **219** and its analogs containing these components could be used as lead compounds. The aforementioned distinctive aspects prompted us to optimize the reaction conditions.

We commenced our optimization study with (*E*)-4-(2-cinnamoylphenyl) 1-methylpyridin-1-ium iodide **205** as the model substrate after identifying the unprecedented

Table 9: Optimization of reaction parameters with **205**



205a **219a** (major) **219a'**(minor)

Entry	Base (1.1 eq.)	Solvent	Time (h)	Yield of 219 [%][a]
1	NaH	Acetamide	24	23
2	NaH	MeCN	24	30
3[b]	**NaH**	**DMF**	**3**	**86**
4[c]	NaH	DMF	12	39
5[d]	NaH	DMF	3	75
6[e]	NaH	DMF	24	79
7[f]	NaH	DMF	24	76
8	KO^{t}Bu	DMF	24	15
9	CS_2CO_3	DMF	24	-
10	K_2CO_3	DMF	24	-
11	DBU	DMF	24	-
12	Guanidine	DMF	24	-

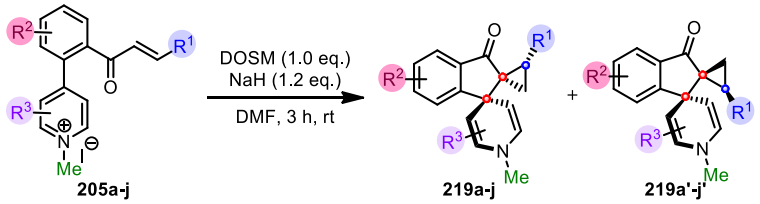
[b]Isolated yield after column chromatography. [b]Obtained in 3.5:1 *dr*. [c]At 0 °C. [d]At 60 °C. [f]In the presence of 1.5 eq. of NaH. [g]In the presence of 2.0 eq. of NaH.

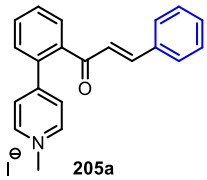
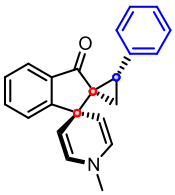
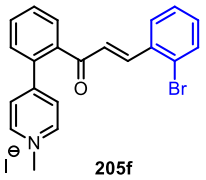
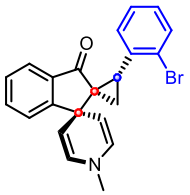
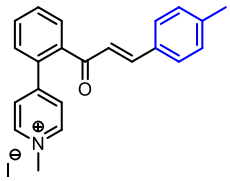
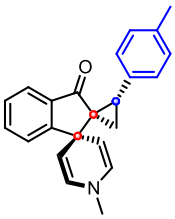
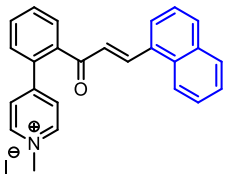
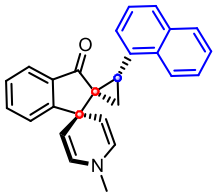
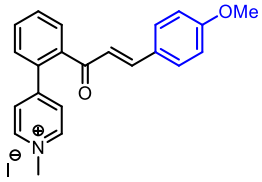
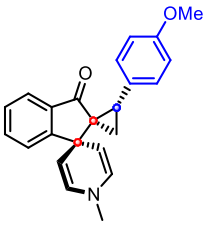
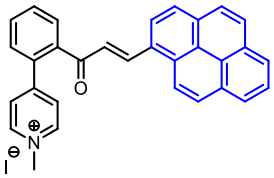
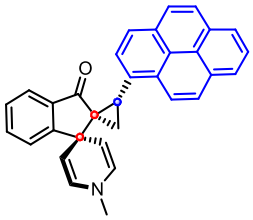
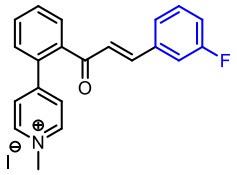
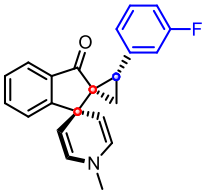
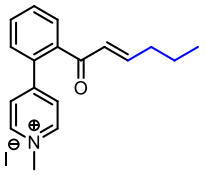
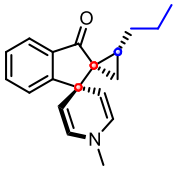
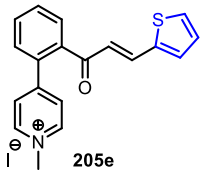
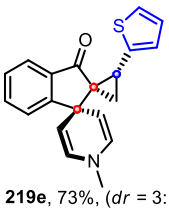
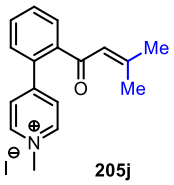
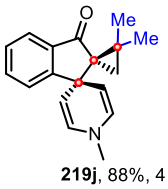
synthesis of **219a** and **219a'** from **205**, the reaction parameters were optimized. Table **9**. summarises the results of evaluating a number of bases and solvent combinations. NaH was the most effective in delivering the desired product **219** in good yields among the typically used organic or inorganic bases (K_2CO_3, K^{t}OBu, NaH DBU, and Guanidine). The initial solvent screening demonstrated a considerable increase in reaction efficiency in DMF (entry 1-3, Table **9**), with the desired product **219** producing in 86% yield in a short reaction time. For better results, the influence of temperature was investigated on reaction mixture. The reaction of **205a** at 0 ^oC generated **219** in a moderate yield, whereas the product was identified in a 75% yield at 60 ^oC. (entries 4 and 5). Contrary to our expectations, even with a longer reaction time and with increased base amounts we didn't observe efficient results (entries 6 and 7). As a result, the optimal reaction condition for a successful outcome was found to be a mixture of NaH and DMF at ambient temperature.

With the optimal reaction condition in hand, we next investigated the scope and generality of the reaction. The *iC-C* process produces a diverse range of synthetically demanding bis-spirocyclic indanones in good to outstanding yields and moderate to high diastereoselectivities. A wide range of enone-tethered pyridinium salts **205a-205j** was subjected to the optimized reaction conditions to generate the respective bis-spirocyclic indanones **219a-219j** in good to excellent yields (Table **10**). The electronic (such as electron-donating and electron-withdrawing groups) and steric roles of the substituents on the enone moiety (R^1) were thoroughly investigated and found to be well-tolerated under the optimized conditions. The substrates bearing electron-donating groups (such as *p*–OMe, *p*-Me) on their enone moiety's of aromatic backbones afforded the respective bis-spirocyclic indanones **219b-219c** in excellent yields with a diastereomeric ratio (*dr*) of 3:1, Table **10**.

Because of their particular biological features, fluorinated chemicals are highly essential. Despite our expectations, the presence of fluorine group on the aryl moiety resulted in high yields of fluorinated bis-spirocyclic indanones **219d** with *dr* = 2.3:1. The sterically hindered substituents of the enone part, such as *ortho*-bromo, 1-naphthyl, and 1-pyrenyl, had a significant impact on the diastereoselectivity of the reaction, yielding bis-spirocyclic indanones (**219f-219h**) in high yields maximal *dr* 1:5. The substrate containing an aliphatic group on the enone moiety produced the desired product **219i** in excellent yield, with *dr* = 9:1. After demonstrating the efficacy and ease of transformation of *β*- monosubstituted

Table 10: Substrate scope: Vicinal bis-spirocyclic indanones **219a-219j** (Variations at R^1)[a,b]



Entry	Substrate	Product[a,b]	Entry	Substrate	Product[a,b]
1	 **205a**	 **219a**, 86%, (*dr* = 3.5:1)	6	 **205f**	 **219f**, 77%, (*dr* = 1:4)
2	 **205b**	 **219b**, 81%, (*dr* = 3:1)	7	 **205g**	 **219g**, 76%, (*dr* = 1:5)
3	 **205c**	 **219c**, 74%, (*dr* = 3:1)	8	 **205h**	 **219h**, 80%, (*dr* = 1:4)
4	 **205d**	 **219d**, 81%, (*dr* = 2.3:1)	9	 **205i**	 **219i**, 74%, *dr* = 9:1
5	 **205e**	 **219e**, 73%, (*dr* = 3:1)	10	 **205j**	 **219j**, 88%, 4 h

[a]Isolated yields after column chromatography. [b]The *dr* was estimated from the analysis of the crude ^{1}H-NMR data.

enones, the sterically demanding substrate such as *β, β*-disubstituted enone produced the bis-spirocyclic indanone **219j** in excellent yield.

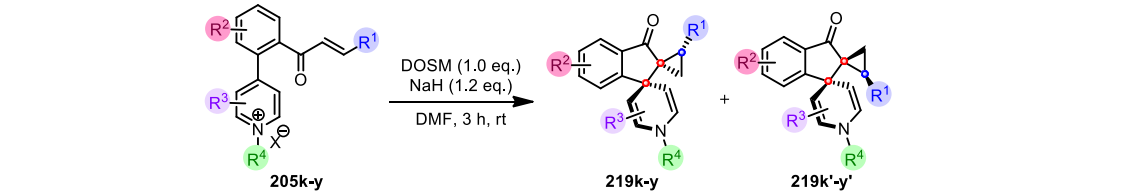
To extend our strategy, we successfully assembled bis-spirocyclic indanone derivatives **219k-219y** having various substituents on the arene backbone (R^2) and pyridine core (R^3) in excellent yields with moderate to high diastereoselectivities (Table **11**). Enone tethered

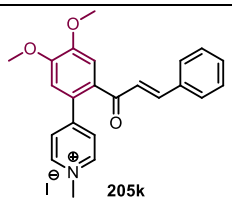
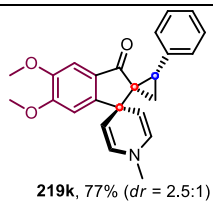
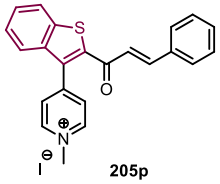
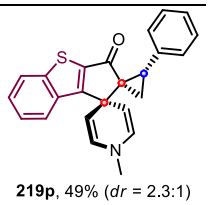
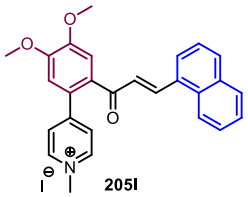
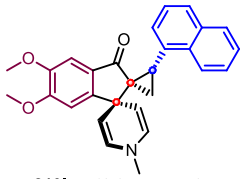
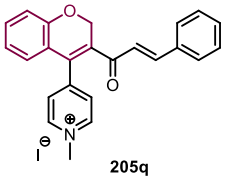
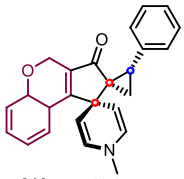
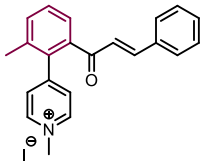
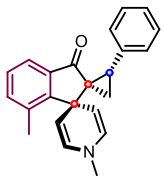
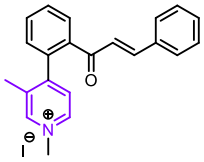
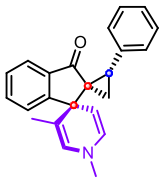
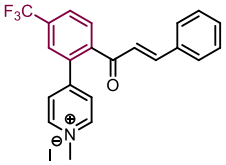
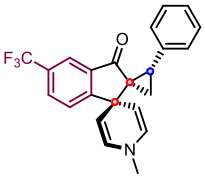
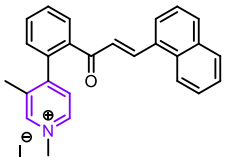
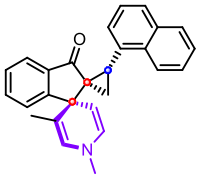
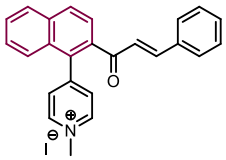
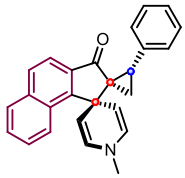
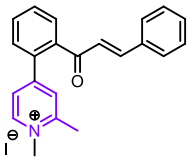
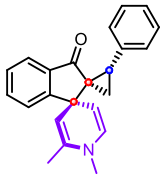
pyridinium salts with electron-donating (-OMe or -Me) **205k-205m** and withdrawing (-CF_3) **205n** groups on the arene's backbone (R^2) had no significant effect on the yields of the reaction while yielding corresponding bis-spirocyclic indanones **219k-219m** and **219n**, Table **11**. The reaction was quite efficient with naphthalene backbone substrates (**205o**). Furthermore, the method's adaptability is demonstrated using the heteroaryl-based substrate **205p**, which satisfactorily provided benzothiophene fused bis-spirocyclic cyclopentanone **219p** in good yield. Interestingly, a non-aromatic backbone, such as chromene-based enone pyridinium salt **205q**, produced chromene-linked bis-spirocyclic cyclopentanone **219q** in a high yield under the optimal conditions. Encouraged by these results, we started investigating the reaction's broader scope and versatility to synthesize bis-spirocyclic indanone derivatives with substitution R^3 on the pyridine core. Notwithstanding our concerns about the outcome of the C-3 substituted pyridinium salts, we achieved the corresponding products (**219r** and **219s**) in good yields. However, the reaction of C-2 substituted pyridinium salt **205t** did not provide the anticipated result.

Following that, we looked into the role of *N*-substituents (R^4) and counter ions (X^-) of pyridinium salts in the process. Various linear and branched alkyl systems were also well accommodated, providing excellent results. Hexylpyridinium iodide enone **205v** produced *N*-hexylated bis-spirocyclic indanone **219v** with a 78% yield with *dr* = 6.5:1. Furthermore, bromo anion-based pyridinium salts with *N*-substituents like butyl **205u**, benzyl **205w**, 3,5-dimethoxybenzyl **205x**, and benzo[*b*]thiophen-2-ylmethyl **205y** were also well-tolerated, yielding the desired products **219u, 219w-219y** in good yields with maximum diastereoselectivity of up to 7:1.

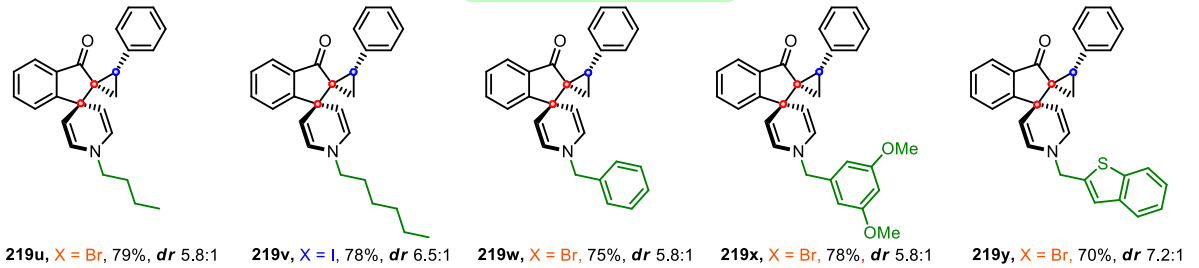
Overall, the impact of R^1, R^2, R^3, R^4, and counter ions (X^-) demonstrated that the transformation is exceptionally robust, with a broad scope and the ability to accommodate substituents with different electronic and steric characteristics. This trait is essential in early drug development during hit-to-lead (H2L) screening.

Table 11: Substrate scope: Bis-spirocyclic indanones **219k-y** (Variations at R^2, R^3, R^4)[a,b]



Entry	Substrate	Product[a,b]	Entry	Substrate	Product[a,b]
1	 **205k**	 **219k**, 77% (*dr* = 2.5:1)	6	 **205p**	 **219p**, 49% (*dr* = 2.3:1)
2	 **205l**	 **219l**, 71% (*dr* = 1:2.5)	7	 **205q**	 **219q** , 78% (*dr* = 4.3:1)
3	 **205m**	 **219m**, 71% (*dr* = 4.5:1)	8	 **205r**	 **219r**, 65%, (*dr* = 2:1)
4	 **205n**	 **219n**, 78%, (*dr* = 3:1)	9	 **205s**	 **219r**, 69%, (*dr* = 1.6:1)
5	 **205o**	 **219o**, 73% (*dr* = 4.6:1)	10	 **205t**	 **219t**, 0%

Variation at R^4, X (counter ion)

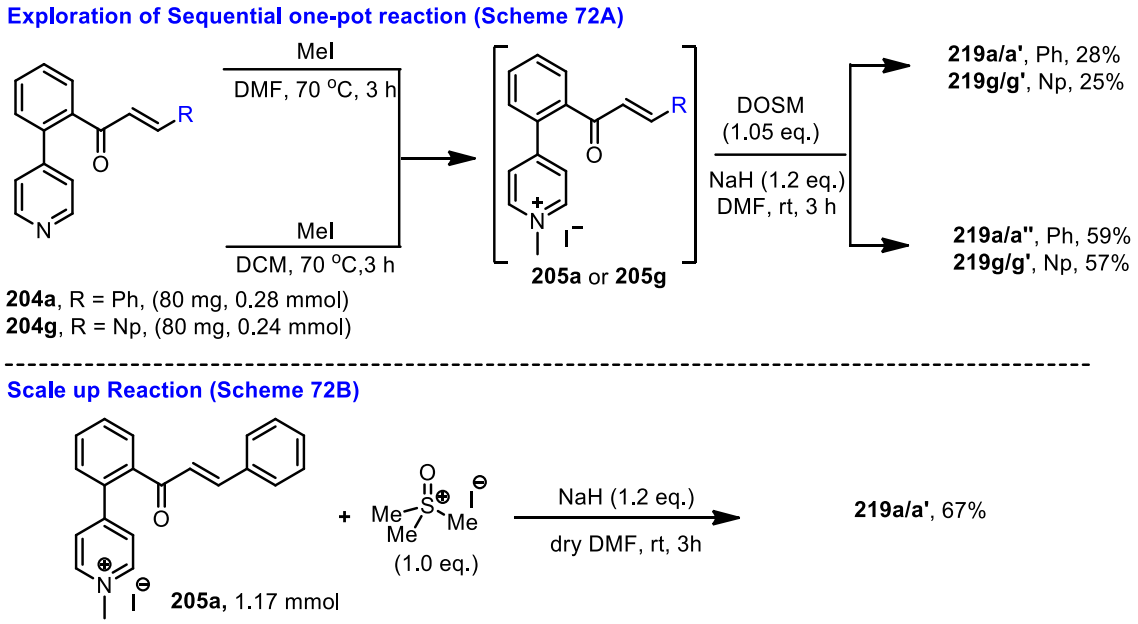


219u, X = Br, 79%, ***dr*** 5.8:1 | **219v**, X = I, 78%, ***dr*** 6.5:1 | **219w**, X = Br, 75%, ***dr*** 5.8:1 | **219x**, X = Br, 78%, ***dr*** 5.8:1 | **219y**, X = Br, 70%, ***dr*** 7.2:1

[a]Isolated yields after column chromatography. [b]The *dr* was estimated from the analysis of the crude ^{1}H-NMR data.

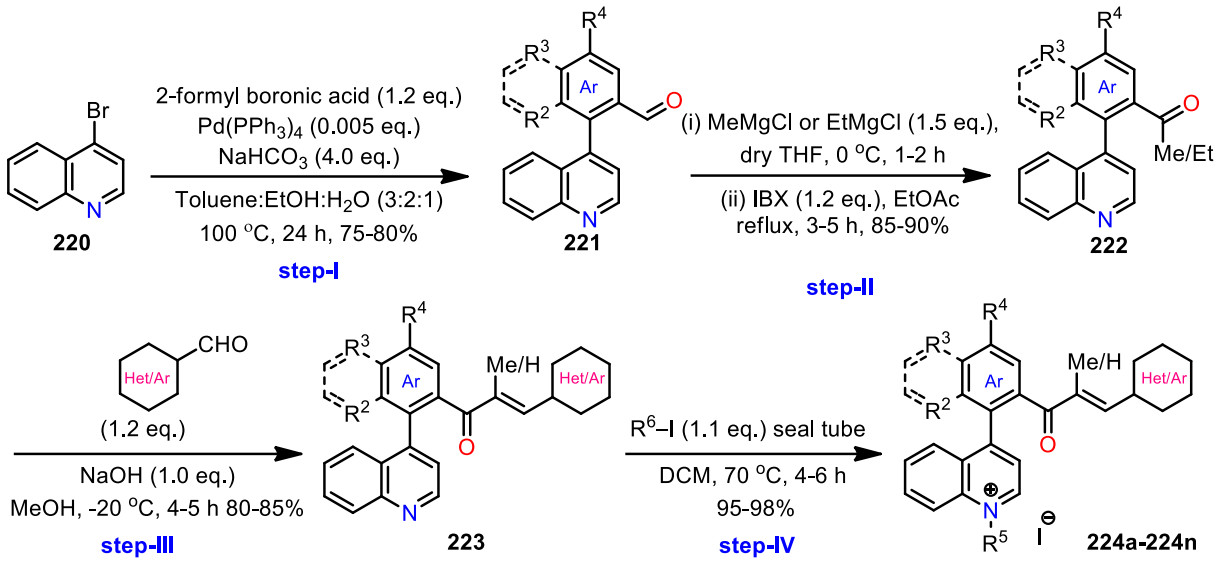
Next, we plan to assess the method's applicability. Towards this, we carried out scale-up and one-pot reactions under prototype conditions, and the corresponding products were obtained in good yields. We intended to establish a sequential protocol because the solvent

requirements for salt synthesis and cascade spiro-cyclization reactions were different. As a result, a mixture of **204a** or **204g** enone-tethered pyridine substrates in DCM and methyl iodide was heated at 70 ^{o}C in a sealed tube for 3 h. The reaction was then carried out with DOSM in the presence of NaH after the production of pyridinium salt **205a** or **205g** on TLC, replacing the solvent with DMF (in Step **2**), and the title compounds **219a/a'** and **219g/g'** was obtained in 59 and 57% yield, respectively (Scheme **72A**). When we tried the one pot reaction of **204a** and **204g** with MeI in DMF and further with DOSM, NaH using DMF as solvent in one-pot, the yield of **219a**/**219a'** and **219g**/**219g'** dropped to to 28 and 25%. Further, 1.17 mmol of 205a was treated with DOSM under conventional reaction conditions to test the suitability of this new synthesis technique on a larger scale, and **219a/a'** was synthesized in a yield of 67% (Scheme **72B**).



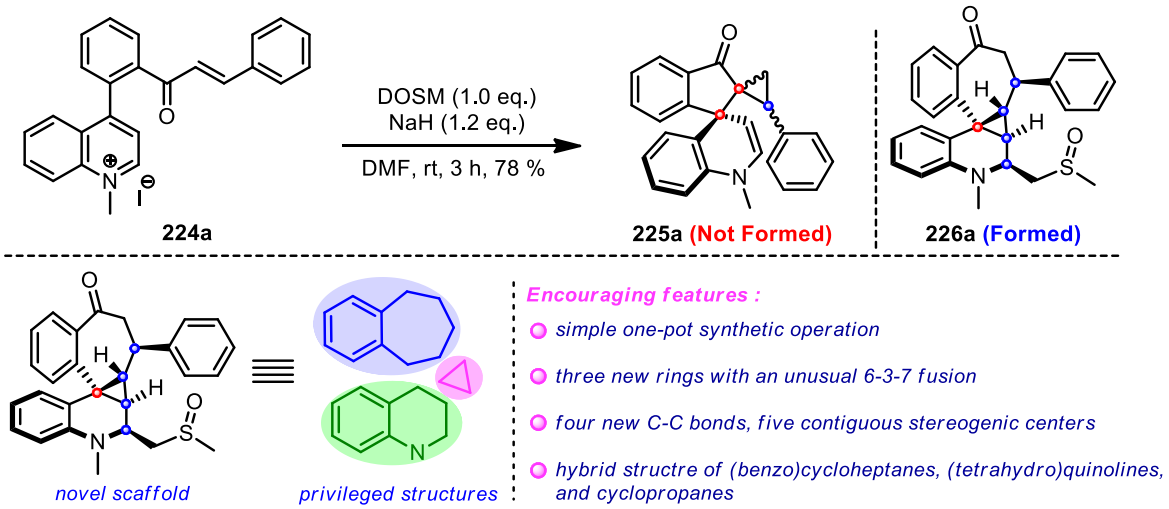
Scheme 72: Exploration of sequential one-pot and scale up reaction

After establishing a practical and efficient iC-C for synthesizing a diverse range of bis-spirocyclic indanones incorporating a dihydro-piperidine ring, we intend to extend this strategy for producing tetrahydroquinolone scaffolds having two contiguous all-carbon spiro-rings fused to an indane moiety from enone-tethered quinolinium salt. In this context, enone-tethered quinolinium salts **224a-224n** were synthesised by following the analogous procedure used for pyrdinium salts (Scheme **73**).



Scheme 73: Synthesis of enone-tethered quinolinium salts **224a-224n.**

To check our hypothesis, enone-tethered quinolinium salt **224a** as model substrate and DOSM were subjected to reaction conditions and delivered an unexpected product **226a** in 78% yield as a single isomer instead of expected product **225a**, Scheme **74**. The structure of polycyclic benzocycloheptanones **226a** were carefully deduced from the IR, NMR, HRMS data. The presence of a sharp band at 1711 cm^{-1} indicates the presence of a carbonyl group in the IR spectrum, indicating the formation of the product **226a.** In the ^{1}H- NMR spectrum (see Figure **42**), the presence of the multiplet at δ 2.11 – 2.00 ppm, a dd at δ 1.86 ppm (J = 10.5, 5.2 Hz) due to methyl (C-1) and cyclopropane protons (C-4, C-6). The presence of multiplet at δ 2.91 – 2.74 ppm due to *N*-methyl (C-10), and $–CH_2$- (C-8), The presence of multiplet at δ 3.93 ppm indicates C-7 methine proton.



Scheme 74: Unexpected result obtained with enone-tethered quinolinium salt **224a**.

In ^{13}C-NMR spectrum (see Figure **43**), the presence of nine aliphatic carbon signals confirms the product **226a** formation. The presence of a peak at δ 206.19 ppm indicates the ketone (C-9), and the peaks at δ 61.7 ppm indicates spiro carbon (C-5) and at δ 34.66, 31.06 ppm are due to the rest of cyclopropane carbons (C-4, C-6). Thus the ^{1}H- and ^{13}C-NMR data confirmed the formation of the product **226a**. In the high-resolution mass spectrum, the presence of a molecular ion peak at *m*/*z* 442.1832 $(M+H)^+$ confirmed the structure of **226a**. The structure and the relative stereochemistry of **226a** were confirmed from the single-crystal X-ray diffraction analysis (Figure **41**).

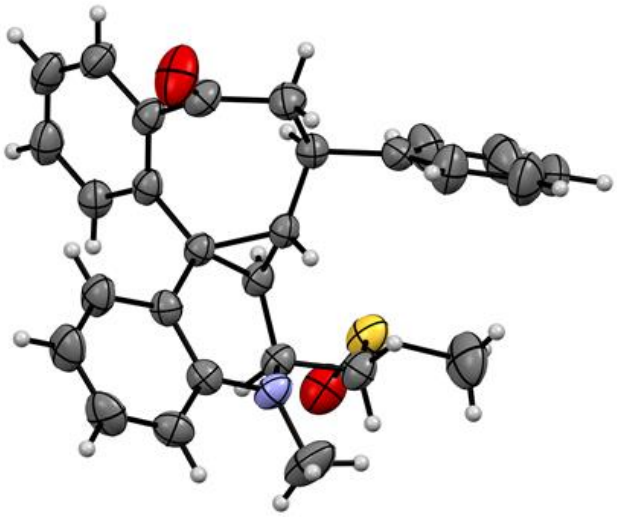


Figure 41: ORTEP diagram of **226a** ellipsoid probability (50%)

The formation of three novel rings with an unusual *6-3-7* fusion, four new C-C bonds, five contiguous stereogenic centers, and a fully functionalized quinoline core combined with a methylene sulfoxide moiety in a highly diastereoselective manner in a single step astonished us. A combination of favored structures such as (benzo) cycloheptanes, (tetrahydro) quinolines, and cyclopropanes might be envisioned as the unprecedented pentacyclic core **226a** (Scheme **74**). We started investigating the method's generality in the hope of finding applications in developing novel classes of bioactive compounds and creating a new template for drug development.

In order to broaden the protocol's applicability, a variety of quinolinium salts with varying electronic features were treated under optimum conditions, and the results were compiled in Table **12**. Exploring the substrate scope with an extended range of enone-tethered

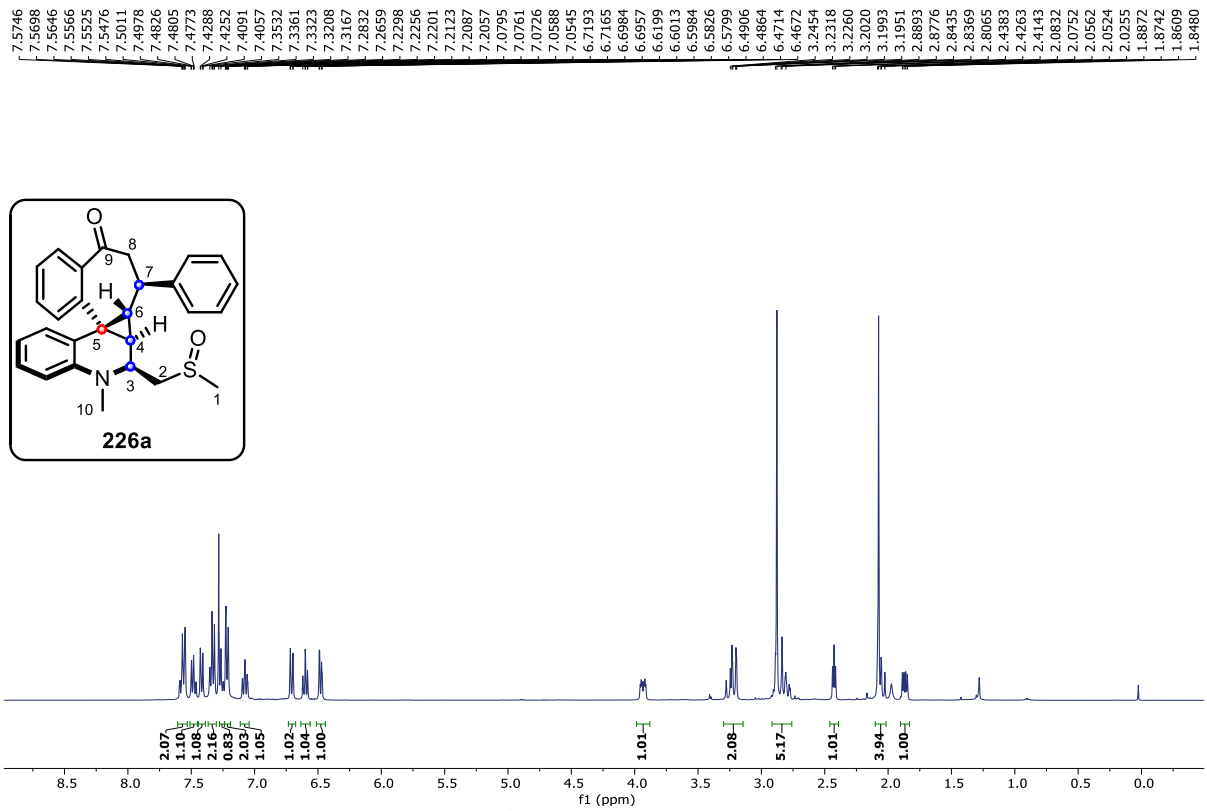


Figure 42: ^{1}H-NMR spectrum of **226a**

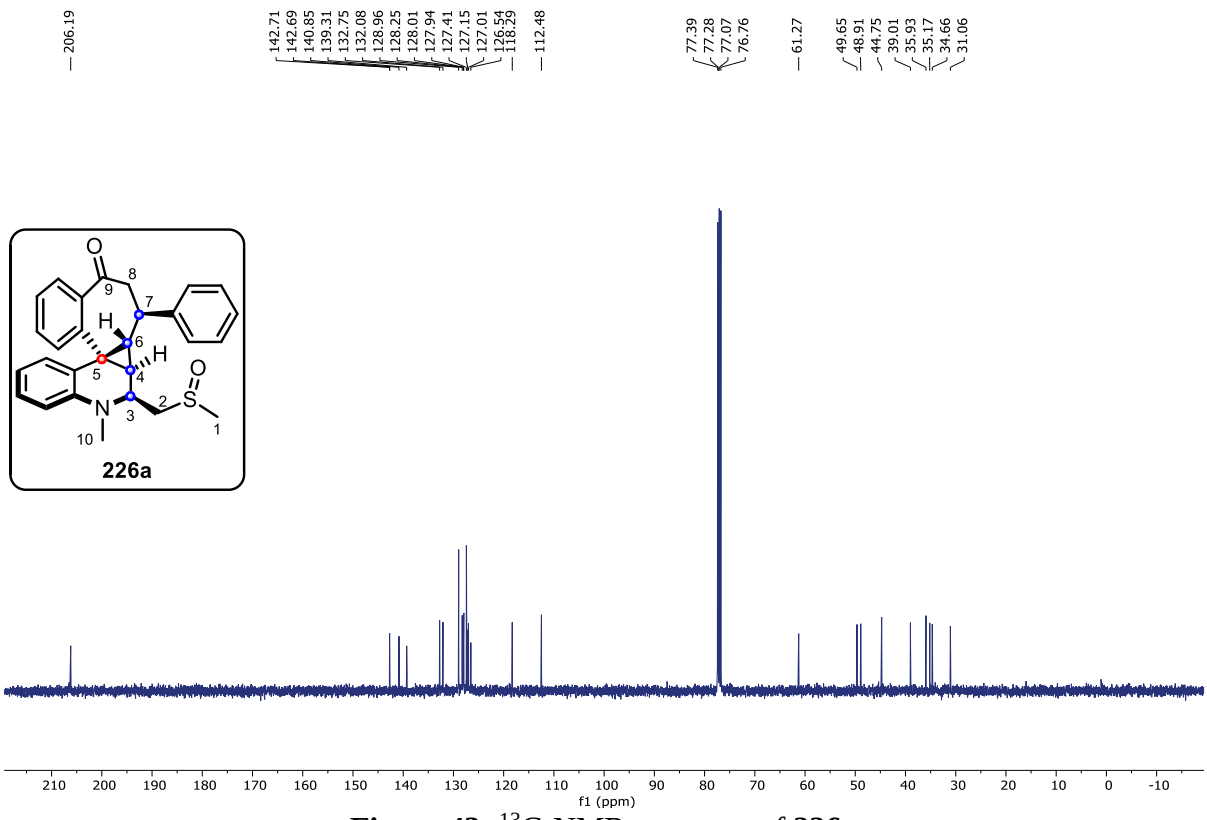
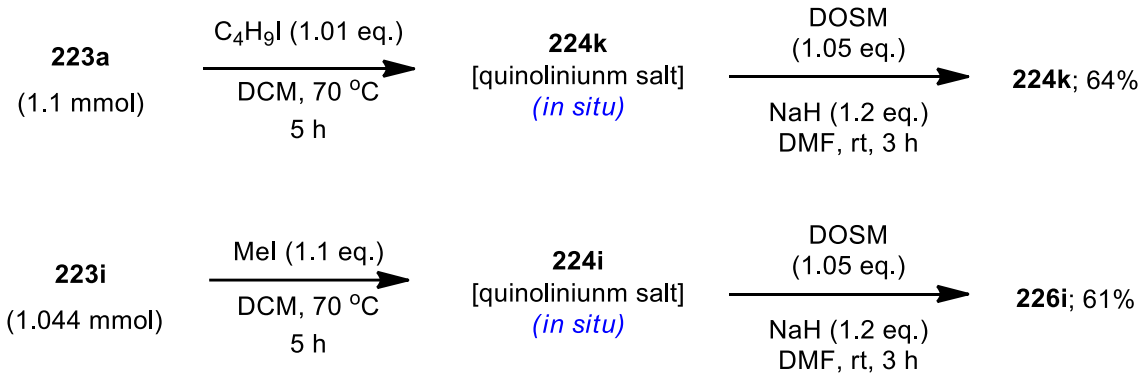


Figure 43: ^{13}C-NMR spectrum of **226a**

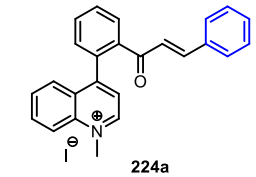
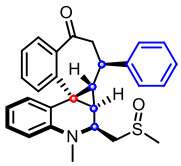
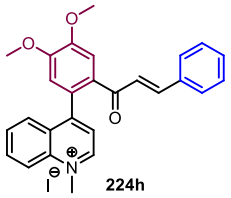
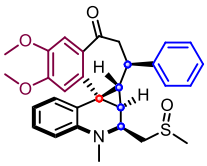
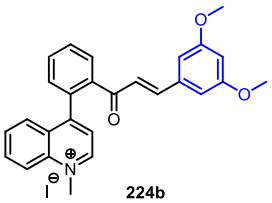
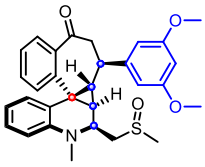
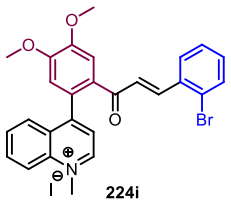
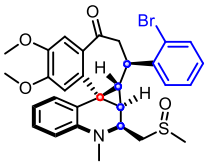
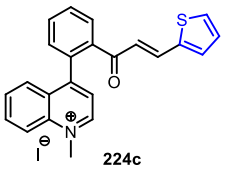
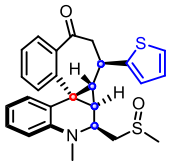
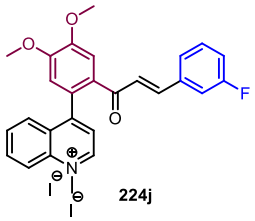
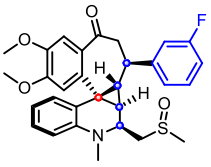
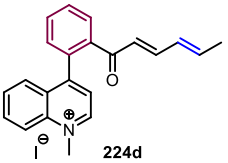
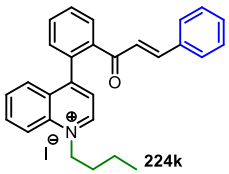
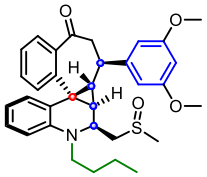
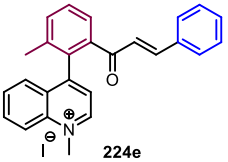
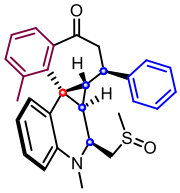
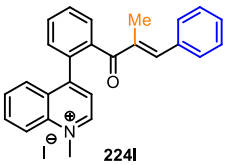
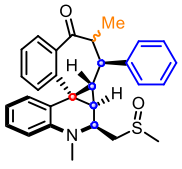
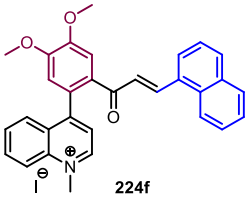
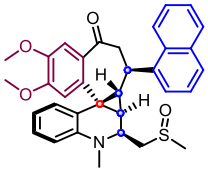
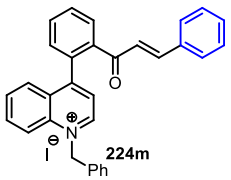
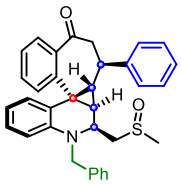
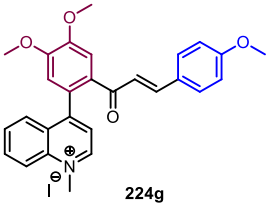
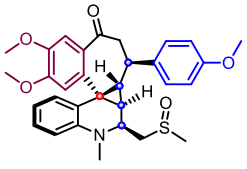
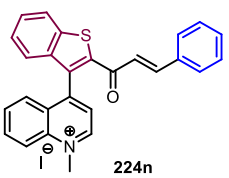
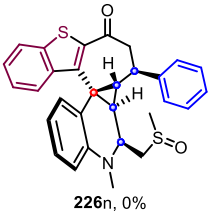
quinolinium salts proved the method's versatility in generating a sequence of intricate spiro-fused benzocycloheptanones **226a-226l**, Table **12**. The influence of substituents on the enone moiety and the arene backbone (R^1 and R^2, R^3) was thoroughly investigated. At R^1, electron-rich arene **224b** and heteroarene moiety **224c** were also tolerated, resulting in high yields of **226b** and **226c**. The substrates with methoxy and methyl groups on the arene backbones (R^2) were also tested in combination with different substituents at R^1, and they all performed admirably under the reaction conditions. Despite being unfavorable for the first Michael addition of the sulfur ylide, an arene ring with electron-donating methoxy groups delivered the predicted consequence **226f-226j** in high yield. A narrow yield range (68-76%) over various substrates demonstrates the method's robustness. Remarkably, benzocycloheptanone with six contiguous stereocenters **226l** was readily synthesized utilizing this method from α,β-substituted enone-quinolinium salt (R^3) **224l**. On the other hand, this approach allows *N*-substituents (R^4) such as methyl group and ^{n}Bu group (**224k)**, resulting in excellent yields of the corresponding products **226a-k**. Unfortunately, substrates comprising an *N*-benzyl group **224m** and heteroarene backbone (**224n**) failed to provide the expected outcome. Meanwhile, this approach rapidly and efficiently generates a novel class of hitherto unavailable polycyclic benzocycloheptanones.

Sequential scale-up batch reactions with **223a** on a 1.044 mmol and **223k** on 1.1 mmol scale were performed to demonstrate the method's generality and practicality, as shown in Scheme **75**. The corresponding products **226k** and **226l** were isolated in 61% and 64% yields in 3 h.



Scheme 75: Sequential one-pot scale up reactions of **223a** and **223l**.

Table 12: Substrate scope: Polycyclic benzocycloheptanones (**226a-226n**)[a,b]

Entry	Substrate	Product[a,b]	Entry	Substrate	Product[a,b]
1	 **224a**	 **226a**, 3h, 78%	8	 **224h**	 **226h**, 4h, 76%
2	 **224b**	 **226b**, 3h, 74%	9	 **224i**	 **226i**, 4h, 77%
3	 **224c**	 **226c**, 3h, 69%	10	 **224j**	 **226j**, 3h, 70%
4	 **224d**	Complex mixture	11	 **224k**	 **226k**, 4h, 72%
5	 **224e**	 **226e**, 4h, 71%	12	 **224l**	 **226l**, 3h, 75% *dr*~ 5:1
6	 **224f**	 **226f**, 4h, 73%	13	 **224m**	 **226m**, 0 %
7	 **224g**	 **226g**, 3h, 70%	14	 **224n**	 **226n**, 0%

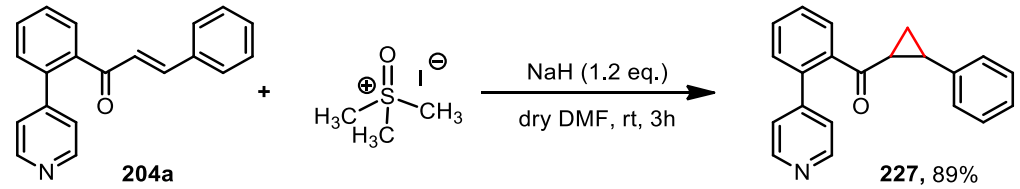
[a]Isolated yields after column chromatography. [b]The *dr* was estimated from the analysis of the crude ^{1}H-NMR data.

3.3: Plausible mechanism

To gain the mechanistic insights of the aforementioned transformations, we have performed a few control experiments as described below.

3.3.1: Reaction of DOSM with enone tethered pyridine

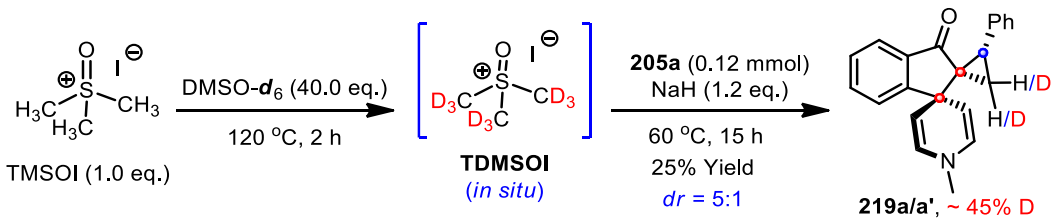
The pyridine ring's C4 position should be more electrophilic for simultaneous dearomatizing spirannulation, which requires activation. Under typical reaction conditions, the reaction of **204a** (without activating reagent) generates the regular C-C product **227** with an 89% yield (Scheme **76**). This result revealed that an activating group was required to produce bis-spiro indanone **219a**.



Scheme 76: Reaction of DOSM with enone tethered pyridine **204a**.

3.3.2: Deuterium experiment and reaction of 205a in the presence of Proton sponge

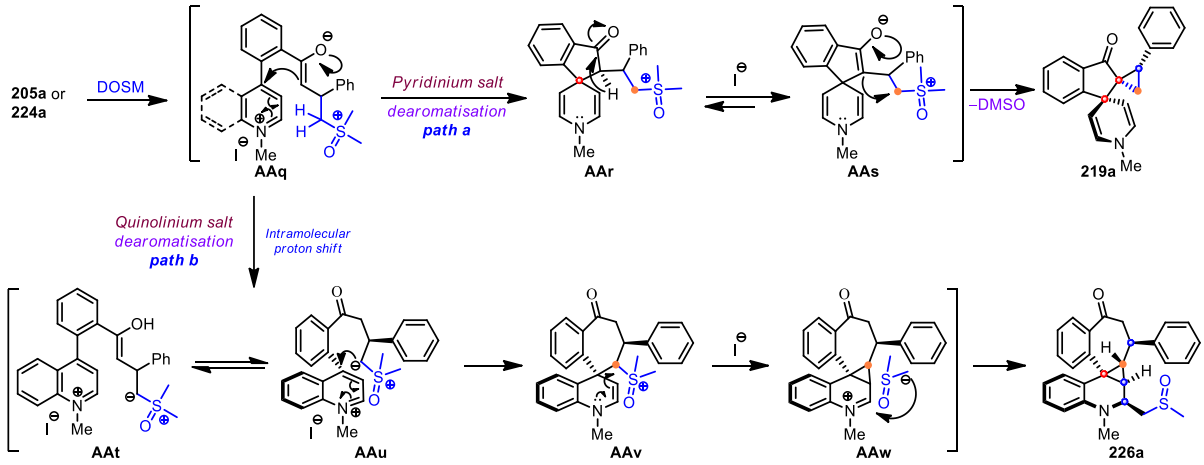
A metathesis reaction between DMSO-d_6 and trimethylsulfoxonium iodide (TMSOI) yielded the final bis-spiro indanone product xx with 45% deuterium incorporation by a one-pot reaction of pyridinium salt **205a** with *in situ* generated TDMSOI (a trideuteromethylation reagent) (Scheme **77**). This result implies that sulfur ylide is the Me source in the final product of **219a/a'-D**.



Scheme 77: Deuterium experiment.

As illustrated in Scheme **78**, all enone tethered azaarenium salts **205a-y** and **224a-224n** delivered their products by reacting with the ylide (DOSM), most likely through simultaneous dearomatizing spirannulation of azaarenium salts and an iC-C reaction. The intermolecular Michael addition of ylide to enone **205a or 224a** initiates the reaction, resulting in the intermittent enolate **AAq**. On the nucleophilic attack of the enolate on the pyridine's *ipso* site, the enolate **AAq** experiences an intramolecular nucleophilic dearomative reaction *via* path a, generating the **AAr** containing a spiro-indanone fused-dihydropyridine ring. Upon eventual deprotonation by counter ion (iodide) the enolate **AAs** may be delivered, which enables the

formation of **219a** by displacing the dimethylsulfoxide group. On the other hand, quinolinium salt **224a** follows path b; due to steric constraints on quinoline rotation, **AAq** undergoes intramolecular 1,3 or 1,5-proton shifts instead of nucleophilic attack on the C4 position of quinoline, resulting in zwitterionic species **AAt or AAu**. Subsequently, **AAu** undergoes an intramolecular nucleophilic dearomative reaction to generate the enamine species **AAv**. The resulting enamine undergoes an enamine-mediated alkylation, leading to benzocycloheptanone-fused cyclopropane containing iminium species **AAw**, which may be further concertedly trapped by sulphoxide ions to afford the desired product **226a** with high diastereoselectivity.



Scheme 78: Plausible mechanism for formation of vicinal bis-spirocyclic indanones and benzocycloheptanone**s.**

In conclusions, we developed a set of diastereoselective cyclopropanoids utilizing a hybrid strategy based on azaarenium salts and sulfur ylide. Through an iC-C reaction, simultaneous dearomatizing spirannulation of designed azaarenium salts allows access to novel scaffolds. This fusion method combines the nucleophilic features of sulfur ylides with the electrophilic properties of azaarenium salts to create new classes of spirocarbocyclic-piperidines/ quinolones with at least three contiguous stereocenters (one being an all-carbon spiro center). This strategy provides efficient routes to access functionally-rich bis-spirocyclic indanones and spirannulated benzocycloheptanones' excellent yields. These new scaffolds disclosed here are mechanistically fascinating and signify the occurrence of numerous bioactive compounds with similar molecular architecture. The generality and practicality of the methodology were carefully evaluated during the course of the study.

Conclusions

In conclusion, we have developed an efficient protocol for synthesis of cyclopentene-fused arenes (with a tertiary carbon) and heteroarenes *via* palladium catalyzed Nazarov-type cyclization of allylic acetates under neutral conditions. This acid-free Nazarov-type cyclization was utilized for the first total synthesis of *β*-diasarone, and other natural products like complex cyclopentanoids.

Next, we have demonstrated an efficient unprecedented Pd(II)-prompted carbocyclization similar to acid-free Nazarov-type cyclization to synthesize fused cyclopentenes with an all-carbon quaternary/spiro center. Natural products (taiwaniaquinone H and dichroanone) and pharmaceutically relevant compounds were synthesized efficiently without the use of any external oxidant, base, addition, or ligand, demonstrating the method's generality and practicability.

In last chapter, we have developed a series of diastereoselective cyclopropanoids utilizing a hybrid strategy based on azaarenium salts and sulfur ylide. An interrupted Corey-Chakovsky reaction of azaarenium salts and sulfur ylide allows access to novel scaffolds such as bis-spirocyclic indanones and spiro-annulated benzocycloheptanones with atleast three contiguous stereocenters (one being an all-carbon spiro center) in good to excellent yields.

Cyclopentannulated arenes and heteroarenes are important molecular structures that can be found in a wide range of bioactive chemicals. Associating such complex compounds with exciting biological activities molecules due to the presence of vicinal stereogenic centres will pique interest in their complete synthesis, heralding a slew of future innovation possibilities. This series of reactions is appealing for sophisticated natural product synthesis because one or more quaternary carbons can be generated in a single reaction. These accomplishments can be viewed as the next steps in taking organic synthesis to the next level. Nonetheless, as new chiral catalysts become viable, more and more efficient enantioselective actions will be used to generate contiguous quaternary carbon stereocenters, and will find extensive application in natural product and pharmaceutical synthesis.

Experimental Section

General experimental methods: All the reagents, solvents and catalysts employed in this study were procured from Sigma-Aldrich and were used without further purification. For thin-layer chromatography (TLC), silica aluminum 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 pellets, as indicated, with ν_{max} in inverse centimeters. Melting points were recorded on a digital melting point apparatus Stuart SMP30. 1H NMR and 13C 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 $CDCl_3$ or in $(CD_3)_2SO$ (δ 2.50 ppm) or in $(CD_3)_2CO$ (δ 2.05 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) or in $(CD_3)_2CO$ at δ 29.9 and 206.7 ppm. Single crystal X-ray analysis was carried on a Bruker Apex II diffractometer. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. Optical rotations were recorded on Rudolph APIII/2W. GC-MS analysis was carried out on Agilent 8890 system connected with 5977B inert GC/MSD with DB-Wax column.

General procedure-1: Synthesis of allylic acetates (13a-t)

A representative procedure for synthesis of 13a-13h, 13k-13l, 13n-t (Scheme 8a, Step-1): An oven dried 25 mL long neck RB flask was charged with aryl bromide **16** (1.2 eq.), anhydrous THF (5 mL) and stirred at –78 °C. *n*-BuLi (1.6 M in hexanes, 1.1 eq.) was added dropwise at the same temperature and stirred for 1 hour. Aldehyde **15** (1.0 eq.) dissolved in anhydrous THF (1 mL) was added dropwise over 15 min and stirred at room temperature for 30 min. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with *aq.* NH_4Cl solution and extracted with EtOAc (2x4 mL). The combined organic

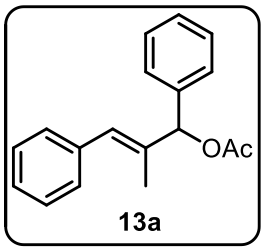
layers were dried over anhydrous Na_2SO_4 and concentrated. The crude alcohol **16** was subjected to next step without purification.

A representative procedure for (Scheme 8a, Step-2): Alcohol **16** (1.0 eq.) was dissolved in dry DCM (6.0 mL), and triethylamine (1.2 eq.), acetic anhydride (1.1 eq.) and DMAP (0.1 eq.) were added at room temperature. Then the reaction mixture was stirred until the completion of starting material (monitored by TLC). The reaction mixture was then quenched by adding saturated *aq.* NH_4Cl solution and extracted with DCM (2x5 mL). The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane as an eluent to afford **13a-13h, 13k-13l, 13n-t** (75-90% yield).

A representative procedure for synthesis of 13i, 13j, 13m (Scheme 8b): A mixture of **18** (1.2 eq.), magnesium (1.2 eq.) and iodine (catalytic) in anhydrous THF (10 mL) was stirred at room temperature, and then cooled in an ice bath. To the reaction mixture, a solution of aldehyde **15** (1.0 eq.) in anhydrous THF (9 mL) was slowly added. The reaction mixture was stirred at ice bath for one hour. Upon completion of reaction (monitored by TLC), the reaction mixture was quenched with *aq.* NH_4Cl and extracted with EtOAc (2x5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The crude alcohol **19** was subjected to acylation without purification as mentioned in Scheme S8a.

(*E*)-2-Methyl-1,3-diphenylallyl acetate (13a).

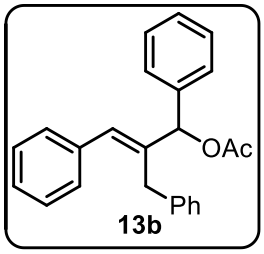
This compound was isolated as colourless liquid by following the general procedure **1**. 250 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 424 mg of **13a** (93% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3028, 1738, 1600, 1493, 1449, 1370, 1232, 1020, 920, 744, 698. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39-7.36 (m, 2H), 7.31-7.27 (m, 2H), 7.25-7.21 (m, 5H), 7.16-7.11 (m, 1H), 6.71 (s, 1H), 6.37 (s, 1H), 2.04 (s, 3H), 1.74 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.3, 138.6, 136.8, 135.7, 128.9 (2C), 128.2 (2C), 127.9 (2C), 127.7, 127.3, 126.7 (2C), 126.6, 79.7, 20.9, 14.3. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{15}$ [M-OAc]$^+$: 207.1174. Found: 207.1168.



13a

(*E*)-2-Benzyl-1,3-diphenylallyl acetate (13b).

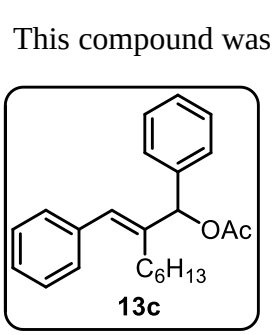
This compound was isolated as colourless liquid by following the general procedure **1**. 200 mg of **15** (Ar^1 = Ph, R^1 = -CH_2Ph) afforded 277 mg of **13b** (90% yield). R_f = 0.5 (Hexane/EtOAc



= 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3028, 1741, 1601, 1494, 1453, 1370, 1232, 1027, 923, 699, 554. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.36-7.32 (m, 2H), 7.30-7.20 (m, 9H) 7.17-7.12 (m, 4H), 6.93 (s, 1H), 6.32 (s, 1H), 3.68 (d, *J* = 15.8 Hz, 1H), 3.41 (d, *J* = 15.8 Hz, 1H), 1.86-1.82 (m, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 169.5, 138.8, 138.5, 137.9, 136.6, 129.3, 128.5 (2C), 128.4 (2C), 128.41 (2C), 128.4 (2C), 128.3 (2C), 128.0, 127.3 (2C), 127.1, 126.1, 78.0, 34.3, 20.8. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{19}$ [M-OAc]$^+$: 283.1487. Found: 283.1496.

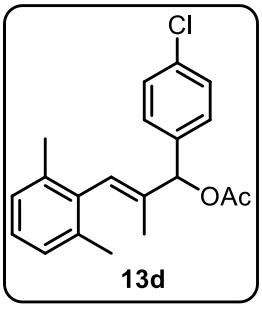
(*E*)-2-Benzylidene-1-phenyloctyl acetate (13c).

This compound was isolated as colorless liquid by following the general procedure **1**. 240 mg of **15** (Ar^1 = Ar^2 = Ph, R^1 = Hex) afforded 248 mg of **13c** (90% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3033, 2929, 1742, 1675, 1595, 1494, 1455, 1370, 1232, 1023, 746, 699. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.34-7.31 (m, 2H), 7.28-7.16 (m, 7H), 7.14-7.11 (m, 1H), 6.56 (s, 1H), 6.32 (s, 1H), 2.19-2.13 (m, 1H), 2.05 (s, 3H), 1.96-1.91 (m, 1H), 1.36-1.30 (m, 2H), 1.17-1.08 (m, 6H), 0.75 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 169.9, 140.9, 138.9, 137.3, 128.8 (2C), 128.5 (2C), 128.3 (2C), 128.1, 127.5 (2C), 127.2, 126.8, 78.3, 31.5, 29.5, 28.9, 28.5, 22.6, 21.4, 14.1. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{25}$ [M-OAc]$^+$: 277.1956. Found: 277.1948.

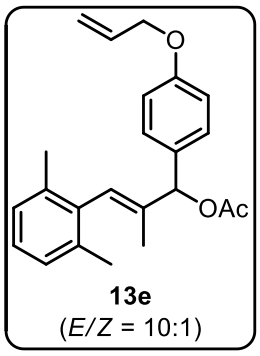


(*E*)-1-(4-Chlorophenyl)-3-(2,6-dimethylphenyl)-2-methylallyl acetate (13d).

This compound was isolated as colorless oil by following the general procedure **1**. 150 mg of **15** (Ar^1 = 2,6-dimethylphenyl, R^1 = Me) afforded 249 mg of **13d** (88% yield). R_f = 0.7 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2916, 1739, 1489, 1369 1226, 1089, 1013, 969, 804, 736. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.39-7.32 (m, 4H), 7.08-7.02 (m, 3H), 6.53 (s, 1H), 6.31 (s, 1H), 2.17-2.13 (m, 9H), 1.31 (d, *J* = 1.2 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 169.81, 137.46, 136.48, 135.91, 133.79, 128.72 (3C), 128.22 (3C), 127.20 (2C), 126.84, 126.49, 78.86, 21.24, 21.22, 20.25, 13.66. **HRMS (ESI):** m/z calcd for $C_{18}H_{18}(^{35}Cl)$ [M-OAc]$^+$: 269.1097. Found: 269.1088.



(*E*)-1-(4-(Allyloxy)phenyl)-3-(2,6-dimethylphenyl)-2-methylallyl acetate (13e).

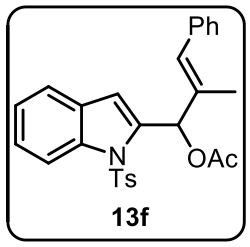


13e
(*E*/*Z* = 10:1)

This compound was isolated as colorless oil by following the general procedure **1**. 180 mg of **15** (Ar^1 = 2,6-dimethylphenyl, R^1 = Me) afforded 282 mg of **13e** (78% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2917, 1736, 1610, 1509, 1463, 1369, 1226, 1020, 997, 966, 756, 736. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36 (d, *J* = 8.64 Hz, 2H), 7.07-7.0 (m, 3H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.50 (s, 1H), 6.28 (s, 1H), 6.09-6.0 (m, 1H), 5.41 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.28 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.53 (dt, *J* = 5.3, 1.6 Hz, 2H), 2.15-2.09 (m, 9H), 1.32 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.98, 158.43, 137.01, 136.27, 136.24, 133.24, 131.05, 128.39 (3C), 127.15 (2C), 126.69, 125.17, 117.77, 114.68 (2C), 79.05, 68.86, 21.32, 21.29, 20.28, 14.08. **HRMS (ESI):** m/z calcd for $C_{21}H_{23}O$ $[M\text{-}OAc]^+$: 291.1749. Found:291.1747.

(*E*)-2-Methyl-3-phenyl-1-(1-tosyl-1*H*-indol-2-yl)allyl acetate (13f).

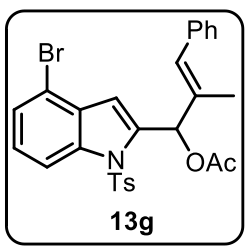
This compound was isolated as pale-yellow solid by following the general procedure **1**. 200 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 535 mg of **13f** (85% yield). M.P = 108-110 °C. R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 3056, 1741, 1598, 1451, 1372, 1229, 1175, 1021, 971, 580, 545. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.41-7.34 (m, 5H), 7.30-7.26 (m, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.12 (s, 1H), 6.84 (s, 1H), 6.69 (s, 1H), 2.34 (s, 3H), 2.23 (s, 3H), 1.99 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.9, 144.9, 138.3, 137.4, 136.9, 135.6, 134.6, 129.8 (2C), 129.15, 129.11 (2C), 128.9, 128.2 (2C), 126.9, 126.8 (2C), 125.1, 123.8, 121.1, 114.9, 111.6, 73.7, 21.5, 21.2, 15.9. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{22}NO_2S$ $[M\text{-}OAc]^+$: 400.1371. Found: 400.1357.



13f

(*E*)-1-(4-bromo-1-tosyl-1*H*-indol-2-yl)-2-methyl-3-phenylallyl acetate (13g).

This compound was isolated as pale-yellow sticky liquid by following the general procedure **1**. 150 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 452 mg of **13g** (82% yield). R_f = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 2924, 1739, 1597, 1422, 1371, 1230, 1091, 734. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.07 (d, *J* = 8.4 Hz, 1H), 7.88-7.76 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.37-7.27 (m, 4H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.20-7.13 (m, 2H), 7.05 (s,

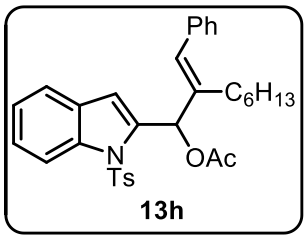


13g

1H), 6.79 (s, 1H), 6.59 (s, 1H), 2.31 (s, 3H), 2.19 (s, 3H), 1.93 (d, *J* = 1.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$-*d*):** δ 169.9, 145.3, 139.2, 137.4, 136.9, 135.3, 134.2, 129.9 (2C), 129.6, 129.6, 129.1 (2C), 128.1 (2C), 126.9, 126.9 (2C), 126.7, 125.8, 114.7, 113.9, 110.8, 73.6, 21.5, 21.1, 15.8. **HRMS (ESI):** m/z calcd for $C_{25}H_{21}(^{79}Br)NO_2S$ $[M\text{-}OAc]^+$: 478.0476. Found: 478.0467.

(*E*)-2-Benzylidene-1-(1-tosyl-1*H*-indol-2-yl)octyl acetate (13h).

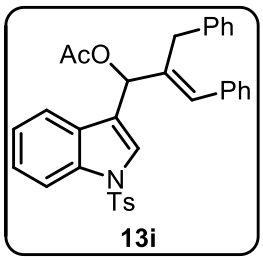
This compound was isolated as off-white semi-solid by following the general procedure **1**. 150 mg of **15** (Ar^1 = Ph, R^1 = Hex) afforded 337 mg of **13h** (92% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 2932, 1743, 1451, 1371, 1228, 1174, 754, 680, 579. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.08 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.28-7.24 (m, 2H), 7.20-7.11 (m, 7H), 6.89 (s, 1H), 6.68 (s, 1H), 6.47 (s, 1H), 2.37-2.30 (m, 1H), 2.25 (s, 3H), 2.07 (s, 3H), 1.99-1.93 (m, 1H), 1.46-1.36 (m, 2H), 1.19-1.13 (m, 6H), 0.77 (t, *J* = 6.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.9, 145.0, 139.9, 138.4, 137.7, 137.1, 136.1, 129.9 (2C), 128.8 (3C), 128.4, 128.3 (2C), 126.9, 126.8 (2C), 125.3, 123.8, 121.2, 115.0, 112.5, 71.6, 31.6, 30.4, 29.7, 28.5, 22.8, 21.7, 21.3, 14.2. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{32}NO_2S$ $[M\text{-}OAc]^+$: 470.2154. Found: 470.2143.



13h

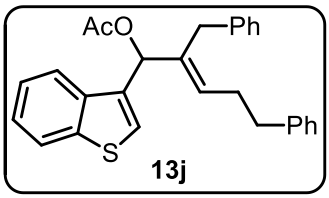
(*E*)-2-Benzyl-3-phenyl-1-(1-tosyl-1*H*-indol-3-yl)allyl acetate (13i).

This compound was isolated as brownish semi-solid by following the general procedure **1**. 150 mg of **15** (Ar^1 = Ph, R^1 = -CH_2Ph) afforded 282 mg of **13i** (78% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 3061, 1598, 1493, 1446, 1371, 1225, 1174, 1088, 998, 702, 665, 573. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.34-7.18 (m, 13H), 7.12-7.07 (m, 3H), 6.70 (s, 1H), 3.94 (d, *J* = 15.8 Hz, 1H), 3.75 (d, *J* = 15.8 Hz, 1H), 2.24 (s, 3H), 1.95 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.8, 145.2, 138.3, 136.6, 135.5, 135.3, 134.9, 132.9, 132.2, 129.8 (2C), 129.2, 128.8 (2C), 128.7 (2C), 128.4 (2C), 128.2 (2C), 127.3, 127.2 (2C), 126.2, 126.0, 124.1, 119.9, 114.9, 103.0, 72.1, 35.4, 21.6, 20.6. **HRMS (ESI):** *m/z* calcd for $C_{31}H_{26}NO_2S$ $[M\text{-}OAc]^+$: 476.1684. Found: 476.1668.



13i

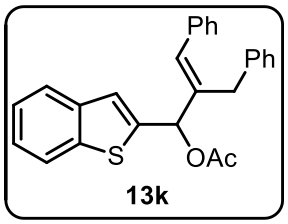
(*E*)-1-(Benzo[*b*]thiophen-3-yl)-2-benzyl-5-phenylpent-2-en-1-yl acetate (13j).



This compound was isolated as pale-yellow viscous oil by following the general procedure **1**. 150 mg of **15** (Ar^1 = -CH_2CH_2Ph, R^1 = -CH_2Ph) afforded 204 mg of **13j** (80% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3030, 1738, 1493, 1451, 1370, 1230, 1023, 738, 698. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.81-7.78 (m, 1H), 7.60-7.57 (m, 1H), 7.31-7.27 (m, 2H), 7.23-7.16 (m, 6H), 7.15-7.12 (m, 1H), 7.08 (d, *J* = 7.0 Hz, 2H), 7.01 (d, *J* = 6.7 Hz, 2H), 6.56 (s, 1H), 5.87 (t, *J* = 6.5 Hz, 1H), 3.34 (q, *J* = 15.5 Hz, 2H), 2.68 (t, *J* = 7.1 Hz, 2H), 2.52-2.47 (m, 2H), 1.86-1.85 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.9, 141.5, 140.7, 139.3, 137.3, 135.3, 133.5, 130.7, 128.64 (2C), 128.45 (3C), 128.39 (3C), 126.0 (2C), 124.8, 124.5, 124.1, 122.8, 122.6, 74.1, 35.6, 33.8, 30.2, 20.9. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{23}S$ $[M\text{-}OAc]^+$: 367.1520. Found: 367.1508.

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-benzyl-3-phenylallyl acetate (13k).

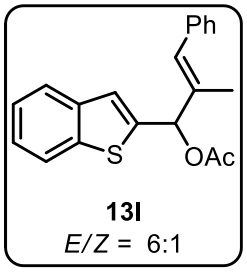
This compound was isolated as pale-yellow sticky oil by following the general procedure **1**.



200 mg of **15** (Ar^1 = Ph, R^1 = -CH_2Ph) afforded 340 mg of **13k** (95% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3060, 1744, 1601, 1495, 1370, 1226, 1075, 1024, 749, 699. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.73-7.71 (m, 1H), 7.65-7.62 (m, 1H), 7.29-7.21 (m, 7H), 7.19-7.15 (m, 3H), 7.12-7.10 (m, 3H), 6.99 (s, 1H), 6.51 (s, 1H), 3.73 (d, *J* = 15.8 Hz, 1H), 3.49 (d, *J* = 15.9 Hz, 1H), 1.83 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.7, 143.1, 140.0, 139.4, 138.8, 137.4, 136.5, 129.8, 128.74 (2C), 128.68 (2C), 128.58 (4C), 127.5, 126.4, 124.7, 124.5, 123.9, 123.5, 122.5, 74.3, 34.5, 20.9. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{19}S$ $[M\text{-}OAc]^+$: 339.1207. Found: 339.1197.

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-methyl-3-phenylallyl acetate (13l).

This compound was isolated as off-white solid by following the general procedure **1**. 150 mg

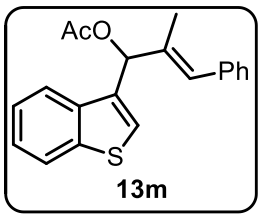


of **15** (Ar^1 = Ph, R^1 = Me) afforded 291 mg of **13l** (88% yield). M.P = 88-90 °C. R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3060, 1742, 1494, 1436, 1369, 1231, 1018, 968, 831, 726, 553. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.80 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.39-7.30 (m, 8H), 6.80 (s, 1H), 6.63 (s, 1H), 2.20 (s, 3H), 1.91 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.8, 143.2, 139.9, 139.5, 136.9, 135.2, 129.2 (2C), 128.3

(2C), 128.2, 127.1, 124.6, 124.5, 123.8, 122.7, 122.5, 76.4, 21.3, 14.8. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{15}S$ $[M\text{-}OAc]^+$: 263.0895. Found: 263.0882.

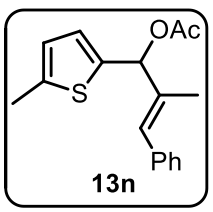
(*E*)-1-(Benzo[*b*]thiophen-3-yl)-2-methyl-3-phenylallyl acetate (13m).

This compound was isolated as pale-yellow liquid by following the general procedure **1**. 300 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 536 mg of **13m** (81% yield). R_f = 0.5(Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2924, 1739, 1599, 1428, 1369 1230, 1018, 761, 733. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91-7.85 (m, 2H), 7.47 (s, 1H), 7.37-7.28 (m, 6H), 7.25-7.23 (m, 1H), 6.82 (s, 1H), 6.74 (s, 1H), 2.18 (s, 3H), 1.84 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.0, 140.8, 137.3, 137.1, 134.9, 133.7, 129.2 (2C), 128.4, 128.3 (2C), 127.0, 124.8, 124.7, 124.4, 122.9, 122.5, 75.6, 21.4, 15.0. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{15}S$ $[M\text{-}OAc]^+$: 263.0895. Found: 263.0886.



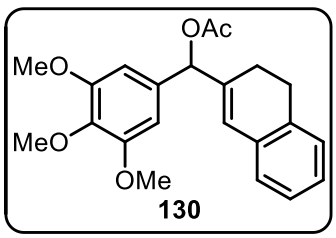
(*E*)-2-Methyl-1-(5-methylthiophen-2-yl)-3-phenylallyl acetate (13n).

This compound was isolated as yellowish-brown liquid by following the general procedure **1**. 200 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 365 mg of **13n** (93% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2861, 1737, 1599, 1444, 1369, 1234, 1109, 1017, 960, 749, 699. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28-7.18 (m, 5H), 6.75 (d, *J* = 3.6 Hz, 1H), 6.66 (s, 1H), 6.60-6.58 (m, 1H), 6.26 (s, 1H), 2.39 (s, 3H), 2.07 (s, 3H), 1.77 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.9, 140.4, 138.8, 138.1, 132.3, 128.5 (2C), 128.2, 127.9, 126.9 (2C), 125.2, 121.6, 80.2, 21.4, 15.2 (2C). **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}S$ $[M\text{-}OAc]^+$: 227.0894. Found: 227.0884.



(3,4-Dihydronaphthalen-2-yl)(3,4,5-trimethoxyphenyl)methyl acetate (13o).

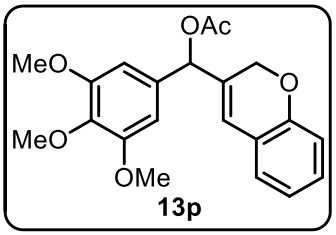
This compound was isolated as yellowish-brown oil by following the general procedure **1**. 150 mg of **15** (Ar^1 = -Ph-, R^1 = -CH_2CH_2-Ph) afforded 269 mg of **13o** (77% yield). R_f = 0.5 (Hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max} /cm^{-1} 3028, 1741, 1601, 1494, 1453, 1370, 1232, 1027, 923, 699, 554. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.17-7.08 (m, 4H), 6.62 (s, 2H), 6.54 (d, *J* = 0.8 Hz, 1H), 6.32 (s, 1H), 3.85 (s, 6H), 3.84 (s, 3H), 2.79 (td, *J* = 8.2, 3.2 Hz, 2H), 2.22-2.15 (m, 5H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.1, 153.3 (2C), 138.3, 137.9, 134.9, 134.0, 133.7, 127.42, 127.40, 126.7, 126.6, 124.1, 104.6



(2C), 77.8, 60.9, 56.2 (2C), 27.9, 24.2, 21.4. **HRMS (ESI):** m/z calcd for $C_{20}H_{21}O_3$ $[M\text{-}OAc]^+$: 309.1491. Found: 309.1477.

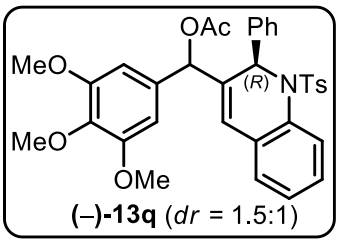
(2*H*-Chromen-3-yl)(3,4,5-trimethoxyphenyl)methyl acetate (13p).

This compound was isolated as pale-yellow liquid by following the general procedure **1**. 200 mg of **15** (Ar^1 = -Ph-, R^1 = -CH_2O-Ph) afforded 364 mg of **13p** (75% yield). R_f = 0.5 (Hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max} /cm^{-1} 2939, 1735, 1592, 1459, 1236, 1127, 758. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.09 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.0 Hz, 1H), 6.88-6.83 (m, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.61 (s, 2H), 6.44 (s, 1H), 6.31 (s, 1H), 4.67 (d, J_{AB} = 14.3 Hz, 1H), 4.60 (d, J_{AB} = 14.2 Hz, 1H), 3.85 (s, 9H), 2.17 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.7, 153.4 (2C), 153.3, 137.9, 132.5, 131.6, 129.4, 127.0, 121.9, 121.5 (2C), 115.6, 104.2 (2C), 75.3, 65.4, 60.7, 56.1, 56.08, 21.1. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{19}O_4$ $[M\text{-}OAc]^+$: 311.1283. Found: 311.1273.



((*R*)-2-Phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)(3,4,5-trimethoxyphenyl)methyl acetate ((–)-13q).

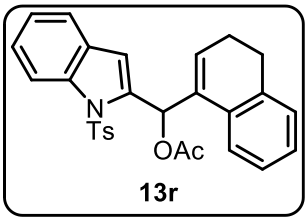
This compound was isolated as yellowish-brown semi-solid by following the general procedure **1**. 180 mg of **15** (Ar^1 = -Ph-, R^1 = -CH(Ph)NTs-) afforded 230 mg of **13q** (83% yield). R_f = 0.5 (Hexane/EtOAc = 1/1). **Optical rotation:** $[\alpha]_D^{25}$ –119.8 (c 0.26, $CHCl_3$). **IR (thin film, neat):** ν_{max} /cm^{-1} 2938, 1744, 1593, 1455, 1344, 1232, 1165, 1127, 662, 578. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.59 (t, *J* = 8.9 Hz, 1H), 7.20 (s, 4H), 7.18-7.09 (m, 3H), 7.06-7.00 (m, 3H), 6.94 (s, 1H), 6.46 (s, 1H), 6.35 (s, 2H), 6.20 (d, *J* = 14.5 Hz, 1H), 6.00 (s, 1H), 3.93 (s, 1H), 3.84 (s, 3H), 3.82 (s, 6H), 2.33 (s, 3H), 1.99 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.5, 153.3, 143.2, 138.0, 137.1, 136.0, 135.7, 133.0, 132.1, 129.1 (2C), 128.7 (2C), 128.6 (2C), 128.4, 128.3, 127.9 (2C), 127.7, 127.1, 126.96 (2C), 126.92, 126.4, 122.3, 104.2, 75.6, 60.9, 58.2, 57.2, 56.2, 21.0, 20.6. **HRMS (ESI):** m/z calcd for $C_{34}H_{33}NO_7SNa$ $[M+Na]^+$: 622.1875. Found: 622.1871.



(3,4-Dihydronaphthalen-2-yl)(1-tosyl-1*H*-indol-2-yl)methyl acetate (13r).

This compound was isolated as yellowish-brown sticky liquid by following the general procedure **1**. 100 mg of **15** (Ar^1 = -CH_2CH_2Ph-, R^1 = -Ph-) afforded 267 mg of **13r** (90% yield).

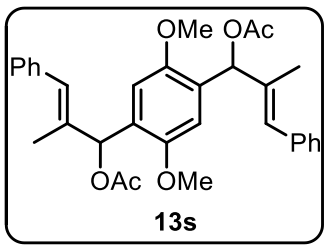
R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 2938, 1739, 1590, 1428, 1369, 1230, 1018, 761, 733. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.31-7.27 (m, 1H), 7.23-7.19 (m, 1H), 7.14-7.07 (m, 6H), 7.00-6.98 (m, 1H), 6.77 (s, 1H), 6.47 (s, 1H), 2.88-2.78 (m, 2H), 2.38-2.30 (m, 2H), 2.26 (s, 3H), 2.15 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.8, 144.9, 138.0, 137.4, 136.9, 135.7, 135.1, 133.5, 129.8 (2C), 128.9, 127.6, 127.4, 126.8 (3C), 126.6, 126.4, 125.1, 123.8, 121.2, 114.9, 111.6, 71.9, 27.9, 25.0, 21.6, 21.2. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{22}NO_2S$ [M-OAc]$^+$: 412.1371. Found: 412.1364.



13r

(2*E*,2'*E*)-(2,5-Dimethoxy-1,4-phenylene)bis(2-methyl-3-phenylprop-2-ene-1,1-diyl) diacetate (13s).

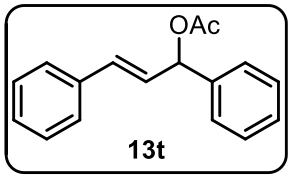
This compound was isolated as off-white solid by following the general procedure **1**, 140 mg of **B** (Ar^1 = Ph, Ar^2 =2,5 dimethoxyphenyl, R^1 = Me) afforded 146 mg of **7u** (87% yield). M.P = 112-114 ^{o}C. R_f = 0.5 (Hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max} /cm^{-1} 2955, 1737, 1502, 1465, 1405, 1233, 1035, 757, 597. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.34-7.30 (m, 4H), 7.26 (d, *J* = 7.2 Hz, 4H), 7.23-7.18 (m, 2H), 6.96 (s, 2H), 6.73 (s, 2H), 6.61 (s, 2H), 3.83 (s, 6H), 2.16 (s, 6H), 1.84 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.8 (2C), 151.1 (2C), 137.4 (2C), 135.5 (2C), 129.1 (5C), 128.2 (5C), 127.6 (2C), 127.1 (2C), 126.7 (2C), 110.9 (2C), 73.8 (2C), 56.5, 21.4, 14.9 (2C). **HRMS (ESI):** *m/z* calcd for $C_{32}H_{34}O_6Na$ [M+Na]$^+$: 537.2253. Found: 537.2250.



13s

***(E)*-1,3-Diphenyl acetate (13t)**.

This compound was isolated as colorless liquid by following the general procedure **1**. 200 mg of **15** (Ar^1 = Ph, R^1 = H) afforded 355 mg of **13t** (93% yield). R_f = 0.4 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3026, 1738, 1495, 1370, 1232, 1018, 963, 697. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43-7.34 (m, 6H), 7.32-7.27 (m, 3H), 7.24-7.21 (m, 1H), 6.66-6.61 (m, 1H), 6.46-6.43 (m, 1H), 6.38-6.31 (m, 1H), 2.12 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.1, 139.3, 136.2, 132.6, 128.7 (2C), 128.6 (2C), 128.2, 128.1, 127.5, 127.1 (2C), 126.8 (2C), 76.2, 21.4. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{13}$ [M-OAc]$^+$: 193.1017. Found: 193.1015.



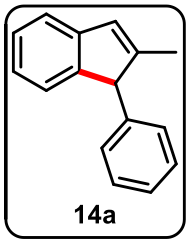
13t

General procedure-2: Synthesis of cyclopenta-fused arenes and heteroarenes (14a-14s)

An oven dried sealed tube was charged with **13a** (0.14 mmol) and dissolved in DCE (2.0 mL). $PdCl_2$ (0.01 mmol) was added and reaction mixture was stirred at 100 ^oC on preheated aluminium blocks until **13a** disappeared a monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc (2x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate as eluent, to afford **14a**.

2-Methyl-1-phenyl-1*H*-indene (14a).

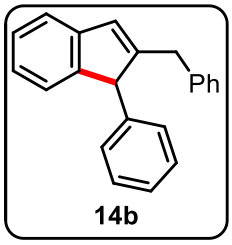
This compound was isolated as off-white solid by following the general procedure **2**. 40 mg of



13a afforded 25 mg of **14a** (81% yield). R_f = 0.5 (Hexane/EtOAc = 10/1). M.P = 40-42 ^oC. **IR (thin film, neat):** ν_{max} /cm^{-1} 3059, 1495, 1447, 1381, 1221, 1079, 1053, 741, 700. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.20-7.11 (m, 5H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.98-6.93 (m, 3H), 6.47 (s, 1H), 4.22 (s, 1H), 1.84 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.0, 148.7, 144.9, 139.9, 128.8 (2C), 128.3 (2C), 127.3, 126.8 (2C), 124.3, 123.8, 119.9, 59.5, 15.3. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{15}$ $[M+H]^+$: 207.1174. Found: 207.1162.

2-Benzyl-1-phenyl-1*H*-indene (14b).

This compound was isolated as colorless viscous liquid by following the general procedure **2**.

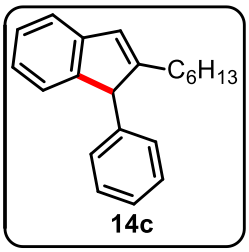


50 mg of **13b** afforded 39 mg of **14b** (78% yield). R_f = 0.5 (Hexane/EtOAc = 20/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3027, 1603, 1493, 1452, 1075, 877, 752, 700, 535. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28-7.16 (m, 8H), 7.12-7.07 (m, 3H), 7.04-6.97 (m, 3H), 6.47 (s, 1H), 4.31 (s, 1H), 3.62 (d, *J* = 15.9 Hz, 1H), 3.38 (d, *J* = 15.8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.8, 149.0, 144.4, 139.9, 139.6, 129.2 (2C), 128.9 (2C), 128.5 (4C), 127.9, 126.96, 126.90, 126.3, 124.7, 123.9, 120.4, 57.8, 36.2. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{17}$ $[M-H]^+$: 281.1331. Found 281.1367.

2-Hexyl-1-phenyl-1*H*-indene (14c).

This compound was isolated as colorless viscous liquid by following the general procedure **2**. 35 mg of **13c** afforded 24 mg of **14c** (83% yield). R_f = 0.5 (Hexane/EtOAc = 10/1). **IR (thin**

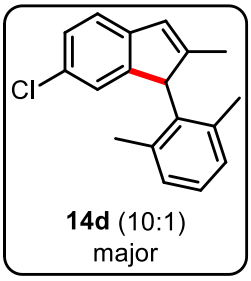
film, neat): ν_{max} /cm^{-1} 2928, 2857, 1611, 1492, 1464, 1073, 878, 750, 732, 699, 644. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.29-7.18 (m, 5H), 7.12-7.09 (m, 1H), 7.05-6.99 (m, 3H), 6.56 (s, 1H), 4.36 (s, 1H), 2.27-2.12 (m, 2H), 1.58-1.46 (m, 2H), 1.31-1.22 (m, 6H), 0.88-0.84 (m, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 155.0, 148.7, 144.8, 140.0, 128.8 (2C), 128.4 (2C), 126.84, 126.80, 126.1, 124.3, 123.9, 120.0, 58.3, 31.8, 29.5, 29.2, 28.7, 22.7, 14.2.



HRMS (ESI): *m/z* calcd for $C_{21}H_{25}$ $[M+H]^+$: 277.1956. Found: 277.1942.

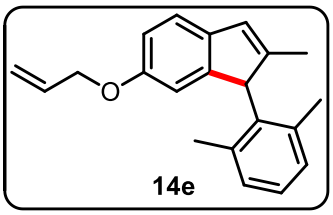
6-Chloro-1-(2,6-dimethylphenyl)-2-methyl-1*H*-indene (14d).

This compound was isolated as colorless oil by following the general procedure **2**. 45 mg of **13d** afforded 30 mg of **14d** (83% yield). R_f = 0.7 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2924, 2852, 1595, 1475, 1463, 1399, 1264, 1089, 1014, 821, 739. **^{1}H NMR (400 MHz, CDCl$_3$): δ** 7.20 (d, *J* = 1.2 Hz, 2H), 7.15-7.11 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.01 (s, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 6.58 (s, 1H), 4.77 (s, 1H), 2.57 (s, 3H), 1.89 (s, 3H), 1.46 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$): δ** 149.8, 148.3, 143.1, 138.2, 137.8, 134.6, 130.0, 129.4, 128.1, 126.9, 126.5, 125.8, 123.0, 120.7, 55.2, 21.9, 17.8, 15.2.



6-(Allyloxy)-1-(2,6-dimethylphenyl)-2-methyl-1*H*-indene (14e).

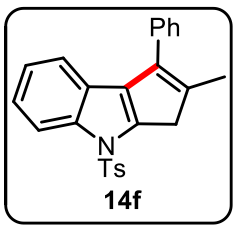
This compound was isolated as colorless oil by following the general procedure **2**. 50 mg of **13e** afforded 27 mg of **14e** (66% yield). R_f = 0.7 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2921,1605, 1576, 1467, 1422, 1134, 849, 767. **^{1}H NMR (400 MHz, CDCl$_3$): δ** 7.18 (d, *J* = 8.2 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 6.80 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.53 (t, *J* = 1.9 Hz, 1H), 6.04-5.94 (m, 1H), 5.34 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.21 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.76 (s, 1H), 4.43 (dt, *J* = 5.4, 1.5 Hz, 2H), 2.56 (s, 3H), 1.86 (s, 3H), 1.47 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$): δ** 156.4, 148.5, 146.7, 138.4, 138.1, 137.7, 135.6, 133.5, 129.3, 128.0, 126.6, 125.9, 120.2, 117.4, 112.5, 110.3, 69.1, 55.3, 21.9, 17.9, 15.1. **HRMS (ESI):** m/z calcd for $C_{21}H_{23}O$ $[M+H]^+$: 291.1749. Found: 291.1752.



2-Methyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (14f).

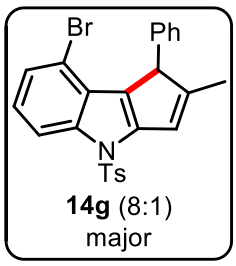
This compound was isolated as pale-yellow solid by following the general procedure **2**. M.P.

= 175-177 °C. 40 mg of **13f** afforded 28 mg of **14f** (80% yield). R_f = 0.3 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 3055, 1693, 1598, 1494, 1448, 1372, 1175, 1090, 814, 737, 667, 541. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.99 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.42-7.35 (m, 3H), 7.29-7.25 (m, 2H), 7.17-7.11 (m, 4H), 7.06 (d, *J* = 7.3 Hz, 1H), 3.64 (s, 2H), 2.24 (s, 3H), 2.11 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 145.1, 142.2, 139.6, 135.7, 135.6, 135.5, 134.6, 130.6, 130.0 (2C), 128.9 (2C), 128.4 (2C), 127.2, 126.6 (2C), 124.9, 123.31, 123.29, 119.7, 114.5, 40.2, 21.7, 14.9. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{22}NO_2S$ $[M+H]^+$: 400.1371. Found: 400.1352.



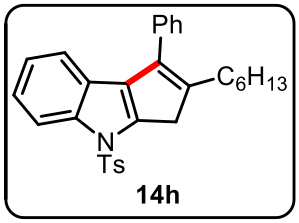
8-Bromo-2-methyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (14g).

This compound was isolated as pale-yellow sticky oil by following the general procedure **2.** 40 mg of **13g** afforded 32 mg of **14g** (90% yield). R_f = 0.6 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 2923, 1596, 1492, 1370, 1356, 1124, 1087, 958, 736,702. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.00 (d, *J* = 8.3 Hz, 1H), 7.77 -7.73 (m, 2H), 7.23-7.16 (m, 6H), 6.97 (t, *J* = 8.1 Hz, 1H), 6.90 (m, 2H), 6.84 (m, 1H), 4.41 (s, 1H), 2.36 (s, 3H), 1.95 (d, *J* = 1.6 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 157.3, 148.0, 145.1, 139.0, 137.8, 134.9, 129.9 (2C), 128.7, 128.4 (2C), 128.1, 127.9, 127.8, 127.0, 126.7 (2C), 126.5, 123.1, 117.7, 113.5, 112.3, 54.6, 21.6, 16.0. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{21}(^{79}Br)NO_2S$ $[M+H]^+$: 478.0476. Found: 478.0476.



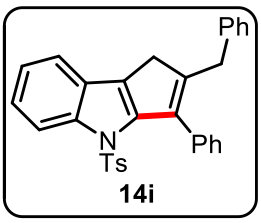
2-Hexyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (14h).

This compound was isolated as viscous liquid by following the general procedure **2**. 30 mg of **13h** afforded 23 mg of **14h** (88% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 2927, 1694, 1596, 1446, 1375, 1175, 1081, 668, 576. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.98 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.39-7.34 (m, 4H), 7.29-7.21 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 3H), 7.03 (t, *J* = 7.6 Hz, 1H), 3.66 (s, 2H), 2.45 (t, *J* = 7.7 Hz, 2H), 2.25 (s, 3H), 2.08 (s, 6H), 1.57-1.49 (m, 2H), 0.81-0.77 (m, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 145.1, 142.4, 140.9, 139.6, 135.7, 135.5, 134.5, 130.6, 130.0 (2C), 128.9 (2C), 128.4 (2C), 127.2, 126.6 (2C), 124.9, 123.2, 123.2, 119.7, 114.5, 37.8, 31.8, 31.1, 30.8, 29.1, 22.7, 21.7, 14.2. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{32}NO_2S$ $[M+H]^+$: 470.2154. Found: 470.2136.



2-Benzyl-3-phenyl-4-tosyl-1,4-dihydrocyclopenta[*b*]indole (14i).

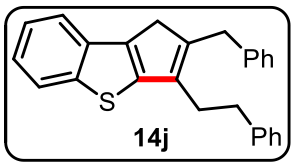
This compound was isolated as brownish-yellow semi-solid by following the general procedure



2. 40 mg of **13i** afforded 25 mg of **14i** (71% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 3061, 1704, 1598, 1494, 1450, 1372, 1175, 1090, 1031, 737, 703, 575. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.21-8.17 (m, 1H), 7.47-7.40 (m, 3H), 7.37-7.30 (m, 5H), 7.28-7.24 (m, 2H), 7.21-7.18 (m, 3H), 7.10-7.06 (m, 4H), 3.65 (s, 2H), 3.17 (s, 2H), 2.30 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 148.3, 146.7, 144.3, 140.86, 140.81, 135.7, 135.33, 135.27, 130.0 (2C), 129.4 (2C), 128.7 (2C), 128.6 (2C), 128.2, 127.9 (2C), 127.5, 127.3, 126.8 (2C), 126.3, 124.1, 123.2, 118.1, 116.5, 36.2, 33.5, 21.7. **HRMS (ESI):** *m/z* calcd for $C_{31}H_{26}NO_2S$ $[M+H]^+$: 476.1684. Found: 476.1662.

2-Benzyl-3-phenethyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene (14j).

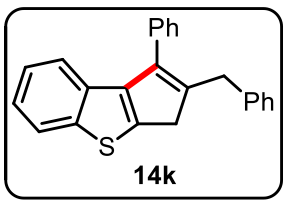
This compound was isolated as viscous liquid by following the general procedure **2**. 45 mg of



13j afforded 34 mg of **14j** (87% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3030, 2923, 1604, 1494, 1458, 1386, 1079, 747, 699. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.29-7.15 (m, 10H), 7.03-7.01 (m, 2H), 3.62 (s, 2H), 3.21 (s, 2H), 3.04-2.99 (m, 2H), 2.93-2.88 (m, 2H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 147.1, 143.6, 142.9, 141.6, 140.8, 139.1, 135.24, 135.19, 128.73 (2C), 128.68 (2C), 128.63 (2C), 128.5 (2C), 126.2 (2C), 124.5, 123.9, 122.4, 120.4, 37.3, 35.2, 35.0, 29.3. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{22}S$ $[M]^+$: 366.1442**.** Found: 366.1446.

2-Benzyl-1-phenyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene (14k).

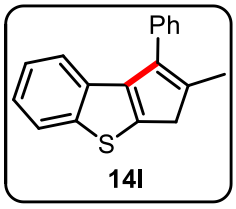
This compound was isolated as pale-yellow oil by following the general procedure **2**. 40 mg of



13k afforded 23 mg of **14k** (68% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 3057, 1706, 1599, 1494, 1452, 1229, 1072, 757, 733, 701. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.80-7.78 (m, 1H), 7.53-7.47 (m, 4H), 7.44-7.40 (m, 1H), 7.37-7.35 (m, 1H), 7.29-7.25 (m, 2H), 7.22-7.15 (m, 5H), 3.80 (s, 2H), 3.45 (s, 2H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 144.9, 144.1, 143.8, 141.7, 141.1, 138.4, 135.7, 132.8, 129.4 (2C), 128.7 (4C), 128.6 (2C), 127.7, 126.2, 124.0, 123.6, 123.2, 121.9, 39.0, 35.3. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{19}S$ $[M+H]^+$: 339.1207. Found: 339.1190.

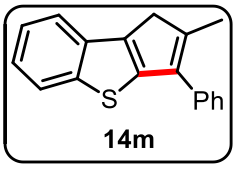
2-Methyl-1-phenyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene (14l).

This compound was isolated as yellowish-brown viscous oil by following the general procedure **2**. 45 mg of **13l** afforded 29 mg of **14l** (78% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2925, 1715, 1664, 1466, 1431, 1384, 1230, 734 701. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.49-7.44 (m, 4H), 7.43-7.36 (m, 2H), 7.22-7.15 (m, 2H), 3.52 (s, 2H), 2.11 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 144.9, 144.5, 141.2, 140.4, 137.2, 135.9, 132.8, 129.5 (2C), 128.4 (2C), 127.3, 123.9, 123.6, 123.1, 121.9, 41.3, 14.9. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{15}S$. $[M+H]^+$: 263.0894. Found: 263.0882.



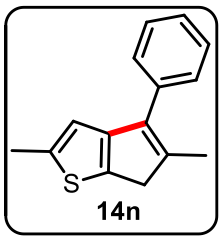
2-Methyl-3-phenyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene (14m).

This compound was isolated as pale-yellow viscous liquid by following the general procedure **2**. 45 mg of **13m** afforded 33 mg of **14m** (91% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2925, 1591, 1491, 1469, 1386, 1248, 1065, 748, 699. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.81 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.60-7.58 (m, 2H), 7.49-7.45 (m, 2H), 7.37-7.31 (m, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 3.52 (s, 2H), 2.31 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 147.4, 142.5, 141.9, 138.2, 135.6, 135.3, 135.1, 128.8 (2C), 128.1 (2C), 127.5, 124.6, 123.8, 122.4, 120.4, 40.4, 16.0. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{13}S$ $[M-H]^+$:261.0738. Found: 261.0727.



2,5-Dimethyl-4-phenyl-6*H*-cyclopenta[*b*]thiophene (14n).

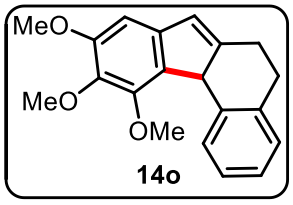
This compound was isolated as pale-yellow liquid by following the general procedure **2**. 30 mg of **13n** afforded 13 mg of **14n** (53% yield). R_f = 0.5 (Hexane/EtOAc = 10/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2925, 2853, 1600, 1466, 1388, 1030, 698. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.39-7.33 (m, 4H), 7.26-7.20 (m, 1H), 6.59 (s, 1H), 3.31 (s, 2H), 2.43 (s, 3H), 2.11 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 151.1, 141.9, 140.1, 136.5, 136.4, 135.9, 128.5 (4C), 126.9, 117.4, 41.2, 16.1, 15.4. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}S$ $[M+H]^+$: 227.0894. Found: 227.0885.



9,10,11-Trimethoxy-6,11b-dihydro-5*H*-benzo[*c*]fluorene (14o).

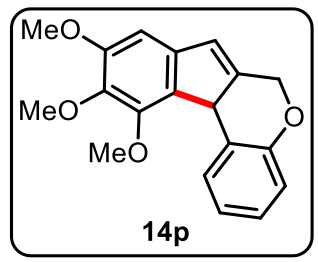
This compound was isolated as yellowish-brown oil by following the general procedure **2**. 30

mg of **13o** afforded 22 mg of **14o** (87% yield). R_f = 0.5 (Hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max} /cm^{-1} 2935, 2366, 1604, 1576, 1465, 1354, 1237, 1109, 1022, 761. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.41 (t, *J* = 4.3 Hz, 1H), 7.22-7.16 (m, 3H), 6.67 (s, 1H), 6.35 (d, *J* = 1.2 Hz, 1H), 4.56 (s, 1H), 4.00 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H), 3.10-2.96 (m, 3H), 2.72-2.63 (m, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 153.8, 150.9, 150.7, 142.7, 138.9, 138.7, 136.2, 127.2, 126.7, 126.5, 126.1, 125.9, 123.0, 100.2, 61.5, 60.0, 56.3, 52.8, 30.1, 24.9. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{21}O_3$ $[M+H]^+$: 309.1491. Found: 309.1461.



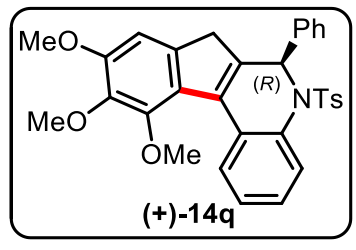
9,10,11-Trimethoxy-6,11b-dihydroindeno[2,1-*c*]chromene (14p).

This compound was isolated as pale-yellow sticky oil by following the general procedure **2**. 40 mg of **13p** afforded 28 mg of **14p** (83% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 2998, 1748, 1675, 1514, 1151, 1008, 758. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.78-7.73 (m, 1H), 7.16-7.11 (m, 1H), 6.93-6.88 (m, 2H), 6.73 (s, 1H), 6.59-6.56 (m, 1H), 5.17 (dd, *J* = 13.2, 1.7 Hz, 1H), 5.03 (dd, *J* = 13.1, 0.4 Hz, 1H), 4.67 (s, 1H), 4.06 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 154.0, 153.9, 150.8, 144.5, 141.1, 140.1, 129.1, 128.2 (2C), 124.8, 124.7, 121.5, 116.8, 101.3, 66.5, 61.4, 60.3, 56.4, 48.2. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283 . Found: 311.1273.



(*R*)-9,10,11-Trimethoxy-6-phenyl-5-tosyl-6,7-dihydro-5*H*-indeno[2,1-*c*]quinoline ((+)-14q).

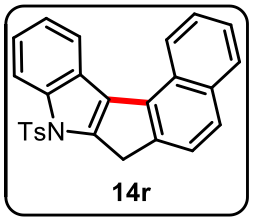
This compound was isolated as yellowish-brown oil by following the general procedure **2**. 28 mg of (–)-**13q** afforded 16 mg of **(+)-14q** (79% yield). R_f = 0.4 (Hexane/EtOAc = 7/3). **Optical rotation:** $[\alpha]_D^{25}$ +70.39 (c 0.04, $CHCl_3$). **IR (thin film, neat):** ν_{max} /cm^{-1} 2926, 1601, 1466, 1345, 1166, 1127, 809, 729, 669, 587, 568. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.22 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.60 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.30-7.22 (m, 4H), 7.19-7.14 (m, 5H), 6.81 (s, 2H), 6.79 (s, 1H), 6.26 (s, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.48 (d, *J* = 22.2 Hz, 1H), 3.46 (s, 3H), 3.13 (d, *J* = 23.5 Hz, 1H), 2.02 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 152.0, 147.6, 143.2, 141.7, 140.5, 139.8, 137.4, 135.5, 135.3, 132.8, 129.4, 128.8 (2C), 128.6 (2C), 128.19, 128.16, 127.9 (2C), 127.8, 127.2, 126.9



(2C), 126.8, 126.6, 104.5, 61.6, 61.4, 58.9, 56.4, 40.3, 21.3. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{30}NO_5S$ $(M+H)^+$: 540.1845. Found: 540.1862.

8-Tosyl-7,8-dihydrobenzo[6,7]indeno[2,1-*b*]indole (14r).

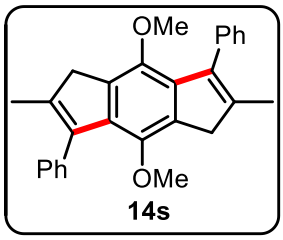
This compound was isolated as greenish-yellow semi-solid by following the general procedure



2. 30 mg of **13r** afforded 21 mg of **14r** (79% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max} /cm^{-1} 2923, 1596, 1491, 1469, 1386, 1248, 1065, 748, 699. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.70 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 7.7 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.77-7.75 (m, 1H), 7.69-7.67 (m, 1H), 7.65-7.60 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.46-7.37 (m, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 4.24 (s, 2H), 2.30 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 146.5, 145.5, 140.5, 140.1, 135.9, 135.3, 133.5, 130.1 (2C), 128.9, 128.1, 127.7, 126.6 (2C), 126.1, 125.7, 125.3, 125.2, 124.9, 124.1, 124.0, 123.3, 121.6, 114.9, 34.7, 21.7. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{19}NO_2S$ $[M]^+$: 409.1136. Found: 409.1114.

4,8-Dimethoxy-2,6-dimethyl-3,7-diphenyl-1,5-dihydro-*s*-indacene (14s).

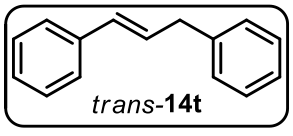
This compound was isolated pale-yellow oil by following the general procedure **2**. 40 mg of



13s afforded 21 mg of **14s** (70% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2947, 1743, 1674, 1591, 1327, 1128, 1003, 758. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.44 (d, *J* = 7.7 Hz, 2H), 7.27-7.21 (m, 2H), 7.18-7.12 (m, 4H), 6.93 (s, 2H), 3.72 (s, 6H), 3.58-3.43 (m, 4H), 2.14 (s, 3H), 2.12 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.35, 151.34, 146.76, 146.73, 142.5, 142.3 (3C), 135.7, 126.19, 126.16, 124.14, 124.12, 123.8 (2C), 123.4 (3C), 119.83, 119.79, 114.62, 114.6, 56.32, 56.31, 43.2 (2C), 15.56, 15.55. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{27}O_2$ $[M+H]^+$: 395.2011. Found: 395.1995.

(*E*)-Prop-1-ene-1,3-diyldibenzene (14t).

This compound was isolated as colourless oil by following the general procedure **2**. 30 mg of



13t afforded 13 mg of **14t** (57% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2924, 1496, 1452, 964, 767, 746, 697. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37-7.22 (m, 10H), 6.46 (d, *J*

= 15.9 Hz, 1H), 6.40-6.32 (m, 1H), 3.55 (d, *J* = 6.6 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 140.3, 137.6, 131.2, 129.4, 128.8 (2C), 128.6 (4C), 127.2, 126.3, 126.2 (2C), 39.5.

General procedure-3: Synthesis of (*E*)-6-((*tert*-butyldimethylsilyl)oxy)-2-methylhept-2-enal (21) (Scheme 10)

A representative procedure for step-I (Scheme 10): To solution of ethyl 3-oxopentanoate **26** (3.5 g, 23.5 mmol, 3.4 mL) and potassium carbonate (4.9 g, 35.5 mmol) in acetone was added prenyl bromide (3.6 g, 23.5 mmol, 2.75 mL). The mixture was stirred at room temperature for 12 h. After completion (monitored by TLC) the solution was quenched with 1 N hydrochloric acid solution. The organic layer was extracted with Et_2O (2x25 mL). The organic extracts were washed with brine, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product **26a** (pale-yellow oil) was used in the next step without further purification.

A representative procedure for step-II (Scheme 10): To a solution of potassium hydroxide (1.7 g, 29.5 mmol) in ethanol:water (1:1) stirred at room temperature was added **26a** (5.0 g, 23.5 mmol). The mixture was immersed in an oil bath and stirred at reflux (100°C) for 3 h. After completion (monitored by TLC), the reaction mixture was cooled to room temperature and extracted with diethyl ether (3x10 mL). The organic extracts were washed with water and brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified *via* flash column chromatography on silica gel using hexane/ethyl acetate (9:1) as eluent to obtain the colorless ketone **27** in 78% yield (over two steps).

A representative procedure for step-III (Scheme 10): To a solution of **27** (1500 mg, 11.9 mmol) in THF:H_2O (4:1) stirred at 0 ^oC temperature was added $NaBH_4$ (428 mg, 17.8 mmol) and mixture was stirred at room temperature for 3 h. After completion (monitored by TLC) the solution was quenched with *aq*. NH_4Cl. The organic layer was extracted with EtOAc (3x10 mL). The organic extracts were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure and crude product was used in the next step without further purification.

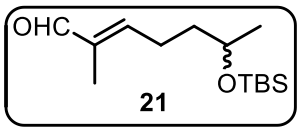
To a solution of alcohol (1500 mg, 11.7 mmol) in DMF (40 mL), imidazole (1593 mg, 23.4 mmol) and TBSCl (2636 mg, 17.6 mmol) were added at 0 °C. The reaction mixture immersed in an oil bath set to 60 °C and stirred for 6 h. After completion of reaction (monitored by TLC) was quenched by the addition of water (50 mL). The organic layer was extracted with EtOAc (3x10 mL), dried over Na_2SO_4. The solvent was evaporated under reduced pressure to

afford the crude product, which was purified by column chromatography using hexane as eluent to give pure silyl ether **28** in 87% yield as colorless oil.

A representative procedure for step-IV (Scheme 10): To a solution of TBS-silyl ether **28** (2500 g, 10.3 mmol) in CH_2Cl_2 (30 mL) at room temperature, *t*-BuOOH (2.5 mL, 5 M in decane, 11.3 mmol) was added and stirred vigorously. Then, SeO_2 (340 mg, 3.09 mmol) was added to the mixture. The resulting mixture was stirred for 2 h, diluted with CH_2Cl_2, and washed with NaOH (10%); then, the organic layer was dried with Na_2SO_4 and concentrated. After 1 h, the reaction mixture was extracted with DCM (2x25 mL) and the separated organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography using hexane/ethyl acetate (9:1) as eluent to give **21** in 56% yield (1480 mg) as a colorless oil.

(*E*)-6-((*tert*-butyldimethylsilyl)oxy)-2-methylhept-2-enal (21).

This compound was prepared by following the general procedure **3** as colorless oil. R_f = 0.4 (hexane/ethyl acetate = 9:1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2857, 2708, 1691, 1472, 1376, 1255, 1136, 1031, 836, 774. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.34 (s, 1H), 6.49-6.44 (m, 1H), 3.86-3.78 (m, 1H), 2.46-2.27 (m, 2H), 1.69 (s, 3H), 1.57-1.52 (m, 2H), 1.14-1.10 (m, 3H), 0.84 (s, 9H), 0.02 (s, 3H), 0.01 (s,3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.3, 154.9, 139.3, 68.0, 38.1, 25.9 (3C), 25.4, 23.8, 18.1, 9.2, -4.2, -4.7. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{27}O_2Si$ $[M-H]^+$: 255.1780. Found: 255.1780.



General procedure-4: Synthesis of indenes 23a-23b (Scheme 11)

A representative procedure for step-I (Scheme 11): The compounds **20a-20b** were synthesized by following literature reports.

A representative procedure for step-II (Scheme 11): An oven dried 25 mL long neck RB flask was charged with aryl bromide **20a** or **20b** (1.0 eq.), dry THF (5 mL) and placed at –78 °C. *n*-BuLi (1.6 M in hexanes, 1.2 eq.) was added dropwise at the same temperature and stirred for 1 hour. Aldehyde **21** (2.0 eq.) dissolved in dry THF (1 mL), was added dropwise over 45 min and stirred at room temperature for 45 min. The reaction mixture was quenched with saturated *aq*. NH_4Cl solution and extracted using EtOAc (2x5 mL). The organic extracts were combined and dried over anhydrous sodium sulphate and concentrated. The crude product **30a**

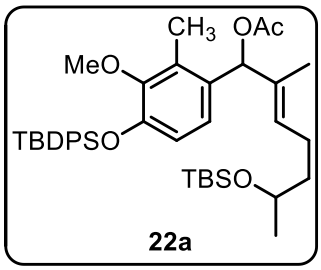
or **30b** was purified by silica gel column chromatography using hexane/ethyl acetate (4:1) as an eluent to afford. [Yield :78% (R = TBDPS) or 83% (R = Me)].

A representative procedure for step-III (Scheme 11): Alcohol **30a** or **30b** (1.0 eq.) was dissolved in dry DCM (6.0 mL) and triethylamine (1.5 eq.), acetic anhydride (1.2 eq.), DMAP (0.05 eq.) ware added to it one by one. Then the reaction mixture was stirred until starting material disappeared (by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM (2x5 mL). The combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as an eluent to afford **22a** (88% yield) and **22b** (91% yield).

A representative procedure for step-IV (Scheme 11): An oven dried 5 mL glass RB flask was charged with **22a** or **22b** (0.20 mmol). DCE (2.0 mL) and $PdCl_2$ (0.02 mmol) were introduced. Stirring continued at 60 ^oC on preheated aluminum blocks until **22a** or **22b** disappeared as monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc (2x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate (9:1) as eluent, to afford **23a** or **23b**.

(*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-1-(4-((*tert*-butyldiphenylsilyl)oxy)-3-methoxy-2-methylphenyl)-2-methylhept-2-en-1-yl acetate (22a).

This compound was isolated as colorless viscous liquid by following the general procedure **4 (Step I-III)**. R_f = 0.5 (Hexane/EtOAc = 8/2). Yield = 88%**. IR (thin film, neat):** ν_{max} /cm^{-1} 2930, 2857, 1740, 1599, 1488, 1369, 1294, 1233, 1045, 833, 774, 701. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77-7.73 (m, 4H), 7.46-7.36 (m, 6H), 6.67 (d, *J* = 8.5 Hz, 1H), 6.35 (d, *J* = 8.5 Hz, 1H), 6.24 (s, 1H), 5.35 (t, *J* = 6.8 Hz, 1H), 3.91 (s, 3H), 3.82-3.72 (d, *J* = 5.7 Hz, 1H), 2.26 (s, 3H), 2.16-2.08 (m, 1H), 2.06 (s, 3H), 2.03-1.95 (m, 1H), 1.49 (s, 3H), 1.46-1.35 (m, 2H), 1.14 (s, 9H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.1, 148.7, 148.2, 135.7 (2C), 135.6 (2C), 133.0, 132.8, 132.4, 130.8, 130.5, 130.0, 128.3, 127.9 (2C), 127.86, 127.82 (2C), 122.2, 117.5, 68.3, 60.5, 39.4, 26.6 (3C), 26.0 (3C), 24.2, 23.9, 21.3, 19.6

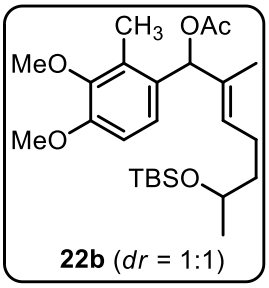


22a

(2C), 18.2, 13.4, 11.6, -4.2, -4.6. **HRMS (ESI):** *m/z* calcd for $C_{40}H_{58}O_5Si_2Na$ $[M+Na]^+$: 697.3720. Found: 697.3731.

(*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-1-(3,4-dimethoxy-2-methylphenyl)-2-methylhept-2-en-1-yl acetate (22b).

This compound was isolated as colorless viscous liquid by following the general procedure **4**

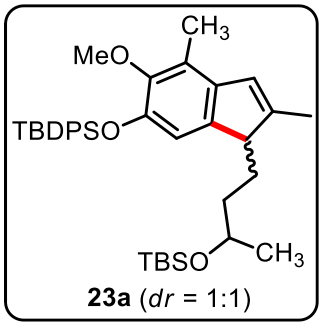


22b (*dr* = 1:1)

(Step I-III). R_f = 0.5 (Hexane/EtOAc = 8/2). Yield = 91%. (R = Me). **IR (thin film, neat):** ν_{max} /cm^{-1} 2929, 1738, 1490, 1236, 1084, 1009, 836, 774. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.83 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.41 (s, 1H), 5.29-5.23 (m, 1H), 3.84 (s, 3H), 3.84-3.81 (m, 1H), 3.77 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H), 1.86-1.79 (m, 1H), 1.76-1.69 (m, 1H), 1.66 (t, *J* = 1.2 Hz, 3H), 1.51-1.39 (m, 2H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.4, 151.6, 135.6, 130.9, 130.0, 126.7, 124.7, 109.0, 79.4, 68.3, 60.3, 55.8, 35.6, 29.2, 25.9 (3C), 24.0, 21.4, 18.2 (2C), 13.3, 12.7, -4.2, -4.6. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{42}O_5SiNa$ $[M+Na]^+$: 473.2699. Found: 473.2690.

***tert*-Butyl((1-(3-((*tert*-butyldimethylsilyl)oxy)butyl)-5-methoxy-2,4-dimethyl-1*H*-inden-6-yl)oxy)diphenylsilane (23a)**.

This compound was isolated as colourless viscous liquid by following the general procedure **4**

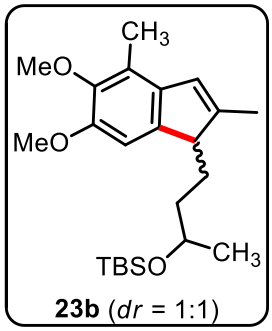


23a (*dr* = 1:1)

(Step IV). R_f = 0.5 (Hexane/EtOAc = 9/1). Yield = 91%. **IR (thin film, neat):** ν_{max} /cm^{-1} 2929, 2857, 1471, 1351, 1254, 701. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.78-7.73 (m, 4H), 7.43-7.32 (m, 6H), 6.38 (s, 1H), 6.28 (s, 1H), 3.90 (s, 3H), 3.40-3.32 (m, 1H), 2.96-2.89 (m, 1H), 2.31 (s, 3H), 1.92 (s, 3H), 1.68-1.60 (m, 1H), 1.35-1.26 (m, 1H), 1.13 (s, 9H), 0.87 (d, *J* = 6.1 Hz, 3H), 0.85 (s, 9H), 0.77-0.69 (m, 1H), 0.51-0.43 (m, 1H), -0.03 (s, 3H), -0.06 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 147.5, 147.3, 145.6, 141.7, 137.9, 135.7 (2C), 135.6 (2C), 133.5, 133.2, 129.9 (2C), 127.9 (2C), 127.8 (2C), 124.7, 122.9, 113.1, 68.8, 60.6, 52.0, 34.2, 26.7 (2C), 26.0 (4C), 25.3, 24.2, 19.7, 18.2, 15.2, 12.4, -4.2, -4.6. **HRMS (ESI):** *m/z* calcd for $C_{38}H_{55}O_3Si_2$ $[M+H]^+$: 615.3690 Found: 615.3676.

***tert*-Butyl((4-(5,6-dimethoxy-2,4-dimethyl-1*H*-inden-1-yl)butan-2-yl)oxy)dimethylsilane (23b)**.

This compound was isolated as pale-yellow viscous liquid by following the general procedure **4 (Step IV).** R_f = 0.5 (Hexane/EtOAc = 8/2). Yield = 91%. **IR (thin film, neat):** ν_{max} /cm^{-1}



23b (*dr* = 1:1)

2928, 2856, 1463, 1343, 1254, 1087, 1005, 836, 773. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 6.81 (s, 1H), 6.45 (s, 1H), 3.86 (d, *J* = 1.6 Hz, 3H), 3.79 (s, 3H), 3.74-3.65 (m, 1H), 3.27-3.24 (m, 1H), 2.30 (s, 3H), 2.03 (s, 3H), 1.97-1.87 (m, 1H), 1.79-1.70 (m, 1H), 1.20-1.09 (m, 1H), 1.07-1.05 (m, 3H), 1.02-0.95 (m, 1H), 0.89 (s, 9H), 0.05-0.01 (m, 6H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 150.1, 146.9, 146.3, 142.3, 137.7, 124.8, 122.9, 105.8, 68.8, 60.5, 56.3, 52.1, 33.9, 26.0 (3C), 25.7, 23.9, 18.2, 15.3, 12.2, -4.2, -4.6. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{38}O_3Si$ $[M]^+$: 390.2590. Found: 390.2584.

General procedure-5: Synthesis of the required starting compound (13m-D):

A representative procedure for step-1 (Scheme 12): An oven dried 25 mL long neck RB flask was charged with benzo[*b*]thiophene **31** (1.34 g, 10.0 mmol), 8 mL dry THF and placed at -78 ^{o}C. *n*-BuLi (1.6*M* in hexanes, 7.5 mL, 12 mmol) was added dropwise at the same temperature and stirred for 2 h. D_2O (0.25 mL) was added and stirring continued for 1 h. The reaction mixture was quenched with saturated aq. NH_4Cl solution and extracted with ethyl acetate. The organic layer was dried and the residue was chromatographed on silica to give **32**.

A representative procedure for step-2 (Scheme 12): To a solution of **32** (1.3 g, 9.6 mmol) in chloroform (20 mL) and acetic acid (20 mL), *N*-bromosuccinimide (1.71 g, 9.6 mmol) was added stepwise and stirred at room temperature for 24 h. The reaction mixture was diluted with chloroform (20 mL) was added and the resulting mixture was successively washed with a saturated sodium thiosulfate solution (20 mL), a saturated sodium carbonate solution (20 mL) and water (15 mL). The extracted organic layer was then dried over $MgSO_4$. The resulting red liquid was then filtered over a pad of silica, eluting with hexane/ethyl acetate to afford **33** as colorless oil.

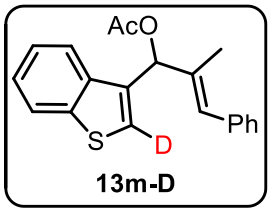
A representative procedure for step-3 (Scheme 12): To a 50 mL RB flask equipped with magnetic stir bar, (*E*)-2-methyl-3-phenylacrylaldehyde (1.1 eq.), anhydrous THF (5.0 ml) were added under N_2 atmosphere and stirred at 0 ^{o}C for 2-3 min. Benzo[*b*]thiophen-3-ylmagnesium bromide solution of **33** which was prepared from magnesium (56 mg, 1.1 eq.), **33** (425 mg, 1.0 eq.) and a catalytic amount of iodine in 10 mL of dry THF was added dropwise with stirring at 0 °C and stirring was continued for 1 h. The reaction mixture was quenched with dil. HCl and

extracted twice with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated and **34** was purified by silica gel column chromatography.

A representative procedure for step-4 (Scheme 12): Alcohol **34** (450 mg, 1.09 mmol) was dissolved in dry DCM (6.0 mL) and triethylamine (0.19 mL, 1.3 mmol), acetic anhydride 0.130 mL, 1.3 mmol), DMAP (13 mg, 0.11 mmol) were added to it one by one. Then the reaction mixture was stirred until starting material disappeared (as detected by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using 10% ethyl acetate/hexane as an eluent to afford **13m-D (**83% yield, 100% D).

1-(2-Deuterobenzo[*b*]thiophen-3-yl)-2 methyl-3-phenylallyl acetate (13m-D).

This compound was isolated as pale-yellow liquid by following the above general procedure.



13m-D

150 mg of **15** (Ar^1 = Ph, R^1 = Me) afforded 291 mg of **13m-D** (88% yield). R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2924, 1739, 1599, 1428, 1369 1230, 1018, 761, 733. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.95–7.88 (m, 2H), 7.45–7.33 (m, 6H), 7.29 (ddt, *J* = 7.9, 6.1, 1.7 Hz, 1H), 6.88 (s, 1H), 6.81 (d, *J* = 1.2 Hz, 1H), 2.240 (s, 3H), 1.901 (d, *J* = 1.9, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** 169.9, 140.7, 137.2, 137.0, 134.8, 133.2, 129.0 (2C), 128.4, 128.2 (2C), 126.9, 124.5, 124.3, 122.9, 122.4, 75.5, 21.3, 14.9. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{14}DS$ $[M\text{-}OAc]^+$: 264.0957. Found: 264.0952.

General procedure-6: The first total synthesis of *β*-diasarone (35)

A representative procedure for step-I (Scheme 15): An oven dried RB flask was charged with NaH (60% oil suspension, 306 mg, 7.65 mmol) and dry THF (6.0 mL). Triethyl 2-phosphonopropionate (1456 mg, 6.12 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and aldehyde **39** (1000 mg, 5.1 mmol) was added. The reaction mixture was stirred until the complete consumption of the starting material (monitored by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq.* NH_4Cl solution and extracted with EtOAc (2x5 mL). The combined organic layers were dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product **40** was taken to the next step without purification.

A representative procedure for step-II (Scheme 15): Compound **40** (1400 mg, 5 mmol) was dissolved in anhydrous THF (7 mL) at -40 °C, then $LiAlH_4$ (209 mg, 5.5 mmol) was added to it and stirred for 12 h at the same temperature. Upon completion, the reaction was quenched by adding saturated *aq*. NH_4Cl solution and extracted with EtOAc (2x5 mL). The combined organic layers were dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was used as such in the next step without purification.

Alcohol (1050 mg, 4.41 mmol) was dissolved in ethyl acetate (10 mL), and IBX (1482 mg, 5.29 mmol) was added. The resulting suspension was immersed in an oil bath set to 75 °C and stirred until alcohol disappeared as monitored by TLC. The reaction was cooled to room temperature and filtered through sintered funnel using celite pad. The filter cake was washed with EtOAc (3x5 mL). Organic extract was extracted 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 (3:1) as eluent to afford the aldehyde **41** (980 mg, yield 83%).

A representative procedure for step-III (Scheme 15): An oven dried 25 mL long neck RB flask was charged with **42** (1-bromo-2,4,5-trimethoxybenzene) (623 mg, 2.54 mmol), 5 mL dry THF and placed at -78 ^oC. *n*-BuLi (1.6 M in hexanes, 1.45 mL, 2.32 mmol), was added dropwise at same temperature and stirred for 1 h. Aldehyde **41** (500 mg, 2.11 mmol) dissolved in 1 mL dry THF, was added dropwise over 15 min and stirred at room temperature for 30 min. The reaction mixture was quenched with saturated *aq*. NH_4Cl solution and extracted using EtOAc (3x5 mL). The organic extracts were combined and dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (2:3) as eluent to afford the alcohol **43** (744 mg, yield 87%).

A representative procedure for step-IV (Scheme 15): Alcohol **43** (200 mg, 0.495 mmol) was dissolved in dry DCM (6.0 mL) and triethylamine (0.150 mL, 1.0 mmol), pivaloyl chloride (0.78 mL, 0.64 mmol), DMAP (3.0 mg, 0.0245 mmol) were added to it one by one. Then the reaction mixture was stirred until starting material disappeared (monitored by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM (3x3 mL). The combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by

silica gel column chromatography using hexane/ethyl acetate (3:2) as an eluent to afford **44** (188 mg, yield 78%).

A representative procedure for step-V (Scheme S5): An oven dried 5 mL glass RB flask was charged with **44** (100 mg, 0.20 mmol). DCE (4.0 mL) and $PdCl_2$ (3.65 mg, 0.02 mmol) were introduced. The reaction mixture was stirred in a preheated aluminum block at 60 ^oC or 100 ^oC until **44** disappeared as monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc (3x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate (3:2) as eluent, to afford **45** as pale-yellow solid (65 mg, yield 83% at 60 ^oC in 1 h, 70 mg, yield 88% at 100 ^oC in 45 min).

A representative procedure for step-VI (Scheme 15): Compound **45** (40 mg, 0.1 mmol) was taken in MeOH (2 mL) followed by the addition of 10% Pd/C (1.07 mg, 0.01 mmol) under argon atmosphere and the resulting reaction mixture was immersed in an oil bath and stirred at 50 ^oC under hydrogen atmosphere for 24 h. After completion, the reaction mixture was filtered through celite pad and washed with EtOAc (3x2 mL). The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (3:1) as an eluent. An oven dried 5 mL glass RB flask was charged with saturated indane (100 mg, 0.26mmol), 1,4-dioxane (4.0 mL) and SeO_2 (31 mg, 0.028 mmol) were introduced to it and stirring continued at 110 ^oC until saturated indane was disappeared as monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc (3x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate (3:1) as eluent, to afford **46** as pale-yellow sticky oil (27 mg, yield 67%).

A representative procedure for step-VII (Scheme 15): A solution of **46** (50 mg, 0.125 mmol) in THF (5 mL) was cooled to -78°C and ethyl magnesium bromide (0.100 mL of a 3 M solution in THF) was added over 10 minutes and stirred for 1 h. After 1h, the resulting mixture was allowed to come to room temperature then stirred for 1 hour and quenched with ammonium chloride solution. Then the reaction was quenched with water and extracted with EtOAc (2x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and

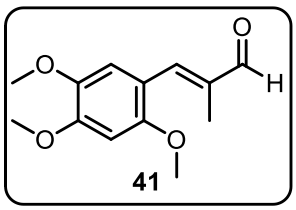
evaporation in vacuo of the combined extracts gave a colorless oil. The crude product was preceded to next step without purification.

To a solution of crude alcohol in toluene (2 mL), Burgess reagent (35 mg, 0.15 mmol) was added at room temperature. The resulting suspension was immersed in an oil bath set to 100°Cstirred until until starting material was disappeared as monitored by TLC. The reaction was quenched with water and extracted with EtOAc (2x2 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate (2:1) as eluent, to afford **47** as colorless oil (32 mg, yield 62%).

A representative procedure for step-VIII (Scheme 15): Compound **47** (30 mg, 0.073 mmol) was taken in MeOH (2 mL) followed by the addition of 10% Pd/C (1.0 mg, 0.01 mmol) under argon atmosphere and stirred at room temperature under hydrogen atmosphere for 24 h. After completion, the reaction mixture was filtered through celite pad and washed with ethyl acetate. The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (2:1) as an eluent, to afford **35** as pale-white crystals (28 mg, yield 92%).

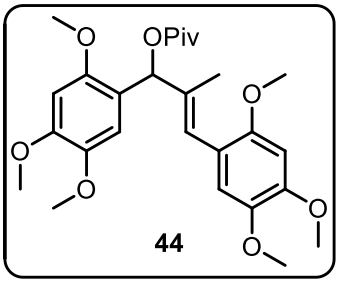
(*E*)-2-Methyl-3-(2,4,5-trimethoxyphenyl)acrylaldehyde (41).

This compound was isolated as pale-yellow solid by following the general procedure **6 (step I-II)**, M.P = 92-95 ^oC. R_f = 0.5 (Hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max} /cm^{-1} 2934, 2833, 1664, 1601, 1286, 1508, 1408, 1286, 1209, 1132, 1029, 883. **^{1}H NMR (400 MHz, $CDCl_3$): δ** 9.57 (s, 1H), 7.59 (d, *J* = 0.7 Hz, 1H), 7.11 (s, 1H), 6.56 (s, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 2.07 (d, *J* = 0.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ** 195.9, 153.5, 151.8, 144.7, 142.7, 136.0, 115.8, 113.5, 96.7, 56.7, 56.5, 56.2, 11.2. **HRMS (ESI):** m/z calcd for $C_{13}H_{17}O_4$ $[M+H]^+$: 237.1127. Found: 237.1087.



(*E*)-2-Methyl-1,3-bis(2,4,5-trimethoxyphenyl)allyl pivalate (44).

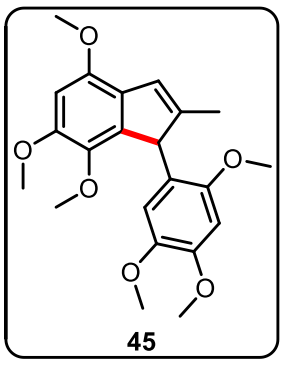
This compound was isolated pale-yellow liquid by following the general procedure **6 (step III-IV)**, 200 mg of **43** afforded 188 mg of **44** (78% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max} /cm^{-1} 2926, 2853, 1728, 1609, 1464, 1398, 1319, 1206, 1153, 1035, 864. **^{1}H NMR (100 MHz, $CDCl_3$): δ** 6.96 (s, 1H), 6.77 (s, 1H), 6.62-6.61 (m, 2H), 6.54 (s, 1H),



6.51 (s, 1H), 3.89 (d, *J* = 4.0 Hz, 6H), 3.85 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H), 1.79 (d, *J* = 0.9 Hz, 3H), 1.26 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$): δ** 177.2, 152.0, 151.7, 149.4, 148.7, 143.2, 142.6, 135.1, 121.3, 119.4, 118.5, 114.3, 111.4, 97.9, 97.8, 73.3, 56.9, 56.83, 56.80, 56.6, 56.23, 56.20, 39.1, 27.4 (3C), 15.3. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{27}O_6$ $[M\text{-}OPiv]^+$: 387.1808 Found: 387.1807.

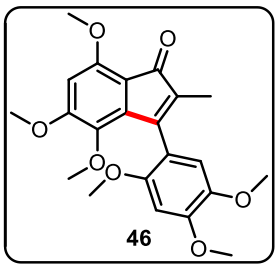
4,6,7-Trimethoxy-2-methyl-1-(2,4,5-trimethoxyphenyl)-1*H*-indene (45).

This compound was isolated as pale-yellow solid by following the general procedure **6 (step V)**, 100 mg of **44** afforded 70 mg of **45** (88% yield). M.P = 94-96 ^oC. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2929, 2853, 1606, 1510, 1464, 1319, 1205, 1036, 983, 831. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.63 (s, 1H), 6.52 (t, *J* = 1.5 Hz, 1H), 6.44 (s, 1H), 6.00 (s, 1H), 5.06 (s, 1H), 3.95 (s, 3H), 3.88 (s, 6H), 3.83 (s, 3H), 3.58 (s, 3H), 3.29 (s, 3H), 1.82 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.4, 150.8, 148.2, 147.9, 147.7, 143.7, 142.7, 139.9, 127.0, 122.1, 119.3, 110.6, 98.7, 97.4, 59.9, 57.6, 56.8, 56.6, 56.3, 56.1, 49.4, 15.0. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{26}O_6Na$ $[M+Na]^+$: 409.1627. Found: 409.1620.



4,5,7-Trimethoxy-2-methyl-3-(2,4,5-trimethoxyphenyl)-1*H*-inden-1-one (46).

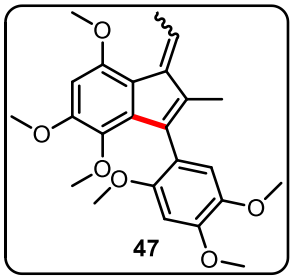
This compound was isolated pale-yellow sticky oil by following the general procedure **6 (step VI);** 40 mg of **45** afforded 27 mg of **46** (67% yield). R_f = 0.5 (Hexane/EtOAc = 20/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2954, 1691, 1461,1377, 1219, 724. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.80 (s, 1H), 6.59 (s, 1H), 6.18 (s, 1H), 3.95 (s, 6H), 3.87 (s, 3H), 3.85 (s, 3H), 3.78 (s, 3H), 3.17 (s, 3H), 1.71 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ** 194.4, 160.8, 154.1, 151.8, 149.9, 148.0, 142.5, 138.7, 138.3, 135.5, 115.1, 113.3, 109.4, 97.1, 95.9, 61.5, 56.8, 56.7, 56.6 (2C), 56.2, 8.9. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{25}O_7$ $[M+H]^+$: 401.1600. Found: 401.1597.



1-Ethylidene-4,5,7-trimethoxy-2-methyl-3-(2,4,5-trimethoxyphenyl)-1*H*-indene (47).

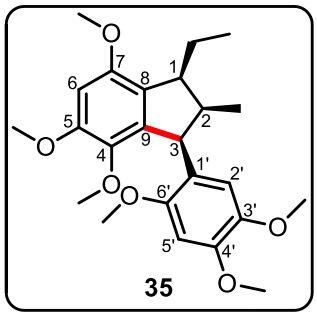
This compound was isolated pale-yellow oil by following the general procedure **5 (step VII);** 50 mg of **46** afforded 32 mg of **47** (62% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film,**

neat): ν_{max} /cm^{-1} 2927, 1461, 1377, 1304, 1206, 965, 722. **^{1}H NMR (500MHz, CDCl$_3$):** δ 7.35 (q, *J* = 8.0 Hz, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 6.35 (s, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.72 (s, 3H), 3.16 (s, 3H), 2.24 (d, *J* = 8.0 Hz, 3H), 2.13 (s, 3H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 152.6, 152.3, 151.7, 148.8, 142.4, 140.3, 137.1, 136.5, 136.2, 135.9, 130.9, 117.6, 116.6, 115.2, 97.6, 94.5, 61.1, 56.8, 56.7, 56.4, 56.2, 55.7, 15.8, 15.7. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{29}O_6$ $[M+H]^+$: 413.1964. Found: 413.1944.



1-Ethyl-4,5,7-trimethoxy-2-methyl-3-(2,4,5-trimethoxyphenyl)-2,3-dihydro-1*H*-indene (35).

This compound was isolated pale-white needle crystals by following the general procedure **6 (step VIII)**; 30 mg of **47** afforded 28 mg of **35** (92% yield).. M.P = 118-120 ^{o}C. R_f = 0.4 (Hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max} /cm^{-1} 2959, 2944, 2832, 1604, 1509, 1494, 1463, 1330, 1253, 1204, 1087, 1036. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 6.53 (s, 1H), 6.44 (s, 1H), 6.22 (s, 1H), 4.82 (d, *J* = 8.7 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 6H), 3.84 (s, 3H), 3.57 (s, 3H), 3.39 (s, 3H), 3.01 (dt, *J* = 8.0, 6.8 Hz, 1H), 2.81-2.89 (m, 1H), 1.57-1.49 (m, 2H), 0.94 (t, *J* = 7.5 Hz, 3H), 0.84 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (125 MHz, CDCl$_3$): δ** 151.9 (2C), 151.8, 147.6, 142.2, 140.3, 139.2, 129.8, 123.1, 115.0, 97.3, 96.9, 60.0, 56.6, 56.5, 56.5, 56.0, 55.4, 47.4, 44.4, 41.8, 24.4, 14.1, 12.0. **Cosy correlation:** δ 0.84/2.81-2.89 [2-Me/2-H], 0.94/1.57-1.49 [Me/CH_2], 1.57-1.49/0.94 [CH_2/Me], 1.57-1.49/1.57-1.49 [CH_2/CH_2], 1.57-1.49/3.01 [CH_2/1-H], 2.81-2.89/0.84 [2-H/2-Me], 2.81-2.89 /2.81-2.89 [2-CH/2-CH], 2.81-2.89 /3.01 [2-H/1-H], 2.81-2.89/4.82 [2-H/3-H], 3.01/1.57-149 [1-H/CH_2], 3.01/2.81-2.89 [1-H/2-CH], 3.01/3.01[1-H/1-H], 4.82/2.81-2.89 [3-H/2-H], 4.8/4.8 [3-CH/3-CH]. **HSQC correlations:** δ 6.53/97.3 [5'-H_{Ar}/5'-C_{Ar}], 6.44/96.9 [6-H_{Ar}/6-C_{Ar}], 6.22/115.0 [2'-H_{Ar}/2'-C_{Ar}], 4.82/44. [3-H/3-C], 3.86-3.39/56.0-60.1 [6(-OMe_{Ar})/6($C_{[6(-OMeAr)]}$], 3.01/47.4 [1-H/1-C], 2.81-2.89/41.8 [2-H/2-C], 1.57-1.49/24.4 [CH_2/C_{CH2}], 0.94/14.1 [Me/C_{Me}], 0.84/12.0 [2-Me/$C_{2\text{-}Me}$]. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{32}O_6Na$ $[M+Na]^+$: 439.2097. Found: 439.2084.



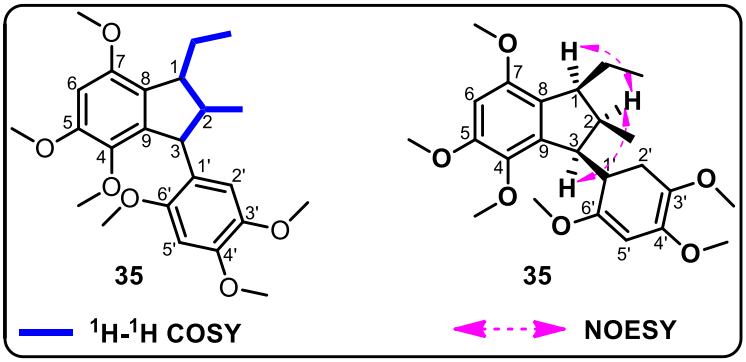


Figure 44: Key NMR correlations of **35** [blue bold lines for ^{1}H–^{1}H COSY, pink dashed two-way arrows for NOESY]

General procedure-7: Synthesis of allylic acetates 148a-148m

A representative procedure for step-1 (Scheme 50): To a solution of isatin **144** (2.94 g, 20.0 mmol) in anhydrous DMF (80 mL) at 0 °C, sodium hydride (60% dispersion in oil, 0.95 g, 24.0 mmol) was added in one portion and stirred for 5 min. Alkyl halide (1.87 mL, 30.0 mmol) was added and the reaction was stirred at 0 °C for 30 min. The reaction mixture was then poured into saturated aqueous ammonium chloride solution and extracted with EtOAc (4 × 30 mL). The combined organic layers were washed with water (3 × 15 mL) and brine (20 mL), then dried over $MgSO_4$, filtered, and concentrated to give crude N-alkyl-isatins **145**, which were used without further purification.

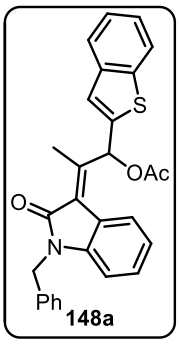
A representative procedure for step-2 (Scheme 50): To a solution of *N*-protected isatin **145** (1.0 g, 4.22 mmol) in THF (8 mL), DBU (130 µL, 0.2 mmol) and propionaldehyde (0.906 µL, 30 mmol) were added, and the reaction mixture was kept at −25 °C for 15 h. After completion of the reaction, the mixture was kept at room temperature followed by the addition of 3:1 mixture of AcOH/H_2O (10 mL) and a few drops of conc. H_2SO_4. This mixture was then refluxed for 45 min. The reaction mixture was diluted with water, extracted with dichloromethane, and washed with brine. The organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by silica column chromatography using hexane−ethyl acetate mixture as eluent to obtain compounds **146** in 60-85% yield.

A representative procedure for step-3 (Scheme 50): An oven dried 25 mL long neck round bottom flask was charged with aryl bromide (399 mg, 2.98 mmol), dry THF (5 mL) and kept at -78 ^{o}C. *n*-BuLi (1.6 *M* in hexane, 1.69 mL, 2.7 mmol), was added dropwise at same temperature and stirred for 2 h. Enal **146** (750 mg, 2.7 mmol) dissolved in dry THF (1 mL) was then added within 2 min and stirred at room temperature for 30 min. The reaction mixture was

quenched with saturated aqueous ammonium chloride solution and extracted using ethyl acetate. The organic extracts were combined and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product **147** obtained was taken to next step without purification. The corresponding alcohols **147** were obtained in 50-73% yield.

A representative procedure for step-4: Alcohol **147** (450 mg, 1.09 mmol) was dissolved in dry DCM (6.0 mL) and triethylamine (0.19 mL, 1.3 mmol), acetic anhydride (0.130 mL, 1.3 mmol), DMAP (13 mg, 0.11 mmol) were added sequentially. Then the reaction mixture was stirred until starting material was consumed (as detected by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexane−ethyl acetate mixture as eluent (90:10 v/v) to obtain compounds **148a-148m** in 70-90% yield.

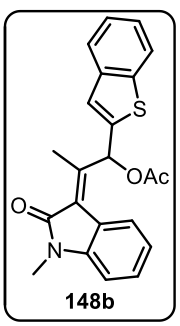
(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-(1-benzyl-2-oxoindolin-3-ylidene)propyl acetate (148a).



148a

This compound was prepared following the general procedure-**7** and isolated as pale yellow oil. R_f = 0.3 (hexane/EtOAc = 9/1**). IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2930, 1745, 1693, 1608, 1467, 1357, 1225, 1181, 1028. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.83 (d, *J* = 0.9 Hz, 1H), 7.77 (dd, *J* = 8.2 and 0.9 Hz, 1H), 7.71 (dd, *J* = 6.9 and 1.8 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.46 (s, 1H), 7.33 – 7.20 (m, 7H), 7.14 (td, *J* = 7.7 and 1.0 Hz, 1H), 6.98 (td, *J* = 7.7 and 1.0 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.8 Hz, 1H), 2.43 (s, 3H), 2.20 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.5, 166.8, 149.9, 142.4, 141.3, 139.6, 139.3, 136.1, 129.0, 128.8 (2C), 127.6, 127.3 (2C), 124.7, 124.5, 124.4 (2C), 123.8, 123.0, 122.3, 122.2, 122.1, 109.0, 69.7, 43.5, 27.0, 16.1. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{20}NOS$ $(M\text{-}OAc)^+$: 394.1266. Found: 394.1241.

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-(1-methyl-2-oxoindolin-3-ylidene)propyl acetate (148b).



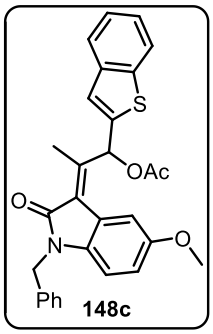
148b

This compound was prepared following the general procedure-**7** and isolated as pale yellow oil. R_f = 0.3 (hexane/EtOAc = 8/2**). IR (thin film, neat):** ν_{max}/cm^{-1} 2924, 2858, 1743, 1694, 1608, 1470, 1371, 1228. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.79 (s, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.43 (s, 1H), 7.35 – 7.16 (m, 3H), 7.01 (t, *J* =7.6 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 3.24 (s, 3H), 2.40 (s, 3H), 2.19 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 166.7, 149.4, 143.2, 141.2, 139.5, 139.3, 129.0, 124.79, 124.4, 124.3, 124.3, 123.7, 122.8, 122.2, 122.1, 122.0, 107.9, 69.5, 25.9, 21.0, 15.91. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}NOS$ $(M\text{-}OAc)^+$: 318.0953. Found: 318.0944**.**

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-(1-benzyl-5-methoxy-2-oxoindolin-3-ylidene)propyl acetate (148c).

This compound was prepared following the general procedure-**7** and isolated as pale reddish

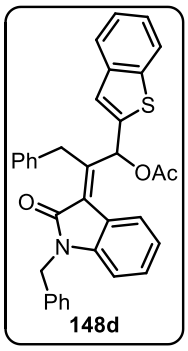


148c

oil. R_f = 0.4 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2854, 1746, 1689, 1593, 1488, 1439, 1367, 1227, 1183. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.84 (d, *J* = 0.8 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.72 (dd, *J* = 6.6 and 1. 6 Hz, 1H), 7.46 (s, 1H), 7.36 – 7.28 (m, 6H), 7.28 – 7.21 (m, 1H), 7.16 (d, *J* = 2.3 Hz, 1H), 6.70 (dd, *J* = 8.5 and 2.4 Hz, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 4.93 (d, *J* = 15.7 Hz, 1H), 3.75 (s, 3H), 2.41 (s, 3H), 2.21 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.5, 166.7, 155.4, 150.3, 141.3, 139.6, 139.4, 136.3, 136.2, 128.8 (2C), 127.5, 127.3 (2C), 125.00, 124.5, 124.4, 124.0, 123.8, 122.3, 122.2, 112.7 (2C), 109.1, 69.7, 56.0, 43.6, 21.1, 16.0. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{22}NO_2S$ $(M\text{-}OAc)^+$: 424.1371. Found: 424.1361**.**

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-2-(1-benzyl-2-oxoindolin-3-ylidene)-3-phenylpropyl acetate (148d).

This compound was prepared following the general procedure-**7** and isolated as pale yellow

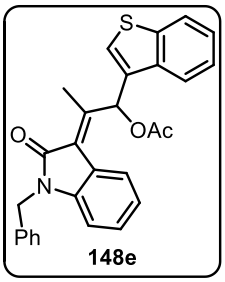


148d

oil. R_f = 0.4 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2925, 1749, 1694, 1608, 1467, 1362, 1223, 1184, 1028. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.97 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 7.4 Hz, 1H), 7.44 (s, 1H), 7.41 – 7.24 (m, 10H), 7.24 – 7.13 (m, 4H), 6.85 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 5.08 (d, *J* = 15.7 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 4.31 (d, *J* = 15.3 Hz, 1H), 4.16 (d, *J* = 15.4 Hz, 1H), 1.49 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.6, 166.9, 150.2, 142.8, 141.6, 139.6, 139.4, 136.5, 136.1, 129.7, 128.9 (2C), 128.8 (2C), 128.2 (2C), 127.7, 127.5 (2C), 127.4, 126.6, 124.5, 124.4, 124.4, 123.7, 122.5, 122.3, 122.0, 122.0, 109.1, 69.6, 43.7, 35.9, 20.1. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{24}NOS$ $(M\text{-}OAc)^+$: 470.1579. Found: 470.1559**.**

(*E*)-1-(Benzo[*b*]thiophen-3-yl)-2-(1-benzyl-2-oxoindolin-3-ylidene)propyl acetate (148e)

This compound was prepared following the general procedure-**7** and isolated as pale reddish

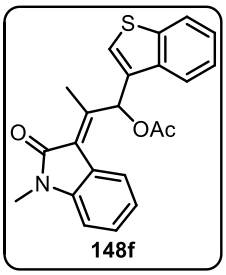


148e

oil. R_f = 0.3 (hexane/EtOAc = 8/1**). IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2930, 1745, 1694, 1608, 1467, 1356, 1228, 1181. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.96 (s, 1H), 8.13 – 8.03 (m, 1H), 7.86 – 7.81 (m, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.48 (s, 1H), 7.39 – 7.30 (m, 6H), 7.30 – 7.22 (m, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.99 (t, *J* = 7.7 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.03 (d, *J* = 15.8 Hz, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 2.40 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.7, 166.8, 149.4, 142.4, 140.3, 137.5, 136.2, 133.4, 129.0, 128.8 (2C), 127.5, 127.3 (2C), 125.2, 124.7, 124.6, 124.6, 124.0, 123.1, 123.0, 122.8, 122.1, 109.0, 68.8, 43.4, 21.2, 16.9. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{20}NOS$ $(M\text{-}OAc)^+$: 394.1266. Found: 394.1250.

(*E*)-1-(Benzo[*b*]thiophen-3-yl)-2-(1-methyl-2-oxoindolin-3-ylidene)propyl acetate (148f).

This compound was prepared following the general procedure-**7** and isolated as pale orange

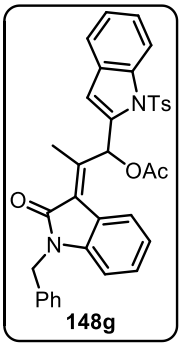


148f

oil. R_f = 0.3 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2932, 1745, 1694, 1633, 1608, 1470, 1374, 1226, 1136, 1013. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.89 (d, *J* = 0.8 Hz, 1H), 8.04 (dd, *J* = 7.0 and 1.1 Hz, 1H), 7.82 (dd, *J* = 7.3 and 1.4 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.43 (s, 1H), 7.40 – 7.32 (m, 2H), 7.32 – 7.23 (m, 1H), 7.02 (td, *J* = 7.7 and 0.9 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 3.25 (s, 3H), 2.38 (s, 3H), 2.16 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.7, 166.7, 149.0, 143.4, 140.3, 137.6, 133.4, 129.1, 125.4, 124.7, 124.6, 124.5, 124.1, 123.0, 122.9, 122.7, 122.0, 108.0, 68.7, 26.0, 21.1, 16.9. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}NOS$ $(M\text{-}OAc)^+$: 318.0953. Found: 318.0938.

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(1-tosyl-1*H*-indol-2-yl)propyl acetate (148g).

This compound was prepared following the general procedure-**7** and isolated as pale yellow



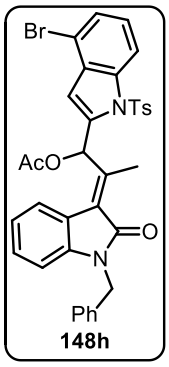
148g

solid. M.P = 180-182 ˚C. R_f = 0.4 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2926, 1746, 1698, 1608, 1467, 1367, 1229, 1175, 1090, 1020, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.69 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.21 (m, 5H), 7.25 – 7.12 (m, 5H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.52 (s, 1H), 4.97 (d, *J* = 15.7 Hz, 1H), 4.90 (d, *J* = 15.7 Hz, 1H), 2.45 (s, 3H), 2.27 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.1, 166.3, 148.8, 144.7, 142.8, 137.9, 137.2, 136.3, 135.4, 129.7 (2C), 129.1, 128.8 (3C), 127.9

(2C), 127.5, 127.4 (2C), 126.0, 125.0, 124.6, 123.6, 123.0, 122.1, 121.1, 114.9, 111.16, 109.0, 69.2, 43.5, 21.7, 21.0, 17.8. **HRMS (ESI):** *m/z* calcd for $C_{33}H_{27}N_2O_3S$ $(M\text{-}OAc)^+$: 531.1742. Found: 531.1743.

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(4-bromo-1-tosyl-1*H*-indol-2-yl)propyl acetate (148h).

This compound was prepared following the general procedure-**7** and isolated as pale yellow

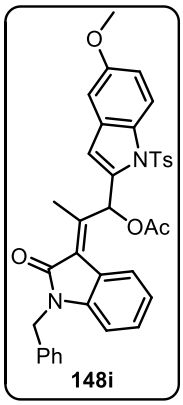


148h

semi solid. R_f = 0.4 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2923, 1747, 1694, 1608, 1467, 1376, 1245, 1171, 1090. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.67 (s, 1H), 8.13 (d, *J* = 7.7 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.36 – 7.27 (m, 5H), 7.29 – 7.17 (m, 4H), 7.12 (t, *J* = 8.1 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.54 (s, 1H), 5.00 (d, *J* = 15.8 Hz, 1H), 4.90 (d, *J* = 15.8 Hz, 1H), 2.47 (s, 3H), 2.30 (s, 3H), 2.20 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.0, 166.3, 148.3, 145.2, 142.8, 138.8, 137.4, 136.2, 135.1, 129.8 (2C), 129.4, 129.2, 128.8 (2C), 127.9 (2C), 127.59, 127.44 (2C), 126.5, 126.2, 125.9, 124.7, 122., 122.1, 114.8, 113.9, 110.4, 109.1, 69.0, 43.5, 21.7, 21.0, 17.8. **HRMS (ESI):** *m/z* calcd for $C_{33}H_{26}(^{79}Br)N_2O_3S$ $(M\text{-}OAc)^+$: 609.0848 Found: 609.0837.

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(5-methoxy-1-tosyl-1*H*-indol-2-yl)propyl acetate (148i).

This compound was prepared following the general procedure-**7** and isolated as pale yellow

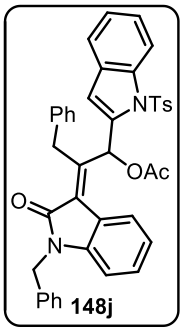


148i

oil. R_f = 0.3 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1746, 1694, 1609, 1467, 1367, 1216, 1163, 1090, 1029. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.68 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 2H), 7.92 (d, *J* = 9.1 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.19 (m, 5H), 7.17 (d, *J* = 7.8 Hz, 3H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 9.3 Hz, 1H), 6.83 (s, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.45 (s, 1H), 4.94 (q, *J* = 15.7 Hz, 2H), 3.74 (s, 3H), 2.43 (s, 3H), 2.27 (s, 3H), 2.18 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.03, 166.24, 156.48, 148.71, 144.66, 142.73, 138.59, 136.31, 135.23, 131.93, 129.78, 129.62 (2C), 129.07, 128.79 (2C), 127.77 (2C), 127.54, 127.45 (2C), 126.02, 124.64, 122.99, 122.04, 115.85, 113.93, 111.34, 108.99, 103.35, 69.18, 55.64, 43.47, 21.65, 21.02, 17.76. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{29}N_2O_4S$ $(M\text{-}OAc)^+$: 561.1848. Found: 561.1918.

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-3-phenyl-1-(1-tosyl-1*H*-indol-2-yl)propyl acetate (148j).

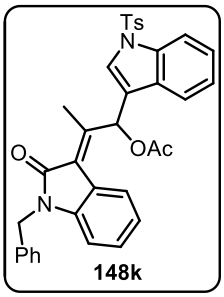
This compound was prepared following the general procedure-**7** and isolated as pale yellow solid. M.P = 182-184 °C. R_f = 0.4 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2924, 1750, 1698, 1607, 1467, 1367, 1224, 1175, 1090, 1021. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.89 (s, 1H), 8.09 (d, *J* = 7.9 Hz, 2H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.41 – 7.24 (m, 7H), 7.26 – 7.12 (m, 9H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.54 (s, 1H), 4.97 (s, 2H), 4.44 (d, *J* = 15.0 Hz, 1H), 4.18 (d, *J* = 15.0 Hz, 1H), 2.27 (s, 3H), 1.56 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.8, 166.3, 149.2, 144.7, 143.1, 138.1, 137.2, 136.2, 135.6, 135.3, 129.75, 129.6 (2C), 128.9 (2C), 128.8, 128.6 (2C), 128.5 (2C), 127.8 (2C), 127.6, 127.6 (3C), 126.5, 124.9, 124.5, 123.5, 122.4, 122.0, 121.0, 114.9, 111.57, 109.1, 68.4, 43.7, 38.0, 21.6, 20.2. **HRMS (ESI):** *m/z* calcd for $C_{39}H_{31}N_2O_3S$ $(M\text{-}OAc)^+$: 607.2055. Found: 607.2074.



148j

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(1-tosyl-1*H*-indol-3-yl)propyl acetate (148k).

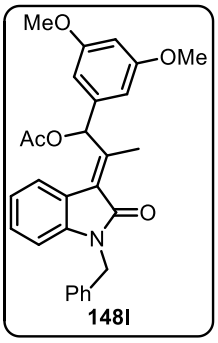
This compound was prepared following the general procedure-**7** and isolated as pale yellow oil. R_f = 0.4 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1746, 1697, 1608, 1467, 1366, 1228, 1175, 1090, 1020. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.68 (s, 1H), 8.12 (d, *J* = 8.3 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.23 (m, 6H), 7.28 – 7.14 (m, 4H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.51 (s, 1H), 4.98 (d, *J* = 15.8 Hz, 1H), 4.91 (d, *J* = 15.8 Hz, 1H), 2.45 (s, 3H), 2.29 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.1, 166.3, 148.8, 144.7, 142.8, 138.0, 137.3, 136.3, 135.4, 129.6 (2C), 129.1, 128.8 (3C), 127.8 (2C), 127.5, 127.5 (2C), 126.0, 125.0, 124.6, 123.6, 123.0, 122.0, 121.1, 114.9, 111.1, 109.0, 69.2, 43.5, 21.6, 21.0, 17.8. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{27}N_2O_3S$ $(M\text{-}OAc)^+$: 531.1742. Found: 531.1734.



148k

(*E*)-2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(3,5-dimethoxyphenyl)propyl acetate (148l).

This compound was prepared following the general procedure-**7** and isolated as pale yellow solid. M.P = 134-137 °C. R_f = 0.4 (hexane/EtOAc = 7/3**)**. **IR (thin film, neat):** ν_{max}/cm^{-1} 2934, 2840, 1744, 1694, 1608, 1467, 1429, 1351, 1230, 1157, 1028. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.62 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.36 – 7.21 (m, 5H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.97 (t,

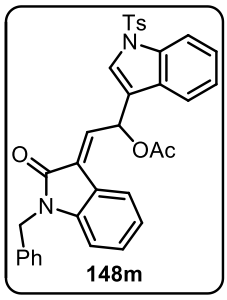


148l

J = 7.6 Hz, 1H), 6.78 – 6.69 (m, 3H), 6.38 (s, 1H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.95 (d, *J* = 15.7 Hz, 1H), 3.75 (s, 6H), 2.28 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.6, 167.0, 160.8 (2C), 151.2, 142.2, 140.8, 136., 128.82, 128.7 (2C), 127.5, 127.3 (3C), 124.4, 123.3, 122.0, 108.8, 104.2 (2C), 99.6, 71.4, 55.4 (2C), 43.4, 21.1, 15.9. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{27}NNaO_5$ $(M+Na)^+$: 480.1787. Found: 480.1802.

2-(1-Benzyl-2-oxoindolin-3-ylidene)-1-(1-tosyl-1*H*-indol-3-yl)ethyl acetate (148m).

This compound was isolated as white semi solid by following the general procedure-**7**. R_f =



148m

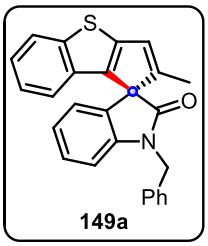
0.4 (hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1740, 1710, 1447 1370, 1697, 1608, 1467, 1366, 1228, 1175, 1090, 1020. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.7 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.34 – 7.22 (m, 4H), 7.22 – 7.12 (m, 7H), 7.04 (dd, *J* = 11.0 and 4.0 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.41 (dd, *J* = 9.1 and 5.3 Hz, 1H), 4.80 (d, *J* = 15.7 Hz, 1H), 4.59 (d, *J* = 15.7 Hz, 1H), 2.27 (s, 3H), 1.90 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 176.8, 170.1, 145.1, 143.3, 135.7, 135.0, 135.0, 129.9 (2C), 128.8, 128.7 (2C), 128.5, 128.1, 127.9, 127.5, 127.4, 127.2 (2C), 126.9 (3C), 124.9, 124.3, 123.4, 122.5, 120.8, 120.3, 113.6, 109.3, 66.3, 43.6, 42.6, 20.9.

General procedure-8: Synthesis of spirocyclic compounds (149a-149l).

An oven dried 5 mL glass vial was charged with **148a-148m** (0.1 mmol) and 1,2-DCE (1.0 mL) and $PdCl_2$ (0.01 mmol) were introduced. The reaction mixture was stirred at 60 ^{o}C until **1** disappeared as monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc. 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 (9:1 to 4:1) to afford **149a-149m**.

1'-Benzyl-2-methylspiro[benzo[*b*]cyclopenta[*d*]thiophene-1,3'-indolin]-2'-one (149a).

This compound was isolated as pale brown solid. Following the general procedure-**8**, 30 mg of



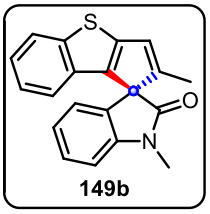
149a

148a afforded 21 mg of **149a** (82% yield). M.P = 168-170 $^\circ$C. R_f = 0.4 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 2853, 1694, 1662, 1618, 1599, 1481, 1362, 1289, 1234, 1089, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.0 Hz, 2H), 7.39 – 7.30 (m,

3H), 7.26 – 7.20 (m, 1H), 7.14 – 7.00 (m, 2H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.92 (td, *J* = 7.6 and 0.7 Hz, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 6.72 (t, *J* = 8.0 Hz, 2H), 5.16 (d, *J* = 15.3 Hz, 1H), 4.97 (d, *J* = 15.3 Hz, 1H), 1.84 (d, *J* = 1.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.7, 150.4, 147.2, 144.1, 143.4, 140.7, 136.0, 133.0, 128.9 (2C), 128.8, 128.0 (3C), 127.0, 125.7, 124.6, 123.8, 123.78, 123.33, 122.8, 119.5, 109.6, 65.2, 44.6, 13.8. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{19}NNaOS$ $(M+Na)^+$: 416.1085. Found: 416.1079.

1',2-Dimethylspiro[benzo[*b*]cyclopenta[*d*]thiophene-1,3'-indolin]-2'-one (149b).

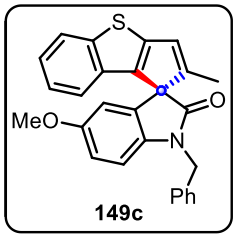
This compound was isolated as a pale brown oil. Following the general procedure-**8**, 30 mg of



148b afforded 18 mg of **149b** (73% yield). R_f = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1716, 1609, 1492, 1468, 1371, 1342, 1259, 1084. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.81 – 7.74 (m, 1H), 7.36 (td, *J* = 7.8, 1.1 Hz, 1H), 7.16 – 7.06 (m, 2H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.98 (dd, *J* = 11.0 and 4.0 Hz, 1H), 6.81 (dd, *J* = 6.6 and 2.3 Hz, 1H), 6.77 – 6.72 (m, 2H), 3.41 (s, 3H), 1.80 (d, *J* = 1.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.6, 150.4, 147.1, 145.0, 143.4, 140.5, 132.9, 128.9, 126.9, 125.6, 124.7, 123.8, 123.6, 123.3, 122.8, 119.2, 108.6, 65.1, 27.2, 13.7. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}NOS$ $(M+H)^+$: 318.0953. Found: 318.0941.

1'-Benzyl-5'-methoxy-2-methylspiro[benzo[*b*]cyclopenta[*d*]thiophene-1,3'-indolin]-2'-one (149c).

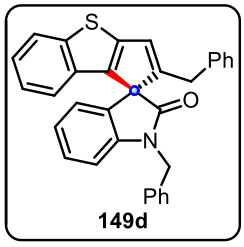
This compound was isolated as reddish brown solid. Following the general procedure-**8**, 25 mg



of **148c** afforded 17 mg of **149c** (77% yield). M.P = 170-173 ˚C. R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 2854, 1712, 1600, 1493, 1439, 1337, 1174. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 6.7 Hz, 2H), 7.37-7.31(m, 3H), 7.17 – 7.10 (m, 1H), 7.08 – 7.03 (m, 1H), 6.86 (d, *J* = 8.6 Hz, 1H), 6.79 – 6.72 (m, 3H), 6.34 (d, *J* = 2.5 Hz, 1H), 5.13 (d, *J* = 15.3 Hz, 1H), 4.95 (d, *J* = 15.3 Hz, 1H), 3.61 (s, 3H), 1.85 (d, *J* = 1.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.4, 156.4, 150.5, 147.2, 143.5, 141.0, 140.8, 137.4, 136.1, 133.0, 128.9 (2C), 128.3, 128.0 (2C), 125.7, 124.6, 123.8, 122.9, 119.6, 113.6, 110.3, 110.1, 65.5, 55.7, 44.7, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{22}NO_2S$ $(M+H)^+$: 424.1371. Found: 424.1357.

1',2-Dibenzylspiro[benzo[*b*]cyclopenta[*d*]thiophene-1,3'-indolin]-2'-one (149d).

This compound was isolated as pale yellow oil. Following the general procedure-**8**, 35 mg of

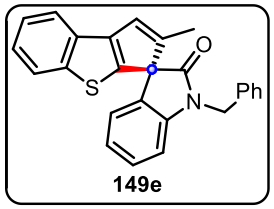


149d

148d afforded 24 mg of **149d** (78% yield). R_f = 0.6 (Hexane/EtOAc = 8/2). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.33 (dd, *J* = 14.8 and 7.1 Hz, 3H), 7.29 – 7.17 (m, 4H), 7.13-7.07 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 8.3 Hz, 2H), 6.52 (s, 1H), 5.11 (d, *J* = 15.3 Hz, 1H), 4.82 (d, *J* = 15.3 Hz, 1H), 3.48 (d, *J* = 16.9 Hz, 1H), 3.33 (d, *J* = 16.9 Hz, 1H). **^{13}C NMR (100 MHZ, $CDCl_3$):** δ 173.4, 154.3, 146.9, 144.1, 143.5, 140.9, 137.7, 136.0, 132.8, 129.5 (2C), 128.9 (2C), 128.9, 128.4 (2C), 128.0 (3C), 126.8, 126.6, 126.4, 124.6, 123.9, 123.8, 123.3, 122.9, 119.6, 109.6, 64.8, 44.6, 35.1. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{24}NOS$ $(M+H)^+$: 470.1579. Found: 470.1560.

1'-Benzyl-2-methylspiro[benzo[*b*]cyclopenta[*d*]thiophene-3,3'-indolin]-2'-one (149e).

This compound was isolated as pale brown oil. Following the general procedure-**8**, 30 mg of

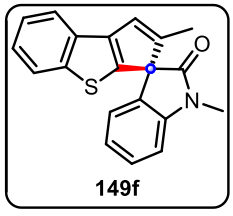


149e

148e afforded 20 mg of **149e** (73% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3058, 2933, 1716, 1609, 1486, 1465, 1428, 1341, 1191, 1079. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.84 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.46 – 7.34 (m, 5H), 7.33 – 7.17 (m, 3H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.91 (s, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 7.4 Hz, 1H), 5.09 (d, *J* = 15.6 Hz, 1H), 4.98 (d, *J* = 15.6 Hz, 1H), 1.81 (s, 3H). **^{13}C NMR (100 MHZ, $CDCl_3$):** δ 173.9, 149.3, 145.8, 145.1, 143.9, 143.1, 135.8, 132.2, 129.1, 129.0 (2C), 127.9, 127.8, 127.5 (2C), 124.8, 124.6, 124.1, 123.8, 123.7, 123.4, 122.0, 109.8, 66.0, 44.5, 14.0. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{19}NNaOS$ $(M+Na)^+$ 416.1085. Found: 416.1094.

1',2-Dimethylspiro[benzo[*b*]cyclopenta[*d*]thiophene-3,3'-indolin]-2'-one (149f).

This compound was isolated as pale reddish oil. Following the general procedure-**8**, 25 mg of



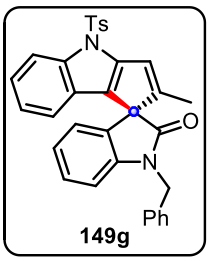
149f

148f afforded 17 mg of **149f** (83% yield). R_f = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2958, 1716, 1608, 1490, 1469, 1340, 1245, 1124, 1086, 1017. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.45 – 7.25 (m, 3H), 7.00 (dd, *J* = 18.4 and 7.5 Hz, 2H), 6.88 (s, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 3.35 (s, 3H), 1.75 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.7, 149.4, 145.9, 145.1, 144.9, 142.7, 132.2, 129.4, 127.8, 124.5, 124.0,

123.8, 123.5, 123.4, 122.0, 108.7, 66.1, 29.8, 27.2, 13.7. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{15}NNaOS$ $(M+Na)^+$: 340.0772. Found: 340.0780.

1'-Benzyl-2-methyl-4-tosyl-4*H*-spiro[cyclopenta[*b*]indole-1,3'-indolin]-2'-one (149g).

This compound was isolated as pale yellow solid. Following the general procedure-**8**, 25 mg

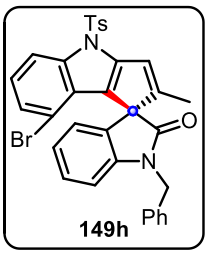


149g

of **148g** afforded 18 mg of **149g** (83% yield). M.P = 187-190 °C. R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 2925, 1716, 1609, 1486, 440, 1372, 1216, 1175. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.38 – 7.28 (m, 3H), 7.22 (dd, *J* = 17.6 and 7.5 Hz, 3H), 7.15 – 7.08 (m, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 2H), 6.65 (d, *J* = 7.1 Hz, 2H), 5.09 (d, *J* = 15.4 Hz, 1H), 4.96 (d, *J* = 15.4 Hz, 1H), 2.33 (s, 3H), 1.84 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.6, 151.9, 147.8, 145.1, 144.1, 138.8, 136.0, 135.1, 130.1 (2C), 128.9 (2C), 128.9, 128.0, 127.7 (3C), 126.9 (2C), 126.6, 125.3, 123.8, 123.5, 123.2, 123.0, 122.6, 117.4, 114.7, 109.7, 62.5, 44.5, 21.7, 14.1. **HRMS (ESI):** *m/z* calcd for $C_{33}H_{26}N_2NaO_3S$ $(M+Na)^+$: 553.1562. Found: 553.1557.

1'-Benzyl-8-bromo-2-methyl-4-tosyl-4*H*-spiro[cyclopenta[*b*]indole-1,3'-indolin]-2'-one (149h).

This compound was isolated as pale brown oil. Following the general procedure-**8**, 40 mg of

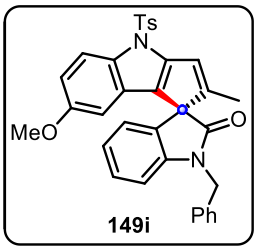


149h

148h afforded 28 mg of **149h** (77% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2930, 1716, 1610, 1487, 1466, 1360, 1171, 1089. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.99 – 7.87 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 7.0 Hz, 2H), 7.39 – 7.30 (m, 3H), 7.28-7.25 (m, 2H), 7.22 (td, *J* = 7.8 and 1.2 Hz, 1H), 7.18 – 7.13 (m, 1H), 7.07 (d, *J* = 1.7 Hz, 1H), 6.99 – 6.86 (m, 3H), 6.62 (d, *J* = 6.8 Hz, 1H), 5.22 (d, *J* = 15.3 Hz, 1H), 4.75 (d, *J* = 15.3 Hz, 1H), 2.35 (s, 3H), 1.78 (d, *J* = 1.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.8, 153.7, 149.7, 145.6, 144.9, 139.0, 135.9, 134.8, 130.2, 128.9 (2C), 128.8, 128.1 (2C), 127.97 (2C), 127.2, 127.1, 127.0, 127.0 (2C), 124.6, 123.7, 123.1, 123.0, 121.0, 113.4, 111.8, 109.5, 63.0, 45.0, 21.7, 14.0. **HRMS (ESI):** *m/z* calcd for $C_{33}H_{26}(^{79}Br)N_2O_3S$ $(M+H)^+$: 609.0848. Found: 609.0837.

1'-Benzyl-7-methoxy-2-methyl-4-tosyl-4*H*-spiro[cyclopenta[*b*]indole-1,3'-indolin]-2'-one (149i).

This compound was isolated as pale yellow oil. Following the general procedure-**8**, 35 mg of

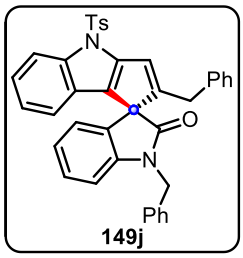


149i

148i afforded 26 mg of **149i** (83% yield). R_f = 0.4 (Hexane/EtOAc = 7/3)**. IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 1716, 1609, 1486, 1455, 1434, 1274, 1171, 1088, 1034. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.87 (d, *J* = 9.1 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.36 – 7.27 (m, 3H), 7.21 (dd, *J* = 14.3 and 8.0 Hz, 3H), 7.09 (s, 1H), 6.90 (dd, *J* = 7.6 and 4.8 Hz, 2H), 6.71 (dd, *J* = 9.0 and 2.3 Hz, 1H), 6.63 (d, *J* = 7.5 Hz, 1H), 6.11 (d, *J* = 2.2 Hz, 1H), 5.11 (d, *J* = 15.4 Hz, 1H), 4.94 (d, *J* = 15.4 Hz, 1H), 3.56 (s, 3H), 2.32 (s, 3H), 1.82 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.6, 156.8, 152.1, 148.7, 145.0, 144.0, 136.0, 134.9, 133.4, 130.0 (2C), 128.9 (2C), 128.9, 127.9, 127.6 (2C), 126.8 (2C), 126.5, 126.4, 126.3, 123.4, 123.3, 122.6, 115.5, 110.8, 109.6, 100.8, 62.4, 55.5, 44.5, 21.7, 14.0. **HRMS (ESI):** *m/z* calcd for $C_{34}H_{28}N_2NaO_4S$ $(M+Na)^+$: 583.1667. Found: 583.1680.

1',2-Dibenzyl-4-tosyl-4*H*-spiro[cyclopenta[*b*]indole-1,3'-indolin]-2'-one (149j).

This compound was isolated as pale yellow oil. Following the general procedure-**8**, 35 mg of

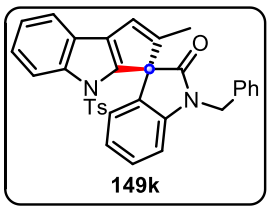


149j

148j afforded 23 mg of **149j** (73% yield). R_f = 0.6 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2919, 2854, 1713, 1609, 1485, 1465, 1342, 1173. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.38 – 7.31 (m, 3H), 7.30 – 7.18 (m, 6H), 7.17 – 7.10 (m, 1H), 7.12 – 7.05 (m, 2H), 7.04 – 6.96 (m, 1H), 6.95 (t, *J* = 1.7 Hz, 1H), 6.93 – 6.85 (m, 2H), 6.64 (dd, *J* = 12.1 and 7.6 Hz, 2H), 5.05 (d, *J* = 15.4 Hz, 1H), 4.80 (d, *J* = 15.4 Hz, 1H), 3.50 (dd, *J* = 16.8 and 1.8 Hz, 1H), 3.35 (dd, *J* = 16.9, 1.0 Hz, 1H), 2.35 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.3, 155.5, 147.6, 145.1, 144.1, 138.8, 137.4, 136.0, 135.1, 130.0 (2C), 129.3 (2C), 128.9 (2C), 128.9, 128.4 (2C), 128.0, 127.7 (2C), 127.1, 126.9 (2C), 126.7, 126.4, 125.2, 123.9, 123.7, 123.2, 123.26, 123.1, 117.6, 114.8, 109.6, 62.2, 44.5, 35.4, 21.7. **HRMS (ESI):** *m/z* calcd for $C_{39}H_{31}N_2O_3S$ $(M+H)^+$: 607.2055. Found: 607.2031.

1'-Benzyl-2-methyl-4-tosyl-4*H*-spiro[cyclopenta[*b*]indole-3,3'-indolin]-2'-one (149k).

This compound was isolated as pale yellow oil. Following the general procedure-**8**, 10 mg of **148k** afforded 7.1 mg of **149k** (79% yield). R_f = 0.4 (Hexane/EtOAc = 9/1). **IR (thin film,**

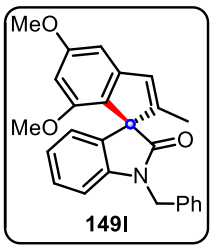


149k

neat): ν_{max}/cm^{-1} 2922, 2847, 1715, 1610, 1466, 1372, 1175, 1089. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.28 (m, 4H), 7.31 – 7.18 (m, 4H), 7.11 (dd, *J* = 8.1 and 6.4 Hz, 3H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 5.09 (d, *J* = 15.4 Hz, 1H), 4.97 (d, *J* = 15.4 Hz, 1H), 2.35 (s, 3H), 1.84 (d, *J* = 1.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 172.8, 152.7, 147.6, 146.3, 144.2, 138.2, 136.9, 134.3, 130.9 (2C), 129.5, 129.2 (2C), 128.2, 127.9 (2C), 127.1 (2C), 126.6, 126.0, 124.9, 124.6, 123.6, 123.5, 123.2, 122.3, 117.3, 114.9, 110.6, 62.3, 43.9, 21.5, 14.0. **HRMS (ESI):** *m/z* calcd for $C_{33}H_{26}N_2NaO_3S$ $(M+Na)^+$: 553.1562. Found: 553.1583.

1'-Benzyl-4,6-dimethoxy-2-methylspiro[indene-1,3'-indolin]-2'-one (148l).

This compound was isolated as pale orange solid. Following the general procedure-**8**, 30 mg

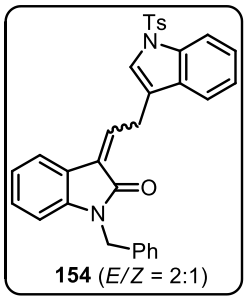


149l

of **148l** afforded 23 mg of **149l** (89% yield). M.P = 135-137 °C. R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2937, 1713, 1604, 1589, 1486, 1465, 1346, 1228, 1171, 1088. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.42 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.24 (m, 1H), 7.14 (t, *J* = 7.7 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 7.3 Hz, 1H), 6.60 (d, *J* = 1.1 Hz, 1H), 6.54 (d, *J* = 1.6 Hz, 1H), 6.19 (d, *J* = 1.5 Hz, 1H), 5.29 (d, *J* = 15.7 Hz, 1H), 4.80 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 3H), 3.47 (s, 3H), 1.68 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 175.2, 161.9, 154.9, 148.4, 148.2, 144.3, 136.3, 130.1, 128.7 (2C), 128.3, 128.0, 127.6, 127.5 (2C), 124.1, 122.7, 122.6, 109.1, 98.8, 95.9, 65.6, 55.7, 55.2, 44.2, 13.1. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{23}NaO_3S$ $(M+Na)^+$ 420.1576. Found: 420.1550.

1-Benzyl-3-(2-(1-tosyl-1*H*-indol-3-yl)ethylidene)indolin-2-one (154).

This compound was isolated as pale brown oil. Following the general procedure-**8**, 30 mg of



154 (*E*/*Z* = 2:1)

148m afforded 20 mg of **154** (73% yield). R_f = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2937, 1701, 1608, 1589, 1466, 1465, 1361, 1171, 1098, 750. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.48 (s, 1H), 7.40 – 7.28 (m, 7H), 7.25 – 7.20 (m, 3H), 7.20 – 7.13 (m, 1H), 7.02 – 6.93 (m, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.00 (s, 2H), 4.48 (d, *J* = 7.0 Hz,

2H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 167.8, 145.0, 143.1, 137.5, 136.0, 135.4, 135.2, 130.4 (2C), 130.0, 129.4, 128.9, 128.9 (2C), 127.7, 127.4 (2C), 126.9 (2C), 125.19, 123.8, 123.5, 123.4, 122.4, 121.9, 119.4, 118.8, 113.9, 109.4, 43.8, 25.3, 21.7. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{27}N_2O_3S$ $(M+H)^+$: 519.1742. Found: 519.1749.

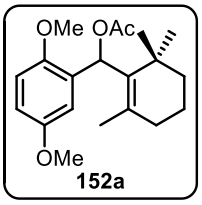
General procedure-9: Synthesis of allylic acetates 152a-152i and 155

A representative procedure for step-1 (Scheme 52): An oven dried 25 mL long neck RB flask was charged with aryl bromide (975 mg, 3.95 mmol), 5 mL dry THF and placed at -78 °C. *n*-BuLi (1.6 *M* in hexanes, 2.26 mL, 3.6 mmol), was added dropwise at same temperature and stirred for 2 h. Enal **150** (500 mg, 3.28 mmol) dissolved in 1 mL dry THF, was added dropwise over 2 mins and stirred at room temperature for 30 min. The reaction mixture was quenched with saturated *aq*. ammonium chloride solution and extracted using ethyl acetate. The organic extracts were combined and dried over anhydrous sodium sulphate and concentrated. The crude product **151** was taken to next step without purification.

A representative procedure for step-2 (Scheme 52): Alcohol **151** (400 mg, 1.25 mmol) was dissolved in dry DCM (6.0 mL) and triethylamine (0.20 mL, 1.3 mmol), acetic anhydride (0.13 mL, 1.3 mmol), DMAP (15 mg, 0.11 mmol) were added. Then the reaction mixture was stirred until starting material disappeared (by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane as an eluent to afford **152a-152i** and **155**.

(2,5-Dimethoxyphenyl)(2,6,6-trimethylcyclohex-1-en-1-yl)methyl acetate (152a).

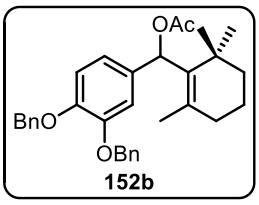
This compound was prepared following the general procedure-**9** and isolated as pale yellow oil. R_f = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2867, 2834, 1739, 1588, 1495, 1464, 1429, 1239. **^{1}H NMR (400 MHz, CDCl3):** δ 6.93 (s, 1H), 6.82 (d, *J* = 1.2 Hz, 2H), 6.76 (s, 1H), 3.80 (s, 3H), 7.76 (s, 3H), 2.14-2.05 (m, 2H), 2.03 (s, 3H), 1.35 (s, 3H), 1.71-1.62 (m, 2H), 1.50-1.43 (m, 2H), 1.24 (s, 3H), 0.77 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 169.5, 152.9, 152.2, 134.2, 134.1, 128.5, 116.8, 112.6, 111.3, 69.5, 55.8, 55.6, 40.0, 34.7, 33.8, 29.0, 27.9, 22.4, 21.1, 19.0. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{25}O_2$ $(M-OAc)^+$: 273.1855. Found: 273.1858.



152a

(3,4-Bis(benzyloxy)phenyl)(2,6,6-trimethylcyclohex-1-en-1-yl)methyl acetate (152b).

This compound was prepared following the general procedure-**9** and isolated as colorless oil.

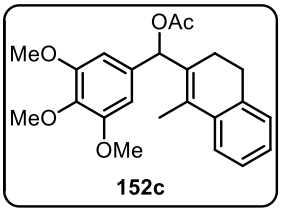


152b

Rf = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 1736, 1509, 1453, 1377, 1235, 1135, 1020, 734. **^{1}H NMR (400 MHz, CDCl3):** δ 7.49-7.47 (m, 2H), 7.43-7.33 (m, 8H), 6.90-6.88 (m, 1H), 6.77-6.74 (m, 2H), 6.60 (s, 1H), 5.19 (s, 4H), 2.11 (s, 3H), 2.00-1.95 (m, 2H), 1.65-1.58 (m, 2H), 1.46-1.42 (m, 2H), 1.43 (s, 3H), 1.04 (s, 3H), 0.87 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.4, 148.1, 147.9, 137.4, 137.3, 135.4, 134.9, 133.7, 128.54 (2C), 128.52 (2C), 127.8, 127.6, 127.3 (2C), 126.9 (2C), 119.9, 114.4, 114.3, 72.4, 71.25, 71.22, 39.8, 34.6, 33.5, 28.7, 28.2, 21.8, 21.4, 19.1. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{33}O_2$ $(M\text{-}OAc)^+$: 425.2481. Found: 425.2500.

(1-Methyl-3,4-dihydronaphthalen-2-yl)(3,4,5-trimethoxyphenyl)methyl acetate (152c).

This compound was prepared following the general procedure-**9** and isolated as colorless oil.

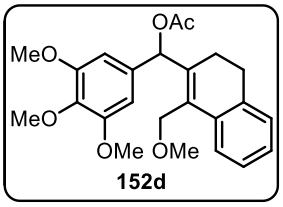


152c

Rf = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2937, 2839, 1739, 1590, 1415, 1234, 1012, 762. **^{1}H NMR (400 MHz, CDCl3):** δ 7.40 (d, *J* = 7.8Hz, 1H), 7.26-7.16 (m, 3H), 6.98 (s, 1H), 6.60 (s, 2H), 3.87 (9H), 2.75-2.71 (m, 2H), 2.37-2.32 (m, 4H), 2.21 (s, 3H), 2.18-2.09 (m, 1H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.0, 153.2 (2C), 137.3, 136.3, 136.0, 134.8, 132.9, 130.0, 127.1, 127.0, 126.5, 123.8, 103.1 (2C), 74.2, 60.8, 56.1 (2C), 28.5, 23.1, 21.2, 14.6. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{23}O_3$ $(M\text{-}OAc)^+$: 323.1647. Fo1und: 323.1662.

(2-(Methoxymethyl)-3,4-dihydronaphthalen-1-yl)(3,4,5-trimethoxyphenyl)methyl acetate (152d).

This compound was prepared following the general procedure-**9** and isolated as pale yellow



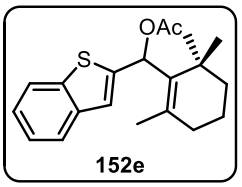
152d

oil. Rf = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2936, 1741. **^{1}H NMR (400 MHz, CDCl3):** δ 7.33 (d, *J* = 7.6 Hz, 1H), 7.19-7.09 (m, 4H), 6.59 (s, 2H), 4.45 (d, *J* = 11.7 Hz, 1H), 4.19 (d, *J* = 12 Hz, 1H), 3.84 (s, 3H), 3.60 (s, 6H), 3.38 (s, 3H), 2.80 (t, *J* = 7.7 Hz, 2H), 2.49 (d, *J* = 8.8 Hz, 2H), 2.18 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.2, 153.2 (2C), 139.3, 137.3, 136.8, 134.6, 133.1, 131.3, 127.2, 126.8, 125.2, 103.5 (2C), 72.2, 72.0, 60.8, 58.4,

56.11 (2C), 56.10, 28.4, 26.4, 21.3. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{25}O_2$ $(M\text{-}OAc)^+$: 273.1855. Found: 273.1858.

Benzo[*b*]thiophen-2-yl(2,6,6-trimethylcyclohex-1-en-1-yl)methyl acetate (152e).

This compound was prepared following the general procedure-**9** and isolated as pale reddish

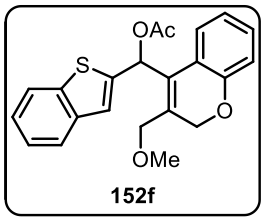


152e

oil. Rf = 0.4 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1}2932, 2867, 1742, 1436, 1458, 1366, 1232, 1014, 957. **^{1}H NMR (400 MHz, CDCl3):** δ 7.82-7.73 (m, 2H), 7.38-7.30 (m, 2H), 7.14 (s, 1H), 6.94 (s, 1H), 2.24 (s, 3H), 2.14-2.12 (m, 2H), 1.78 (s, 3H), 1.74-1.71 (m, 2H), 1.60-1.49 (m, 2H), 1.18 (s, 3H), 1.13 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.1, 146.0, 139.9, 139.5, 136.9, 135.6, 124.2, 124.1, 123.4, 122.1, 121.8, 69.5, 39.8, 34.8, 33.7, 28.9, 28.1, 22.2, 21.3, 19.2. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{21}S$ $(M\text{-}OAc)^+$: 269.1364. Found: 269.1353.

Benzo[*b*]thiophen-2-yl(3-(methoxymethyl)-2H-chromen-4-yl)methyl acetate (152f).

This compound was prepared following the general procedure-**9** and isolated as pale reddish

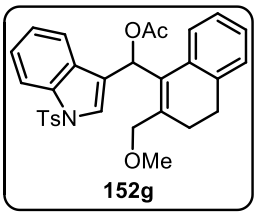


152f

oil. R_f = 0.3 (hexane/EtOAc = 8/1**)**. **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2939, 1457, 1375, 1224, 1098. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 7.1 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.34 (s, 2H), 7.31 – 7.22 (m, 1H), 7.16 (s, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 4.85 (d, *J* = 14.7 Hz, 1H), 4.77 (d, *J* = 14.7 Hz, 1H), 4.44 (d, *J* = 12.7 Hz, 1H), 4.28 (d, *J* = 12.8 Hz, 1H), 3.35 (s, 3H), 2.17 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 169.9, 154.6, 142.6, 139.8, 139.5, 132.7, 129.3, 128.3, 125.9, 124.6, 124.5, 123.8, 122.3, 122.1, 121.4, 121.2, 116.3, 69.4, 68.5, 66.5, 58.6, 21.1. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}O_2S$ $(M\text{-}OAc)^+$: 321.0949. Found: 321.0940.

(2-(Methoxymethyl)-3,4-dihydronaphthalen-1-yl)(1-tosyl-1H-indol-3-yl)methyl acetate (152g).

This compound was prepared following the general procedure-**9** and isolated as pale reddish



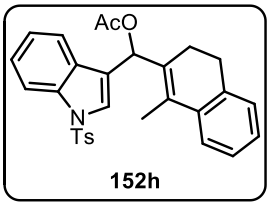
152g

oil. R_f = 0.4 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 1742, 1599, 1447, 1373, 1230, 1175, 1097, 982. **^{1}H NMR (400 MHz, CDCl3):** δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J*= 7.8 Hz, 1H), 7.49-7.46 (m, 2H), 7.43 (d, *J*= 1.0 Hz, 1H), 7.38-7.34 (m, 1H), 7.30-7.26 (m, 1H), 7.22-7.16 (m, 4H), 7.10-7.06 (m, 1H), 4.53 (d, *J* = 11.7 Hz,

1H), 4.23 (d, *J* = 12.0 Hz, 1H), 3.39 (s, 3H), 2.86-2.82 (m, 2H), 2.63-2.48 (m, 2H), 2.37 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.0, 145, 139.6, 136.9, 135.5, 134.9, 133.1, 130.6, 129.9 (2C), 129.0, 127.5, 126.9, 126.8 (2C), 125.9, 125.32, 125.30, 125.06, 123.5, 121.0, 120.2, 113.8, 71.8, 67.3, 58.4, 28.3, 26.3, 21.6, 21.2. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{21}S$ $(M\text{-}OAc)^+$: 269.1364. Found: 269.1353.

(1-Methyl-3,4-dihydronaphthalen-2-yl)(1-tosyl-1*H*-indol-3-yl) methyl acetate (152h).

This compound was prepared following the general procedure-**9** and isolated as pale brownish

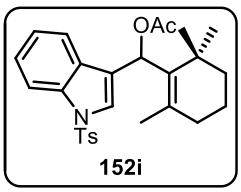


152h

oil. Rf = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 1740, 1598, 1449, 1372, 1229, 1176, 1089, 1021, 920, 812, 757, 663, 575, 540. **^{1}H NMR (400 MHz, CDCl3):** δ 8.00-7.97 (m, 1H), 7.78-7.76 (m, 2H), 7.58 (d, *J* = 1.2 Hz, 1H), 7.43-7.40 (m, 2H), 7.35-7.31 (m, 2H), 7.26-7.24 (m, 4H), 7.20-7.18 (m, 2H), 2.71-2.65 (m, 2H), 2.38-2.37 (m, 6H), 2.32-2.29 (m, 2H) 2.22 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.0, 145.0, 136.1 (2C), 135.4, 135.0, 131.4, 130.6, 129.9 (2C), 128.6, 127.2, 127.1, 126.8 (2C), 126.5, 125.0, 123.9, 123.8, 123.4, 120.8, 119.9, 113.8, 69.4, 28.4, 23.0, 21.6, 21.2, 14.6. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{24}NO_2S$ $(M\text{-}OAc)^+$: 426.1528. Found: 426.1535.

(1-Tosyl-1*H*-indol-3-yl)(2,6,6-trimethylcyclohex-1-en-1-yl)methyl acetate (152i).

This compound was prepared following the general procedure-**9** and isolated as pale yellow

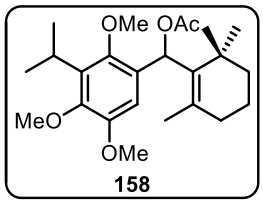


152i

oil. Rf = 0.4 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** νmax/cm^{-1} 2928, 1734, 1597, 1446, 1372, 1174, 1018, 974, 812, 747. **^{1}H NMR (400 MHz, CDCl3):** δ 7.99 (d, *J* = 8.3 Hz, 1H), 7.74-7.72 (m, 2H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 1.2 Hz, 1H), 7.34 (td, *J* = 7.8 Hz, 1H), 7.29-7.21 (m, 4H), 6.83 (s, 1H), 2.35 (s, 3H), 2.22-2.05 (m, 2H), 2.09 (s, 3H), 1.79 (s, 3H), 1.72-1.68 (m, 2H), 1.55-1.51 (m, 2H), 1.18 (s, 3H), 0.87 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 170.1, 145.0, 135.6, 135.02, 135.00, 134.9, 129.8 (2C), 129.5, 126.8 (2C), 126.4, 124.8, 123.5, 122.0, 119.9, 113.8, 66.5, 39.8, 34.6, 33.6, 29.2, 27.8, 22.3, 21.5, 21.3, 19.0. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{28}NO_2S$ $(M\text{-}OAc)^+$: 406.1841. Found: 406.1839.

(3-Isopropyl-2,4,5-trimethoxyphenyl)(2,6,6-trimethylcyclohex-1-en-1-yl)methyl acetate (158).

This compound was prepared following the general procedure-**9** and isolated as pale reddish oil. Rf = 0.4 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 1738, 1480, 1236, 1105, 1042, 954. **^{1}H NMR (400 MHz, CDCl3):** δ 6.82 (s, 1H), 6.77 (s, 1H), 3.88 (s, 3H), 3.78 (s, 3H), 3.70 (s, 3H), 3.42-3.35 (m, 1H), 2.13-2.06 (m, 2H), 2.06 (s, 3H), 1.80 (s, 3H), 1.70-1.60 (m, 2H), 1.52-1.46 (m, 2H), 1.38-1.34 (m, 6H), 1.26 (s, 3H), 0.74 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 169.6, 150.8, 149.3, 148.8, 135.2, 135.0, 133.3, 126.7, 111.8, 70.0, 62.0, 60.6, 55.8, 40.2, 34.7, 33.9, 29.3, 27.9, 26.1, 22.6, 21.9, 21.8, 21.3, 19.0. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{33}O_3$ $(M\text{-}OAc)^+$: 345.2430. Found: 345.2418.

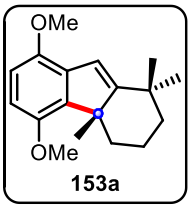


158

General procedure-10: Synthesis of of cyclopentene-fused arenes and heteroarenes

An oven dried 5 mL glass vial was charged with **152a** (0.15 mmol), and solvent (1.0 mL) and catalyst (0.015 mmol) were introduced. Stirring continued at 80 ^oC until **152a** disappeared as monitored by TLC. Then the reaction was quenched with water and extracted with EtOAc. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **153**.

5,8-Dimethoxy-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1*H*-fluorene (153a).

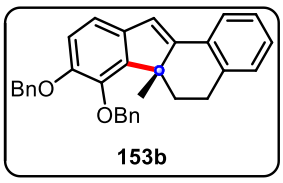


153a

This compound was prepared following the general procedure-**10** and isolated as pale reddish oil. 25 mg of **152a** afforded 22 mg of **153a** (88% yield). Rf = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1752, 1493, 1461, 1383, 1251, 1086. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.71-6.69 (m, 1H), 6.62-6.59 (m, 1H), 6.48 (s, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 2.57-2.52 (m, 1H), 2.00-1.89 (m, 1H), 1.67-1.57 (m, 2H), 1.47 (s, 3H), 1.31 (s, 3H), 1.26 (s, 3H), 1.17-1.01 (m, 2H). **^{13}C NMR (100 MHz, CDCl3):** δ 164.1, 149.9, 147.2, 142.6, 131.8, 116.2, 109.0, 107.4, 55.9, 55.6, 52.5, 42.7, 35.8, 35.6, 31.4, 25.4, 19.9, 19.4. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{25}O_2$ $(M+H)^+$: 273.1855. Found: 273.1844.

7,8-Bis(benzyloxy)-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1*H*-fluorene (153b).

This compound was prepared following the general procedure-**10** and isolated as colorless oil. 30 mg of **152b** afforded 21 mg of **153b** (81% yield). R_f = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2958, 2926, 1614, 1484, 1453, 1317, 1137, 1027, 736. **^{1}H NMR (400**

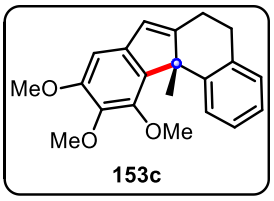


153b

MHz, $CDCl_3$): δ 7.54-7.29 (m, 10H), 6.97 (d, *J* = 12.2 Hz, 2H), 6.30 (s, 1H), 5.22-5.20 (m, 4H), 2.16-2.09 (m, 1H), 2.00-1.96 (m, 1H), 1.71-1.60 (m, 2H), 1.36 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.18-1.10 (m, 1H), 1.05-0.91 (m, 1H). **^{13}C NMR (100 MHz, CDCl3):** δ 163.4, 148.57, 148.51, 146.4, 137.8, 137.7, 135.9, 128.48 (2C), 128.40 (2C), 127.7 (4C), 127.3 (2C), 120.2, 110.5, 108.0, 72.6, 71.7, 50.9, 42.7, 38.2, 35.5, 31.3, 25.3, 23.5, 19.8. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{33}O_2$ $(M+H)^+$: 425.2481. Found**:** 425.2475.

7,8-Bis(benzyloxy)-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1*H*-fluorene (153c).

This compound was prepared following the general procedure-**10** and isolated as colorless oil.

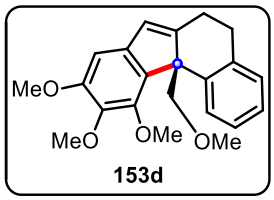


153c

30 mg of **152c** afforded 21 mg of **153c** (80% yield). Rf = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2839, 1601, 166, 1408, 1355, 1199, 1109, 1021, 988. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.20 (d, *J* = 7.8 Hz, 1H), 7.28-7.13 (m, 3H), 6.65 (s, 1H), 6.33 (s, 1H), 4.11 (s, 3H), 3.95 (s, 3H), 3.90 (s, 3H), 3.31-3.26 (m, 1H), 3.05-2.1 (m, 3H), 1.70 (s, 3H). **^{13}C NMR (100 MHz, CDCl3): δ** 156.5, 15.34, 150.8, 142.7, 140.0, 139.7, 136.1, 134.2, 128.9, 128.4, 126.3, 126.2, 121.2, 100.2, 60.9, 56.8, 56.1, 32.6 (2C), 24.7, 23.2. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{23}O_3$ $(M+H)^+$: 323.1647. Found**:** 323.1662.

7,8,9-Trimethoxy-6a-(methoxymethyl)-6,6a-dihydro-5*H*-benzo[*a*]fluorine (153d)

This compound was prepared following the general procedure-**10** and isolated as colorless oil.

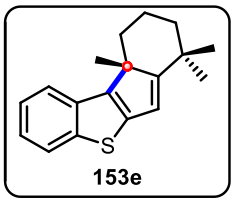


153d

30 mg of **152d** afforded 20 mg of **153d** (78% yield). Rf = 0.5 (Hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2935, 2366, 1604, 1576, 1465, 1354, 1237, 1109, 1022, 761. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.69-7.67 (m, 1H), 7.29-7.23 (m, 3H), 6.79 (s, 1H), 6.77 (s, 1H), 4.02 (s, 3H), 4.01-3.99 (m, 1H), 3.92 (s, 6H), 3.65 (d, *J* = 9.0 Hz, 1H), 3.13 (s, 3H), 2.97-2.79 (m, 2H), 1.64 (dt, *J* = 13.1 and 6.5, 2H). **^{13}C NMR (100 MHz, CDCl3):** δ 153.5, 150.7, 150.2, 140.1, 139.9, 135.7, 133.3, 132.0, 128.9, 127.5, 126.3, 125.3, 123.3, 101, 74.2, 60.9, 60.8, 60.5, 59.5, 56.14, 56.13, 54.6. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{26}O_4$ $(M+H)^+$: 353.1753. Found: 354.1744.

7,7,10a-Trimethyl-8,9,10,10a-tetrahydro-7*H*-benzo[*b*]indeno[1,2-*d*]thiophene (153e).

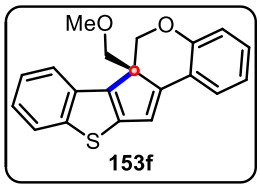
This compound was prepared following the general procedure-**10** and isolated as pale yellow



solid. M.P = 78-80 ºC. 30 mg of **152e** afforded 22 mg of **153e** (87% yield). Rf = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 2863, 1564, 1456, 1424, 1323, 1293, 1186, 756, 729. **^{1}H NMR (400 MHz, CDCl3):** δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.40-7.36 (m, 1H), 7.26-7.22 (m, 1H), 6.48 (s, 1H), 2.44 (dd, *J* = 13.0 and 1.5 Hz, 1H), 2.07-2.02 (m, 1H), 1.69-1.17 (m, 2H), 1.55 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.27-1.17 (m, 2H). **^{13}C NMR (100 MHz, CDCl3):** δ 168.6, 150.5, 143.6, 141.3, 133.9, 124.1, 124.0, 122.0, 119.9, 116.4, 50.6, 43.2, 37.6, 36.3, 31.2, 25.5, 21.7, 19.5. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{20}S$ $(M+H)^+$: 268.1286. Found: 268.1323.

6a-(Methoxymethyl)-6,6a-dihydrobenzo[4',5']thieno[2',3':4,5]cyclopenta[1,2-c] chromene (153f).

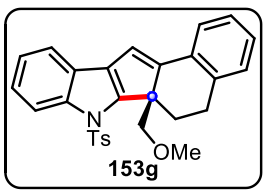
This compound was prepared following the general procedure-**10** and isolated as colorless oil.



23 mg of **152f** afforded 35 mg of **153f** (78% yield). R_f = 0.7 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3057, 2919, 1608, 1580, 1473, 1331, 1212, 1103, 756. **^{1}H NMR (400 MHz, DMSO):** δ 7.98 – 7.91 (m, 2H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.31 – 7.18 (m, 3H), 7.05 – 6.94 (m, 2H), 5.06 (d, *J* = 10.4 Hz, 1H), 3.83 (dd, *J* = 19.0 and 9.1 Hz, 2H), 3.18 (s, 3H), 3.04 (d, *J* = 9.0 Hz,1H). **^{13}C NMR (100 MHz, DMSO):** δ 152.6, 146.4, 146.2, 143.4, 142.9, 134.4, 129.7, 125.0, 124.7, 123.7, 123.1, 122.4, 121.4, 119.9, 119.2, 116.5, 72.3, 69.4, 59.0, 51.5. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{17}O_2S$ $(M+H)^+$: 321.0949. Found: 321.0935.

6a-(Methoxymethyl)-7-tosyl-5,6,6a,7-tetrahydrobenzo[4,5]indeno[1,2-*b*]indole (153g).

This compound was prepared following the general procedure-**10** and isolated as colorless oil.

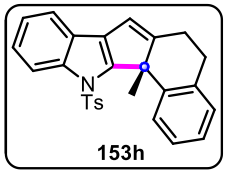


50 mg of **152g** afforded 38 mg of **153g** (86% yield). Rf = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 1596, 1447, 1366, 1173, 1109, 980, 852, 756. **^{1}H NMR (400 MHz, CDCl3):** δ 8.00-7.96 (m, 1H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.62 (dd, *J* = 8.8 Hz and 2.8, 1H), 7.30-7.25 (m, 5H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.00 (s, 1H), 4.41 (d, *J* = 9.0 Hz, 1H), 3.90 (d, *J* = 9.0 Hz, 1H), 3.27-3.12 (m, 2H), 3.10 (s, 3H), 3.05-2.99 (m, 1H), 2.34 (s, 3H), 1.86-1.76 (m, 1H) **^{13}C NMR (100 MHz, CDCl3):** δ 149.4, 148.9, 144.6, 140.3, 135.8, 134.6, 132.4, 131.5, 129.7 (2C), 128.7, 127.1, 126.8 (2C), 126.5, 124.9, 124.4,

123.9, 123.5, 119.8, 116.5, 114.8, 73.2, 59.2, 54.0, 29.7, 26.4, 21.5. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{25}NO_3S$ $(M+H)^+$: 456.1633. Found: 456.1623.

12*b*-Methyl-12-tosyl-5,6,12,12*b*-tetrahydrobenzo[6,7]indeno[1,2-*b*]indole (153h).

This compound was prepared following the general procedure-**10** and isolated as pale reddish

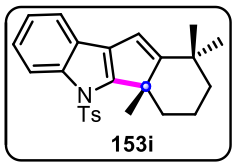


153h

oil. 30 mg of **152h** afforded 20 mg of **153h** (79% yield). Rf = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1}2925, 1598, 1446, 1371, 1175, 1090, 813, 742, 703, 665, 574, 542. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.11 (d, *J* = 8.3 Hz, 1H), 7.76 (td, *J* = 19.5 and 7.5 Hz, 4H), 7.38-7.34 (m, 1H), 7.28-7.14 (m, 6H), 6.92 (s, 1H), 3.34 (dd, *J* = 12.1and 5.5 Hz, 1H), 3.10-3.01 (m, 3H), 2.32 (s, 3H), 1.57 (s, 3H). **^{13}C NMR (100 MHz, CDCl3):** δ 161.4, 144.7, 140.7, 138.9, 136.0, 135.4, 132.1, 129.8 (2C), 128.6, 127.8, 127.1, 126.7 (3C), 126.4, 126.3, 123.7, 122.3, 118.5, 114.7, 114.5, 52.5, 32.4, 26.7, 24.2, 21.5. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{24}NO_2S$ $(M+H)^+$: 426.1528. Found: 426.1506.

1,1,4a-Trimethyl-5-tosyl-1,2,3,4,4a,5-hexahydroindeno[1,2-*b*]indole (153i).

This compound was prepared following the general procedure-**10** and isolated as pale yellow



153i

oil. 30 mg of **152i** afforded 20 mg of **153i** (78% yield). Rf = 0.5 (Hexane/EtOAc = 7/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 3029, 2929, 1487, 1449, 1370, 1075, 963, 761, 694. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.16-8.14 (m, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.53-7.50 (m, 1H), 7.30-7.23 (m, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.43 (s, 1H), 2.98 (dd, *J* = 12.6 and 1.6 Hz, 1H), 2.30 (s, 3H), 2.00 (td, *J* = 13.9 and 3.2 Hz, 1H), 1.75-1.68 (m, 2H), 1.65 (s, 3H), 1.35 (s, 3H), 1.30 (s, 3H), 1.25-1.17 (m, 2H). **^{13}C NMR (100 MHz, CDCl3):** δ 163.4, 152.7, 144.4, 140.9, 135.4, 129.5 (2C), 129.3, 126.7 (2C), 125.1, 123.7, 123.6, 119.3, 115.5, 113.1, 52.0, 42.1, 36.2, 35.1, 31.6, 26.2, 22.1, 21.5, 19.2. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{28}NO_2S$ $(M+H)^+$: 406.1841. Found: 406.1821.

General procedure-11: Synthesis of deuterated allylic acetate 148e-D.

A representative procedure for step-1 (Scheme 55): An oven dried 25 mL long neck RB flask was charged with benzo[*b*]thiophene **31** (1.34 g, 10.0 mmol), 8 mL dry THF and placed at -78 ^{o}C. *n*-BuLi (1.6*M* in hexanes, 7.5 mL, 12 mmol) was added dropwise at the same temperature and stirred for 2 h. D_2O (0.25 mL) was added and stirring continued for 1 h. The

reaction mixture was quenched with saturated aq. NH_4Cl solution and extracted with ethyl acetate. The organic layer was dried and the residue was chromatographed on silica to give **32**.

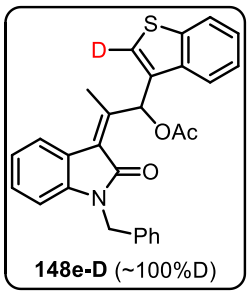
A representative procedure for step-2 (Scheme 55): To a solution of **32** (1.3 g, 9.6 mmol) in chloroform (20 mL) and acetic acid (20 mL), *N*-bromosuccinimide (1.71 g, 9.6 mmol) was added stepwise and stirred at room temperature for 24 h. The reaction mixture was diluted with chloroform (20 mL) was added and the resulting mixture was successively washed with a saturated sodium thiosulfate solution (20 mL), a saturated sodium carbonate solution (20 mL) and water (15 mL). The extracted organic layer was then dried over $MgSO_4$. The resulting red liquid was then filtered over a pad of silica, eluting with hexane/ethyl acetate to afford **33** as colorless oil.

A representative procedure for step-3 (Scheme 55): To a 50 mL RB flask equipped with magnetic stir bar, **146e** (500 mg, 1.8 mmol), anhydrous THF (5.0 ml) were added under N_2 atmosphere and stirred at 0 ^oC for 2-3 min. Benzo[*b*]thiophen-3-ylmagnesium bromide solution of **33** which was prepared from magnesium (56 mg, 2.34 mmol), **33** (425 mg, 2 mmol) and a catalytic amount of iodine in 10 mL of dry THF was added dropwise with stirring at 0 °C and stirring was continued for 1 h. The reaction mixture was quenched with dil. HCl and extracted twice with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated and **147e** was purified by silica gel column chromatography.

A representative procedure for step-4 (Scheme 55): Alcohol **147e** (450 mg, 1.09 mmol) was dissolved in dry DCM (6.0 mL) and triethylamine (0.19 mL, 1.3 mmol), acetic anhydride 0.130 mL, 1.3 mmol), DMAP (13 mg, 0.11 mmol) were added to it one by one. Then the reaction mixture was stirred until starting material disappeared (as detected by TLC). Upon completion, the reaction mixture was quenched by adding saturated *aq*. NH_4Cl solution and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using 10% ethyl acetate/hexane as an eluent to afford **148e-D (**83% yield, 100% D).

1-(2-Deuterobenzo[*b*]thiophen-3-yl)-2-(1-benzyl-2-oxoindolin-3-ylidene)propyl acetate (148e-D).

This compound was prepared following the general procedure-**11** and isolated as pale reddish oil. R_f = 0.3 (hexane/EtOAc = 8/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2930, 1745, 1694, 1608, 1467, 1356, 1228, 1181. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.96 (s, 1H), 8.11 – 8.04 (m, 1H), 7.88 – 7.80 (m, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.37 – 7.29 (m, 6H), 7.29 – 7.21 (m, 1H), 7.16 (td, *J* = 7.7 and 0.9 Hz, 1H), 6.99 (td, *J* = 7.7 and 0.9 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.97 (d, *J* = 15.7 Hz, 1H), 2.40 (s, 3H), 2.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.7, 166.8, 149.4, 142.4, 140.3, 137.5, 136.2, 133.3, 129.0, 128.8 (2C), 127.6, 127.3 (2C), 125.2, 124.7, 124.6, 124.6, 123.2, 123.0, 122.8, 122.1, 109.0, 68.8, 43.5, 21.2, 16.9. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{19}DNOS$ $(M\text{-}OAc)^+$: 395.1328. Found: 395.1315.



148e-D (~100%D)

General procedure-12: Synthesis of enone tethered pyridinium salts (205a-205h, 205k-205o and 205r-t)

A representative procedure for synthesis of 201 (Scheme 67, step I): $Pd(PPh_3)_4$ (0.005 mmol), $NaHCO_3$ (4.0 mmol), 4-bromopyridine hydrochloride (1.0 mmol), corresponding boronic acid (1.2 mmol), and solvent toluene (3.0 mL), EtOH (2.0 mL) and H_2O (2.0 ml) were added to a sealed tube. The reaction mixture was degassed with nitrogen and the resulting solution was stirred at 100 °C for 24 h. After the reaction was completed (TLC), the reaction was quenched with saturated aq. NH_4Cl solution and extracted using ethyl acetate. The organic extracts were combined dried over anhydrous sodium sulfate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford biaryl aldehydes **202** (yield 75-80%).

A representative procedure for synthesis of ketone 203 (Scheme 67, step II): An oven-dried 25 mL RB flask was charged with biaryl aldehyde **202** in 10 mL dry THF and placed at 0 °C under N_2 atmosphere. The methyl magnesium chloride (3.0 M in THF, 1.2 eq.) was added dropwise at the same temperature and stirred for 1 h. Upon completion, the reaction mixture was quenched with water (~2-3 mL) and extracted with ethyl acetate (2x5 mL). The organic extracts were combined and dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was taken to the next step without further purification.

The crude product was dissolved in ethyl acetate, and IBX (1.2 eq.) was added. The suspension was stirred at reflux condition until the alcohol disappeared as monitored by TLC. The mixture was filtered through celite pad. The residue was washed with ethyl acetate (2x6

mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford biaryl ketone **203** (yield 85-90%).

A representative procedure for synthesis of birayl enone 204 (Scheme 67, step III): The biaryl ketone **xx** and the corresponding aldehyde (1.2 eq.) was dissolved in MeOH and KOH (1.0 eq.) was introduced at -20 °C for 2h then transfer to room temperature and stirred for 30 min, monitor the reaction till completion of starting material **203**. The reaction mixture was quenched with saturated aqueous NH_4Cl (~2-3 mL) solution and extracted with ethyl acetate (2x5 mL). The combined organic layers were dried dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford biaryl ketone **204** (yield 85-90%).

A representative procedure for synthesis of 205a-xx (Scheme 67, step IV): In a Seal tube biaryl enone **204** (252 mg) was dissolved in DCM (2.0 mL) and alkyl bromide or iodide (1.2 eq.) was added in one portion, reaction mixture was stirred at 70 °C for 2-5 h monitored the reaction on TLC. After compeletion of Starting material, the solvent was evaporated, crude product was washed with ethyl aceate 4-5 times. Product dried over vacuum to get yellow solid and transferred to final step without any further purification.

General procedure-13: Synthesis of enone tethered pyridinium salts (205i and 205j).

A representative procedure for synthesis of 2-bromoenone (211) (Scheme 69, step I-II): All the 2-bromoenones were synthesized from **209** according to the reported literature.

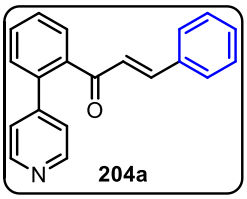
A representative procedure for synthesis of enone-tethered pyridines (212) (Scheme 69, step III): $Pd(PPh_3)_4$ (0.005 mmol), $[HP(^tBu)_3]BF_4$ (0.012 mmol), enone **211** (1.0 mmol), pyridin-4-ylboronic acid (1.2 mmol), KF (3.3 mmol) and H_2O (60.0 mmol) were added to a sealed tube. The reaction tube was degassed with nitrogen and then DMF (2.0 mL) was added using a syringe, and the resulting solution was stirred at 70 °C for 36 h. After the reaction was completed (TLC), the reaction was quenched with saturated aq. NH_4Cl solution and extracted using ethyl acetate. The organic extracts were combined dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford enone tethered pyridines **212**.

A representative procedure for synthesis of enone-tethered pyridinium salts (205i and **205j) (Scheme 69**, **step IV):** In a Seal tube biaryl enone **212** (300 mg) was dissolved in DCM (3.0 mL) and Methyl iodide (1.2 eq.) was added in one portion, reaction mixture was stirred at 70 °C for 2-5 h monitored the reaction on TLC. After compeletion of Starting material, the solvent was evaporated, crude product was washed with ethyl aceate 4-5 times. Product dried over vacuum to get yellow solid and transferred to final step without any further purification.

General procedure-14: Synthesis of enone tethered pyridinium (205p-205q)

A representative procedure for synthesis of 214 (Scheme 70 step I): $Pd(PPh_3)_4$ (0.005 mmol), $NaHCO_3$ (4.0 mmol), bromide **213** (1.0 mmol), pyridin-4-ylboronic acid (1.2 mmol), and solvent toluene (3.0 mL), EtOH (2.0 mL) and H_2O (2.0 ml) were added to a sealed tube. The reaction mixture was degassed with nitrogen and the resulting solution was stirred at 100 °C for 24 h. After the reaction was completed (TLC), the reaction was quenched with saturated aq. NH_4Cl solution and extracted using ethyl acetate. The organic extracts were combined dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to afford biaryl aldehydes **214** (yield 70-77%). The biaryl aldehydes **214** were subjected to further transformation to obtain corresponding enone tethered pyridinium salts **205p** and **205q** as mentioned in (**Scheme 67**, **step II-IV)**.

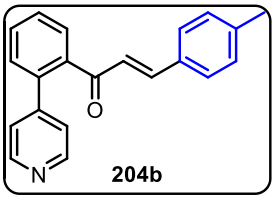
(*E*)-3-Phenyl-1-(2-(pyridin-4-yl)phenyl)prop-2-en-1-one (204a).



This compound was isolated as pale-yellow solid by following the general procedure-**12**. M.P = 82-84 ºC. R_f = 0.4 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2921, 2852, 1667, 1593, 1331, 1209, 1027, 983, 827, 760. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.59 (d, *J* = 6.1 Hz, 2H), 7.66 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.5 Hz, 1H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.40-7.29 (m, 8H), 6.74 (d, *J* = 16.0 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.6, 149.5 (2C), 148.7, 145.7, 139.4, 138.0, 134.1, 130.9, 130.8, 130.0, 128.9 (2C), 128.9, 128.7, 128.3 (2C), 126.5, 123.9 (2C).

(*E*)-1-(2-(Pyridin-4-yl)phenyl)-3-(p-tolyl)prop-2-en-1-one (204b).

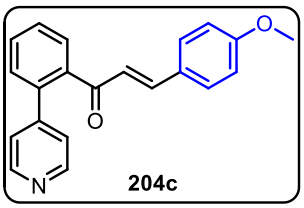
This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.5 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2921, 2851, 1666,1642, 1595,1408, 1326, 1208, 1024, 983, 826, 760. **^{1}H NMR (400 MHz, $CDCl_3$):**



δ 8.62-8.52 (m, 2H), 7.64 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.34 (d, *J* = 16.1 Hz, 1H), 7.31-7.27 (m, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.69 (d, *J* = 16.0 Hz, 1H), 2.33 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 195.8, 149.8 (2C), 148.3, 145.8, 141.4, 139.6, 138.1, 131.4, 130.8, 130.0, 129.7 (2C), 128.9, 128.6, 128.3 (2C), 125.6, 123.8 (2C), 21.5.

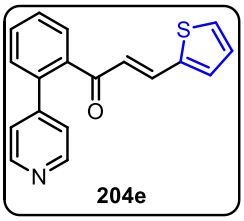
(*E*)-3-(4-Methoxyphenyl)-1-(2-(pyridin-4-yl)phenyl)prop-2-en-1-one (204c)

This compound was isolated as pale-yellow sticky oil by following the general procedure-**12**.



R_f = 0.3 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3054, 3025, 2839, 1663, 1636, 1592, 1569, 1251, 1172, 1025, 828, 775. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.60-8.55 (m, 2H), 7.64 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.30 (dd, *J* = 6.2, 1.8 Hz, 5H), 6.88-6.81 (m, 2H), 6.61 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.8, 161.8, 149.8 (2C), 148.4, 145.6, 139.7, 138.0, 130.7, 130.1 (2C), 129.9, 128.8, 128.6, 126.8, 124.4, 123.8 (2C), 114.4 (2C), 55.4.

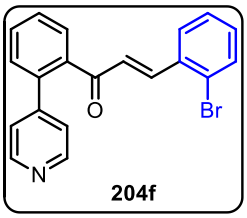
(*E*)-1-(2-(Pyridin-4-yl)phenyl)-3-(thiophen-2-yl)prop-2-en-1-one (204e).This compound



was isolated as reddish-brown oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3105, 3063, 3026, 1658, 1636, 1583, 1474, 1409, 1363, 1282, 1209, 1078, 1023, 827, 761. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63-8.56 (m, 2H), 7.68-7.63 (m, 1H), 7.59 (td, *J* = 7.6, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.52-7.48 (m, 1H), 7.45-7.42 (m, 1H), 7.35 (dt, *J* = 5.0, 1.0 Hz, 1H), 7.30-7.27 (m, 2H), 7.18-7.15 (m, 1H), 7.00 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.51 (d, *J* = 15.7 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 194.8, 149.7 (2C), 148.4, 139.6, 139.4, 138.2, 137.5, 132.0, 130.9, 130.0, 129.5, 128.9, 128.6, 128.3, 125.2, 123.8 (2C).

(*E*)-3-(2-Bromophenyl)-1-(2-(pyridin-4-yl)phenyl)prop-2-en-1-one (204f).

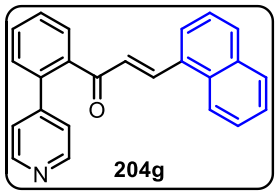
This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 1666, 1644, 1597, 1465, 1440, 1408, 1207, 1025, 828, 760. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.64-



8.58 (m, 2H), 7.71-7.64 (m, 2H), 7.61 (td, *J* = 7.6, 1.5 Hz, 1H), 7.54 (tt, *J* = 7.8, 1.2 Hz, 2H), 7.47 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.33-7.29 (m, 2H), 7.25-7.21 (m, 2H), 7.19-7.14 (m, 1H), 6.59 (d, *J* = 16.0 Hz, 1H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 195.7, 149.9 (2C), 148.2, 143.8, 139.2, 138.1, 134.2, 133.4, 131.5, 131.0, 129.9, 129.1, 129.0, 128.7, 127.7, 127.7, 125.6, 123.9 (2C).

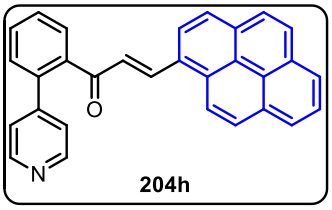
(*E*)-3-(Naphthalen-1-yl)-1-(2-(pyridin-4-yl)phenyl)prop-2-en-1-one (204g)

This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3068, 1664, 1641, 1595, 1509, 1396, 1347, 1311, 1289, 1214, 1027, 979, 827, 779, 762. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.65-8.59 (m, 2H), 8.21 (d, *J* = 15.7 Hz, 1H), 7.91-7.86 (m, 1H), 7.81 (ddd, *J* = 8.2, 7.1, 1.9 Hz, 2H), 7.73 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.5 Hz, 1H), 7.55 (td, *J* = 7.5, 1.4 Hz, 1H), 7.51-7.44 (m, 3H), 7.39 – 7.31 (m, 4H), 6.74 (d, *J* = 15.8 Hz, 1H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 195.3, 149.9 (2C), 148.4, 142.0, 139.7, 138.1, 133.6, 131.6, 131.4, 131.1, 131.0, 130.0, 129.1, 129.0, 128.8 (2C), 127.0, 126.3, 125.4, 125.3, 124.0 (2C), 123.1.



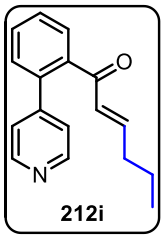
(*E*)-3-(Pyren-1-yl)-1-(2-(pyridin-4-yl)phenyl)prop-2-en-1-one (204h).

This compound was isolated as yellowish-orange solid by following the general procedure-**12**. M.P = 163-167 ºC. R_f = 0.3 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 1659, 1637, 1592, 1580, 1317, 1286, 1214, 1023, 977, 844. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.66-8.59 (m, 2H), 8.49 (d, *J* = 15.7 Hz, 1H), 8.15-8.09 (m, 3H), 8.03-7.98 (m, 2H), 7.97-7.88 (m, 3H), 7.78 (td, *J* = 6.0, 5.6, 3.0 Hz, 2H), 7.60 (ddd, *J* = 14.7, 7.4, 1.5 Hz, 2H), 7.47 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.40-7.34 (m, 2H), 6.88 (d, *J* = 15.7 Hz, 1H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 195.1, 149.9, 148.5, 141.6, 139.9, 138.2, 132.9, 131.2, 131.1, 130.5, 130.1, 130.0, 129.1, 128.8, 128.8, 128.7, 128.2, 127.9, 127.2, 126.3, 126.1, 125.9, 125.0, 124.1, 124.0, 122.1.



(*E*)-1-(2-(Pyridin-4-yl)phenyl)hex-2-en-1-one (212i).

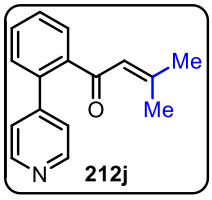
This compound was isolated as pale-yellow oil by following the general procedure-**13**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3064, 2959, 2871, 1650, 1617, 1594, 1209, 1118, 970, 804, 762. **^{1}H NMR (400 MHz, CDCl$_3$):** δ



8.61 – 8.57 (m, 2H), 7.56 – 7.49 (m, 3H), 7.41 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.25 – 7.22 (m, 2H), 6.54 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.07 (dt, *J* = 15.7, 1.5 Hz, 1H), 2.02 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.31 – 1.23 (m, 2H), 0.78 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 96.70, 151.59, 149.83, 148.34 (2C), 139.51, 137.81, 130.85, 130.60, 129.74, 128.76, 128.55, 123.80, 123.75, 34.51, 21.08, 13.59.

3-Methyl-1-(2-(pyridin-4-yl)phenyl)but-2-en-1-one xx (212j).

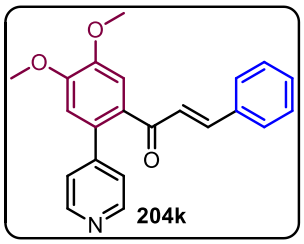
This compound was isolated as reddish-brown solid by following the general procedure-**13**.



M.P. = 92-94 ^{o}C. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1665, 1608, 1585, 1444, 1409, 1239, 1101, 829, 746. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.63 (d, *J* = 5.1 Hz, 2H), 7.63 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.39 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.28 (d, *J* = 4.2 Hz, 2H), 6.03 (s 1H), 2.09 (s 3H), 1.74 (s 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 195.1, 156.9, 149.5 (2C), 148.8, 141.5, 137.7, 130.5, 129.9, 128.6, 128.5 (2C), 124.9, 123.9, 27.6, 20.9.

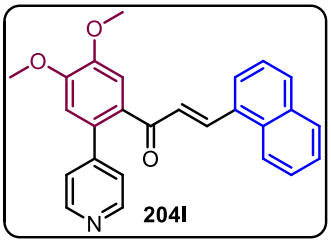
(*E*)-1-(4,5-Dimethoxy-2-(pyridin-4-yl)phenyl)-3-phenylprop-2-en-1-one (204k)

This compound was isolated as off-white solid by following the general procedure-**12**. M.P = 155-158 ^{o}C. R_f = 0.3 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2935, 2849, 1660, 1637, 1596, 1351, 1244, 1156, 1029, 989, 831. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.64 – 8.56 (m, 2H), 7.41 (d, *J* = 15.9 Hz, 1H), 7.38 – 7.27 (m, 6H), 7.26 – 7.21 (m, 2H), 6.91 (s, 1H), 6.56 (d, *J* = 15.9 Hz, 1H), 4.00 (s, 3H), 3.99 (s,3H).–**^{13}C NMR (100 MHz, CDCl$_3$):** δ 194.1, 151.1, 149.9 (2C), 149.1, 148.5, 144.0, 134.4, 132.1, 132.1, 132.1, 132.0, 130.5, 128.9 (2C), 128.2 (2C), 126.4, 124.0, 112.4, 112.1, 56.2.



(*E*)-1-(4,5-Dimethoxy-2-(pyridin-4-yl)phenyl)-3-(naphthalen-1-yl)prop-2-en-1-one (204l)

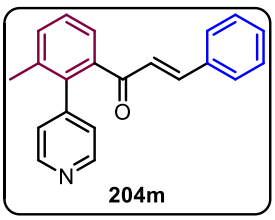
This compound was isolated as reddish-orange solid by following the general procedure-**12**. M.P = 95-96 ^{o}C. R_f = 0.3 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3058, 3009, 2930, 1709, 1659, 1595, 1542, 1516, 1462, 1439, 1413, 1395, 1350, 1322, 1272, 1243, 1218, 1203, 1154, 1026, 788. **^{1}H NMR (400 MHz, CDCl$_3$):** 8.68 –



8.61 (m, 2H), 8.27 (d, *J* = 15.6 Hz, 1H), 7.99 – 7.93 (m, 1H), 7.87 – 7.81 (m, 2H), 7.52 (ddd, *J* = 7.2, 4.9, 1.6 Hz, 2H), 7.41 – 7.34 (m, 4H), 7.16 (dd, *J* = 7.2, 1.1 Hz, 1H), 6.93 (s, 1H), 6.62 (d, *J* = 15.6 Hz, 1H), 4.02 (s, 3H), 4.01 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 193.9, 151.2, 150.0 (2C), 149.2, 148.5, 140.6, 133.6, 132.3, 132.1, 131.8, 131.4, 130.7, 129.0, 128.7, 126.9, 126.2, 125.4, 125.1, 124.2 (2C), 123.2, 112.4, 112.3, 56.2, 56.2.

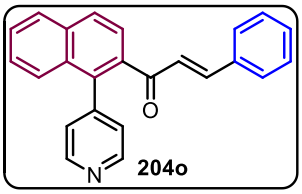
(*E*)-1-(3-Methyl-2-(pyridin-4-yl)phenyl)-3-phenylprop-2-en-1-one (204m).

This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2931, 1668, 1643, 1599, 1574, 1450, 1331, 1286, 1232, 1134, 1083, 1054, 981, 764. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61 – 8.57 (m, 2H), 7.47 – 7.40 (m, 3H), 7.38 – 7.33 (m, 5H), 7.29 (d, *J* = 16.1 Hz, 1H), 7.18 – 7.14 (m, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 2.18 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 195.9, 149.6 (2C), 147.7, 145.7, 140.0, 137.1, 136.3, 134.3, 132.4, 130.7, 128.9 (2C), 128.3 (2C), 128.0, 126.7, 125.7, 124.7 (2C), 20.4. **HRMS (ESI):** m/z calcd for $C_{21}H_{17}NO$ $(M+H)^+$ 300.1388 found: 300.1403.



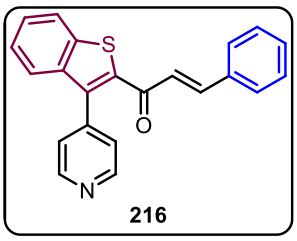
(*E*)-3-Phenyl-1-(1-(pyridin-4-yl)naphthalen-2-yl)prop-2-en-1-one (204o).

This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 1658, 1642, 1598, 1340, 1207, 1051, 978, 824, 766, 750. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.71-8.68 (m, 2H), 8.04 (d, *J* = 8.5 Hz, 1H), 8.00 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.67-7.61 (m, 2H), 7.56-7.52 (m, 1H), 7.38-7.34 (m, 7H), 7.30 (d, *J* = 9.9 Hz, 1H), 6.75 (d, *J* = 16.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.2, 149.5 (2C), 146.0, 137.0, 135.4, 134.2, 134.2, 131.1, 130.8, 128.9 (2C), 128.8, 128.6, 128.3 (2C), 128.3 (2C), 127.4, 127.4, 126.8, 126.3, 125.7, 124.5.



(*E*)-3-Phenyl-1-(3-(pyridin-4-yl)benzo[*b*]thiophen-2-yl)prop-2-en-1-one (216).

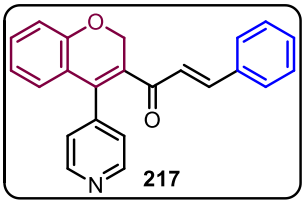
This compound was isolated as reddish-brown solid by following the general procedure-**14**. M.P. = 149.6-151.2 °C. R_f = 0.4 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR**



(thin film, neat): ν_{max}/cm^{-1} 1640, 1594, 1573, 1522, 1483, 1357, 1210, 1179, 991, 974, 762. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.84-8.78 (m, 2H), 7.97-7.91 (m, 1H), 7.68 (d, *J* = 15.6 Hz, 1H), 7.52 (td, *J* = 8.0, 1.0 Hz, 2H), 7.46-7.39 (m, 3H), 7.38-7.30 (m, 3H), 7.23-7.15 (m, 2H), 6.72 (d, *J* = 15.5 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 184.5, 150.2 (2C), 144.2, 143.6, 141.5, 140.8, 139.5, 137.9, 134.3, 130.8, 129.0 (2C), 128.3 (2C), 127.6, 125.4, 125.0 (2C), 124.8, 123.5, 122.8. **HRMS (ESI):** m/z calcd for $C_{22}H_{16}NOS$ $(M+H)^+$ 342.0953, found: 342.0941.

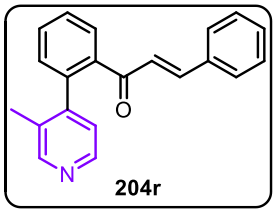
(*E*)-3-phenyl-1-(4-(pyridin-4-yl)-2H-chromen-3-yl)prop-2-en-1-one (217).

This compound was isolated as pale-yellow solid by following the general procedure-**14**. M.P = 87-90 ºC. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3036, 1645, 1591, 1574, 1481, 1449, 1373, 1277, 1239, 1204, 1115, 988, 823, 762. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.74-8.65 (m, 2H), 7.45 (d, *J* = 15.7 Hz, 1H), 7.32-7.25 (m, 6H), 7.08 (dt, *J* = 6.8, 1.6 Hz, 2H), 6.99 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.90 (td, *J* = 7.6, 1.2 Hz, 1H), 6.75 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.20 (d, *J* = 15.8 Hz, 1H), 5.07 (s, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 190.7, 155.5, 150.0 (2C), 144.9, 143.3, 138.9, 134.2, 131.9, 130.6, 129.7, 128.9 (2C), 128.1 (2C), 127.7, 124.9, 124.8 (2C), 122.9, 121.9, 116.7, 66.4.



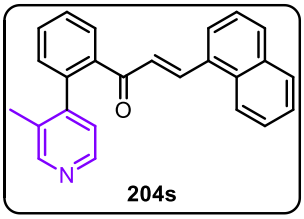
(*E*)-1-(2-(3-Methylpyridin-4-yl)phenyl)-3-phenylprop-2-en-1-one (204r).

This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 2931, 1666, 1638, 1599, 1574, 1454, 1331, 1288, 1232, 1134, 1092, 1054, 983, 764. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.45 (d, *J* = 1.8 Hz, 1H), 8.42 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.77-7.74 (m, 1H), 7.60-7.56 (m, 1H), 7.53 (tt, *J* = 7.5, 1.7 Hz, 1H), 7.42 (dd, *J* = 16.0, 1.9 Hz, 1H), 7.34 (h, *J* = 3.3 Hz, 5H), 7.26 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.09 (dd, *J* = 5.0, 1.8 Hz, 1H), 6.79 (dd, *J* = 15.9, 2.0 Hz, 1H), 2.14 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 194.1, 150.8, 148.6, 146.9, 145.1, 139.1, 138.0, 134.3, 131.2, 130.6, 130.7, 130.0, 128.9 (2C), 128.7, 128.3 (2C), 128.2, 125.4, 123.9, 17.0.



(*E*)-1-(2-(3-Methylpyridin-4-yl)phenyl)-3-(naphthalen-1-yl)prop-2-en-1-one (204s).

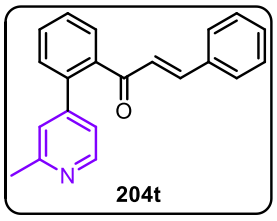
This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2921, 2851, 1666, 1642, 1595, 1408, 1326, 1208, 1024, 983, 826, 760.**^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.48 (s, 1H), 8.46 (d, *J* = 5.0 Hz, 1H), 8.30 (d, *J* = 15.6 Hz, 1H), 8.01 – 7.97 (m, 1H), 7.87 – 7.81 (m, 3H), 7.60 (td, *J* = 7.5, 1.5 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.50 (td, *J* = 7.6, 1.5 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.28 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.13 (d, *J* = 4.9 Hz, 1H), 6.85 (d, *J* = 15.6 Hz, 1H), 2.15 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 193.7, 151.0, 148.6, 147.1, 141.6, 139.2, 138.1, 133.6, 131.7, 131.5, 131.2, 131.1, 130.9, 130.1, 128.9, 128.8, 128.3, 127.7, 127.0, 126.3, 125.4, 125.2, 124.0, 123.1, 17.0.



204s

(*E*)-1-(2-(2-Methylpyridin-4-yl)phenyl)-3-phenylprop-2-en-1-one (204t).

This compound was isolated as pale-yellow oil by following the general procedure-**12**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 1669, 1643, 1603, 1573, 1545, 1494, 1448, 1331, 1261,1209, 763, 752. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.47 (d, *J* = 5.1 Hz, 1H), 7.66 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.60 (td, *J* = 7.6, 1.5 Hz, 1H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.39-7.32 (m, 6H), 7.17 (d, *J* = 1.7 Hz, 1H), 7.11 (dd, *J* = 5.1, 1.7 Hz, 1H), 6.71 (d, *J* = 16.0 Hz, 1H), 2.54 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.9, 158.6, 149.2, 148.7, 145.4, 139.5, 138.5, 134.3, 130.9, 130.7, 129.9, 128.9 (2C), 128.9, 128.5, 128.3 (2C), 126.6, 123.4, 120.9, 24.4.



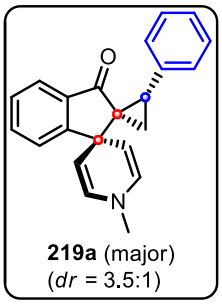
204t

General procedure-15: Synthesis of vicinal bis-spirocyclic indanones (219a-219y).

A mixture of sodium hydride (60% in oil, 12 mg, 0.28 mmol) and trimethyloxosulfonium iodide (52 mg, 0.23 mmol) was placed in an oven dried flask and DMSO (4.0 mL) was added to the mixture. After the evolution of hydrogen ceased, the milky solution turned clear and the reaction mixture was stirred for 15 min. The compound **205a** (100 mg, 0.23 mmol) was dissolved in DMSO (1.0 mL) and was added to the clear solution dropwise over a period of 5-10 min and stirred at rt until the reactant **205a** disappeared as monitored by TLC. The reaction mixture was quenched with ice-water and extracted with diethyl ether. 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.

1''-Methyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219a).

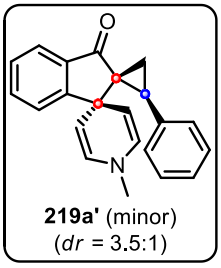
Major: This compound was isolated by following the general procedure-**15**. 100 mg of **205a**



afforded 49 mg of **219a** (67% yield) R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3055, 1697. 1674, 1600, 1497, 1408, 1290, 1113, 1007, 932, 756, 725. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.69-7.65 (m, 2H), 7.57 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.34 (ddd, *J* = 8.0, 4.9, 3.4 Hz, 1H), 7.29 (d, *J* = 4.4 Hz, 4H), 7.25-7.18 (m, 1H), 6.20 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.09 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.32 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.09 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.02 (s, 3H), 2.99 (t, *J* = 8.6 Hz, 1H), 2.10 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.71 (dd, *J* = 9.1, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 202.9, 162.6, 136.4, 134.6, 134.4, 130.4, 129.9, 129.2 (2C), 127.7 (2C), 127.7, 127.4, 126.52, 121.56, 101.9, 101.8, 52.9, 46.1, 40.5, 33.6, 18.7. **HRMS (ESI):** m/z calcd for $C_{22}H_{18}NO$ $(M-H)^+$ 312.1388 found: 312.1395.

1''-Methyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219a').

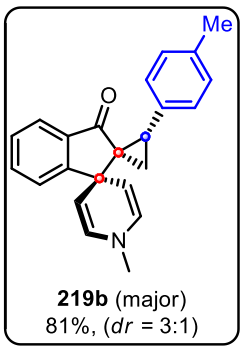
Minor: This compound was isolated by following the general procedure-**15**. 100 mg of **205a**



afforded 14 mg of **219a'** (19% yield), R_f = 0.5 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3055, 1697. 1674, 1600, 1497, 1408, 1290, 1113, 1007, 932, 756, 725. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.72-7.69 (m, 1H), 7.64 (ddd, *J* = 7.8, 7.1, 1.2 Hz, 1H), 7.57 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.35 (ddd, *J* = 7.7, 7.1, 1.1 Hz, 1H), 7.21-7.10 (m, 6H), 5.96 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.90 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.12 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.52 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.20 (dd, *J* = 9.3, 7.9 Hz, 1H), 2.71 (s, 3H), 2.02 (dd, *J* = 7.9, 4.2 Hz, 1H), 1.57 (dd, *J* = 9.3, 4.1 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 204.9, 164.0, 137.5, 134.8, 132.6, 130.5, 129.3 (2C), 127.6, 127.5, 127.4, 127.0 (2C), 125.68, 121.52, 104.2, 100.2, 53.2, 45.2, 40.1, 32.6, 18.8. **HRMS (ESI):** m/z calcd for $C_{22}H_{18}NO$ $(M-H)^+$ 312.1388 found: 312.1395.

1''-Methyl-2-(p-tolyl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219b).

This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**.

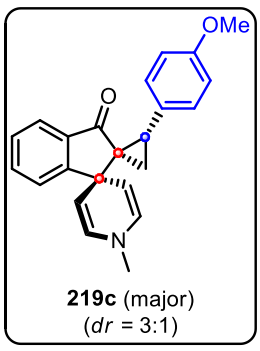


219b (major)
81%, (*dr* = 3:1)

IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2965, 2854, 1701, 1671, 1600, 1517, 1462, 1378, 1208, 1022, 1008, 821, 765, 709. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.65-7.60 (m, 2H), 7.54 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.30 (ddd, *J* = 7.6, 5.2, 3.1 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 7.7 Hz, 2H), 6.16 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.05 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.28 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.06 (dd, *J* = 7.8, 3.0 Hz, 1H), 2.98 (s, 3H), 2.93 (t, *J* = 8.6 Hz, 1H), 2.29 (s, 3H), 2.04 (dd, *J* = 8.2, 4.2 Hz, 1H), 1.65 (dd, *J* = 9.1, 4.3 Hz, 1H). **^{13}C (126 MHz, $CDCl_3$):** δ 202.9, 162.6, 135.9, 134.7, 134.3, 133.2, 130.4, 129.8 129.1 (2C), 128.5 (2C), 127.6, 127.4, 121.5, 102.0, 101.9, 52.8, 46.1, 40.4, 33.4, 21.1, 18.7.

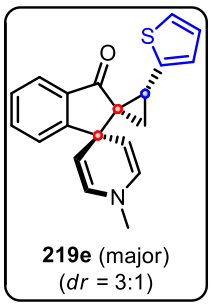
2-(4-Methoxyphenyl)-1''-methyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219c).

This compound was isolated as pale-yellow solid by following the general procedure-**15**. M.P = 135-142 °C. R_f = 0.2 (15:85 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2929, 2834, 1698, 1671, 1599, 1513, 1462, 1320, 1209, 1175, 1007, 973, 800, 726, 708. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.70 -7.64 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.34 (ddd, *J* = 8.0, 4.8, 3.3 Hz, 1H), 7.23-7.18 (m, 2H), 6.85-6.81 (m, 2H), 6.19 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.08 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.29 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.08 (dd, *J* = 7.8, 2.9 Hz, 1H), 3.79 (s, 3H), 3.01 (s, 3H), 2.95 (t, *J* = 8.6 Hz, 1H), 2.06 (dd, *J* = 8.1, 4.2 Hz, 1H), 1.69 (dd, *J* = 9.0, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 203.0, 162.7, 158.1, 134.7, 134.4, 130.5, 130.2 (2C), 129.8, 128.3, 127.7, 127.4, 121.5, 113.2 (2C), 102.0, 101.8, 55.1, 52.9, 46.1, 40.5, 33.2, 18.9. **HRMS (ESI):** m/z calcd for $C_{23}H_{22}NO_2$ $(M+H)^+$) 344.1651 found: 344.1663.



219c (major)
(*dr* = 3:1)

1''-Methyl-2-(thiophen-2-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219e).



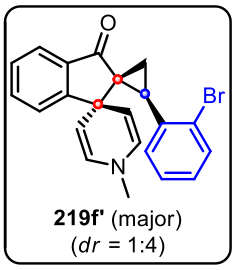
219e (major)
(*dr* = 3:1)

This compound was isolated as reddish- brown semi-solid by following the general procedure-**15**. R_f = 0.2 (15:85 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2963, 2911, 1700, 1671, 1599, 1462, 1315, 1222, 1105, 993, 765, 695. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.72-7.64 (m, 2H), 7.62 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.36 (ddd, *J* = 8.0, 5.0, 3.2

Hz, 1H), 7.14 (dd, *J* = 4.4, 1.9 Hz, 1H), 6.96 (d, *J* = 4.5 Hz, 2H), 6.19 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.08 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.26 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.06 (dd, *J* = 7.8, 2.9 Hz, 1H), 3.01 (m, 4H), 2.08 (dd, *J* = 7.8, 4.2 Hz, 1H), 1.79 (dd, *J* = 9., 4.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 202.1, 162.4, 140.3, 134.6, 134.4, 130.6, 130.0, 127.7, 127.5, 126.5, 126.3, 123.9, 121.6, 101.7, 101.4, 53.0, 46.1, 40.5, 27.7, 20.3. **HRMS (ESI):** m/z calcd for $C_{20}H_{18}NOS$ $(M+H)^+$ 320.1109 found: 320.1120.

2-(2-Bromophenyl)-1''-methyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219f').

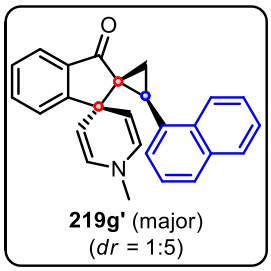
This compound was isolated as greenish semi-solid by following the general procedure-**15**. R_f = 0.2 (15:85 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3054, 2956, 2920, 2836, 1699, 1674, 1600, 1463, 1378, 1292, 1208, 1023, 1007, 765, 748, 719. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.76 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.67 (td, *J* = 7.4, 1.2 Hz, 1H), 7.59 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.45 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.39 (td, *J* = 7.4, 1.1 Hz, 1H), 7.18 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.13 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.07 (dd, *J* = 7.5, 1.9 Hz, 1H), 5.92 (dd, *J* = 7.8, 1.7 Hz, 1H), 4.87 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.06 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.86 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.31 (t, *J* = 8.6 Hz, 1H), 2.63 (s, 3H), 2.05 (dd, *J* = 8.1, 4.2 Hz, 1H), 1.61 (dd, *J* = 9.1, 4.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 204.4, 163.6, 137.7, 134.8, 132.8, 131.6, 130.3, 128.8, 128.7, 127.6, 127.5, 127.4, 127.2, 126.0, 121.7, 102.2, 100.1, 52.2, 45.2, 39.9, 33.4, 18.4.



219f' (major)
(*dr* = 1:4)

1''-Methyl-2-(naphthalen-1-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219g').

This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.2 (15:85 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3051, 2953. 2907, 2834, 1695, 1673, 1599, 1462, 1293, 1083, 797. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.05 – 7.97 (m, 1H), 7.85-7.78 (m, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.64 (td, *J* = 7.4, 1.2 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.42 (ddd, *J* = 8.2, 5.0, 1.4 Hz, 3H), 7.39-7.33 (m, 1H), 7.31 – 7.26 (m, 1H), 5.90 (dd, *J* = 7.8, 1.7 Hz, 1H), 4.32 (dd, *J* = 7.8, 1.7 Hz, 1H), 4.08 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.76 (t, *J* = 8.6 Hz, 1H), 3.16 (dd, *J* = 7.8, 2.9 Hz, 1H), 2.55 (s, 3H), 2.30 (dd, *J* = 8.0, 4.0 Hz, 1H), 1.74 (dd, *J* = 9.2, 4.0 Hz, 1H). **^{13}C NMR (100 MHz,**

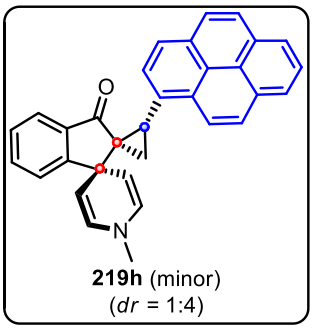


219g' (major)
(*dr* = 1:5)

$CDCl_3$): δ 205.2, 163.9, 134.8, 134.7, 134.1, 133.0, 132.7, 130.2, 128.2, 127.6, 127.4, 127.0, 126.6, 125.9, 125.3, 124.5, 124.3, 124.3, 121.6, 103.1, 99.9, 53.3, 45.3, 39.9, 30.1, 18.5. **HRMS (ESI):** m/z calcd for $C_{22}H_{19}BrNO$ $(M+H^+)$ 392.0650 found: 392.0643.

1''-Methyl-2-(pyren-2-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219h).

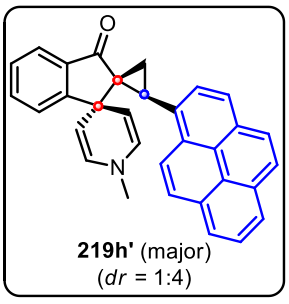
This compound was isolated as yellowish semi-solid by following the general procedure-**15**.



R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2929, 1700, 1674, 1601, 1463, 1384, 1360, 1206, 1104, 1006, 845, 726. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.15 (dd, *J* = 8.6, 1.7 Hz, 2H), 8.12 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.06-8.01 (m, 3H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.92 (t, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 9.2 Hz, 1H), 7.76 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.2 Hz, 1H), 7.38 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.28 (td, *J* = 7.3, 1.1 Hz, 1H), 6.34 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.12 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.73 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.17 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.54 (t, *J* = 8.4 Hz, 1H), 3.05 (s, 3H), 2.35 (dd, *J* = 7.8, 4.3 Hz, 1H), 1.97 (dd, *J* = 9.0, 4.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 202.5, 162.4, 134.6, 134.5, 131.6, 131.3, 131.1, 130.7, 130.3, 129.6, 128.1, 127.6, 127.6, 127.5, 126.9, 126.7, 125.5, 124.9, 124.8, 124.70, 124.3, 123.5, 121.6, 103.2, 100.2, 52.9, 46.6, 40.5, 31.5, 19.4. **HRMS (ESI):** m/z calcd for $C_{32}H_{24}NO$ $(M+H)^+$ 438.1858 found: 438.1859.

1''-Methyl-2-(pyren-1-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219h').

This compound was isolated as pale-yellow sticky oil by following the general procedure-**15**.

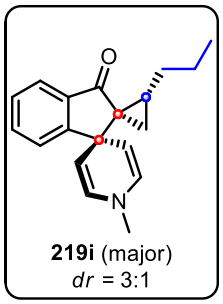


R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2929, 1700, 1674, 1601, 1463, 1384, 1360, 1206, 1104, 1006, 845, 726. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.22 (d, *J* = 9.3 Hz, 1H), 8.14 – 8.08 (m, 2H), 8.03 – 7.96 (m, 4H), 7.94 (t, *J* = 7.6 Hz, 1H), 7.83 – 7.76 (m, 2H), 7.58 (td, *J* = 7.4, 1.3 Hz, 1H), 7.45 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.37 (td, *J* = 7.5, 1.0 Hz, 1H), 5.83 (dd, *J* = 7.8, 1.7 Hz, 1H), 4.07 (dd, *J* = 7.8, 3.0 Hz, 1H), 4.02 (t, *J* = 8.6 Hz, 1H), 3.85 (dd, *J* = 7.8, 1.7 Hz, 1H), 3.14 (dd, *J* = 7.8, 3.0 Hz, 1H), 2.44 (dd, *J* = 8.0, 4.1 Hz, 1H), 2.31 (s, 3H), 1.83 (dd, *J* = 9.2, 4.1 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 205.0, 163.9, 134.8, 133.0,

131.8, 131.7, 131.3, 130.9, 130.4, 129.9, 127.6, 127.4, 127.3 (2C), 127.1, 126.7, 125.8, 125.1, 125.0, 124.8, 124.7, 124.1, 124.1, 123.5, 121.6, 102.8, 99.8, 53.4, 45.4, 39.6, 30.6, 18.88.

1''-Methyl-2-propyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219i)

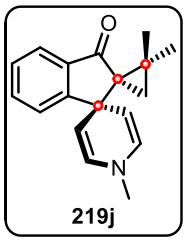
Major: This compound was isolated as reddish-brown oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3055, 1697. 1674, 1600, 1497, 1408, 1290, 1113, 1007, 932, 756, 725. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.71 – 7.59 (m, 3H), 7.37 (ddd, *J* = 8.0, 6.8, 1.5 Hz, 1H), 6.04 (ddd, *J* = 28.4, 7.8, 1.8 Hz, 2H), 4.03 (ddd, *J* = 35.0, 7.8, 2.9 Hz, 2H), 2.96 (s, 3H), 1.78 – 1.66 (m, 3H), 1.39 (dq, *J* = 7.9, 3.8 Hz, 2H), 1.33 – 1.19 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 205.7, 162.8, 134.7, 134.3, 130.0, 129.6, 127.6, 127.3, 121.2, 102.1, 102.0, 49.5, 46.0, 40.4, 30.3, 28.0, 23.1, 21.4, 13.9.



219i (major)
dr = 3:1

1'',2,2-Trimethyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219j)

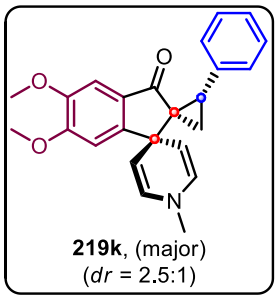
This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3055, 1697. 1674, 1600, 1497, 1408, 1290, 1113, 1007, 932, 756, 725. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.70 – 7.59 (m, 3H), 7.38 – 7.31 (m, 1H), 6.05 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.79 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.25 (dd, *J* = 7.9, 3.0 Hz, 1H), 4.09 (dd, *J* = 7.9, 2.9 Hz, 1H), 2.99 (s, 3H), 1.57 (s, 3H), 1.40 (s, 3H), 1.30 (d, *J* = 3.3 Hz, 1H), 1.19 (d, *J* = 3.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 206.2, 163.1, 134.3, 133.5, 130.6, 128.3, 127.4, 127.2, 121.2, 105.8, 100.9, 51.9, 46.2, 40.5, 30.3, 30.0, 25.0, 20.0.



219j

5',6'-Dimethoxy-1''-methyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219k).

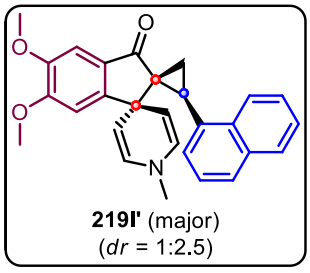
This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{1} 2929,1689, 1670, 1593, 1494, 1359, 1279, 1121, 1018, 869, 722. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.30-7.24 (m, 4H), 7.23 – 7.16 (m, 1H), 7.05 (s, 1H), 7.02 (s, 1H), 6.19 (dd, *J* = 7.8,



1.7 Hz, 1H), 6.08 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.28 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.07 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.02 (s, 3H), 3.87 (s, 3H), 3.02 (s, 3H), 2.93 (t, *J* = 8.6 Hz, 1H), 2.04 (dd, *J* = 8.1, 4.3 Hz, 1H), 1.66-1.62 (m, 1H). **^{13}C{1H} NMR (126 MHz, CDCl$_3$):** δ 201.5, 157.8, 155.2, 149.4 (2C), 136.7, 130.5, 129.9, 129.2 (2C), 127.7 (2C), 126.3, 108.5, 102.3, 102.1, 101.9, 56.3, 56.11, 53.0, 45.9, 40.5, 32.8, 17.9.

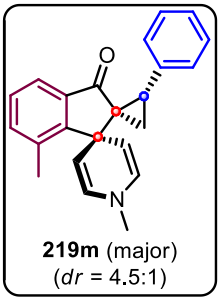
5',6'-Dimethoxy-1''-methyl-2-(naphthalen-1-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219l').

This compound was isolated as reddish-brown oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.03-7.92 (m, 1H), 7.80-7.76 (m, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.42-7.36 (m, 2H), 7.32 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.24 (dt, *J* = 7.2, 1.1 Hz, 1H), 7.22 (s, 1H), 6.88 (s, 1H), 5.87 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.29 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.02 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 3.66 (t, *J* = 8.6 Hz, 1H), 3.11 (dd, *J* = 7.8, 3.0 Hz, 1H), 2.54 (s, 3H), 2.20 (dd, *J* = 8.0, 4.0 Hz, 1H), 1.67 (dd, *J* = 9.2, 4.0 Hz, 1H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 203.5, 159.3, 155.6, 134.5, 130.2, 128.1, 127.2, 126.5, 125.9, 125.8, 125.2, 124.5, 124.4, 124.2, 108.5, 103.3, 102.2, 100.2, 56.2, 56.2, 53.4, 45.1, 39.8, 29.6, 17.7. **HRMS (ESI):** m/z calcd for $C_{28}H_{26}NO_3$ $(M+H)^+$ 424.1913 found: 424.1919.



1'',7'-Dimethyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219m).

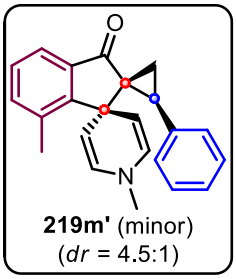
This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2927, 2854, 1697, 1671, 1599, 1478, 1379, 1217, 1199, 1015, 765, 694. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.44 (ddd, *J* = 7.6, 1.3, 0.7 Hz, 1H), 7.38 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.28-7.22 (m, 5H), 7.20-7.15 (m, 1H), 6.12 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.05 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.21 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.97 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.00 (s, 4H), 2.50 (s, 3H), 2.07 (dd, *J* = 8.3, 4.2 Hz, 1H), 1.72 (dd, *J* = 9.1, 4.2 Hz, 1H). **^{13}C (125 MHz, CDCl$_3$):** δ 203.2, 157.0, 138.2, 136.9, 136.5, 135.3, 130.8, 130.6, 129.2 (2C), 127.7, 127.7 (2C), 126.4, 119.6,



100.7, 100.2, 53.4, 46.0, 40.5, 33.6, 18.7, 17.9. **HRMS (ESI):** m/z calcd for $C_{23}H_{22}NO_2$ $(M+H)^+$ 328.1701 found: 328.1701.

(1R,2R)-1'',7''-Dimethyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219m').

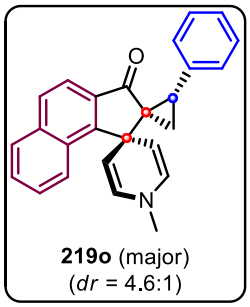
This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**.



R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2927, 2854, 1697, 1671, 1599, 1478, 1379, 1217, 1199, 1015, 765, 694. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.62 (ddd, *J* = 7.6, 1.3, 0.7 Hz, 1H), 7.37 (ddt, *J* = 7.4, 1.5, 0.8 Hz, 1H), 7.27 (d, *J* = 9.5 Hz, 3H), 7.22 – 7.15 (m, 4H), 7.15 – 7.10 (m, 1H), 5.89 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.86 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.07 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.44 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.22 (dd, *J* = 9.3, 8.0 Hz, 1H), 2.73 (s, 3H), 2.41 (d, *J* = 0.8 Hz, 3H), 2.09 (dd, *J* = 8.0, 4.1 Hz, 1H), 1.58 (dd, *J* = 9.3, 4.1 Hz, 1H). **^{13}C (125 MHz, $CDCl_3$):** δ 205.3, 157.9, 138.3, 137.7, 137.6, 133.2, 130.7, 129.5, 128.5, 127.7, 127.0, 125.6, 119.7, 101.8, 99.1, 53.6, 45.37, 40.24, 32.9, 18.8, 17.9. **HRMS (ESI):** m/z calcd for $C_{23}H_{22}NO_2$ $(M+H)^+$ 328.1701 found: 328.1701.

1''-Methyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-cyclopenta[*a*]naphthalene-1',4''-pyridin]-3'-one (219o).

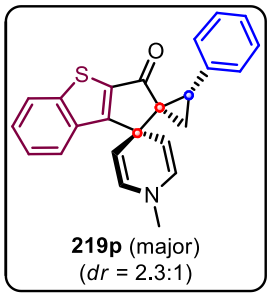
This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.4



(1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2929, 2958, 1711, 1699, 1674, 1594, 1454, 1310, 1221, 1038, 1006, 764, 700. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61-8.56 (m, 1H), 7.95-7.89 (m, 1H), 7.81-7.76 (m, 1H), 7.64-7.54 (m, 3H), 7.32-7.22 (m, 5H), 7.21-7.16 (m, 1H), 6.21 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.14 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.41 (dd, *J* = 7.9, 3.0 Hz, 1H), 4.17 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.13 (s, 3H), 3.10 (t, *J* = 8.7 Hz, 1H), 2.11 (dd, *J* = 8.3, 4.3 Hz, 1H), 1.81 (dd, *J* = 9.2, 4.3 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.4, 159.1, 137.7, 136.5, 133.1, 131.0, 130.5, 130.3, 129.3, 129.2 (3C), 127.9, 127.7 (2C), 126.5, 126.3, 126.1, 118.4, 103.0, 102.3, 54.0, 46.5, 40.7, 32.7, 18.1. **HRMS (ESI):** m/z calcd for: $C_{26}H_{22}NO$ $(M+H)^+$ 364.1701 found 364.1708.

1''-methyl-2-phenyl-1''*H*,3'*H*-dispiro[cyclopropane-1,2'benzo[*b*]cyclopenta[*d*]thiophene-1',4''-pyridin]-3'-one (219p).

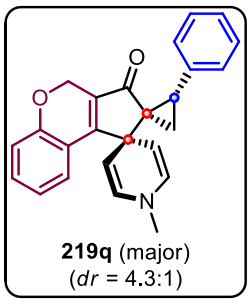
This compound was isolated as yellowish-orange oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.05-7.99 (m, 1H), 7.90-7.85 (m, 1H), 7.47-7.40 (m, 2H), 7.31-7.25 (m, 4H), 7.20 (ddt, *J* = 8.6, 7.2, 1.9 Hz, 1H), 6.23 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.16 (dd, *J* = 7.8, 1.7 Hz, 1H), 4.39 (dd, *J* = 7.8, 3.0 Hz, 1H), 4.15 (dd, *J* = 7.8, 2.9 Hz, 1H), 3.10 (s, 3H), 3.00 (t, *J* = 8.8 Hz, 1H), 2.07-2.04 (m, 1H), 1.74 (dd, *J* = 9.3, 4.5 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 195.2, 167.7, 148.1, 138.3, 136.2, 134.7, 131.3, 131.2, 129.3 (2C), 127.8 (2C), 127.3, 126.5, 124.6, 124.6, 124.39, 100.94, 100.5, 56.8, 44.8, 40.6, 32.0, 17.3. **HRMS (ESI):** m/z calcd for $C_{24}H_{19}NOS$ $(M+H)^+$370.1266 found: 370.1270.



219p (major)
(*dr* = 2.3:1)

1''-Methyl-2-phenyl-5a',9a'-dihydro-1''H,3'H,4'H-dispiro[cyclopropane-1,2'-cyclopenta[*c*]chromene -1',4''-pyridin]-3'-one (219q).

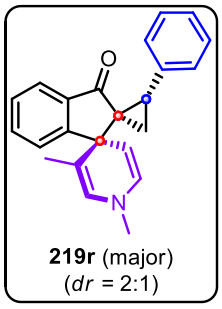
This compound was isolated as pale-yellow sticky oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2929, 2854, 1711, 1684, 1670, 1601, 1566, 1496, 1450, 1345, 1227, 1038, 993, 762, 750, 696. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.81 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.29-7.22 (m, 5H), 7.21-7.16 (m, 1H), 6.92 (td, *J* = 7.6, 1.2 Hz, 1H), 6.86 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.16 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.09 (dd, *J* = 7.9, 1.8 Hz, 1H), 5.00-4.90 (m, 2H), 4.30 (dd, *J* = 7.9, 3.0 Hz, 1H), 4.07 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.05 (s, 3H), 2.89 (t, *J* = 8.7 Hz, 1H), 1.92 (dd, *J* = 8.2, 4.4 Hz, 1H), 1.65 (dd, *J* = 9.2, 4.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 200.3, 156.9, 136.2, 132.0, 131.5, 131.4, 129.1 (2C), 128.4, 127.7 (2C), 126.9, 126.4, 121.0, 120.3, 116.7, 101.4, 100.7, 63.1, 53.8, 46.9, 40.6, 31.7, 17.0.



219q (major)
(*dr* = 4.3:1)

1'',3''-Dimethyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219r).

This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2954, 2927, 1703, 1682, 1602, 1498, 1464, 1292, 1266, 1105, 1081, 765, 749, 700. **^{1}H NMR (500**

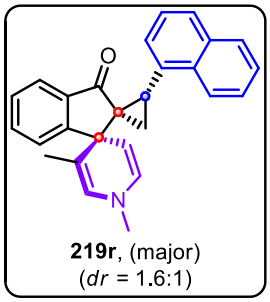


219r (major)
(*dr* = 2:1)

MHz, $CDCl_3$): δ 7.71 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.65-7.58 (m, 2H), 7.35 (ddd, *J* = 7.6, 6.8, 1.4 Hz, 1H), 7.20 (dq, *J* = 6.9, 2.9, 2.5 Hz, 2H), 7.18-7.11 (m, 3H), 6.01 (dd, *J* = 7.7, 1.7 Hz, 1H), 4.69 (p, *J* = 1.3 Hz, 1H), 4.07 (d, *J* = 7.7 Hz, 1H), 3.16 (dd, *J* = 9.3, 7.9 Hz, 1H), 2.72 (s, 3H), 1.96 (dd, *J* = 7.9, 4.1 Hz, 1H), 1.54 (dd, *J* = 9.3, 4.1 Hz, 1H), 0.72 (d, *J* = 1.3 Hz, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 204.7, 162.4, 136.7, 134.7, 134.2, 130.2, 128.7 (2C), 127.3, 126.8 (3C), 126.0, 125.5, 121.4, 107.1, 99.2, 50.6, 48.6, 39.9, 31.7, 19.8, 16.5. **HRMS (ESI):** m/z calcd for $C_{23}H_{22}NO$ $(M+H)^+$ 328.1701 found: 328.1711.

1'',3''-dimethyl-2-(naphthalen-1-yl)-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (205s).

This compound was isolated as pale-yellow sticky oil by following the general procedure-**15**.

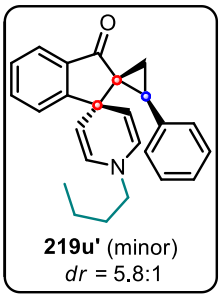


219r, (major)
(*dr* = 1.6:1)

R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3053, 2920, 1698, 1682, `1600, 1463, 1293, 1264, 1240, 1084, 983, 776, 765. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.25-8.21 (m, 1H), 7.8 (ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H), 7.83-7.73 (m, 3H), 7.67 (t, *J* = 8.7 Hz, 1H), 7.59 (dddd, *J* = 8.3, 7.3, 4.7, 1.2 Hz, 1H), 7.52 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.48 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.43-7.22 (m, 7H), 7.16 (d, *J* = 7.3 Hz, 1H), 5.97 (dd, *J* = 7.6, 1.7 Hz, 1H), 4.28 (p, *J* = 1.3 Hz, 1H), 4.05 (d, *J* = 7.6 Hz, 1H), 3.91 (dd, *J* = 9.3, 8.0 Hz, 1H), 2.97 (d, *J* = 7.7 Hz, 1H), 2.60 (s, 3H), 2.55 (s, 1H), 2.25 (dd, *J* = 7.9, 4.0 Hz, 1H), 1.62 (dd, *J* = 9.3, 4.0 Hz, 1H), 1.16 (d, *J* = 1.2 Hz, 1H), 0.31 (d, *J* = 1.3 Hz, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 204.8, 134.6, 134.6, 134.5, 134.0, 133.4, 132.8, 130.3, 128.2, 128.2, 128.1, 127.4, 127.3, 127.3, 127.1, 126.7, 126.7, 126.0, 125.9, 125.4, 125.3, 125.2, 125.1, 124.5, 124.4, 124.3, 124.2, 123.7, 121.9, 121.6, 107.7, 101.4, 99.0, 52.8, 48.8, 39.9, 39.8, 33.0, 27.9, 19.7, 19.6, 17.0, 16.6. **HRMS (ESI):** m/z calcd $C_{27}H_{24}NO$ $(M+H)^+$ 378.1858 found: 378.1862.

1''-Butyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219u').

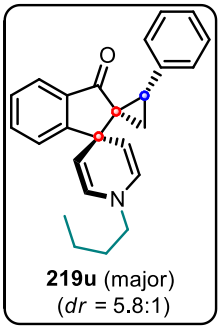
This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light).**IR (thin film, neat):** ν_{max}/cm^{-1} 2955, 2863, 1699, 1669, 1599, 1497, 1461, 1321, 1029, 998, 766, 696. **^{1}H NMR (500 MHz,**



CDCl$_3$): δ 7.70 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.64 (td, *J* = 7.4, 1.2 Hz, 1H), 7.56 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.35 (td, *J* = 7.4, 1.1 Hz, 1H), 7.22 – 7.14 (m, 4H), 7.13 – 7.07 (m, 1H), 6.02 (dd, *J* = 7.9, 1.8 Hz, 1H), 5.04 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.11 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.49 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.17 (dd, *J* = 9.3, 8.0 Hz, 1H), 2.97 – 2.89 (m, 1H), 2.85 (q, *J* = 7.1 Hz, 1H), 1.99 (dd, *J* = 8.0, 4.1 Hz, 1H), 1.63 – 1.56 (m, 1H), 1.46 – 1.37 (m, 2H), 1.34 – 1.24 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 205.0, 164.2, 137.5, 134.8, 132.4, 129.7, 129.3, 127.6, 127.3, 127.2, 126.8, 125.6, 121.4, 103.9, 100.3, 52.9, 52.8, 45.6, 33.2, 32.1, 19.7, 19.0, 13.8. **HRMS (ESI):** m/z calcd for $C_{25}H_{26}NO$ $(M+H)^+$ 356.2014 found: 356.2027.

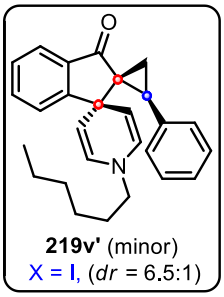
1''-Butyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219u).

This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2955, 2863, 1699, 1669, 1599, 1497, 1461, 1321, 1029, 998, 766, 696. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.65-7.60 (m, 2H), 7.53 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.29 (ddd, *J* = 7.6, 4.8, 3.4 Hz, 1H), 7.27-7.23 (m, 4H), 7.17 (dt, *J* = 5.2, 1.8 Hz, 1H), 6.20 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.09 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.27 (dd, *J* = 7.8, 3.0 Hz, 1H), 4.04 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.14 (t, *J* = 7.0 Hz, 2H), 3.01-2.91 (m, 1H), 2.07 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.67 (dd, *J* = 9.1, 4.3 Hz, 1H), 1.61-1.49 (m, 2H), 1.40-1.30 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 202.9, 162.7, 136.5, 134.6, 134.4, 129.7, 129.2 (2C), 129.1, 127.7 (2C), 127.7, 127.4, 126.5, 121.5, 101.6, 101.5, 53.2, 53.1, 46.5, 33.6, 32.2, 19.8, 18.7, 13.8. **HRMS (ESI):** m/z calcd for $C_{25}H_{26}NO$ $(M+H)^+$ 356.2014 found: 356.2027.



1''-Hexyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219v').

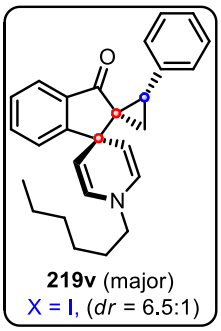
This compound was isolated as pale-yellow oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2952, 2926, 2857, 1699, 1671, 1600, 1498, 1461, 1375, 1147, 1114, 1007, 931, 724, 695. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.70 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.56 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.27 – 7.24 (m, 1H), 7.18 – 7.10 (m, 4H), 6.02 (dd, *J* = 7.9, 1.8



Hz, 1H), 5.03 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.11 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.49 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.17 (dd, *J* = 9.3, 8.0 Hz, 1H), 2.94 – 2.89 (m, 1H), 2.86 – 2.80 (m, 1H), 1.99 (dd, *J* = 8.0, 4.1 Hz, 1H), 1.62 – 1.59 (m, 1H), 1.45 – 1.40 (m, 2H), 1.36 – 1.28 (m, 6H), 0.92 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 205.0, 164.2, 137.5, 134.8, 132.4, 129.7, 129.2 (2C), 127.6, 127.3, 127.2 (2C), 126.8, 125.6, 121.4, 103.9, 100.3, 53.2, 52.8, 45.6, 33.2, 31.5, 29.9, 26.2, 22.6, 19.0, 14.0. **HRMS (ESI):** m/z calcd for $C_{27}H_{30}NO$ $(M+H)^+$ 384.2327 found: 384.2339.

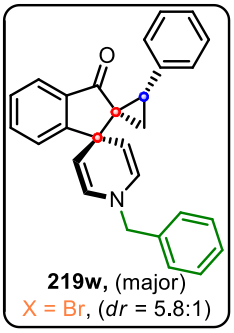
1''-Hexyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219v).

This compound was isolated as pale-yellow semi-solid by following the general procedure-**15**.



R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2952, 2926, 2857, 1699, 1671, 1600, 1498, 1461, 1375, 1147, 1114, 1007, 931, 724, 695. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.64-7.61 (m, 2H), 7.53 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.32-7.27 (m, 1H), 7.27-7.23 (m, 4H), 7.19-7.15 (m, 1H), 6.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.09 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.27 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.04 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.14 (t, *J* = 7.0 Hz, 2H), 3.00-2.93 (m, 1H), 2.07 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.67 (dd, *J* = 9.1, 4.3 Hz, 1H), 1.57 (t, *J* = 7.0 Hz, 2H), 1.33 (qd, *J* = 5.3, 3.6, 3.0 Hz, 6H), 0.94-0.88 (m, 3H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 202.9, 162.7, 136.5, 134.6, 134.4, 129.7, 129.2 (2C), 129.1, 127.8 (2C), 127.7, 127.4, 126.5, 121.5, 101.6, 101.5, 53.5, 53.0, 46.5, 33.6, 31.5, 30.1, 26.2, 22.6, 18.7, 14.0. **HRMS (ESI):** m/z calcd for $C_{27}H_{30}NO$ $(M+H)^+$ 384.2327 found: 384.2339.

1''-Benzyl-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219w).

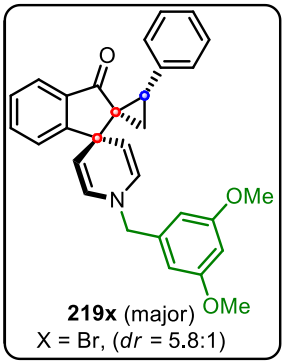


This compound was isolated as reddish-orange oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3085, 3062, 3027, 1700, 1670, 1601, 1496, 1403, 1324, 1209, 1021, 766, 733. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.72 – 7.65 (m, 2H), 7.59 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.44 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.36 (ddd, *J* = 7.9, 5.7, 2.1 Hz, 2H), 7.33 – 7.28 (m, 6H), 7.23

(ddd, *J* = 8.4, 3.9, 2.3 Hz, 1H), 6.33 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.22 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.40 (d, *J* = 8.0 Hz, 3H), 4.17 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.04 (t, *J* = 8.6 Hz, 1H), 2.14 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.74 (dd, *J* = 9.1, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 202.8, 162.48, 138.3, 136.3, 134.7, 134.5, 130.1, 129.4 (2C), 129.3, 128.8 (2C), 127.7 (2C), 127.7, 127.6, 127.5, 127.0 (2C), 126.5, 121.6, 102.6, 102.5, 57.0, 52.9, 46.3, 33.7, 18.7.

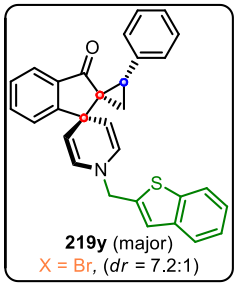
1''-(3,5-Dimethoxybenzyl)-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219x).

This compound was isolated as pale-yellow solid by following the general procedure-**15**. M.P = 94-96 ^{o}C. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2955, 2923, 2853, 16999, 1671, 1596, 1462, 1429, 1402, 1321, 1204, 1155, 1064, 1021, 1010, 766, 733, 696. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.73-7.65 (m, 2H), 7.59 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.39-7.33 (m, 1H), 7.31 (d, *J* = 4.4 Hz, 4H), 7.26-7.20 (m, 1H), 6.44 (s, 3H), 6.32 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.21 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.40 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.34 (s, 2H), 4.18 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.85 (s, 6H), 3.04 (t, *J* = 8.6 Hz, 1H), 2.14 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.74 (dd, *J* = 9.1, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 202.7, 162.4, 161.2 (2C), 140.9, 136.3, 134.7, 134.5, 130.1, 129.5 (2C), 129.2 (2C), 127.7, 127.7, 127.5, 126.5, 121.6, 104.7 (2C), 102.5, 102.4, 99.3, 57.0, 55.4, 55.3, 52.8, 46.3, 33.7, 18.7.



1''-(Benzo[b]thiophen-2-ylmethyl)-2-phenyl-1''H,3'H-dispiro[cyclopropane-1,2'-indene-1',4''-pyridin]-3'-one (219y).

This compound was isolated as reddish-brown oil by following the general procedure-**15**. R_f = 0.4 (1:9 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3052, 2920, 2854, 1698, 1671, 1601, 1461, 1399, 1322, 1206, 1190, 1018, 766, 748. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.86 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.78 (dd, *J* = 7.1, 1.8 Hz, 1H), 7.70-7.64 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.36 (dtd, *J* = 13.9, 6.3, 5.6, 2.1 Hz, 3H), 7.29 (d, *J* = 4.5 Hz, 4H), 7.22 (d, *J* = 4.2 Hz, 2H), 6.36 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.24 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.62 (d, *J* = 1.0 Hz, 2H), 4.44 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.22 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.03 (t, *J* = 8.6 Hz, 1H), 2.12 (dd, *J* = 8.2, 4.3 Hz, 1H), 1.74 (dd, *J* = 9.1, 4.3 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 202.7, 162.2, 142.4, 139.8, 139.4, 136.2, 134.7, 134.5, 129.3, 129.3



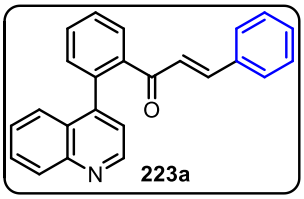
(2C), 128.7, 127.8 (2C), 127.7, 127.6, 126.5, 124.5, 124., 123.5, 122.5, 122.0, 121.6, 103.6, 103.4, 53.1, 52.6, 46.2, 33.7, 18.7.

General procedure-16: Synthesis of enone tethered quinolinium salts (224a-224n) (Scheme 73)

All enone tethered quinolinium salts were prepared by following the **general procedure-12** applied for pyindinum based salt by employing 4-bromo quinoline as coupling partner.

(*E*)-3-Phenyl-1-(2-(quinolin-4-yl)phenyl)prop-2-en-1-one (223a).

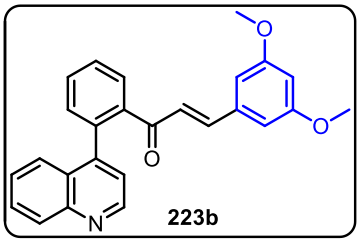
This compound was isolated as pale-yellow semi-solid by following the general procedure-**16**.



R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 1667, 1642, 1604, 1331, 1277, 1209, 1017, 981, 959, 764, 750. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.87 (d, *J* = 4.3 Hz, 1H), 8.13 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.85-7.81 (m, 1H), 7.76 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.69 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.62 (td, *J* = 6.8, 1.7 Hz, 2H), 7.50 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.47-7.44 (m, 1H), 7.30-7.24 (m, 3H), 7.23-7.17 (m, 2H), 7.05-7.00 (m, 2H), 6.59 (d, *J* = 16.0 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.4, 149.7, 148.3, 147.3, 144.7, 140.3, 136.6, 134.1, 130.1, 130.8, 130.5, 129.9, 129.5, 129.0, 128.7 (2C), 128.7, 128.1 (2C), 127.1, 127.0, 125.6, 125.5, 122.0.

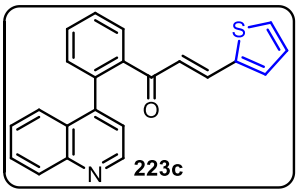
(*E*)-3-(3,5-Dimethoxyphenyl)-1-(2-(quinolin-4-yl)phenyl)prop-2-en-1-one (223b).

This compound was isolated as pale-yellow solid by following the general procedure-**16**. M.P = 113.4-116 °C. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 2933, 2838, 1667, 1642, 1586, 1507, 1457, 1425, 1284, 1203, 1154, 1061, 1020, 979, 925, 843, 767, 734. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.88 (d, *J* = 4.4 Hz, 1H), 8.17-8.09 (m, 1H), 7.86-7.80 (m, 1H), 7.79 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.66-7.60 (m, 2H), 7.55-7.43 (m, 2H), 7.28 (d, *J* = 4.9 Hz, 1H), 7.21 (d, *J* = 15.8 Hz, 1H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.38 (t, *J* = 2.2 Hz, 1H), 6.17 (d, *J* = 2.2 Hz, 2H), 3.65 (d, *J* = 1.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.2, 160.7 (2C), 149.7, 148.4, 147.1, 144.6, 140.2, 136.5, 135.9, 131.0, 130.81, 129.9, 129.5, 129.1, 128.7, 127.0, 126.9, 125.8, 125.7, 122.1, 105.8 (2C), 103.15, 55.34, 55.31.



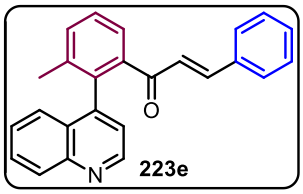
(*E*)-1-(2-(Quinolin-4-yl)phenyl)-3-(thiophen-2-yl)prop-2-en-1-one (223c).

This compound was isolated as reddish-brown oil by following the general procedure-**16**. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2954, 2924, 2853, 1660, 1639, 1582, 1508, 1420, 1387, 1364, 1280, 1209, 1018, 969, 853, 766, 709. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.89 (d, *J* = 4.4 Hz, 1H), 8.17-8.09 (m, 1H), 7.86-7.80 (m, 1H), 7.75-7.67 (m, 2H), 7.62 (td, *J* = 6.4, 1.3 Hz, 2H), 7.50 (ddd, *J* = 8.5, 7.0, 1.4 Hz, 1H), 7.47-7.43 (m, 1H), 7.39 (d, *J* = 15.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.24 (d, *J* = 5.1 Hz, 1H), 6.96 (d, *J* = 3.6 Hz, 1H), 6.90 (ddd, *J* = 4.9, 3.6, 1.1 Hz, 1H), 6.40 (d, *J* = 15.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 193.5, 149.7 (2C), 148.3, 147.2, 140.2, 139.5, 136.8, 136.6, 131.8, 131.0, 130.8, 129.9, 129.5, 129.2, 128.9, 128.7, 128.1, 127.0, 125.6, 124.1, 121.9.



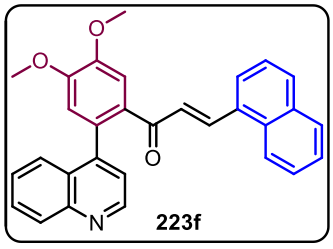
(*E*)-1-(3-Methyl-2-(quinolin-4-yl)phenyl)-3-phenylprop-2-en-1-one (223e).

This compound was isolated as pale-yellow solid by following the general procedure-**16**. M.P = 86-89 °C. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 2922, 1668, 1643, 1601, 1574, 1505, 1448, 1330, 1266, 1055, 979, 845, 828, 761, 734, 701. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.88 (d, *J* = 4.4 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.62-7.56 (m, 2H), 7.53-7.47 (m, 3H), 7.26 (dd, *J* = 8.3, 6.0 Hz, 2H), 7.20 (dd, *J* = 7.4, 5.4 Hz, 3H), 7.04-7.00 (m, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 2.01 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.9, 150.0, 148.2, 146.3, 144.6, 140.8, 137.3, 135.5, 134.1, 132.5, 130.4, 130.1, 129.4, 128.7 (2C), 128.4, 128.15(2C), 127.31, 127.2, 126.0, 125.8, 125.6, 122.2, 20.2.



(*E*)-1-(4,5-Dimethoxy-2-(quinolin-4-yl)phenyl)-3-(naphthalen-1-yl)prop-2-en-1-one (223f).

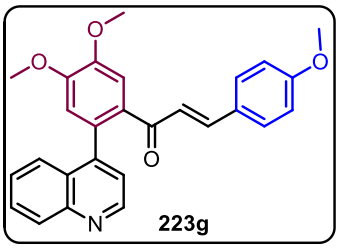
This compound was isolated as pale-yellow solid by following the general procedure-**16**. M.P = 157-159.4 °C. R_f = 0.3 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2955, 2931, 2852, 1654, 1596, 1570, 1513, 1464, 1348, 1274, 1265, 1248, 1213, 1147, 1088, 1028, 976, 804, 777, 749. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.91 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.20-8.12 (m, 2H), 8.10 (d, *J* = 15.5 Hz, 1H), 7.86-7.80 (m, 1H), 7.80-7.72 (m, 3H), 7.61-7.54 (m, 1H), 7.52 (s, 1H), 7.48-7.40 (m, 2H), 7.38 (dd, *J* = 8.5, 4.2



Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.94 (s, 1H), 6.62 (d, *J* = 7.3 Hz, 1H), 6.42 (d, *J* = 15.4 Hz, 1H), 4.07 (s, 3H), 3.97 (s, 3H). **^{13}C NMR (100 MHz, DMSO-*d*$_6$):** δ 188.1, 146.4, 145.8, 144.0, 143.5, 134.7, 134.3, 129.4, 128.7, 128.7, 127.2, 127.0, 126.5, 125.6, 124.9, 124.29, 123.8, 123.7, 123.1, 122.7, 121.9, 121.3, 120.4, 120.0, 118.4, 116.9, 109.1, 107.2, 51.5, 51.4.

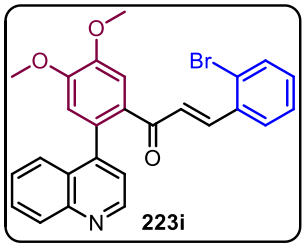
(*E*)-1-(4,5-Dimethoxy-2-(quinolin-4-yl)phenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (223g).

This compound was isolated as pale-yellow solid by following the general procedure-**16**. M.P = 153-156 ^{o}C. R_f = 0.4 (5:5 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2921, 1651, 1595, 1570, 1510, 1463, 1250, 1100, 991, 828, 806. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.91 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15-8.04 (m, 2H), 7.72 (dd, *J* = 8.6, 7.1 Hz, 1H), 7.51 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.44 (s, 1H), 7.38 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.19 (d, *J* = 15.7 Hz, 1H), 6.91 (s, 1H), 6.85-6.78 (m, 2H), 6.71-6.65 (m, 2H), 6.20 (d,*J* = 15.7 Hz, 1H), 4.04 (s, 3H), 3.94 (s, 3H), 3.76 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ 193.0, 161.3, 150.9, 150.4, 148.7, 148.2, 142.6, 139.1, 134.2, 133.6, 131.6, 129.6, 129.5, 128.8, 128.1, 127.4, 127.0, 123.2, 121.5, 114.0, 113.8, 111.9, 55.3.



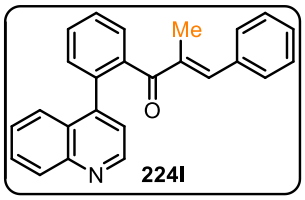
(*E*)-3-(2-Bromophenyl)-1-(4,5-dimethoxy-2-(quinolin-4-yl)phenyl)prop-2-en-1-one (223i)

This compound was isolated as pale-yellow semi-solid by following the general procedure-**16**. R_f = 0.3 (4:6 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2954, 2923, 2853, 1656, 1593, 1564, 1513, 1464, 1439, 1345, 1275, 1200, 1145, 1100, 1026, 805, 757, 733. **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.91 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 – 8.07 (m, 2H), 7.72 – 7.64 (m, 2H), 7.50 – 7.44 (m, 3H), 7.11 – 6.99 (m, 3H), 6.92 (s, 1H), 6.42 (dd, *J* = 7.6, 1.9 Hz, 1H), 6.22 (d, *J* = 15.7 Hz, 1H), 4.05 (s, 3H), 3.96 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$):** δ 192.7, 151.1, 149.6, 149.0, 148.2, 147.8, 143.3, 134.2, 132.9, 130.5, 130.2, 129.7, 129.6, 128.6, 127.9, 127.3, 127.3, 125.7, 125.3, 122.3, 113.2, 112.0, 56.2.



(*E*)-2-Methyl-3-phenyl-1-(2-(quinolin-4-yl)phenyl)prop-2-en-1-one (224l).

This compound was isolated as pale-yellow solid by following the general procedure-**16**. M.P = 132.8-134 ^{o}C. R_f = 0.4 (3:7 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film,**

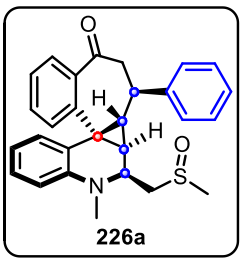


neat): ν_{max}/cm^{-1} 2923, 1649, 1583, 1508, 1444, 1419, 1357, 1240, 1011, 764. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.81 (d, *J* = 4.4 Hz, 1H), 8.12 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.74-7.69 (m, 1H), 7.65-7.60 (m, 3H), 7.50-7.46 (m, 1H), 7.39 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.20-7.15 (m, 4H), 6.87 (d, *J* = 1.6 Hz, 1H), 6.77-6.72 (m, 2H), 1.60 (d, *J* = 1.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 200.5, 149.5, 148.3, 147.2, 142.9, 140.7, 137.9, 136.3, 135.0, 130.4, 129.9, 129.7, 129.5, 129.1 (2C), 129.0, 128.6, 128.4, 128.1 (2C), 126.9, 126.7, 126.0, 121.9, 12.9.

General procedure-15: Synthesis of Polycyclic Benzocycloheptanones (226a-226n).

A mixture of sodium hydride (60% in oil, 10 mg, 0.25 mmol) and trimethyloxosulfonium iodide (56 mg, 0.21 mmol) was placed in an oven dried flask and DMSO (4.0 mL) was added to the mixture. After the evolution of hydrogen ceased, the milky solution turned clear and the reaction mixture was stirred for 15 min. The compound **224a** (100 mg, 0.21 mmol) was dissolved in DMSO (1.0 mL) and was added to the clear solution dropwise over a period of 5-10 min and stirred at rt until the reactant **224a** disappeared as monitored by TLC. The reaction mixture was quenched with ice-water and extracted with diethyl ether. 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.

1-Methyl-2-((methylsulfinyl)methyl)-3-phenyl-2,2a,3,4-tetrahydro-1*H*benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226a).

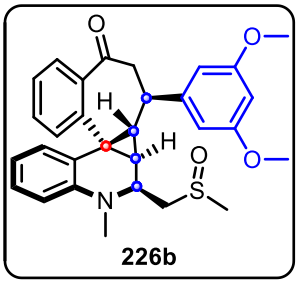


This compound was isolated as pale-yellow solid by following the general procedure-**17**. M.P = 225-227 ^oC. R_f = 0.3 (9:1 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3028, 2920, 1679, 1598, 1497, 1282, 1230, 1050, 750. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.57 (ddd, *J* = 8.7, 7.0, 1.8 Hz, 2H), 7.51 – 7.47 (m, 1H), 7.41 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.34 (ddd, *J* = 7.6, 6.4, 1.7 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.24 – 7.19 (m, 2H), 7.08 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 6.71 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.60 (td, *J* = 7.5, 1.1 Hz, 1H), 6.48 (dd, *J* = 7.6, 1.7 Hz, 1H), 3.93 (ddd, *J* = 10.9, 4.4, 2.8 Hz, 1H), 3.29 – 3.17 (m, 2H), 2.91 – 2.74 (m, 5H), 2.42 (t, *J* = 4.8 Hz, 1H), 2.11 – 2.00 (m, 4H), 1.86 (dd, *J* = 10.5, 5.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 206.1, 142.7, 140.8, 139.3, 132.7, 132.0, 128.9,

128.2, 128.0, 127.9, 127.4, 127.1, 127.0, 126.5, 118.2, 112.4, 61.2, 49.6, 48.9, 44.7, 39.0, 35.9, 35.1, 34.6, 31.0. **HRMS (ESI):** m/z calcd for $C_{28}H_{29}NO_2S$ $(M+H^+)$ 442.1841 found: 442.1832.

3-(3,5-Dimethoxyphenyl)-1-methyl-2-((methylsulfinyl)methyl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226b).

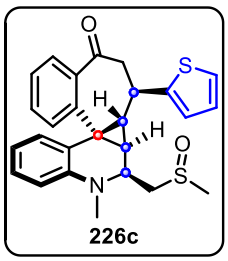
This compound was isolated as off-white solid by following the general procedure-**17**. M.P = 102-105 ^oC. R_f = 0.3 (9:1 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 2871, 2850, 1679, 1595, 1483, 1362, 1204, 1057, 845, 830, 750. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.61 – 7.53 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.11 – 7.05 (m, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.36 (s, 3H), 3.94 (dt, *J* = 11.2, 3.1 Hz, 1H), 3.78 (s, 6H), 3.30 – 3.18 (m, 2H), 2.89 (s, 3H), 2.80 – 2.70 (m, 1H), 2.43 (t, *J* = 4.7 Hz, 1H), 2.23 (s, 3H), 2.15 (t, *J* = 11.5 Hz, 1H), 1.84 (dd, *J* = 10.8, 5.2 Hz, 1H), 1.68 (d, *J* = 4.7 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 205.9, 161.1, 145.0, 142.7, 140.8, 139.3, 132.7, 132.1, 128.2, 128.0, 127.8, 127.0, 126.5, 118.2, 112.5, 105.2, 98.6, 61.5, 55.3, 49.6, 48.4, 44.9, 38.9, 35.9, 35.2, 34.9, 30.9. **HRMS (ESI):** m/z calcd for $C_{30}H_{32}NO_4S$ $(M+H^+)$ 502.2052 found: 502.2040.



226b

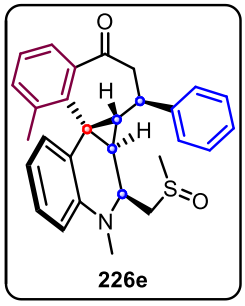
1-Methyl-2-((methylsulfinyl)methyl)-3-(thiophen-2-yl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226c).

This compound was isolated as reddish-brown solid by following the general procedure-**17**. M.P = 190-193 ^oC. R_f = 0.3 (8:2 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 2853, 1674, 1595, 1494, 1361, 1276, 1041, 963, 764, 701. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.56 (ddd, *J* = 15.2, 7.6, 1.6 Hz, 2H), 7.48 (td, *J* = 7.5, 1.3 Hz, 1H), 7.42 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.20 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.08 (ddd, *J* = 8.6, 7.3, 1.7 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.87 (dd, *J* = 3.5, 1.2 Hz, 1H), 6.72 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.61 (td, *J* = 7.5, 1.1 Hz, 1H), 6.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 4.01 – 3.93 (m, 1H), 3.34 – 3.27 (m, 1H), 3.27 – 3.13 (m, 2H), 2.97 (d, *J* = 15.6 Hz, 1H), 2.91 (s, 3H), 2.45 (t, *J* = 4.8 Hz, 1H), 2.36 (dd, *J* = 12.3, 10.8 Hz, 1H), 2.30 (s, 3H), 1.92 (dd, *J* = 10.2, 5.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 205.3, 146.0, 142.8, 139.1, 132.8, 132.1, 128.3, 128.0, 127.9, 127.0, 126.4, 124.0, 123.6, 118.4, 112.6, 61.3, 50.3, 49.8, 39.9, 39.3, 35.8, 35.7, 34.8, 30.9, 29.7. **HRMS (ESI):** m/z calcd for $C_{26}H_{26}NO_2S_2$ $(M+H)^+$ 448.1405 found: 448.1394.



226c

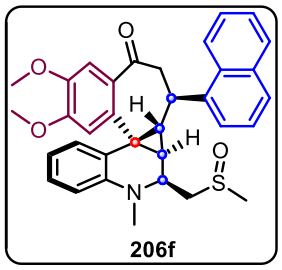
1,9-Dimethyl-2-((methylsulfinyl)methyl)-3-phenyl-1,2,2a,2b,3,4-hexahydro-5*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5-one (226e).



This compound was isolated as pale-yellow oil by following the general procedure-**17**. R_f = 0.3 (8:2 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2960, 2927, 1676, 1598, 1493, 1270, 1220, 1041, 764. **^{1}H NMR (500 MHz, $CDCl_3$):** ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.34 (m, 2H), 7.31 (ddd, *J* = 7.6, 6.3, 1.8 Hz, 3H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.19 (m, 2H), 7.05 (ddd, *J* = 8.3, 7.2, 1.8 Hz, 1H), 6.67 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.56 (td, *J* = 7.4, 1.1 Hz, 1H), 6.51 (dd, *J* = 7.7, 1.8 Hz, 1H), 3.96 (ddd, *J* = 10.9, 4.5, 2.6 Hz, 1H), 3.22 – 3.13 (m, 2H), 2.87 (s, 3H), 2.84 – 2.80 (m, 1H), 2.80 – 2.76 (m, 1H), 2.22 (dd, *J* = 5.4, 4.5 Hz, 1H), 2.18 (s, 3H), 2.08 – 2.01 (m, 4H), 1.84 (dd, *J* = 10.8, 5.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 207.0, 142.7, 142.6, 142.1, 139.2, 134.2, 128.9, 128.2, 127.4, 127.1, 127.1, 127.0, 125.6, 124.9, 118.27, 112.42, 61.4, 49.5, 48.9, 44.7, 39.1, 36.1, 36.0, 34.6, 29.7, 20.3. **HRMS (ESI):** m/z calcd for $C_{29}H_{30}NO_2S$ $(M+H)^+$ 456.1997 found: 456.1972.

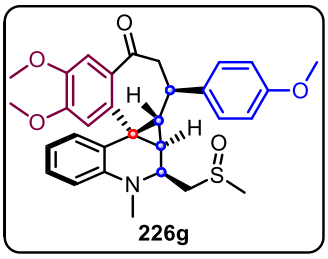
7,8-Dimethoxy-1-methyl-2-((methylsulfinyl)methyl)-3-(naphthalen-1-yl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226f).

This compound was isolated as pale-yellow oil by following the general procedure-**17**. R_f = 0.4 (9:1 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 2850, 1710, 1664, 1597, 1511, 1363, 1263, 1212, 1038, 750. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.88 (td, *J* = 7.1, 6.3, 3.8 Hz, 2H), 7.75 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.54 – 7.43 (m, 4H), 7.24 (s, 1H), 7.08 (ddd, *J* = 8.3, 7.3, 1.7 Hz, 1H), 6.83 (s, 1H), 6.70 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.62 (td, *J* = 7.4, 1.1 Hz, 1H), 6.56 – 6.47 (m, 1H), 4.00 (s, 3H), 3.93 (s, 3H), 3.83 (s, 2H), 3.45 (d, *J* = 18.2 Hz, 1H), 3.06 – 2.90 (m, 2H), 2.82 (s, 3H), 2.47 (t, *J* = 4.7 Hz, 1H), 1.97 (s, 1H), 1.78 (t, *J* = 11.5 Hz, 1H), 1.69 (d, *J* = 18.5 Hz, 2H), 1.53 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 204.2, 153.2, 148.9, 142.8, 133.6, 132.6, 130.8, 128.9, 127.7, 127.2, 126.9, 126.6, 126.1, 125.8, 118.3, 113.9, 112.5, 111.0, 56.3, 56.1, 49.6, 38.4, 35.93, 29.70. **HRMS (ESI):** m/z calcd for $C_{34}H_{34}NO_4S$ $(M+H)^+$ 552.2209 found: 552.2200.



(7,8-Dimethoxy-3-(4-methoxyphenyl)-1-methyl-2-((methylsulfinyl)methyl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226g).

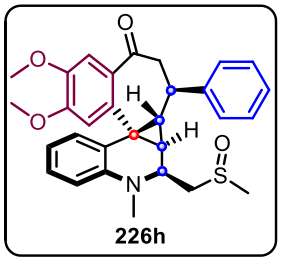
This compound was isolated as off-white solid by following the general procedure-**17**. M.P = 242-244 ºC. R_f = 0.3 (10:0 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2927, 2850, 1664, 1596, 1505, 1448, 1362, 1211, 1146, 1018, 743 **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.11 (dd, *J* = 7.0, 1.7 Hz, 3H), 7.06 (ddd, *J* = 8.2, 7.2, 1.7 Hz, 1H), 6.88 – 6.81 (m, 2H), 6.76 (s, 1H), 6.69 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.59 (td, *J* = 7.4, 1.1 Hz, 1H), 6.48 (dd, *J* = 7.6, 1.7 Hz, 1H), 3.96 (s, 3H), 3.92 (ddd, *J* = 10.9, 4.4, 2.8 Hz, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 3.26 – 3.14 (m, 2H), 2.87 (s, 3H), 2.84 – 2.74 (m, 2H), 2.39 (dd, *J* = 5.3, 4.4 Hz, 1H), 2.13 (s, 3H), 2.08 (dd, *J* = 12.2, 10.7 Hz, 1H), 1.77 (dd, *J* = 10.6, 5.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 204.6, 158.6, 152.9, 148.7, 142.6, 135.0, 133.3, 132.9, 128.2, 127.7, 126.9, 126.9, 118.2, 114.2, 113.6, 112.3, 110.8, 61.6, 56.2, 56.0, 55.3, 49.7, 49.3, 43.8, 39.1, 36.2, 36.0, 34.5, 30.9.



226g

7,8-Dimethoxy-1-methyl-2-((methylsulfinyl)methyl)-3-phenyl-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226h).

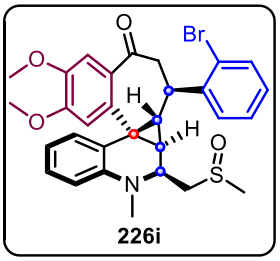
This compound was isolated as pale-yellow oil by following the general procedure-**17**. R_f = 0.3 (10:0 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2930, 2831, 1712,1674, 1595, 1498, 1445, 1265, 1205, 1171, 1035, 884, 747. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31 (dd, *J* = 8.0, 6.7 Hz, 2H), 7.26 – 7.22 (m, 1H), 7.22 – 7.18 (m, 2H), 7.13 (s, 1H), 7.07 (ddd, *J* = 8.5, 7.3, 1.7 Hz, 1H), 6.77 (s, 1H), 6.69 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.59 (td, *J* = 7.5, 1.1 Hz, 1H), 6.49 (dd, *J* = 7.7, 1.7 Hz, 1H), 3.96 (s, 3H), 3.92 (ddd, *J* = 10.7, 4.5, 2.7 Hz, 1H), 3.89 (s, 3H), 3.25 – 3.14 (m, 2H), 2.87 (s, 3H), 2.40 (dd, *J* = 5.2, 4.4 Hz, 1H), 2.06 (s, 4H), 1.81 (dd, *J* = 10.5, 5.3 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 204.4, 152.9, 148.8, 143.0, 142.6, 133.3, 128.9, 127.8, 127.3, 127.0, 126.9, 126.8, 118.2, 113.7, 112.3, 110.8, 61.6, 56.2, 56.0, 49.6, 49.1, 44.7, 39.1, 36.1, 36.0, 34.54, 31.02. **HRMS (ESI):** m/z calcd for $C_{30}H_{32}NO_4S$ $(M+H)^+$ 502.2052 found: 502.2067.



226h

3-(2-Bromophenyl)-7,8-dimethoxy-1-methyl-2-((methylsulfinyl)methyl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226i).

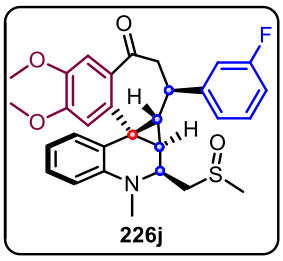
This compound was isolated as reddish-brown solid by following the general procedure-**17**. M.P = 217-219 ºC. R_f = 0.3 (8:2 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1}2929, 2856, 1710, 1665, 1597, 1511, 1497, 1467, 1361, 1262, 1212, 1171, 1035, 874, 751, 731. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.16 (s, 1H), 7.11 (ddd, *J* = 8.0, 6.8, 2.2 Hz, 1H), 7.07 (ddd, *J* = 8.3, 7.3, 1.7 Hz, 1H), 6.77 (s, 1H), 6.70 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.60 (td, *J* = 7.4, 1.1 Hz, 1H), 6.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 3.97 (s, 3H), 3.97 – 3.92 (m, 1H), 3.90 (s, 3H), 3.21 (dt, *J* = 17.8, 7.0 Hz, 2H), 2.89 (s, 3H), 2.81 (dd, *J* = 18.7, 2.5 Hz, 1H), 2.54 (t, *J* = 4.9 Hz, 1H), 2.16 (s, 4H), 1.70 (s, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 203.9, 153.0, 142.7, 142.3, 133.4, 133.1, 132.5, 128.4, 128.1, 127.9, 127.0, 126.9, 118.3, 113.7, 112.5, 110.8, 61.8, 56.2, 56.0, 50.1, 39.2, 36.1, 34.5, 30.6.



226i

3-(3-Fluorophenyl)-7,8-dimethoxy-1-methyl-2-((methylsulfinyl)methyl)-2,2a,3,4-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-*c*]quinolin-5(2b*H*)-one (226j).

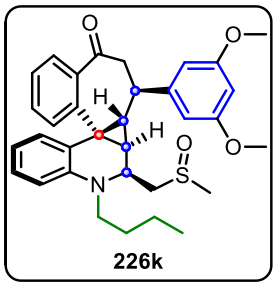
This compound was isolated as off-white solid by following the general procedure-**17** M.P = 242-245 ºC R_f = 0.3 (8:2 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 3004, 2960, 2932, 2915, 2837, 1667, 1598, 1512, 1463, 1362, 1260, 1212, 1176, 1052, 1035, 750. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.30 (td, *J* = 7.9, 5.9 Hz, 1H), 7.13 (s, 1H), 7.07 (ddd, *J* = 8.3, 7.3, 1.7 Hz, 1H), 7.00 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.98 – 6.90 (m, 2H), 6.77 (s, 1H), 6.70 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.60 (td, *J* = 7.4, 1.1 Hz, 1H), 6.48 (dd, *J* = 7.7, 1.7 Hz, 1H), 3.96 (s, 3H), 3.95 – 3.91 (m, 1H), 3.89 (s, 3H), 3.29 – 3.15 (m, 2H), 2.88 (s, 3H), 2.84 (dd, *J* = 16.5, 3.0 Hz, 1H), 2.44 (dd, *J* = 5.2, 4.3 Hz, 1H), 2.20 (s, 3H), 2.07 (dd, *J* = 12.3, 10.7 Hz, 1H), 1.84 –1.74 (m, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 203.8, 153.1, 148.8, 142.7, 133.2, 132.6, 130.5, 130.4, 127.8, 127.0, 126.8, 122.9, 122.9, 118.3, 114.4, 114.2, 114.0, 113.8, 113.7, 112.5, 110.8, 61.2, 56.2, 56.0, 49.7, 48.7, 44.37, 39.06, 35.9, 35.7, 34.6, 30.8.



226j

1-Butyl-3-(3,5-dimethoxyphenyl)-2-((methylsulfinyl)methyl)-1,2,2a,2b,3,4-hexahydro-5H-benzo[6',7']cyclohepta[1',2':2,3]cyclopropa[1,2-c]quinolin-5-one (226k).

This compound was isolated as yellowish-green solid by following the general procedure-**17**. M.P = 212-214 ºC. R_f = 0.3 (9:1 EtOAc:Hexanes, visualized by 254 nm UV light). **IR (thin film, neat):** ν_{max}/cm^{-1} 2955, 2928, 1677, 1594, 1495, 1430, 1202, 1152, 1053, 835, 735. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.59 – 7.51 (m, 2H), 7.47 (ddd, J = 8.1, 7.2, 1.3 Hz, 1H), 7.40 (dd, J = 8.2, 1.2 Hz, 1H), 7.05 (ddd, J = 8.6, 7.2, 1.8 Hz, 1H), 6.66 (dd, J = 8.5, 1.0 Hz, 1H), 6.56 (td, J = 7.4, 1.0 Hz, 1H), 6.46 (dd, J = 7.6, 1.7 Hz, 1H), 6.35 (s, 3H), 4.08 (ddd, J = 11.0, 4.4, 2.6 Hz, 1H), 3.77 (d, J = 8.4 Hz, 6H), 3.36 (ddd, J = 15.9, 11.0, 5.0 Hz, 1H), 3.29 – 3.12 (m, 3H), 2.98 – 2.90 (m, 1H), 2.87 (dd, J = 18.7, 3.0 Hz, 1H), 2.74 (ddd, J = 13.3, 10.6, 3.1 Hz, 1H), 2.42 (t, J = 4.8 Hz, 1H), 2.22 (s, 3H), 2.17 – 2.08 (m, 1H), 1.78 (dd, J = 10.7, 5.2 Hz, 2H), 1.39 (q, J = 7.5 Hz, 2H), 0.99 (t, J = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 205.9, 161.1 (2C), 145.1, 141.5, 140.7, 139.5, 132.7, 132.1, 128.2, 128.1, 128.0, 126.9, 126.4, 117.7, 112.5, 105.2 (2C), 98.7, 61.6, 55.4, 55.3, 48.5, 48.1, 47.7, 44.9, 39.05, 35.1, 34.8, 30.7, 28.4, 20.2, 13.9.

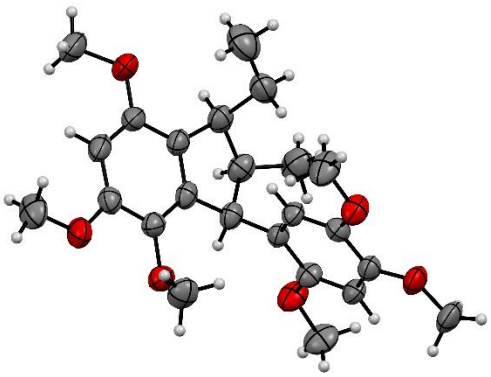


226k

Crystal structure of *β*-35 (CCDC 2109017): The structure of ***β*-35** was confirmed by single-crystal X-ray diffraction analysis.

Table 13. Crystal data and structure refinement for *β*-35

Identification code	***β*-35**
Empirical formula	$C_{24}H_{32}O_6$
Formula weight	416.49
Temperature/K	296.0(2)
Crystal system	orthorhombic
Space group	$Pca2_1$
a/Å	35.515(3)
b/Å	8.2303(7)
c/Å	7.6266(7)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2229.2(3)
Z	4

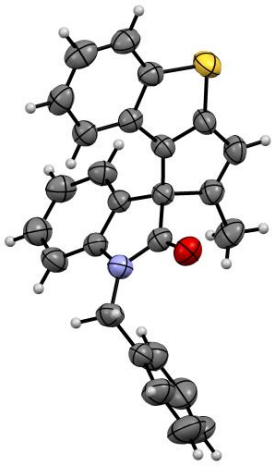


ρ_{calc}g/cm^3	1.241
μ/mm^{-1}	0.088
F(000)	896.0
Crystal size/mm^3	0.18 × 0.14 × 0.07
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.95 to 55.092
Index ranges	-46 ≤ h ≤ 46, -10 ≤ k ≤ 10, -9 ≤ l ≤ 9
Reflections collected	21690
Independent reflections	5124 [R_{int} = 0.0855, R_{sigma} = 0.0818]
Data/restraints/parameters	5124/1/279
Goodness-of-fit on F^2	0.978
Final R indexes [I>=2σ (I)]	R_1 = 0.0536, wR_2 = 0.1083
Final R indexes [all data]	R_1 = 0.1286, wR_2 = 0.1392
Largest diff. peak/hole / e Å^{-3}	0.18/-0.17
Flack parameter	0.0(10)

Crystal Structure of 149a (CCDC 1965370): Structure of the spiroxindole **149a** was confirmed by single crystal X-ray diffraction analysis.

Crystal data and structure refinement for 149a

Identification code	**149a**
Empirical formula	$C_{26}H_{19}NOS$
Formula weight	393.48
Temperature/K	298.0(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.8555(12)
b/Å	9.9916(8)
c/Å	11.3490(15)
α/°	90
β/°	114.698(16)
γ/°	90
Volume/Å^3	1015.3(2)

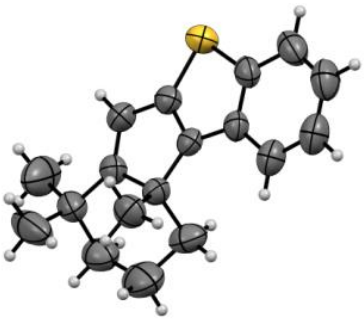


Z	2
ρ_{calc}g/cm^3	1.287
μ/mm^{-1}	0.176
F(000)	412.0
Crystal size/mm^3	0.21 × 0.16 × 0.09
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.678 to 50
Index ranges	-11 ≤ h ≤ 11, -11 ≤ k ≤ 11, -13 ≤ l ≤ 13
Reflections collected	7711
Independent reflections	3578 [R_{int} = 0.0326, R_{sigma} = 0.0592]
Data/restraints/parameters	3578/1/263
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0455, wR_2 = 0.0850
Final R indexes [all data]	R_1 = 0.0706, wR_2 = 0.1002
Largest diff. peak/hole / e Å^{-3}	0.17/-0.21
Flack parameter	0.03(5)

Crystal Structure of 153e (CCDC 1965374): Structure of the cyclopentannulated heteroarene **153e** was confirmed by single crystal X-ray diffraction analysis.

Crystal data and structure refinement for 153e

Identification code	**153e**
Empirical formula	$C_{18}H_{20}S$
Formula weight	268.40
Temperature/K	298.00(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.0356(14)
b/Å	9.5429(9)
c/Å	16.215(2)
α/°	90
β/°	104.664(13)
γ/°	90

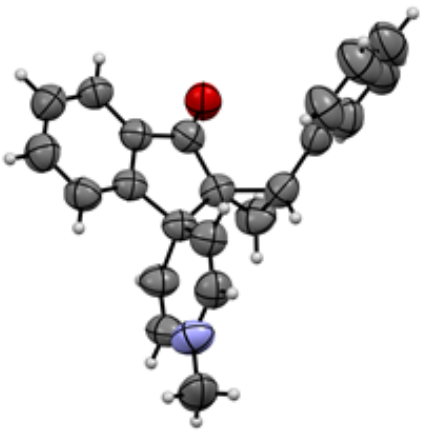


Volume/Å^3	1502.3(3)
Z	4
ρ_{calc}g/cm^3	1.187
μ/mm^{-1}	0.200
F(000)	576.0
Crystal size/mm^3	0.3 × 0.25 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.996 to 49.978
Index ranges	-11 ≤ h ≤ 11, -11 ≤ k ≤ 11, -19 ≤ l ≤ 19
Reflections collected	5325
Independent reflections	2636 [R_{int} = 0.0469, R_{sigma} = 0.0726]
Data/restraints/parameters	2636/0/175
Goodness-of-fit on F^2	1.115
Final R indexes [I>=2σ (I)]	R_1 = 0.1098, wR_2 = 0.2943
Final R indexes [all data]	R_1 = 0.1569, wR_2 = 0.3510
Largest diff. peak/hole / e Å^{-3}	1.16/-0.47

Crystal Structure of 219a (CCDC 2133525): Structure of the cyclopentannulated heteroarene **219a** was confirmed by single crystal X-ray diffraction analysis.

Crystal data and structure refinement for 219a (Major).

Identification code	**219a** (Major)
Empirical formula	$C_{22}H_{19}NO$
Formula weight	311.407
Temperature/K	289
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.4984(6)
b/Å	13.6723(8)
c/Å	12.6001(8)
α/°	90
β/°	108.468(7)
γ/°	90

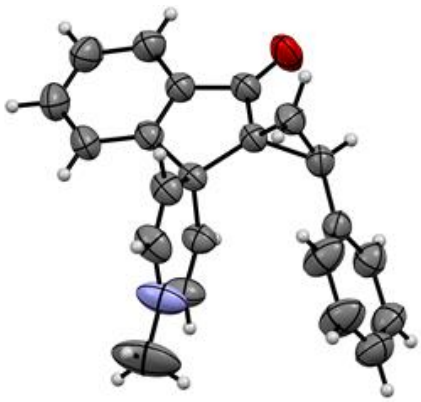


Volume/Å^3	1715.44(19)
Z	4
ρ_{calc}g/cm^3	1.206
μ/mm^{-1}	0.072
F(000)	660.3
Crystal size/mm^3	0.3 × 0.2 × 0.2
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.06 to 65.54
Index ranges	-14 ≤ h ≤ 15, -9 ≤ k ≤ 18, -19 ≤ l ≤ 17
Reflections collected	10342
Independent reflections	5728 [R_{int} = 0.0279, R_{sigma} = 0.0405]
Data/restraints/parameters	5728/0/218
Goodness-of-fit on F^2	1.143
Final R indexes [I>=2σ (I)]	R_1 = 0.0623, wR_2 = 0.1825
Final R indexes [all data]	R_1 = 0.1075, wR_2 = 0.2261
Largest diff. peak/hole / e Å^{-3}	0.28/-0.23

Crystal Structure of 219a' (CCDC 2133527): Structure of the cyclopentannulated heteroarene **219a'** was confirmed by single crystal X-ray diffraction analysis.

Crystal data and structure refinement for 219a' (minor).

Identification code	**219a' (minor)**
Empirical formula	$C_{22}H_{19}NO$
Formula weight	313.402
Temperature/K	298
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.2759(4)
b/Å	18.6849(8)
c/Å	11.6613(6)
α/°	90
β/°	106.981(5)
γ/°	90

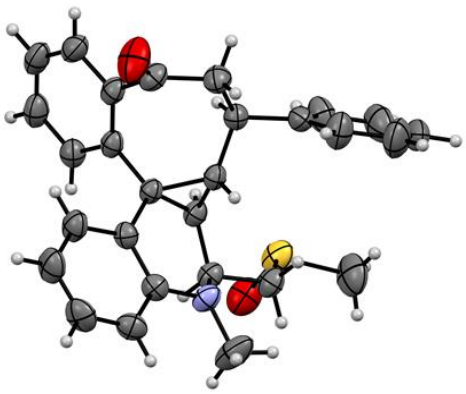


Volume/Å^3	1724.62(15)
Z	4
ρ_{calc}g/cm^3	1.207
μ/mm^{-1}	0.074
F(000)	664.3
Crystal size/mm^3	0.6 × 0.3 × 0.2
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.74 to 65.34
Index ranges	-7 ≤ h ≤ 11, -28 ≤ k ≤ 23, -17 ≤ l ≤ 11
Reflections collected	8796
Independent reflections	5576 [R_{int} = 0.0188, R_{sigma} = 0.0323]
Data/restraints/parameters	5576/0/218
Goodness-of-fit on F^2	1.211
Final R indexes [I>=2σ (I)]	R_1 = 0.0577, wR_2 = 0.1745
Final R indexes [all data]	R_1 = 0.0778, wR_2 = 0.1994
Largest diff. peak/hole / e Å^{-3}	0.27/-0.19

Crystal Structure of 226a (CCDC 2143316): Structure of the cyclopentannulated heteroarene **226a** was confirmed by single crystal X-ray diffraction analysis.

Crystal data and structure refinement for 226a.

Identification code	**226a**
Empirical formula	$C_{28}H_{27}NO_2S$
Formula weight	441.56
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	9.0157(3)
b/Å	11.1293(4)
c/Å	11.8264(3)
α/°	88.918(3)
β/°	87.476(3)
γ/°	74.544(3)



Volume/Å^3	1142.58(6)
Z	2
ρ_{calc}g/cm^3	1.283
μ/mm^{-1}	0.167
F(000)	468.0
Crystal size/mm^3	0.12 × 0.08 × 0.04
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.354 to 54.952
Index ranges	-11 ≤ h ≤ 10, -14 ≤ k ≤ 14, -14 ≤ l ≤ 15
Reflections collected	16391
Independent reflections	4891 [R_{int} = 0.0484, R_{sigma} = 0.0464]
Data/restraints/parameters	4891/0/291
Goodness-of-fit on F^2	1.120
Final R indexes [I>=2σ (I)]	R_1 = 0.0502, wR_2 = 0.1363
Final R indexes [all data]	R_1 = 0.0743, wR_2 = 0.1490
Largest diff. peak/hole / e Å^{-3}	0.38/-0.34

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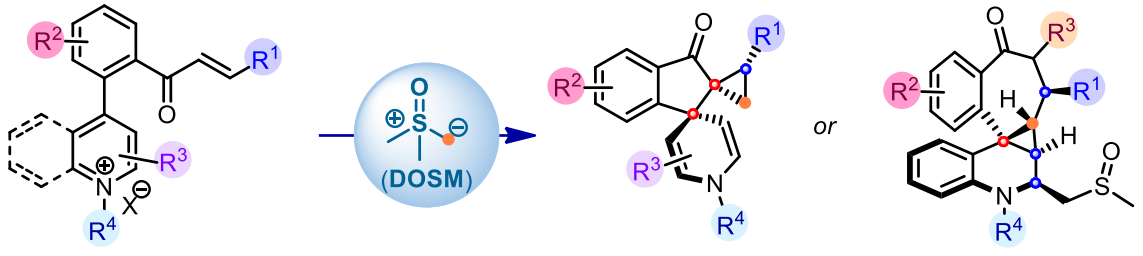

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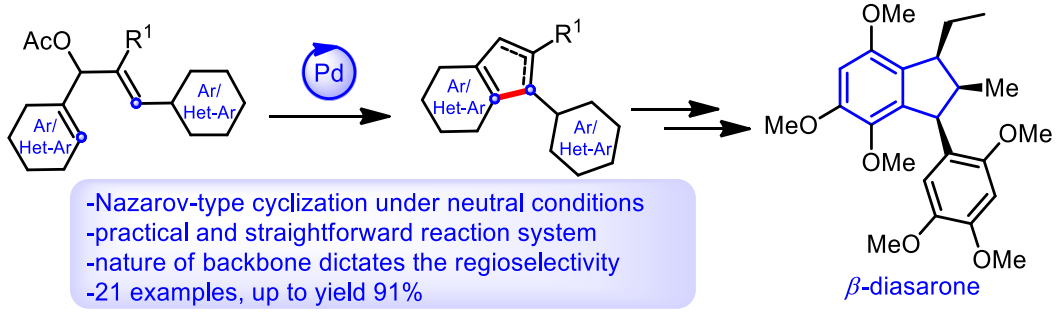

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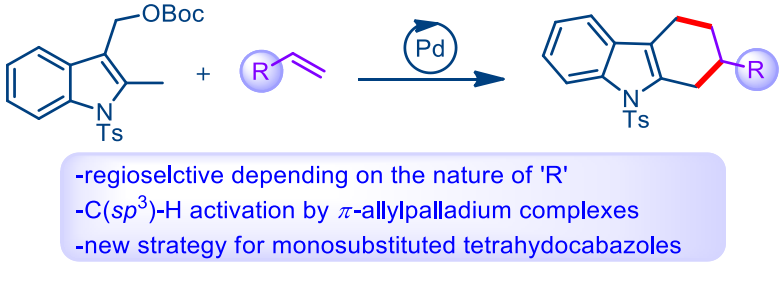

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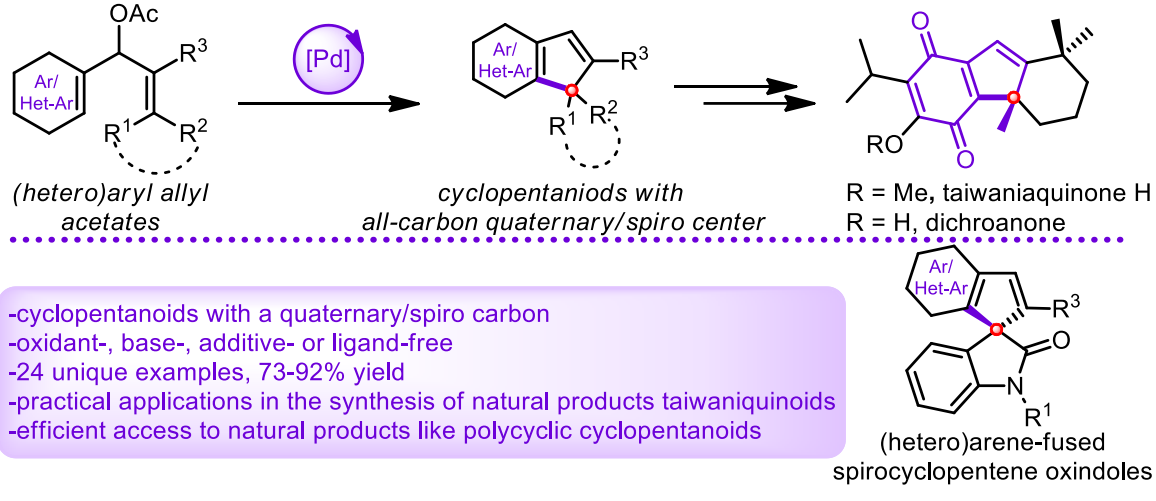

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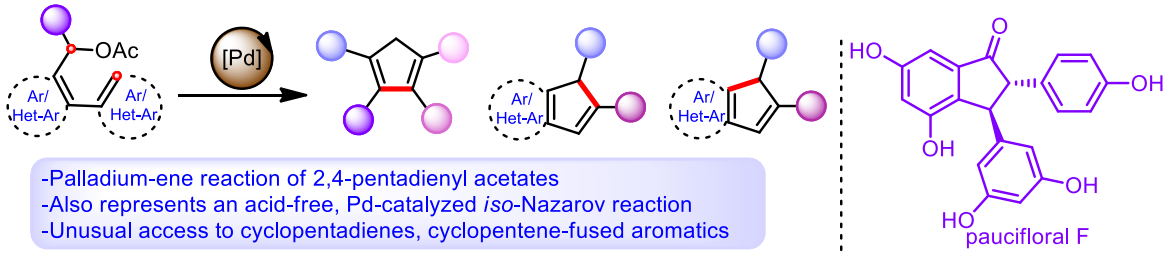

About the Author

The author, Mr. Bara Singh, was born in 1991 and raised at Ludhiana, Punjab. After his initial schooling from Government Multipurpose Senior Secondary School, he received a B.Sc. degree S.C.D. Government College, Ludhiana, (*affiliated to* Panjab University, Chandigarh) in 2012. After obtaining a M.Sc. degree from Department of Chemistry, College of Basic Sciences and Humanities, Punjab Agricultural University, Ludhiana, Punjab, India in 2014, he joined the research group of Dr. S. S. V. Ramasastry at the Indian Institute of Science Education and Research (IISER) Mohali, as a Ph.D. student in August 2016. He passed the comprehensive examination in August 2017. Presently, he is working as a Senior Research Fellow of IISER Mohali in the Department of Chemical Sciences.

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- Delivered an oral presentation in the ***16th Junior National Organic Symposium (J-NOST)*** at The Indian Institute of Science (IISC), Bangalore, India held on October 31 - November 1, 2020). (*First J-NOST Virtual Conference)*.
- Participated in ***Recent advances in Bio-organic and Medicinal Chemistry (RABMC)*** at NIPER-Mohali, held on August 30, 2019.
- Presented a poster in the ***15th Junior National Organic Symposium (J-NOST)*** at Department of Chemistry, University of Delhi, India held on October 18-21, 2019.
- Participated in ***Recent advances in Organic and Bio-organic Chemistry (RAOBC)*** at IISER-Mohali, held on March 22-24, 2019.
- American Chemical Society (ACS) on Campus held at IISER Mohali on February 9, 2018.
- Participated in the ***Royal Society of Chemistry (RSC) Roadshow*** at IISER Mohali, held on November 14, 2017.
- Participated in the ***National Conference on Liquid Crystal (NCLC)*** at IISER Mohali, held on October 11-13, 2017.