Lewis acid catalyzed synthetic approaches toward unsymmetrical diaryl- and triarylmethanes

A thesis submitted for the partial fulfilment of

the degree of Doctor of Philosophy

by

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August 2017

Dedicated

To

My beloved Parents

&

My life-partner Soujanya

DECLARATION

The work presented in this thesis titled ***"Lewis acid catalyzed synthetic approaches toward unsymmetrical diaryl- and triarylmethanes"*** has been carried out by me under the supervision of **Dr. R. Vijaya Anand** in the Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, Punjab.

This work has not been submitted in part or full for a degree, diploma or a fellowship to any other university or institute.

Whenever contributions of others are involved, every effort is made to indicate this clearly with due 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.

S Mahesh

Date:

Place:

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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Date:

Place:

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Abstract

The research work carried out is primarily focused on the Lewis acid catalyzed 5-*endo*-dig cyclization and/or conjugate addition approaches for the synthesis of unsymmetrical diaryl- and triarylmethanes using 2-(2-enynyl)-pyridines or *p*-quinone methides (*p*-QMs) as synthetic precursors.

This thesis is divided into **four chapters**:

Chapter 1: General introduction on the Synthesis and applications of diaryl- and triarylmethane derivatives

In recent years, diaryl- and triarylmethanes have gained recognition due to their enthralling applications in various fields. For instance, diarylmethane derivatives trimethoprim (**1**) and papavarine (**2**) are well known active pharmaceutical ingredients, and triarylmethanes **3** & **4** possess remarkable anti-fungal and anti-tuberculosis activities, respectively (**Figure 1**). Some of the diarylmethanes are also found as subunits of supramolecules. Considering the importance of these derivatives, many different synthetic approaches have been reported. Among them, Brønsted or Lewis acid catalyzed Friedel-Crafts alkylation of electron-rich arenes with benzyl alcohol was found to be the dominant route for their synthesis. Besides, transition-metal catalyzed coupling reactions between diarylmethanol derivatives and aryl coupling partners have also been established.

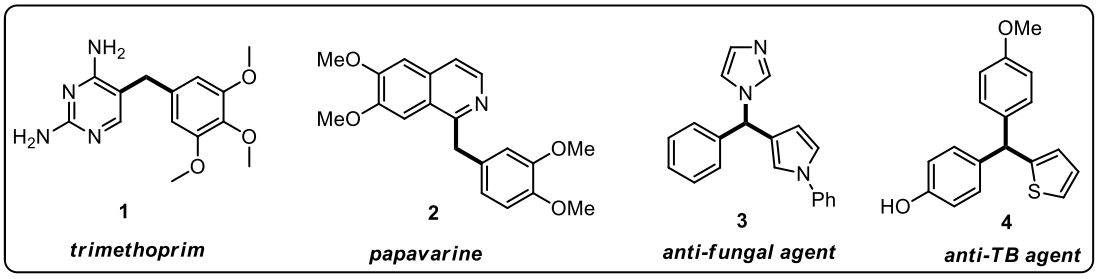
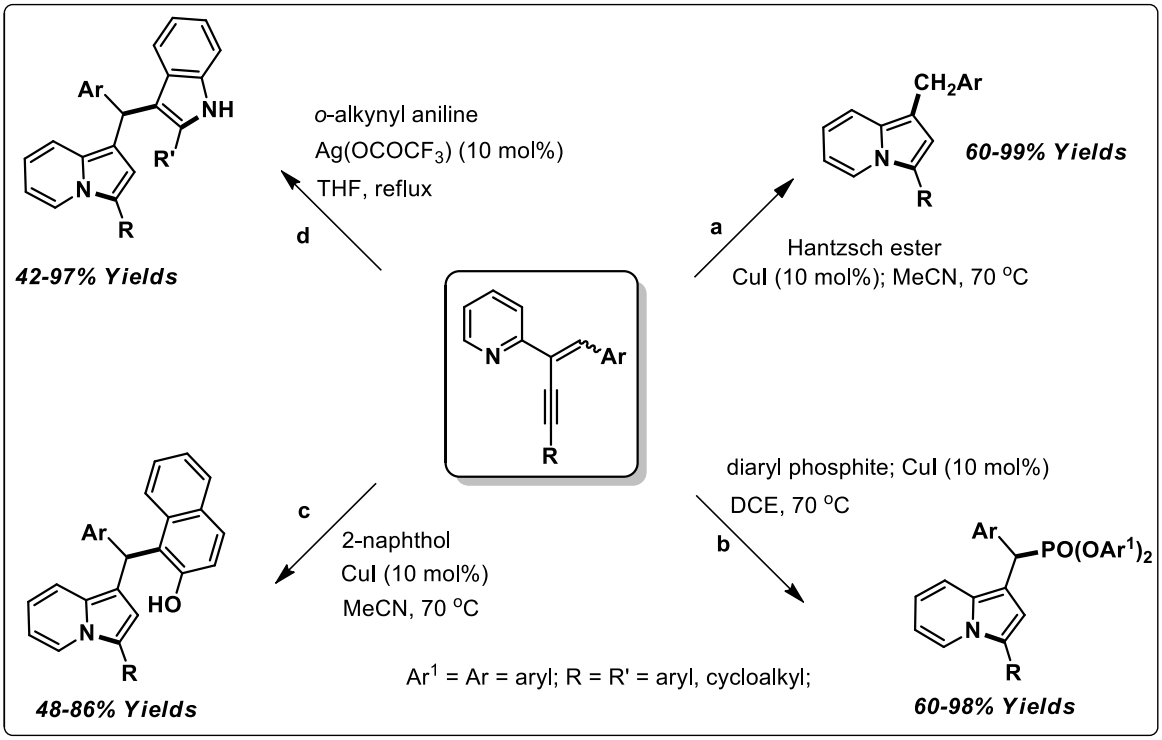


Figure 1. Some biologically active diaryl- and triarylmethanes

Chapter 2: Metal catalyzed diversity-oriented approaches toward indolizine containing unsymmetrical diaryl- and triarylmethane derivatives

In this chapter, a brief introduction about the synthesis of indolizines and related natural products is discussed. While working on the development of new protocols for the synthesis of unsymmetrical diaryl- and triarylmethane derivatives, we envisaged that it is possible to

synthesize indolizine containing diaryl- and triarylmethanes through a metal catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by a remote addition of a variety of nucleophiles under certain reaction conditions. In this context, we have developed an efficacious protocol to access a wide range of indolizine containing unsymmetrical diarylmethanes through a Cu-catalyzed reductive cyclization of 2-(2-enynyl)-pyridines using Hantzsch ester as a reducing agent (**a**, **Scheme 1**).



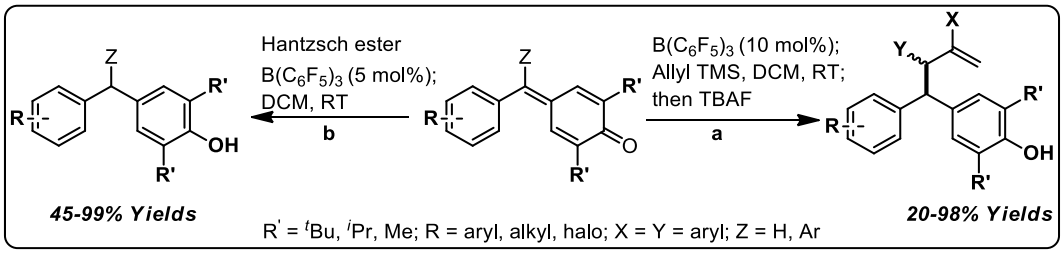
Scheme 1. Synthesis of indolizine containing unsymmetrical diaryl- and triarylmethanes

Another strategy was developed for the synthesis of indolizine containing diarylmethyl phosphonates through a Cu-catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by remote hydrophosphonylation (**b**, **Scheme 1**). Through this method, a variety of indolizine containing diarylmethyl phosphonates could be prepared in moderate to excellent yields. After completing the synthesis of unsymmetrical diarylmethanes, we shifted our attention to develop a couple of protocols to synthesize indolizine containing unsymmetrical triarylmethanes using appropriate nucleophiles. Consequently, we have developed a protocol to access indolizine containing unsymmetrical triarylmethanes through 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by a nucleophile

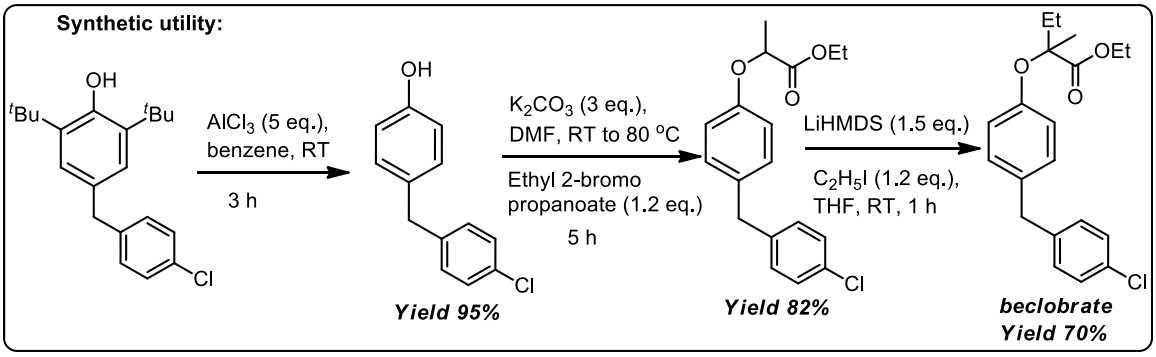
addition of 2-naphthols (**c**, **Scheme 1**). Out of many catalysts screened, CuI was found to be the best catalyst to drive this transformation. In continuation of this protocol, a Ag-catalyzed double 5-*endo*-dig cyclization strategy was established for the synthesis of unsymmetrical triarylmethanes containing indolizine and indole together in the same molecule (**d**, **Scheme 1**).

Chapter 3: Divergent approaches toward unsymmetrical diarylmethane derivatives through 1,6-conjugate addition reactions of *p*-quinone methides

A concise introduction about the syntheses and synthetic elaborations of *p*-quinone methides (*p*-QMs) is discussed in this chapter. Allylation of carbon electrophiles is acknowledged to be one of the important methods in carbon–carbon bond forming transformations, and a variety of 1,2- as well as 1,4-allylation approaches have been developed. However, the vinylogous allylation *i.e.*, the 1,6-conjugate allylation of dienones is under explored till date, though there are a very few reports available for the 1,6-conjugate addition of other alkylmetal reagents. Recently, we have disclosed a Lewis acid catalyzed highly regio-selective allylation of *p*-quinone methides using a variety of allyl silanes (**a**, **Scheme 2**). Interestingly, $B(C_6F_5)_3$ was found to catalyze this transformation effectively and a diverse range of allylated products were obtained in good yields. In continuation of this methodology, we have also developed a general protocol to access unsymmetrical diaryl- and triarylmethanes through a $B(C_6F_5)_3$ catalyzed regio-selective reduction of *p*-QMs and fuchsones, respectively (**b**, **Scheme 2**). This protocol was also elaborated for the total synthesis of a pharmaceutically active drug, called beclobrate (**Scheme 3**).



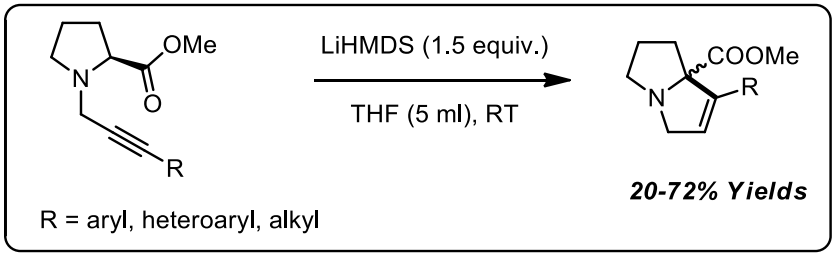
Scheme 2. 1,6-Conjugate addition approach towards diaryl- and triarylmethanes



Scheme 3: Synthetic elaboration to beclobrate

Chapter 4: Base mediated 5-*endo*-dig cyclization of *N*-propargyl-L-proline ester derivatives: an expeditious entry to pyrrolizidine alkaloids

A general introduction about pyrrolizidine alkaloids is discussed in this chapter. Since the *5-endo*-dig cyclization strategy has been proved to be a prevalent strategy for the assembly of cyclic or bicyclic core of many valuable molecules, we were interested in employing this approach for the construction of the pyrrolizidine scaffold. We thought that the bicyclic core of pyrrolizidine could be easily assembled from *N*-propargyl-L-proline esters through a base facilitated *5-endo*-dig cyclization. Screening of a variety of reaction conditions revealed that LiHMDS was the best base and THF was found to be the most appropriate solvent. Having optimized the reaction condition, the scope and limitations were investigated using a wide range of substituted *N*-propargyl-L-proline-methyl esters (**Scheme 4**).



Scheme 4. Synthesis of pyrrolizidine alkaloids

ABBREVIATIONS

Acac	Acetylacetone
Ac	Acetyl
MeCN	Acetonitrile
aq	Aqueous
B_2Pin_2	Bis(pinacolato)diboron
Bz	Benzoyl
Bn	Benzyl
OBn	Benzyloxy
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene
dppf	1,1'-Bis(diphenylphosphino)ferrocene
DPPPent	1,5-Bis(diphenylphosphino)pentane)
n-Bu	Butyl
calcd	Calculated
CDI	1,1'-Carbonyldiimidazole
Cbz	Carboxybenzyl
cm	Centimeter
δ	Chemical shift
$CDCl_3$	Chloroform-D
TMSCl	Chlorotrimethylsilane
J	Coupling constant
Cy	Cyclohexyl
cod	1,5-Cyclooctadiene
CPME	Cyclopentyl methyl ether
°C	Degree celsius
DMP	Dess-Matin periodinane
dr	Diastereomeric ratio
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-Diazabicyclo(5.4.0)undec-7-ene
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DCE	Dichloroethane
DCM	Dichloromethane
Xphos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl
Et_2O	Diethyl ether
DEAD	Diethylazodicarboxylate
DIPEA	Diisopropylethylamine
DME	Dimethoxyethane
DMAc	Dimethylacetamide
DMF	*N*,*N*'-Dimethyl formamide

d	Doublet
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
dt	Doublet of triplets
EWG	Electron withdrawing
ESI	Electrospray ionization
ee	Enantiomeric excess
er	Enantiomeric ratio
EtOH	Ethanol
EtOAc	Ethylacetate
EDCI	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
equiv	Equivalents
FT-IR	Fourier transform infrared spectroscopy
HEH	Hantzschester
Hz	Hertz
HMPA	Hexamethylphosphoramide
HRMS	High-resolution Mass Spectrum
HFIP	Hexafluoroisopropanol
h	Hour(s)
i-Pr	*iso*-Propyl
LiHMDS	Lithium bis(trimethylsilyl)amide
LDA	Lithium diisopropylamide
^{t}BuOLi	Lithium-*tert*-butoxide
m/z	Mass/Charge
MHz	Mega Hertz
m.p.	Melting point
Mes	Mesityl
MeOH	Methanol
MOM	Methoxymethyl
MPPIM	Methyl 1-(3-phenylpropanoyl)-2-oxaimidazolidine-4(***S***)-carboxylate
mg	Milligram(s)
mL	Milliliter(s)
mmol	Millimole(s)
min	Minute(s)
M.S.	Molecular sieves
m	Multiplet
NHC	*N*-heterocyclic carbene
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile

$POCl_3$	Phosphoryl chloride
Phen	1,10-Phenanthroline
Piv	Pivaloyl
^{t}BuOK	Potassium-*tert*-butoxide
PEG	Polyethyleneglycol
q	Quartet
R_f	Retention factor
RT	Room temperature
SIPr	1,3-Bis(2,6-diisopropylphenyl)imidazolinium
s	Singlet
sept	Septet
tert	Tertiary
^{t}Bu	*tert*-Butyl
Boc	*tert*-Butyloxycarbonyl
TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
TBS	*tert*-butylsilyl
OTBS	*tert*-butylsilyloxy
TBAI	Tetrabutylammonium iodide
TBAF	Tetrabutylammonium fluoride
THF	Tetrahydrofuran
TMS	Tetramethylsilane
TPCD	Tetra Pyridine Cobalt (II) Dichromate
TIPS	Triisopropylsilyl
TFSA/TfOH	Trifluoromethanesulfonic acid
TFE	Trifluoroethanol
TFA	Trifluoroaceticacid
t	Triplet
td	Triplet of doublets
tt	Triplet of triplet

Contents

Chapter 1: General introduction on the synthesis and applications of diaryl- and triarylmethane derivatives

1. Diarylmethanes:

Although the concept of diarylmethanes being a part of supramolecular assembly had been believed since 1944, Georghiou[1a] was the first to report these supramolecular building blocks through the synthesis of all the isomers of calix[4]naphthalene (**1a**) from 1-naphthol in 1995. Diarylmethane unit is found as an integral part of many natural and unnatural biologically significant compounds (**Figure 1**).[2]. Some of the diarylmethane derivatives, such as GC 1 (**1b**), were well studied as thyroid hormone analogues.[2a,2b] Beclobrate (**1c**)[2c] is being sold as a cholesterol and triglyceride-lowering drug. Papaverine (**1d**)[2d] is being used to study the functional status of coronary arteries. Trimethoprim (**1e**)[2e] is an antibiotic, used especially in the treatment of urinary tract infections.

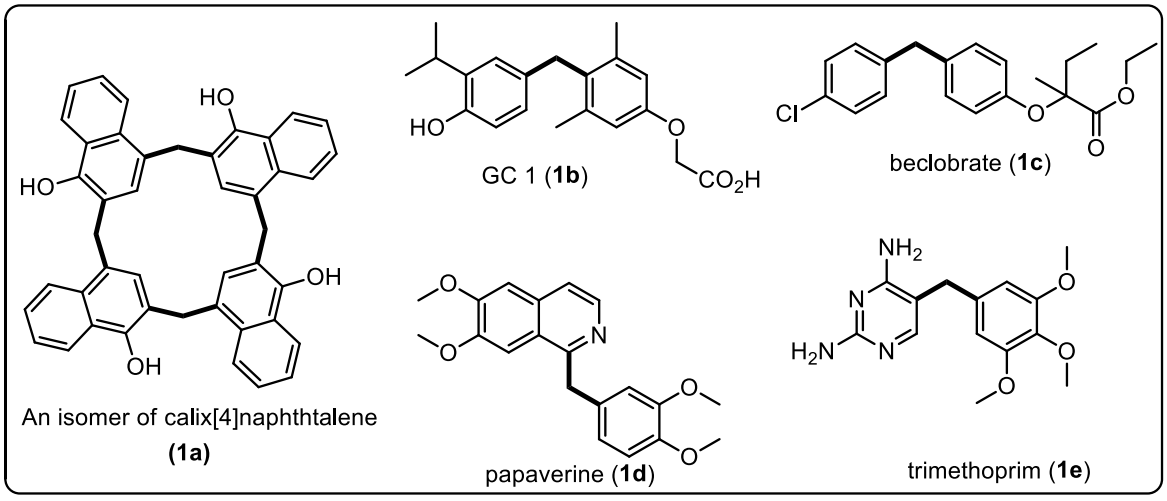
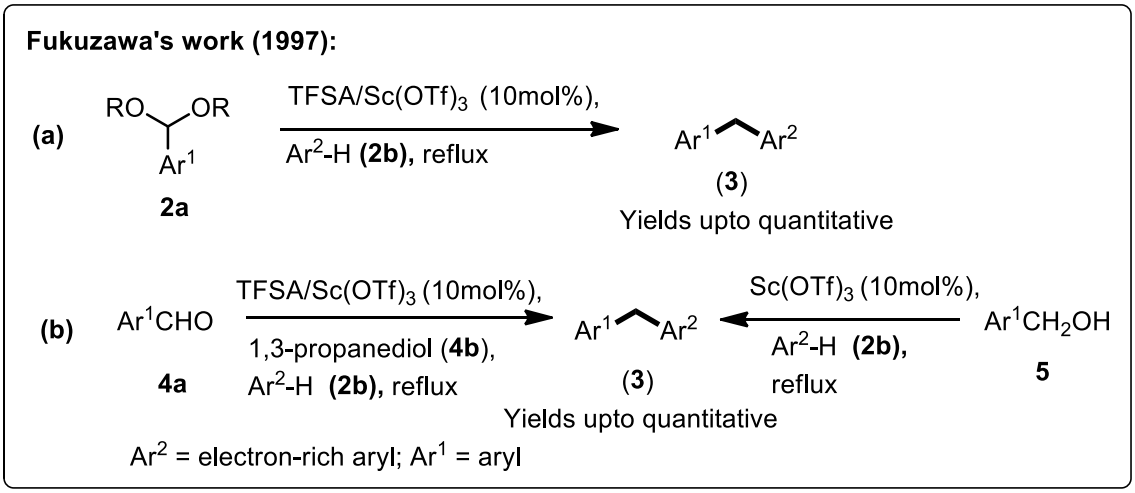


Figure 1. Therapeutically active diarylmethanes

Although there are several divergent ways to access symmetrical and/or unsymmetrical diarylmethanes,[3-13] Lewis acid/Brønsted acid catalyzed Friedel-Crafts reactions and the metal catalyzed cross-coupling reactions were found to be the prominent and convenient approaches. The following section describes the literature precedence on the synthesis of symmetrical and/or unsymmetrical diarylmethanes through the above-mentioned synthetic approaches.

1a. Synthesis of diarylmethanes through Fridel-Crafts approach:

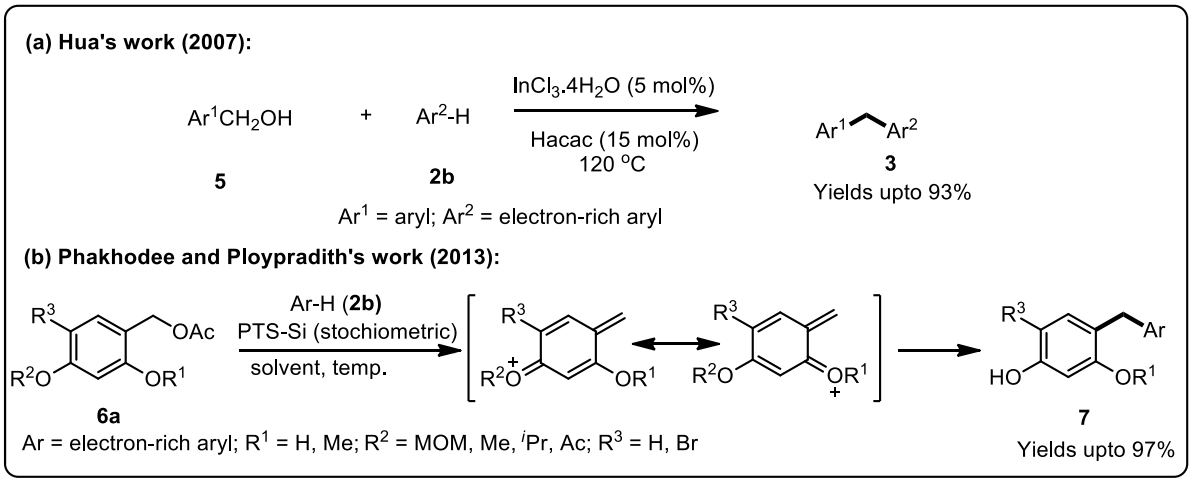
As mentioned earlier, Friedel-Crafts alkylation of electron-rich arenes with benzyl alcohol was a very popular route for the synthesis of diarylmethane derivatives.[3,5,13] Explicitly, the typical Friedel-Crafts reaction of aromatic aldehydes with arenes usually provides a complex mixture of products along with diarylmethane in the presence of stoichoimetric amount of an acid.[4] Comprehended with this drawback, an alternative strategy was developed and a couple of reports were disclosed by Fukuzava and co-workers in 1997 solely for the synthesis of diarylmethanes (**Scheme 1**). Initial report divulged a super-acid (triflic acid) catalyzed Friedel-Crafts alkylation of arenecarbaldehyde-acetals (**2a**) with arenes (**2b**), through a redox process, to access diarylmethanes (**3**) in moderate to excellent yields. Additionally, they elaborated their studies to an acid catalyzed Friedel-Crafts benzylation of arenes using arene-carbaldehyde (**4a**) and 1,3-propanediol (**4b**). Notably, there was no reaction with arene-carbaldehyde (**4a**) in the absence of 1,3-propanediol (**4b**) (**a**, **Scheme 1**).[4d]



Scheme 1. Synthesis of diarylmethanes through Brønsted acid catalysis

Soon after, they came up with an improved version of the present protocol by replacing the super-acid with a mild Lewis acid [$Sc(OTf)_3$] under environmentally benign conditions. Through this version, Friedel-Crafts benzylation of arenes (**2b**) with benzyl alcohols (**5**) led to the respective diarylmethanes in excellent yields using catalytic amounts of $Sc(OTf)_3$. Interestingly, in this case, the catalyst was recovered and reused for three times with approximately equal efficiency (**b**, **Scheme 1**).[4e]

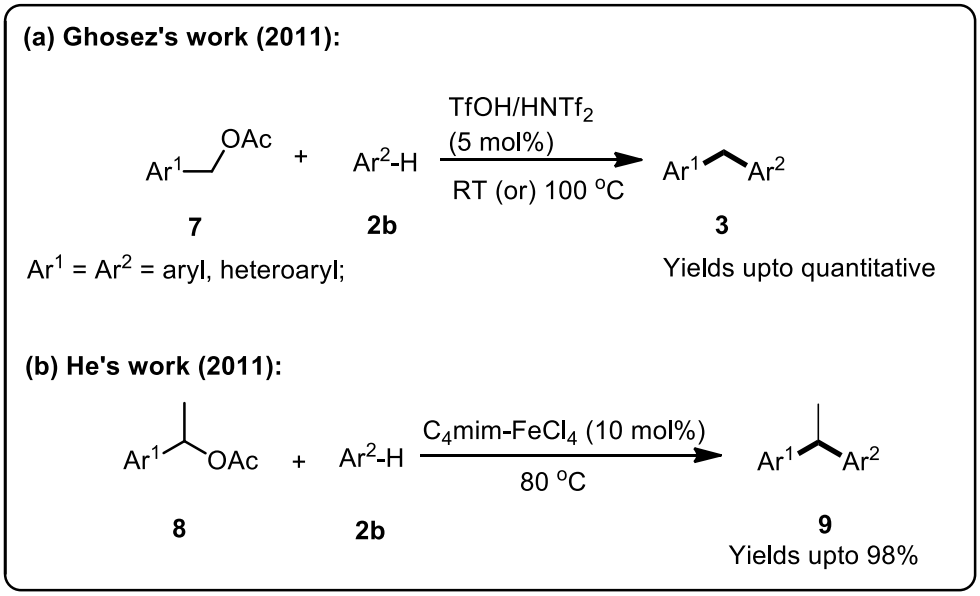
Later on, while working on the air stable and water tolerant Lewis acids catalyzed organic transformations, Hua and co-workers developed an indium catalyzed Friedel-Crafts reaction of arenes (**2b**) with benzyl alcohols (**5**) for the synthesis of unsymmetrical diarylmethanes (**3**). It was found that in the absence of additive (acetylacetone), the reaction took place only at 150 °C. The addition of acetyl acetone enhanced the reaction rate at 120 °C and the desired products (**3**) were isolated with moderate to excellent yields (**a, Scheme 2**).[5a] Besides the plethora[3-5] of Lewis/Brønsted acid catalyzed approaches, Phakhodee and Ploypradith jointly accounted the solid supported acid (PTS-Si) mediated benzylation of a diverse range of electron rich arenes (**2b**) with benzyl acetates (**6a**) for the regio-selective synthesis of diarylmethanes (**7**) in moderate to excellent yields. Since simple unsubstituted benzyl acetates failed to react under the reaction conditions, the mechanism of the reaction was believed to proceed through quinone methides (**b, Scheme 2**).[5b]



Scheme 2. Diarylmethanes synthesis through divergent approaches

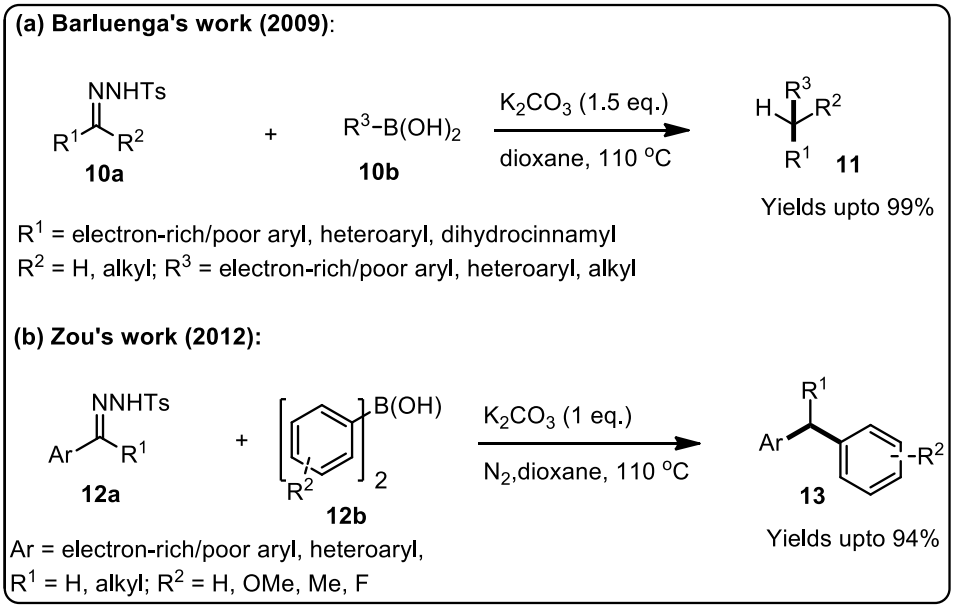
Ghosez and co-workers established a worthwhile and environmentally friendly benzylation strategy through the triflicacid/triflimide catalyzed reaction of non-genotoxic benzyl acetates (**7a**) with electron-rich arenes and heteroarenes (**2b**) for the synthesis of wide array of diarylmethanes (**3**) under mild reaction conditions (**a**, **Scheme 3**).[6a] At the same time, an operationally simple and improved version of this methodology was reported by He and co-workers, which describes an ionic liquid catalyzed benzylation of arenes (**2b**) using benzyl

acetates (**8a**) [**b**, **Scheme 3**].[6b] Additionally, the catalyst was recovered and reused at least for five times without any loss in its activity.



Scheme 3. Diarylmethane synthesis through Friedel-Crafts alkylation

Apart from the Lewis acid acid catalyzed Friedel-Crafts reactions, a few metal few approaches have been developed for the synthesis of unsymmetrical diarylmethanes. Considering the *N*-tosylhydrazones (**10a**) as a potential source of active diazo compound, Barluenga and co-workers have introduced an operationally simple and metal free reductive coupling of electron-rich, electron-poor and heteroaryl based *N*-tosylhydrazones (**10a**) with aromatic/aliphatic boronic acids (**10b**) for the synthesis of broad range unsymmetrical diarylmethanes (**11**). Since tosylhydrazones are the derivatives of carbonyl compounds, a one-pot reductive coupling of carbonyl compounds with boronic acids *via* the respective hydrozones was also described (**a**, **Scheme 4**).[7a] Further, the present protocol was elaborated with the high-order aryl borons (**12b**) by Zou and co-workers in 2012. They accounted the synthesis of unsymmetrical diarylmethanes (**13**) through reductive coupling between diaryl boronic acids (**12b**) and *N*-tosylhydrozones (**12a**) under similar reaction conditions (**b**, **Scheme 4**).[7b]

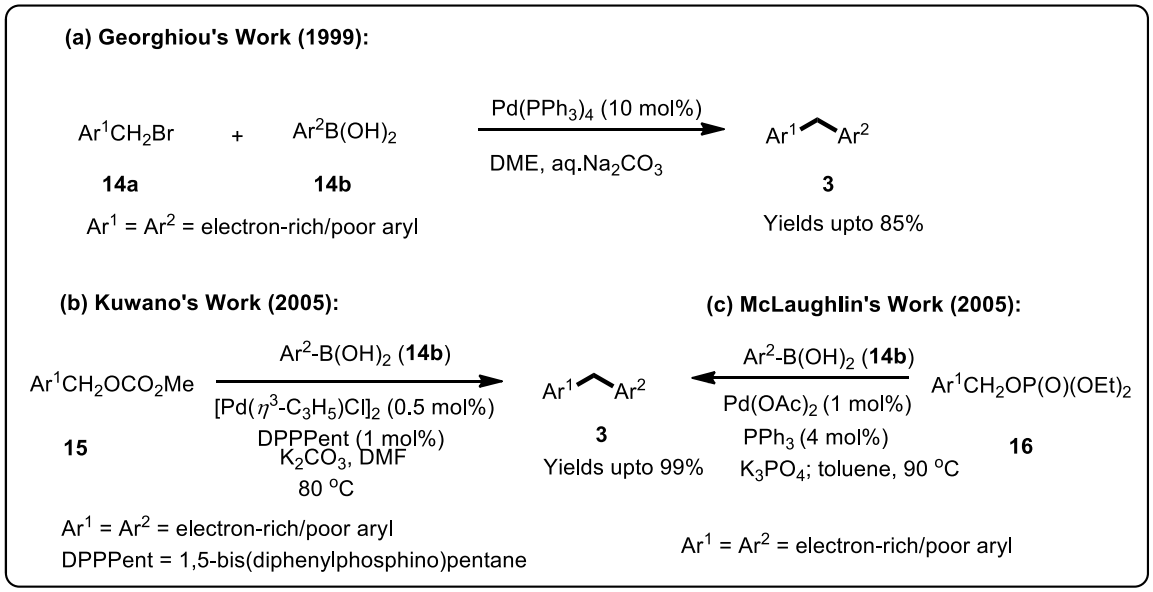


Scheme 4. Metal free approaches for the synthesis of diarylmethanes

1b. Synthesis of diarylmethanes through metal catalyzed coupling reactions:

After the revolutionary discovery of calix[4]naphthalenes, Georghiou and co-workers have extended the well-established Suzuki-Miyaura methodology through the metal catalyzed cross-coupling between benzyl halides (**14a**) and aryl boronic acids (**14b**) for the synthesis of unsymmetrical diarylmethanes (**3**) in 1999. The present cross-coupling method was found to be equally effective for the electron-donating as well as the electron-withdrawing substituents on the benzyl halides. Additionally, this method was applied not only for the synthesis of simple diarylmethanes (**3**) but also for the mixed *endo*- and *exo*-functionalized calix[4]naphthalenes through the cross-coupling between fused-aryl substrates (**a**, **Scheme 4**).[8a] In continuation of Geoghiou's seminal work, Kuwano and McLaughlin disclosed a couple of protocols independently to prepare diarylmethane derivatives through Suzuki-Miyaura cross-coupling. Kuwano described that the *in situ* generated palladium complex catalyzed the cross-coupling between benzyl carbonates (**15**) and aryl boronic acids (**14b**), which led to the formation of a variety of functionalized diarylmethanes (**3**) (**b**, **Scheme 4**).[8b] Later on, they elaborated this method to the synthesis of triarylmethanes under similar reaction conditions.[8c] Whereas, McLaughlin's work revealed the cross-coupling of benzylic phosphates (**16**) with aryl boronic

acids (**14b**) in the presence of a readily available catalytic system (palladium acetate and PPh_3) (**c**, **Scheme 4**).[8d]

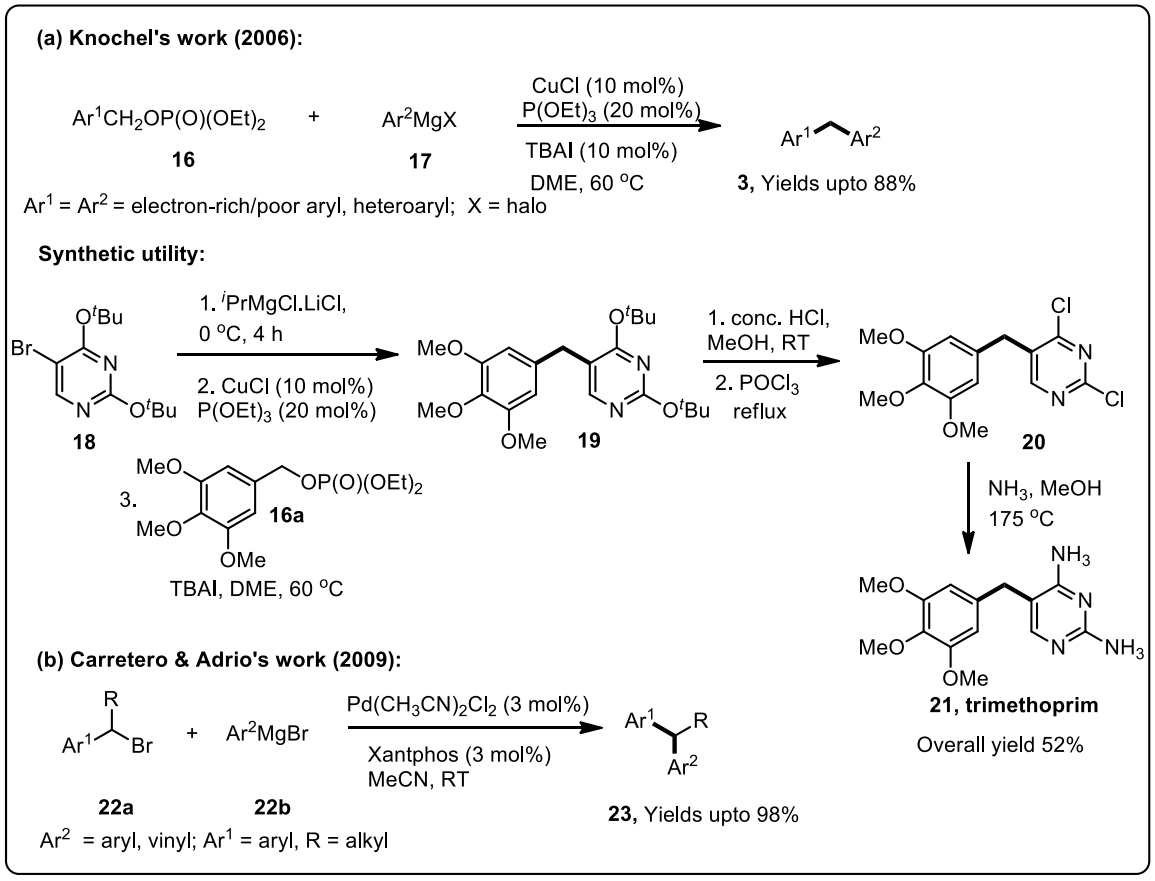


Scheme 4. Synthesis of diarylmethanes through Suzuki-Miyaura cross-coupling reaction

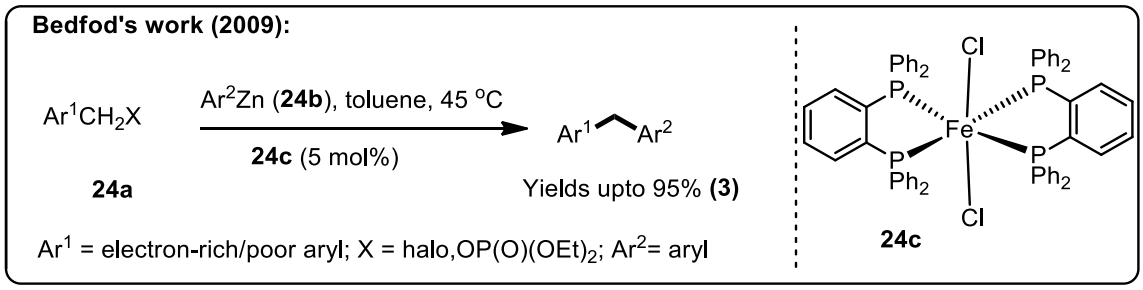
While working on the synthesis of poly-functionalized Grignard reagents, Knochel and co-workers have developed a mild and efficient Cu-based catalytic system for the synthesis of assortment of functionalized diarylmethanes (**3**). The present protocol describes a cross-coupling reaction between aryl-magnesium halides (**17**) with benzylic phosphates (**16**). Additionally, the antibiotic trimethoprim (**21**) was accessed using the present Cu-catalyzed cross-coupling as a key step with 52% overall yield (**a**, **Scheme 5**).[9a] Carretero and Adrio's report illustrates the air stable Pd-catalyzed Kumada-Corriu reaction of secondary benzyl bromides (**22a**) with Grignard reagents (**22b**) to access a variety of diarylmethanes (**23**) under mild reaction conditions. Minimizing the highly competitive β-hydride elimination was achieved using xantphos as a ligand (**b**, **Scheme 5**).[9b]

In another report, Bedford and co-workers unveiled an iron (**24c**) catalyzed synthesis of diarylmethanes through the Negishi coupling of benzyl halides and phosphates (**24a**) with the diaryl/aryl zinc (**24b**) reagents for the synthesis of diarylmethanes (**3**). Notably, diaryl zinc reactivity was found to be better than simple aryl zinc halide reagents. Interestingly, the diaryl

zinc species not only acts as arylating reagents but also as a stabilizer for the active catalyst (**Scheme 6)**.[10a]



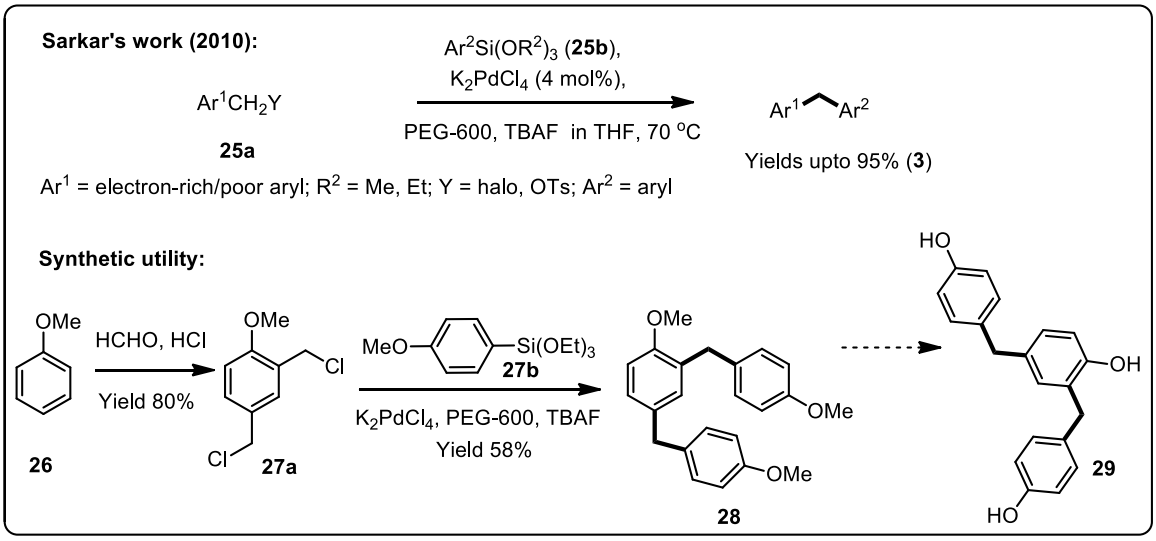
Scheme 5. Metal catalyzed cross-coupling approach



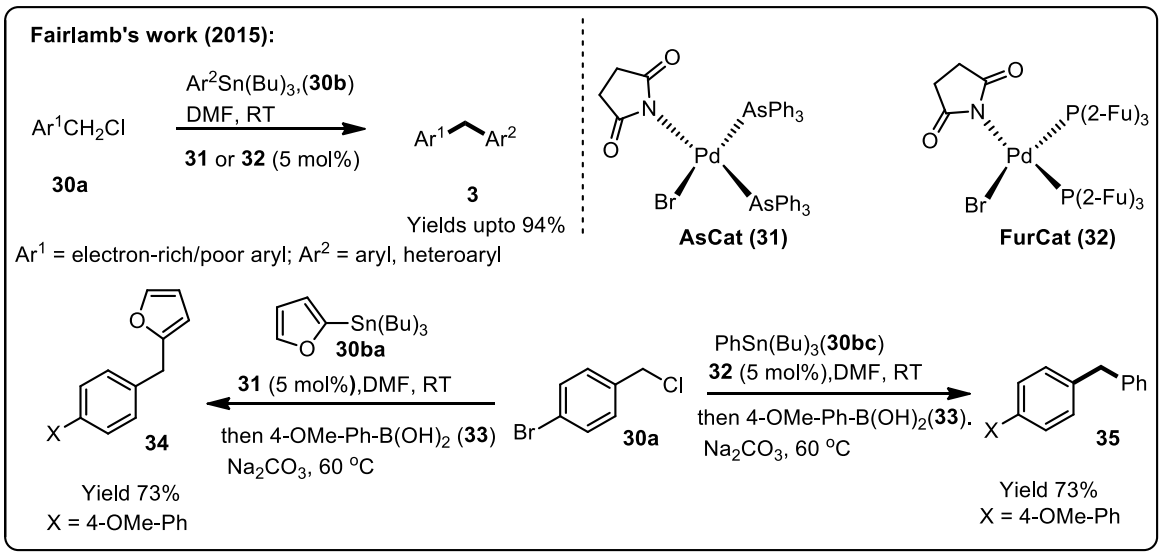
Scheme 6. Diarylmethanes synthesis using Negishi coupling

Prompted by the high surface to volume ratio of metal nanoparticles, Pd-nanoparticle catalyzed Hiyama coupling of benzyl halides was developed by Sarkar and co-workers. The current cross-coupling portrays the reaction between benzylic halides (**25a**) and aryl trialkoxysilanes (**25b**) for the production of diverse range of diarylmethanes (**3**). Moreover, this protocol was also well-

suited for the benzyl tosylates (**25a**) as well. Remarkably, by using this protocol, a natural product [2,4-bis(4-hydroxybenzyl)phenol (**29**)] was accessed in three steps (**Scheme 7**).[11]



Scheme 7. Diarylmethanes synthesis *via* Hiyama coupling

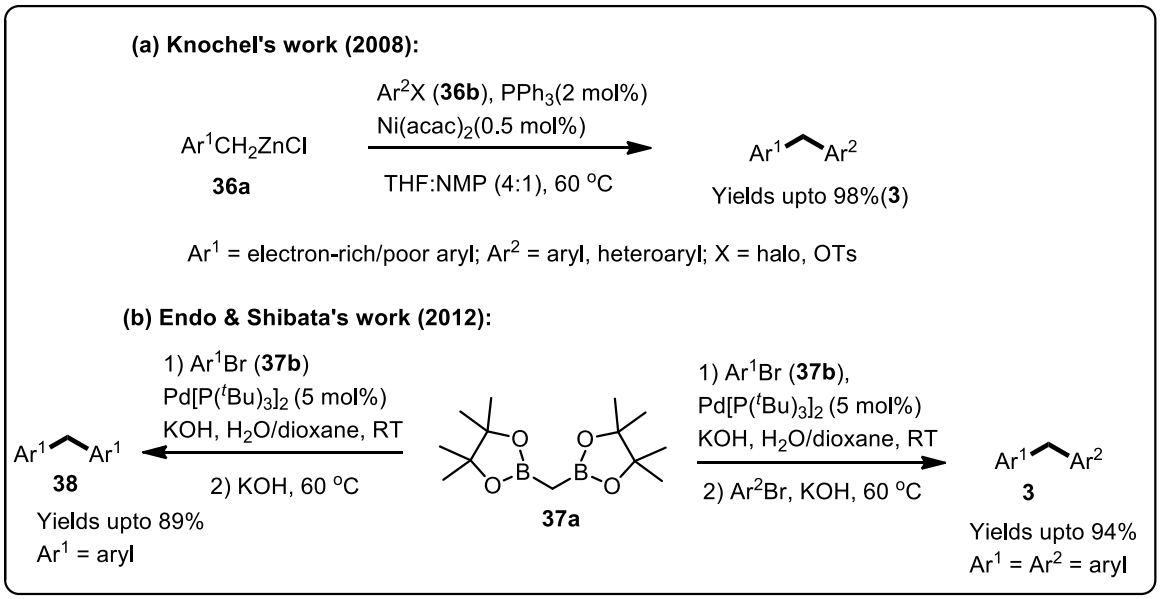


Scheme 8. Synthesis of diarylmethanes through Stille coupling

While working on the development of new catalysts for the effective Stille cross-coupling, Fairlamb reported a palladium (**31** or **32**) catalyzed cross-coupling reaction between benzyl chlorides (**30a**) and aryl tin reagents (**30b**) to synthesize polyfunctionalized diarylmethanes (**3**). Additionally, the reaction mixture of 4-bromobenzyl chloride (**30a**) and stannanes (**30ba** or

30bc) was further subjected to Suzuki-Miyaura coupling with 4-methoxyphenyl boronic acid (**33**) in a one-pot manner to access biphenyl systems (**34**, **35**) [**Scheme 8**].[12a]

Though the traditional metal catalyzed cross-coupling methods involving aryl coupling partners are well-known for their practical applicability in the synthetic chemistry, benzylic analogues are found to be another interesting coupling partners, especially, for the synthesis of diarylmethanes. For instance, while working on the synthesis of highly functionalized benzylic Zn-reagents, Knochel anticipated that diarylmethanes could be accessed through the cross-coupling of benzylic Zn-reagents with suitable electrophilic aryl partners. As a result, they realized a Ni-catalyzed cross-coupling between benzylic Zn-species (**36a**) and aryl halides/tosylates (**36b**) to prepare functionalized diarylmethanes (**3**) [**a**, **Scheme 9**].[13a]



Scheme 9. Synthesis of diarylmethanes using benzylic metal reagents

Further, a one-pot cross-coupling reaction of diboryl methane (**37a**) with aryl bromide (**37b**) to access symmetrical as well as unsymmetrical diarylmethanes was realized by Endo and Shibata independently (**b**, **Scheme 9**). Through this method, a wide array of functionalized symmetrical (**38**) and unsymmetrical (**3**) diarylmethanes could be accessed. Notably, the reaction temperature and amount of base are found to be the controlling factors for the effective synthesis of the desired products.[13b]

2. Triarylmethanes:

In recent years, triarylmethanes (TAMs) have gained attention due to their wide range of applications in various fields.[14a] Some stable quinoid form of TAM derivatives such as, malachite green (**39a**), sunset orange (**39b**) and crystal violet (**39c**) are important components in dye industry (**Figure 2**).[14a] In addition, crystal violet derivatives have been studied for photo-toxicity in tumor cells.[14b] The photo-chemical and photo-physical properties of TAM dyes such as, absorption spectra, photo deactivation of excited states, photo-oxidation, photo-reduction process are very well studied.[14c]

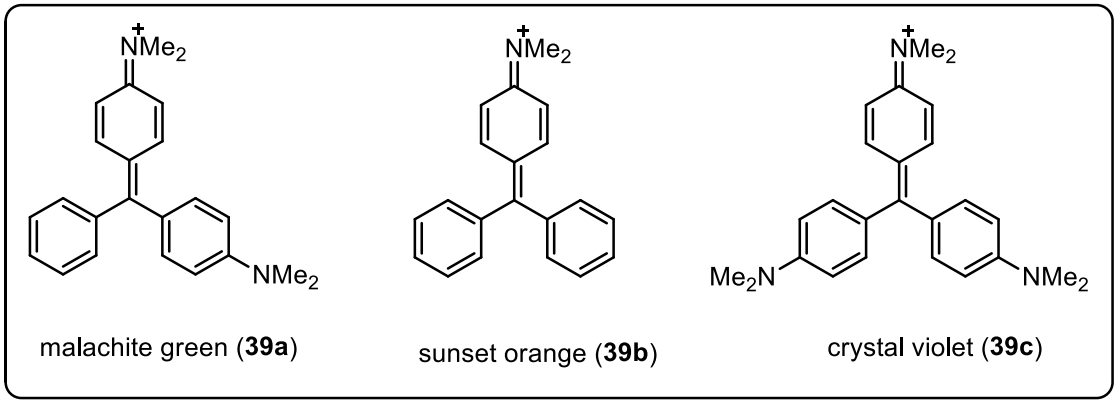


Figure 2: Stable quinoid structures of triarylmethanes

Some of the TAMs also show remarkable therapeutic activities, for example; unsymmetrical TAMs such as **40a, 40b** & **40c** exhibit anti-breast cancer, aromatase-sulfatase inhibition and anti-fungal activities respectively.[15] Apart from these, a wide range of biological activities of indole based TAMs are reported and reviewed.[14d] For instance, **40e** had shown a remarkable cytotoxic activity to renal cancer cells[16] and **40f** is used for lung cancer treatment.[17] Anti-tumor activity against leukemia p-388 in mice was tested using quinoline based TAM **40d** (**Figure 3**).[18]

Though the heterocyclic analogues of TAM radicals[19] have been known since 1968, Nakayama was the first to report the complete structural elucidation of dimer of tri-2-thienyl methyl radical in 1990.[20] In addition; numerous investigations have been carried out on reactivity of simple triarylcarbenium ions and heteroarylcarbenium ions. Their application in material science is notable as a few of the triarylmethanes could be used as fluorescent probes[21] and metal ion sensors.[22,23] TAMs were used as a unique protecting group source for the synthesis of

polyamide nucleic acid analogues.[24,14e] Steric effects with *ortho*-substitution of these derivatives were also studied for the chiral helical conformation.[25]

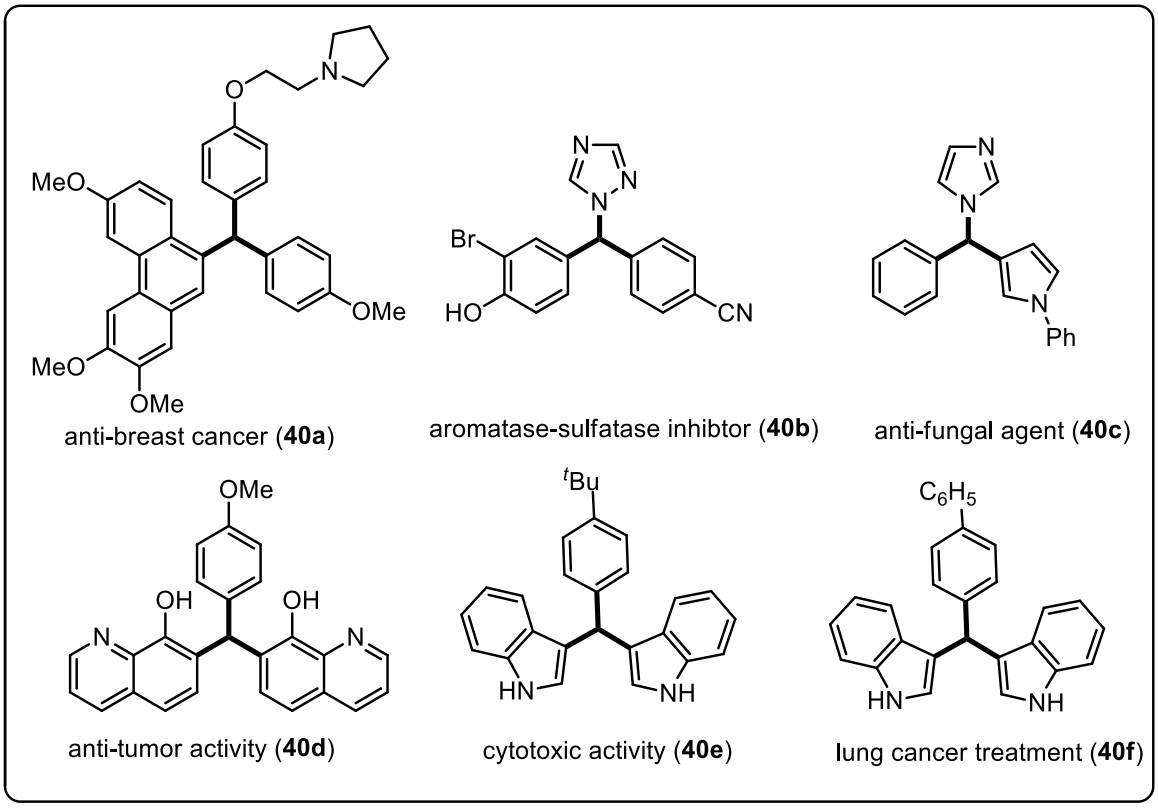


Figure. 3: Therapeutically active triarylmethanes

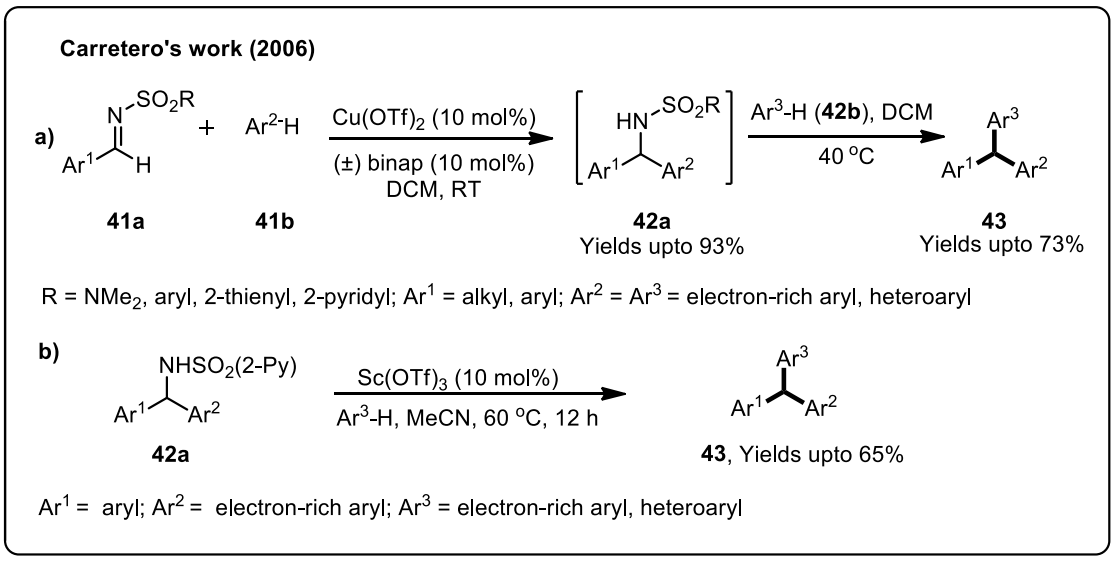
Extensive literature survey revealed that the symmetrical and/or unsymmetrical triarylmethanes could be accessed majorly through the following ways.[14a,14f]

1) Lewis acid/Brønsted acid catalyzed Friedel-Crafts reaction
2) Metal catalyzed cross-coupling reactions

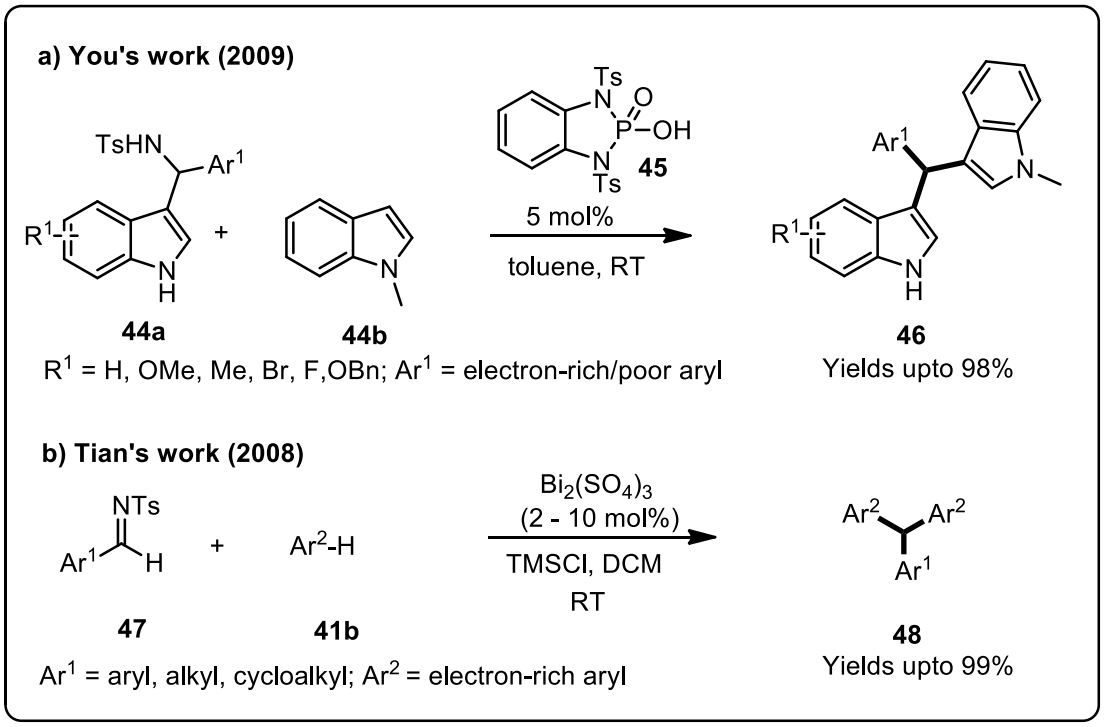
2a. Synthesis of triarylmethanes through Lewis acid/ Brønsted acid catalyzed Friedel-Crafts reactions:

A Cu-catalyzed aza Freidel-Crafts reaction of *N*-sulfonated aldimines (**41a**) with electron-rich aryl sources (**3b**) as a nucleophile for the synthesis of triarylmethanes (**43**) was reported by Carretero and co-workers in 2006. Having the *N*-(2-pyridylsulfonyl) group as a directing unit,

the authors could prepare a variety of *N*-diarylmethylsulfonamide (**42a**) and TAMs (**43**). Moreover, 2-pyridyl sulfonyl derived *N*-diarylmethylsulfonamides (**42a**) could be converted to **43** by employing scandium triflate as a catalyst **(Scheme 10)**.[26a]



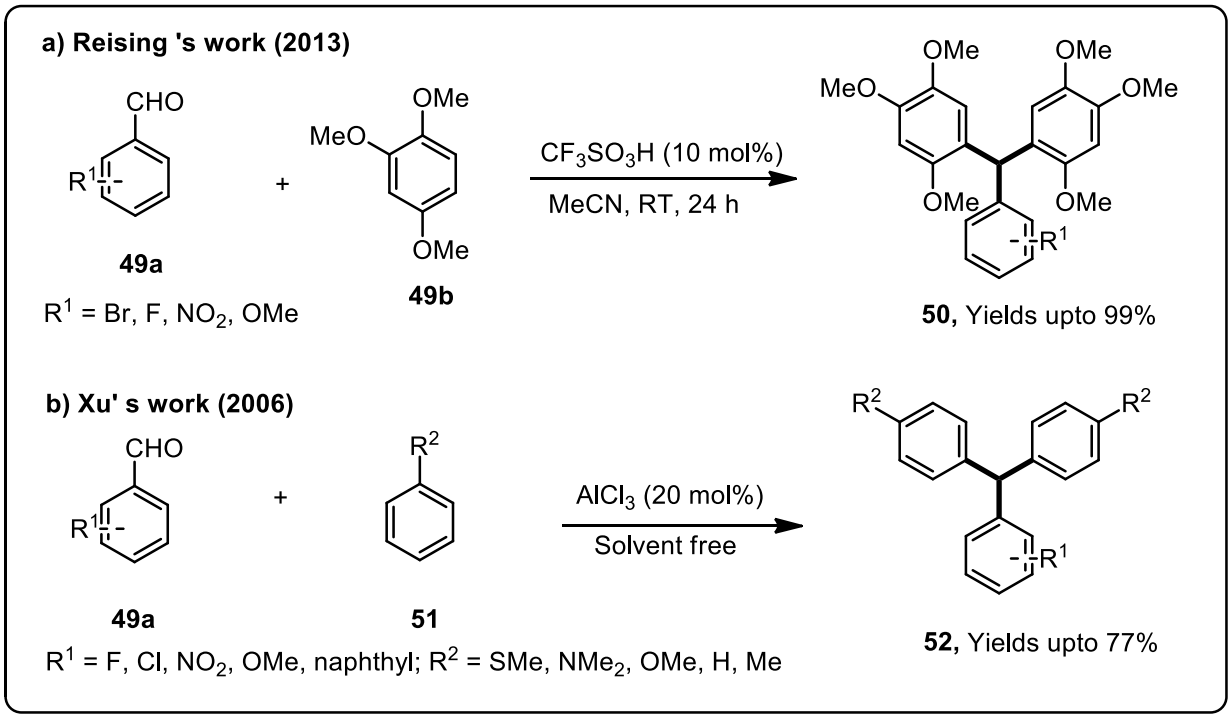
Scheme 10: TAM synthesis through a Lewis acid catalyzed Friedel-Crafts alkylation



Scheme 11: TAM synthesis through Lewis/Brønsted acid catalyzed Friedel-Crafts alkylation

While working on the chiral phosphoric acid[27a] catalyzed Friedel-Crafts addition of indole to *N*-tosyl aldimines, You and co-workers observed aryl bis(3-indolyl)methanes **46** as a side-product along with the chiral Friedel-Crafts adducts. Triggered with this observation, they have developed an achiral version of this transformation using **45** as a catalyst. Many aryl bis(3-indolyl)methanes **46** could be accessed through this method (**a, Scheme 11**).[27b]

Considering the significant improvement in the Lewis acidity[(28a, 28b)] of metal and chlorosilane pair, Tian and co-workers reported an environmentally benign, bismuth catalyzed highly regio-selective Friedel-Crafts alkylation of *N*-tosylimines (**47a**) with electron-rich arenes (**41b**) for the synthesis of symmetrical TAMs (**48**) [**b, Scheme 11**].[28c] They have also demonstrated that even imines derived from aliphatic aldehydes underwent smooth conversion to their respective alkyl diarylmethanes in good yields.[28c]

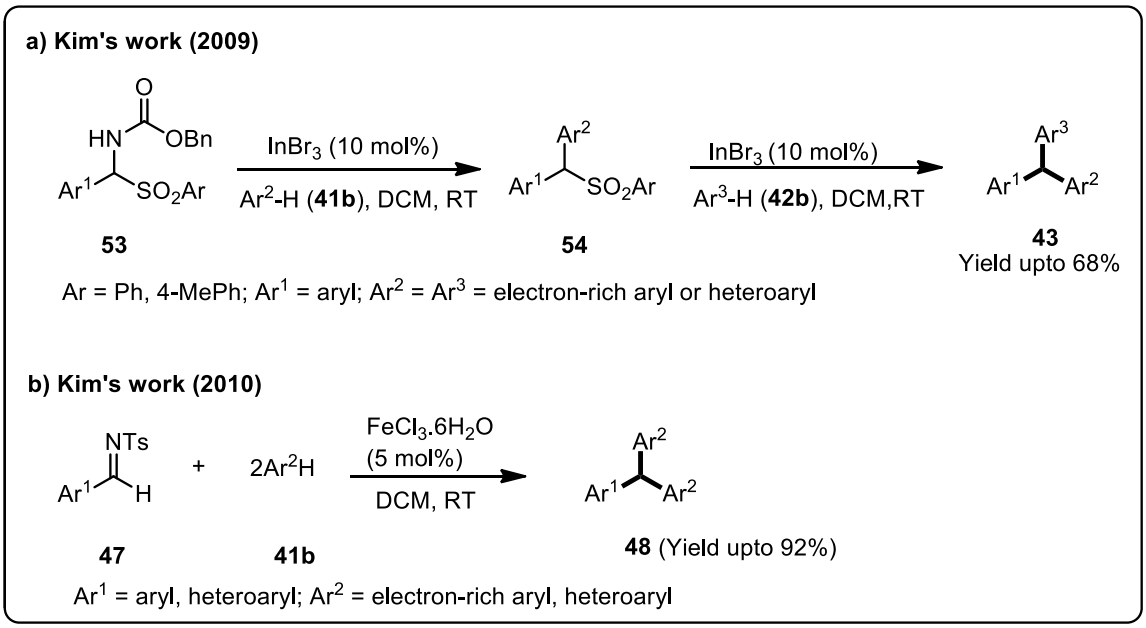


Scheme 12: TAM synthesis through Friedel-Crafts alkylation

A couple of different approaches had been independently developed by Reissig and Xu for the synthesis of triarylmethanes (**50** and **52**) from aromatic aldehydes (**49a**) and electron rich arenes (**49b, 51**). Reissig's work basically involves trifluoromethane sulphonicacid promoted simple

double arylation of aromatic aldehydes (**49a**) under mild reaction conditions (**a**, **Scheme 12**).[29] Xu's group demonstrated a Lewis acid catalyzed solvent-free Friedel-Crafts alkylation of aryl aldehydes using electron-rich thioanisole, anisole, N, N-dimethylaniline (**51**) etc. Notably, Xu's protocol was found to be inefficient for the alkylation of electron poor aldehydes (NO_2, Cl) [**49a**] with arenes (**51**) bearing weak electron donating groups (H, Me) [**b**, **Scheme 12**].[30]

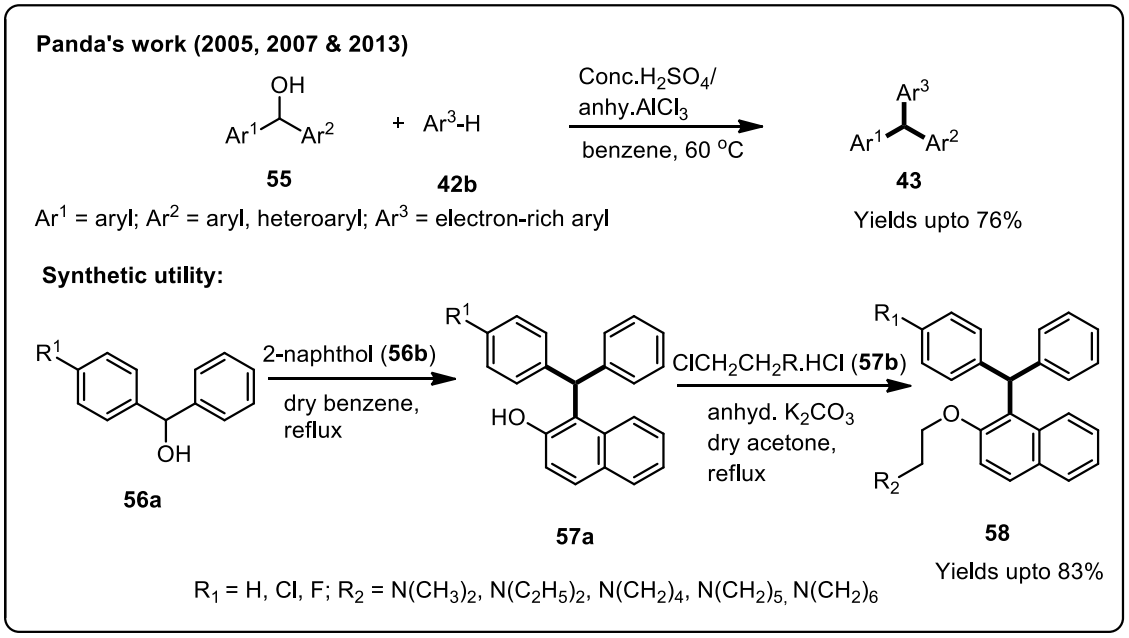
α-Amido sulfones (**53**) were employed by Kim and co-workers for the synthesis of triarylmethanes (**43**) through indium catalyzed sequential arylation process. According to them, initial arylation of α-amido sulfones (**53**) provided arylsulfones (**54**), which on sequential arylation led to triarylmethanes (**43**). Further, the authors had come up with an improved version of this methodology in 2010, where even low amounts of $FeCl_3$ were sufficient to catalyze this transformation. The present iron catalyzed version was found to be highly compatible in comparison with the other literature methods for the synthesis of symmetrical TAMs (**Scheme 13**).[31]



Scheme 13: Metal catalyzed TAM synthesis from alpha-amidosulfones and aldimines

Another interesting and adaptable synthetic precursor in the synthesis of TAMs was diarylcarbinol (**55**). A Brønsted acid catalyzed alkylation of diarylcarbinol for the synthesis of a series of unsymmetrical triarylmethanes (**43**) was reported by G. Panda and co-workers.[32b] They

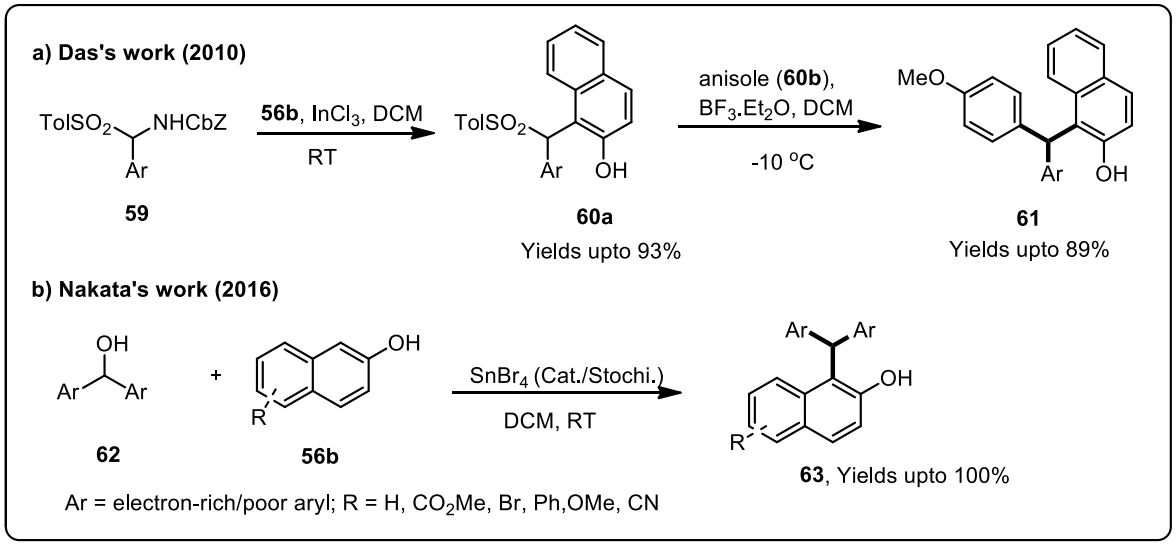
have also described the synthesis of many diarylnaphthylmethanes (**57a**) by Friedel-Crafts alkylation of diarylcarbinols (**56a**) with 2-naphthols (**56b**). Further, the products were elaborated to biologically active target analogues (**58**). Moreover, the *in vitro* studies of the targeted diaylmethyl naphthyloxy-ethylamines (**58**) showed promising activity towards cancer cells.[32c] Moreover, the products of the present protocol were also found to be potential intermediates to prepare tetra-substituted methanes (**Scheme 14**). [32a-c]



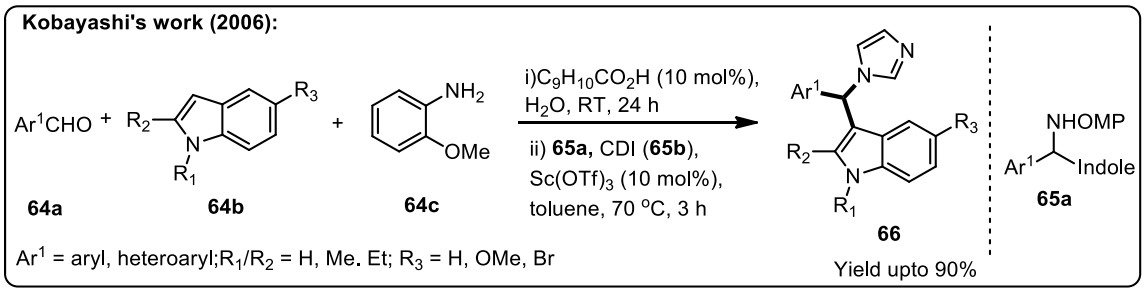
Scheme 14: Brønsted acid catalyzed TAM synthesis and synthetic utility

As discussed earlier, α-amido sulfones are predicted to be a potential source for the typical Friedel-Crafts alkylation. In 2010, Das and co-workers divulged a $InCl_3$ catalyzed Friedel-Crafts alkylation of α-amido sulfones (**59**) with 2-naphthols. It was proposed that *N*-benzyloxycarbonylamino sulfones (**59**) first generate respective imines, which then undergoes a nucleophilic addition with 2-naphthol (**56b**) to give aryl sulfones (**60a**). These sulfone derivatives (**60a**) were further elaborated to triarylmethanes (**61**) using $BF_3.Et_2O$ as a promotor (**a**, **Scheme 15**).[32d] In another report, $SnBr_4$ promoted Friedel-Crafts alkylation of diarylmethanol (**62**) with 2-Naphthols (**56b**) was described by Nakata and co-workers (**b**, **Scheme 15**).[32e]

A three component aza Friedel-Crafts reaction using aldehyde (**64a**), primary amine (**64c**) and indole (**64b**) was developed by Kobayashi and co-workers under metal-free and environmentally benign conditions. A wide range of diarylmethylamines (**65a**) with high selectivity were obtained in good yields over the competitive bis-indolyl arylmethanes formation through simple addition of indole to aldehydes. Further, this method was elaborated to the one-pot synthesis biologically active nonsteroidal aromatase inhibitor and its analogues (**66**) in the presence of carbonyl diimidazole (**65b**) (**Scheme 16**).[33]



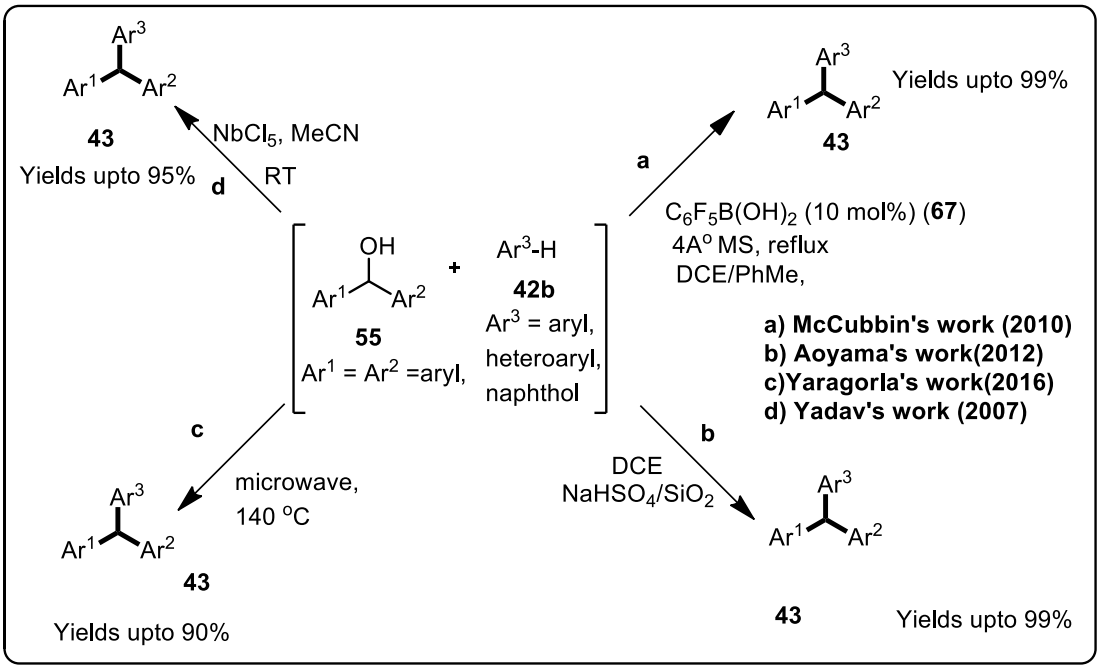
Scheme 15: Lewis / Brønsted acid catalyzed approaches using 2-naphthols



Scheme 16: A three component approach for biologically active TAM analogues

An organo-catalytic protocol for the preparation of triarylmethanes (**43**) was developed by McCubbin and co-workers using a commercially available and recoverable pentafluorophenyl boronic acid (**67**) as a catalyst. A variety of elctron-rich arenes, heteroarenes and naphthol

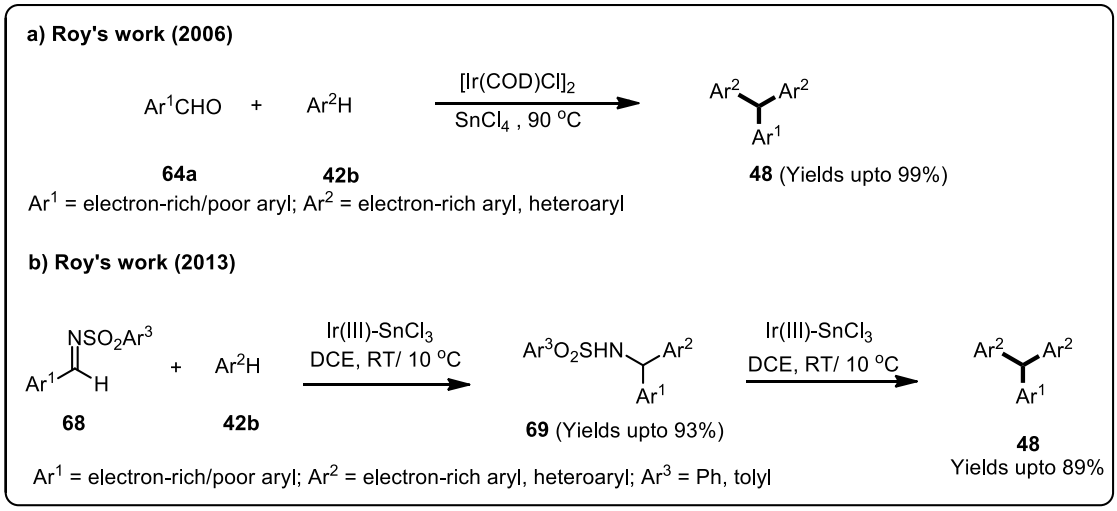
derivatives (**42b**) were treated with diphenyl carbinols (**55**) under the optimized reaction conditions to get the desired triarylmethanes **43** (**a, scheme 17**).[34a]



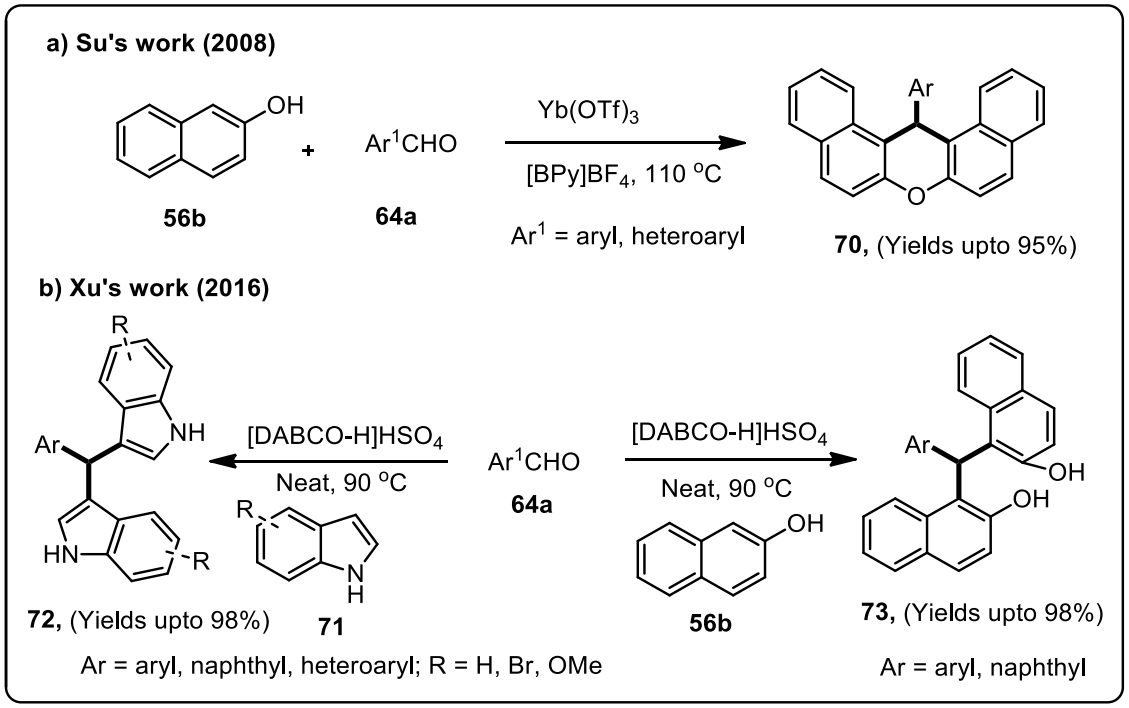
Scheme 17: Other Friedel-Crafts based approaches to TAMs

Aoyama and co-workers reported an efficient heterogeneous protocol for the synthesis of triarylmethanes (**43**) from electron-rich arenes (**42b**) and diarylcarbinols (**55**) using silica gel supported $NaHSO_4$. Notably, the catalyst was easily recovered and reused at least for eight times without any loss in its activity (**b, scheme 17**).[34b] Microwave conditions were also found to be highly appropriate for the synthesis of TAMs as reported by Yaragorla and co-workers (**c, scheme 17**).[34c] $NbCl_5$ is another competitive and versatile catalyst, described by Yadav and co-workers, for the synthesis of triaylmethanes (**43**) [**d, scheme 17**].[34d]

Roy and co-workers developed a bimetallic system, based on iridium and tin, for the synthesis of triarylmethanes (**48**), through bis-arylation of aromatic aldehydes (**64a**) under solvent free conditions.[35a] Later, they disclosed an efficient method for the synthesis of diarylmethylsulfonamides (**69**) and triarylmethanes (**48**) through an aza-Friedel-Crafts reaction of *N*-sulfonyl aromatic aldimines (**68**) using the same bimetallic catalyst (**Scheme 18**).[35b]



Scheme 18: TAM synthesis through catalysis by a bimetallic system

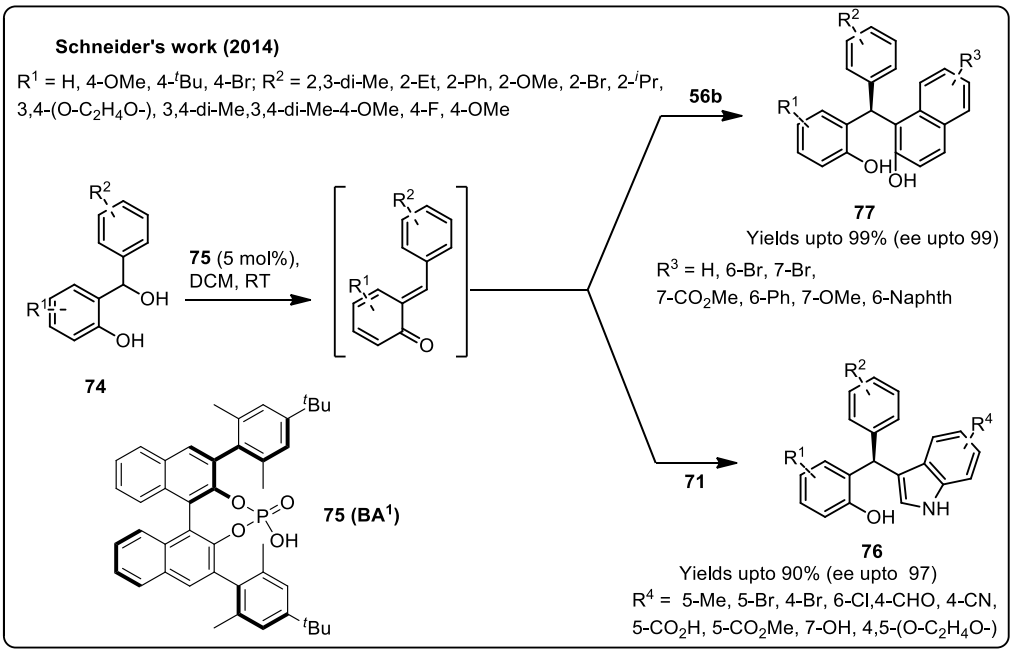


Scheme 19: Synthesis of TAMs in ionic liquids

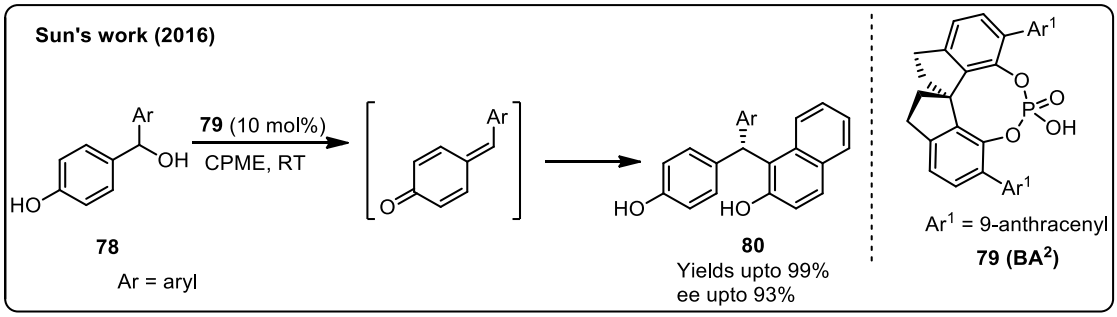
Therapeutically important benzoxanthene derivatives are a class of triarylmethanes that were synthesized by Su and co-workers, using a simple Lewis acid [$Yb(OTf)_3$] catalyzed condensation of two equivalents of 2-naphthol (**56b**) with a variety of benzaldehyde derivatives (**64a**) in ionic liquid media. This method illustrates the synthesis of a wide range of benzoxanthene (**70**) derivatives bearing electron-donating groups as well as electron-withdrawing groups (**a**, **Scheme 19**).[36a] Recently, a solvent free and ionic liquid catalyzed protocol for the condensation of arenes

(**71, 56b**) with aromatic aldehydes (**64a**) to generate bisindolyl (**72**) and bisnaphthyl (**73**) based triarylmethanes was reported by Xu and co-workers (**b**, **Scheme 19**).[36b] Notably, the present protocols are important from green chemistry perspective.

In addition to other applications,[37a-c] quinone methides (QMs) could also serve as versatile intermediates in the preparation of diaryl- and triarylmethane derivatives. Schneider and co-workers demonstrated a chiral Brønsted acid (**75**) catalyzed Friedel-Crafts alkylation of *in situ* generated *o*-quinone methides with indoles (**71**) and 2-naphthols (**56b**) for the preparation of enantiomerically enriched diarylindolylmethanes (**76**) and triarylmethanes (**77**) [**Scheme 20**].[37d]



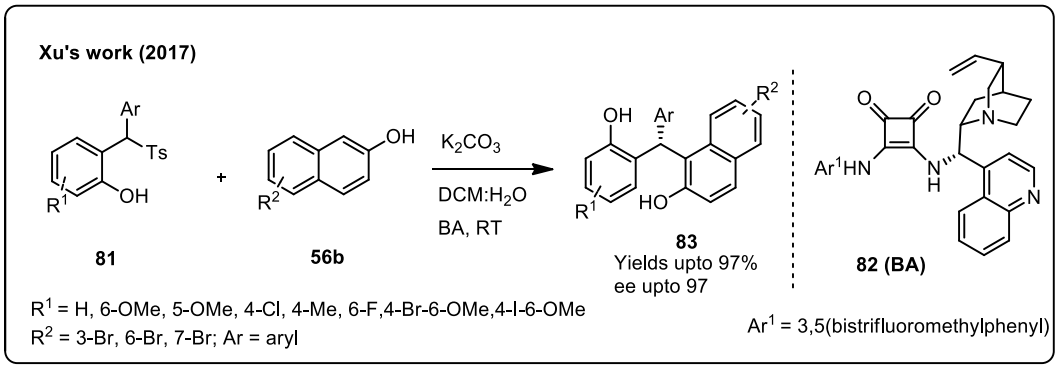
Scheme 20: Brønsted acid catalyzed enantioselective synthesis of TAMs



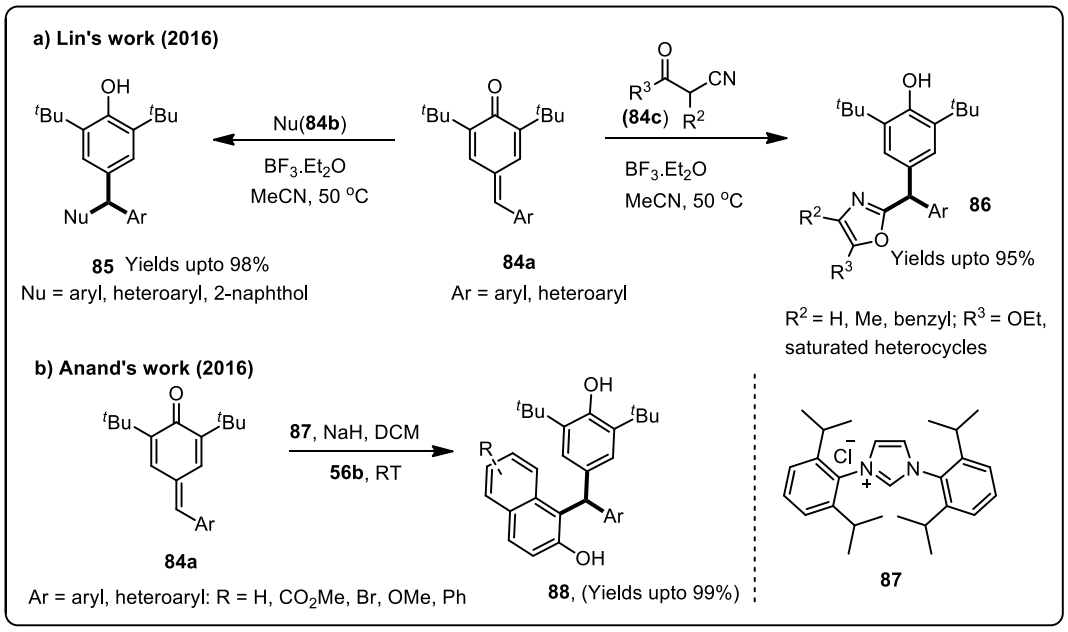
Scheme 21: Chiral Brønsted acid catalyzed enantioselective synthesis of TAMs

Moreover, this protocol was also extended for the enantio-selective phosphoric acid (**79**) catalyzed addition of 2-naphthols to *in situ* generated *p*-quinone methide from diarylcarbinol (**78**). Sun's work accomplishes the synthesis of high enantiomerically pure triarylmethanes (**80**) (**Scheme 21**).[37e]

Xu and co-workers have divulged a competitive version for the enantioselective synthesis of triarylmethanes (**83**). The current methodology describes a chiral bifunctional amine-squaramide catalyzed (**82**) highly enantioselective Friedel-Crafts alkylation of 2-naphthol with *o*-quinone methides (**Scheme 22**).[37f]



Scheme 22: Enantioselective TAM synthesis in biphasic media

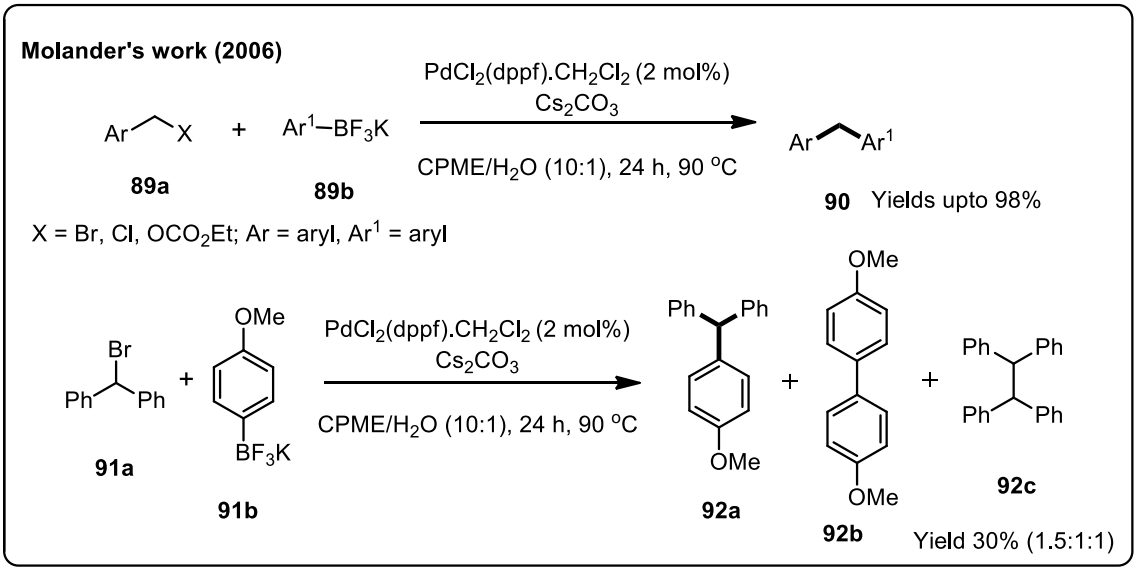


Scheme 23: Recent advances in metal free approaches toward TAM synthesis

Lin and co-workers disclosed a $BF_3.Et_2O$ catalyzed 1,6-conjugate addition of various aryl sources (**84b**) and α-isocyanoacetamides (**84c**) to *p*-quinone methides (**84a**) to access unsymmetrical triarylmethane derivatives (**85, 86**) [**a**, **Scheme 23**].[37g] Our research group also contributed in the development of effective methods for the preparation of unsymmetrical triarylmethanes. Recently, we have reported an *N*-heterocyclic carbene (**87**) catalyzed addition of 2-naphthol (**56b**) to *p*-quinone methides (**84a**). Broad range of naphthalene containing unsymmetrical triarylmethanes (**88**) could be prepared through this method (**b**, **Scheme 23**).[37h]

2b. Synthesis of triarylmethanes through metal catalyzed coupling reactions:

Although the Friedel-Crafts approach was found to be the dominant approach for the synthesis of triarylmethanes, there are a few drawbacks in this method such as, the requirement of electron-rich arenes, harsh reaction conditions, poor regio-selectivity etc. Moreover, there are only a handful of approaches are known for the synthesis of structurally complex unsymmetrical triarylmethanes. To overcome the above-mentioned limitations, in recent years, many transition-metal catalyzed approaches have been developed for the synthesis of such unsymmetrical triarylmethanes.

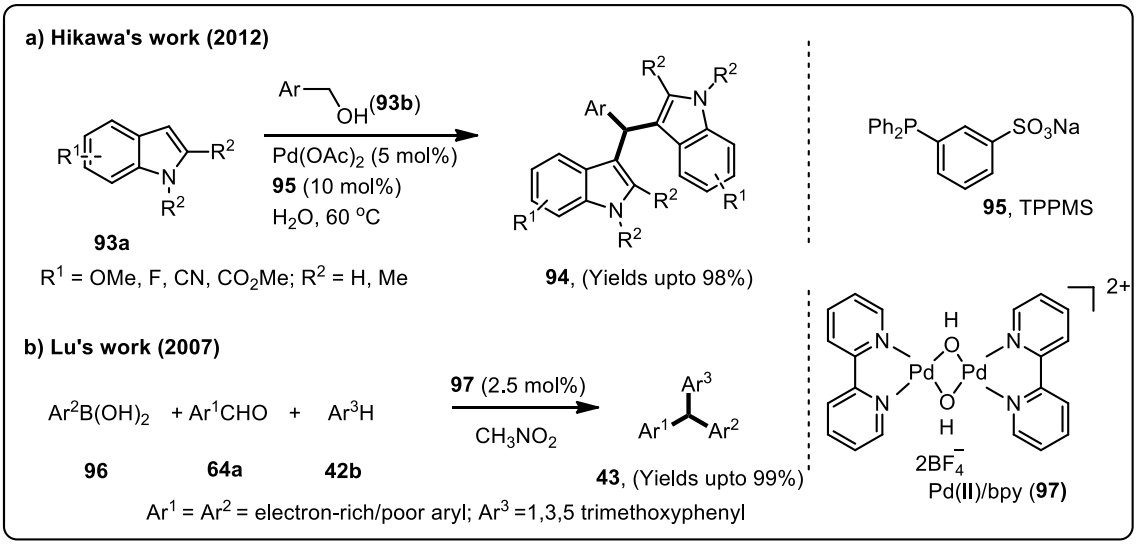


Scheme 24: Pd-catalyzed coupling approach to di- and triarylmethanes

In a seminal contribution, Molander's group developed a Pd-catalyzed cross-coupling reaction to access unsymmetrical diaryl- and triarylmethanes. The present work describes a Pd-catalyzed

Suzuki-Miyaura coupling of potassium aryltrifluoroborates (**89b**) with benzyl halides (**89a**). Variety of simple diarylmethane (**90**) could be prepared using this method. This method was also elaborated to the synthesis of symmetrical triarylmethane (**92a**), however the chemo- and regio-selectivities were found to be very poor (**Scheme 24**).[38b]

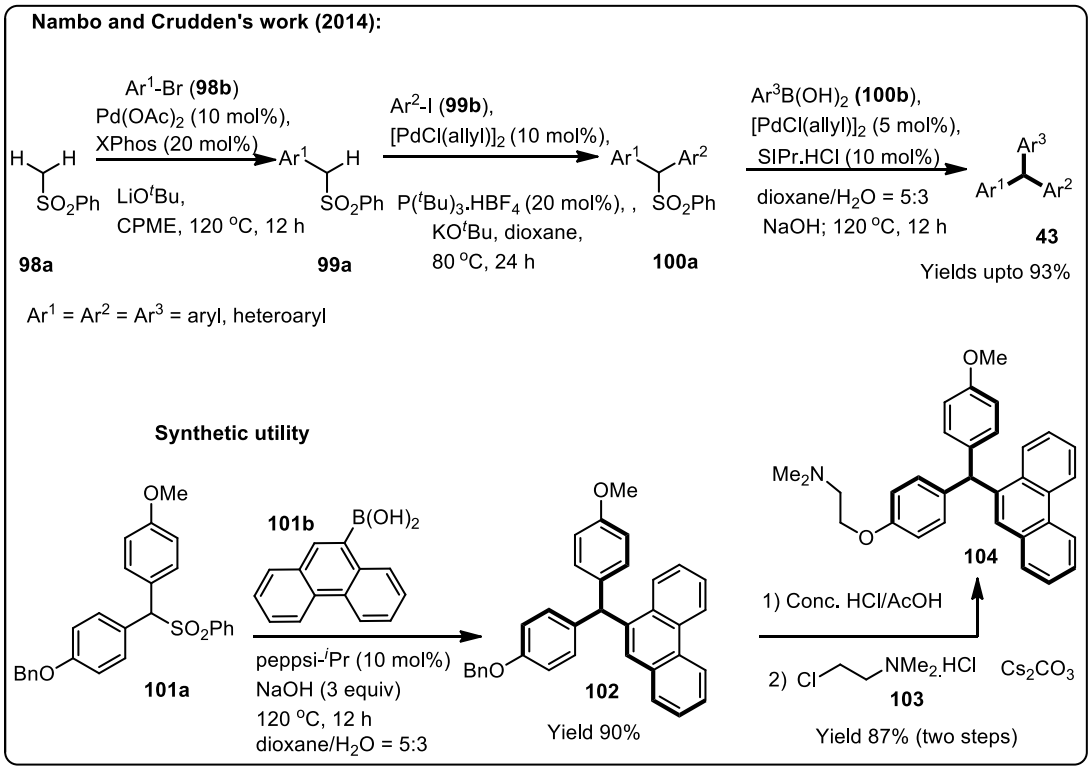
In addition to Pd-catalyzed approaches[38a-e] toward the synthesis of triarylmethanes, Hikawa and co-workers introduced a new C-H activation strategy using a (π-benzyl)-complex of palladium as a catalyst. Through this method, the synthesis of a diverse range of bis-indolyl arylmethanes (**94**) could be achieved. It was anticipated that this reaction proceeds through the C–H activation of the C_3-position of indole (**93a**) followed by benzylic C–H functionalization of benzyl alcohol (**a**, **Scheme 25**).[39a] Another interesting approach based on cationic Pd(II) (**97**)-catalyzed addition of aryl boronic acids (**96**) to aryl aldehydes (**64a**) was established by Lu and co-workers for the one-pot synthesis of unsymmetrical triarylmethanes (**43**). It was proposed that the addition of aryl-palladium species, derived from aryl boronic acid (**96**), reacts with aldehydes and generates diarylmethanol (**55**), which again undergoes arylation with electron-rich 1,3,5-trimethoxy benzene (**42b**) to provide unsymmetrical triarylmethanes (**43**) (**b**, **Scheme 25**).[40]



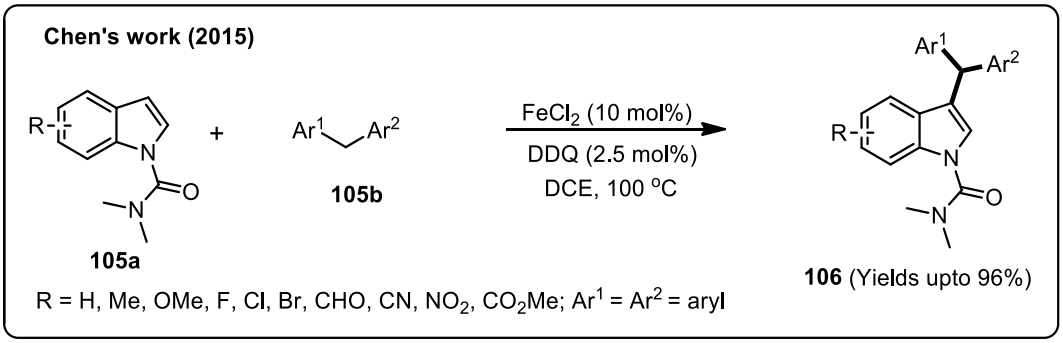
Scheme 25: TAM synthesis through Pd-catalysis

Nambo and Crudden developed a sequential Pd-catalyzed C-H arylations of a readily available methyl surrogate (**98a**) (Methyl phenylsulfone) to make unsymmetrical TAMs. The present

protocol consists of 3 steps, out of which, the first two steps involve the successive arylation of **98a** through coupling with aryl halides **98b** and **99b** respectively. Subsequent desulfonylative arylation with aryl boronic acids (**100b**) at elevated temperature provided the unsymmetrical triarylmethanes (**43**) in moderate to excellent yields. Further, this methodolgy was elaborated to the synthesis of anti-breast cancer agent **104** in a very good overall yield (**scheme 26**).[41]



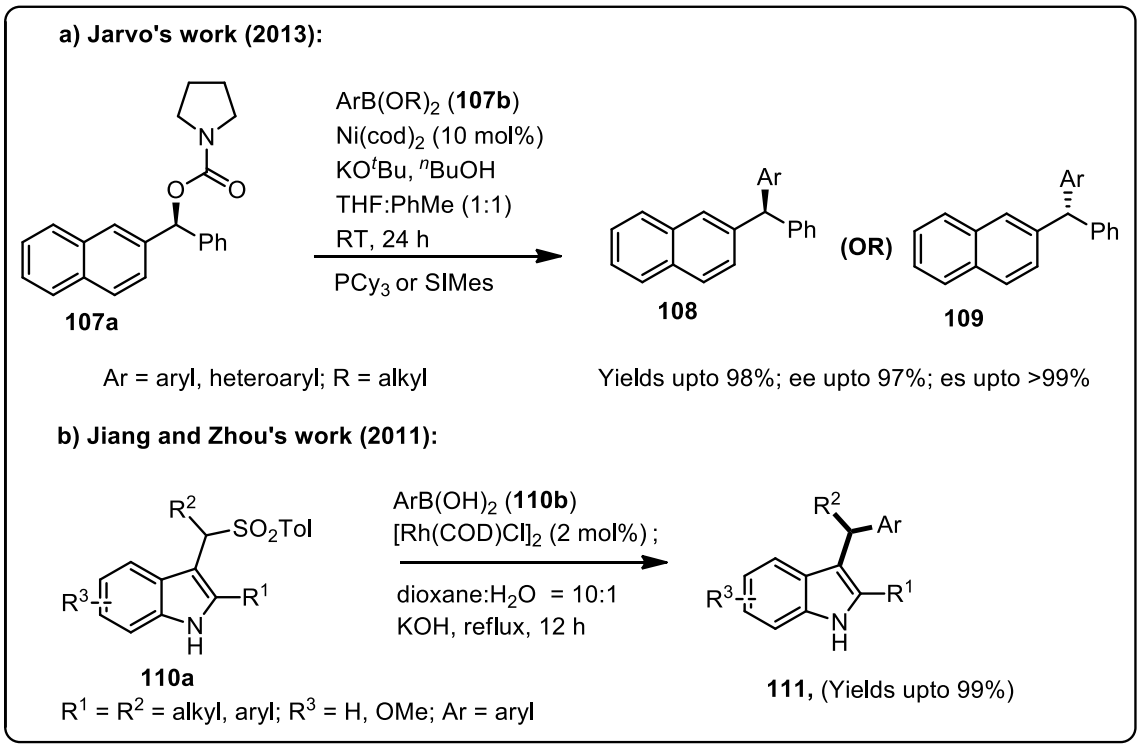
Scheme 26: Pd-catalyzed sequential arylation for the synthesis of TAMs



Scheme 27: Cross dehydrogenative coupling approach to TAMs

Chen and co-workers disclosed an iron catalyzed oxidative crossdehydrogenative coupling between *N*,*N*-dimethylcarboxamide (**105a**) and diarylmethanes (**105b**) to access indole-containing unsymmetrical TAMs (**106)** [**Scheme 27**].[42]

Jarvo and co-workers portrayed a Ni-catalyzed Suzuki-Miyaura cross-coupling reaction of benzylic carbamates (**107a**) with aryl boronic esters (**107b**) for the synthesis of enantiomerically enriched triarylmethanes (**108**/**109**). The significance of this method is that the achiral ligand controls whether the reaction proceeds with inversion or retention at the electrophilic carbon (**a**, **scheme 28**).[43]

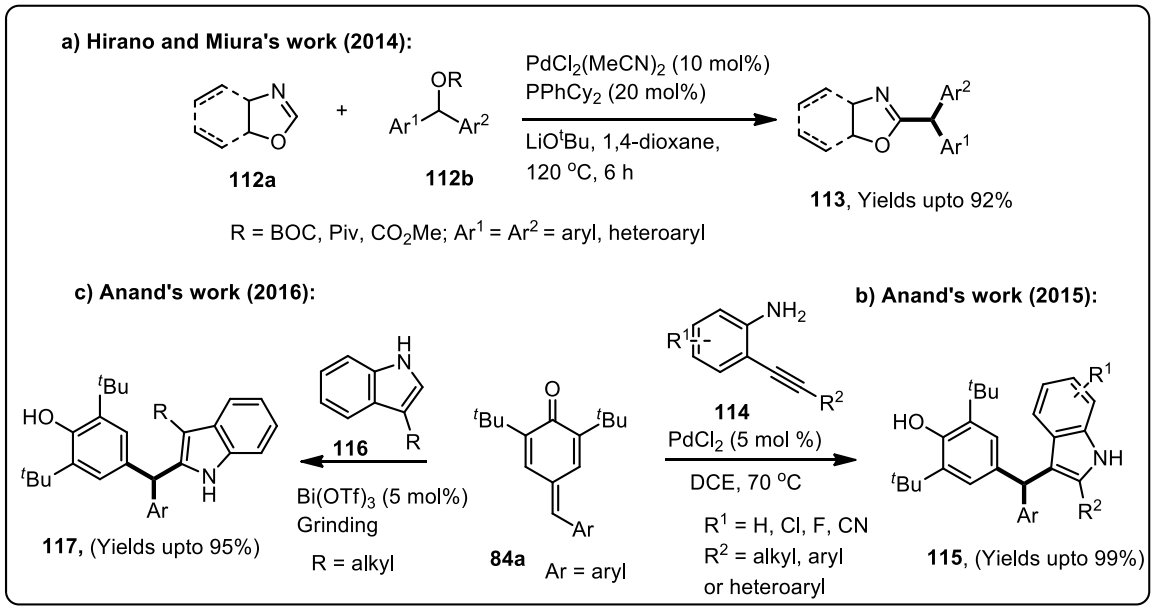


Scheme 28: TAM synthesis through metal catalysis

Jiang and Zhou developed a Rh-catalyzed method for the addition of aryl boronic acids (**110b**) to *in situ* generated imines from sulfonyl indoles (**110a**). Through this approach, broad range of diaryl- and triarylmethanes (**111**) were accessed in good yields (**b**, **scheme 28**).[44]

Hirano and Miura realized a Pd-catalyzed oxazole (**112a**) coupling with diarylmethylcarbonates or pivalates (**112b**) to furnish corresponding triarylmethanes (**113**). Notably, the precursors utilized in this are non-halodenated and non-metalated which is complementary to the standard cross-coupling approaches (**a**, **scheme 29**).[45] Our research group, very recently, developed a

couple of reports for the synthesis of TAMs using *p*-quinone methide as a key synthetic precursor. First report unveiled a Pd-catalyzed cyclization-addition sequence of *o*-alkynyl anilines (**114**) *via* 1,6-conjugate addition to *p*-quionone methides (**84a**) for the synthesis of wide range of densely-substituted unsymmetrical diarylindolylmethane derivatives (**115**) with 100% atom economy (**b, Scheme 29**).[46a] Subsequent report discloses a solvent-free 1,6-conjugate addition of 3-substituted indoles (**116**) to *p*-quionone methides (**84a**) for the preparation of unsymmetrical diaryl indolylmethane derivatives (**117**) [**c, Scheme 29**].[46b]



Scheme 29: Heteroaryl based TAM syntheses through divergent approaches

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Chapter 2: Metal catalyzed diversity-oriented approaches toward indolizine containing unsymmetrical diaryl- and triarylmethane derivatives

1. Introduction:

Indolizines are a class of nitrogen containing unsaturated bicyclic heterocycles having the nitrogen atom shared between 5- and 6-membered rings. They are also known as pyrrocoline, pyrrolo[1,2-*a*]pyridine, pyrindole etc. Indolizine core is found as an integral part in many biologically active complex natural products.[1a] Moreover, many unnatural indolizine derivatives possess remarkable therapeutic activities (**Figure 1**).[2] Besides, some of them are known to exhibit noteworthy photo-physical properties.[3]

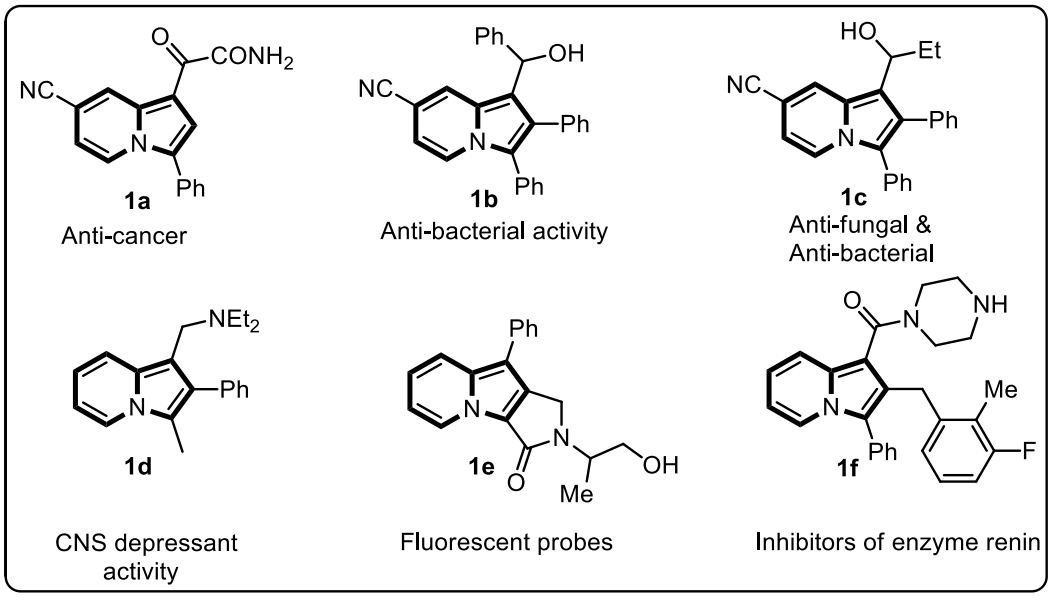
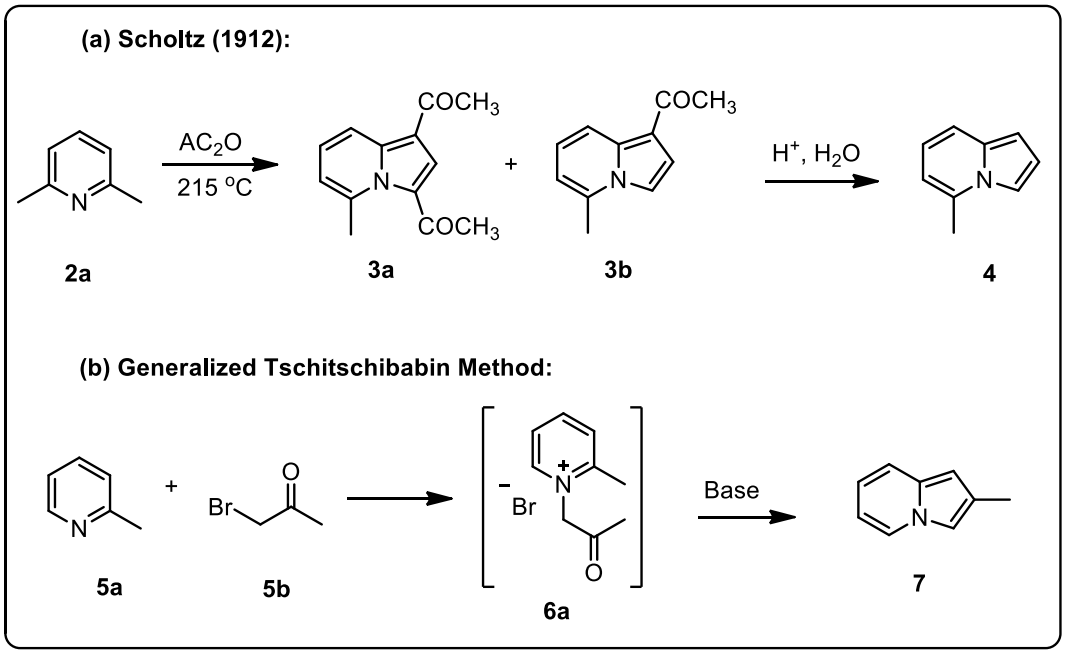


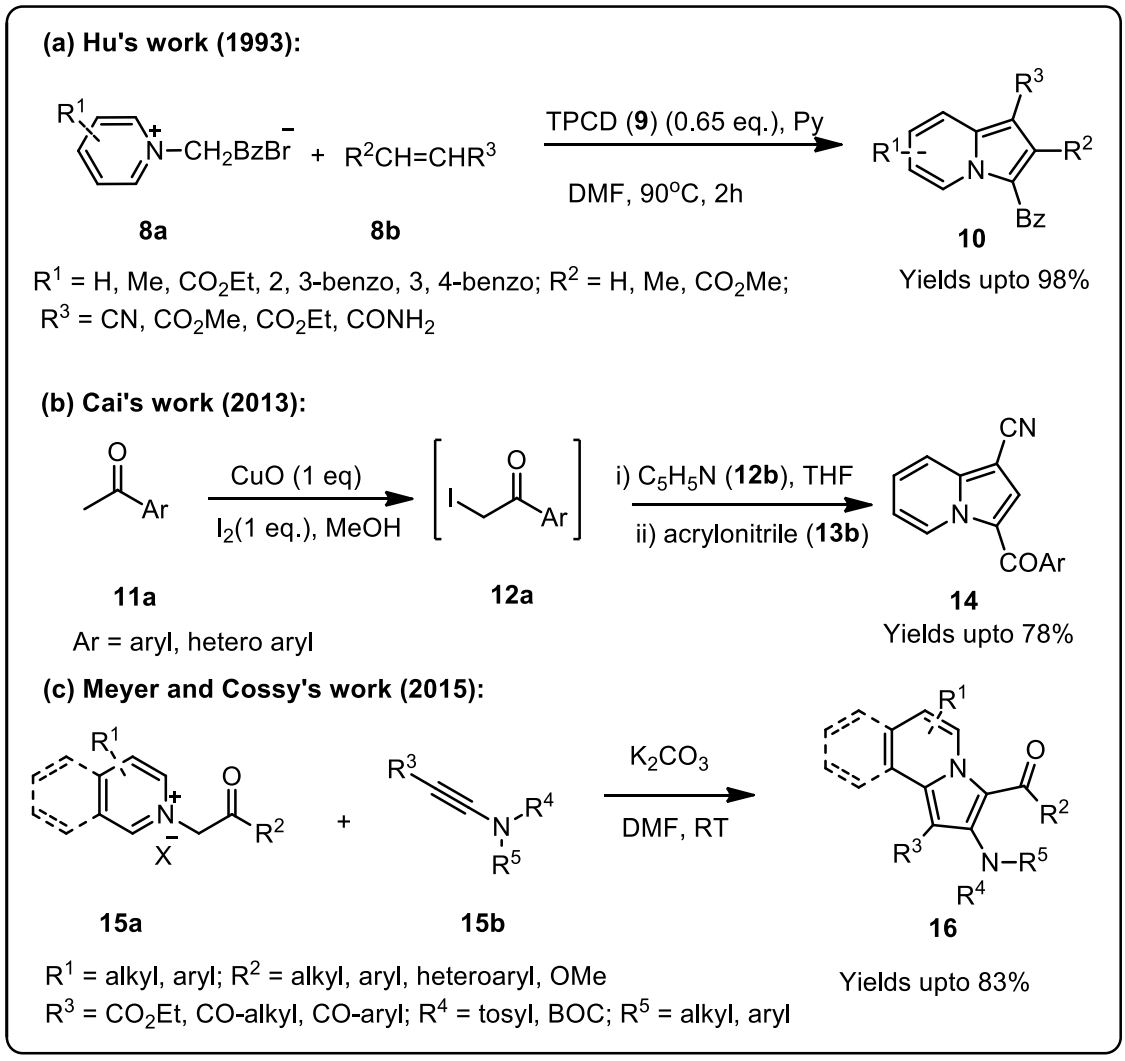
Figure 1. Biologically important indolizine derivatives

The classical approaches for assembling indolizine core comprise Scholtz reaction and Tschitschibabin's protocol. In Scholtz process, a mixture of 2,6-lutidine (**2a**) and Ac_2O was heated at 215 °C to furnish the acetyl derivatives of methylpyrrocoline (**3**), which on acidic hydrolysis provided 5-methyl pyrrocoline (**4**) [**a**, **Scheme 1**].[4] The typical procedure for the Tschitschibabin method comprises the reaction of the quaternary pyridinium salt (**6a**) under basic media to generate indolizine derivatives (**7**) [**b**, **Scheme 1**].[5]



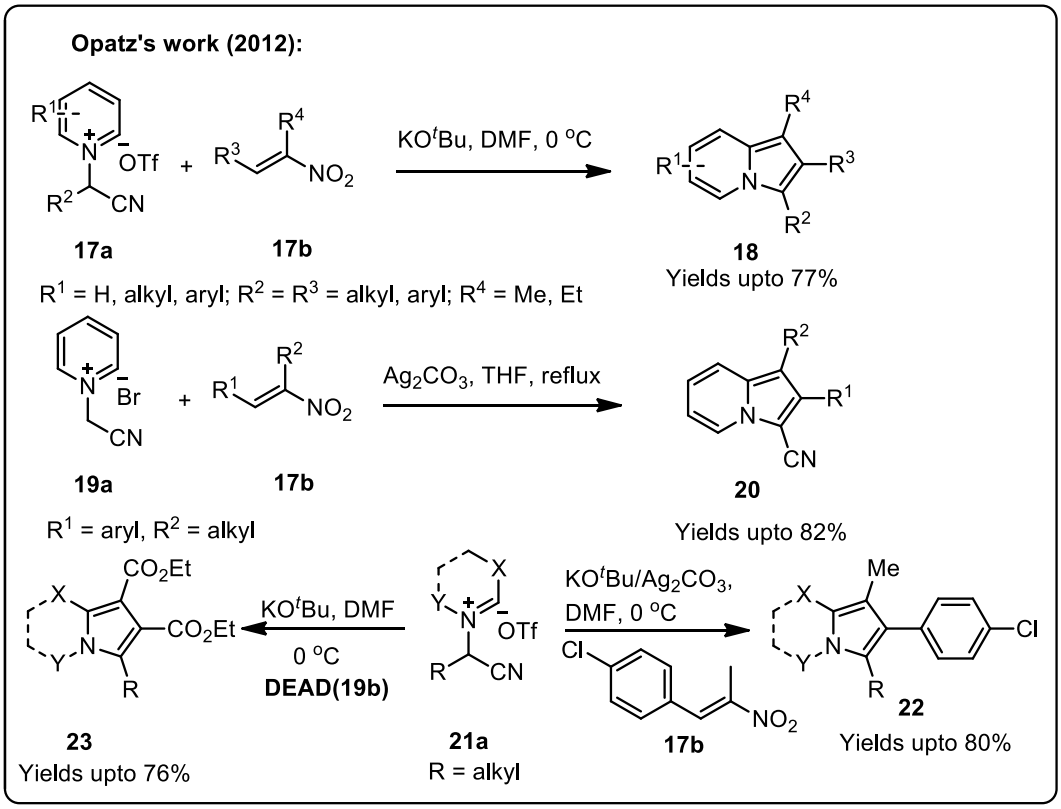
Scheme 1. Traditional methods for the synthesis of indolizine derivatives

Apart from the above-mentioned traditional methods, 1,3-dipolar cycloaddition approach has been found to be a prevalent strategy for the construction of indolizine derivatives, in which either olefine or acetylene derivatives are used as dipolarophiles and pyridine derivatives as 1,3-dipole.[6] In general, the pyridinium ylides generated from α-halonitriles/ketones or cyanohydrin triflates serve as precursors for the synthesis of indolizines. Hu and co-workers reported the 1,3-dipolar cycloaddition between a wide array of pyridine based ylides (**8a**) with dipolarophiles (**8b**) for the preparation of lead derivatives (**10**) in the presence of an oxidant TPCD (**9**) [Tetra Pyridine Cobalt (II) Dichromate] (**a, Scheme 2**).[6a] A tandem approach for the construction of indolizines (**14**) using readily available precursors such as ketone, pyridine and acrylonitrile was reported by Cai *et.al.*, which illustrates an one-pot synthesis pyridinium ylide followed by 1,3-dipolar cycloaddition with acrylonitrile (**13b**) [**b, Scheme 2**].[6b] Very recently, 1,3-dipolar cycloaddition of pyridinium or isoquinolinium based ylides (**15a**) with ynamides (**15b**) was developed by Meyer and Cossy for the synthesis of structurally complex indolizine derivatives (**16**) [**c, Scheme 2**].[6c]



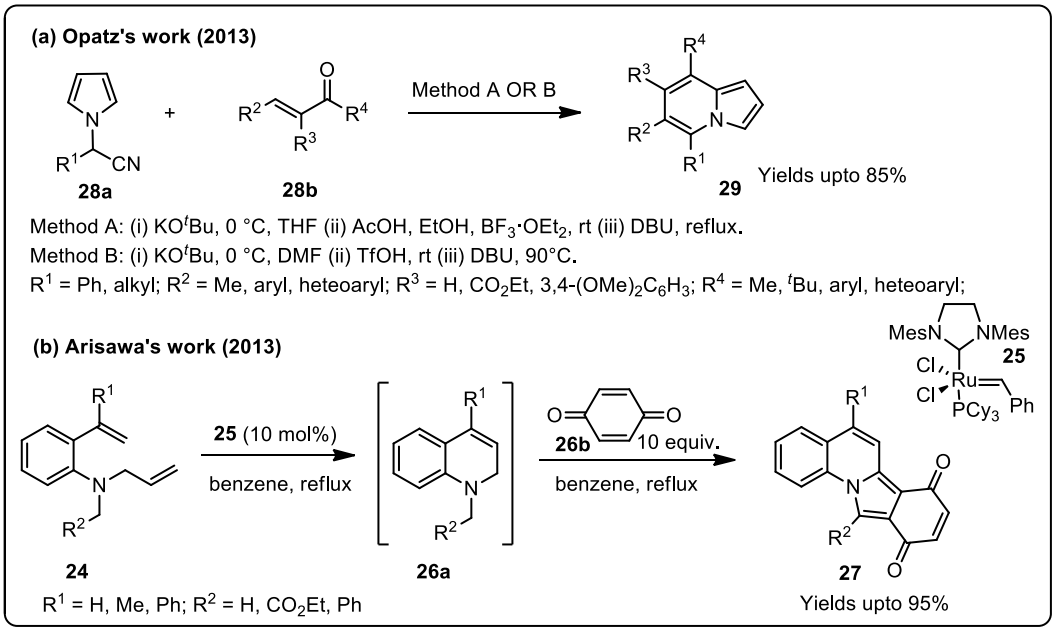
Scheme 2. Indolizine synthesis through 1,3-dipolar cycloaddition strategy

Opatz and co-workers reported the synthesis of poly-substituted indolizines (**18**, **20**), using nitro-olefines (**17b**) as coupling partners, by altering the reaction conditions according to the counter ion of ylides (**17a**, **19a**). Utilizing this protocol, they could prepare a variety of indolizine derivatives (**22** & **23**) such as pyrroloisoquinoline, pyrrolophthalazine, pyrroloimidazole, and pyrrolobenzothiazole from their respective heterocyclic precursors (**Scheme 3**).[6d]

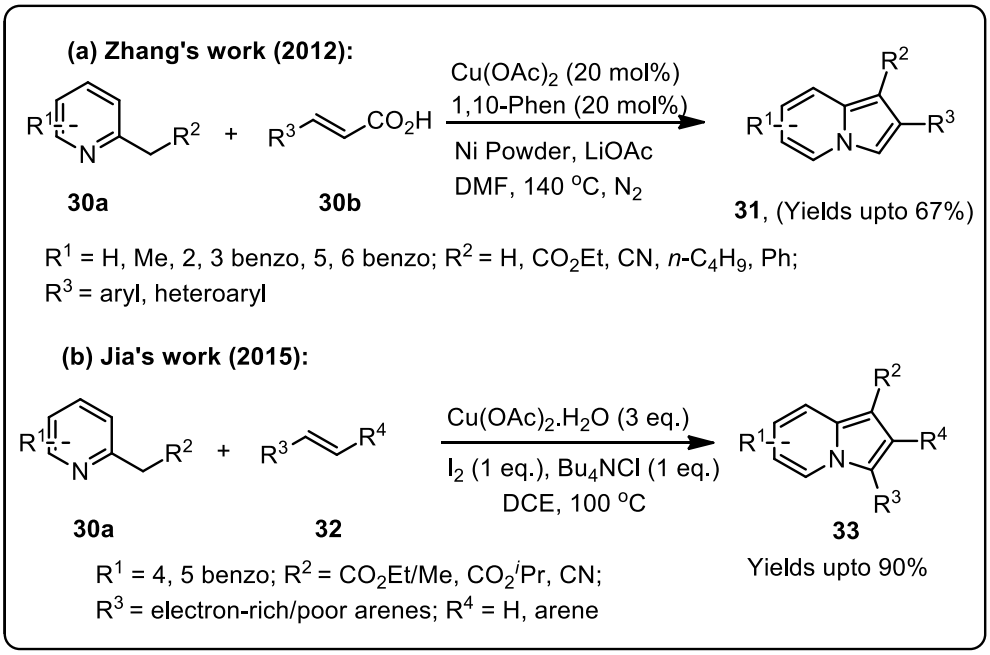


Scheme 3. Opatz approaches toward indolizine synthesis

Besides the numerous reports using pyridine derivatives as precursors, only a handful of reports are known for the annulation of pyrrole for the synthesis of indolizines.[6e] Opatz and co-workers have come up with another interesting approach for the synthesis of densely substituted indolizine derivatives (**29**), which involves a one-pot conjugate addition/ cyclodehydration/dehydrocyanation sequence starting from 2-(1H-pyrrol-1-yl)nitriles (**28a**) and α,β-unsaturated ketones or aldehydes (**28b**) (**a**, **Scheme 4**).[6e] Arisawa and co-workers developed a new '*assisted tandem method*' in 2013.[7a] This method disclosed a ruthenium catalyzed ring closing metathesis followed by 1,3-dipolar cycloaddition of the precursor **24** in an one-pot manner for the synthesis of indolizine (**27**). It was proposed that the azomethine equivalent, 1,2-dihydroquinoline (**26a**), was generated as an intermediate from the ruthenium-alkylidene-catalyzed (**25**) ring closing metathesis of **24**, which further underwent a ruthenium catalyzed 1,3-dipolar cycloaddition with dipolarophile (**26b**) to produce isoindolo[2,1-*a*]quinoline (**27**) derivatives (**b**, **Scheme 4**).[7a]



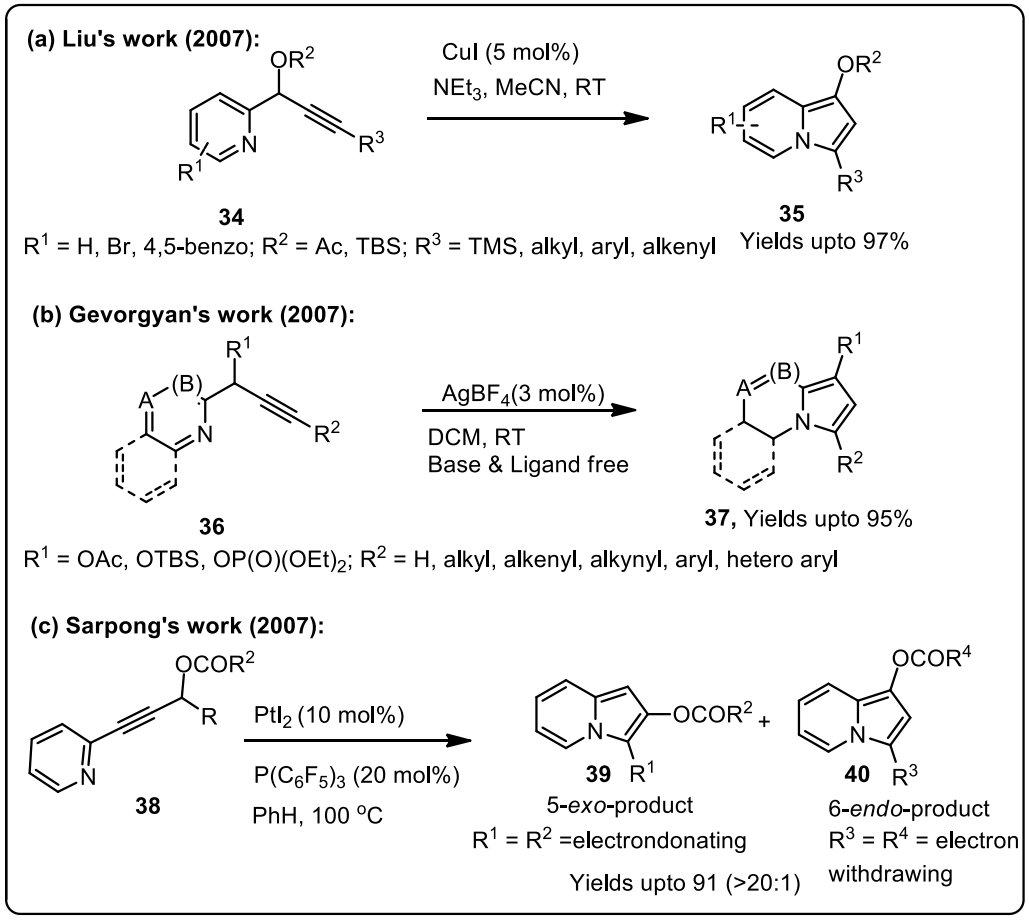
Scheme 4. Miscellaneous approaches in 1,3-dipolar cycloaddition



Scheme 5: Oxidative cross-coupling approaches for indolizine synthesis

Zhang and co-workers developed a novel Cu-catalyzed annulation of 2-alkyl pyridines (**30a**) towards α,β-unsaturated carboxylic acids (**30b**) for the efficient production of indolizines (**31**). The present method divulged a C-H olefination and decarboxylative amination of readily

available pyridine derivatives which furnished a broad range of C-2 arylated indolizines (**a**, **Scheme 5**).[7d] A straight forward and convenient protocol for the synthesis of structurally diverse 1,3-disubstituted and 1,2,3-trisustituted indolizines (**33**) was reported by Jia and co-workers, through Cu/I_2 mediated oxidative cross-coupling of the pyridine derivatives (**30a**) with olefines (**32**). It was proposed that olefine addition to pyridine-2-acetate derivatives occurs in a radical fashion followed by cyclization and oxidation leads to the desired products (**33**) [**b**, **Scheme 5**].[7f]

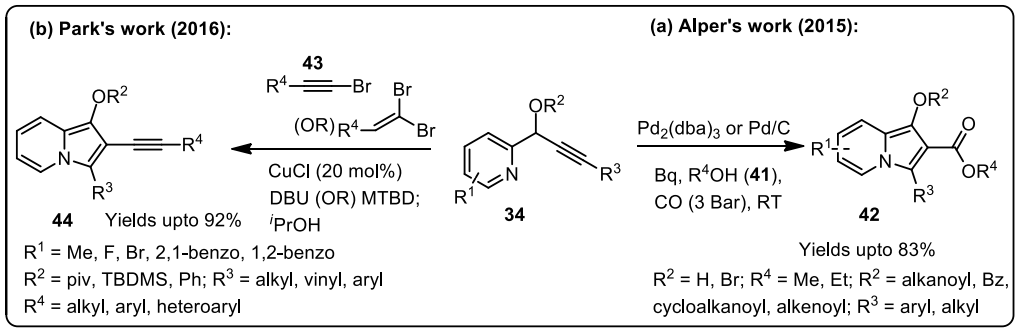


Scheme 6: Cycloisomerization of pyridine derivatives for the synthesis of indolizines

Encouraged by the high demand of the application potential of pyridine-2-propargyl derivatives as precursors, various groups have come up with different strategies for the preparation of *N*-fused bicycle systems by employing a variety of metal catalysts.[8,9] Liu's protocol discloses a base-mediated simple cycloisomerization of propargylic pyridine derivatives (**34**) for the synthesis of indolizines (**35**) (**a**, **Scheme 6**).[8a] Sarpong and co-workers reported a Pt-catalyzed 5-

exo-dig/6-*endo*-dig cyclization of similar propargylic analogues (**38**) for the synthesis of 2,3-disubstituted/1,3-disubstituted indolizines (**39** & **40**) [**c**, **Scheme 6**].[9d] While developing a few cycloisomerization strategies[8,9] for the synthesis of a library of indolizine derivatives, Gevorgyan and co-workers came up with an alternative strategy to both Liu's and Sarpong's work, which involves a Ag-catalyzed, base and ligand free, cycloisomerization of similar propargylic pyridine derivatives (**34**) to furnish the indolizines (**35**) [**b**, **Scheme 6**].[8b]

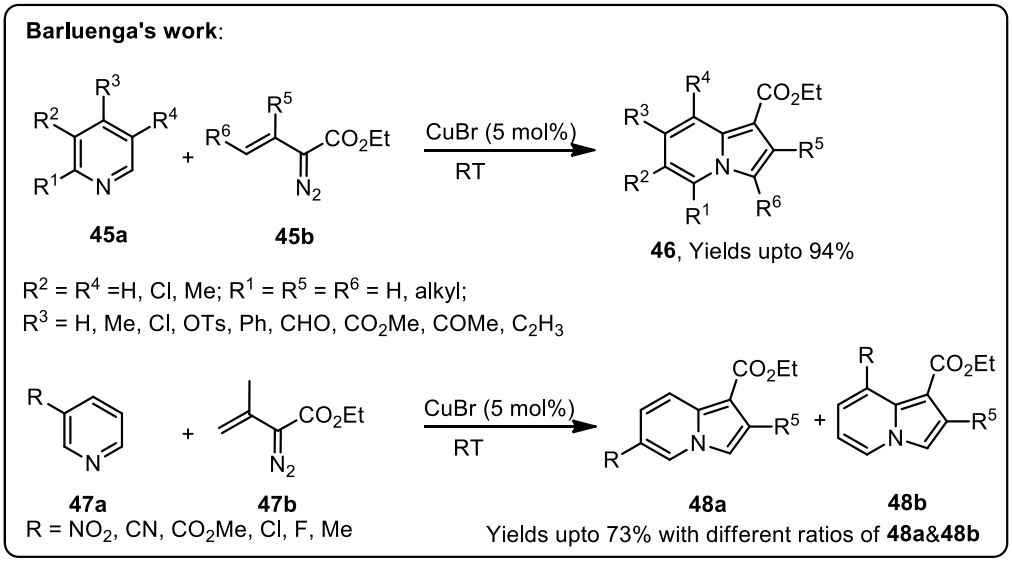
One-pot applications for the synthesis of C_2-substituted indolizine have become an exceptionally attractive research area, which majorly comprises cycloisomerization of pyridine propargyl derivatives followed by trapping with an electrophile. For instance, Pd-catalyzed oxidative carbonylation of propargylic pyridines (**34**) was divulged by Alper and co-workers for the synthesis of indolizines. Through this method, a broad range of heavily substituted and potentially useful indolizines (**42**) were assembled under mild reaction conditions (**a, Scheme 7**).[8c] Further, a base controlled and Cu-catalyzed tandem cyclization followed by alkynylation was revealed by Park and co-workers in 2016. They proposed that the reaction actually proceeds through 5-*endo*-dig amino-cupration of **34** followed by a Cu-catalyzed coupling with alkynyl bromide or alkenyl bromides (**43**) to provide highly functionalized indolizine derivatives (**44**) [**b, Scheme 7**].[8d]



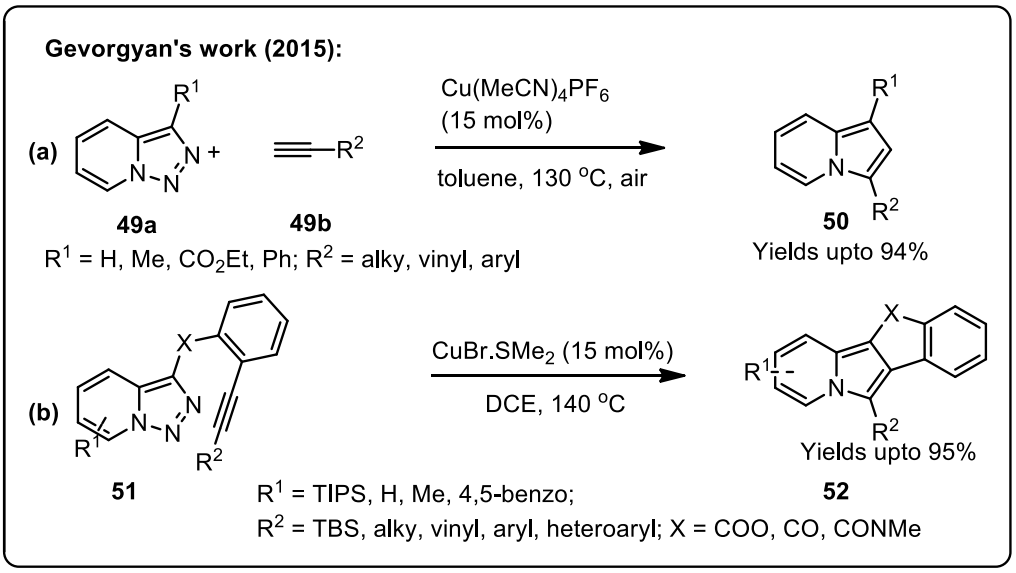
Scheme 7: Cycloisomerization of pyridine derivatives for the synthesis of indolizines

Vinyl diazoacetates are considered to be other interesting coupling partners in the synthesis of indolizines. Barluenga and co-workers reported a metal-catalyzed cyclization of π-deficient heterocyclic system with alkenyl diazo compounds (**45b**, **47b**). The present strategy has proven that the commercially cheaper transition metal (Cu) catalyzes the regioselective annulation of

pyridine derivatives (**45a**, **47a**) with **45a** & **45b** to prepare a diverse range of indolizine derivatives (**46**, **48**) [**Scheme 8**].[10a]



Scheme 8: Vinyl diazoacetates derived indolizine synthesis

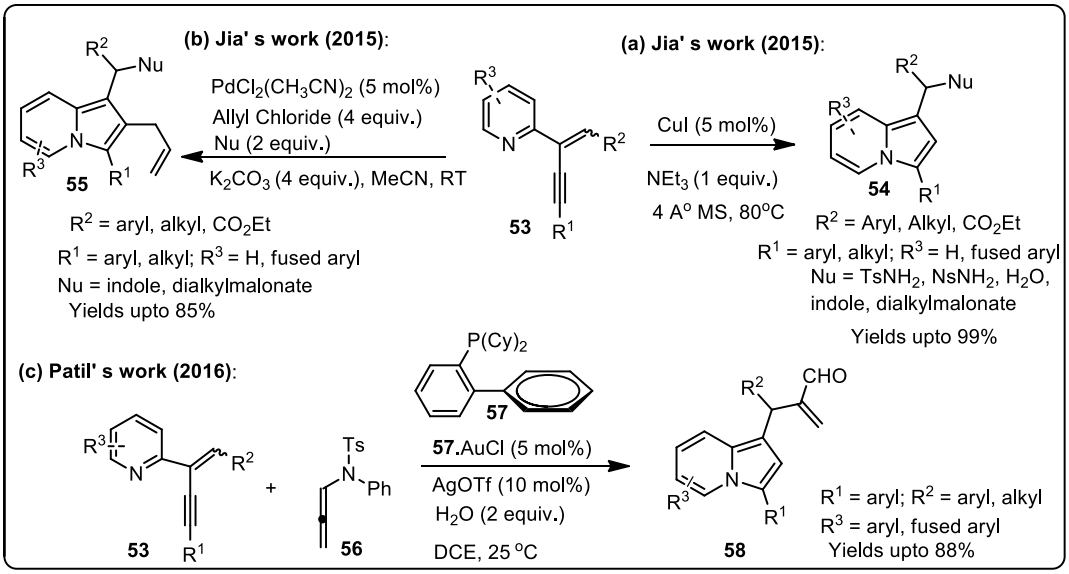


Scheme 9: Indolizine synthesis through pyridotriazoles

Very recently a couple of reports appeared from Gevorgyan's group, displaying the synthesis of indolizines (**50**)/polycyclic indolizines (**52**) through a Cu-catalyzed transannulation of

unactivated pyridotriazoles (**49a** and **51**) with acetylenes through inter- or intra-molecular cyclization (**Scheme 9**).[11b,11c]

Very recently, a Cu-catalyzed cyclization of 2-(2-enynyl)-pyridines (**53**) in the presence of various nucleophiles through a concurrent C–N bond formation and a remote nucleophile addition was developed by Jia and co-workers in 2015. Variety of nucleophiles such as malonates, indoles, amides, alcohols and even water were employed for the synthesis of a wide array of functionalized indolizine derivatives (**54**). [12a] Additionally, 2-(2-enynyl)-pyridines were also converted into its cyclopropyl counterparts [2-(1-alkynyl-cyclopropyl)pyridines] and were subjected to Au-catalyzed ring-opening reactions with nucleophiles for the synthesis of extended carbon analogues of **54** in good yields (**a**, **Scheme 10**).[(12a, 12b)] Further, this protocol was elaborated to a Pd-catalyzed three component cascade reaction for the synthesis of heavily substituted indolizine derivatives (**55**). The present cascade reaction unveiled that the cyclization of 2-(2-enynyl)-pyridines (**53**) with a remote nucleophile addition followed by allyl trapping led to indolizines (**55**) in which two C-C and a C-N bonds formation occurs simultaneously (**b**, **Scheme 10**).[12c]



Scheme 10. Indolizine synthesis from 2-(2-enynyl)-pyridines

Later, Patil and co-workers developed a co-operative Au/Ag catalyst system for the synthesis of indolizine derivatives (**58**) using 2-(2-enynyl)-pyridines (**53**) and *N*-allenamide (**56**) as a nucleophilic enal equivalent (**c**, **Scheme 10**).[12d]

2. Objectives:

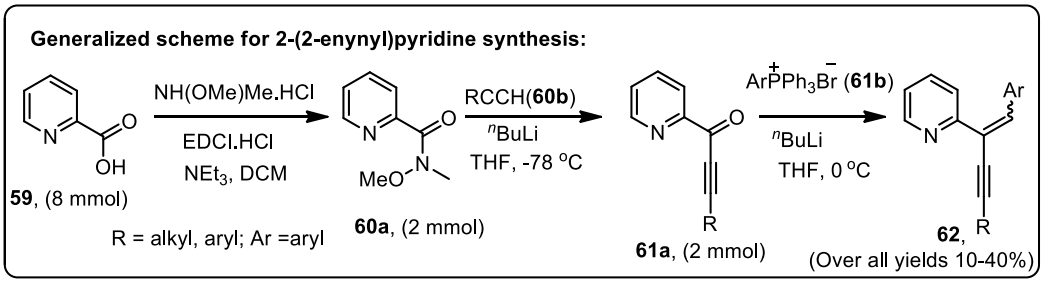
a) *To synthesize indolizine containing diarylmethanes through a Lewis acid catalyzed reductive cyclization of 2-(2-enynyl)-pyridines.*

b) *To access indolizine containing diarylmethyl phosphonates through a metal catalyzed hydrophosphonylation of 2-(2-enynyl)-pyridines.*

c) *To prepare indolizine containing unsymmetrical triarylmethanes through a Lewis acid catalyzed 5-endo-dig cyclization of 2-(2-enynyl)-pyridine followed by a remote addition of 2-naphthols.*

d) *To develop a double 5-endo-dig cyclization cascade reaction for the synthesis of hetero-arylated unsymmetrical triarylmethanes from 2-(2-enynyl)-pyridine and o-alkynyl anilines.*

The 5-*endo*-dig cyclization approach has proved to be a prevalent strategy for the construction of many valuable bicyclic heterocycles as shown in the introduction part (**Schemes 6**, **7** and **10**). We became interested to employ this approach for the preparation of indolizine containing unsymmetrical diaryl- and triarylmethanes from 2-(2-enynyl)-pyridines (**62**). In this regard, we have prepared broad range of 2-(2-enynyl)-pyridines (**62**) by adapting a known literature procedure (**Scheme 11**).[12a-c]



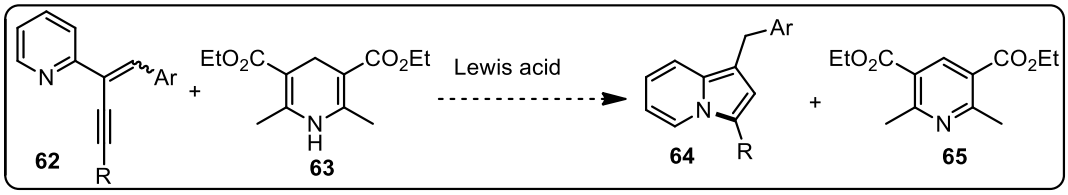
Scheme 11: Synthesis of 2-(2-enynyl)-pyridines

2a. Synthesis of diarylmethanes through a Lewis acid catalyzed reductive cyclization of 2-(2-enynyl)-pyridines:

Apart from the seminal contribution by Noyori and co-workers in the field of the transition metal-based asymmetric hydrogenations[13], organocatalytic transfer hydrogenations using organic hydride donors has become a prevalent strategy to the synthetic community.[14] Among various hydrogen sources, Hantzsch ester, a 1,4-dihydropyridine derivative, has been widely used for the transfer hydrogenation reaction. For instance, Hantzsch ester mediated 1,2-addition of hydrogen for the reduction of imines,[15a] enamines,[15b] carbonyls[15c] as well as 1,4-addition of hydrogen for the reduction of α,β-unsaturated carbonyls[16] are very common in the literature .

Results and discusion:

While working on the synthesis of unsymmetrical diaryl- and triarylmethane derivatives,[17] we anticipated that it is possible to synthesize indolizine containing unsymmetrical diarylmethanes (**64**) starting from 2-(2-enynyl)-pyridine derivatives (**62**) and Hantzsch ester (**63**) as a reductant (**Scheme 12**). To the best of our knowledge, hydride sources have not been utilized as nucleophiles for this transformation so far. Herein, we disclose a Cu-catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines (**62**) followed by a remote addition of hydride leading to unsymmetrical indolizine based diarylmethanes (**64**).[17f]

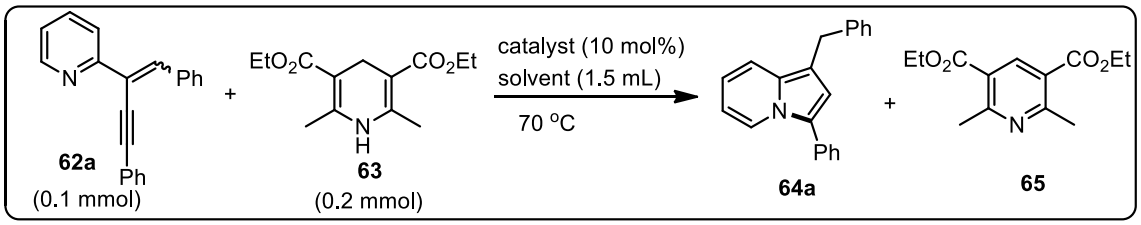


Scheme 12: Our proposed approach towards indolizine based diaryl methanes

We began the optimization studies with 2-(2-enynyl)-pyridine (**62a)** and Hantzsch ester (**63**) [as a hydride surrogate] under various reaction conditions. Our initial optimization experiments revealed that silver based catalysts, such as $AgSbF_6$, $AgBF_4$ and AgOAc were found to be effective to drive this transformation at 70 °C in acetonitrile and the desired product **64a** was obtained in 80-86% yields (Entries 1-3). Other metal catalysts

such as $PdCl_2$, $Pd(OAc)_2$, $Sc(OTf)_3$ and $Bi(OTf)_3$ were also found to be suitable for this transformation; however, the yield of **64a** was found to be moderate or less (20-65%) when compared to silver catalysts (Entries 4-7).

Table 1: Optimization studies[a,b]



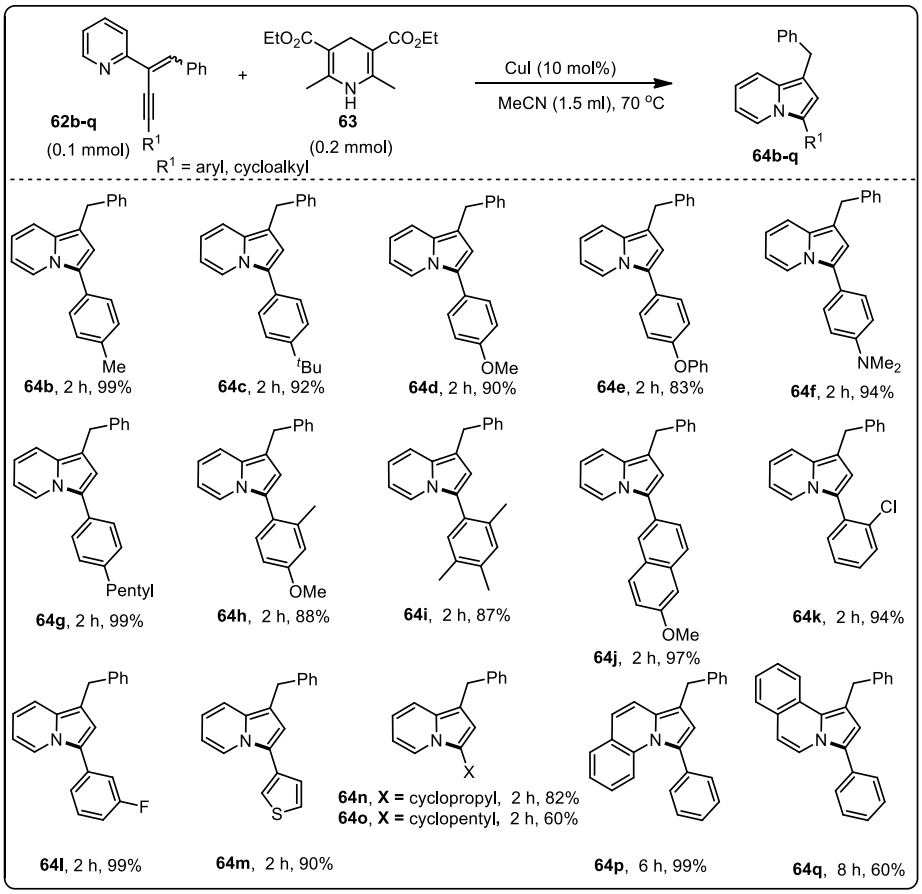
Entry	Lewis acid	Solvent	Time [h]	Yield [%][c]
1	$AgSbF_6$	MeCN	2	80
2	$AgBF_4$	MeCN	2	86
3	Ag(OAc)	MeCN	2	82
4	$PdCl_2$	MeCN	8	20
5	$Pd(OAc)_2$	MeCN	4	47
6	$Sc(OTf)_3$	MeCN	6	65
7	$Bi(OTf)_3$	MeCN	6	60
8	$Cu(OTf)_2$	MeCN	3	79
9	Cu(OTf)	MeCN	3	82
10	CuCl	MeCN	3	75
11	**CuI**	**MeCN**	**3**	**95**
12	CuI	DCE	3	89
13	CuI	Toluene	3	79
14	CuI	THF	3	61
15	---	MeCN	24	NR
16[d]	CuI	MeCN	24	80
17[e]	CuI	MeCN	5	88

[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62a** in solvent. [b]2 Equivalents of Hantzsch ester (**63**) was found to be optimal. [c]Isolated yield. [d]Reaction was done at room temperature (25-27 °C). [e]Reaction was carried out in 1.42 mmol of **62a** in 10 mL of MeCN.

Further optimization studies revealed that copper based catalysts, like Cu(OTf).PhMe, $Cu(OTf)_2$, and CuCl also catalyzed the reaction and, in those cases, the product **64a** was obtained in the range of 75-82% yields within a short reaction time (Entries 8-10). Remarkably, the yield of **64a** was improved to 95% when the reaction was carried out with CuI as a catalyst in acetonitrile at 70 °C (Entry 11). Heartened by this observation, we elaborated the optimization studies using CuI as a catalyst in different solvents. However, unfortunately, in all those cases (Entries 12-14) the yield of the desired product **64a** was inferior (61-89%) when compared to entry 11. No product was observed in the absence of any catalyst even after 24 h (Entry 15). The reaction also progressed at room temperature in the presence of CuI in acetonitrile and provided the product **64a** in 80% yield; however, the reaction took a very long time (24 h) to complete (Entry 16). A relatively large scale reaction was carried out with 400 mg (1.42 mmol) of **62a** under the standard conditions (Entry 11), and in this case, the product **64a** was isolated in 88% yield after 5 h (Entry 17).

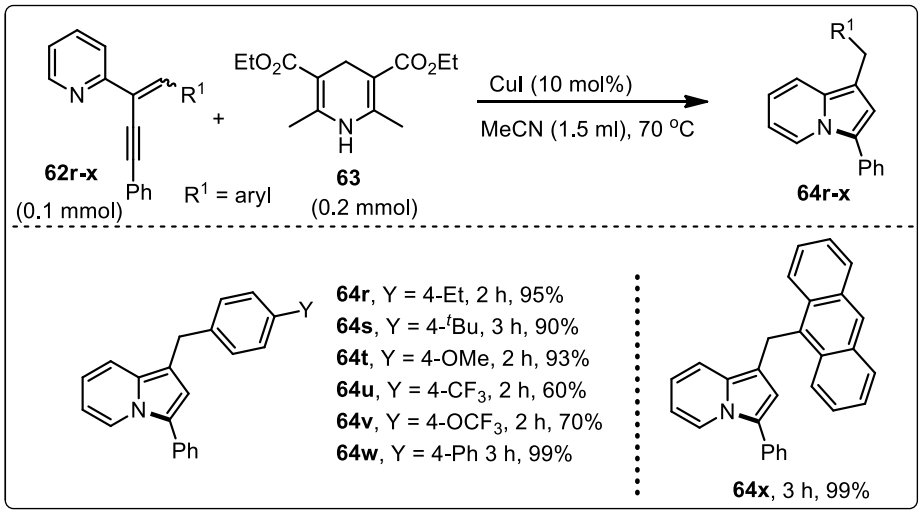
After establishing the optimal conditions (Entry 11, Table 1), the substrate scope of the reaction was investigated by using a wide range of substituted 2-(2-enynyl)-pyridines and the results are summarized in Table 2 and Table 3. The results projected in Table 2 attest that this method worked very well with the 2-(2-enynyl)-pyridines (**62b-l**), which were derived from terminal acetylenes, substituted with electron-rich as well as electron-poor arenes, and in all the cases, the expected diarylmethanes (**64b-l**) were isolated in good to excellent yields (83-99%). Under the standard conditions, the anticipated heteroaryl substituted diarylmethane (**64m**) was isolated with 90% yield from **62m**. Even electronically inactive cycloalkyl-substituted derivatives (**62n** and **62o**) underwent cyclization to lead the products **64n** and **64o** in 82% and 60% isolated yields, respectively. Moreover, quinoline (**62p**) and isoquinoline (**62q**) based diarylmethanes furnished the desired products (**64p** and **64q**) with 99% and 60% yields, respectively.

Table 2. Substrate scope with different 2-(2-enynyl)-pyridines



[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62** in solvent at 70 °C. Yields reported are isolated yields.

Table 3. Substrate scope with different 2-(2-enynyl)-pyridines



[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62** in solvent at 70 °C. Yields reported are isolated yields.

The efficiency of the reaction was also tested using a few 2-(2-enynyl)-pyridine (**62r-x**) derivatives having substitution at the olefinic part (Table 3), and in all those cases, the respective diarylmethane derivatives (**64r-x**) were isolated in moderate to excellent yields (60-99%).

2b. Synthesis of diarylmethyl phosphonates through a metal catalyzed hydrophosphonylation of 2-(2-enynyl)-pyridines:

A brief introduction on the synthesis and applications of organophosphorous compounds is included in this section.

Organophosphorous derivatives are accredited to be an important class of compounds in the area of organic as well as inorganic chemistry.[18] Some of the organophosphorous derivatives exhibit intriguing applications in various fields.[19] For instance, diarylmethanephosphonate **65a** is used as a potassium channel modulator. Moreover, **65b** and **65c** have been utilized in the preparation of chemiluminescence materials[20] and as flame retardants[21] respectively (**Figure 2**). Moreover, arylated methylphosphonates have found many applications in organic synthesis, especially as reagents in Horner–Wadsworth–Emmons reaction.[22]

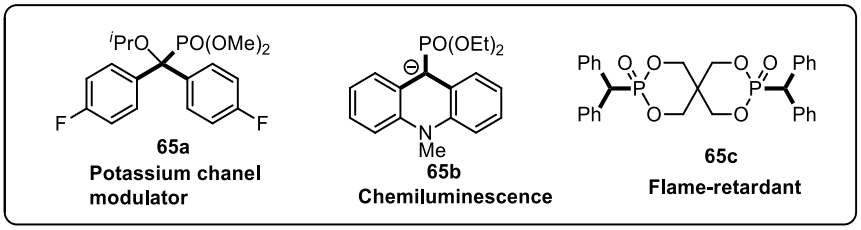
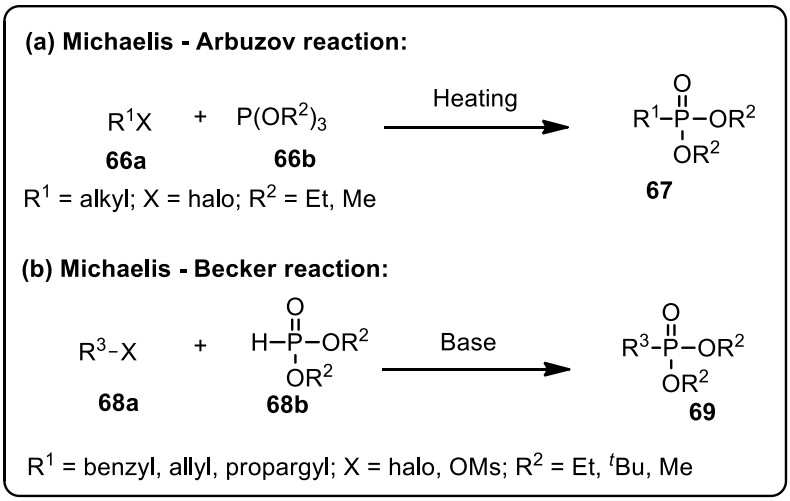


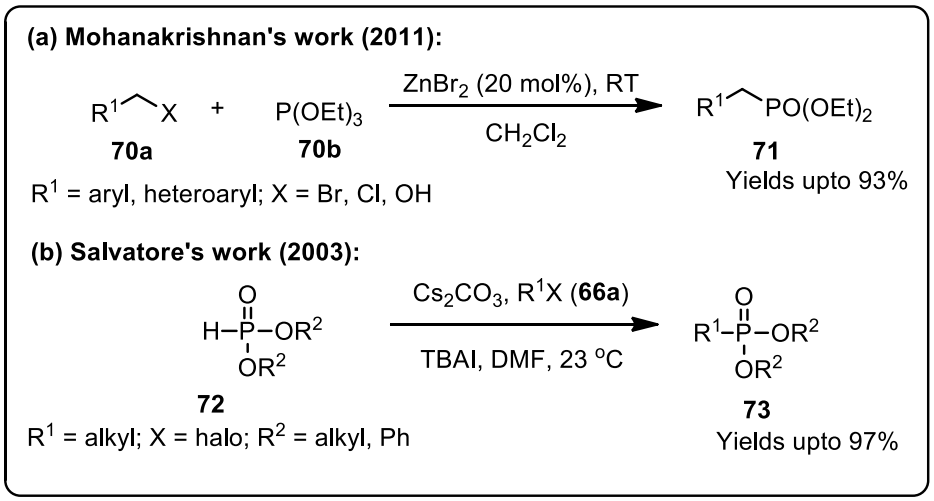
Figure 2. Applications of diarylmethylphosphonates

The traditional approaches for the synthesis of phosphonate derivatives involve the Michaelis–Arbuzov and Michaelis–Becker reaction between tri/di-alkylphosphites (**66b**/**68b**) and the alkyl halides or alkyl mesylates (**66a**/**68a**). Though, they are well established in the derivatization of phosphorous compounds, harsh reaction conditions and narrow substrate scope makes them less

attractive (**Scheme 13**).[23] Moreover, recently few developments in this area were also reported in the literature.[23]



Scheme 13. Traditional methods for the synthesis of phosphonates

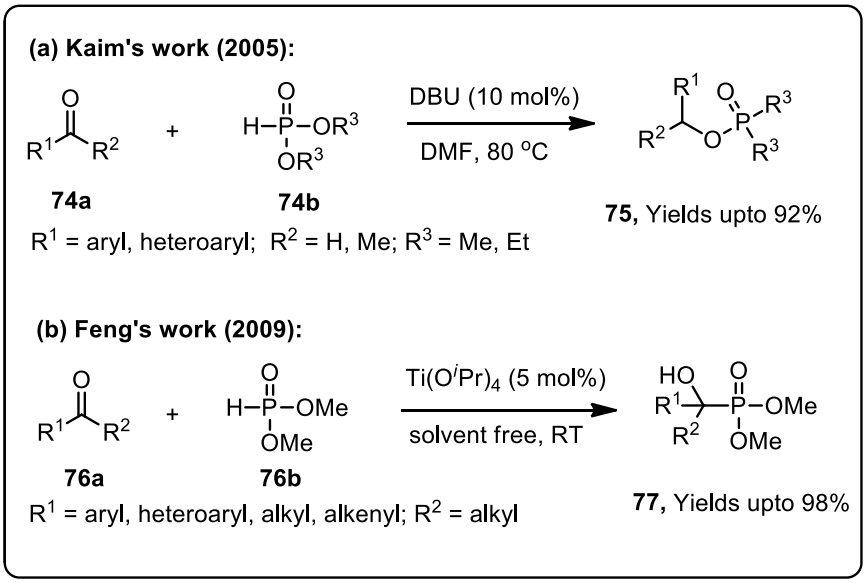


Scheme 14. Recent developments in the synthesis of phosphonates

Mohanakrishnan and co-workers disclosed the improved version of Michaelis–Arbuzov method in 2011. The present work describes a Lewis acid mediated synthesis of arylmethylphosphonates (**71**) through the reaction between triethylphosphite (**70b**) and alkylhalides (**70a**) at room temperature (**a**, **Scheme 14**).[24] Salvatore and co-workers reported an attractive method for the synthesis of phosphonates (**73**) through alkylation of dialkyl or diarylphosphite (**72**) with alkyl

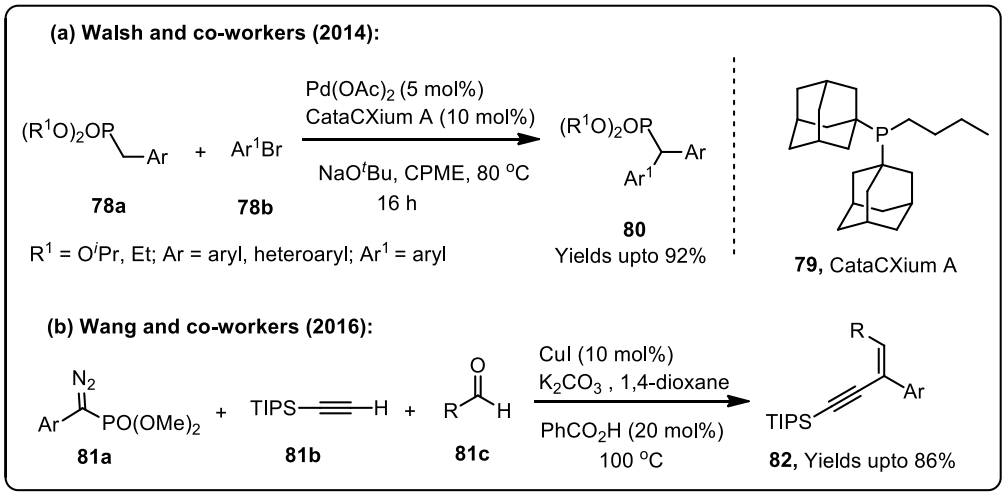
halides (**66a**) in the presence of Cs_2CO_3 and TBAI under mild reaction conditions. (**b**, **Scheme 14**).[25]

Base catalyzed phospha-Brook rearrangement was realized by Kaim for the preparation of broad spectrum of phosphonates (**75**). They described DBU catalyzed hydrophosphonylation of carbonyls (**74a**) with diakylphosphite (**74b**) followed by 1,2-phosphonate rearrangement, which led to phosphonates (**a**, **Scheme 15**).[26a] Lewis acid catalyzed hydrophosphonylation of ketones (**76a**) with dimethylphosphite (7**6b**) for the preparation of α-hydroxy phosphonates (**77**) was demonstrated by Feng and co-workers (**b**, **Scheme 15**).[26b]

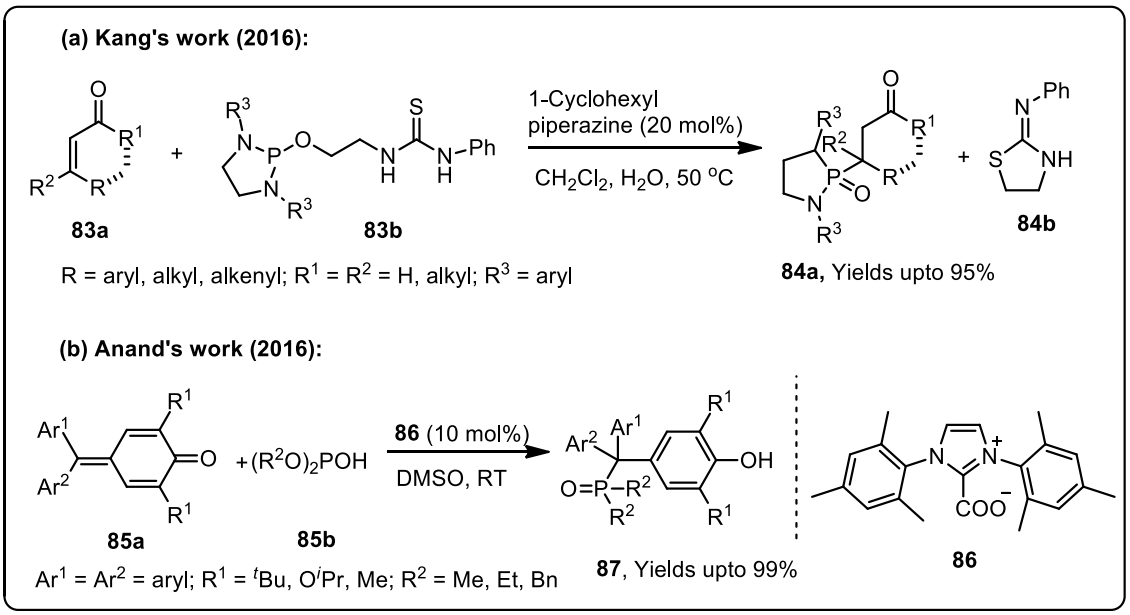


Scheme 15. Hydrophosphonylation of carbonyl compounds

Walsh and co-workers reported a palladium catalyzed of α-arylation of benzylic phosphonates (**78a**) via a deprotonative cross coupling process. The present work describes the synthesis of diarylmethylphosphonates (**80**) from diisopropylphosphonate (**78a**) and bromobenzene (**78b**). Weakly acidic sp^3 C-H (pK_a = 27) functionalization is the prominent feature of this work (**a**, **Scheme 16**).[27a] While developing the cross-coupling reactions, Wang and co-workers developed a Cu (I) catalyzed cross-coupling of α-diazo phosphonates (**81a**) and alkynes (**81b**) followed by Horner-Wadsworth-Emmons reaction with aldehydes (**81c**) to prepare a range of enynes (**82**) in good yields and high stereo-selectivities (**b**, **Scheme 16**).[27b]



Scheme 16. Metal catalyzed derivatization of organo phosphorous compounds



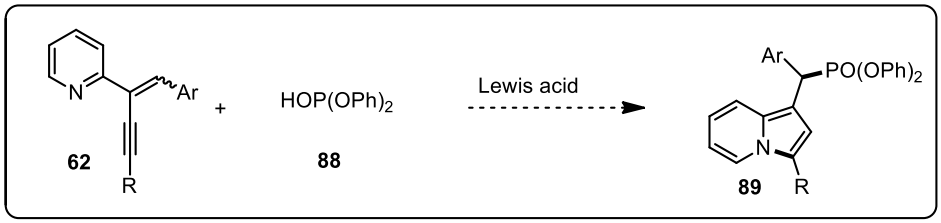
Scheme 17. Conjugate additions in phosphonylation reactions

Very recently, Kang and co-workers developed an interesting approach for the synthesis of phosphonates (**84a**) through a phospha-Michael reaction of α,β-unsaturated carbonyl compounds (**83a**) with multi-functional *N*-heterocyclic phosphine-thiourea (**83b**) [**a**, **Scheme 17**].[28] Our research group also contributed in the development of effective methods for the synthesis of organophosphorous derivatives. Recently, we have reported an *N*-heterocyclic carbene (**86**)

catalyzed 1,6-conjugate addition of dialkylphosphites (**85b**) to *p*-quinonemethides (**85a**) for the preparation of diarylmethylphosphonates (**87**) [**b**, **Scheme 17**].[17b]

Results and discussion:

While developing practical methods for the synthesis of unsymmetrical diaryl- and triarylmethane derivatives,[17] we envisaged that it is possible to synthesize indolizine containing unsymmetrical diarylmethylphosphonates (**89**) starting from 2-(2-enynyl)-pyridine derivatives (**62**) [**Scheme 18**]. To the best of our knowledge, phosphorous based nucleophiles have not been utilized for this transformation so far. Herein, we disclose a Cu-catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines (**62a**) followed by a remote addition of diarylphosphites (**88**) leading to unsymmetrical indolizine based diarylmethylphosphonates (**89**).[17g]

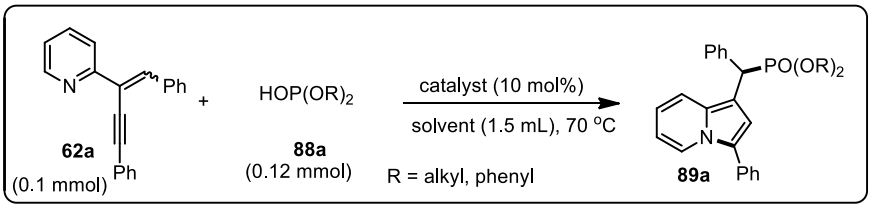


Scheme 18. Proposed approach for the synthesis of diarylmethyl phosphonates

We commenced the optimization studies by employing readily available 2-(2-enynyl)-pyridine derivatives **62a**[12] and diphenylphosphite **88** under various reaction conditions and the results are revealed in Table 4. To our pleasure, the initial attempt itself gave a fruitful output as the expected product **89a** was isolated in 63% yield within 3 h, when $AgSbF_6$ was used as a catalyst in DCE at 70 °C (Entry 1). Delighted by this result, we performed further optimization studies to find out the best reaction conditions. Other silver salts such as $AgBF_4$ and AgOTf have also been found to be effective to drive this transformation and afforded **89a** in 85 and 66% yields respectively (Entries 2 & 3). Palladium based catalysts, such as $PdCl_2$ and $Pd(OAc)_2$, also gave the expected product **89a** in 70% yield (Entries 4 & 5). The reaction did work well even with copper catalysts such as Cu(II) and Cu(I) triflates and, **89a** was obtained in 85 and 80% yields respectively in those cases (Entries 6 & 7). When the reaction was carried out with CuI as a catalyst, the indolizine derivative **89a** was isolated in 90% yield within 3 h (Entry 8). This clearly indicates that CuI was superior in effecting this transformation when compared to other catalysts.

Further optimization studies were performed using CuI as a catalyst in other solvents such as toluene, THF and acetonitrile. However, the yield of **89a** in all those solvents was found to be inferior when compared to DCE (Entries 9-11). An experiment was also performed in DCE at room temperature using CuI as a catalyst and **89a** was isolated only in 70% yield even after 24 h (Entry 12). Unfortunately, only a complex mixture was observed when dimethyl- and diethylphosphites were used as nucleophiles (Entries 13 & 14). When the reaction was performed without any catalyst at 70 °C, merely 41% of **89a** was isolated and the reaction was not reaching completion even after 36 h (Entry 15). A relatively large scale reaction was carried out with 500 mg (1.8 mmol) of **62a** under the standard conditions (Entry 8), and in this case, the product **89a** was isolated in 80% yield after 5 h (Entry 17).

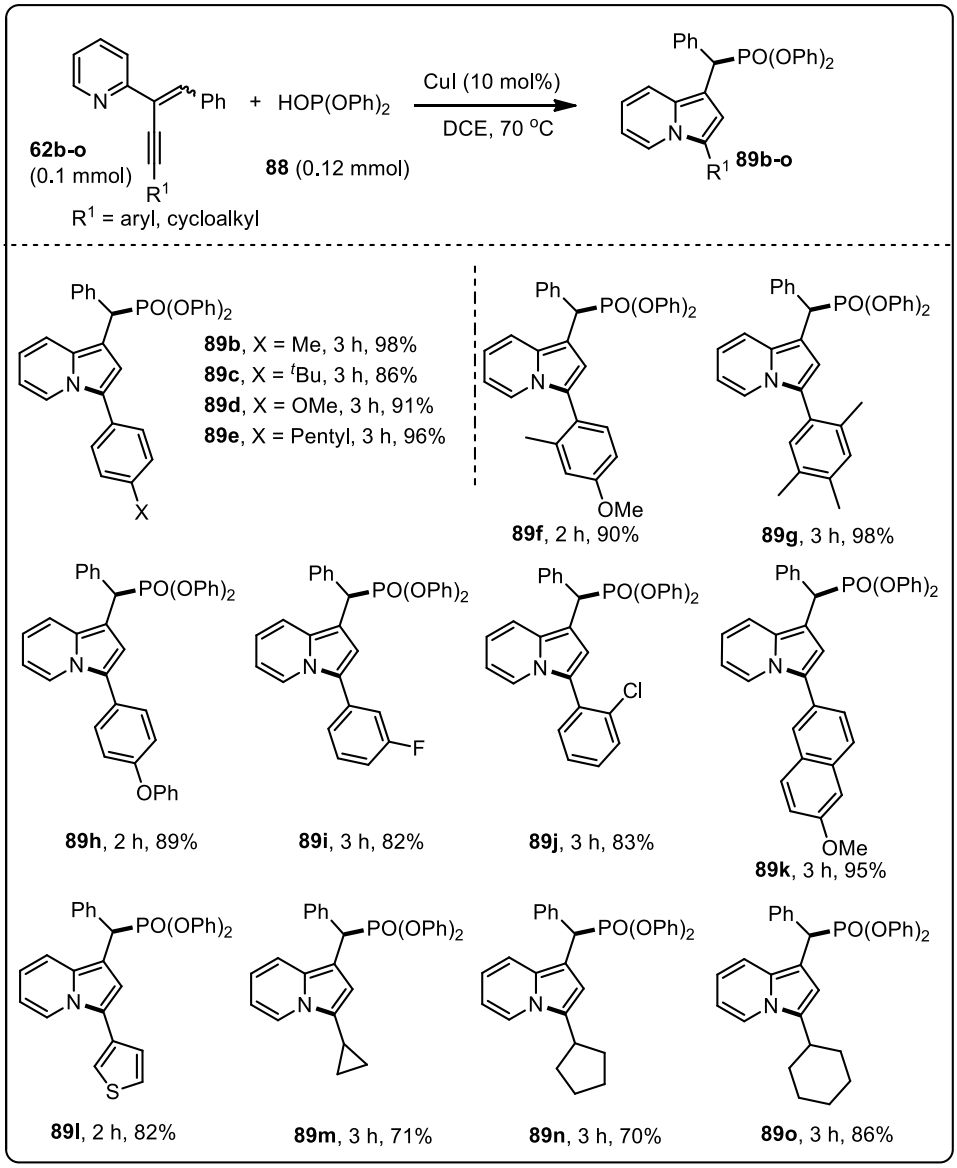
Table 4. Optimization Studies [a]



Entry	Lewis acid	Solvent	Time [h]	Yield [%][b]
1	$AgSbF_6$	DCE	3	63
2	$AgBF_4$	DCE	1	85
3	AgOTf	DCE	2	66
4	$PdCl_2$	DCE	10	70
5	$Pd(OAc)_2$	DCE	5	70
6	$Cu(OTf)_2$	DCE	1	85
7	CuOTf	DCE	1	80
8	**CuI**	**DCE**	**3**	**90**
9	CuI	Toluene	6	76
10	CuI	THF	6	74
11	CuI	MeCN	3	74
12 [c]	CuI	DCE	24	70
13[d]	CuI	DCE	24	CM[f]
14[e]	CuI	DCE	24	CM[f]
15	---	DCE	36	41
16[g]	CuI	DCE	5	80

[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62a** in solvent. [b]Isolated yield. [c]Reaction was done at room temperature (25 °C -27 °C). [d]$HOP(OMe)_2$ was used instead of $HOP(OPh)_2$. [e]$HOP(OEt)_2$ was used. [f]CM = Complex mixture. [g]Reaction was performed with 1.8 mmol of **62a**.

Table 5. Substrate scope with different 2-(2-enynyl)-pyridines

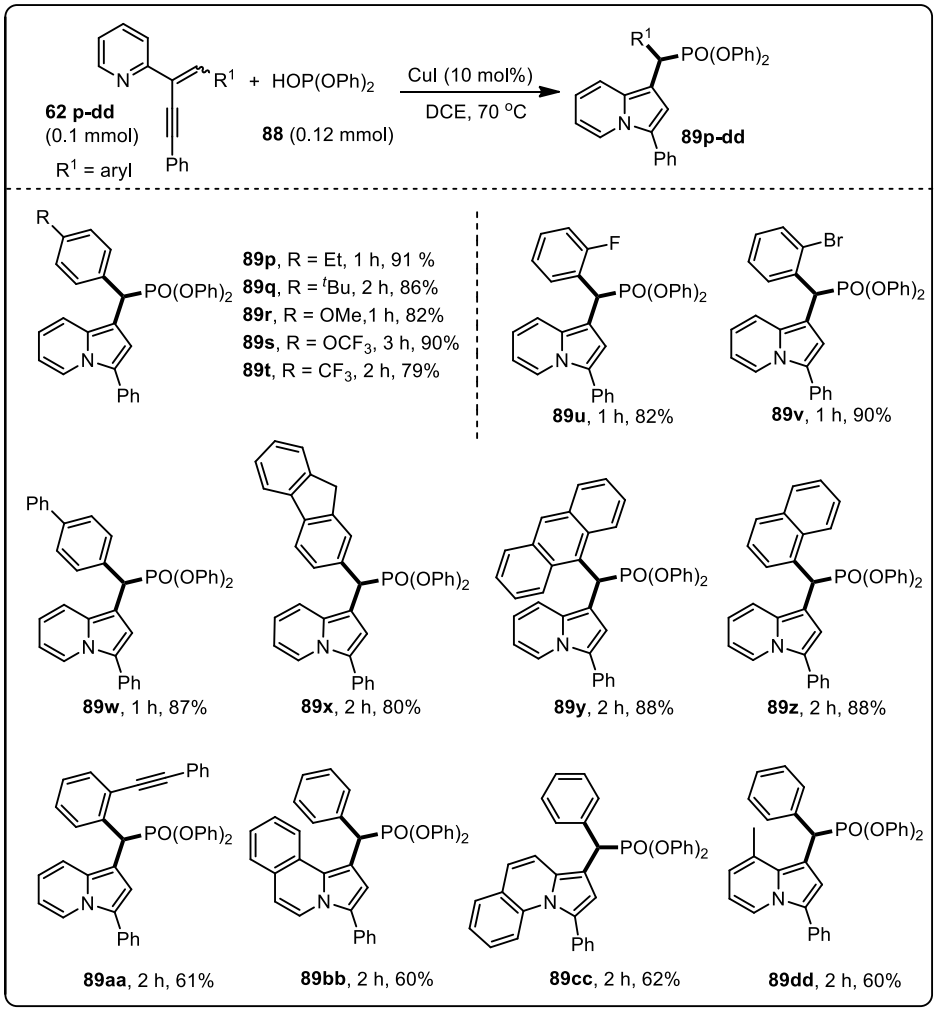


[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62b-o** in solvent at 70 °C. Yields reported are isolated yields

Having optimized the reaction conditions (Entry 8, Table 1), the substrate scope and limitations were appraised using a wide range of 2-(2-enynyl)-pyridines (**62b-o**), and the results are summarized in Table 5. We found that electronic nature of the aryl group present in the alkyne part had a very minimal influence in the reaction as most of the 2-(2-enynyl)-pyridines underwent smooth cyclization to give the indolizine derivatives in good to excellent yields. For example, 2-(2-enynyl)-pyridines (**62b-h**) derived from alkynes fastened with electron rich aryl

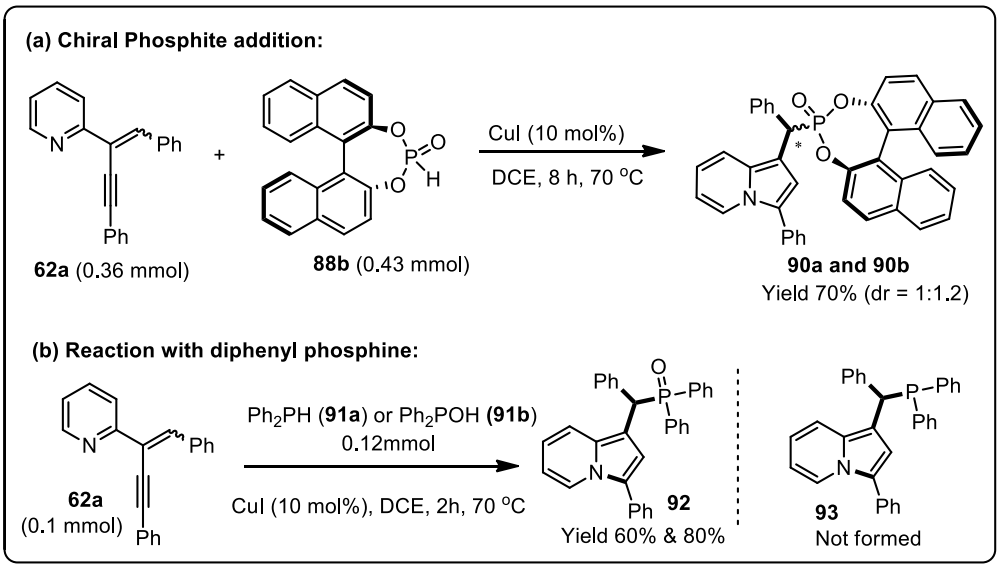
group gave the anticipated products (**89b-h**) in excellent yields (86-98%). The precursors (**62i** and **62j**) derived from halo-substituted phenylacetylenes were also converted effortlessly to their corresponding diarylmethylphosphonates (**89i** and **89j**) in 82 and 83% yields respectively. 2-(2-Enynyl)-pyridines tethered with methoxy-naphthyl (**62k**) and thiophene (**62l**) gave the expected products (**89k** and **89l**) in excellent yields under the optimal conditions. Even the precursors (**62m-o**), derived from cycloalkyl alkynes underwent this transformation to afford the indolizine derivatives (**89m-o**) in good yields (70-86%).

Table 6. Substrate scope with different 2-(2-enynyl)-pyridines



[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62p-dd** in solvent at 70 °C. Yields reported are isolated yields.

After exploring the substrate scope of 2-(2-enynyl)-pyridines having various aryl and cycloalkyl substituents in the alkyne part (Table 5), we subsequently focused our attention to evaluate the scope of this transformation by varying the aryl group at the olefinic position of **62**, and the results are divulged in Table 6. The reaction was found to be very effective in the cases of 2-(2-enynyl)-pyridines (**62p-v**) substituted with electron-rich as well as electron-poor aryl groups at the olefinic position, and the desired indolizine containing diarylmethylphosphonates (**89p-v**) were isolated in very good yields (79-91%). Other precursors, substituted with biaryl (**62w**), fused-aryl (**62x-z**) and alkynyl-aryl (**62aa**) derivatives, were also subjected to ring-closure followed by hydrophosphonylation to provide the corresponding indolizine derivatives (**89w-aa**) in moderate to good yields (61-88%). This transformation was also extended to the precursors (**62bb-dd**), derived from other heterocycles such as isoquinoline, quinoline and 3-methylpyridine derivatives. In all these cases, the expected products (**89bb-dd**) were obtained in moderate yields (60-62%).

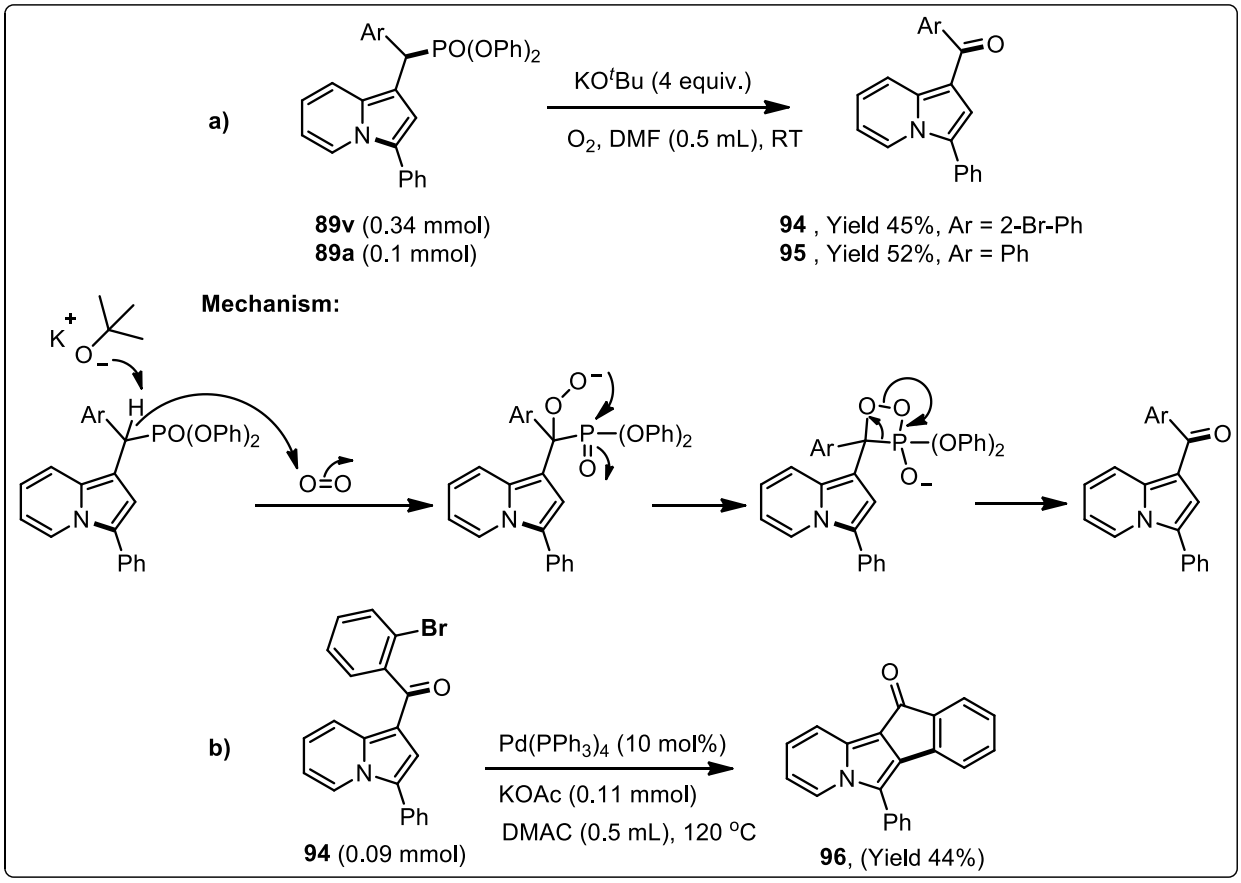


Scheme 19. Addition of different phosphites to 2-(2-enynyl)-pyridines

To elaborate this methodology further, an experiment was performed using a chiral (*R*)-BINOL based phosphite (**88b**) as a nucleophile. However, in this case, the diastereoselectivity was found to be very poor as this reaction provided both the diastereomers (**90a** and **90b**) in 1:1.2 ratio (**a, Scheme 19**). Other P-H nucleophile Ph_2PH (**91a**) (freshly prepared from Ph_2PCl and Zn

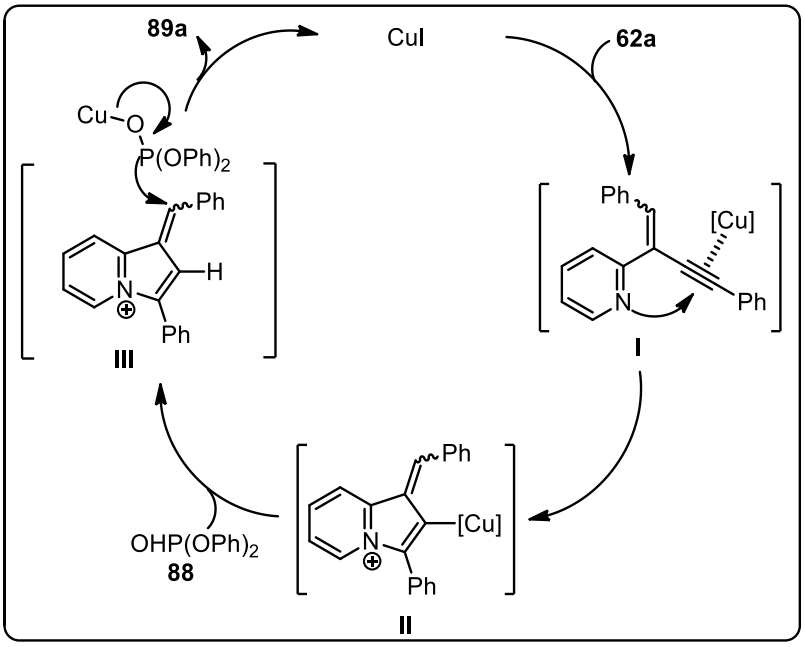
powder)[29] was also considered as a nucleophile for this transformation. Interestingly in this case, the expected product **93** was not observed. Instead, the oxidized product **92** was obtained in 60 % yield under the optimized conditions. We believe that Ph_2PH (**91a**) was oxidized[30] to Ph_2POH (**91b**) under the reaction conditions prior to the reaction with 2-(2-enynyl)-pyridine (**62a**). To confirm this, another experiment was carried out with Ph_2POH (**91b**) and, in this case, product **92** was obtained in 80% yield. It is clear from this experiment that Ph_2PH (**91a**) is oxidized to Ph_2POH (**91b**) under the reaction conditions (**b**, **Scheme 19**).

To portray the synthetic utility of this methodology, a couple of the products **89v** and **89a** was converted to the ketone **94** and **95** in 45% and 52% yield respectively through oxy-Wittig reaction (**a**, **Scheme 20**). Interestingly, **94** underwent intramolecular Heck type coupling in the presence of Pd(0) catalyst to form the tetracyclic-indolizine derivative (**96**) in 44% yield (**b**, **Scheme 20**).



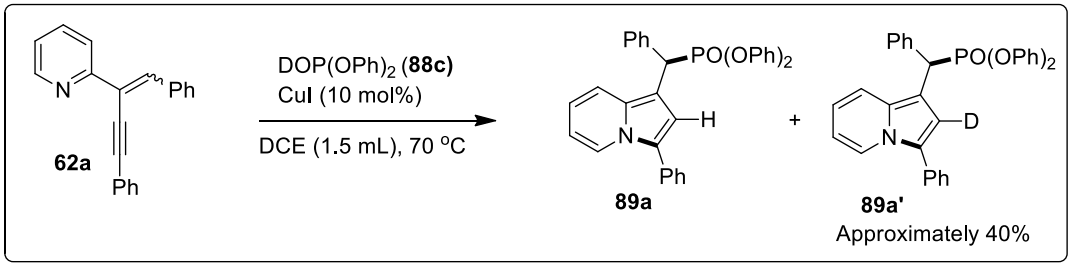
Scheme 20. Synthetic elaboration of the phosphonates through oxy-Wittig reaction

Although the mechanism of this transformation is not clearly understood, based on the outcome of this methodology and on previous reports,[31] we propose a plausible mechanism for this transformation. In the initial step, Cu-catalyst activates the alkyne part of **62a** and the subsequent 5-*endo-dig* cyclization leads to pyridinium salt **II**. The organocopper intermediate **II** then undergoes protonation with $HOP(OPh)_2$ (**88**) to provide intermediate **III** and Cu-$OP(OPh)_2$.[31c] Nucleophilic attack of Cu-$OP(OPh)_2$ at the olefinic part of **III** leads to the formation of **89a** with the extrusion of Cu catalyst **(Scheme 21)**.



Scheme 21. Plausible mechanism

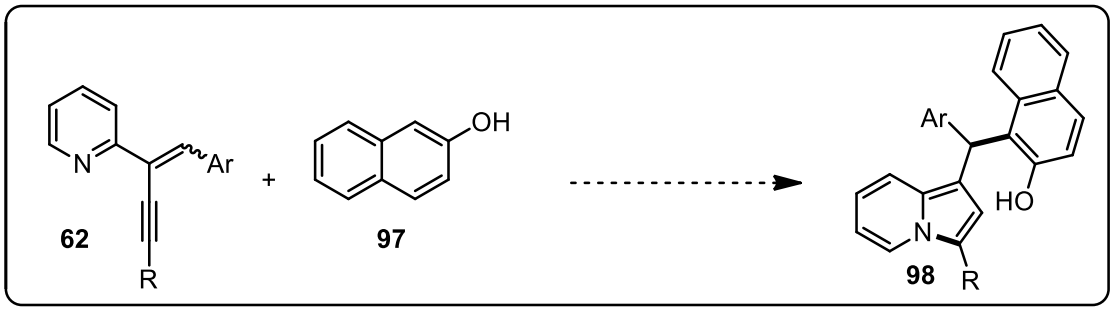
To confirm that $HOP(OPh)_2$ (**88**) is actually acting as a proton source in the conversion of **II** into **III**, another experiment was performed with $DOP(OPh)_2$ (**88c**) [freshly prepared from CD_3OD and $HOP(OPh)_2$].[32b] As expected, the product **89a** was obtained with approximately 40% deuterium incorporation (based on HRMS analysis), which clearly supports the conclusion that $HOP(OPh)_2$ acts as a proton source in the conversion of **II** into **III** (**Scheme 22**). Unfortunately, we were unable to confirm the deuterium incorporation at the indolizine moiety (**89a′**) by ^1H NMR spectroscopic analysis due to the corresponding C–H proton (δ = 7.33 ppm) overlaps with signals in the aromatic region. However, we could confirm the deuterium incorporation (ca. 40 %) by HRMS analysis in the positive mode (*m*/*z* calcd. 517.1792; found 517.1776).



Scheme 22. Hydrophosphonylation reaction using deuterated phosphite-**88c**

2c. Synthesis of indolizine containing unsymmetrical triarylmethanes through a metal catalyzed 5-endo-dig cyclization of 2-(2-enynyl)-pyridine followed by a remote addition of 2-naphthols:

In continuation with the synthesis of indolzine containing diarylmethane derivatives,[17] we conceived that it is possible to synthesize structurally complex indolizine containing unsymmetrical triarylmethanes from 2-(2-enynyl)-pyridines using appropriate aryl nucleophiles. In this regard, we thought of utilizing 2-naphthols as nucleophiles (**Scheme 23**). Herein, we unveil a Cu-catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by a remote addition of 2-naphthols leading to unsymmetrical indolizine based triarylmethanes.[17f]



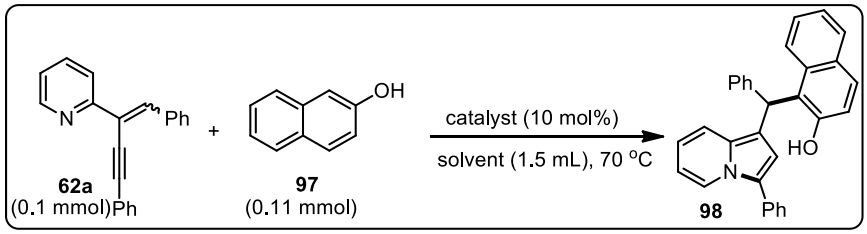
Scheme 23. Our proposed approach toward naphthol based triarylmethanes

Results and discussion:

We commenced the optimization studies with 2-(2-enynyl)-pyridine (**62a)** using 2-naphthol (**97**) as a nucleophile under various reaction conditions (Table 7). The initial optimization experiments revealed that metal catalysts such as copper and palladium

catalysts promote this transformation; however, the yield of the product **98** was low to moderate (Entries 1-4). $Bi(OTf)_3$ failed to drive the reaction even after 24 h (Entry 5).

Table 7: Optimization studies[a]



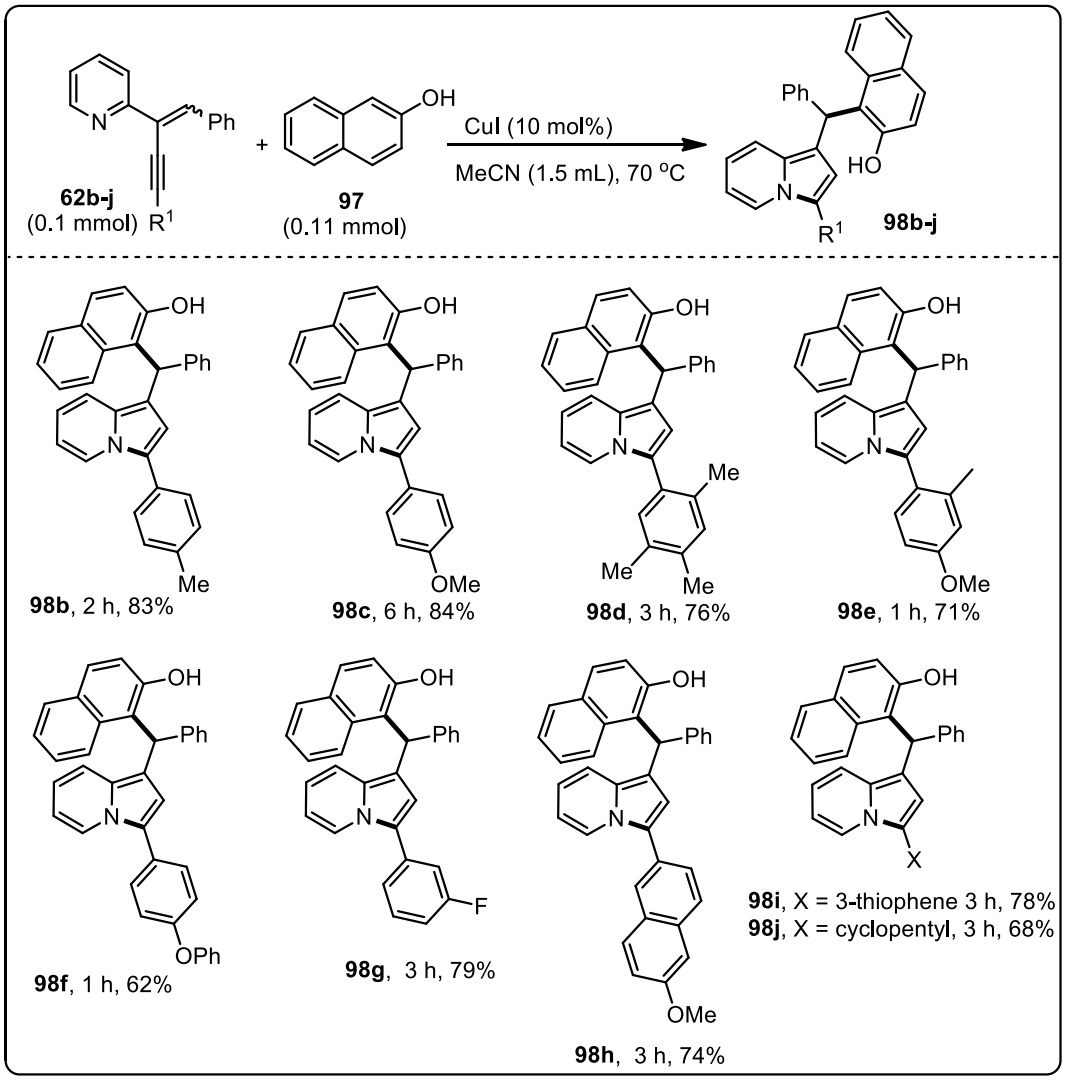
Entry	Lewis acid	Solvent	Time [h]	Yield [%][b]
1	CuOTf.PhMe	MeCN	2	56
2	$Cu(OTf)_2$	MeCN	3	60
3	$Pd(OAc)_2$	MeCN	3	57
4	$PdCl_2$	MeCN	24	20
5	$Bi(OTf)_3$	MeCN	24	NR
6	$AgSbF_6$	MeCN	2	50
7	$AgCF_3COO$	MeCN	3	42
8	$AgBF_4$	MeCN	3	40
9	AgOTf	MeCN	4	32
10	**CuI**	**MeCN**	**3**	**84**
11	CuI	Toluene	4	79
12	CuI	THF	10	24
13	CuI	DMF	8	CM
14	CuI	DCE	3	63
15	---	MeCN	24	NR
16[c]	CuI	MeCN	24	60

[a]*Reaction conditions:* 0.067M of **62a** in solvent. [b]Isolated yield. [c]Reaction done at room temperarture. 1.1 equivalents of **97** with respect to **62a** were found to be optimal.

Although many silver salts were found to be suitable to drive this transformation, the yield of **98** was not satisfactory, in those cases (Entries 6-9). When the reaction was carried out using CuI as a catalyst in acetonitrile, **98** was isolated in 84% yield in 3 h (Entry 10). Encouraged by this observation, further optimization studies were carried out

in different solvents. However, in all those cases, the yield of **98** was found to be inferior (Entries 11-14). No product was observed in the absence of catalyst even after 24 h (Entry 15). Notably, when the reaction was carried out at room temperature in the presence of 10 mol% of CuI in acetonitrile, the expected product was obtained in 60% yield; however, the reaction did not reach to completion even after 24 h (Entry 16).

Table 8: Substrate scope using different 2-(2-enynyl)-pyridines

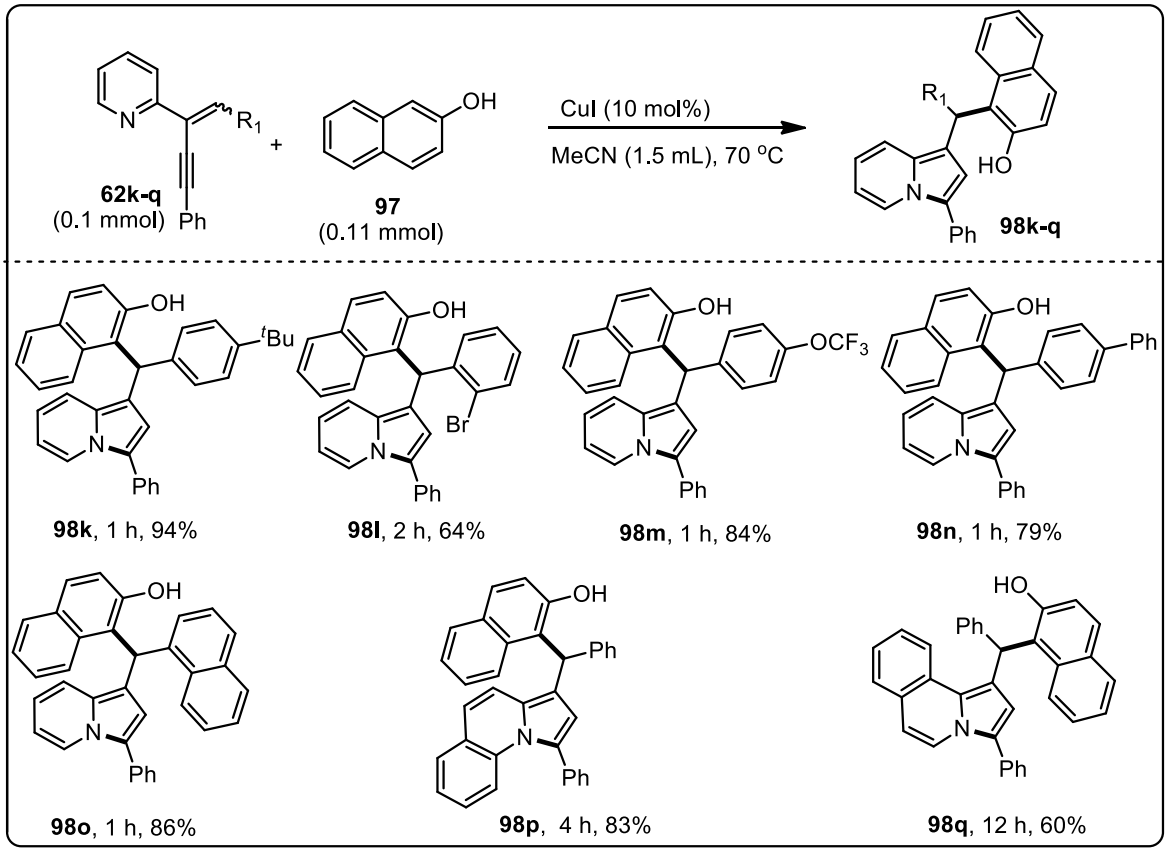


[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62** in MeCN at 70 °C. Yields reported are isolated yields.

The generality of the substrate scope was evaluated by employing 2-naphthol (**97**) as a nucleophile with 2-(2-enynyl)-pyridines (**62b-j**) and the results are summarized in Table 8

and Table 9. It is evident from Table 8 that the present protocol works certainly well with the 2-(2-enynyl)-pyridines bearing aryl, heteroaryl, cycloalkyl substituents at the alkyne parts to furnish the corresponding products (**98b-j**) in moderate to good yields (62-84%). The substrate scope of this methodology was also elaborated with a few variations at olefinic part of 2-(2-enynyl)-pyridines (Table 9). For instance, the derivatives of 2-(2-enynyl)-pyridines bearing electron-rich (**62k**) and moderately electron poor (**62l** and **62m**) substituents provided the corresponding triarylmethanes (**98k-m**) in good yields (64-84%). Other precursors substituted with biaryl and naphthalene was also under went smooth conversion to afford the respective triarylmethane derivatives (**98n** and **98o**) with 79 and 86% yields, respectively. Under the optimal conditions, quinoline (**98p**) and isoquinoline (**98q**) derived triarylmethanes were isolated with 83% and 60% yields, respectively.

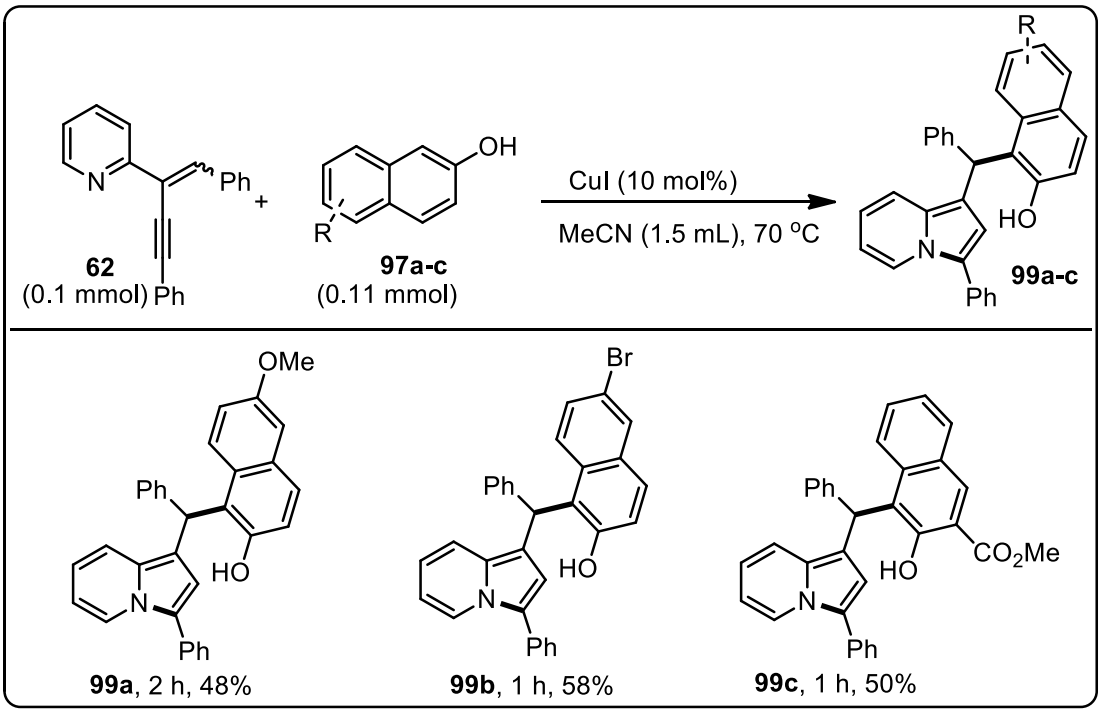
Table 9: Substrate scope with different 2-(2-enynyl)-pyridines



[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62** in MeCN at 70 °C. Yields reported are isolated yields.

After exploring the substrate scope of 2-(2-enynyl)-pyridines (**62a-q**) having various substitutions at both alkyne part as well as olefinic position, we subsequently focused our attention to evaluate the scope of this reaction with other 2-naphthol derivatives (**97a-c**) [Table 10]. It is apparent from Table 10 that electron-rich (**97a)** and electron-poor **(97c**) 2-naphthol derivatives worked well under standard conditions in accessing the corresponding triarylmethanes (**99a** and **99c**) in moderate yields. Even, 2-naphthol derivative 6-bromo-2-naphthol (**97b**) reacted smoothly with **62** for the synthesis of desired product **99b** with a moderate yield (58%).

Table 10: Substrate scope with different 2-naphthols

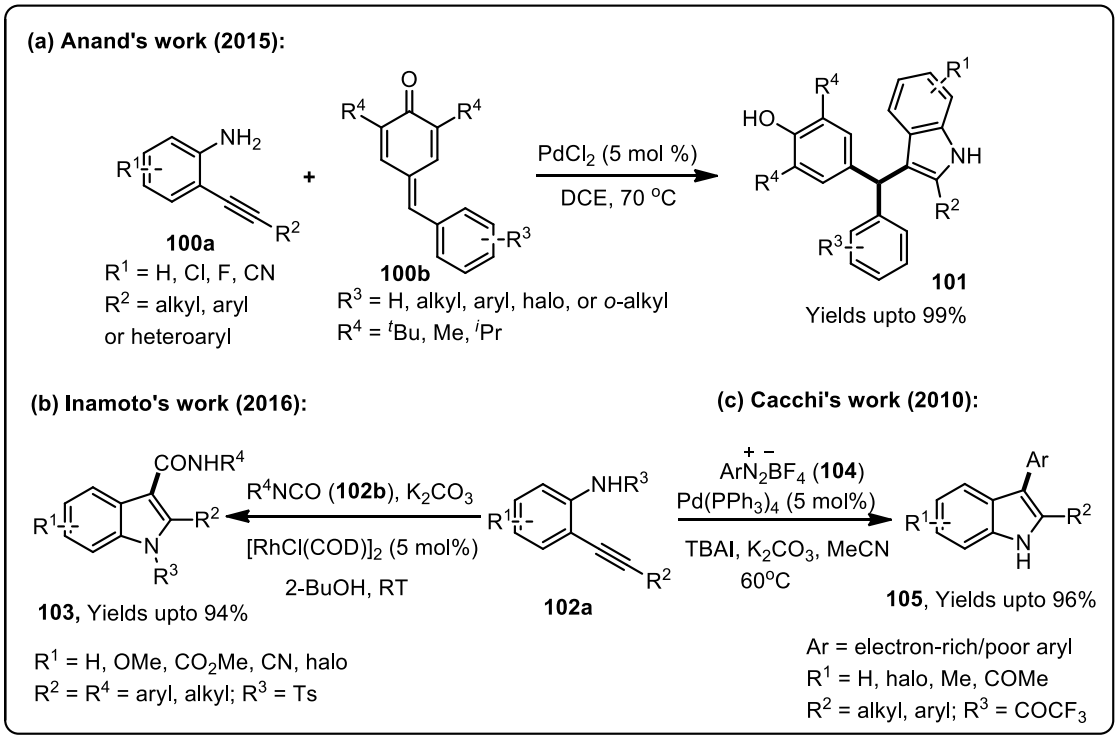


[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62** in MeCN at 70 °C. Yields reported are isolated yields.

2d. Synthesis of hetero-arylated unsymmetrical triarylmethanes through a metal catalyzed double 5-endo-dig cyclization cascade:

Transition metal catalyzed domino electrophilic cyclization[33] of *o*-alkynyl aniline followed by trapping with an electrophile trapping is a powerful strategy for the synthesis of 2,3-disubstituted indoles. For instance, recently, our research group developed a Pd-catalyzed domino cyclization-

1,6-conjugate addition cascade to prepare indole containing unsymmetrical triarylmethanes (**101**) with 100% atom economy (**a, Scheme 24**).[33a]



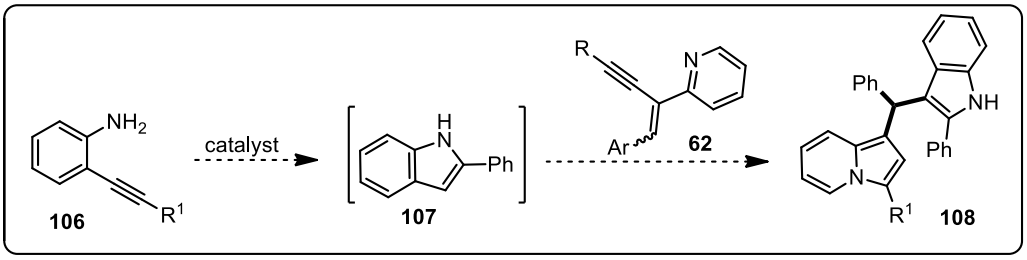
Scheme 24. Domino cyclization approaches toward indole construction

Further, a Rh-metal catalyzed tandem type approach was disclosed by Inamoto and co-workers for the synthesis of indole-3-carboxamides derivatives (**103**), which demonstrates the cyclization of 2-alkynyl anilines (**102a**) followed by coupling with isocyanates (**102b**) under basic medium to afford a vast range of highly functionalized 2,3-disubstituted indoles (**103**) [**b, Scheme 24**][33b] Cacchi and co-workers reported a Pd-catalyzed approach for the synthesis of 2,3-disubstituted indoles (**105**) through domino cyclization of 2-alkynyltrifluoroacetanilides (**102a**) followed by coupling with arene diazonium salts (**104**) [**c, Scheme 24**].[33c]

Results and discussion:

Our proposed synthetic approach to access hetero-arylated unsymmetrical triarylmethane derivatives is presented in **Scheme 25.**[17h] This proposed transformation basically involves two consecutive 5-*endo*-dig cyclizations followed by a remote nucleophilic attack. We thought of utilizing 2-alkynyl anilines and 2-(2-enynyl)-pyridines as precursors to synthesize the lead

compounds (**108**) in a one-pot manner using a metal catalyst. The results are discussed in this section.

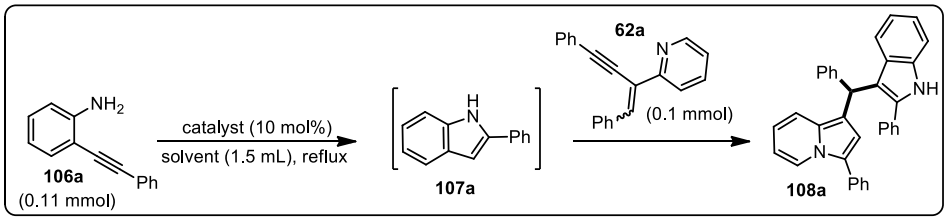


Scheme 25: Proposed approach for double 5-*endo*-dig cyclization cascade reaction

We have chosen readily available *o*-alkynyl aniline (**106a**) and 2-(2-enynyl)-pyridine (**62a**) as model substrates for the optimization studies, and Table 11 reveals the results. Since this transformation involves two steps (*i.e.*, the initial formation of 2-substituted indole **107a** followed by reaction with **62a**), **62a** was added to the reaction mixture after the complete conversion of **106a** to **107a** (by TLC). A preliminary experiment was performed using CuI as a catalyst in refluxing THF (Entry 1). However, unfortunately, this catalyst was found to be ineffective for the first step (*i.e.*, the formation of **107a**). To our pleasure, when $Cu(OTf)_2$ was used as a catalyst, the expected product **108** was isolated in 25% yield (Entry 2). $PdCl_2$ was found to be efficient for the formation of **107a**, but ineffective to drive the second step (Entry 3). $Bi(OTf)_3$ failed to effect even the first cyclization (Entry 4). Yet, when the reaction was carried out with $AgSbF_6$, **108** was obtained in 45% yield (Entry 5). Encouraged by this result, further optimization studies were performed using other silver salts in THF (Entries 6-9). Though most of the silver salts are effective to catalyze this transformation, $Ag(OCOCF_3)$ was found to be the best, and in that case, **108** was obtained in 90% isolated yield within a few hours (Entry 6). The yield of **108** was lower when the reaction was conducted in other solvents such as DMF, MeOH, MeCN etc. (Entries 10-14). The reaction also worked at room temperature (Entry 15); however, it required a very long time (70 h) for the complete conversion of **106a** to **107a**. When a reaction was carried out in the absence of silver catalyst, even the formation of **107a** was not observed (Entry 16). Similarly, another experiment was carried out, in which, **107a** was refluxed along with **62a** in THF without any catalyst and, in this case, **108** was detected only in traces even after 24 h (Entry 17). These two experiments clearly indicate that a catalyst is required to drive both the steps. In addition to that, another experiment was done, in which **107a** was treated with **62a**

in the presence of $Ag(OCOCF_3)$ catalyst in refluxing THF and, as expected, **108** was obtained in 93% isolated yield in an hour (Entry 18).

Table 11. Optimization studies [a,b]

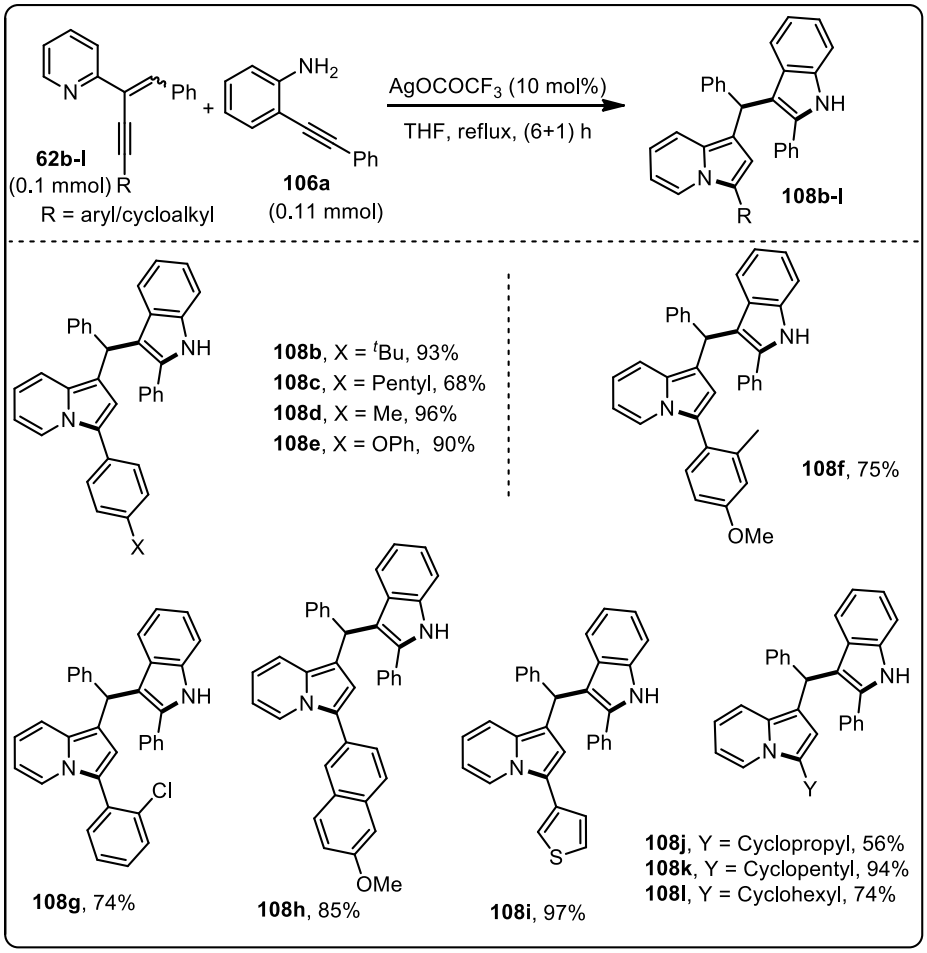


Entry	Lewis acid	Solvent	Time [h]	Yield [%][c]
1	CuI	THF	24+0	---
2	$Cu(OTf)_2$	THF	12+8	25
3	$PdCl_2$	THF	5+48	---
4	$Bi(OTf)_3$	THF	24+0	---
5	$AgSbF_6$	THF	4+4	45
6	**$Ag(OCOCF_3)$**	**THF**	**6+1**	**90**
7	$AgBF_4$	THF	4+4	55
8	$AgNO_3$	THF	4+4	70
9	Ag(OTf)	THF	4+4	35
10[d]	$Ag(OCOCF_3)$	DMF	5+2	80
11	$Ag(OCOCF_3)$	MeOH	5+5	50
12	$Ag(OCOCF_3)$	DCE	3+3	60
13	$Ag(OCOCF_3)$	MeCN	24+4	74
14	$Ag(OCOCF_3)$	Toluene	5+5	60
15[e]	$Ag(OCOCF_3)$	THF	70+2	85
16[f]	---	THF	24+0	---
17[g]	---	THF	0+24	Traces
18[h]	$Ag(OCOCF_3)$	THF	0+1	93
19	$Ag(OCOCF_3)$	THF	8	Traces

[a]*Reaction conditions:* All reactions were carried out with 0.067 M of **62a** in solvent under reflux conditions. [b]In all experiments, **62a** was added to the reaction mixture after the complete consumption of **106a**. [c]Isolated yield. [d]Reaction was performed at 100 °C. [e]Reaction was done at room temperature (25-27 °C). [f]Reaction was performed without any catalyst. [g]Reaction was performed with isolated **107a** without any catalyst. [h]Reaction performed with isolated **107a**.

This observation evidently signifies that the reaction is actually proceeding through indole derivative **107a**. When a mixture of **106a** and **62a** was refluxed together in THF with $Ag(OCOCF_3)$ catalyst, many unidentified products were observed along with traces of expected product **108** (Entry 19).

Table 12. Substrate scope with different 2-(2-enynyl)-pyridines

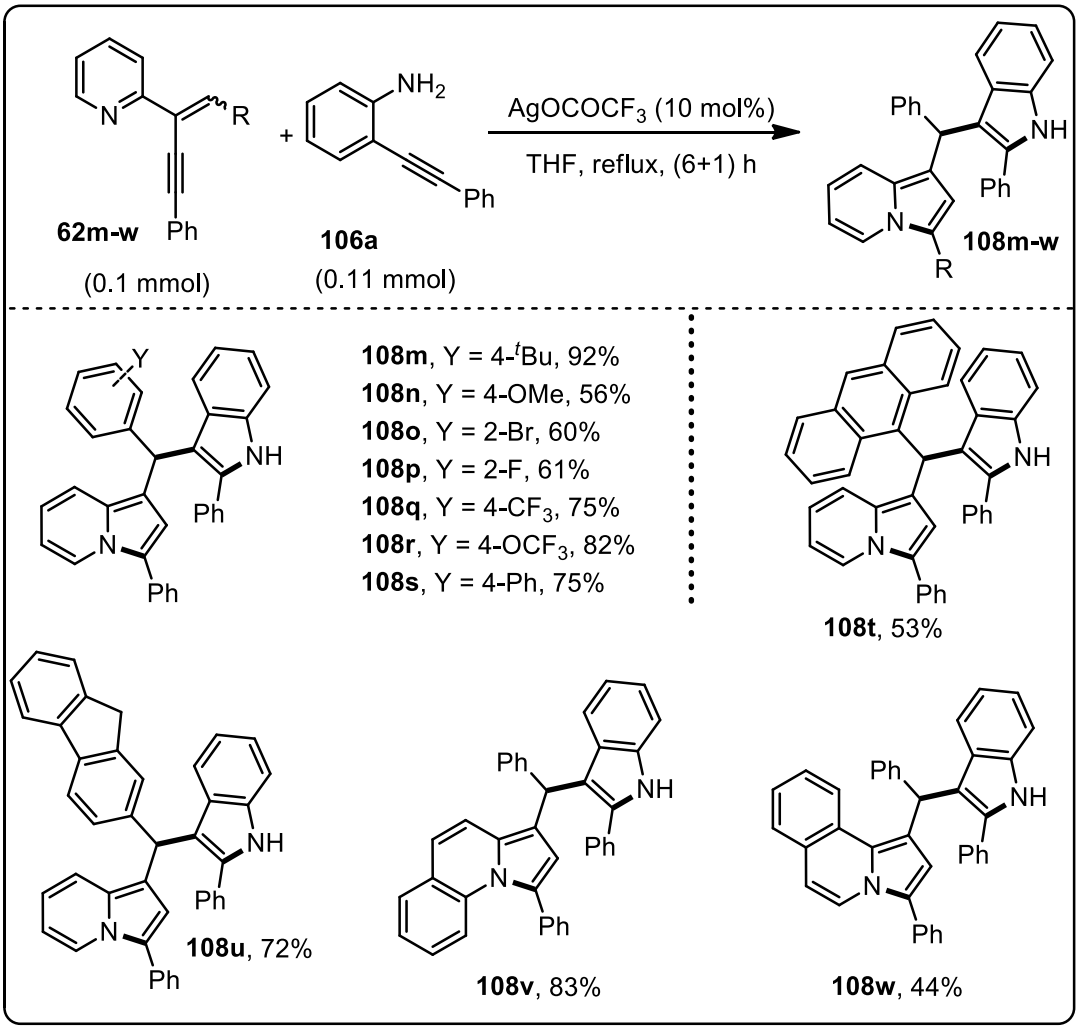


[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62b-l** in refluxing THF. In all these experiments, **106a** was refluxed in THF along with 10 mol% of $Ag(OCOCF_3)$ for 6 h before the addition of **62b-l**, and the reaction was continued for another hour. Yields reported are isolated yields.

The generality of this transformation was investigated by employing a diverse range of substituted *o*-alkynyl anilines and 2-(2-enynyl)-pyridines under the optimized conditions (Entry 6, Table 11). Table 12 reveals the substrate scope with a variety of substituted 2-(2-enynyl)-pyridines. 2-(2-Enynyl)-pyridines (**62b-i**) having different aryl groups at the alkyne part worked astoundingly well, and in all those cases, the expected products (**108b-i**) were obtained in good

to excellent yields (68-97%). 2-(2-Enynyl)-pyridines (**62j-l**) substituted with alicyclic compounds (such as cyclopropyl, cyclopentyl and cyclohexyl) were also found to be suitable for this reaction, and the respective products (**108j-l**) were obtained in 56-94% isolated yields under the standard reaction conditions.

Table 13. Substrate scope with different 2-(2-enynyl)-pyridines



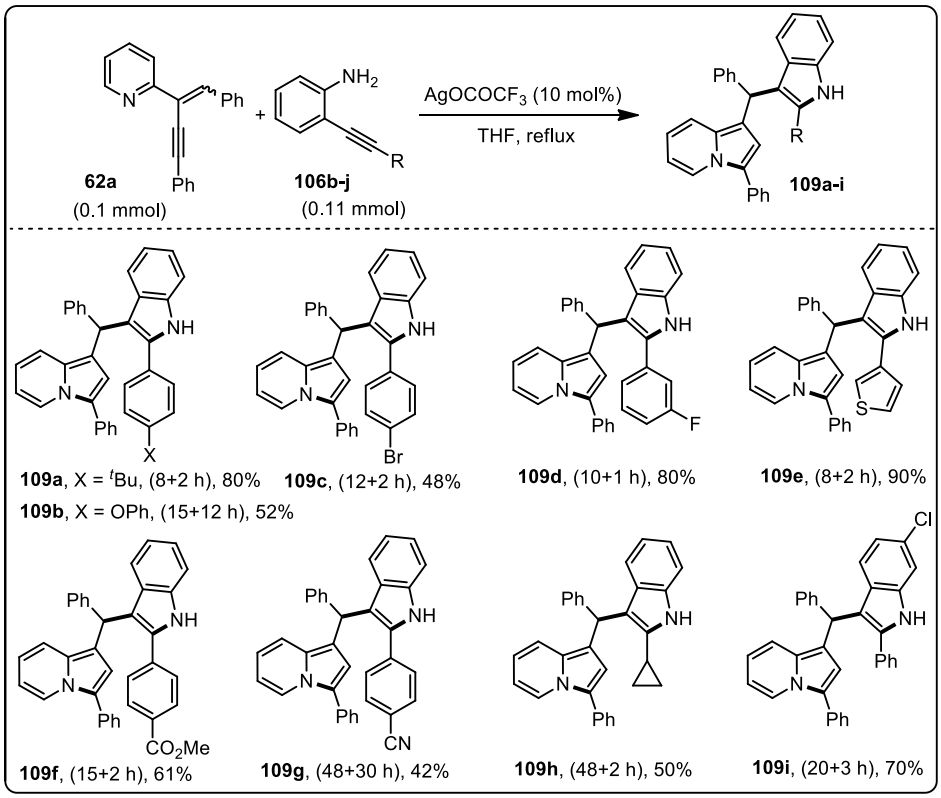
[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62m-w** in refluxing THF. In all these experiments, **106a** was refluxed in THF along with 10 mol% of $Ag(OCOCF_3)$ for 6 h before the addition of **62m-w**, and the reaction was continued for another hour. Yields reported are isolated yields.

Then, we went on to investigate the substrate scope with other 2-(2-enynyl)-pyridines (**62m-u**) having different aryl substituents (both electron-rich and electron-poor) at the alkene part (Table 13). To our delight, in all those cases, the expected triarylmethanes (**108m-u**) were formed in the

range of 53-95% yields. In the case of **62v**, which was derived from quinoline-2-carboxylic acid, the product **108v** was obtained in 83% yield. However, the precursor **62w** (prepared from isoquinoline-1-carboxylic acid) afforded the product **108w** only in 44% yield under the reaction conditions.

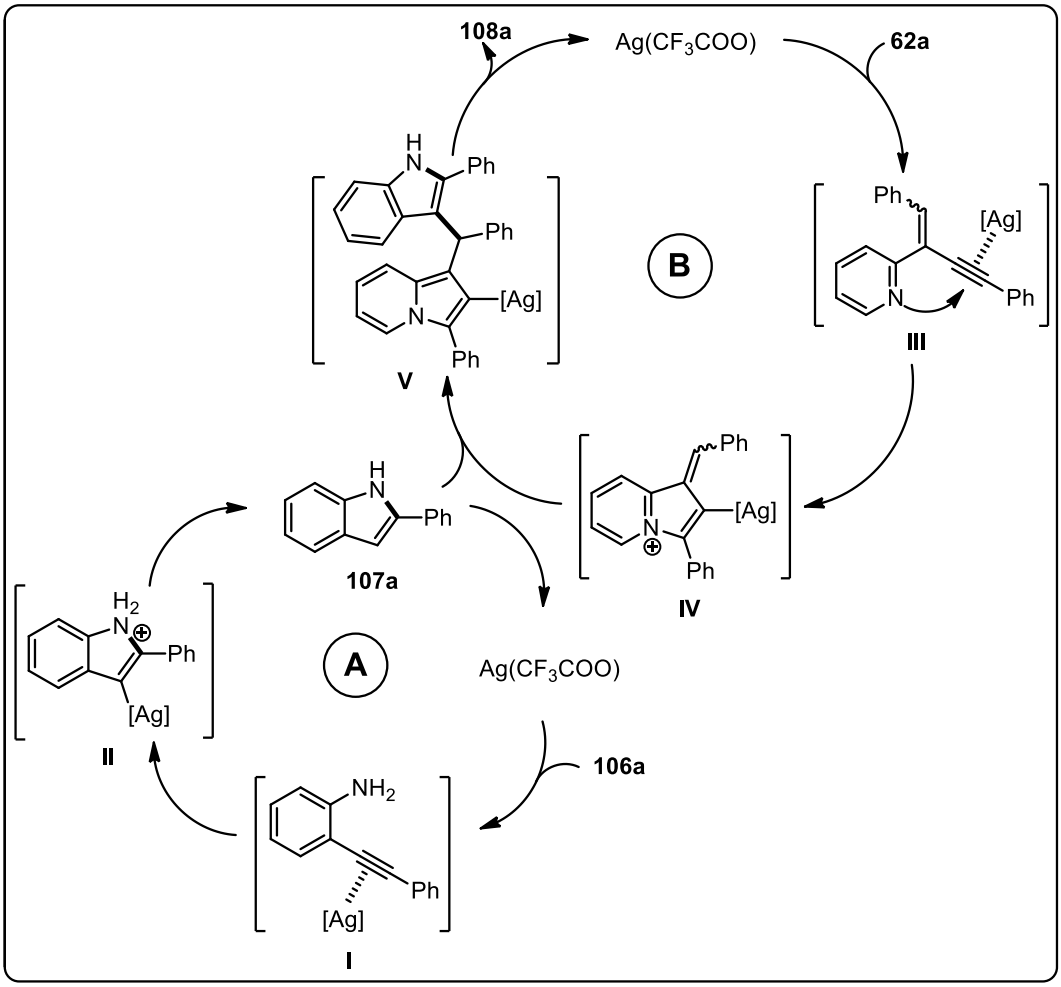
The substrate scope studies were also elaborated to different *o*-alkynyl anilines (**106b-j**), substituted with a range of aryl or alkyl groups at the alkyne part, under the optimal conditions and the results are summarized in Table 14. Most of *o*-alkynyl anilines (**106b-f**), tethered with divergent aryl substituents, underwent a smooth conversion to their corresponding triarylmethane derivatives (**109a-e**) in moderate to good yields. Nevertheless, *o*-alkynyl anilines (**106g, 106h**), substituted with electron-poor aryl groups, provided the products **109f** & **109g** in relatively less yields (61 and 42% respectively). In case of **106i** (having cyclopropane at the alkyne part), the desired product **109h** was obtained in 50% yield. Another *o*-alkynyl aniline **106j**, derived from 6-chloroaniline derivative, gave the corresponding product **109i** in 70% yield.

Table 14. Substrate scope with different *o*-alkynylanilines



[a]*Reaction conditions*: Reactions were carried out with 0.067 M of **62a** in refluxing THF. In all these experiments, **106b-j** was refluxed in THF along with 10 mol% of $Ag(OCOCF_3)$ before the addition of **62a**, and the reaction was continued until **62a** completely consumed. Yields reported are isolated yields.

A plausible mechanism for this one-pot transformation has been proposed (**Scheme 26**). In the initial step, silver catalyst activates the alkyne part of **106a**, and a successive 5-*endo*-dig cyclization leads to intermediate **II**, which then undergoes proton isomerization to give the indole derivative **107a** with the expulsion of the catalyst (cycle **A**). In the subsequent step, activation of the alkyne part of **62a** by silver catalyst followed by 5-*endo*-dig cyclization leads to indolizinium salt **IV**, in which the exocyclic alkene part becomes relatively more electrophilic due to the formation of hypervalent nitrogen (cycle **B**). Remote nucleophilic addition of **107a** to the exocyclic olefinic center of **IV** generates another intermediate **V**, which then undergoes aromatization followed by proton transfer to afford **108a** along with the regeneration of silver catalyst.



Scheme 26. Proposed mechanism

3. Conclusion:

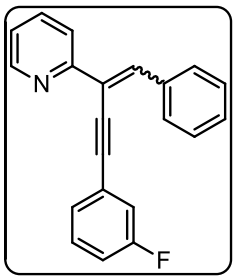
In summary, we have developed an efficacious protocol to access a wide range of indolizine containing unsymmetrical diarylmethanes through a Cu-catalyzed reductive cyclization of 2-(2-enynyl)-pyridines using Hantzsch ester as a reducing agent. Another strategy was also developed for the synthesis of indolizine containing diarylmethyl phosphonates through a Cu-catalyzed 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by remote hydrophosphonylation. Through these methods, a variety of indolizine containing diarylmethane derivatives could be prepared in moderate to excellent yields. Further, our studies were also extended to the synthesis of unsymmetrical triarylmethanes. Consequently, we have developed a protocol to access indolizine containing unsymmetrical triarylmethanes through 5-*endo*-dig cyclization of 2-(2-enynyl)-pyridines followed by a nucleophilic addition of 2-naphthols. In continuation of this protocol, a Ag-catalyzed double 5-*endo*-dig cyclization strategy was established for the synthesis of unsymmetrical triarylmethanes containing indolizine and indole together in the same molecule.

4. Experimental section:

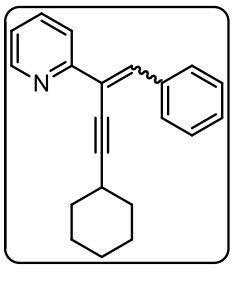
General methods: Most of the reagents and starting materials used were purchased from commercial sources and used as such. All the 2-(2-enynyl)-pyridines and (*R*)-2,2'-binaphthyl phosphite were prepared by following a known literature procedure.[34] Melting points were recorded on SMP20 melting point apparatus and are uncorrected. ^{1}H, ^{13}C, ^{31}P and ^{19}F spectra were recorded in $CDCl_3$ (400, 100, 162 and 376 MHz respectively) on Bruker FT-NMR spectrometer. Chemical shift values are reported in parts per million relative to TMS (for ^{1}H and ^{13}C), H_3PO_4:D_2O [85:15] (for ^{31}P) and $BF_3.Et_2O$ (for ^{19}F). High resolution mass spectra were recorded on Waters Q-TOF Premier-HAB213 spectrometer. FT-IR spectra were recorded on a Perkin – Elmer FT-IR spectrometer. Specific rotation recorded on Rudloph autopol III polarimter. Thin layer chromatography was performed on Merck silica gel 60 F_{254} TLC plates using EtOAc/Hexane as an eluent. Column chromatography was carried out through silica gel (100-200 mesh) using ethyl acetate/hexane mixture as an eluent.

Characterization data of 2-(2-enynyl)-pyridines:

2-[4-(3-Fluorophenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 1582, 1430, 1147, 782 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (d, J = 4.2 Hz, 1H), 8.24 (s, 1H), 8.09 (d, J = 7.9 Hz, 2H), 7.94 (d, J = 7.9 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.39 – 7.35 (m, 3H), 7.29 – 7.22 (m, 2H), 7.12 – 7.07 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.6 (d, J = 245 Hz), 155.1, 149.2, 138.0, 137.0, 136.3, 130.3 (d, J = 8.7 Hz), 129.9, 129.2, 128.5, 127.5 (d, J = 3.1 Hz), 125.1 (d, J = 9.4 Hz), 122.7, 121.8, 119.5, 118.4 (d, J = 22.6 Hz), 116.1 (d, J = 21.1 Hz), 96.1 (d, J = 3.5 Hz), 88.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.55 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{15}FN$ $[M+H]^+$: 300.1188; found: 300.1175.

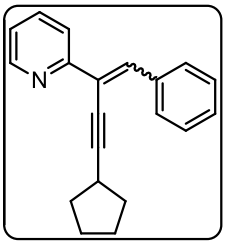


2-(4-Cyclohexyl-1-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3053, 2929, 2853, 2204, 1584, 784 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.60 (d, J = 4.7 Hz, 1H), 8.12 – 8.10 (m, 3H), 7.91 (d, J = 8.0 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.41 – 7.38 (m, 2H), 7.34 – 7.30 (m, 1H), 7.20 – 7.17 (m, 1H), 2.80 – 2.75 (m, 1H), 2.01 – 1.98 (m, 2H), 1.83 – 1.78 (m, 2H), 1.69 – 1.56 (m, 3H), 1.46 – 1.39 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.9, 148.9, 136.8, 136.6, 135.6, 129.7, 128.6, 128.2, 122.4, 121.8, 120.4, 103.5, 78.8, 32.6, 30.4, 26.0, 25.1 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{22}N$ $[M+H]^+$: 288.1752; found: 288.1744.

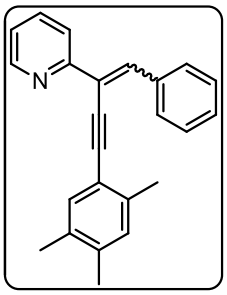


2-(1-Phenyl-4-(*p*-tolyl)but-1-en-3-yn-2-yl)pyridine: FT-IR 3051, 1429, 783, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (d, J = 4.5 Hz, 1H), 8.25 (s, 1H), 8.17 (d, J = 7.9 Hz, 2H), 8.01 (d, J = 7.9 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.52 (d, J = 7.8 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.22 (d, J = 8.0 Hz, 3H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 149.0, 139.0, 136.9, 136.7, 136.5, 131.5, 129.9, 129.4, 128.9, 128.4, 122.5, 121.9, 120.2, 119.9, 97.9, 87.3, 21.7 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{18}N$ $[M+H]^+$: 296.1439; found: 296.1431.

2-(4-Cyclopentyl-1-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3051, 2960, 2869, 2210, 1584, 1466, 784 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.60 (d, J = 4.7 Hz, 1H), 8.10 – 8.08 (m, 3H) 7.89 (d, J = 7.9 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.41 – 7.37 (m, 2H), 7.33 – 7.30 (m, 1H), 7.20 –

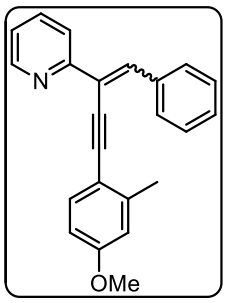


7.17 (m, 1H), 3.05 – 3.00 (m, 1H), 3.09 – 2.04 (m, 2H), 1.87 – 1.84 (m, 3H), 1.70 – 1.64 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.9, 148.9, 136.8, 136.6, 135.6, 129.7, 128.6, 128.2, 122.4, 121.8, 120.4, 103.7, 78.6, 33.8, 31.5, 25.2 ppm. HRMS (ESI): *m/z* calcd for $C_{20}H_{20}N$ $[M+H]^+$: 274.1595; found: 274.1610.

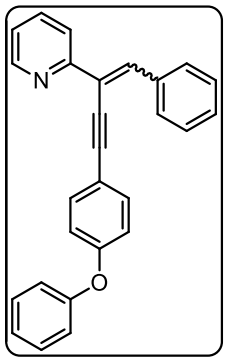


2-[1-Phenyl-4-(2,4,5-trimethylphenyl)but-1-en-3-yn-2-yl]pyridine: FT-IR 3018, 1586, 1467, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.71 (d, *J* = 4.6 Hz, 1H), 8.31 (s, 1H), 8.25 (d, *J* = 7.6 Hz, 2H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.51 – 7.47 (m, 2H), 7.42 – 7.39 (m, 2H), 7.26 – 7.23 (m, 1H), 7.08 (s, 1H), 2.57 (s, 3H), 2.30 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 148.9, 137.7, 137.4, 136.8, 136.5, 136.2, 134.0, 133.1, 131.1, 129.8, 128.7, 128.3, 122.4, 121.8, 120.2, 120.18, 97.4, 90.5, 20.5, 20.0, 19.2 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{22}N$ $[M+H]^+$: 324.1752; found: 324.1739.

2-[4-(4-methoxy-2-methylphenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3006, 2186,



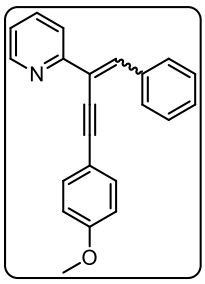
1498, 1239, 783 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (d, *J* = 4.6 Hz, 1H), 8.18 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.36 – 7.32 (m, 1H), 7.24 – 7.21 (m, 1H), 6.81 (s, 1H), 6.79 – 6.76 (m, 1H), 3.83 (s, 3H), 2.55 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.0, 155.7, 149.1, 142.1, 136.9, 136.6, 136.1, 133.7, 129.8, 128.8, 128.4, 122.5, 121.9, 120.4, 115.5, 115.4, 111.6, 97.1, 90.3, 55.4, 21.5 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{20}NO$ $[M+H]^+$: 326.1545; found: 326.1531.



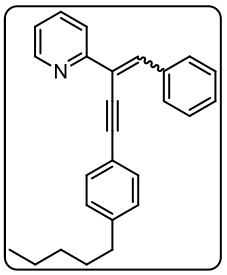
2-[4-(4-Phenoxyphenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 1586, 1488, 1241, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (d, *J* = 4.6 Hz, 1H), 8.21 (s, 1H), 8.13 (d, *J* = 7.9 Hz, 2H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.33 (m, 5H), 7.26 – 7.21 (m, 1H), 7.19 – 7.15 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 156.4, 155.4, 149.1, 137.0, 136.9, 136.5, 133.3, 130.1, 129.9, 128.9, 128.4, 124.1, 122.6, 121.9,

119.9, 119.7, 118.6, 117.8, 97.3, 87.4 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{20}NO$ $[M+H]^+$: 374.1545; found: 374.1529.

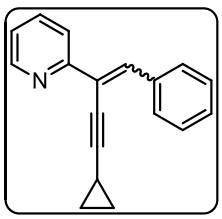
2-[4-(4-Methoxyphenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 2193, 1509, 1250, 783 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 4.6 Hz, 1H), 8.19 (s, 1H), 8.15 (d, *J* = 7.9 Hz, 2H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.33 (m, 1H), 7.23 – 7.20 (m, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.0, 155.4, 149.1, 136.9, 136.6, 136.4, 133.1, 129.9, 128.8, 128.4, 122.5, 121.9, 120.1, 115.4, 114.3, 97.8, 86.7, 55.5 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{18}NO$ $[M+H]^+$: 312.1388; found: 312.1377 ppm.



2-[4-(4-pentylphenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 2957, 2929, 2855, 1584, 1466, 783 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.65 (d, *J* = 4.6 Hz, 1H), 8.23 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 2H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.47 – 7.43 (m, 2H), 7.38 – 7.34 (m, 1H), 7.26 – 7.21 (m, 3H), 2.65 (t, *J* = 7.6 Hz, 2H), 1.69 – 1.62 (m, 2H), 1.40 – 1.35 (m, 4H), 0.94 – 0.91 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 149.0, 144.0, 136.9, 136.7, 136.5, 131.5, 129.9, 128.9, 128.8, 128.4, 122.6, 121.9, 120.4, 120.0, 98.0, 87.3, 36.0, 31.6, 31.1, 22.7, 14.1 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}N$ $[M+H]^+$: 352.2065; found: 352.2051.



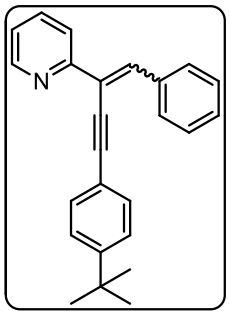
2-[1-Phenyl-4-(thiophen-3-yl)but-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 2206, 1584, 1466, 782 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 4.7 Hz, 1H), 8.21 (s, 1H), 8.12 (d, *J* = 7.7 Hz, 2H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.59 – 7.52 (m, 1H), 7.45 – 7.41 (m, 2H), 7.36 – 7.33 (m, 2H), 7.27 – 7.26 (m, 1H), 7.23 – 7.20 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.2, 149.1, 137.1, 137.0, 136.4, 129.9, 129.7, 129.04, 128.98, 128.4, 125.8, 122.6, 122.4, 121.9, 119.8, 92.9, 87.4 ppm. HRMS (ESI): *m/z* calcd for $C_{19}H_{14}NS$ $[M+H]^+$: 288.0847; found: 288.0836.



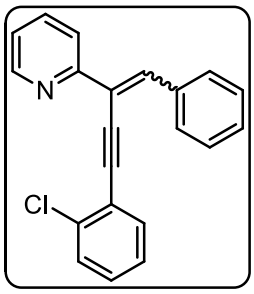
2-(4-Cyclopropyl-1-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 2920, 2344, 1545, 1178, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.61 – 8.59 (m, 1H), 8.11 (s, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.69 (td, *J* = 7.7, 1.8 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.34 – 7.31 (m, 1H), 7.18 – 7.15 (m,

1H), 1.64 – 1.57 (m, 1H), 0.98 – 0.89 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.7, 148.8, 136.7, 136.5, 135.8, 129.4, 128.6, 128.2, 122.3, 121.7, 120.2, 102.3, 74.1, 8.8, 0.8 ppm. HRMS (ESI): *m/z* calcd for $C_{18}H_{16}N$ $[M+H]^+$: 246.1282; found: 246.1772.

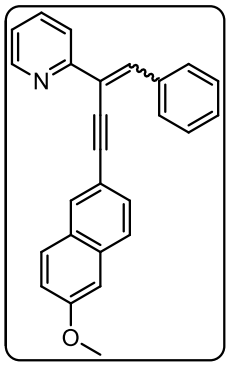
2-[4-(4-(*tert*-Butyl)phenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 2957, 2924, 2042, 1586, 1112, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 – 8.66 (d, 1H), 8.27 (s, 1H), 8.19 (d, *J* = 7.4 Hz, 2H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H), 7.59 – 7.57 (m, 2H), 7.48 – 7.44 (m, 4H), 7.39 – 7.35 (m, 1H), 7.24 – 7.20 (m, 1H), 1.38 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 152.1, 149.0, 136.9, 136.8, 136.5, 131.4, 129.9, 128.9, 128.4, 125.6, 122.5, 121.8, 120.3, 119.9, 98.0, 87.3, 34.9, 31.2 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{24}N$ $[M+H]^+$: 338.1908; found: 338.1893.



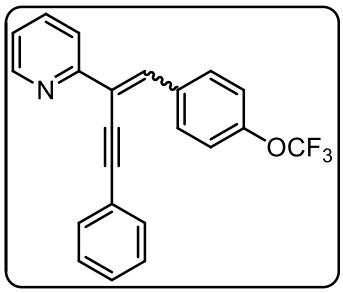
2-[4-(2-Chlorophenyl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3054, 1584, 1466, 1429, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (d, *J* = 4.7 Hz, 1H), 8.35 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.49 – 7.45 (m, 3H), 7.41 – 7.37 (m, 1H), 7.29 – 7.25 (m, 2H), 7.23 – 7.20 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.9, 148.9, 137.8, 136.9, 136.1, 135.8, 133.4, 130.0, 129.6, 129.5, 129.1, 128.3, 126.7, 123.2, 122.6, 121.9, 119.4, 94.5, 92.8 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{15}ClN$ $[M+H]^+$: 316.0893; found: 316.0881.



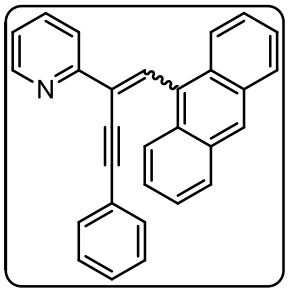
2-[4-(6-methoxynaphthalen-2-yl)-1-phenylbut-1-en-3-yn-2-yl]pyridine: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.68 (d, *J* = 4.5 Hz, 1H), 8.29 (s, 1H), 8.23 (d, *J* = 7.6 Hz, 2H), 8.07 (d, *J* = 7.9 Hz, 1H), 8.04 (s, 1H), 7.80 – 7.74 (m, 3H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42 – 7.38 (m, 1H), 7.26 – 7.19 (m, 2H), 7.13 (s, 1H), 3.92 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.5, 155.3, 149.0, 136.9, 136.8, 136.5, 134.4, 131.4, 129.9, 129.5, 128.9, 128.7, 128.5, 128.4, 127.1, 122.5, 121.9, 120.0, 119.7, 118.1, 105.9, 98.4, 87.6, 55.4 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{20}NO$ $[M+H]^+$: 362.1545; found: 362.1561.



2-[4-Phenyl-1-(4-(trifluoromethoxy)phenyl)but-1-en-3-yn-2-yl]pyridine: FT-IR 3055, 1584, 1259, 1167, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (d, *J* = 4.6 Hz, 1H), 8.22 (s, 1H), 8.16 (d, *J* = 8.6 Hz, 2H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.60 – 7.58 (m, 2H),

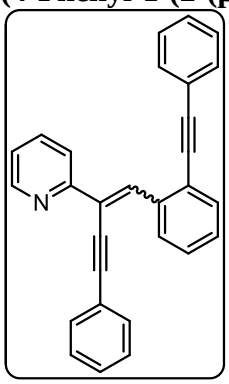


7.43 – 7.39 (m, 3H), 7.27 (d, J = 8.4 Hz, 2H), 7.22 – 7.19 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.8, 149.13 (d, $J_{C\text{-}F}$ = 1.7 Hz), 149.05, 136.9, 135.2, 135.1, 131.6, 131.2, 128.9, 128.7, 123.0, 122.8, 121.9, 120.6, 120.58 (q, $J_{C\text{-}F}$ = 256.0 Hz), 120.55 (s), 98.2, 87.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.5 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{15}F_3NO$ $[M+H]^+$: 366.1105; found: 366.1091.



2-[1-(Anthracen-9-yl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3050, 2210, 1583, 1430, 736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.18 (s, 1H), 8.80 – 8.79 (m, 1H), 8.50 (s, 1H), 8.36 – 8.34 (m, 2H), 8.09 – 8.06 (m, 3H), 7.84 (td, J = 7.7, 1.3 Hz, 1H), 7.51 – 7.49 (m, 4H), 7.35 – 7.32 (m, 1H), 7.17 – 7.13 (m, 1H), 7.10 – 7.06 (m, 2H), 6.74 (d, J = 7.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.2, 149.5, 137.1, 136.0, 131.7, 131.5, 131.3, 129.6, 128.7, 128.3, 128.1, 127.4, 127.3, 126.9, 125.5, 125.3, 123.1, 122.8, 122.0, 97.4, 87.2 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{20}N$ $[M+H]^+$: 382.1595; found: 382.1591.

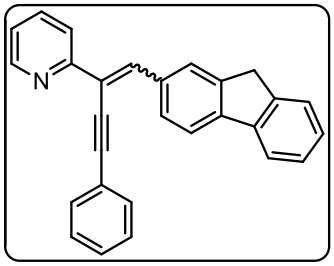
2-(4-Phenyl-1-(2-(phenylethynyl)phenyl)but-1-en-3-yn-2-yl)pyridine: FT-IR 2994, 2027, 1583, 1466, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (d, J = 4.8 Hz, 1H), 7.72 (s, 1H), 7.62 – 7.60 (m, 2H), 7.55 – 7.53 (m, 3H), 7.40 – 7.31 (m, 7H), 7.21 – 7.16 (m, 3H), 7.01 – 6.97 (m, 1H), 6.84 – 6.82 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.4, 149.9, 137.9, 137.3, 136.5, 132.4, 131.9, 131.8, 129.5, 128.6, 128.5, 128.4, 128.3, 127.8, 127.7, 125.4, 124.6, 123.4, 123.3, 122.7, 95.1, 91.2, 91.1, 88.0 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{20}N$ $[M+H]^+$: 382.1595; found: 382.1584.



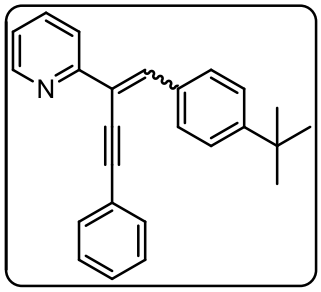
2-(1,4-diphenylbut-1-en-3-yn-2-yl)quinolone: FT-IR 3061, 2027, 1594, 1503, 1424, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.42 (s, 1H), 8.23 – 8.15 (m, 5H), 7.83 (d, J = 8.1 Hz, 1H), 7.77 – 7.73 (m, 1H), 7.66 – 7.63 (m, 2H), 7.55 – 7.52 (m, 1H), 7.50 – 7.37 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 147.9, 138.7, 136.8, 136.5, 131.7, 130.1, 129.9, 129.7, 129.2, 128.8, 128.7, 128.5, 127.7, 127.6, 126.4, 123.4, 120.3,

120.1, 97.9, 88.4 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{18}N$ $[M+H]^+$: 332.1439; found: 332.1423.

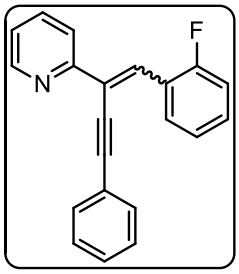
2-[1-(9H-Fluoren-2-yl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3059, 2920, 1583, 1431, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.67 (d, *J* = 4.7 Hz, 1H), 8.45 (s, 1H), 8.33 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.79 – 7.75 (m, 1H), 7.66 – 7.64 (m, 2H), 7.58 – 7.56 (m, 1H), 7.47 – 7.37 (m, 4H), 7.35 – 7.32 (m, 1H), 7.26 – 7.21 (m, 1H), 3.96 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 149.1, 144.0, 143.3, 142.7, 141.5, 137.6, 136.9, 135.1, 131.6, 129.4, 128.7, 128.69, 127.2, 127.0, 126.2, 125.2, 123.5, 122.4, 121.8, 120.3, 119.8, 118.9, 97.9, 88.5, 37.1 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{20}N$ $[M+H]^+$: 370.1595; found: 370.1588.



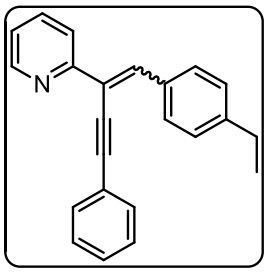
2-[1-(Naphthalen-1-yl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3061, 1584, 1467, 1430, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.03 (s, 1H), 8.74 – 8.73 (m, 1H), 8.48 (d, *J* = 7.3 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.93 – 7.90 (m, 2H), 7.80 (td, *J* = 7.7, 1.8 Hz, 1H), 7.62 – 7.52 (m, 3H), 7.49 – 7.45 (m, 2H), 7.37 – 7.33 (m, 3H), 7.29 – 7.26 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.0, 149.3, 137.0, 134.9, 133.7, 133.5, 132.3, 131.7, 129.2, 128.7, 128.6, 128.5, 127.3, 126.4, 126.0, 125.3, 124.5, 123.3, 122.8, 122.4, 122.0, 96.2, 87.8 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{18}N$ $[M+H]^+$: 332.1439; found: 332.1426



2-[1-(4-(*tert*-Butyl)phenyl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 2962, 1584, 1464, 1430, 755 cm^{-1}**;** ^1H NMR (400 MHz, $CDCl_3$) δ = 8.65 – 8.63 (m, 1H), 8.21 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.75 (td, *J* = 7.8, 1.8 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.42 – 7.39 (m, 3H), 7.23 – 7.20 (m, 1H), 1.36 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 152.4, 149.1, 137.0, 136.97, 133.6, 131.6, 129.8, 128.7, 128.66, 125.5, 123.5, 122.5, 121.8, 118.8, 97.7, 88.2, 35.0, 31.4 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{24}N$ $[M+H]^+$: 338.1908; found: 338.1894.

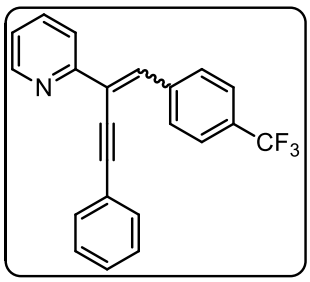


2-[1-(2-Fluorophenyl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 3058, 1584, 1465, 1429, 754 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 – 8.61 (m, 2H), 8.43 (s, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.58 – 7.56 (m, 2H), 7.40 – 7.39 (m, 3H), 7.36 – 7.31 (m, 1H), 7.26 – 7.20 (m, 2H), 7.15 – 7.11 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.3 (d, *J* = 250.0 Hz), 155.0, 149.3 (d, *J* = 1.9 Hz), 137.0, 131.7, 130.5, 130.4 (d, *J* = 1.0 Hz), 129.4 (d, *J* = 1.3 Hz), 128.9, 128.7, 128.6 (d, *J* = 2.8 Hz), 124.6 (d, *J* = 11.4 Hz), 123.8, 123.1, 122.9, 121.9, 121.70 (d, *J* = 1.8 Hz), 115.5 (d, *J* = 22.0 Hz), 97.8, 87.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -114.6 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{15}FN$ $[M+H]^+$: 300.1188; found: 300.1177.

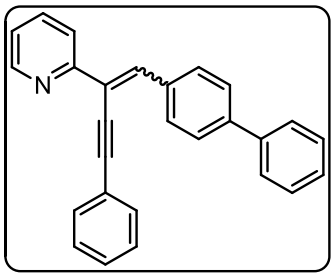


2-[1-(4-Ethylphenyl)-4-phenylbut-1-en-3-yn-2-yl]pyridine: FT-IR 2964, 1584, 1466, 1430, 755 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 4.6 Hz, 1H), 8.20 (s, 1H), 8.08 (d, *J* = 8.1 Hz, 2H), 7.99 – 7.97 (m, 1H), 7.75 (td, *J* = 7.6, 1.2 Hz, 1H), 7.62 – 7.60 (m, 2H), 7.43 – 7.37 (m, 3H), 7.29 – 7.26 (m, 2H), 7.23 – 7.20 (m, 1H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 149.1, 145.6, 137.2, 137.0, 133.9, 131.6, 130.1, 128.7, 128.6, 128.0, 123.5, 122.5, 121.8, 118.8, 97.6, 88.2, 29.0, 15.5 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310.1595; found: 310.1609.

2-[4-Phenyl-1-(4-(trifluoromethyl)phenyl)but-1-en-3-yn-2-yl]pyridine: FT-IR 3056, 1585, 1324, 1069, 756 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 – 8.65 (m, 1H), 8.24 (s, 1H), 8.21 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.79 (td, *J* = 7.7, 1.7 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.60 – 7.57 (m, 2H), 7.43 – 7.41 (m, 3H), 7.28 – 7.25 (m, 1H) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.57 ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.7, 149.2, 139.8, 137.1, 135.2, 131.7, 130.2 (q, *J* = 32.2 Hz), 129.9, 129.2, 128.8(2C), 125.4 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 270.4 Hz), 123.2, 122.9, 122.2, 98.6, 87.3 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{15}F_3N$ $[M+H]^+$: 350.1156; found: 350.1146.

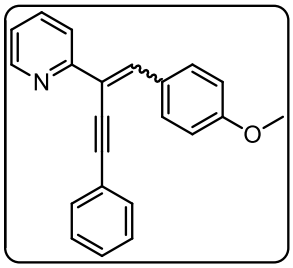


2-(1-([1,1'-Biphenyl]-4-yl)-4-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3058, 1583, 1466, 1430, 756 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 – 8.65 (m, 1H), 8.27 (s, 1H), 8.23 (d, *J* = 8.3 Hz, 2H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.78 (td, *J* = 7.6, 1.4 Hz, 1H), 7.70 – 7.66 (m, 4H), 7.64 – 7.62 (m, 2H), 7.48 – 7.35 (m, 6H), 7.26 – 7.23 (m, 1H) ppm. ^{13}C NMR (100

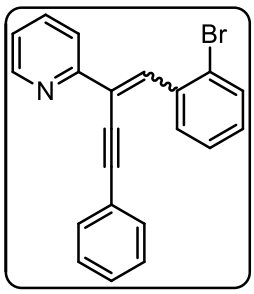


MHz, $CDCl_3$) δ = 155.3, 149.1, 141.6, 140.7, 137.0, 136.7, 135.5, 131.7, 130.4, 129.0, 128.8, 128.7, 127.7, 127.2, 127.1, 123.3, 122.6, 121.9, 119.7, 98.0, 88.1 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{20}N$ $[M+H]^+$: 358.1595; found: 358.1610.

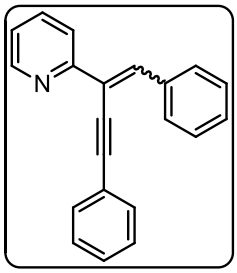
2-(1-(4-Methoxyphenyl)-4-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3055, 2835, 1509, 1257, 756 cm^{-1}**;** ^1H NMR (400 MHz, $CDCl_3$) δ = 8.63 – 8.62 (m, 1H), 8.17 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.74 (td, *J* = 7.6, 1.8 Hz, 1H), 7.62 – 7.59 (m, 2H), 7.43 – 7.38 (m, 3H), 7.22 – 7.19 (m, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.3, 155.6, 149.0, 137.0, 136.8, 131.63, 131.60, 129.3, 128.7, 128.6, 123.5, 122.3, 121.6, 117.4, 113.9, 97.4, 88.3, 55.5 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{18}NO$ $[M+H]^+$: 312.1388; found: 312.1402.



2-(1-(2-Bromophenyl)-4-phenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3056, 1584, 1464, 1431, 754 cm^{-1}**;** ^1H NMR (400 MHz, $CDCl_3$) δ = 8.69 (d, *J* = 4.0 Hz, 1H), 8.48 (s, 1H), 8.44 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68 – 7.65 (m, 1H), 7.54 – 7.50 (m, 2H), 7.41 – 7.35 (m, 4H), 7.27 – 7.19 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.8, 149.4, 136.9, 136.5, 136.2, 132.9, 131.7, 130.4, 129.9, 128.8, 128.6, 126.9, 125.7, 123.0, 122.9, 122.5, 122.0, 96.9, 87.1 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{15}BrN$ $[M+H]^+$: 360.0388; found: 360.0403.



2-(1,4-Diphenylbut-1-en-3-yn-2-yl)pyridine: FT-IR 3050, 2196, 1582, 1429, 756 cm^{-1}**;** ^1H NMR (400 MHz, $CDCl_3$) δ = 8.65 – 8.64 (m, 1H), 8.22 (s, 1H), 8.13 (d, *J* = 7.6 Hz, 2H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.76 (td, *J* = 7.8, 1.8 Hz, 1H), 7.61 – 7.59 (m, 2H), 7.46 – 7.34 (m, 6H), 7.26 – 7.22 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 149.1, 137.2, 137.0, 136.4, 131.7, 130.0, 129.0, 128.8, 128.7, 128.5, 123.3, 122.7, 121.9, 119.8, 97.7, 87.9 ppm.



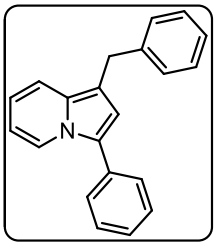
General procedure for the synthesis of diarylmethanes:

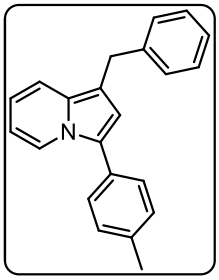
Hantzsch ester (0.2 mmol) was added to a mixture of 2-(2-enynyl)-pyridine (0.1 mmol) and CuI (0.01 mmol) in 1.5 ml of MeCN, and the resultant mixture was stirred at 70 °C until the 2-(2-

enynyl)-pyridine was completely consumed (by T.L.C.). The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using ethyl acetate/hexane mixture as an eluent to get the pure indolizine containing diarylmethanes.

Characterization of the products:

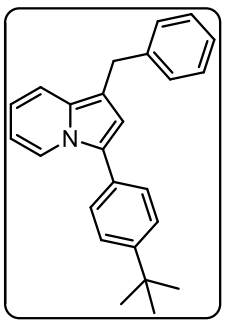
1-Benzyl-3-phenylindolizine (64a) : Yellow oil; yield 95% (27 mg); R_f = 0.8 (5% EtOAc in hexane); FT-IR 3027, 1452, 735, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.2 Hz, 1H), 7.59 – 7.57 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 1H), 7.35 – 7.29 (m, 5H), 7.25 – 7.20 (m, 1H), 6.74 (s, 1H), 6.67 – 6.63 (m, 1H), 6.46 (t, *J* = 6.8 Hz, 1H), 4.19 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.0, 132.6, 131.1, 129.0, 128.6, 128.5, 127.9, 127.0, 125.9, 124.7, 122.3, 117.8, 116.2, 115.1, 112.9, 110.6, 32.1 ppm.



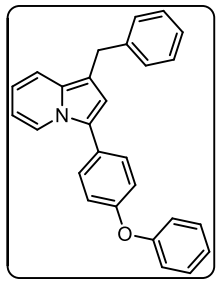


1-Benzyl-3-(*p*-tolyl)indolizine (64b): Yellow solid; yield 99% (29.5 mg); R_f = 0.8 (5% EtOAc in hexane); M.P. 116–118 °C; FT-IR 2923, 1481, 1260, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, *J* = 7.2 Hz, 1H), 7.45 – 7.43 (m, 2H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.30 – 7.25 (m, 6H), 7.22 – 7.17 (m, 1H), 6.68 (s, 1H), 6.63 – 6.59 (m, 1H), 6.45 – 6.41 (m, 1H), 4.16 (s, 2H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.1, 136.8, 130.9, 129.7 (2C), 128.6, 128.5, 128.0, 125.9, 124.7, 122.4, 117.8, 116.0, 114.8, 112.7, 110.5, 32.1, 21.4 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{20}N$ $[M+H]^+$: 298.1596; found: 298.1583.

1-Benzyl-3-[4-(*tert*-butyl)phenyl]indolizine (64c): White solid; yield 92% (31.2 mg); R_f = 0.6 (5% EtOAc in hexane); M.P. 126–128 °C; FT-IR 2962, 1493, 1301, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.1 Hz, 1H), 7.51 – 7.47 (m, 4H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.30 – 7.26 (m, 4H), 7.23 – 7.19 (m, 1H), 6.70 (s, 1H), 6.64 – 6.60 (m, 1H), 6.44 (t, *J* = 6.8 Hz, 1H), 4.17 (s, 2H), 1.38 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.0, 142.1, 130.9, 129.7, 128.6, 128.5, 127.7, 125.93, 125.91, 124.7, 122.5, 117.8, 116.0, 115.0, 112.7, 110.4, 34.8, 32.1, 31.5 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{26}N$ $[M+H]^+$: 340.2066; found: 340.2054.

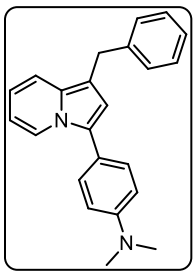


1-Benzyl-3-(4-methoxyphenyl)indolizine (64d): Yellow oil; yield 90% (28.2 mg); R_f = 0.3 (5% EtOAc in hexane); FT-IR 2836, 1524, 1248, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.31 – 7.26 (m, 4H), 7.24 – 7.18 (m, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.66 (s, 1H), 6.63 – 6.59 (m, 1H), 6.43 (t, *J* = 6.9 Hz, 1H), 4.18 (s, 2H), 3.87 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.8, 142.1, 130.6, 129.5, 128.6, 128.5, 125.9, 125.1, 124.4, 122.2, 117.8, 115.8, 114.6, 114.5, 112.6, 110.4, 55.5, 32.1 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{20}NO$ $[M+H]^+$: 314.1546; found: 314.1532.

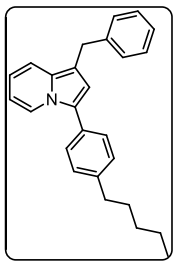


1-Benzyl-3-(4-phenoxyphenyl)indolizine (64e): Yellow oil; yield 83% (31 mg); R_f = 0.4 (5% EtOAc in hexane); FT-IR 3029, 1489, 1239, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.38 (m, 3H), 7.33 – 7.30 (m, 4H), 7.26 – 7.20 (m, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.13 – 7.11 (m, 4H), 6.71 (s, 1H), 6.67 – 6.63 (m, 1H), 6.47 (t, *J* = 6.9 Hz, 1H), 4.20 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.1, 156.4, 142.0, 130.9, 129.9, 129.5, 128.6, 128.5, 127.6, 125.9, 124.1, 123.6, 122.2, 119.3, 119.2, 117.8, 116.0, 114.9, 112.8, 110.6, 32.1 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{22}NO$ $[M+H]^+$: 376.1702; found: 376.1688.

4-(1-Benzylindolizin-3-yl)-N,N-dimethylaniline (64f): Yellow oil; yield 94% (30.6 mg); R_f = 0.3 (5% EtOAc in hexane); FT-IR 2892, 1612, 1443, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.19 (d, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.33 – 7.26 (m, 4H), 7.24 – 7.17 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.65 (s, 1H), 6.61 – 6.57 (m, 1H), 6.42 (t, *J* = 6.7 Hz, 1H), 4.18 (s, 2H), 3.02 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.5, 142.3, 130.3, 129.2, 128.6, 128.4, 125.8, 125.1, 122.4, 121.0, 117.7, 115.4, 114.2, 113.0, 112.4, 110.1, 40.8, 32.2 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{23}N_2$ $[M+H]^+$: 327.1862; found: 327.1849.

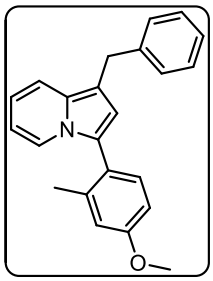


1-Benzyl-3-(4-pentylphenyl)indolizine (64g): Yellow oil; yield 99% (35 mg); R_f = 0.5(5% EtOAc in hexane); FT-IR 2929, 1607, 1266, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.2 Hz, 1H), 7.50 – 7.48 (m, 2H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.32 – 7.28 (m, 6H), 7.24 – 7.20 (m, 1H), 6.72 (s, 1H), 6.65 – 6.61 (m, 1H), 6.45 (t, *J* = 6.8 Hz, 1H), 4.19 (s, 2H), 2.68 (t, *J* = 7.6

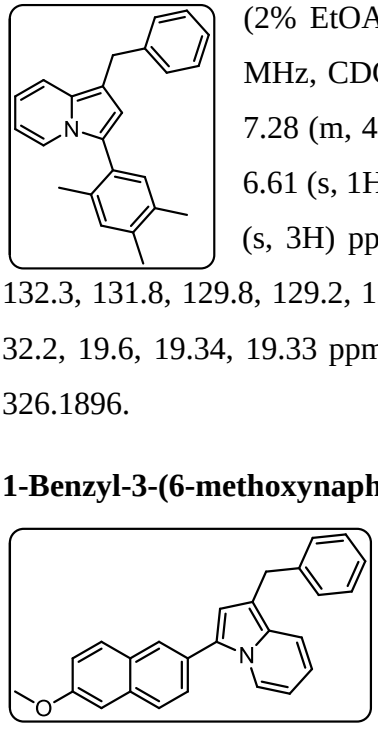


Hz, 2H), 1.73 – 1.66 (m, 2H), 1.43 – 1.38 (m, 4H), 0.96 (t, *J* = 6.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.1, 141.9, 130.9, 129.9, 129.0, 128.6, 128.5, 127.9, 125.9, 124.8, 122.4, 117.8, 115.9, 114.9, 112.7, 110.4, 35.8, 32.1, 31.7, 31.3, 22.7, 14.2 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{28}N$ $[M+H]^+$: 354.2222; found: 354.2209.

1-Benzyl-3-(4-methoxy-2-methylphenyl)indolizine (64h): Yellow oil; yield 88% (28.8 mg); R_f = 0.7 (5% EtOAc in hexane); FT-IR 2936, 1607, 1242, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 7.2 Hz, 1H), 7.37 – 7.35 (m, 1H), 7.31 – 7.25 (m, 5H), 7.23 – 7.16 (m, 1H), 6.89 (d, *J* = 2.6 Hz, 1H), 6.83 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.62 – 6.58 (m, 1H), 6.58 (s, 1H), 6.41 – 6.37 (m, 1H), 4.20 (s, 2H), 3.86 (s, 3H), 2.12 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6, 142.3, 139.9, 132.5, 129.8, 128.6, 128.4, 125.8, 124.3, 123.4, 122.7, 117.5, 115.8, 115.4, 115.3, 111.6, 111.4, 110.0, 55.4, 32.2, 20.2 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{22}NO$ $[M+H]^+$: 328.1702; found: 328.1688.



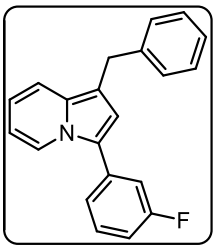
1-Benzyl-3-(2,4,5-trimethylphenyl)indolizine (64i): Yellow oil; yield 87% (28.3 mg); R_f = 0.7 (2% EtOAc in hexane); FT-IR 2919, 1494, 1307, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55 (d, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.31 – 7.28 (m, 4H), 7.24 – 7.17 (m, 1H), 7.15 – 7.13 (m, 2H), 6.63 – 6.59 (m, 1H), 6.61 (s, 1H), 6.42 – 6.38 (m, 1H), 4.21 (s, 2H), 2.32 (s, 3H), 2.28 (s, 3H), 2.10 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.3, 136.7, 135.3, 134.1, 132.3, 131.8, 129.8, 129.2, 128.6, 128.4, 125.8, 123.9, 122.8, 117.5, 115.4, 115.2, 111.7, 109.9, 32.2, 19.6, 19.34, 19.33 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{24}N$ $[M+H]^+$: 326.1909; found: 326.1896.



1-Benzyl-3-(6-methoxynaphthalen-2-yl)indolizine (64j): Yellow oil; yield 97% (35.2 mg); R_f = 0.7 (5% EtOAc in hexane); FT-IR 2904, 1607, 1266, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 7.1 Hz, 1H), 7.95 (s, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.37 – 7.32 (m, 4H), 7.26 – 7.20 (m, 3H), 6.83 (s, 1H), 6.69 – 6.65 (m, 1H), 6.49 (t, *J* = 6.8 Hz, 1H), 4.23 (s, 2H), 3.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 142.1, 133.6, 131.1, 129.5, 129.3, 128.6,

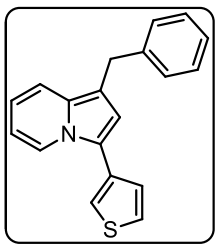
128.5, 127.8, 127.4, 127.0, 126.1, 125.9, 124.7, 122.3, 119.3, 117.9, 116.2, 115.2, 113.0, 110.7, 105.9, 55.4, 32.1 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{22}NO$ $[M+H]^+$: 364.1702; found: 364.1689.

1-Benzyl-3-(2-chlorophenyl)indolizine (64k): Yellow oil; yield 94% (29.8 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3060, 1494, 1307, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.64 (d, J = 7.1 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.49 – 7.44 (m, 1H), 7.42 – 7.40 (m, 1H), 7.37 – 7.29 (m, 6H), 7.24 – 7.20 (m, 1H), 6.75 (s, 1H), 6.71 – 6.67 (m, 1H), 6.50 – 6.47 (m, 1H), 4.22 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.0, 134.5, 132.9, 131.4, 130.8, 130.1, 129.2, 128.6, 128.5, 127.0, 125.9, 123.4, 121.4, 117.5, 116.3, 116.2, 112.2, 110.2, 32.2 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{17}ClN$ $[M+H]^+$: 318.1050; found: 318.1039.

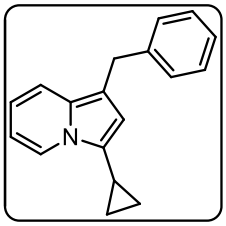


1-Benzyl-3-(3-fluorophenyl)indolizine (64l): Yellow oil; yield 99% (29.8 mg); R_f = 0.7 (2% EtOAc in hexane); FT-IR 3061, 1612, 1584, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, J = 7.2 Hz, 1H), 7.43 – 7.32 (m, 4H), 7.29 – 7.28 (m, 3H), 7.27 – 7.18 (m, 2H), 7.02 – 6.97 (m, 1H), 6.72 (s, 1H), 6.68 – 6.64 (m, 1H), 6.51 – 6.47 (m, 1H), 4.15 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.3 (d, J_{C-F} = 244.4 Hz), 141.9, 134.7 (d, J_{C-F} = 8.3 Hz), 131.6, 130.5 (d, J_{C-F} = 8.7 Hz), 128.6 (d, J_{C-F} = 8.6 Hz), 126.0, 123.4 (d, J_{C-F} = 2.4 Hz), 123.3 (d, J_{C-F} = 2.8 Hz), 122.3, 118.0, 116.7, 115.6, 114.42 (d, J_{C-F} = 21.9 Hz), 113.8, 113.6 113.2, 111.0, 32.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.5 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{17}FN$ $[M+H]^+$: 302.1346; found: 302.1332.

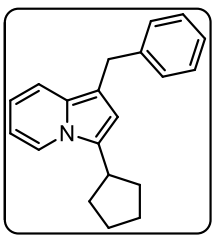
1-Benzyl-3-(thiophen-3-yl)indolizine (64m): Yellow oil; yield 90% (26 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3022, 1493, 1301, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, J = 7.1 Hz, 1H), 7.44 – 7.43 (m, 1H), 7.39 – 7.38 (m, 2H), 7.34 – 7.33 (m, 1H), 7.31 – 7.30 (m, 4H), 7.24 – 7.19 (m, 1H), 6.75 (s, 1H), 6.66 – 6.62 (m, 1H), 6.50 (t, J = 6.9 Hz, 1H), 4.17 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.0, 133.0, 130.9, 128.6, 128.5, 127.6, 126.0, 125.9, 122.7, 120.3, 120.2, 117.8, 116.0, 115.0, 112.6, 110.7, 32.1 ppm. HRMS (ESI): *m/z* calcd for $C_{19}H_{16}NS$ $[M+H]^+$: 290.1004; found: 290.0993.



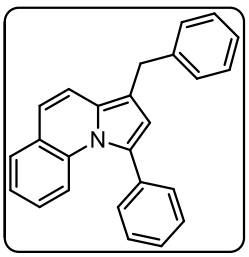
1-Benzyl-3-cyclopropylindolizine (64n): Yellow oil; yield 82% (20.2 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3030, 1658, 1587, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.02 (d, *J* = 7.0 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.28 – 7.24 (m, 4H), 7.20 – 7.17 (m, 1H), 6.63 – 6.59 (m, 1H), 6.51 (t, *J* = 6.8 Hz, 1H), 6.37 (s, 1H), 4.11 (s, 2H), 1.87 – 1.80 (m, 1H), 0.98 – 0.93 (m, 2H), 0.68 – 0.64 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.4, 129.7, 128.6, 128.4, 125.8, 125.3, 122.3, 117.4, 115.2, 112.4, 110.7, 109.7, 32.1, 6.3, 5.4 ppm. HRMS (ESI): *m/z* calcd for $C_{18}H_{18}N$ $[M+H]^+$: 248.1440; found: 248.1429.



1-Benzyl-3-cyclopentylindolizine (64o): Yellow solid; yield 60% (16.5 mg); R_f = 0.7 (2% EtOAc in hexane); M.P. 106-108 °C; FT-IR 2954, 1656, 1494, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 7.1 Hz, 1H), 7.32 – 7.23 (m, 5H), 7.19 – 7.15 (m, 1H), 6.57 – 6.53 (m, 1H), 6.46 – 6.43 (m, 1H), 6.44 (s, 1H), 4.12 (s, 2H), 3.29 – 3.21 (m, 1H), 2.19 – 2.10 (m, 2H), 1.81 – 1.65 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.5, 129.7, 128.6, 128.4, 128.1, 125.8, 122.2, 117.6, 114.5, 110.8, 110.7, 109.6, 36.6, 32.2, 31.5, 25.2 ppm. HRMS (ESI): *m/z* calcd for $C_{20}H_{22}N$ $[M+H]^+$: 276.1753; found: 276.1741.



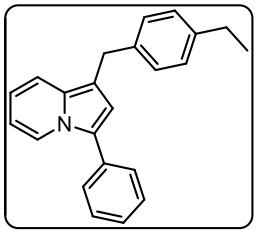
3-Benzyl-1-phenylpyrrolo[1,2-*a*]quinoline (64p): Yellow oil; yield 99% (33 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3059, 1599, 1448, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.61 – 7.59 (m, 1H), 7.52 – 7.47 (m, 3H), 7.46 – 7.40 (m, 3H), 7.36 – 7.31 (m, 5H), 7.24 – 7.20 (m, 2H), 7.12 – 7.08 (m, 1H), 6.99 – 6.96 (m, 1H), 6.55 (s, 1H), 4.17 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.8, 135.7, 134.5, 130.0, 129.6, 129.3, 128.7, 128.6, 128.5, 128.47, 127.6, 126.4, 126.0, 125.6, 123.3, 118.5, 117.7, 117.5, 117.4, 115.9, 32.0 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{20}N$ $[M+H]^+$: 334.1596; found: 334.1580.



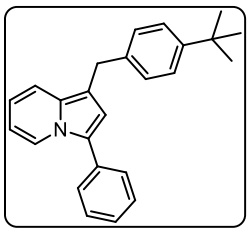
1-Benzyl-3-phenylpyrrolo[2,1-*a*]isoquinoline (64q): Yellow oil; yield 60% (20 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3027, 1457, 1340, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.03 (m, 2H), 7.56 – 7.54 (m, 3H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.29 (m, 7H), 7.26 – 7.21 (m, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 6.54 (s, 1H), 4.50 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.6,

132.3, 129.0, 128.9, 128.7, 128.6, 127.8, 127.7, 127.44, 127.40, 127.0, 126.8, 126.1, 126.0, 125.0, 122.9, 122.5, 116.5, 115.4, 111.0, 35.0 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{20}N$ $[M+H]^+$: 334.1596; found: 334.1580.

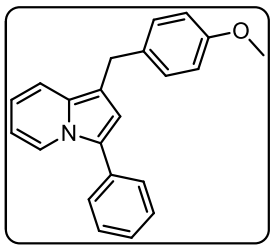
1-(4-Ethylbenzyl)-3-phenylindolizine (64r): Yellow oil; yield 95% (29.6 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 2962, 1604, 1269, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.2 Hz, 1H), 7.58 – 7.56 (m, 2H), 7.48 – 7.44 (m, 2H), 7.40 (d, *J* = 9.0 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.24 – 7.22 (m, 2H), 7.15 – 7.13 (m, 2H), 6.73 (s, 1H), 6.65 – 6.62 (m, 1H), 6.47 – 6.43 (m, 1H), 4.15 (s, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.8, 139.2, 132.7, 131.1, 129.0, 128.5, 128.0, 127.93, 126.9, 124.6, 122.3, 117.9, 116.1, 115.1, 113.2, 110.6, 31.7, 28.6, 15.8 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{22}N$ $[M+H]^+$: 312.1753; found: 312.1740.



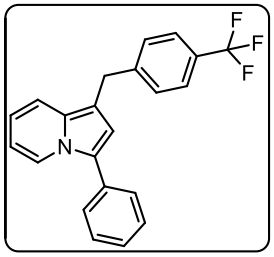
1-(4-(*tert*-Butyl)benzyl)-3-phenylindolizine (64s): Yellow oil; yield 90% (30.5 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 2962, 1604, 1257, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.2 Hz, 1H), 7.58 – 7.56 (m, 2H), 7.48 – 7.40 (m, 3H), 7.34 – 7.30 (m, 3H), 7.26 – 7.23 (m, 2H), 6.75 (s, 1H), 6.66 – 6.62 (m, 1H), 6.47 – 6.44 (m, 1H), 4.15 (s, 2H), 1.33 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.7, 139.0, 132.7, 131.1, 129.0, 128.2, 127.9, 127.0, 125.4, 124.6, 122.3, 117.9, 116.1, 115.1, 113.1, 110.6, 34.5, 31.56, 31.51 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{26}N$ $[M+H]^+$: 340.2066; found: 340.2050.



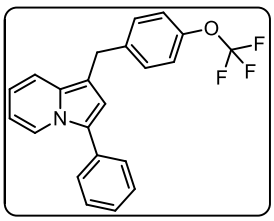
1-(4-Methoxybenzyl)-3-phenylindolizine (64t): Yellow oil; yield 90% (28.2 mg); R_f = 0.4 (5% EtOAc in hexane); FT-IR 2836, 1511, 1248, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, *J* = 7.2 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.47 – 7.43 (m, 2H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.70 (s, 1H), 6.65 – 6.61 (m, 1H), 6.45 (t, *J* = 6.6 Hz, 1H), 4.11 (s, 2H), 3.79 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 134.1, 132.6, 131.1, 129.5, 129.0, 127.9, 127.0, 124.5, 122.4, 117.9, 116.2, 115.1, 113.9, 113.4, 110.6, 55.4, 31.2 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{20}NO$ $[M+H]^+$: 314.1546; found: 314.1531.



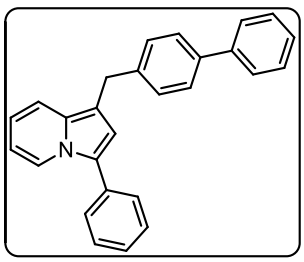
3-Phenyl-1-(4-(trifluoromethyl)benzyl)indolizine (64u): Yellow solid; yield 60% (21 mg); R_f = 0.6 (5% EtOAc in hexane); M.P. 134–136 °C; FT-IR 2932, 1326, 1123, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, J = 6.4 Hz, 1H), 7.56 – 7.52 (m, 4H), 7.47 – 7.44 (m, 2H), 7.39 – 7.37 (m, 2H), 7.34 – 7.31 (m, 2H), 6.68 (s, 1H), 6.68 – 6.63 (m, 1H), 6.47 (t, J = 6.8 Hz, 1H), 4.21 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.2, 132.4, 131.1, 129.1, 128.9, 128.0, 127.2, 125.4 (q, J_{C-F} = 3.7 Hz), 124.9, 122.5, 121.8 (q, J_{C-F} = 270.1 Hz), 117.6, 116.6, 115.0, 111.7, 110.8, 32.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.2 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{17}F_3N$ $[M+H]^+$: 352.1314; found: 352.1297.



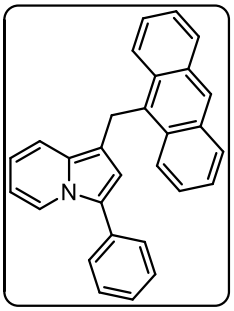
3-Phenyl-1-(4-(trifluoromethoxy)benzyl)indolizine (64v): Yellow solid; yield 70% (25.7 mg); R_f = 0.7 (2% EtOAc in hexane); M.P. 103–105 °C; FT-IR 2927, 1508, 1262, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 – 8.26 (m, 1H), 7.57 – 7.54 (m, 2H), 7.48 – 7.44 (m, 2H), 7.36 – 7.32 (m, 2H), 7.31 – 7.28 (m, 2H), 7.14 – 7.12 (m, 2H), 6.70 (s, 1H), 6.67 – 6.63 (m, 1H), 6.49 – 6.45 (m, 1H), 4.16 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.5 (q, J = 1.8 Hz), 140.8, 132.5, 131.1, 129.8, 129.1, 128.0, 127.1, 124.9, 122.4, 121.1, 120.7 (q, J_{C-F} = 254.9 Hz), 117.6, 116.5, 115.0, 112.2, 110.7, 31.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.9 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{17}F_3NO$ $[M+H]^+$: 368.1263; found: 368.1248.



1-([1,1'-Biphenyl]-4-ylmethyl)-3-phenylindolizine (64w): Yellow oil; yield 99% (35.5 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 2923, 1600, 1487, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.29 (d, J = 6.8 Hz, 1H), 7.61 – 7.54 (m, 6H), 7.49 – 7.34 (m, 9H), 6.78 (s, 1H), 6.68 – 6.64 (m, 1H), 6.49 – 6.46 (m, 1H), 4.23 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.2, 141.17, 138.9, 132.6, 131.1, 129.0 (2C), 128.8, 127.9, 127.2, 127.1, 127.09, 127.0, 124.7, 122.4, 117.8, 116.3, 115.1, 112.7, 110.6, 31.8 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{22}N$ $[M+H]^+$: 360.1753; found: 360.1738.



1-(Anthracen-9-ylmethyl)-3-phenylindolizine (64x): Yellow solid; yield 99% (38 mg); R_f = 0.5 (5% EtOAc in hexane); M.P. 176–178 °C; FT-IR 3057, 1602, 1348, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.43 (s, 1H), 8.35 – 8.33 (m, 2H), 8.24 (d, J = 7.2 Hz, 1H), 8.05 – 8.03 (m, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.47 – 7.45 (m, 4H), 7.36 – 7.29 (m, 4H), 7.21 – 7.18 (m, 1H),

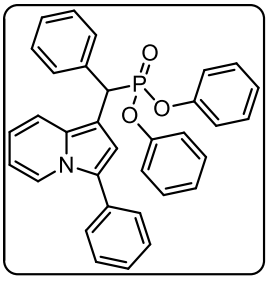


6.75 – 6.72 (m, 1H), 6.49 (d, J = 6.6 Hz, 1H), 6.20 (s, 1H), 5.10 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.2, 132.4, 131.8, 130.5, 130.1, 129.2, 128.8, 127.8, 126.9, 126.2, 125.8, 125.2, 125.0, 124.6, 122.4, 117.7, 116.2, 114.8, 113.2, 110.6, 24.5 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{22}N$ $[M+H]^+$: 384.1753; found: 384.1734.

General procedure for the Cu-catalyzed synthesis of indolizine phosphonates: Diaryl phosphite (0.12 mmol) was added to a mixture of 2-(2-enynyl)-pyridine (0.1 mmol) and CuI (0.01 mmol) in 1.5 ml of DCE and the resultant mixture was stirred at 70 °C until the 2-(2-enynyl)-pyridine was completely consumed (by T.L.C.). The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using 10 – 20% ethyl acetate/hexane mixture as an eluent to get the pure indolizine phosphonate.

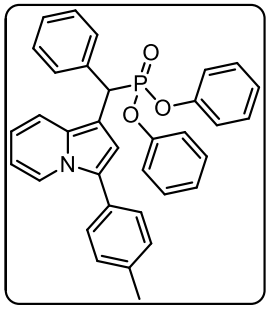
Characterization of the products:

Diphenyl (phenyl(3-phenylindolizin-1-yl)methyl)phosphonate (89a): Green semi-solid; yield



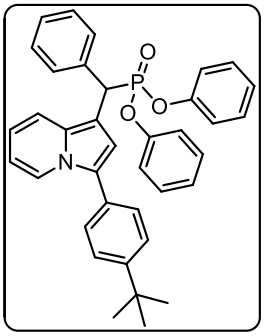
90% (46 mg); R_f = 0.2 (20% EtOAc in hexane); FT-IR 1490, 1271, 1187, 934 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, J = 7.2 Hz, 1H), 7.69 – 7.68 (m, 2H), 7.54 – 7.51 (m, 2H), 7.48 – 7.41 (m, 3H), 7.36 – 7.32 (m, 4H), 7.28 – 7.24 (m, 1H), 7.22 – 7.12 (m, 4H), 7.10 – 7.02 (m, 2H), 6.87 (t, J = 8.6 Hz, 4H), 6.69 (dd, J = 9.0, 6.4 Hz, 1H), 6.47 (td, J = 7.4, 1.0 Hz, 1H), 5.12 (d, J_{H-P} = 26.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.6 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 136.5 (d, J_{C-P} = 4.6 Hz), 132.2, 131.6 (d, J_{C-P} = 14.3 Hz), 129.7, 129.6, 129.4, 129.0, 128.8 (d, J_{C-P} = 1.9 Hz), 128.3, 127.5 (d, J_{C-P} = 2.7 Hz), 127.3, 125.4, 125.0 (d, J_{C-P} = 0.8 Hz), 124.9 (d, J_{C-P} = 0.8 Hz), 122.5, 120.7 (d, J_{C-P} = 4.3 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.5, 117.3 (d, J_{C-P} = 1.4 Hz), 115.4 (d, J_{C-P} = 4.4 Hz), 111.0, 106.7 (d, J_{C-P} = 5.9 Hz), 42.6 (d, J_{C-P} = 140.4 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.1 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{27}NO_3P$ $[M+H]^+$: 516.1729; found: 516.1710.

Diphenyl [phenyl(3-(*p*-tolyl)indolizin-1-yl)methyl]phosphonate (89b): Green solid; yield 98%



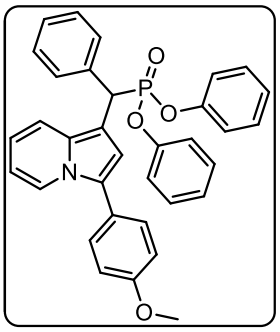
(52 mg); R_f = 0.4 (20% EtOAc in hexane); M.P. 140 – 144 °C; FT-IR 1490, 1273, 1189, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.20 (d, J = 7.1 Hz, 1H), 7.70 (d, J = 7.4 Hz, 2H), 7.43 (d, J = 8.2 Hz, 3H), 7.37 – 7.32 (m, 3H), 7.29 – 7.26 (m, 3H), 7.23 – 7.13 (m, 4H), 7.11 – 7.03 (m, 2H), 6.89 (t, J = 9.4 Hz, 4H), 6.68 (dd, J = 8.5, 6.6 Hz, 1H), 6.46 (t, J = 6.9 Hz, 1H), 5.13 (d, J_{H-P} = 26.2 Hz, 1H), 2.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.7 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 137.2, 136.5 (d, J_{C-P} = 4.6 Hz), 131.4 (d, J_{C-P} = 14.4 Hz), 129.68, 129.66, 129.6, 129.4, 129.3, 128.8 (d, J_{C-P} = 1.9 Hz), 128.2, 127.4 (d, J_{C-P} = 2.7 Hz), 125.5, 125.0 (d, J_{C-P} = 0.8 Hz), 124.8 (d, J_{C-P} = 0.6 Hz), 122.5, 120.7 (d, J_{C-P} = 4.3 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.3, 117.2 (d, J_{C-P} = 1.4 Hz), 115.1 (d, J_{C-P} = 4.4 Hz), 110.8, 106.4 (d, J_{C-P} = 5.9 Hz), 42.6 (d, J_{C-P} = 140.3 Hz), 21.4 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{29}NO_3P$ $[M+H]^+$: 530.1886; found: 530.1866.

Diphenyl [(3-(4-(*tert*-butyl)phenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89c): Yellow

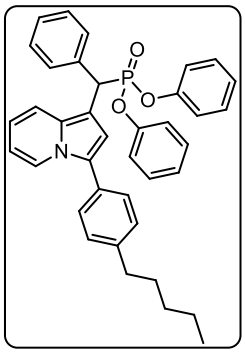


oil; yield 86% (49.0 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1272, 1190, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, J = 7.1 Hz, 1H), 7.72 (d, J = 7.4 Hz, 2H), 7.53 – 7.48 (m, 4H), 7.44 (d, J = 9.0 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.29 (d, J = 7.1 Hz, 1H), 7.24 – 7.15 (m, 4H), 7.12 – 7.05 (m, 2H), 6.93 – 6.88 (m, 4H), 6.69 (dd, J = 8.7, 6.8 Hz, 1H), 6.46 (t, J = 6.9 Hz, 1H), 5.15 (d, J_{H-P} = 26.2 Hz, 1H), 1.41 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.7 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 150.3, 136.5 (d, J_{C-P} = 4.6 Hz), 131.4 (d, J_{C-P} = 14.4 Hz), 129.6 (d, J_{C-P} = 7.6 Hz), 129.5, 129.4, 129.3, 128.8 (d, J_{C-P} = 1.8 Hz), 127.9, 127.4 (d, J_{C-P} = 2.7 Hz), 125.9, 125.4, 125.0, 124.8, 122.6, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.3, 117.2 (d, J_{C-P} = 1.2 Hz), 115.2 (d, J_{C-P} = 4.3 Hz), 110.8, 106.4 (d, J_{C-P} = 5.9 Hz), 42.6 (d, J_{C-P} = 140.4 Hz), 34.8, 31.4 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm.; HRMS (ESI): *m/z* calcd for $C_{37}H_{35}NO_3P$ $[M+H]^+$: 572.2355; found: 572.2330.

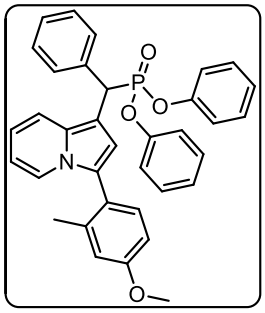
Diphenyl [(3-(4-methoxyphenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89d): Green solid; yield 91% (49.6 mg); R_f = 0.2 (20% EtOAc in hexane); M.P. 152 – 154 °C; FT-IR 1489, 1251, 1188, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.14 (d, J = 7.2 Hz, 1H), 7.71 – 7.69 (m, 2H), 7.46 – 7.41(m, 3H), 7.35 (t, J = 7.5 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.23 – 7.19 (m, 2H), 7.17 – 7.13 (m, 2H), 7.11 – 7.03 (m, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.91 – 6.86 (m, 4H), 6.67 (dd, J = 9.0, 6.4 Hz, 1H), 6.45 (td, J = 7.3, 1.1 Hz, 1H), 5.13 (d, J_{H-P} = 26.1 Hz, 1H), 3.87 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.0, 150.8 (d, J_{C-P} = 9.7 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 136.5 (d, J_{C-P} = 4.6 Hz), 131.1 (d, J_{C-P} = 14.4 Hz), 129.8, 129.6, 129.5, 129.4, 128.8 (d, J_{C-P} = 1.8 Hz), 127.4 (d, J_{C-P} = 2.7 Hz), 125.2, 125.0 (d, J_{C-P} = 0.6 Hz), 124.8 (d, J_{C-P} = 0.6 Hz), 124.6, 122.4, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.2 (d, J_{C-P} = 1.5 Hz), 117.1, 114.9 (d, J_{C-P} = 4.3 Hz), 114.4, 110.8, 106.3 (d, J_{C-P} = 5.9 Hz), 55.5, 42.6 (d, J_{C-P} = 140.4 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{29}NO_4P$ $[M+H]^+$: 546.1835; found: 546.1816.



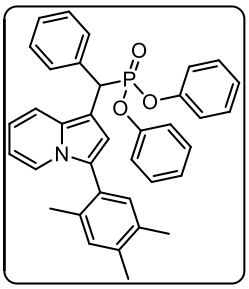
Diphenyl [(3-(4-pentylphenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89e): Green thick oil; yield 96% (56.4 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1274, 1189, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, J = 7.1 Hz, 1H), 7.73 – 7.71 (m, 2H), 7.47 – 7.42 (m, 3H), 7.38 – 7.34 (m, 3H), 7.31 – 7.28 (m, 3H), 7.24 – 7.20 (m, 2H), 7.18 – 7.14 (m, 2H), 7.12 – 7.04 (m, 2H), 6.92 – 6.88 (m, 4H), 6.68 (dd, J = 9.0, 6.4 Hz, 1H), 6.46 (td, J = 7.3, 1.0 Hz, 1H), 5.15 (d, J_{H-P} = 26.2 Hz, 1H), 2.68 (t, J = 7.6 Hz, 2H), 1.70 (quintet, J = 7.3 Hz, 2H), 1.43 – 1.36 (m, 4H), 0.95 (t, J = 6.8 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.7 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 142.2, 136.5 (d, J_{C-P} = 4.6 Hz), 131.3 (d, J_{C-P} = 14.3 Hz), 129.6 (d, J_{C-P} = 7.6 Hz), 129.5, 129.4, 129.4 (d, J_{C-P} = 0.4 Hz), 129.0, 128.8 (d, J_{C-P} = 1.9 Hz), 128.2, 127.4 (d, J_{C-P} = 2.7 Hz), 125.5, 125.0 (d, J_{C-P} = 0.6 Hz), 124.8 (d, J_{C-P} = 0.4 Hz), 122.6, 120.7 (d, J_{C-P} = 4.3 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.2, 117.1 (d, J_{C-P} = 1.2 Hz), 115.1 (d, J_{C-P} = 4.3 Hz), 110.8, 106.4 (d, J_{C-P} = 5.9 Hz), 42.6 (d, J_{C-P} = 140.4 Hz), 35.8, 31.7, 31.3, 22.7, 14.2 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{38}H_{37}NO_3P$ $[M+H]^+$: 586.2512; found: 586.2488.



Diphenyl [(3-(4-methoxy-2-methylphenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89f):

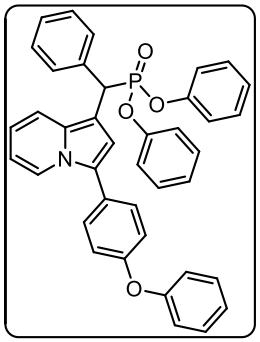


Green solid; yield 90% (50 mg); R_f = 0.4 (20% EtOAc in hexane); M.P. 145 – 147 °C; FT-IR 1490, 1273, 1190, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.72 – 7.71 (m, 2H), 7.52 (d, J = 7.1 Hz, 1H), 7.44 (d, J = 9.1 Hz, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.30 – 7.28 (m, 1H), 7.25 – 7.19 (m, 4H), 7.17 – 7.13 (m, 2H), 7.11 – 7.03 (m, 2H), 6.92 – 6.89 (m, 3H), 6.86 – 6.82 (m, 3H), 6.67 (dd, J = 9.2, 6.6 Hz, 1H), 6.43 (td, J = 7.3, 1.0 Hz, 1H), 5.18 (d, J_{H-P} = 26.2 Hz, 1H), 3.86 (s, 3H), 2.09 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.7, 150.8 (d, J_{C-P} = 9.8 Hz), 150.7 (d, J_{C-P} = 10.1 Hz), 139.9, 136.6 (d, J_{C-P} = 4.5 Hz), 132.6, 130.4 (d, J_{C-P} = 14.3 Hz), 129.7 (d, J_{C-P} = 7.4 Hz), 129.6 (d, J_{C-P} = 0.5 Hz), 129.4 (d, J_{C-P} = 0.4 Hz), 128.8 (d, J_{C-P} = 1.9 Hz), 127.4 (d, J_{C-P} = 2.7 Hz), 125.0 (d, J_{C-P} = 0.8 Hz), 124.8 (d, J_{C-P} = 0.6 Hz), 124.2, 123.7, 122.8, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 116.9 (d, J_{C-P} = 1.4 Hz), 116.8, 115.8, 115.5 (d, J_{C-P} = 1.2 Hz), 111.4, 110.4, 105.5 (d, J_{C-P} = 6.0 Hz), 55.4, 42.7 (d, J_{C-P} = 140.6 Hz), 20.1 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.3 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{31}NO_4P$ $[M+H]^+$: 560.1991; found: 560.1972.

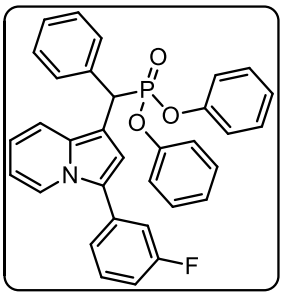


Diphenyl [phenyl(3-(2,4,5-trimethylphenyl)indolizin-1-yl)methyl]phosphonate (89g): dark brown thick oil; yield 98% (54.6 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1273, 1190, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, J = 7.5 Hz, 2H), 7.55 (d, J = 7.0 Hz, 1H), 7.44 (d, J = 9.0 Hz, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.29 (d, J = 7.0 Hz, 1H), 7.26 – 7.20 (m, 3H), 7.17 – 7.03 (m, 6H), 6.92 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.69 – 6.66 (m, 1H), 6.43 (t, J = 6.8 Hz, 1H), 5.18 (d, J_{H-P} = 26.2 Hz, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 2.06 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, J_{C-P} = 9.8 Hz), 150.7 (d, J_{C-P} = 10.1 Hz), 136.9, 136.7 (d, J_{C-P} = 4.5 Hz), 135.3, 134.2, 132.5, 131.8, 130.4 (d, J_{C-P} = 14.4 Hz), 129.7, 129.65 (d, J_{C-P} = 7.4 Hz), 129.6, 129.4, 128.7 (d, J_{C-P} = 1.8 Hz), 128.6, 127.3 (d, J_{C-P} = 2.7 Hz), 124.9, 124.8 (d, J_{C-P} = 0.4 Hz), 124.6, 123.0, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.0 (d, J_{C-P} = 1.4 Hz), 116.8, 115.5 (d, J_{C-P} = 4.4 Hz), 110.4, 105.5 (d, J_{C-P} = 6.0 Hz), 42.7 (d, J_{C-P} = 140.4 Hz), 19.6, 19.3 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.3 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{33}NO_3P$ $[M+H]^+$: 558.2199; found: 558.2180.

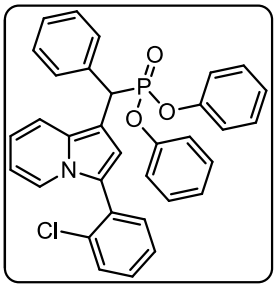
Diphenyl [(3-(4-phenoxyphenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89h): Green thick oil; yield 89% (54.0 mg); R_f = 0.3 (20% EtOAc in hexane); FT-IR 1490, 1238, 1188, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.19 (d, J = 7.2 Hz, 1H), 7.73 – 7.71 (d, J = 7.6 Hz, 2H), 7.48 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 9.1 Hz, 1H), 7.42 – 7.33 (m, 5H), 7.31 – 7.26 (m, 1H), 7.22 (t, J = 7.7 Hz, 2H), 7.18 – 7.14 (m, 3H), 7.13 – 7.04 (m, 6H), 6.92 – 6.87 (m, 4H), 6.70 (dd, J = 9.0, 6.4 Hz, 1H), 6.48 (td, J = 7.4, 1.1 Hz, 1H), 5.16 (d, J_{H-P} = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.0, 156.7, 150.8 (d, J_{C-P} = 9.1 Hz), 150.7 (d, J_{C-P} = 9.8 Hz), 136.5 (d, J_{C-P} = 4.6 Hz), 131.4 (d, J_{C-P} = 14.3 Hz), 130.0, 129.8, 129.6, 129.5, 129.4, 128.8 (d, J_{C-P} = 1.8 Hz), 127.5 (d, J_{C-P} = 2.7 Hz), 127.1, 125.0 (d, J_{C-P} = 0.5 Hz), 124.9 (d, J_{C-P} = 0.6 Hz), 124.8, 123.6, 122.4, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 119.2 (d, J_{C-P} = 4.6 Hz), 117.3, 117.2 (d, J_{C-P} = 1.1 Hz), 115.6, 115.2 (d, J_{C-P} = 4.4 Hz), 111.0, 106.5 (d, J_{C-P} = 5.9 Hz), 42.6 (d, J_{C-P} = 140.5 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{31}NO_4P$ $[M+H]^+$: 608.1991; found: 608.1966.



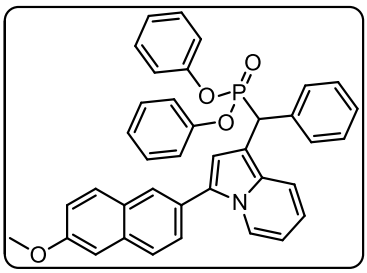
Diphenyl [(3-(3-fluorophenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89i): Green solid; yield 89% (54.0 mg); R_f = 0.4 (20% EtOAc in hexane); M.P. 150 – 152 °C; FT-IR 1490, 1267, 1189, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, J = 7.1 Hz, 1H), 7.69 (d, J = 7.4 Hz, 2H), 7.45 (d, J = 9.0 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.36 (s, 1H), 7.33 – 7.26 (m, 3H), 7.23 – 7.14 (m, 5H), 7.11 – 7.00 (m, 3H), 6.89 (dd, J = 7.7, 4.1 Hz, 4H), 6.72 (dd, J = 9.0, 6.5 Hz, 1H), 6.51 (t, J = 6.9 Hz, 1H), 5.13 (d, J_{H-P} = 26.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.2 (d, J_{C-F} = 244.7 Hz), 150.8 (d, J_{C-P} = 9.6 Hz), 150.7 (d, J_{C-P} = 9.9 Hz), 136.3 (d, J = 4.7 Hz), 134.2 (d, J = 8.3 Hz), 132.0 (d, J_{C-P} = 14.3 Hz), 130.6 (d, J_{C-F} = 8.7 Hz), 129.62, 129.6, 129.5, 129.4, 128.9 (d, J_{C-P} = 1.8 Hz), 127.5 (d, J_{C-P} = 2.7 Hz), 125.0 (d, J_{C-P} = 0.9 Hz), 124.9 (d, J_{C-P} = 0.6 Hz), 123.7 (d, J_{C-P} = 2.8 Hz), 122.4, 120.6 (d, J_{C-P} = 4.3 Hz), 120.5 (d, J_{C-P} = 4.2 Hz), 117.9, 117.3 (d, J_{C-P} = 1.4 Hz), 115.8 (d, J_{C-P} = 4.4 Hz), 114.7 (d, J_{C-F} = 22.0 Hz), 114.1 (d, J_{C-F} = 21.0 Hz), 111.4, 107.0 (d, J_{C-P} = 5.8 Hz), 42.5 (d, J_{C-P} = 140.6 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.4 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.0 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{26}FNO_3P$ $[M+H]^+$: 534.1635; found: 534.1615.



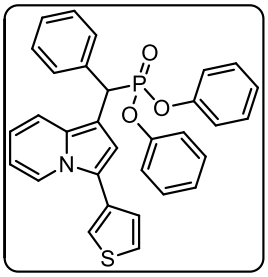
Diphenyl [(3-(2-chlorophenyl)indolizin-1-yl)(phenyl)methyl]phosphonate (89j): Green thick oil; yield 83% (45.6 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1272, 1162, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.72 – 7.70 (m, 2H), 7.61 (d, J = 7.1 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.45 (d, J = 9.1 Hz, 1H), 7.43 – 7.41 (m, 1H), 7.38 – 7.33 (m, 5H), 7.30 – 7.28 (m, 1H), 7.23 – 7.19 (m, 2H), 7.16 – 7.12 (m, 2H), 7.11 – 7.02 (m, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 6.73 (dd, J = 9.0, 6.5 Hz, 1H), 6.50 (td, J = 7.4, 1.0 Hz, 1H), 5.16 (d, $J_{H\text{-}P}$ = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.0 Hz), 136.5 (d, $J_{C\text{-}P}$ = 4.6 Hz), 134.7, 133.2, 131.3 (d, $J_{C\text{-}P}$ = 14.2 Hz), 131.0, 130.1, 129.7 (d, $J_{C\text{-}P}$ = 7.4 Hz), 129.6 (d, $J_{C\text{-}P}$ = 0.5 Hz), 129.5, 129.5, 128.8 (d, $J_{C\text{-}P}$ = 1.9 Hz), 127.4 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.1, 125.0 (d, $J_{C\text{-}P}$ = 0.8 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.8 Hz), 123.6, 122.3, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 117.7, 116.9 (d, $J_{C\text{-}P}$ = 1.4 Hz), 116.5 (d, $J_{C\text{-}P}$ = 4.4 Hz), 110.6, 106.0 (d, $J_{C\text{-}P}$ = 5.9 Hz), 42.6 (d, $J_{C\text{-}P}$ = 140.5 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{26}ClNO_3P$ $[M+H]^+$: 550.1340; found: 550.1322.



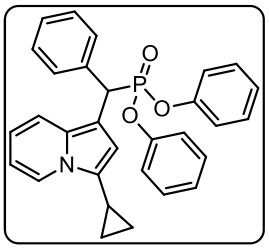
Diphenyl [(3-(6-methoxynaphthalen-2-yl)indolizin-1-yl)(phenyl)methyl]phosphonate (89k): Dark brown thick oil; yield 95% (56.5 mg); R_f = 0.2 (20% EtOAc in hexane); FT-IR 1490, 1270, 1217, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, J = 7.2 Hz, 1H), 7.90 (s, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.73 – 7.71 (m, 2H), 7.61 (dd, J = 8.5, 1.7 Hz, 1H), 7.45 (d, J = 9.1 Hz, 1H), 7.42 (s, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.30 – 7.28 (m, 1H), 7.24 – 7.14 (m, 6H), 7.11 – 7.03 (m, 2H), 6.90 (t, J = 8.3 Hz, 4H), 6.71 (dd, J = 9.1, 6.4 Hz, 1H), 6.49 (td, J = 7.3, 1.0 Hz, 1H), 5.16 (d, $J_{H\text{-}P}$ = 26.2 Hz, 1H), 3.96 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 150.9 (d, $J_{C\text{-}P}$ = 9.5 Hz), 150.8 (d, $J_{C\text{-}P}$ = 9.9 Hz), 136.5 (d, $J_{C\text{-}P}$ = 4.6 Hz), 133.8, 131.6 (d, $J_{C\text{-}P}$ = 14.4 Hz), 129.7 (d, $J_{C\text{-}P}$ = 7.5 Hz), 129.6, 129.5, 129.4, 129.2, 128.8 (d, $J_{C\text{-}P}$ = 1.9 Hz), 127.5, 127.4, 127.3, 127.0, 126.7, 125.6, 125.0 (d, $J_{C\text{-}P}$ = 0.6 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.5 Hz), 122.5, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.2 Hz), 119.4, 117.5, 117.3 (d, $J_{C\text{-}P}$ = 1.3 Hz), 115.5 (d, $J_{C\text{-}P}$ = 4.4 Hz), 111.0, 106.7 (d, $J_{C\text{-}P}$ = 5.8 Hz), 105.9, 55.5, 42.6 (d, $J_{C\text{-}P}$ = 140.4 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{38}H_{31}NO_4P$ $[M+H]^+$: 596.1991; found: 596.1967.



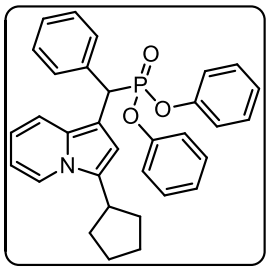
Diphenyl [phenyl(3-(thiophen-3-yl)indolizin-1-yl)methyl]phosphonate (89l): Green solid; yield 82% (42.7 mg); R_f = 0.2 (20% EtOAc in hexane); M.P. 133 – 135 °C; FT-IR 1490, 1271, 1189, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.19 (d, J = 7.1 Hz, 1H), 7.67 (d, J = 7.5 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.35 – 7.30 (m, 4H), 7.28 – 7.24 (m, 1H), 7.22 – 7.13 (m, 4H), 7.10 – 7.03 (m, 2H), 6.87 (dd, J = 7.7, 3.9 Hz, 4H), 6.69 (dd, J = 8.6, 6.6 Hz, 1H), 6.51 (t, J = 6.8 Hz, 1H), 5.11 (d, J_{H-P} = 26.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.7 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 136.5 (d, J_{C-P} = 4.7 Hz), 132.6, 131.3 (d, J_{C-P} = 14.5 Hz), 129.7, 129.6, 129.4, 128.8 (d, J_{C-P} = 1.9 Hz), 127.7, 127.5 (d, J_{C-P} = 2.7 Hz), 126.1, 125.0 (d, J_{C-P} = 0.7 Hz), 124.9 (d, J_{C-P} = 0.7 Hz), 122.9, 121.2, 120.9, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.3, 117.2 (d, J_{C-P} = 1.5 Hz), 115.3 (d, J_{C-P} = 4.4 Hz), 111.1, 106.4 (d, J_{C-P} = 5.8 Hz), 42.5 (d, J_{C-P} = 141.4 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.1 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{25}NO_3PS$ $[M+H]^+$: 522.1294; found: 522.1274.



Diphenyl [(3-cyclopropylindolizin-1-yl)(phenyl)methyl]phosphonate (89m): Green thick oil; yield 71% (31.9 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1273, 1190, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.01 (d, J = 7.0 Hz, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.36 – 7.30 (m, 3H), 7.26 – 7.17 (m, 3H), 7.14 – 7.06 (m, 3H), 7.05 – 7.01 (m, 1H), 6.97 (s, 1H), 6.86 (d, J = 7.7 Hz, 2H), 6.78 (d, J = 7.7 Hz, 2H), 6.68 – 6.64 (m, 1H), 6.52 (t, J = 6.7 Hz, 1H), 5.06 (d, J_{H-P} = 26.2 Hz, 1H), 1.83 – 1.76 (m, 1H), 0.94 (d, J = 8.1 Hz, 2H), 0.70 – 0.57 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, J_{C-P} = 9.6 Hz), 150.7 (d, J_{C-P} = 10.0 Hz), 136.7 (d, J_{C-P} = 4.3 Hz), 130.3 (d, J_{C-P} = 14.4 Hz), 129.6 (d, J_{C-P} = 3.9 Hz), 129.5 (d, J_{C-P} = 3.0 Hz), 129.3 (d, J_{C-P} = 0.5 Hz), 128.7 (d, J_{C-P} = 1.9 Hz), 127.3 (d, J_{C-P} = 2.7 Hz), 126.1, 124.9 (d, J_{C-P} = 0.9 Hz), 124.8 (d, J_{C-P} = 0.8 Hz), 122.5, 120.7 (d, J_{C-P} = 4.3 Hz), 120.5 (d, J_{C-P} = 4.2 Hz), 116.8 (d, J_{C-P} = 1.7 Hz), 116.6 (d, J_{C-P} = 0.7 Hz), 113.0 (d, J_{C-P} = 4.3 Hz), 110.1, 104.3 (d, J_{C-P} = 6.0 Hz), 42.6 (d, J_{C-P} = 140.2 Hz), 6.3, 5.6, 5.4 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.3 ppm. HRMS (ESI): *m/z* calcd for $C_{30}H_{27}NO_3P$ $[M+H]^+$: 480.1729; found: 480.1712.

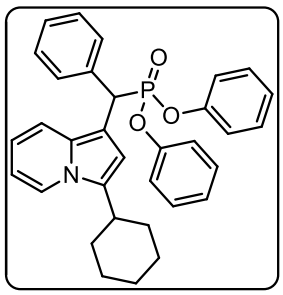


Diphenyl [(3-cyclopentylindolizin-1-yl)(phenyl)methyl]phosphonate (89n): Dark brown solid; yield 70% (35.5 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 104 – 106 °C; FT-IR 1490, 1273, 1190, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.74 (d, J = 7.0 Hz, 1H), 7.64 (d, J = 7.4

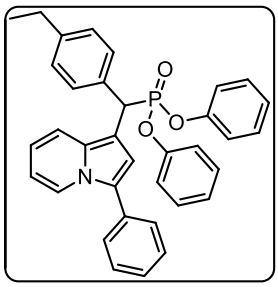


Hz, 2H), 7.36 – 7.30 (m, 3H), 7.26 – 7.18 (m, 3H), 7.13 – 7.08 (m, 3H), 7.06 – 7.00 (m, 1H), 7.04 (s, 1H), 6.88 (d, J = 7.7 Hz, 2H), 6.78 (d, J = 7.7 Hz, 2H), 6.63 – 6.59 (m, 1H), 6.47 (t, J = 6.8 Hz, 1H), 5.08 (d, $J_{H\text{-}P}$ = 26.3 Hz, 1H), 3.22 (q, J = 7.6 Hz, 1H), 2.14 – 2.10 (m, 2H), 1.79 – 1.61 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.1 Hz), 136.8 (d, $J_{C\text{-}P}$ = 4.4 Hz), 130.4 (d, $J_{C\text{-}P}$ = 14.5 Hz), 129.6, 129.5, 129.3 (d, $J_{C\text{-}P}$ = 0.4 Hz), 128.8, 128.7 (d, $J_{C\text{-}P}$ = 1.9 Hz), 127.3 (d, $J_{C\text{-}P}$ = 2.7 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.9 Hz), 124.7 (d, $J_{C\text{-}P}$ = 0.8 Hz), 122.4, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.1 Hz), 116.9 (d, $J_{C\text{-}P}$ = 1.7 Hz), 115.9 (d, $J_{C\text{-}P}$ = 0.7 Hz), 111.1 (d, $J_{C\text{-}P}$ = 4.3 Hz), 110.1, 104.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 42.6 (d, $J_{C\text{-}P}$ = 140.1 Hz), 36.5, 31.4 (d, $J_{C\text{-}P}$ = 8.3 Hz), 25.2 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.4 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{31}NO_3P$ $[M+H]^+$: 508.2042; found: 508.2049.

Diphenyl [(3-cyclohexylindolizin-1-yl)(phenyl)methyl]phosphonate (89o): Dark brown oil;



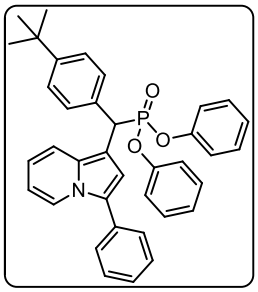
yield 86% (44.8 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1271, 1190, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.73 (d, J = 7.1 Hz, 1H), 7.65 (d, J = 7.5 Hz, 2H), 7.37 – 7.31 (m, 3H), 7.27 – 7.25 (m, 1H), 7.20 (t, J = 7.8 Hz, 2H), 7.14 – 7.08 (m, 3H), 7.07 – 7.01 (m, 1H), 7.03 (s, 1H), 6.89 (d, J = 7.8 Hz, 2H), 6.78 (d, J = 7.8 Hz, 2H), 6.59 (dd, J = 8.4, 6.5 Hz, 1H), 6.46 (t, J = 6.9 Hz, 1H), 5.09 (d, $J_{H\text{-}P}$ = 26.3 Hz, 1H), 2.80 – 2.74 (m, 1H), 2.05 (brs, 2H), 1.88 – 1.78 (m, 3H), 1.55 – 1.27 (m, 5H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.8 (d, $J_{C\text{-}P}$ = 10.1 Hz), 136.8 (d, $J_{C\text{-}P}$ = 4.2 Hz), 130.0, 129.6, 129.6, 129.5, 129.3, 128.7 (d, $J_{C\text{-}P}$ = 1.9 Hz), 127.3 (d, $J_{C\text{-}P}$ = 2.7 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.6 Hz), 124.7 (d, $J_{C\text{-}P}$ = 0.7 Hz), 122.0, 120.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.2 Hz), 117.1 (d, $J_{C\text{-}P}$ = 1.3 Hz), 115.8, 110.9, 110.1, 104.8, 42.7 (d, $J_{C\text{-}P}$ = 140.1 Hz), 35.4, 31.8 (d, $J_{C\text{-}P}$ = 8.1 Hz), 26.7, 26.5 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.4 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{33}NO_3P$ $[M+H]^+$: 522.2199; found: 522.2217.



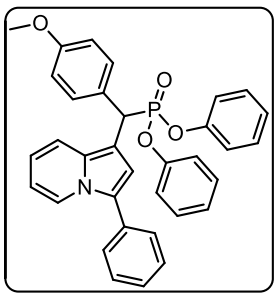
Diphenyl [(4-ethylphenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89p): Green semi- solid; yield 91% (49.4 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1272, 1189, 932 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 7.2 Hz, 1H), 7.59 (dd, J = 8.2, 2.1 Hz, 2H), 7.54 – 7.51 (m, 2H), 7.47 – 7.42 (m, 3H), 7.33 (s, 1H), 7.35

– 7.31 (m, 1H), 7.21 – 7.12 (m, 6H), 7.10 – 7.02 (m, 2H), 6.89 – 6.85 (m, 4H), 6.68 (dd, J = 9.1, 6.4 Hz, 1H), 6.46 (td, J = 7.4, 1.2 Hz, 1H), 5.09 (d, $J_{H\text{-}P}$ = 26.1 Hz, 1H), 2.62 (q, J = 7.6 Hz, 2H), 1.21 (t, J = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.8 (d, $J_{C\text{-}P}$ = 10.0 Hz), 143.5 (d, $J_{C\text{-}P}$ = 3.0 Hz), 133.6 (d, $J_{C\text{-}P}$ = 4.8 Hz), 132.3, 131.5 (d, $J_{C\text{-}P}$ = 14.4 Hz), 129.5 (d, $J_{C\text{-}P}$ = 0.5 Hz), 129.5 (d, $J_{C\text{-}P}$ = 7.4 Hz), 129.4 (d, $J_{C\text{-}P}$ = 0.4 Hz), 129.0, 128.3 (d, $J_{C\text{-}P}$ = 1.9 Hz), 128.2, 127.3, 125.4, 124.9, 124.8 (d, $J_{C\text{-}P}$ = 0.8 Hz), 122.5, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, J = 4.2 Hz), 117.4, 117.3 (d, $J_{C\text{-}P}$ = 1.4 Hz), 115.4 (d, $J_{C\text{-}P}$ = 4.4 Hz), 110.9, 106.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 42.2 (d, $J_{C\text{-}P}$ = 140.4 Hz), 28.6, 15.8 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.3 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{31}NO_3P$ $[M+H]^+$: 544.2042; found: 544.2036.

Diphenyl [(4-(*tert*-butyl)phenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89q): dark brown oil; yield 86% (49.1 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1491, 1271, 1190, 932 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, J = 7.2 Hz, 1H), 7.62 (dd, J = 8.4, 2.1 Hz, 2H), 7.54 (d, J = 7.2 Hz, 2H), 7.47 (t, J = 7.8 Hz, 3H), 7.37 – 7.32 (m, 4H), 7.21 – 7.13 (m, 4H), 7.09 – 7.03 (m, 2H), 6.86 (dd, J = 10.4, 8.9 Hz, 4H), 6.69 (dd, J = 9.0, 6.4 Hz, 1H), 6.47 (t, J = 6.4 Hz, 1H), 5.11 (d, $J_{H\text{-}P}$ = 26.1 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 10.0 Hz), 150.8 (d, $J_{C\text{-}P}$ = 9.7 Hz), 150.3 (d, $J_{C\text{-}P}$ = 3.0 Hz), 133.2 (d, $J_{C\text{-}P}$ = 4.7 Hz), 132.2, 131.5 (d, $J_{C\text{-}P}$ = 14.4 Hz), 129.5, 129.4, 129.3 (d, $J_{C\text{-}P}$ = 7.4 Hz), 129.0, 128.2, 127.3, 125.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 125.4, 124.9 (d, $J_{C\text{-}P}$ = 0.6 Hz), 124.8 (d, $J_{C\text{-}P}$ = 0.7 Hz), 122.5, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.2 Hz), 117.4, 117.3 (d, $J_{C\text{-}P}$ = 1.5 Hz), 115.4 (d, $J_{C\text{-}P}$ = 4.4 Hz), 110.9, 106.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 42.2 (d, $J_{C\text{-}P}$ = 140.2 Hz), 34.6, 31.4 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.4 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{35}NO_3P$ $[M+H]^+$: 572.2355; found: 572.2379.

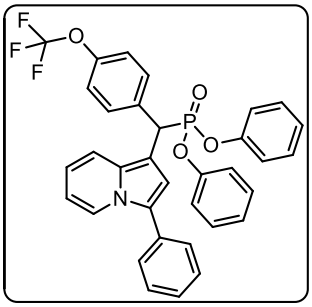


Diphenyl [(4-methoxyphenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89r): Green semi-solid; yield 82% (44.7 mg); R_f = 0.2 (20 % EtOAc in hexane); FT-IR 1490, 1252, 1187, 931 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, J = 7.2 Hz, 1H), 7.59 (dd, J = 8.8, 2.1 Hz, 2H), 7.54 – 7.51 (m, 2H), 7.48 – 7.40 (m, 3H), 7.36 – 7.31 (m, 1H), 7.31 (s, 1H), 7.23 – 7.19 (m, 2H), 7.16 – 7.12 (m, 2H), 7.11 – 7.07 (m, 1H), 7.06 – 7.02 (m, 1H), 6.93 – 6.91(m, 2H), 6.88 – 6.85 (m, 4H), 6.68 (dd, J = 9.1, 6.4 Hz, 1H), 6.46 (td,



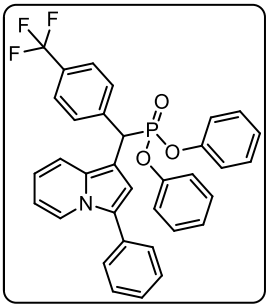
J = 7.4, 1.2 Hz, 1H), 5.07 (d, J_{H-P} = 26.1 Hz, 1H), 3.78 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.9 (d, J_{C-P} = 2.7 Hz), 150.9 (d, J_{C-P} = 9.8 Hz), 150.8 (d, J_{C-P} = 10.1 Hz), 132.2, 131.5 (d, J_{C-P} = 14.4 Hz), 130.7 (d, J_{C-P} = 7.4 Hz), 129.6, 129.4, 129.0, 128.5 (d, J_{C-P} = 4.8 Hz), 128.2, 127.3, 125.4, 125.0, 124.8, 122.5, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 117.4, 117.3 (d, J_{C-P} = 1.4 Hz), 115.3 (d, J_{C-P} = 3.9 Hz), 114.2 (d, J_{C-P} = 1.7 Hz), 110.9, 107.0 (d, J_{C-P} = 5.4 Hz), 55.4 (d, J_{C-P} = 2.6 Hz), 41.7 (d, J_{C-P} = 141.1 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.4 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{29}NO_4P$ $[M+H]^+$: 546.1835; found: 546.1831.

Diphenyl [(3-phenylindolizin-1-yl)(4-(trifluoromethoxy)phenyl)methyl]phosphonate (89s):



Green solid; yield 90% (53.9 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 125 – 127 °C; FT-IR 1490, 1262, 1214, 934 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, J = 7.1 Hz, 1H), 7.71(d, J = 8.4 Hz, 2H), 7.53 (d, J = 7.4 Hz, 2H), 7.47 (t, J = 7.1 Hz, 2H), 7.41 (d, J = 9.0 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.32 (s, 1H), 7.24 – 7.03 (m, 8H), 6.91 (d, J = 7.8 Hz, 2H), 6.86 (d, J = 7.8 Hz, 2H), 6.74 – 6.70 (m, 1H), 6.50 (t, J = 6.6 Hz, 1H), 5.14 (d, J_{H-P} = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.7 (d, J_{C-P} = 9.7 Hz,), 150.6 (d, J_{C-P} = 9.9 Hz), 148.6 – 148.5 (m), 135.3 (d, J_{C-P} = 4.5 Hz), 132.0, 131.6 (d, J_{C-P} = 14.4 Hz), 131.0 (d, J_{C-P} = 7.2 Hz), 129.7, 129.5 (d, J_{C-P} = 4.2 Hz), 129.1, 128.3, 127.5, 125.7, 125.1 (d, J_{C-P} = 0.7 Hz), 125.0 (d, J_{C-P} = 0.8 Hz), 122.6, 121.3, 120.6 (q, J_{C-F} = 255 Hz), 120.5 (d, J_{C-P} = 4.4 Hz), 120.5 (d, J_{C-P} = 4.3 Hz), 117.8, 117.0 (d, J_{C-P} = 1.4 Hz), 115.2 (d, J_{C-P} = 4.3 Hz), 111.1, 106.0 (d, J_{C-P} = 5.9 Hz), 41.9 (d, J_{C-P} = 140.9 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.8 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 17.4 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{26}F_3NO_4P$ $[M+H]^+$: 600.1552; found: 600.1528.

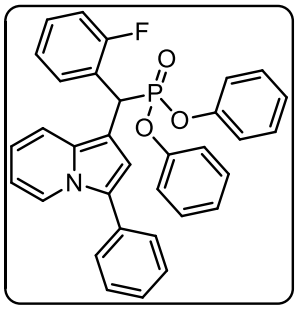
Diphenyl [(3-phenylindolizin-1-yl)(4-(trifluoromethyl)phenyl)methyl]phosphonate (89t):



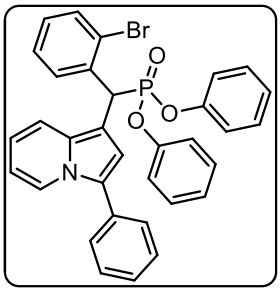
Light green solid; yield 79% (46.1 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 122–125 °C; FT-IR 1490, 1326, 1163, 935 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, J = 7.1 Hz, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 8.1 Hz, 2H), 7.54 – 7.52 (m, 2H), 7.50 – 7.46 (m, 2H), 7.42 (d, J = 9.0 Hz, 1H), 7.38 – 7.36 (m, 1H), 7.34 (s, 1H), 7.26 – 7.22 (m, 2H), 7.19 – 7.11 (m, 3H), 7.08 – 7.05 (m, 1H), 6.96 (d, J = 7.9 Hz, 2H), 6.87 (d, J =

7.9 Hz, 2H), 6.73 (dd, J = 8.9, 6.4 Hz, 1H), 6.51 (t, J = 6.7 Hz, 1H), 5.22 (d, $J_{H\text{-}P}$ = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.7 (d, $J_{C\text{-}P}$ = 9.7 Hz), 150.5 (d, $J_{C\text{-}P}$ = 10.0 Hz), 140.7 (dd, $J_{C\text{-}F}$ = 4.2, $J_{C\text{-}P}$ = 1.1 Hz), 131.9, 131.6 (d, $J_{C\text{-}P}$ = 14.2 Hz), 130.0, 129.9, 129.7, 129.5 (d, $J_{C\text{-}P}$ = 0.4 Hz), 129.1, 128.3, 127.5, 125.8 – 125.7 (m), 125.2 (d, $J_{C\text{-}P}$ = 0.6 Hz), 125.1 (d, $J_{C\text{-}P}$ = 0.7 Hz), 124.2 (q, $J_{C\text{-}F}$ = 271.2 Hz), 122.6, 120.5 (d, J = 4.3 Hz), 120.4 (d, J = 4.2 Hz), 117.9, 116.9 (d, J = 1.3 Hz), 115.5, 115.2 (d, $J_{C\text{-}P}$ = 4.3 Hz), 111.1, 105.6 (d, $J_{C\text{-}P}$ = 6.2 Hz), 42.4 (d, $J_{C\text{-}P}$ = 140.9 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.5 (d, $J_{F\text{-}P}$ = 1.8 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 16.9 (d, $J_{P\text{-}F}$ = 1.6 Hz) ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{26}F_3NO_3P$ $[M+H]^+$: 584.1603; found: 584.1625.

Diphenyl [(2-fluorophenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89u): Brown thick oil; yield 82% (43.7 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1272, 1188, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 7.2 Hz, 1H), 8.01 (tt, J = 7.7, 2.0 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.48 – 7.44 (m, 2H), 7.37 (d, J = 1.0 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.24 – 7.20 (m, 3H), 7.17 – 7.03 (m, 6H), 6.97 – 6.95 (m, 2H), 6.90 – 6.88 (m, 2H), 6.72 (dd, J = 9.1, 6.4 Hz, 1H), 6.48 (td, J = 7.4, 1.4 Hz, 1H), 5.60 (d, $J_{H\text{-}P}$ = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.2 (dd, $J_{C\text{-}F}$ = 244.1, $J_{C\text{-}P}$ = 9.6 Hz), 150.8 (d, $J_{C\text{-}P}$ = 9.6 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.0 Hz), 132.1, 131.7 (d, $J_{C\text{-}P}$ = 14.4 Hz), 131.3 (dd, J = 4.8, 2.6 Hz), 129.6, 129.4 (d, $J_{C\text{-}P}$ = 0.4 Hz), 129.1 (d, J = 2.6 Hz), 129.0, 128.2, 127.4, 125.5, 125.0 (d, $J_{C\text{-}P}$ = 0.6 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.8 Hz), 124.7 – 124.6 (m), 124.1 (dd, $J_{C\text{-}F}$ = 14.6, $J_{C\text{-}P}$ = 3.4 Hz), 122.5, 120.6 (d, J = 1.4 Hz), 120.5 (d, J = 1.6 Hz), 117.7, 117.2, 115.5 (dd, $J_{C\text{-}F}$ = 22.6, $J_{C\text{-}P}$ = 1.1 Hz), 115.2 (d, J = 4.1 Hz), 111.1, 105.9 (d, J = 5.5 Hz), 33.2 (dd, $J_{C\text{-}P}$ = 145.4, $J_{C\text{-}F}$ = 4.0 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -118.3 (d, $J_{F\text{-}P}$ = 5.8 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 17.3 (d, $J_{P\text{-}F}$ = 5.6 Hz) ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{26}FNO_3P$ $[M+H]^+$: 534.1635; found: 534.1652.

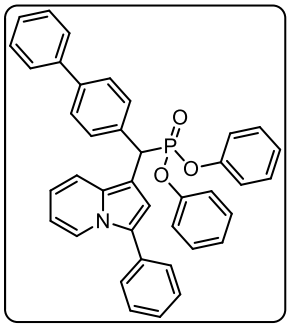


Diphenyl [(2-bromophenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89v): Brown solid; yield 90% (53.5 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 150 – 152 °C; FT-IR 1490, 1272, 1189, 934 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 7.2 Hz, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.53 – 7.51 (m, 2H), 7.46 (t, J = 7.7 Hz, 2H), 7.37 (s, 1H), 7.37 – 7.29



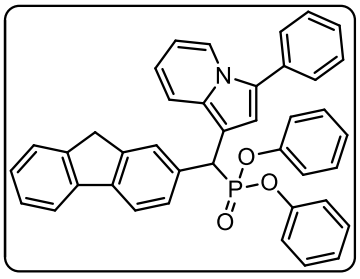
(m, 2H), 7.23 – 7.13 (m, 4H), 7.12 – 7.03 (m, 3H), 6.96 – 6.94 (m, 2H), 6.90 – 6.88 (m, 2H), 6.72 (dd, J = 9.1, 6.4 Hz, 1H), 6.48 (td, J = 7.4, 1.1 Hz, 1H), 5.85 (d, $J_{H\text{-}P}$ = 26.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, $J_{C\text{-}P}$ = 9.6 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.0 Hz), 136.3 (d, $J_{C\text{-}P}$ = 2.3 Hz), 133.0 (d, $J_{C\text{-}P}$ = 1.0 Hz), 132.1, 131.9 (d, $J_{C\text{-}P}$ = 14.5 Hz), 131.7, 131.6, 129.6, 129.4, 129.0, 128.9 (d, $J_{C\text{-}P}$ = 2.5 Hz), 128.2, 128.1 (d, $J_{C\text{-}P}$ = 2.6 Hz), 127.3, 125.6, 125.1, 125.0 (d, $J_{C\text{-}P}$ = 0.8 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.8 Hz), 122.5, 120.5 (d, $J_{C\text{-}P}$ = 4.2 Hz), 120.4 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.7, 115.2 (d, $J_{C\text{-}P}$ = 4.2 Hz), 111.1, 106.1 (d, $J_{C\text{-}P}$ = 5.5 Hz), 40.8 (d, $J_{C\text{-}P}$ = 143.3 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 17.4 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{26}BrNO_3P$ $[M+H]^+$: 594.0834; found: 594.0837.

Diphenyl ([1,1'-biphenyl]-4-yl(3-phenylindolizin-1-yl)methyl)phosphonate (89w): Green



solid; yield 87% (51.4 mg); R_f = 0.4 (20% EtOAc in hexane); M.P. 158 – 160 °C; FT-IR 1488, 1272, 1212, 932 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, J = 7.2 Hz, 1H), 7.75 (dd, J = 8.2, 1.9 Hz, 2H), 7.57 – 7.53 (m, 6H), 7.48 – 7.41 (m, 5H), 7.36 – 7.32 (m, 3H), 7.22 – 7.13 (m, 4H), 7.11 – 7.03 (m, 2H), 6.93 (d, $J_{C\text{-}P}$ = 8.2 Hz, 2H), 6.88 (d, $J_{C\text{-}P}$ = 8.2 Hz, 2H), 6.71 (dd, J = 8.9, 6.6 Hz, 1H), 6.48 (t, J = 6.6 Hz, 1H), 5.16 (d, $J_{H\text{-}P}$ = 26.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.8 (d, $J_{C\text{-}P}$ = 9.6 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.0 Hz), 140.9 (d, $J_{C\text{-}P}$ = 1.0 Hz), 140.3 (d, $J_{C\text{-}P}$ = 3.0 Hz), 135.5 (d, $J_{C\text{-}P}$ = 4.6 Hz), 132.2, 131.6 (d, $J_{C\text{-}P}$ = 14.3 Hz), 130.0, 130.0, 129.6, 129.4, 129.0, 128.9, 128.3, 127.6 (d, $J_{C\text{-}P}$ = 2.0 Hz), 127.4 (d, $J_{C\text{-}P}$ = 4.0 Hz), 127.2, 125.5, 125.0 (d, $J_{C\text{-}P}$ = 0.7 Hz), 124.9, 122.6, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.2 Hz), 117.6, 117.2 (d, $J_{C\text{-}P}$ = 1.4 Hz), 115.4 (d, $J_{C\text{-}P}$ = 4.4 Hz), 111.0, 106.5 (d, $J_{C\text{-}P}$ = 5.8 Hz), 42.3 (d, $J_{C\text{-}P}$ = 140.5 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.0 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{31}NO_3P$ $[M+H]^+$: 592.2042; found: 592.2050.

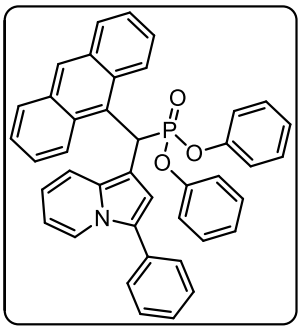
Diphenyl [(9H-fluoren-2-yl)(3-phenylindolizin-1-yl)methyl]phosphonate (89x): Light brown



solid; yield 80% (48.2 mg); R_f = 0.2 (20% EtOAc in hexane); M.P. 162 – 164 °C; FT-IR 1490, 1272, 1190, 932 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, J = 7.1 Hz, 1H), 7.86 (s, 1H), 7.76 (dd, J = 7.5, 4.0 Hz, 2H), 7.70 – 7.68 (m, 1H), 7.54 (t, J = 8.0 Hz, 3H), 7.49 – 7.44 (m, 3H), 7.39 (s, 1H), 7.39 – 7.26 (m, 3H), 7.20 – 7.13 (m, 4H), 7.08 – 7.03 (m, 2H), 6.91 (t, J = 7.1 Hz, 4H), 6.72 – 6.68 (m, 1H), 6.47 (t, J = 6.8 Hz,

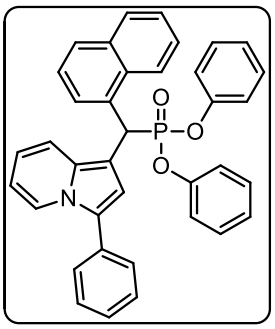
1H), 5.20 (d, J_{H-P} = 26.2 Hz, 1H), 3.87 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, J_{C-P} = 9.9 Hz), 150.8 (d, J_{C-P} = 10.1 Hz), 143.9 (d, J_{C-P} = 2.0 Hz), 143.6, 141.4 (d, J_{C-P} = 1.0 Hz), 141.1 (d, J_{C-P} = 2.9 Hz), 134.9 (d, J_{C-P} = 4.8 Hz), 132.2, 131.6 (d, J_{C-P} = 14.5 Hz), 129.6, 129.4, 129.0, 128.4 (d, J_{C-P} = 7.8 Hz), 128.2, 127.3, 126.8 (d, J_{C-P} = 2.3 Hz), 126.2 (d, J_{C-P} = 7.3 Hz), 125.4, 125.1, 125.0 (d, J_{C-P} = 0.8 Hz), 124.9, 122.5, 120.7 (d, J_{C-P} = 4.2 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 120.1 (d, J_{C-P} = 1.8 Hz), 120.0, 117.5, 117.3 (d, J_{C-P} = 1.3 Hz), 115.4 (d, J_{C-P} = 4.4 Hz), 111.0, 106.9 (d, J_{C-P} = 5.6 Hz), 42.6 (d, J_{C-P} = 140.3 Hz), 37.0 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.2 ppm. HRMS (ESI): *m/z* calcd for $C_{40}H_{31}NO_3P$ $[M+H]^+$: 604.2042; found: 604.2028.

Diphenyl [anthracen-9-yl(3-phenylindolizin-1-yl)methyl]phosphonate (89y): Dark brown



solid; yield 88% (54.1 mg); R_f = 0.4 (20% EtOAc in hexane); M.P. 69 – 71 °C; FT-IR 1490, 1275, 1212, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.10 – 9.08 (m, 1H), 8.54 (d, *J* = 9.0 Hz, 1H), 8.41 (d, *J* = 3.0 Hz, 1H), 8.21 – 8.19 (m, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.90 – 7.88 (m, 1H), 7.73 (s, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.59 – 7.57 (m, 2H), 7.54 – 7.45 (m, 3H), 7.37 – 7.26 (m, 5H), 7.18 – 7.14 (m, 3H), 6.89 – 6.81 (m, 4H), 6.71 – 6.68 (m, 1H), 6.42 – 6.40 (m, 2H), 6.34 – 6.27 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, J_{C-P} = 10.1 Hz), 150.6 (d, J_{C-P} = 9.5 Hz), 132.3, 132.1 (d, J_{C-P} = 3.7 Hz), 131.9 (d, J_{C-P} = 19.3 Hz), 131.7 (d, J_{C-P} = 2.4 Hz), 131.4 (d, J_{C-P} = 4.9 Hz), 130.8, 130.7, 130.1 (d, J_{C-P} = 0.8 Hz), 129.7, 129.1, 129.0, 128.8 (d, J_{C-P} = 4.9 Hz), 128.6, 128.3, 128.1, 128.0, 127.3, 127.0, 125.3, 125.2, 124.7, 124.7, 124.4, 123.3, 122.4, 121.1 (d, J_{C-P} = 4.2 Hz), 119.7 (d, J_{C-P} = 4.5 Hz), 117.8, 117.1, 116.0 (d, J_{C-P} = 4.5 Hz), 110.8, 107.9 (d, J_{C-P} = 2.4 Hz), 37.6 (d, J_{C-P} = 142.2 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.4 ppm. HRMS (ESI): *m/z* calcd for $C_{41}H_{31}NO_3P$ $[M+H]^+$: 616.2042; found: 616.2063.

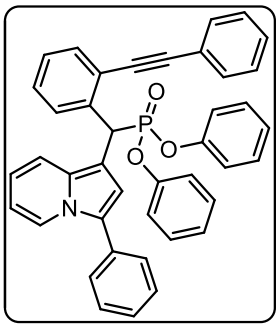
Diphenyl [naphthalen-1-yl(3-phenylindolizin-1-yl)methyl]phosphonate (89z): Brown thick



oil; yield 88% (49.7 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1271, 1189, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.32 (ddd, *J* = 7.2, 2.7, 1.0 Hz, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.21 (d, *J* = 7.2 Hz, 1H), 7.88 (d, *J* = 7.4 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.53 – 7.48 (m, 5H), 7.47 – 7.42 (m, 2H), 7.34 – 7.31 (m, 1H), 7.30 (d, *J* = 1.1 Hz, 1H), 7.17 – 7.09 (m, 4H), 7.07 – 7.00 (m, 2H), 6.90 – 6.88 (m, 2H),

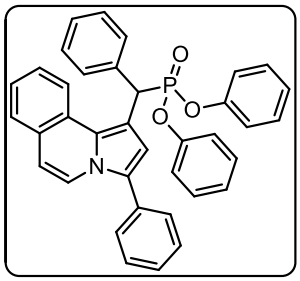
6.78 – 6.76 (m, 2H), 6.68 (dd, J = 9.0, 6.4 Hz, 1H), 6.45 (td, J = 7.4, 1.2 Hz, 1H), 6.01 (d, $J_{H\text{-}P}$ = 26.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.1 Hz), 134.2, 132.5 (d, $J_{C\text{-}P}$ = 2.6 Hz), 132.2, 131.7 (d, $J_{C\text{-}P}$ = 10.5 Hz), 131.6, 131.4, 129.5 (d, $J_{C\text{-}P}$ = 0.8 Hz), 129.3, 129.0, 128.2, 128.2, 128.1 (d, $J_{C\text{-}P}$ = 6.2 Hz), 127.3, 126.6, 125.7 (d, $J_{C\text{-}P}$ = 2.6 Hz), 125.7, 125.4, 124.8, 124.8 (d, $J_{C\text{-}P}$ = 0.7 Hz), 123.0, 122.6, 120.5, 120.5, 117.6, 117.4 (d, $J_{C\text{-}P}$ = 1.6 Hz), 116.0 (d, $J_{C\text{-}P}$ = 4.3 Hz), 110.9, 107.0 (d, $J_{C\text{-}P}$ = 6.3 Hz), 37.1 (d, $J_{C\text{-}P}$ = 143.6 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.5 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{29}NO_3P$ $[M+H]^+$: 566.1886; found: 566.1901.

Diphenyl [(2-(phenylethynyl)phenyl)(3-phenylindolizin-1-yl)methyl]phosphonate (89aa):



Light green oil; yield 60% (36.9 mg); R_f = 0.4 (20% EtOAc in hexane); FT-IR 1491, 1275, 1190, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 7.2 Hz, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.54 – 7.52 (m, 6H), 7.47 – 7.39 (m, 6H), 7.33 (t, J = 7.4 Hz, 2H), 7.24 – 7.16 (m, 3H), 7.12 – 7.00 (m, 4H), 6.95 (d, J = 8.2 Hz, 2H), 6.89 (d, J = 8.3 Hz, 2H), 6.59 (dd, J = 9.0, 6.5 Hz, 1H), 6.45 – 6.42 (m, 1H), 5.99 (d, $J_{H\text{-}P}$ = 25.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.9 Hz), 150.9 (d, $J_{C\text{-}P}$ = 9.6 Hz), 138.4 (d, $J_{C\text{-}P}$ = 3.4 Hz), 132.4 (d, $J_{C\text{-}P}$ = 0.7 Hz), 132.3, 131.9 (d, $J_{C\text{-}P}$ = 14.9 Hz), 131.7, 130.0 (d, $J_{C\text{-}P}$ = 4.7 Hz), 129.6, 129.5, 129.1 (d, $J_{C\text{-}P}$ = 2.7 Hz), 129.0, 128.7, 128.6, 128.2, 127.3, 127.2 (d, $J_{C\text{-}P}$ = 2.5 Hz), 125.6, 124.9 (d, $J_{C\text{-}P}$ = 0.8 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.5 Hz), 123.2 (d, $J_{C\text{-}P}$ = 10.7 Hz), 123.2, 122.4, 120.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 120.5 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.6 (d, $J_{C\text{-}P}$ = 1.3 Hz), 117.5, 115.2 (d, $J_{C\text{-}P}$ = 4.3 Hz), 111.0, 107.0 (d, $J_{C\text{-}P}$ = 5.4 Hz), 94.2, 88.2 (d, $J_{C\text{-}P}$ = 1.5 Hz), 39.2 (d, $J_{C\text{-}P}$ = 141.4 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 17.8 ppm. HRMS (ESI): *m/z* calcd for $C_{41}H_{31}NO_3P$ $[M+H]^+$: 616.2042; found: 616.2062.

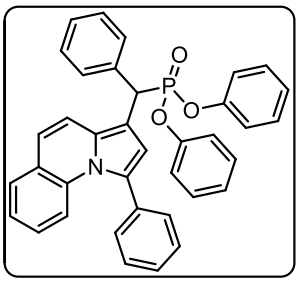
Diphenyl {phenyl(3-phenylpyrrolo[2,1-a]isoquinolin-1-yl)methyl}phosphonate (89bb):



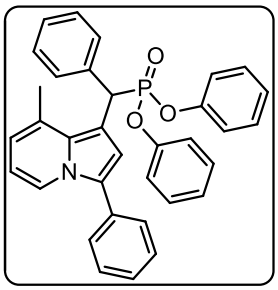
Green solid; yield 60% (33.9 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 170 – 172 °C; FT-IR 1489, 1275, 1211, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 (d, J = 8.2 Hz, 1H), 8.02 (d, J = 7.5 Hz, 1H), 7.75 – 7.73 (m, 2H), 7.55 – 7.47 (m, 6H), 7.45 – 7.34 (m, 5H), 7.32 – 7.27 (m, 1H), 7.21 (t, J = 7.7 Hz, 2H), 7.13 – 7.07 (m, 3H), 7.02 (t, J = 7.2 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.69 (d,

J = 7.5 Hz, 1H), 5.65 (d, $J_{H\text{-}P}$ = 28.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.7 Hz), 150.7 (d, $J_{C\text{-}P}$ = 9.9 Hz), 135.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 131.8, 130.3 (d, $J_{C\text{-}P}$ = 6.5 Hz), 129.6 (d, $J_{C\text{-}P}$ = 0.4 Hz), 129.4 (d, $J_{C\text{-}P}$ = 0.5 Hz), 129.0, 128.9, 128.9 (d, $J_{C\text{-}P}$ = 2.8 Hz), 128.2, 127.9, 127.7, 127.6 (d, $J_{C\text{-}P}$ = 3.3 Hz), 127.5, 127.1, 126.9 (d, $J_{C\text{-}P}$ = 1.2 Hz), 126.7, 126.6, 125.6, 125.0 (d, $J_{C\text{-}P}$ = 0.8 Hz), 124.9 (d, $J_{C\text{-}P}$ = 0.9 Hz), 122.5 (d, $J_{C\text{-}P}$ = 15.4 Hz), 120.7 (d, $J_{C\text{-}P}$ = 0.6 Hz), 120.6, 115.3 (d, $J_{C\text{-}P}$ = 5.4 Hz), 111.4, 111.0 (d, $J_{C\text{-}P}$ = 4.6 Hz), 44.2 (d, $J_{C\text{-}P}$ =138.5 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.3 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{29}NO_3P$ $[M+H]^+$: 566.1886; found: 566.1906.

Diphenyl {phenyl(1-phenylpyrrolo[1,2-a]quinolin-3-yl)methyl}phosphonate (89cc): Yellow solid; yield 60% (36.9 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 156 – 158 °C; FT-IR 1490, 1271, 1190, 934 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70 – 7.68 (m, 2H), 7.59 (d, J = 7.8 Hz, 1H), 7.47 – 7.40 (m, 6H), 7.38 – 7.33 (m, 3H), 7.29 – 7.26 (m, 1H), 7.23 – 7.18 (m, 3H), 7.15 – 7.06 (m, 5H), 7.04 – 7.00 (m, 2H), 6.89 (d, J = 8.3 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.12 (d, $J_{H\text{-}P}$ = 26.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.8 Hz), 150.7 (d, $J_{C\text{-}P}$ = 10.2 Hz), 136.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 135.3, 134.3, 130.5 (d, $J_{C\text{-}P}$ = 14.3 Hz), 130.1 (d, $J_{C\text{-}P}$ = 1.1 Hz), 129.7, 129.6, 129.5, 129.5, 128.9 (d, $J_{C\text{-}P}$ = 1.8 Hz), 128.6, 128.6, 127.8, 127.5 (d, $J_{C\text{-}P}$ = 2.7 Hz), 126.7, 125.4, 125.0, 124.9, 123.6, 120.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 120.6 (d, $J_{C\text{-}P}$ = 4.2 Hz), 119.8 (d, $J_{C\text{-}P}$ = 0.7 Hz), 117.8, 117.5 (d, $J_{C\text{-}P}$ = 4.3 Hz), 116.5 (d, $J_{C\text{-}P}$ = 1.8 Hz), 109.9 (d, $J_{C\text{-}P}$ = 5.9 Hz), 42.6 (d, $J_{C\text{-}P}$ = 140.6 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 17.9 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{29}NO_3P$ $[M+H]^+$: 566.1886; found: 566.1865.

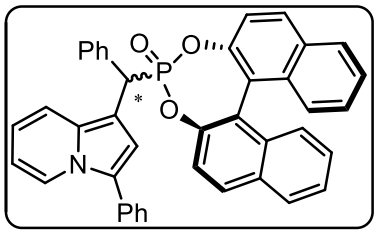


Diphenyl [(8-methyl-3-phenylindolizin-1-yl)(phenyl)methyl]phosphonate (89dd): Green thick oil; yield 60% (31.7 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 1490, 1274, 1190, 931 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 6.9 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.54 – 7.53 (m, 1H), 7.50 (dd, J = 9.2, 1.1 Hz, 2H), 7.48 – 7.43 (m, 2H), 7.36 – 7.29 (m, 3H), 7.27 – 7.23 (m, 1H), 7.20 (t, J = 7.7, 8.1 Hz, 2H), 7.13 (t, J = 7.6, 8.2 Hz, 2H), 7.10 – 7.02 (m, 2H), 6.90 – 6.88 (m, 2H), 6.84 – 6.82 (m, 2H), 6.40 – 6.39 (m, 1H), 6.36 – 6.32 (m, 1H), 5.59 (d, $J_{H\text{-}P}$ = 27.5 Hz, 1H), 2.56 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9 (d, $J_{C\text{-}P}$ = 9.7 Hz), 150.8 (d, $J_{C\text{-}P}$ = 9.9 Hz), 137.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 132.4,



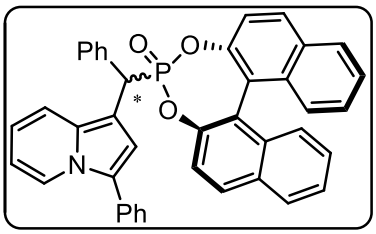
131.9, 131.1 (d, J_{C-P} = 15.1 Hz), 129.9 (d, J_{C-P} = 6.9 Hz), 129.6, 129.4, 129.0, 128.9, 128.8, 128.7, 128.5, 127.4, 127.3 (d, J_{C-P} = 3.0 Hz), 125.7, 125.0 (d, J_{C-P} = 0.9 Hz), 124.9 (d, J_{C-P} = 0.8 Hz), 121.2, 120.7 (d, J_{C-P} = 4.3 Hz), 120.6 (d, J_{C-P} = 4.2 Hz), 119.0, 116.5 (d, J_{C-P} = 4.6 Hz), 110.5, 107.4 (d, J_{C-P} = 5.2 Hz), 43.1 (d, J_{C-P} = 138.3 Hz), 21.1 ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 18.8 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{29}NO_3P$ $[M+H]^+$: 530.1886; found: 530.1870.

4-(Phenyl(3-phenylindolizin-1-yl)methyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide (90b): Green solid; yield 70% (153 mg); R_f = 0.3 (30% EtOAc in hexane); M.P. 182 – 186



°C; FT-IR 1285, 1225, 961 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 7.1 Hz, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.94 (t, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.9 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.59 (s, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 3H), 7.47 – 7.42 (m, 3H), 7.36 (t, *J* = 7.0 Hz, 2H), 7.32 – 7.20 (m, 6H), 6.82 (d, *J* = 8.8 Hz, 1H), 6.72 (dd, *J* = 8.7, 6.5 Hz, 1H), 6.54 (t, *J* = 6.9 Hz, 1H), 4.81 (d, J_{H-P} = 24.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.9 (d, J_{C-P} = 10.2 Hz), 146.3 (d, J_{C-P} = 10.1 Hz), 136.2 (d, J_{C-P} = 5.1 Hz), 132.6 (d, J_{C-P} = 0.8 Hz), 132.5 (d, J_{C-P} = 1.2 Hz), 132.2, 131.9 (d, J_{C-P} = 1.1 Hz), 131.7 (d, J_{C-P} = 0.8 Hz), 131.4 (d, J_{C-P} = 15.8 Hz), 131.2 (d, J_{C-P} = 0.8 Hz), 130.9, 129.4, 129.3, 129.1, 128.8 (d, J_{C-P} = 1.8 Hz), 128.6, 128.5, 128.3, 127.5, 127.4, 127.1, 126.8, 126.7, 125.9, 125.8, 125.7, 122.8, 122.1 (d, J_{C-P} = 2.6 Hz), 121.9 (d, J_{C-P} = 1.9 Hz), 121.6 (d, J_{C-P} = 1.6 Hz), 120.7 (d, J_{C-P} = 3.4 Hz), 117.5, 117.3, 115.6 (d, J_{C-P} = 4.5 Hz), 111.1, 106.6 (d, J_{C-P} = 4.5 Hz), 40.1 (d, J_{C-P} = 132.1 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 35.2 ppm. Specific rotation: $[\alpha]_D^{20}$ = -254.1 (C = 0.17 $CHCl_3$). HRMS (ESI): *m/z* calcd for $C_{41}H_{29}NO_3P$ $[M+H]^+$: 614.1886; found: 614.1863.

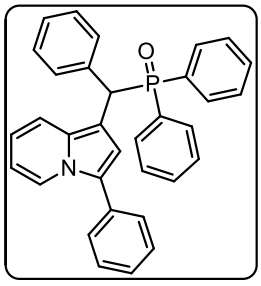
4-(Phenyl(3-phenylindolizin-1-yl)methyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide (90a): Green solid; yield 70% (153 mg); R_f = 0.3 (30% EtOAc in hexane); M.P. 182 – 186



°C; FT-IR 1285, 1224, 961 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 3H), 7.54 (dd, *J* = 8.9, 0.9 Hz, 1H), 7.50 (d, *J* = 8.9 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.42 – 7.37 (m, 5H), 7.34 – 7.29 (m, 2H), 7.25 – 7.19 (m, 5H), 6.93 (dd, *J* = 7.6, 1.7 Hz, 2H), 6.88 (s, 1H), 6.70 – 6.66 (m, 2H), 6.46 (td, *J* = 7.2, 1.0 Hz, 1H), 5.10 (d, J_{H-P} = 26.0 Hz,

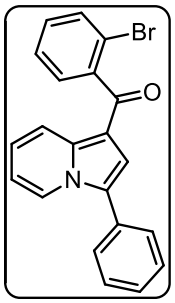
1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.0 (d, J_{C-P} = 10.7 Hz), 145.9 (d, J_{C-P} = 10.1 Hz), 136.1 (d, J_{C-P} = 3.2 Hz), 132.7 (d, J_{C-P} = 1.5 Hz), 132.4, 132.0 (d, J_{C-P} = 1.0 Hz), 131.6, 131.4, 131.3 (d, J_{C-P} = 13.3 Hz), 131.2 (d, J_{C-P} = 1.2 Hz), 130.0, 129.5, 129.4, 129.0 (d, J_{C-P} = 1.3 Hz), 128.8, 128.6, 128.5, 127.9, 127.6 (d, J_{C-P} = 2.3 Hz), 127.4, 127.1 (d, J_{C-P} = 3.3 Hz), 126.6 (d, J_{C-P} = 6.4 Hz), 125.7, 125.6, 125.5, 122.6, 122.3 (d, J_{C-P} = 2.8 Hz), 121.7 (d, J_{C-P} = 1.9 Hz), 120.4 (d, J_{C-P} = 1.5 Hz), 120.2 (d, J_{C-P} = 3.9 Hz), 117.7, 117.1 (d, J_{C-P} = 1.4 Hz), 115.3 (d, J_{C-P} = 3.5 Hz), 110.9, 106.2 (d, J_{C-P} = 6.7 Hz), 41.5 (d, J_{C-P} = 131.0 Hz) ppm. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 35.2 ppm. Specific rotation: $[\alpha]_D^{20}$ = -195.5 (C = 0.11 $CHCl_3$). HRMS (ESI): *m/z* calcd for $C_{41}H_{29}NO_3P$ $[M+H]^+$: 614.1886; found: 614.1900.

Diphenyl[phenyl(3-phenylindolizin-1-yl)methyl]phosphine Oxide (92): Green solid; R_f = 0.2



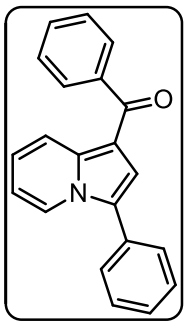
(40% EtOAc in hexane); M.P. 254–256 °C; FT-IR 3058, 1600, 1438, 740, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 7.1 Hz, 1 H), 7.71–7.67 (m, 2 H), 7.59–7.55 (m, 2 H), 7.51–7.49 (m, 2 H), 7.44–7.26 (m, 13 H), 7.17–7.09 (m, 3 H), 6.58 (dd, J = 8.6, 6.4 Hz, 1 H), 6.41–6.37 (m, 1 H), 5.07 (d, J = 10.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4 (d, $J_{C–P}$ = 4.3 Hz), 133.3 (d, $J_{C–P}$ = 2.7 Hz), 132.4 (d, $J_{C–P}$ = 3.8 Hz), 132.3, 131.6, 131.5, 131.46, 131.41, 131.40, 131.36, 131.31, 129.8 (d, $J_{C–P}$ = 5.7 Hz), 128.9, 128.4, 128.3, 128.1, 127.1, 126.8 (d, $J_{C–P}$ = 2.0 Hz), 125.3, 122.4, 117.0 (d, $J_{C–P}$ = 4.8 Hz), 115.9 (d, $J_{C–P}$ = 4.5 Hz), 110.7, 108.7 (d, $J_{C–P}$ = 4.6 Hz), 44.8 (d, $J_{C–P}$ = 67.5 Hz) ppm. ^{31}P NMR (162 MHz, CDCl3): δ = 31.6 ppm. HRMS (ESI):*m/z* calcd. for $C_{33}H_{26}NOPNa$ $[M + Na]^+$ 506.1652; found 506.1635.

[2-Bromophenyl](3-phenylindolizin-1-yl)methanone (94): Brown semi-solid; yield 45% (57

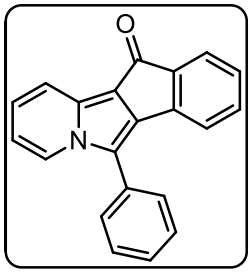


mg); R_f = 0.3 (20% EtOAc in hexane); FT-IR 3055, 2925, 1615, 1498, 1421, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.35 – 8.33 (m, 1H), 7.65 (dd, J = 8.0, 0.9 Hz, 1H), 7.52 – 7.44 (m, 5H), 7.42 – 7.37 (m, 2H), 7.32 – 7.24 (m, 2H), 6.86 (td, J = 6.8, 1.2 Hz, 1H), 6.82 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.4, 143.1, 137.4, 133.2, 130.8, 130.4, 129.3, 128.9, 128.8, 128.5, 127.4, 127.2, 125.1, 123.8, 121.2, 119.6, 118.4, 114.4, 112.8 ppm.

Phenyl(3-phenylindolizin-1-yl)methanone (95): Green semi-solid; R_f = 0.3 (20% EtOAc in hexane); FT-IR 3056, 1614, 1498, 1418, 1241, 873 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.59 (dt, *J* = 9.0, 1.2 Hz, 1H), 8.36 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.57 – 7.46 (m, 7H), 7.44 – 7.39 (m, 1H), 7.23 (ddd, *J* = 9.0, 6.7, 1.0 Hz, 1H), 7.14 (s, 1H), 6.84 (td, *J* = 6.9, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.6, 141.3, 137.7, 131.1, 130.9, 129.3, 129.1, 129.0, 128.4, 128.3, 126.7, 124.3, 123.5, 121.3, 118.5, 114.1, 112.6 ppm. HRMS (ESI):*m*/*z* calcd. for $C_{21}H_{16}NO$ $[M + H]^+$ 298.1232; found 298.1219.



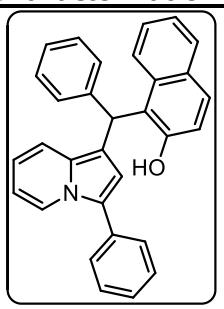
6-phenyl-11H-indeno[2,1-a]indolizin-11-one (96): Brown semi-solid; yield 45% (57 mg); R_f = 0.1 (20% EtOAc in hexane); FT-IR 3061, 1667, 1633, 1498, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.02 – 8.00 (m, 1H), 7.75 – 7.72 (m, 1H), 7.64 – 7.55 (m, 5H), 7.52 – 7.48 (m, 1H), 7.22 – 7.14 (m, 3H), 7.09 – 7.05 (m, 1H), 6.59 (td, *J* = 6.9, 1.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 185.4, 142.7, 139.0, 135.7, 132.7, 132.4, 129.8, 129.6, 129.56, 129.1, 128.3, 125.8, 125.1, 123.7, 120.8, 120.7, 119.2, 113.8, 113.0 ppm. HRMS (ESI):*m*/*z* calcd. for $C_{21}H_{14}NO$ $[M + H]^+$ 296.1075; found 296.1061.



General procedure for the synthesis of 2-naphthol derived triarylmethanes:

2-naphthol (0.11 mmol) was added to a mixture of 2-(2-enynyl)-pyridine (0.1 mmol) and CuI (0.01 mmol) in 1.5 ml of MeCN**,** and the resultant mixture was stirred at 70 °C until the 2-(2-enynyl)-pyridine was completely consumed (by T.L.C.). The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using ethyl acetate/hexane mixture as an eluent to get the pure indolizine containing triarylmethanes.

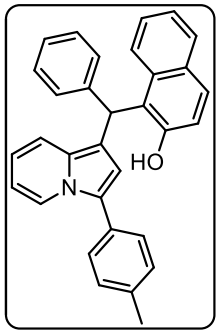
Characterization of the products:



1-(phenyl(3-phenylindolizin-1-yl)methyl)naphthalen-2-ol (98a): Green solid; yield 84% (35.7 mg); R_f = 0.6 (10% EtOAc in hexane); M.P. 158–160 °C; FT-IR 3384, 2926, 1280, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 6.8 Hz, 1H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.46 – 7.39 (m, 5H), 7.36 – 7.29

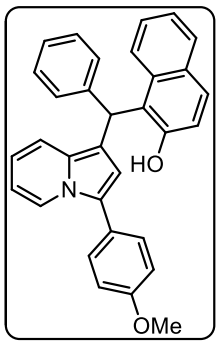
(m, 5H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.58 (s, 1H), 6.58 – 6.49 (m, 2H), 6.49 (s, 1H), 6.08 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7, 142.0, 133.1, 131.9, 131.5, 129.7, 129.5, 129.1, 129.0, 128.9, 128.8, 128.2, 127.5, 127.0, 126.9, 125.4, 123.2, 122.68, 122.66, 119.9, 119.3, 118.0, 117.7, 114.6, 112.9, 111.7, 41.0 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{24}NO$ $[M+H]^+$: 426.1859; found: 426.1843.

1-[Phenyl{3-(*p*-tolyl)indolizin-1-yl}methyl]naphthalen-2-ol (98b) : Green oil; yield 83% (36.4



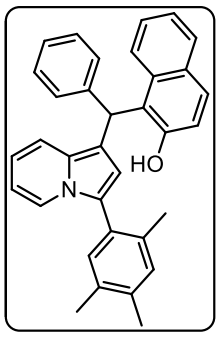
mg); R_f = 0.4 (10% EtOAc in hexane); FT-IR 3391, 3059, 1514, 1234, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, *J* = 6.9 Hz, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.44 – 7.40 (m, 4H), 7.38 – 7.33 (m, 3H), 7.29 – 7.25 (m, 3H), 7.09 (d, *J* = 8.8 Hz, 1H), 7.00 – 6.98 (m, 1H), 6.61 (s, 1H), 6.57 – 6.50 (m, 2H), 6.49 (s, 1H), 6.15 (s, 1H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7, 142.1, 137.3, 133.1, 131.2, 129.7 (2C), 129.6, 129.4, 129.0, 128.97, 128.92, 128.8, 128.1, 126.94, 126.88, 125.4, 123.1, 122.7, 119.8, 119.4, 118.0, 117.4, 114.2, 112.7, 111.6, 41.0, 21.4 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{26}NO$ $[M+H]^+$: 440.2015; found: 440.1997.

1-[(3-(4-Methoxyphenyl)indolizin-1-yl)(phenyl)methyl]naphthalen-2-ol (**98c**): Green semi-



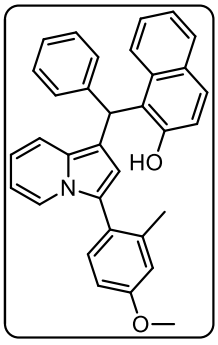
solid; yield 84% (38.2 mg); R_f = 0.3 (10% EtOAc in hexane); FT-IR 3324, 3060, 1601, 1255, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (d, *J* = 6.8 Hz, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.44 – 7.42 (m, 4H), 7.38 – 7.33 (m, 3H), 7.29 – 7.25 (m, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 6.99 – 6.97 (m, 3H), 6.61 (s, 1H), 6.55 – 6.47 (m, 2H), 6.45 (s, 1H), 6.16 (s, 1H), 3.85 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.1, 153.7, 142.1, 133.1, 131.0, 129.7, 129.6, 129.4, 129.0, 128.9, 128.8, 126.9, 126.89, 125.2, 124.4, 123.2, 122.7, 122.6, 119.8, 119.4, 117.9, 117.3, 114.5, 114.0, 112.5, 111.5, 55.5, 41.1 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{26}NO_2$ $[M+H]^+$: 456.1964; found: 456.1947.

1-[Phenyl(3-(2,4,5-trimethylphenyl)indolizin-1-yl)methyl]naphthalen-2-ol (98d): Green oil;

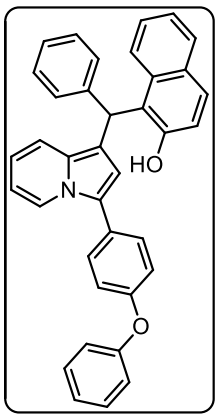


yield 76% (35.5 mg); R_f = 0.5 (10% EtOAc in hexane); FT-IR 3337, 2923, 1514, 1235, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 6.5 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.43 – 7.41 (m, 2H), 7.37 – 7.31 (m, 3H), 7.26 – 7.22 (m, 1H), 7.09 – 7.06 (m, 3H), 6.96 – 6.93 (m, 1H), 6.62 (s, 1H), 6.55 – 6.51 (m, 1H), 6.46 (t, *J* = 6.7 Hz, 1H), 6.35 (s, 1H), 6.22 (s, 1H), 2.29 (s, 3H), 2.24 (s, 3H), 2.04 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 142.2, 137.2, 135.4, 134.2, 133.1, 132.4, 131.9, 130.2, 129.6, 129.4, 128.9(2C), 128.8(2C), 128.3, 126.9, 124.7, 123.15, 123.10, 122.7, 119.9, 119.3, 117.7, 117.1, 114.5, 111.9, 111.2, 41.3, 19.6, 19.28, 19.27 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{29}NO$ $[M+H]^+$: 468.2328; found: 468.2310.

1-[(3-(4-Methoxy-2-methylphenyl)indolizin-1-yl)(phenyl)methyl] naphthalen-2-ol (98e):



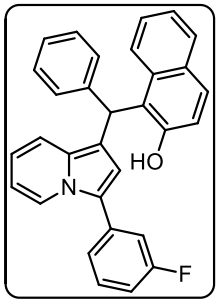
Green oil; yield 73% (34.2 mg); R_f = 0.3 (10% EtOAc in hexane); FT-IR 3320, 2925, 1606, 1242, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* = 8.11 (d, *J* = 8.6 Hz, 1H), 7.82 – 7.80 (m, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 7.0 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.41 – 7.39 (m, 2H), 7.36 – 7.30 (m, 3H), 7.25 – 7.20 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 1H), 6.85 – 6.84 (m, 1H), 6.79 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.60 (s, 1H), 6.54 – 6.50 (m, 1H), 6.46 (td, *J* = 7.0, 1.2 Hz, 1H), 6.33 (s, 1H), 6.20 (s, 1H), 3.83 (s, 3H), 2.06 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) *δ* = 159.9, 153.9, 142.2, 140.0, 133.1, 132.6, 130.2, 129.6, 129.4, 128.9(2C), 128.85(2C), 126.9, 124.2, 123.4, 123.1, 123.0, 122.7, 119.8, 119.3, 117.7, 117.1, 115.9, 114.6, 111.8, 111.5, 111.3, 55.4, 41.2, 20.1 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{28}NO_2$ $[M+H]^+$: 470.2121; found: 470.2103.



1-[(3-(4-Phenoxyphenyl)indolizin-1-yl)(phenyl)methyl]naphthalen-2-ol (98f): Yellow solid; yield 62% (32.2 mg); R_f = 0.3 (10% EtOAc in hexane); M.P. 96–98 °C; FT-IR 3384, 3060, 1489, 1240, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* = 8.23 (d, *J* = 6.8 Hz, 1H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 3H), 7.41 – 7.31 (m, 7H), 7.28 – 7.24 (m, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.08 – 7.05 (m, 5H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.58 (s, 1H), 6.58 – 6.50 (m, 2H), 6.46 (s, 1H),

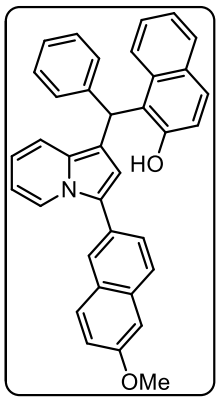
6.08 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.0, 156.8, 153.7, 142.0, 133.1, 131.3, 130.0, 129.8, 129.7, 129.5, 129.0, 128.9, 128.8, 127.0, 126.9, 126.88, 124.8, 123.7, 123.2, 122.7, 122.6, 119.8, 119.4, 119.3, 119.2, 118.0, 117.5, 114.4, 112.8, 111.7, 41.0 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{28}NO_2$ $[M+H]^+$: 518.2121; found: 518.2100.

1-[(3-(3-Fluorophenyl)indolizin-1-yl)(phenyl)methyl]naphthalen-2-ol (98g): Green solid;



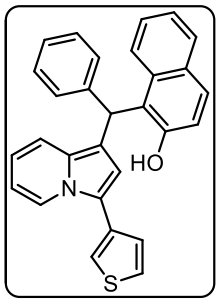
yield 79% (35 mg); R_f = 0.3 (10% EtOAc in hexane); M.P. 103–105 °C; FT-IR 3399, 3064, 2925, 1612, 1265, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 6.9 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.42 – 7.40 (m, 2H), 7.38 – 7.34 (m, 4H), 7.30 – 7.26 (m, 2H), 7.24 – 7.20 (m, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.61 – 6.54 (m, 4H), 6.02 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.2 (d, J_{C-F} = 245.0 Hz), 153.6, 141.9, 134.0 (d, J_{C-F} = 8.3 Hz), 133.1, 131.9, 130.6 (d, J_{C-F} = 8.7 Hz), 129.7, 129.5, 129.1, 129.0, 128.8, 127.1, 126.9, 124.0 (d, J_{C-F} = 2.3 Hz), 123.6 (d, J_{C-F} = 2.8 Hz), 123.2, 122.7, 122.6, 119.8, 119.4, 118.1, 118.05, 115.0, 114.7 (d, J_{C-F} = 21.9 Hz), 114.2 (d, J_{C-F} = 20.1 Hz), 113.3, 112.1, 40.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.2 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{23}FNO$ $[M+H]^+$: 444.1764; found: 444.1747.

1-[(3-(6-Methoxynaphthalen-2-yl)indolizin-1-yl)(phenyl)methyl] naphthalen-2-ol (98h):



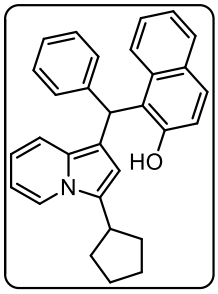
Green semi-solid; yield 74% (37.4 mg); R_f = 0.5 (20% EtOAc in hexane); FT-IR 3399, 3059, 1624, 1268, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.36 – 8.34 (m, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 0.8 Hz, 1H), 7.84 – 7.72 (m, 4H), 7.58 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.44 – 7.42 (m, 2H), 7.37 – 7.33 (m, 3H), 7.29 – 7.26 (m, 1H), 7.19 – 7.15 (m, 2H), 7.09 (d, *J* = 8.8 Hz, 1H), 7.02 – 7.00 (m, 1H), 6.63 (s, 1H), 6.60 – 6.51 (m, 2H), 6.58 (s, 1H), 6.15 (s, 1H), 3.94 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 153.7, 142.1, 133.8, 133.1, 131.4, 129.7, 129.5, 129.48, 129.2, 129.0(2C), 128.9, 128.87 (2C), 127.5, 127.1, 127.0, 126.9, 126.6, 125.5, 123.2, 122.7, 119.9, 119.5, 119.4, 118.0, 117.7, 114.6, 113.0, 111.8, 105.9, 55.5, 41.04 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{28}NO_2$ $[M+H]^+$: 506.2121; found: 506.2101.

1-[Phenyl(3-(thiophen-3-yl)indolizin-1-yl)methyl]naphthalen-2-ol (98i): White solid; yield



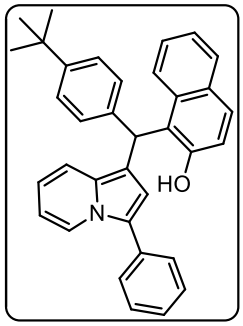
78% (33.6 mg); R_f = 0.3 (10% EtOAc in hexane); M.P. 200–202 °C; FT-IR 3388, 2925, 2854, 1268, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.25 – 8.22 (m, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.47 – 7.39 (m, 3H), 7.37 – 7.31 (m, 6H), 7.28 – 7.24 (m, 1H), 7.06 (d, *J* = 8.8 Hz, 1H), 6.99 – 6.95 (m, 1H), 6.57 – 6.54 (m, 3H), 6.50 (s, 1H), 6.02 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7, 142.0, 133.1, 132.3, 131.2, 129.7, 129.5, 129.0, 128.9, 128.8, 127.5, 127.0, 126.9, 126.3, 123.2, 123.1, 122.7, 121.3, 120.8, 119.8, 119.4, 117.9, 117.5, 114.5, 112.6, 111.9, 41.0 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{22}NOS\,[M+H]^+$: 432.1423; found: 432.1408.

1-[(3-Cyclopentylindolizin-1-yl)(phenyl)methyl]naphthalen-2-ol (98j): Yellow solid; yield



68% (28.4 mg); R_f = 0.5 (10% EtOAc in hexane); M.P. 173–175 °C; FT-IR 3376, 2956, 1210, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 7.1 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.39 – 7.32 (m, 5H), 7.28 – 7.25 (m, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.56 (s, 1H), 6.54 – 6.45 (m, 2H), 6.22 (s, 1H), 6.14 (s, 1H), 3.28 – 3.20 (m, 1H), 2.18 – 2.06 (m, 2H), 1.80 – 1.59 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 142.3, 133.1, 130.3, 129.6, 129.3, 129.0, 128.9(2C), 126.8, 123.1, 122.7, 122.6, 119.9, 119.5, 117.8, 116.2, 110.9, 110.7, 110.0, 41.3, 36.6, 31.5, 31.4, 25.18, 25.16 ppm. HRMS (ESI): *m/z* calcd for $C_{30}H_{28}NO\,[M+H]^+$: 418.2172; found: 418.2154.

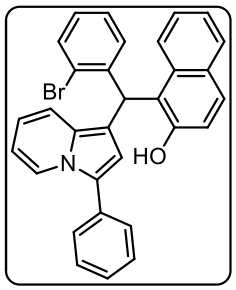
1-[(4-(*tert*-Butyl)phenyl)(3-phenylindolizin-1-yl)methyl]naphthalen-2-ol (98k): Green solid



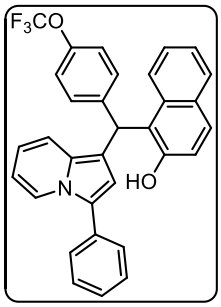
yield 76% (36.6 mg); R_f = 0.4 (10% EtOAc in hexane); M.P. 171–173 °C; FT-IR 3399, 2963, 1513, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.0 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.53 – 7.51 (m, 2H), 7.49 – 7.42 (m, 3H), 7.37 – 7.30 (m, 6H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.57 (s, 1H), 6.55 (s, 1H), 6.57 – 6.48 (m, 2H), 6.07 (s, 1H), 1.31 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.6, 149.7, 138.6, 133.2, 132.1, 131.4, 129.6, 129.4, 129.1, 128.9, 128.4, 128.2, 127.4, 126.9, 125.9, 125.3, 123.1, 122.7, 122.6, 119.9, 119.8, 118.1, 117.5, 114.6, 113.2,

111.6, 40.3, 34.6, 31.5 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{32}NO$ $[M+H]^+$: 482.2485; found: 482.2467.

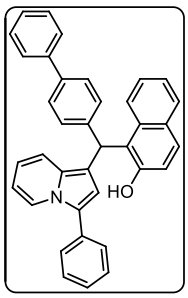
1-[(2-Bromophenyl)(3-phenylindolizin-1-yl)methyl]naphthalen-2-ol (98l): White solid; yield



64% (32.2 mg); R_f = 0.4 (10% EtOAc in hexane); M.P. 144–146 °C; FT-IR 3387, 3060, 1467, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 6.8 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.40 – 7.31 (m, 3H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.14 (td, *J* = 7.7, 1.5 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.98 – 6.96 (m, 1H), 6.86 (s, 1H), 6.59 – 6.52 (m, 2H), 6.37(s, 1H), 6.36 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.4, 141.2, 133.3, 133.1, 131.8, 131.7, 130.4, 129.8, 129.6, 129.1, 128.9, 128.7, 128.24, 128.22, 127.5, 127.2, 125.7, 125.1, 123.3, 122.8, 122.7, 119.8, 118.3, 118.0, 117.9, 114.1, 112.0, 110.7, 41.6 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{23}BrNO$ $[M+H]^+$: 504.0964; found: 504.0945.



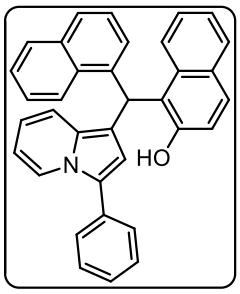
1-[(3-Phenylindolizin-1-yl)(4-(trifluoromethoxy)phenyl)methyl] naphthalen-2-ol (98m): Green oil; yield 84% (42.8 mg); R_f = 0.2 (10% EtOAc in hexane); FT-IR 3414, 3064, 1601, 1260, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.29 (d, *J* = 6.8 Hz, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.52 – 7.50 (m, 2H), 7.48 – 7.41 (m, 5H), 7.39 – 7.32 (m, 2H), 7.19 – 7.17 (m, 2H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.97 – 6.95 (m, 1H), 6.60 (s, 1H), 6.60 – 6.51 (m, 2H), 6.47 (s, 1H), 6.08 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7, 148.1 (q, J_{C-F} = 1.7 Hz), 140.7, 132.9, 131.8, 131.5, 130.3, 129.8, 129.7, 129.15, 129.1, 128.2, 127.6, 127.0, 125.5, 123.3, 122.7, 122.5, 121.3, 120.6 (d, J_{C-F} = 255.3 Hz), 119.9, 118.8, 117.95, 117.93, 114.2, 112.4, 111.9, 40.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.8 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{23}F_3NO_2$ $[M+H]^+$: 510.1682; found: 510.1660.



1-([1,1'-Biphenyl]-4-yl(3-phenylindolizin-1-yl)methyl)naphthalen-2-ol (98n): White solid; yield 79% (39.5 mg); R_f = 0.2 (10% EtOAc in hexane); M.P. 152–154 °C; FT-IR 3400, 3059, 2924, 1600, 749cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 6.9 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 8.9 Hz, 1H), 7.59 – 7.55 (m, 3H), 7.52 – 7.40 (m, 9H),

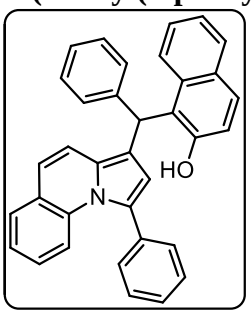
7.37 – 7.30 (m, 3H), 7.26 (s, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.62 – 6.51 (m, 4H), 6.15 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7, 141.1, 140.9, 139.8, 133.1, 131.9, 131.5, 129.7, 129.5, 129.3, 129.1, 129.0, 128.9, 128.2, 127.7, 127.5, 127.3, 127.1, 127.0, 125.4, 123.2, 122.70, 122.69, 119.9, 119.3, 118.0, 117.7, 114.6, 112.8, 111.8, 40.7 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{28}NO$ $[M+H]^+$: 502.2172; found: 502.2152.

1-[Naphthalen-1-yl(3-phenylindolizin-1-yl)methyl]naphthalen-2-ol (98o): White solid; yield



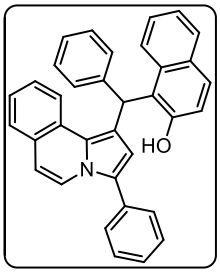
86% (41 mg); R_f = 0.3 (10% EtOAc in hexane); M.P. 172–174 °C; FT-IR 3398, 3059, 1265, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31 (d, *J* = 7.0 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.85 – 7.77 (m, 3H), 7.52 – 7.49 (m, 1H), 7.45 – 7.32 (m, 9H), 7.30 – 7.26 (m, 2H), 7.10 – 7.06 (m, 2H), 6.61 – 6.51 (m, 2H), 6.33 (s, 1H), 6.27 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.5, 137.4, 134.3, 133.1, 131.82, 131.80, 131.3, 129.7, 129.6, 129.1, 129.0, 128.9, 128.1 (2C), 127.4, 127.1, 126.5, 126.4, 126.0, 125.8, 125.6, 124.2, 123.2, 122.8, 122.6, 119.8, 119.1, 118.0, 117.8, 114.9, 112.5, 111.8, 38.0 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}NO$ $[M+H]^+$: 476.2015; found: 476.1997.

1-(Phenyl(1-phenylpyrrolo[1,2-*a*]quinolin-3-yl)methyl)naphthalen-2-ol (98p): Yellow solid;

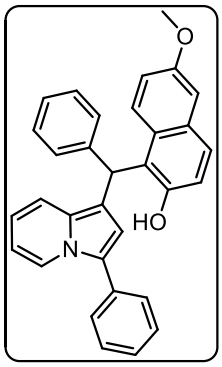


yield 83% (39.4 mg); R_f = 0.4 (10% EtOAc in hexane); M.P. 112-114 °C; FT-IR 3408, 3059, 1448, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.51 – 7.38 (m, 9H), 7.36 – 7.31 (m, 3H), 7.27 – 7.22 (m, 2H), 7.14 – 7.10 (m, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 7.00 – 6.98 (m, 1H), 6.90 – 6.87 (m, 1H), 6.61 (s, 1H), 6.34 (s, 1H), 6.02 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.6, 141.9, 135.1, 134.3, 133.1, 130.4, 130.1, 129.7, 129.55, 129.49, 129.1, 129.0, 128.8, 128.70, 128.66, 128.0, 127.05, 126.97, 126.8, 125.6, 123.9, 123.2, 122.7, 119.9, 119.7, 117.9, 117.1, 116.6, 115.9, 40.8 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}NO$ $[M+H]^+$: 476.2015; found: 476.1996.

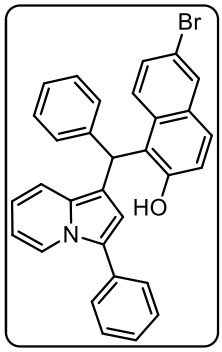
1-(Phenyl(3-phenylpyrrolo[2,1-*a*]isoquinolin-1-yl)methyl)naphthalene-2-ol (98q): White solid; yield 60% (28.5 mg); R_f = 0.4 (10% EtOAc in hexane); M.P. 221–223 °C; FT-IR 3406, 2924, 1337, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.03 (m, 2H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.31 (m, 11H), 7.28 – 7.20 (m, 2H), 7.03 – 6.98 (m, 2H), 6.81 (s, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 6.35 (s, 1H), 6.21 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.0, 142.6, 133.3, 131.6, 129.7, 129.2, 129.0, 128.9, 128.2, 127.9, 127.88, 127.6, 127.20, 126.9, 126.89, 126.8, 125.5, 123.5, 123.2, 122.6, 122.3, 120.0, 118.2, 117.3, 114.0, 112.2, 43.6 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}NO$ $[M+H]^+$: 476.2015; found: 476.1997.



6-Methoxy-1-(phenyl(3-phenylindolizin-1-yl)methyl)naphthalen-2-ol (99a): Yellow solid; yield 48% (22 mg); R_f = 0.3 (10% EtOAc in hexane); M.P. 110–112 °C; FT-IR 3404, 3061, 1606, 1241, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 6.9 Hz, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.51 – 7.49 (m, 2H), 7.44 – 7.38 (m, 4H), 7.35 – 7.31 (m, 3H), 7.29 – 7.24 (m, 1H), 7.15 – 7.12 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.54 (s, 1H), 6.58 – 6.49 (m, 2H), 6.49 (s, 1H), 5.88 (s, 1H), 3.90 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.7, 152.1, 142.1, 131.9, 131.4, 130.6, 129.1, 129.0, 128.8, 128.3, 128.2 (2C), 127.4, 127.0, 125.3, 124.3, 122.7, 120.3, 119.8, 119.0, 118.0, 117.6, 114.6, 113.0, 111.7, 107.4, 55.5, 41.1 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{26}NO_2$ $[M+H]^+$: 456.1964; found: 456.1946

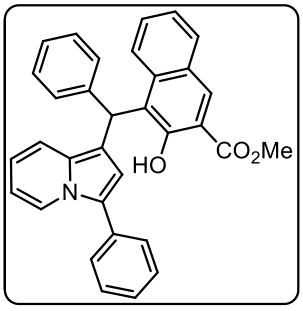


6-Bromo-1-[phenyl(3-phenylindolizin-1-yl)methyl]naphthalen-2-ol (99b): Brown semi-solid; yield 58% (29.2 mg); R_f = 0.5 (10% EtOAc in hexane); FT-IR 3316, 3061, 1494, 1345, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.29 (d, *J* = 7.0 Hz, 1H), 7.97 – 7.95 (m, 2H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.51 – 7.49 (m, 3H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.38 – 7.26 (m, 6H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 6.60 – 6.48 (m, 2H), 6.52 (s, 1H), 6.48 (s, 1H), 6.12 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.0, 141.7, 131.8, 131.7, 131.4, 130.9, 130.8, 130.0, 129.1, 128.7, 128.6, 128.2, 128.0, 127.5, 127.1, 125.5, 124.7,



122.7, 121.0, 119.7, 117.86, 117.84, 116.9, 114.5, 112.4, 111.8, 41.0 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{23}BrNO$ $[M+H]^+$: 504.0964; found: 504.0943.

Methyl 3-hydroxy-4-(phenyl(3-phenylindolizin-1-yl)methyl)-2-naphthoate (99c): Yellow

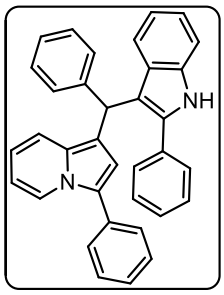


solid; yield 50% (24 mg); R_f = 0.7 (10% EtOAc in hexane); M.P. 100–102 °C; FT-IR 3170, 3058, 1679, 1441, 1209, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 11.11 (s, 1H), 8.50 (s, 1H), 8.26 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.80 – 7.78 (m, 1H), 7.51 – 7.48 (m, 3H), 7.42 – 7.38 (m, 2H), 7.31 – 7.22 (m, 7H), 7.19 – 7.16 (m, 1H), 7.02 (s, 1H), 6.78 (s, 1H), 6.64 – 6.60 (m, 1H), 6.48 – 6.44 (m, 1H), 4.03 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.9, 154.1, 144.2, 136.6, 132.7, 132.1, 130.3, 128.9 (2C), 128.4, 128.2, 128.0 (2C), 127.9, 126.9, 126.1, 125.7, 124.6, 124.5, 123.4, 122.3, 118.5, 116.5, 115.6, 114.2, 113.9, 110.8, 52.8, 37.6 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{26}NO_3$ $[M+H]^+$: 484.1913; found: 484.1934.

General procedure for the Ag-catalyzed synthesis of indole based triarylmethanes:

$Ag(OCOCF_3)$ (0.01 mmol) was added to a solution of *o*-alkynyl aniline (0.11 mmol) in THF (1.5 ml) and the resultant mixture was refluxed until the complete consumption of *o*-alkynyl aniline was observed (by T.L.C.). 2-(2-Enynyl)-pyridine (0.1 mmol) was then added to the reaction mixture and stirring was continued under reflux condition until 2-(2-enynyl)-pyridine was completely consumed (by T.L.C.). The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using 10 – 20% ethyl acetate/hexane mixture as an eluent to get the pure triarylmethanes.

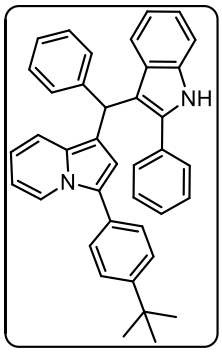
Characterization of the products:



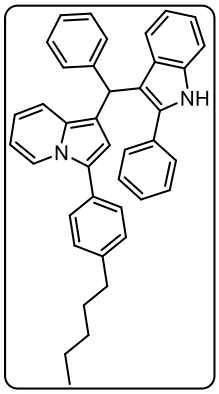
2-Phenyl-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (108a): Light yellow solid; yield 90% (42.7 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 86–89 °C; FT-IR 3412, 3058, 1450, 130, 741, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.1 Hz, 1H), 8.07 (s, 1H), 7.53 – 7.50 (m, 4H), 7.44 – 7.35 (m, 6H), 7.32 – 7.30 (m, 3H), 7.27 – 7.23 (m, 3H), 7.20 – 7.17 (m, 1H), 7.15 – 7.11 (m, 1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.92 (t, *J* = 7.9 Hz, 1H), 6.75 (s, 1H), 6.51 – 6.47 (m, 1H), 6.42 (t, *J* = 7.0 Hz, 1H), 6.11 (s, 1H) ppm. ^{13}C NMR (100

MHz, $CDCl_3$) δ = 144.7, 136.4, 135.2, 133.2, 132.7, 130.9, 128.9, 128.8 (2C), 128.7, 128.5, 128.2, 127.9, 126.8, 125.9, 124.4, 122.3, 122.0, 121.8, 119.6, 118.2, 116.4, 116.2, 116.1, 115.7, 115.67, 110.8, 110.6, 39.3 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{27}N_2$ $[M+H]^+$: 475.2175; found: 475.2153.

[3-((3-(4-(*tert*-Butyl)phenyl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108b): Off

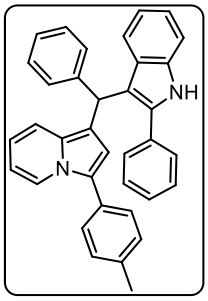


white solid; yield 93% (49.3 mg); R_f = 0.7 (20% EtOAc in hexane); M.P. 140–142 °C; FT-IR 3415, 3059, 2962, 1457, 1269, 741, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.53 – 7.51 (m, 2H), 7.49 – 7.31 (m, 11H), 7.27 – 7.23 (m, 2H), 7.21 – 7.17 (m, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 6.92 (t, *J* = 7.7 Hz, 1H), 6.75 (s, 1H), 6.50 – 6.46 (m, 1H), 6.43 – 6.39 (m, 1H), 6.12 (s, 1H), 1.37 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.9, 144.7, 136.4, 135.1, 133.3, 130.7, 129.9, 128.9 (2C), 128.7, 128.5, 128.1, 127.9, 127.6, 125.9, 125.8, 124.3, 122.5, 122.0, 121.8, 119.6, 118.1, 116.3, 116.2, 115.9, 115.6, 110.8, 110.4, 39.3, 34.7, 31.5 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{35}N_2$ $[M+H]^+$: 531.2801; found: 531.2778.



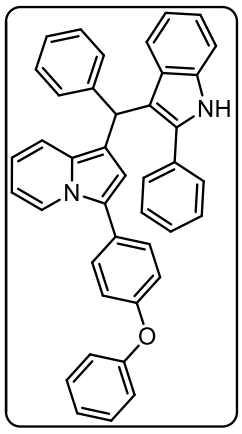
[3-((3-(4-Pentylphenyl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108c) : Green solid; yield 68% (37 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 130–132 °C; FT-IR 3412, 3059, 2928, 1457, 1303, 741, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.54 – 7.52 (m, 2H), 7.46 – 7.32 (m, 10H), 7.28 – 7.24 (m, 3H), 7.22 – 7.18 (m, 1H), 7.14 (t, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 1H), 6.95 – 6.92 (m, 1H), 6.75 (s, 1H), 6.50 – 6.47 (m, 1H), 6.43 – 6.40 (m, 1H), 6.13 (s, 1H), 2.65 (t, *J* = 7.6 Hz, 2H), 1.67 (quintet, *J* = 7.4 Hz, 2H), 1.41 – 1.36 (m, 4H), 0.94 (t, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7, 141.7, 136.4, 135.2, 133.2, 130.7, 130.0, 128.9, 128.84, 128.82, 128.7, 128.5, 128.1, 127.9 (2C), 125.9, 124.5, 122.4, 121.9, 121.8, 119.6, 118.1, 116.2, 116.19, 115.8, 115.5, 110.8, 110.4, 39.3, 35.8, 31.6, 31.3, 22.7, 14.2 ppm. HRMS (ESI): *m/z* calcd for $C_{40}H_{37}N_2$ $[M+H]^+$: 545.2957; found: 545.2934.

[2-Phenyl-3-(phenyl(3-(*p*-tolyl)indolizin-1-yl)methyl)]-1H-indole (108d): Green solid; yield 96% (47 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 190–192 °C; FT-IR 3415, 3058, 1449, 1300, 741, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, *J* = 7.1 Hz, 1H), 8.08 (s, 1H), 7.53 – 7.51 (m, 2H), 7.44 – 7.30 (m, 10H), 7.26 – 7.22 (m, 3H), 7.20 – 7.17 (m, 1H), 7.15 – 7.11 (m,



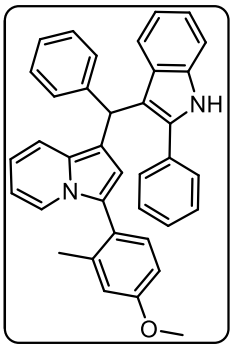
1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.94 – 6.90 (m, 1H), 6.73 (s, 1H), 6.49 – 6.45 (m, 1H), 6.42 – 6.38 (m, 1H), 6.11 (s, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7, 136.6, 136.4, 135.2, 133.2, 130.7, 129.8, 129.6, 128.83, 128.83, 128.7, 128.5, 128.1, 127.9 (2C), 127.8, 125.9, 124.4, 122.3, 121.9, 121.8, 119.5, 118.1, 116.2, 116.17, 115.8, 115.4, 110.8, 110.4, 39.3, 21.4 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{29}N_2$ $[M+H]^+$: 489.2331; found: 489.2313.

[3-((3-(4-Phenoxyphenyl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108e): Off



white solid; yield 90% (51 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 118–120 °C; FT-IR 3419, 3058, 1489, 1238, 741, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 7.1 Hz, 1H), 8.07 (s, 1H), 7.52 – 7.30 (m, 13H), 7.27 – 7.23 (m, 2H), 7.21 – 7.17 (m, 1H), 7.15 – 7.11 (m, 2H), 7.06 (d, *J* = 8.6 Hz, 4H), 6.98 (d, *J* = 8.9 Hz, 1H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.73 (s, 1H), 6.51 – 6.47 (m, 1H), 6.44 – 6.41 (m, 1H), 6.12 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.2, 156.2, 144.7, 136.4, 135.2, 133.2, 130.7, 129.9, 129.5, 128.84, 128.83, 128.7, 128.5, 128.2, 127.9, 127.8, 125.9, 123.8, 123.5, 122.2, 122.0, 121.7, 119.6, 119.3, 119.0, 118.1, 116.3, 116.2, 116.0, 115.5, 110.9, 110.6, 39.3 ppm. HRMS (ESI): *m/z* calcd for $C_{41}H_{31}N_2O$ $[M+H]^+$: 567.2437; found: 567.2412.

[3-((3-(4-Methoxy-2-methylphenyl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole



(108f): Light brown solid; yield 75% (39 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 115–117 °C; FT-IR 3411, 2926, 1450, 1276, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (s, 1H), 7.55 – 7.53 (m, 2H), 7.49 (d, *J* = 7.1 Hz, 1H), 7.46 – 7.42 (m, 2H), 7.40 – 7.30 (m, 4H), 7.28 – 7.22 (m, 4H), 7.20 – 7.17 (m, 1H), 7.13 – 7.09 (m, 1H), 6.95 (d, *J* = 9.0 Hz, 1H), 6.90 – 6.86 (m, 2H), 6.79 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.60 (s, 1H), 6.47 – 6.43 (m, 1H), 6.37 – 6.33 (m, 1H), 6.14 (s, 1H), 3.84 (s, 3H), 2.10 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.5, 145.0, 140.0, 136.4, 135.0, 133.3, 132.5, 129.4, 128.9, 128.86, 128.7, 128.6, 128.1, 127.9, 125.9, 124.4, 123.0, 122.6, 121.9, 121.8, 119.4, 117.8, 116.4, 115.9, 115.8, 115.3, 115.29, 111.3, 110.8, 109.9, 55.4, 39.4, 20.2 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{31}N_2O$ $[M+H]^+$: 519.2437; found: 519.2417.

[3-((3-(2-Chlorophenyl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108g): Off white solid; yield 74% (37.6 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 98–100 °C; FT-IR 3411, 3058, 1448, 1307, 741, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.08 (s, 1H), 7.60 (d, J = 7.0 Hz, 1H), 7.54 – 7.49 (m, 3H), 7.45 – 7.37 (m, 4H), 7.36 – 7.24 (m, 8H), 7.21 – 7.17 (m, 1H), 7.14 – 7.10 (m, 1H), 6.98 (d, J = 9.0 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.73 (s, 1H), 6.54 – 6.50 (m, 1H), 6.45 – 6.41 (m, 1H), 6.14 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.8, 136.4, 135.1, 134.7, 133.3, 133.0, 131.6, 130.4, 130.0, 129.1, 128.9, 128.89, 128.7, 128.6, 128.2, 128.0, 126.9, 125.9, 123.3, 122.0, 121.9, 121.2, 119.6, 117.8, 116.8, 116.3, 116.2, 115.8, 110.8, 110.1, 39.5 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}ClN_2$ $[M+H]^+$: 509.1785; found: 509.1768.

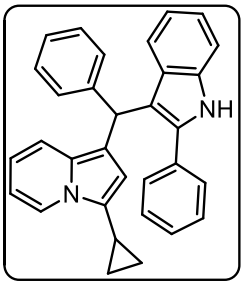
[3-((3-(6-Methoxynaphthalen-2-yl)indolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole

(108h) : Light yellow solid; yield 85% (47.1 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 98–100 °C; FT-IR 3411, 2927, 1606, 1275, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, J = 7.0 Hz, 1H), 8.09 (s, 1H), 7.90 (s, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.72 (d, J = 8.7 Hz, 1H), 7.60 (dd, J = 8.5, 1.5 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.44 – 7.32 (m, 7H), 7.28 – 7.24 (m, 2H), 7.21 – 7.12 (m, 4H), 7.00 (d, J = 8.9 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.83 (s, 1H), 6.52 – 6.49 (m, 1H), 6.46 – 6.42 (m, 1H), 6.14 (s, 1H), 3.94 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 144.7, 136.4, 135.2, 133.5, 133.2, 131.0, 129.5, 129.3, 128.9 (2C), 128.7, 128.6, 128.2, 128.0, 127.9, 127.3, 127.1, 126.0, 125.9, 124.5, 122.3, 122.0, 121.8, 119.6, 119.3, 118.2, 116.5, 116.2, 116.1, 115.8, 110.8, 110.6, 105.9, 55.5, 39.3 ppm. HRMS (ESI): *m/z* calcd for $C_{40}H_{31}N_2O$ $[M+H]^+$: 555.2437; found: 555.2411.

[2-Phenyl-3-(phenyl(3-(thiophen-3-yl)indolizin-1-yl)methyl)]-1H-indole (108i): Green solid; yield 97% (46.6 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 126–128 °C; FT-IR 3411, 3058, 1449, 742, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 6.4 Hz, 1H), 8.09 (s, 1H), 7.51 – 7.49 (m, 2H), 7.43 – 7.33 (m, 6H), 7.29 – 7.22 (m, 6H), 7.20 – 7.11 (m, 2H), 6.98 (d, J = 7.9 Hz, 1H), 6.91 (t, J = 7.3 Hz, 1H), 6.77 (s, 1H), 6.51 – 6.44 (m, 2H), 6.10 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 136.4, 135.2, 133.19, 133.1, 130.6, 128.9, 128.8, 128.7, 128.5, 128.2, 128.0, 127.7, 125.9, 125.87, 122.7, 122.0, 121.7, 120.2,

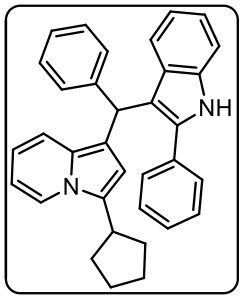
119.9, 119.6, 118.0, 116.2, 116.0, 115.9, 115.5, 110.8, 110.7, 39.2 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{25}N_2S$ $[M+H]^+$: 481.1739; found: 481.1725.

[3-((3-Cyclopropylindolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108j): Green solid;



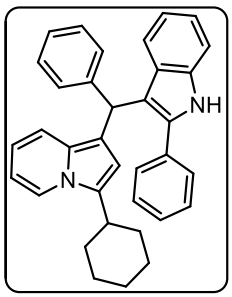
yield 56% (24.6 mg); R_f = 0.7 (20% EtOAc in hexane); M.P. 190–192 °C; FT-IR 3404, 3059, 1450, 1422, 742, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.06 (s, 1H), 8.01 – 8.00 (m, 1H), 7.48 – 7.47 (m, 2H), 7.41 – 7.34 (m, 4H), 7.26 – 7.10 (m, 7H), 6.93 – 6.89 (m, 2H), 6.47 – 6.44 (m, 2H), 6.39 (s, 1H), 6.06 (s, 1H), 1.83 – 1.77 (m, 1H), 0.93 – 0.84 (m, 2H), 0.64 – 0.54 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.0, 136.4, 135.0, 133.3, 129.4, 128.8, 128.78, 128.7, 128.5, 128.1, 127.9, 125.8, 125.0, 122.3, 121.9, 121.8, 119.5, 117.7, 116.6, 115.0, 114.1, 113.0, 110.8, 109.6, 39.2, 6.4, 5.5, 5.46 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{27}N_2$ $[M+H]^+$: 439.2175; found: 439.2157.

[3-((3-Cyclopentylindolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108k): Green solid;



yield 94% (44 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 171–173 °C; FT-IR 3404, 3059, 2957, 1450, 1309, 741, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.09 (s, 1H), 7.74 – 7.72 (m, 1H), 7.49 – 7.47 (m, 2H), 7.42 – 7.34 (m, 5H), 7.26 – 7.21 (m, 4H), 7.19 – 7.16 (m, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.92 – 6.88 (m, 2H), 6.47 (s, 1H), 6.42 – 6.37 (m, 2H), 6.07 (s, 1H), 3.25 – 3.18 (m, 1H), 2.18 – 2.02 (m, 2H), 1.74 – 1.56 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 136.4, 135.1, 133.3, 129.5, 128.8 (2C), 128.7, 128.6, 128.0, 127.9, 127.7, 125.7, 122.2, 121.87, 121.8, 119.4, 117.8, 116.6, 114.3, 114.26, 111.2, 110.8, 109.5, 39.3, 36.7, 31.44, 31.37, 25.17, 25.15 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{31}N_2$ $[M+H]^+$: 467.2488; found: 467.2465.

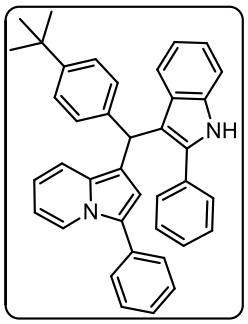
[3-((3-Cyclohexylindolizin-1-yl)(phenyl)methyl)]-2-phenyl-1H-indole (108l): Green solid;



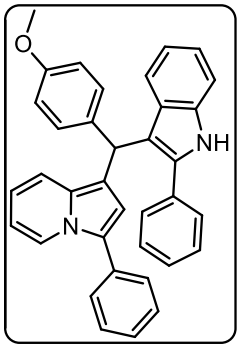
yield 74% (35.5 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 161–163 °C; FT-IR 3403, 3060, 2928, 1450, 742, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.08 (s, 1H), 7.71 (d, *J* = 6.5 Hz, 1H), 7.49 – 7.47 (m, 2H), 7.42 – 7.33 (m, 4H), 7.26 – 7.21 (m, 5H), 7.19 – 7.16 (m, 1H),), 7.12 (t, *J* = 7.4 Hz, 1H), 6.92 – 6.87 (m, 2H), 6.42 (s, 1H), 6.42 – 6.35 (m, 2H), 6.06 (s, 1H), 2.79 – 2.73 (m, 1H), 2.07 – 1.96 (m, 2H), 1.82 – 1.73 (m, 3H), 1.45 – 1.31 (m, 5H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.1, 136.4, 135.0, 133.3, 129.1, 128.9, 128.8 (2C),

128.7, 128.6, 128.0, 127.9, 125.7, 121.9, 121.86, 121.7, 119.4, 118.0, 116.6, 114.5, 114.2, 110.9, 110.8, 109.5, 39.3, 35.4, 31.8, 31.7, 26.7, 26.7, 26.5 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{33}N_2$ $[M+H]^+$: 481.2644; found:481.2628.

[3-((4-(*tert*-Butyl)phenyl)(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108m):

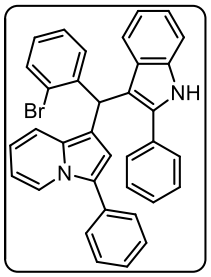


Green solid; yield 92% (49 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 153–155 °C; FT-IR 3408, 3059, 2963, 1449, 1300, 742, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.52 – 7.51 (m, 4H), 7.43 – 7.35 (m, 7H), 7.29 – 7.21 (m, 5H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.97 – 6.91 (m, 2H), 6.77 (s, 1H), 6.48 – 6.44 (m, 1H), 6.39 (t, *J* = 6.5 Hz, 1H), 6.08 (s, 1H), 1.29 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.5, 141.4, 136.4, 135.1, 133.3, 132.8, 130.9, 128.9, 128.8, 128.5, 128.4, 128.0, 127.9, 127.8, 126.8, 125.0, 124.3, 122.2, 122.0, 121.9, 119.5, 118.2, 116.8, 116.4, 116.0, 115.6, 110.8, 110.5, 38.7, 34.5, 31.6 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{35}N_2$ $[M+H]^+$: 531.2801; found: 531.2782.



[3-((4-Methoxyphenyl)(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108n): Light green solid; yield 56% (28.2 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 216–218 °C; FT-IR 3407, 3060, 2927, 1462, 1262, 746, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 – 8.24 (m, 1H), 8.08 (s, 1H), 7.52 – 7.49 (m, 4H), 7.44 – 7.34 (m, 6H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.20 (d, *J* = 8.3 Hz, 2H), 7.14 – 7.10 (m, 1H), 6.97 – 6.94 (m, 1H), 6.93 – 6.89 (m, 1H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.73 (s, 1H), 6.49 – 6.45 (m, 1H), 6.42 – 6.38 (m, 1H), 6.06 (s, 1H), 3.77 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.7, 136.8, 136.4, 135.0, 133.2, 132.7, 130.8, 129.8, 128.9, 128.8, 128.7, 128.5, 127.9, 126.8, 124.3, 122.3, 122.0, 121.8, 119.6, 118.2, 116.8, 116.4, 116.0, 115.7, 115.6, 113.5, 110.8, 110.6, 55.3, 38.5 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{29}N_2O$ $[M+H]^+$: 505.2281; found: 505.2259.

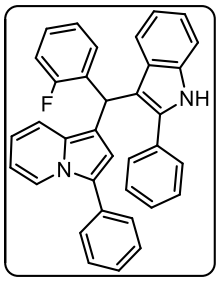
[3-((2-Bromophenyl)(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108o): Green



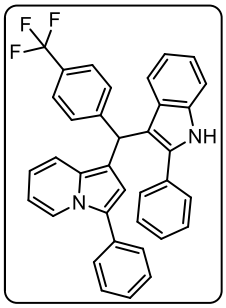
solid; yield 60% (33.1 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 122–124 °C; FT-IR 3412, 3060, 2925, 1461, 1267, 745, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 6.9 Hz, 1H), 8.12 (s, 1H), 7.62 – 7.57 (m, 4H), 7.45 – 7.30 (m, 10H), 7.26 – 7.22 (m, 1H), 7.19 – 7.09 (m, 2H), 7.00 – 6.96 (m, 2H), 6.70 (s, 1H), 6.52 – 6.48 (m, 1H), 6.43 (t, *J* = 6.6 Hz, 1H), 6.35 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.6, 136.2, 135.9, 133.2, 133.1, 132.6, 131.1, 130.7, 128.9, 128.86, 128.6, 128.5, 128.4, 127.9, 127.8, 127.2, 126.8, 125.1, 124.1, 122.2, 121.8, 121.0, 119.6, 118.1, 116.2, 115.9, 115.4, 114.0, 110.9, 110.7, 40.4 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}BrN_2$ $[M+H]^+$: 553.1280; found: 553.1257.

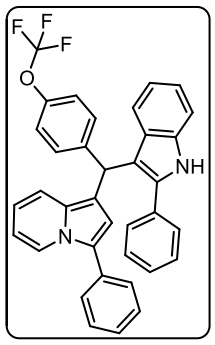
[3-((2-Fluorophenyl)(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108p): Light yellow solid; yield 61% (30 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 136–138 °C; FT-IR 3417, 3060, 1455, 1302, 739, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, *J* = 7.1 Hz, 1H), 8.10 (s, 1H), 7.53 – 7.51 (m, 2H), 7.47 – 7.35 (m, 10H), 7.29 – 7.26 (m, 1H), 7.21 – 7.16 (m, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.05 – 6.90 (m, 4H), 6.68 (s, 1H), 6.48 – 6.44 (m, 1H), 6.40 (t, *J* = 6.1 Hz, 1H), 6.31 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.0 (d, J_{C-F} = 245.4 Hz), 136.2, 135.3, 133.2, 132.7, 131.7 (d, J_{C-F} = 13.7 Hz), 130.6 (d, J_{C-F} = 4.0 Hz), 130.5, 128.9, 128.8, 128.7, 128.6, 128.0, 127.93, 127.9, 126.8, 124.1, 123.8 (d, J_{C-F} = 3.4 Hz), 123.0, 121.9, 121.1, 119.6, 118.2, 116.1, 115.8, 115.4 (d, J_{C-F} = 21.8 Hz), 115.0, 114.4, 110.9, 110.7, 33.6 (d, J_{C-F} = 2.9 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -116.0 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}FN_2$ $[M+H]^+$: 493.2081; found: 493.2059.



2-Phenyl-[3-((3-phenylindolizin-1-yl)(4-(trifluoromethyl)phenyl)methyl)]-1H-indole (108q): Green solid; yield 75% (40.7 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 130–132 °C; FT-IR 3411, 3061, 2926, 1450, 1325, 1121, 741, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.1 Hz, 1H), 8.13 (s, 1H), 7.52 – 7.37 (m, 13H), 7.30 – 7.25 (m, 3H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.97 – 6.92 (m, 2H), 6.72 (s, 1H), 6.54 – 6.50 (m, 1H), 6.44 (t, *J* = 6.5 Hz, 1H), 6.12 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.9, 136.4, 135.5, 133.0, 132.5, 130.9, 129.1, 129.0 (2C), 128.9, 128.7, 128.2, 128.0, 127.1 (q, J_{C-F} = 242.5 Hz), 127.0, 125.1 (q, J_{C-F} = 3.8 Hz), 124.7, 123.2, 122.4, 122.2, 121.4, 119.8, 117.9, 116.5, 115.5, 115.3, 115.2, 111.0, 110.7, 39.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.1 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{26}F_3N_2$ $[M+H]^+$: 543.2049; found: 543.2026.

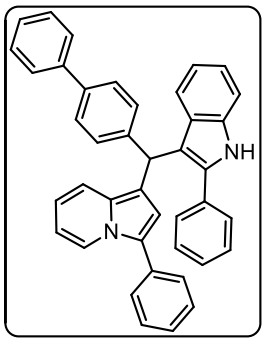


2-Phenyl-[3-((3-phenylindolizin-1-yl)(4-(trifluoromethoxy)phenyl)methyl)]-1H-indole (108r): Green semi solid; yield 82% (45.8 mg); R_f = 0.7 (20% EtOAc in hexane); FT-IR 3413, 3061, 1505, 1262, 740, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.1 Hz, 1H), 8.11 (s, 1H), 7.53 – 7.48 (m, 4H), 7.45 – 7.36 (m, 6H), 7.30 – 7.26 (m, 4H), 7.17 – 7.13 (m, 1H), 7.08



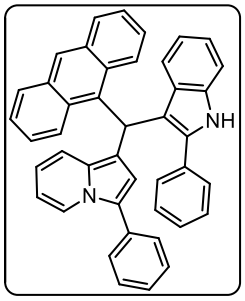
– 7.06 (m, 2H), 6.99 – 6.93 (m, 2H), 6.75 (s, 1H), 6.54 – 6.51 (m, 1H), 6.46 – 6.42 (m, 1H), 6.09 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.4, 143.4, 136.4, 135.4, 133.0, 132.6, 130.8, 130.1, 129.0, 128.9, 128.7, 128.2, 128.1, 128.0, 127.0, 124.6, 122.4, 122.2, 121.5, 120.7 (q, $J_{C\text{-}F}$ = 254.9 Hz), 120.6, 119.7, 117.9, 116.4, 115.8, 115.6, 115.4, 111.0, 110.7, 38.7 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.8 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{26}F_3N_2O$ $[M+H]^+$: 559.1998; found: 559.1972.

{3-([1,1'-Biphenyl]-4-yl(3-phenylindolizin-1-yl)methyl)}-2-phenyl-1H-indole (108s): Off



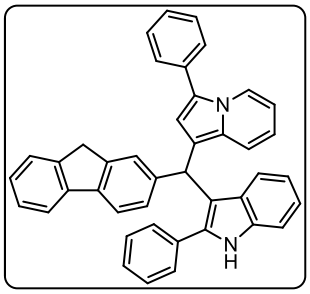
white solid; yield 75% (41.2 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 176–178 °C; FT-IR 3415, 3057, 1487, 1301, 744, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.29 (d, *J* = 7.1 Hz, 1H), 8.08 (s, 1H), 7.60 (d, *J* = 7.2 Hz, 2H), 7.55 – 7.53 (m, 4H), 7.50 – 7.48 (m, 2H), 7.46 – 7.37 (m, 11H), 7.33 – 7.26 (m, 2H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.01 (d, *J* = 9.0 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.81 (s, 1H), 6.53 – 6.49 (m, 1H), 6.45 – 6.42 (m, 1H), 6.15 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 141.2, 138.6, 136.4, 135.3, 133.2, 132.7, 131.0, 129.3, 128.9, 128.88, 128.8, 128.76, 128.50, 128.0, 127.96, 127.1, 127.0, 126.9 (2C), 124.4, 122.3, 122.0, 121.8, 119.6, 118.2, 116.3, 116.2, 116.1, 115.7, 110.9, 110.6, 39.0 ppm. HRMS (ESI): *m/z* calcd for $C_{41}H_{31}N_2$ $[M+H]^+$: 551.2488; found: 551.2471.

[3-(Anthracen-9-yl(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108t): Yellow

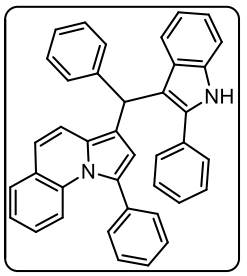


solid; yield 53% (30.4 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 132–135 °C; FT-IR 3415, 3052, 1450, 1265, 734, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.49 – 8.47 (m, 2H), 8.33 (s, 1H), 8.17 (d, *J* = 7.1 Hz, 1H), 7.95 – 7.92 (m, 3H), 7.50 (s, 1H), 7.40 – 7.28 (m, 7H), 7.24 – 7.17 (m, 3H), 7.13 (d, *J* = 9.0 Hz, 1H), 7.08 – 7.04 (m, 1H), 7.01 – 6.95 (m, 3H), 6.90 – 6.86 (m, 2H), 6.73 (d, *J* = 3.8 Hz, 2H), 6.58 (s, 1H), 6.49 – 6.45 (m, 1H), 6.39 – 6.36 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.7, 135.7, 135.2, 133.3, 132.7, 131.9, 130.8, 130.7, 129.1, 128.8, 128.7, 128.6, 127.9, 127.3, 127.2, 127.15, 126.7, 125.7, 125.1, 124.5, 124.2, 122.2, 121.8, 120.9, 119.6, 118.2, 116.7, 116.4, 116.3, 116.1, 110.6, 110.5, 36.1 ppm. HRMS (ESI): *m/z* calcd for $C_{43}H_{31}N_2$ $[M+H]^+$: 575.2488; found: 575.2465.

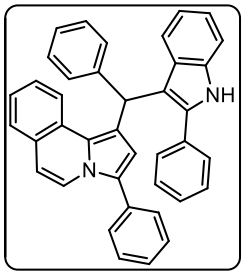
[3-((9H-Fluoren-2-yl)(3-phenylindolizin-1-yl)methyl)]-2-phenyl-1H-indole (108u): Green solid; yield 72% (40.5 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 226–228 °C; FT-IR 3412, 3056, 1455, 1301, 738, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.29 (d, *J* = 7.1 Hz, 1H), 8.12 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.55 – 7.53 (m, 4H), 7.50 – 7.47 (m, 2H), 7.45 – 7.32 (m, 9H), 7.29 – 7.23 (m, 2H), 7.15 – 7.10 (m, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.92 – 6.88 (m, 1H), 6.78 (s, 1H), 6.51 – 6.47 (m, 1H), 6.43 (td, *J* = 7.1, 1.4 Hz, 1H), 6.18 (s, 1H), 3.79 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.7, 143.5, 143.4, 141.9, 139.6, 136.4, 135.1, 133.2, 132.7, 130.9, 128.9, 128.8, 128.7, 128.6, 127.94, 127.91, 127.6, 126.8, 126.7, 126.3, 125.4, 125.1, 124.4, 122.3, 122.0, 121.8, 119.7, 119.6, 119.5, 118.2, 116.6, 116.4, 116.1, 115.8, 110.8, 110.6, 39.5, 37.1 ppm. HRMS (ESI): *m/z* calcd for $C_{42}H_{31}N_2$ $[M+H]^+$: 563.2488; found: 563.2463.



[1-Phenyl-3-(phenyl(2-phenyl-1H-indol-3-yl)methyl)]pyrrolo[1,2-*a*]quinoline (108v) : Pale yellow solid; yield 83% (43.5 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 140–142 °C; FT-IR 3413, 3057, 2925, 1448, 1309, 741, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.09 (s, 1H), 7.56 – 7.35 (m, 13H), 7.31 – 7.21 (m, 5H), 7.19 – 7.15 (m, 2H), 7.14 – 7.06 (m, 2H), 6.97 (d, *J* = 9.3 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 9.4 Hz, 1H), 6.58 (s, 1H), 6.10 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.5, 136.4, 135.8, 135.3, 134.5, 133.2, 129.7, 129.4, 129.3, 128.9, 128.8, 128.7, 128.5, 128.46, 128.4, 128.2, 128.0, 127.4, 126.3, 126.0, 125.6, 123.2, 122.0, 121.7, 119.7, 119.3, 118.4, 118.0, 117.8, 117.6, 116.1, 110.9, 39.1 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{29}N_2$ $[M+H]^+$: 525.2331; found: 525.2310.

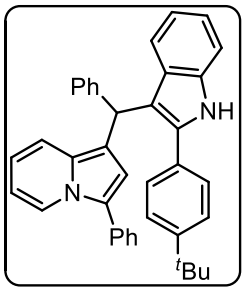


[3-Phenyl-1-(phenyl(2-phenyl-1H-indol-3-yl)methyl)]pyrrolo[2,1-*a*]isoquinoline (108w): Off white solid; yield 44% (23 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 148–150 °C; FT-IR 3418, 3057, 2925, 1455, 1337, 740, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.12 (s, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.41 (m, 8H), 7.37 – 7.30 (m, 8H), 7.28 – 7.24 (m, 1H), 7.21 – 7.17 (m, 2H), 7.14 – 7.10 (m, 1H), 7.04 – 7.00 (m, 1H), 6.92 – 6.88 (m, 1H), 6.65 (d, *J* = 7.5 Hz, 1H), 6.59 (s, 1H), 6.37 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6, 136.4, 135.5, 133.2, 132.4, 129.2, 129.1, 128.9, 128.8 (2C), 128.4, 128.38, 127.9, 127.8, 127.4, 127.3, 127.1, 126.8, 126.4, 126.1, 125.8, 124.7, 123.7, 122.5, 122.0, 121.7, 121.0, 119.7,



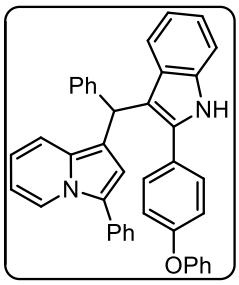
115.7, 115.5, 111.0, 110.8, 42.0 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{29}N_2$ $[M+H]^+$: 525.2331; found: 525.2312.

2-(4-(*tert*-Butyl)phenyl)-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109a): Green



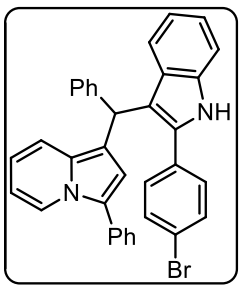
solid; yield 80% (42.4 mg); R_f = 0.7 (20% EtOAc in hexane); M.P. 129–131 °C; FT-IR 3407, 2962, 1456, 1268, 838, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.0 Hz, 1H), 8.04 (s, 1H), 7.53 – 7.51 (m, 2H), 7.44 – 7.23 (m, 13H), 7.20 – 7.17 (m, 1H), 7.12 (t, *J* = 7.3 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.73 (s, 1H), 6.50 – 6.47 (m, 1H), 6.42 (t, *J* = 6.6 Hz, 1H), 6.13 (s, 1H), 1.36 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.0, 144.7, 136.3, 135.2, 132.8, 130.9, 130.3, 128.9 (2C), 128.7, 128.3, 128.1, 127.9, 126.8, 125.9, 125.8, 124.3, 122.3, 121.8, 121.6, 119.5, 118.3, 116.5, 116.0, 115.9, 115.8, 110.7, 110.5, 39.4, 34.8, 31.5 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{35}N_2$ $[M+H]^+$: 531.2801; found: 531.2782.

2-(4-Phenoxyphenyl)-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109b): Green



solid; yield 52% (29.4 mg); R_f = 0.5 (20% EtOAc in hexane); M.P. 124–126 °C; FT-IR 3412, 3058, 1488, 1241, 1106, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.52 – 7.50 (m, 2H), 7.45 – 7.34 (m, 7H), 7.31 – 7.22 (m, 6H), 7.20 – 7.10 (m, 3H), 7.06 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.71 (s, 1H), 6.51 – 6.47 (m, 1H), 6.41 (t, *J* = 6.5 Hz, 1H), 6.08 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.3, 156.9, 144.6, 136.3, 134.7, 132.7, 130.9, 130.1, 130.0, 128.9, 128.8, 128.6, 128.2, 128.1, 127.9, 126.8, 126.0, 124.4, 123.8, 122.3, 121.9, 121.6, 119.6, 119.4, 118.8, 118.1, 116.3, 116.1, 116.0, 115.7, 110.8, 110.6, 39.4 ppm. HRMS (ESI): *m/z* calcd for $C_{41}H_{31}N_2O$ $[M+H]^+$: 567.2437; found: 567.2429.

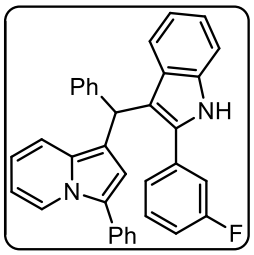
2-(4-Bromophenyl)-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109c): Green



solid; yield 48% (26.5 mg); R_f = 0.7 (20% EtOAc in hexane); M.P. 136–138 °C; FT-IR 3405, 3058, 2926, 1452, 1301, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, *J* = 7.1 Hz, 1H), 8.10 (s, 1H), 7.51 – 7.49 (m, 4H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.36 – 7.31 (m, 3H), 7.29 – 7.22 (m, 6H), 7.20 – 7.16 (m, 1H), 7.15 – 7.11 (m, 1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.94 – 6.90 (m, 1H), 6.69 (s, 1H), 6.53 – 6.49 (m, 1H), 6.44 – 6.41 (m, 1H), 6.03 (s, 1H)

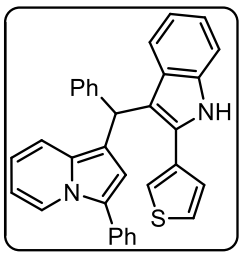
ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.4, 136.4, 133.9, 132.6, 132.1, 131.9, 130.8, 130.2, 128.9, 128.8, 128.5, 128.2, 127.9, 126.9, 126.1, 124.4, 122.4, 122.3, 122.1, 121.7, 119.8, 118.0, 116.7, 116.3, 116.0, 115.7, 110.9, 110.6, 39.4 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}BrN_2$ $[M+H]^+$: 553.1280; found: 553.1255.

2-(3-Fluorophenyl)-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109d): Off white



solid; yield 80% (39.4 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 196–198 °C; FT-IR 3404, 3060, 1453, 1300, 741, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.53 – 7.51 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.31 – 7.24 (m, 7H), 7.21 – 7.18 (m, 2H), 7.17 – 7.13 (m, 1H), 7.06 (td, *J* = 8.4, 1.8 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 1H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.72 (s, 1H), 6.54 – 6.50 (m, 1H), 6.45 – 6.41(m, 1H), 6.10 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.9 (d, J_{C-F} = 245.0 Hz), 144.4, 136.5, 135.3 (d, J_{C-F} = 8.1 Hz), 133.8 (d, J_{C-F} = 2.3 Hz), 132.6, 130.8, 130.3 (d, J_{C-F} = 8.5 Hz), 128.9, 128.8, 128.4, 128.2, 127.9, 126.9, 126.0, 124.41, 124.40, 122.3 (d, J_{C-F} = 1.9 Hz), 121.8, 119.8, 118.0, 116.9, 116.3, 116.0, 115.6, 115.5 (d, J_{C-F} = 22.1 Hz), 114.8, 114.6, 111.0, 110.6, 39.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.2 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}FN_2$ $[M+H]^+$: 493.2081; found: 493.2062.

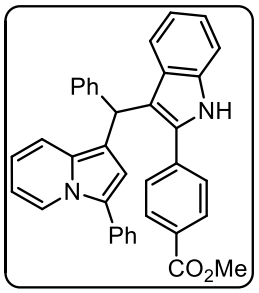
3-[Phenyl(3-phenylindolizin-1-yl)methyl]-2-(thiophen-3-yl)-1H-indole (109e): Green solid;



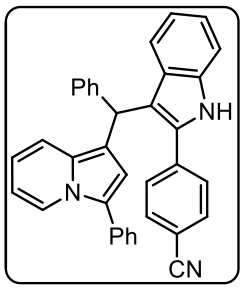
yield 90% (43.2 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 160–162 °C; FT-IR 3412, 3057, 2926, 1460, 1106, 741, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 7.1 Hz, 1H), 8.07 (s, 1H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.42 – 7.38 (m, 3H), 7.35 – 7.23 (m, 8H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 9.0 Hz, 1H), 6.90 – 6.86 (m, 1H), 6.67 (s, 1H), 6.52 – 6.49 (m, 1H), 6.42 (t, *J* = 6.4 Hz, 1H), 6.14 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.5, 136.1, 133.7, 132.7, 130.9, 130.7, 128.9, 128.85, 128.6, 128.2, 127.9, 127.5, 126.8, 126.3, 126.0, 124.4, 122.9, 122.4, 122.0, 121.5, 119.6, 118.1, 116.2, 116.21, 116.16, 115.7, 110.8, 110.6, 39.5 ppm. HRMS (ESI): *m/z* calcd for $C_{33}H_{25}N_2S$ $[M+H]^+$: 481.1739; found: 481.1720.

Methyl 4-[(3-(phenyl(3-phenylindolizin-1-yl)methyl)-1H-indol-2-yl)]benzoate (109f): Green solid; yield 61% (32.4 mg); R_f = 0.3 (20% EtOAc in hexane); M.P. 194–196 °C; FT-IR 3408, 3058, 1722, 1435, 1281, 742, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 (d, *J* = 7.1 Hz, 1H), 8.23 (s, 1H), 8.05 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.51 – 7.50 (m, 2H), 7.40 (t,

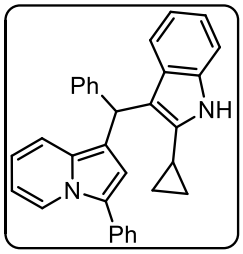
J = 7.5 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.31 – 7.23 (m, 6H), 7.20 – 7.19 (m, 1H), 7.17 – 7.13 (m, 1H), 6.99 (d, *J* = 9.0 Hz, 1H), 6.92 (t, *J* = 7.8 Hz, 1H), 6.71 (s, 1H), 6.54 – 6.50 (m, 1H), 6.43 (t, *J* = 6.9 Hz, 1H), 6.10 (s, 1H), 3.94 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.0, 144.3, 137.7, 136.7, 133.9, 132.6, 130.8, 130.0, 129.1, 128.9, 128.8, 128.5, 128.4, 128.2, 127.9, 126.9, 126.1, 124.5, 122.6, 122.4, 121.9, 119.9, 117.9, 117.7, 116.4, 115.9, 115.6, 111.0, 110.7, 52.4, 39.4 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{29}N_2O_2$ $[M+H]^+$: 533.2230; found: 533.2207.



4-[(3-(Phenyl(3-phenylindolizin-1-yl)methyl)-1H-indol-2-yl)]benzonitrile (109g): Yellow solid; yield 42% (21 mg); R_f = 0.3 (20% EtOAc in hexane); M.P. 188–190 °C; FT-IR 3354, 2925, 2222, 1602, 1451, 739, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, *J* = 7.0 Hz, 1H), 8.11 (s, 1H), 7.63 – 7.61 (m, 2H), 7.54 – 7.52 (m, 2H), 7.51 – 7.46 (m, 2H), 7.43 – 7.37 (m, 3H), 7.30 – 7.16 (m, 8H), 6.96 – 6.92 (m, 2H), 6.64 (s, 1H), 6.55 – 6.51 (m, 1H), 6.46 – 6.43 (m, 1H), 6.05 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.0, 137.7, 136.8, 133.0, 132.5, 132.4, 130.7, 129.0, 128.9, 128.8, 128.5, 128.3, 127.9, 127.0, 126.3, 124.6, 123.1, 122.5, 122.0, 120.2, 118.9, 118.4, 117.8, 116.6, 115.7, 115.6, 111.1, 111.0, 110.8, 39.5 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{26}N_3$ $[M+H]^+$: 500.2127; found: 500.2106.

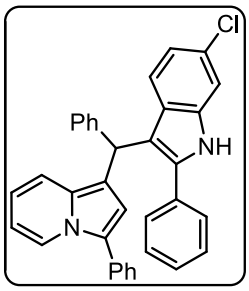


2-Cyclopropyl-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109h): Green solid; yield 50% (22 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 108–110 °C; FT-IR 3415, 3058, 2926, 1428, 1300, 744, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 7.2 Hz, 1H), 7.64 (s, 1H), 7.53 – 7.50 (m, 2H), 7.42 – 7.38 (m, 2H), 7.35 – 7.33 (m, 2H), 7.29 – 7.26 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 3H), 7.21 – 7.16 (m, 3H), 7.06 – 7.02 (m, 1H), 6.90 – 6.56 (m, 1H), 6.66 (s, 1H), 6.55 – 6.51 (m, 1H), 6.44 – 6.41 (m, 1H), 6.18 (s, 1H), 2.00 – 1.94 (m, 1H), 0.93 – 0.85 (m, 2H), 0.76 – 0.65 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7, 136.1, 134.9, 132.8, 131.1, 128.9, 128.8, 128.6, 128.1, 127.9, 126.8, 125.9, 124.2, 122.3, 121.0, 120.0, 119.3, 118.3, 116.4, 116.3, 116.0, 115.7, 110.6, 110.3, 39.2, 7.9, 6.7, 6.4 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{27}N_2$ $[M+H]^+$: 439.2175; found: 439.2157.

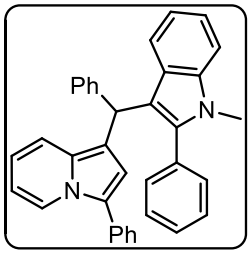


6-Chloro-2-phenyl-[3-(phenyl(3-phenylindolizin-1-yl)methyl)]-1H-indole (109i): Off white solid; yield 70% (35.6 mg); R_f = 0.6 (20% EtOAc in hexane); M.P. 150–152 °C; FT-IR 3411,

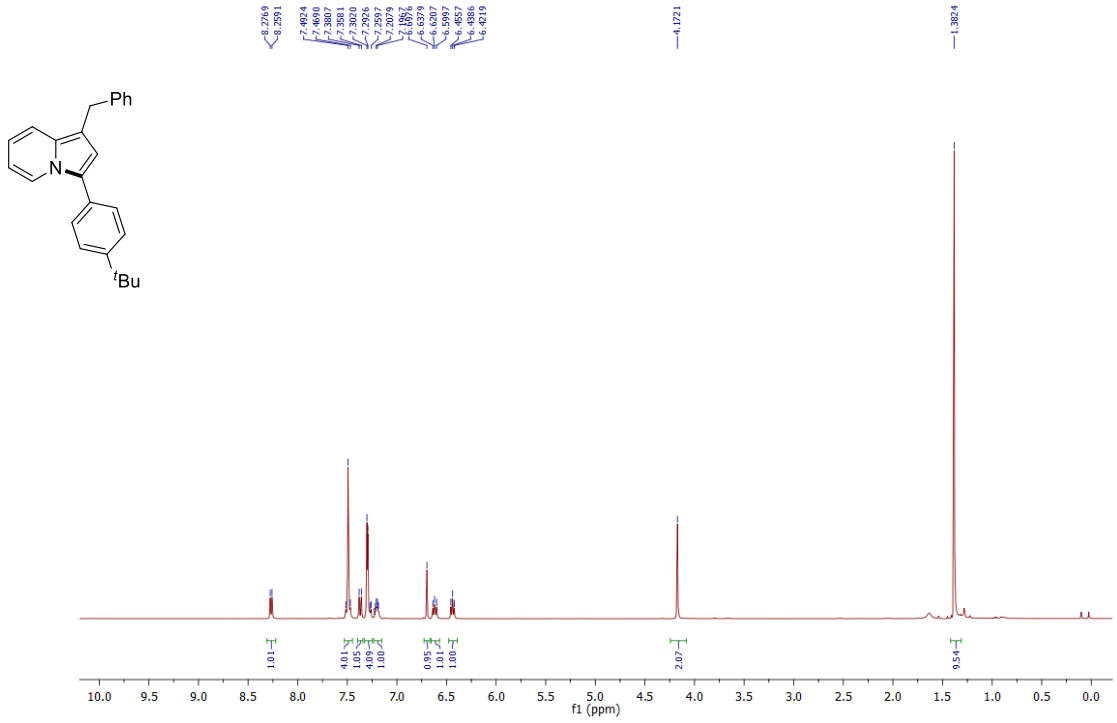
3059, 1449, 1301, 740, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 – 8.26 (m, 1H), 8.08 (s, 1H), 7.53 – 7.47 (m, 4H), 7.44 – 7.36 (m, 5H), 7.33 (d, *J* = 1.7 Hz, 1H), 7.30 – 7.24 (m, 5H), 7.23 – 7.19 (m, 1H), 7.18 – 7.16 (m, 1H), 6.97 – 6.94 (m, 1H), 6.87 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.68 (s, 1H), 6.52 – 6.48 (m, 1H), 6.43 (td, *J* = 7.1, 1.4 Hz, 1H), 6.07 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.4, 136.8, 135.8, 132.7, 132.6, 130.9, 129.0, 128.9, 128.8, 128.6, 128.3, 128.2, 127.9, 127.8, 127.2, 126.9, 126.1, 124.5, 122.5, 122.4, 120.4, 118.1, 116.3, 116.28, 116.0, 115.5, 110.8, 110.7, 39.2 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}ClN_2$ $[M+H]^+$: 509.1785; found: 509.1764.



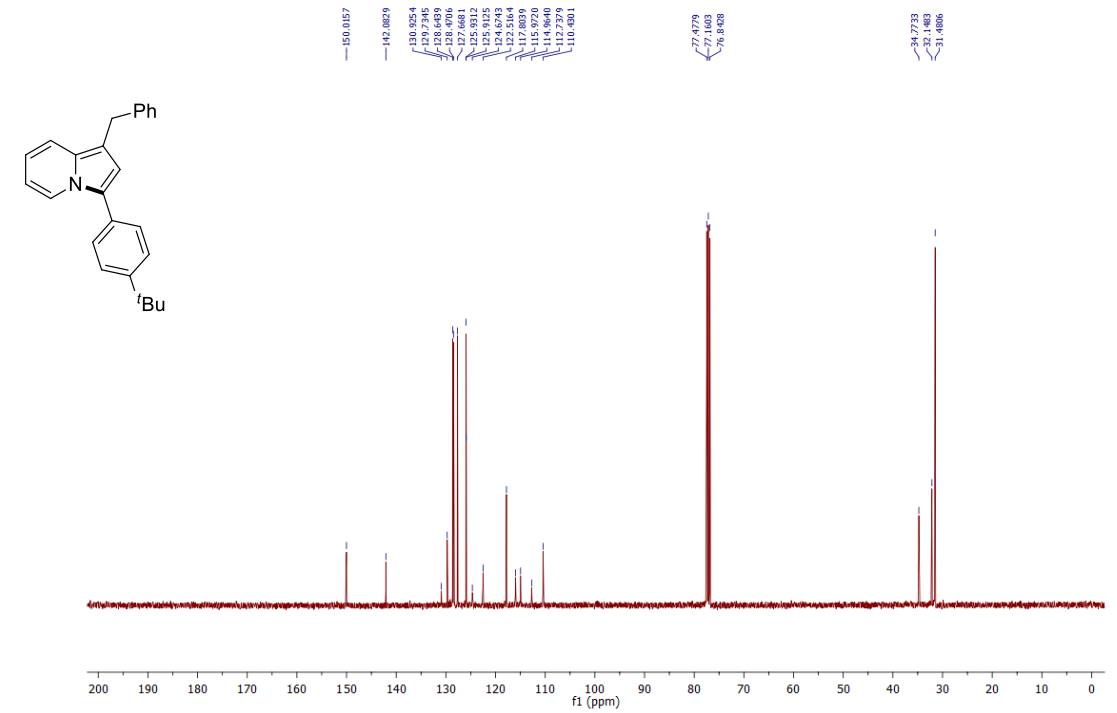
1-Methyl-2-phenyl-3-[phenyl(3-phenylindolizin-1-yl)methyl]-1H-indole (109j): Yellow solid; yield 58% (30 mg); R_f = 0.5 (10% EtOAc in hexane); M.P. 100–102 °C; FT-IR 3057, 2926, 1468, 741, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.23 (d, *J* = 7.0 Hz, 1H), 7.51 – 7.49 (m, 2H), 7.42 – 7.37 (m, 6H), 7.34 – 7.32 (m, 3H), 7.29 – 7.26 (m, 3H), 7.24 – 7.14 (m, 4H), 6.95 (t, *J* = 7.3 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 1H), 6.72 (s, 1H), 6.46 – 6.42 (m, 1H), 6.38 (t, *J* = 6.6 Hz, 1H), 5.83 (s, 1H), 3.61 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.0, 138.3, 137.7, 132.8, 132.1, 130.9, 130.8, 128.9, 128.7 (2C), 128.4, 128.2, 128.1, 127.9, 127.1, 126.7, 125.8, 124.3, 122.2, 121.5, 119.2, 118.2, 116.7, 116.2, 115.8, 115.6, 110.5, 109.3, 39.5, 31.0 ppm. HRMS (ESI): *m/z* calcd for $C_{36}H_{29}N_2$ $[M+H]^+$: 489.2331; found: 489.2313.



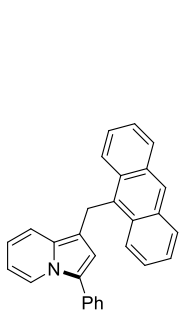
^{1}H Spectrum of 64c

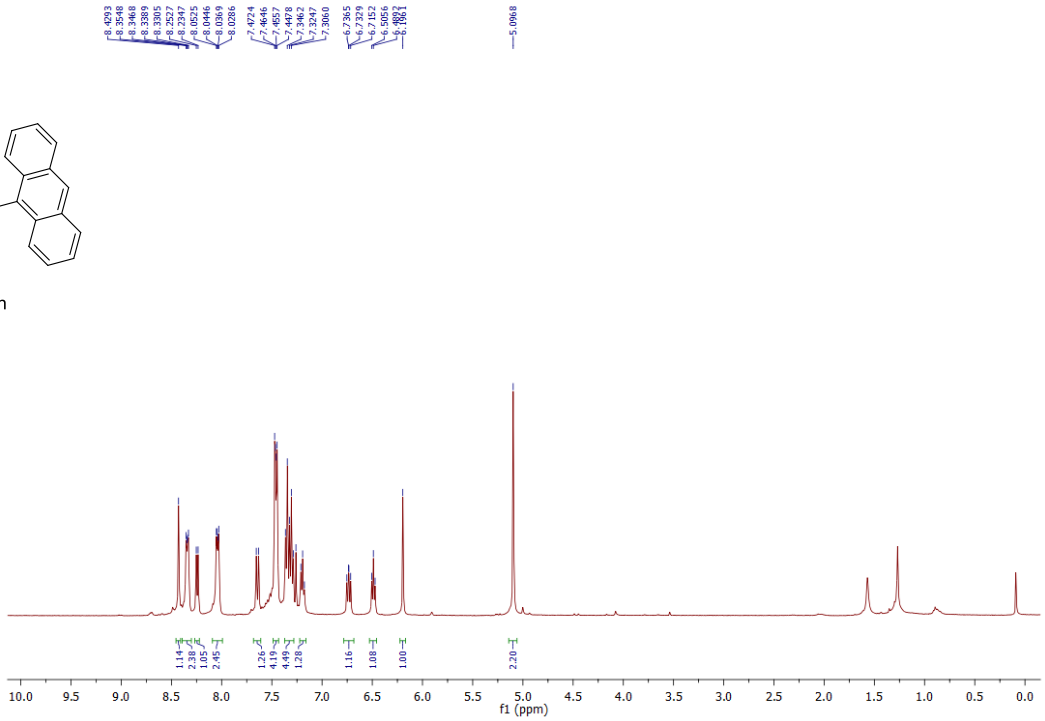


^{13}C Spectrum of 64c

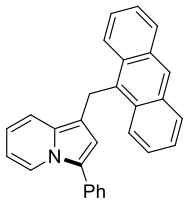


^{1}H Spectrum of 64x

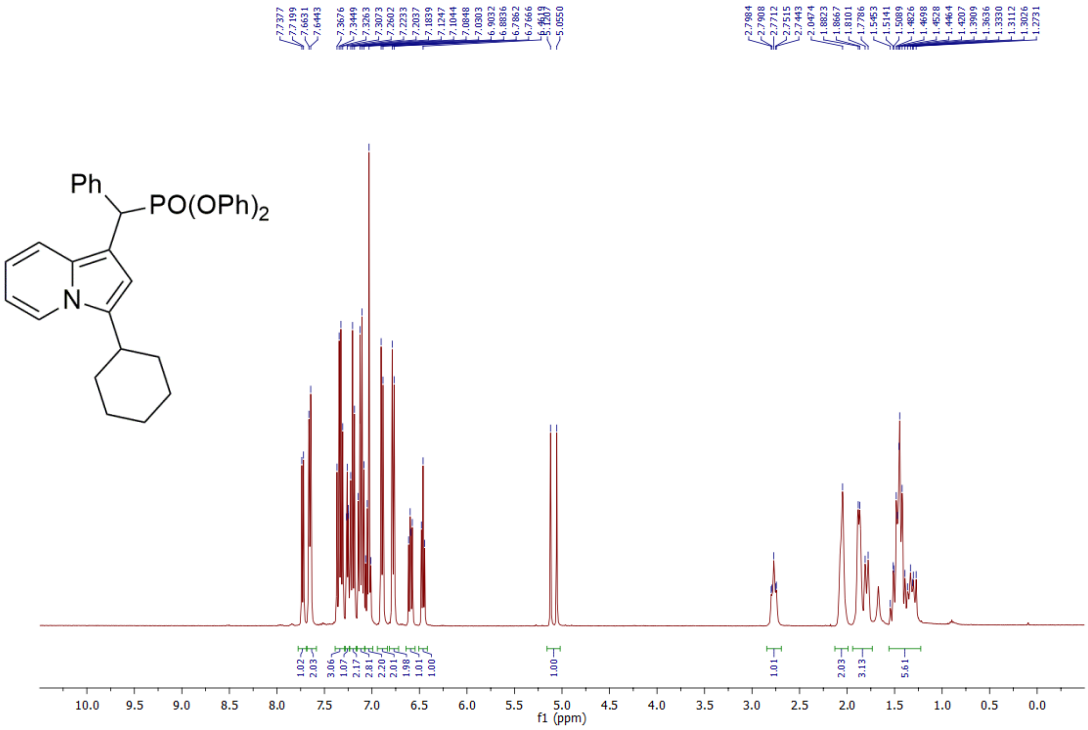




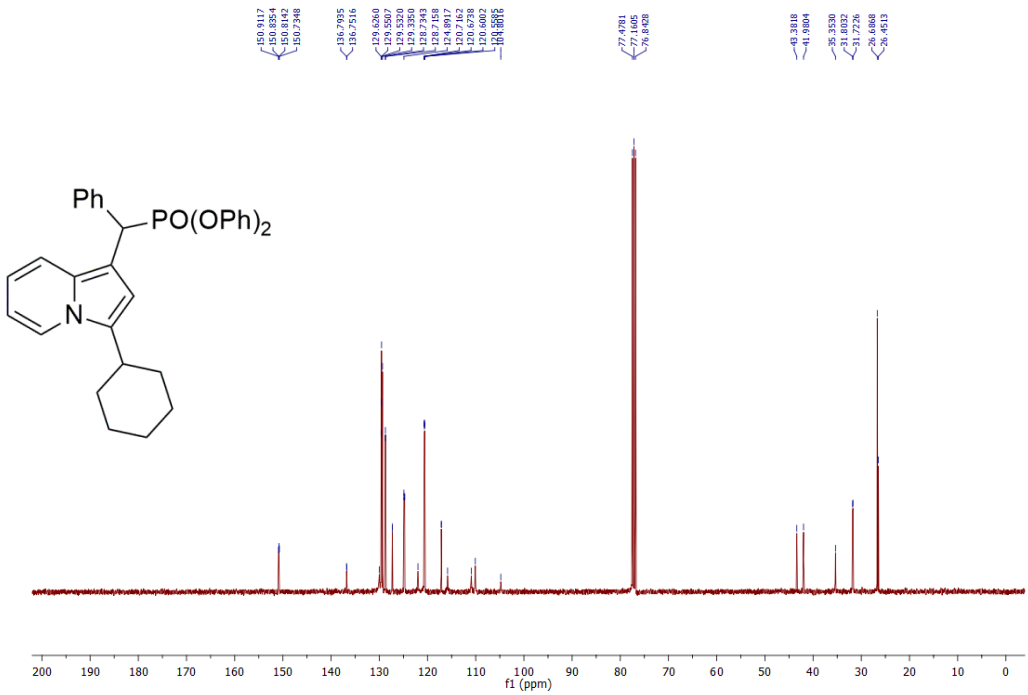
^{13}C Spectrum of 64x



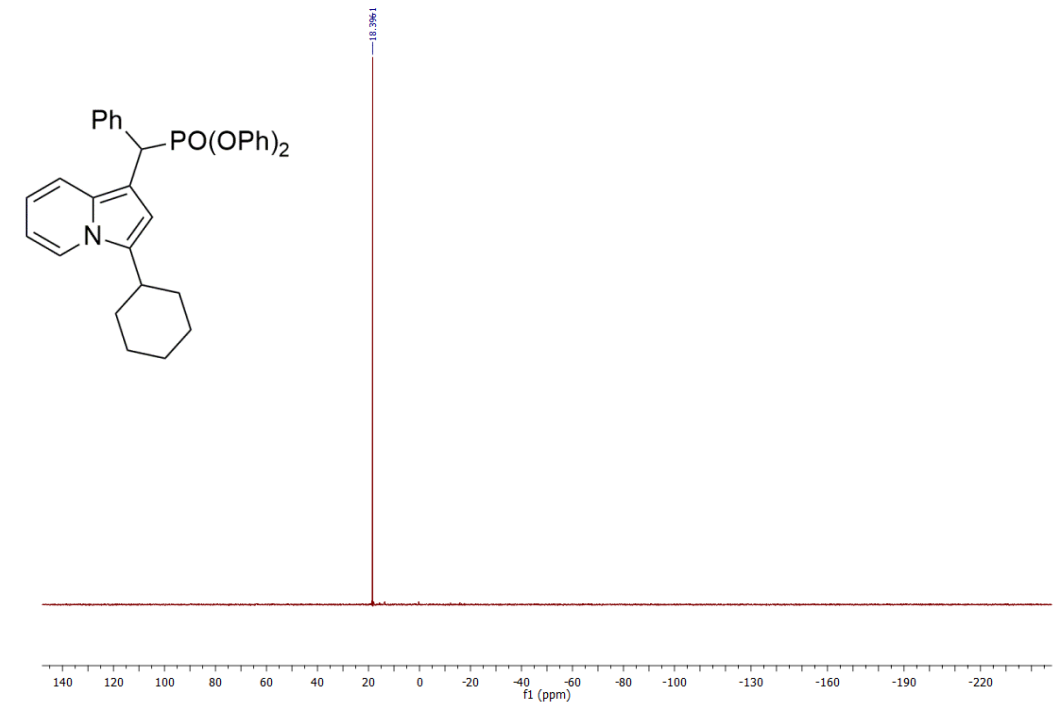
^{1}H NMR SPECTRUM OF 89o



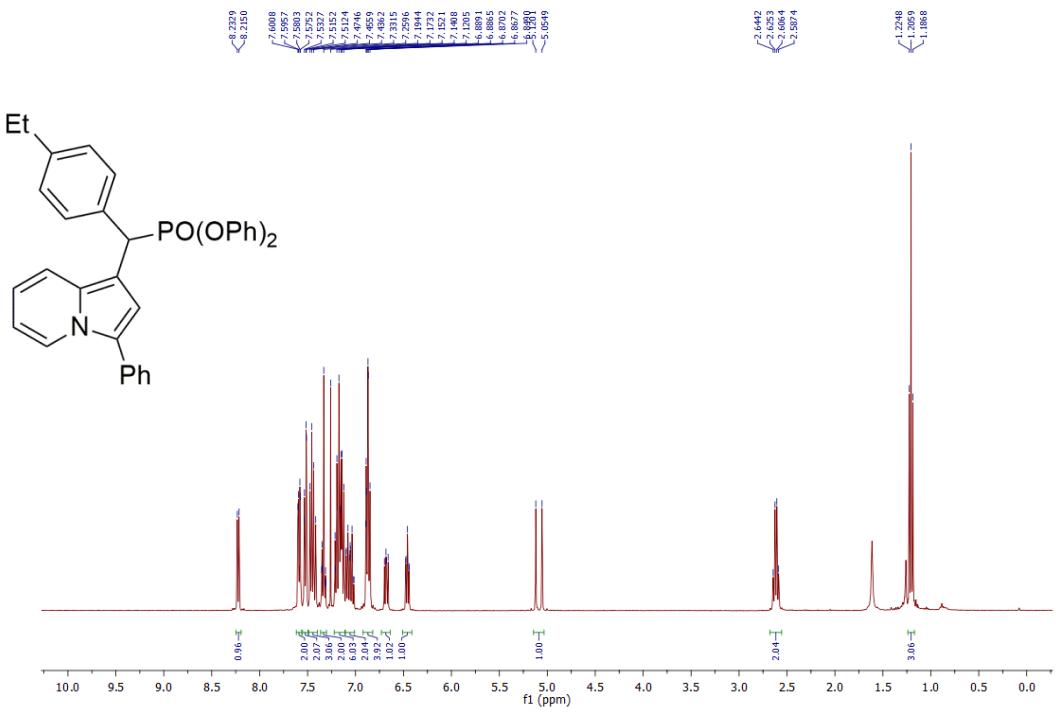
^{13}C NMR SPECTRUM OF 89o



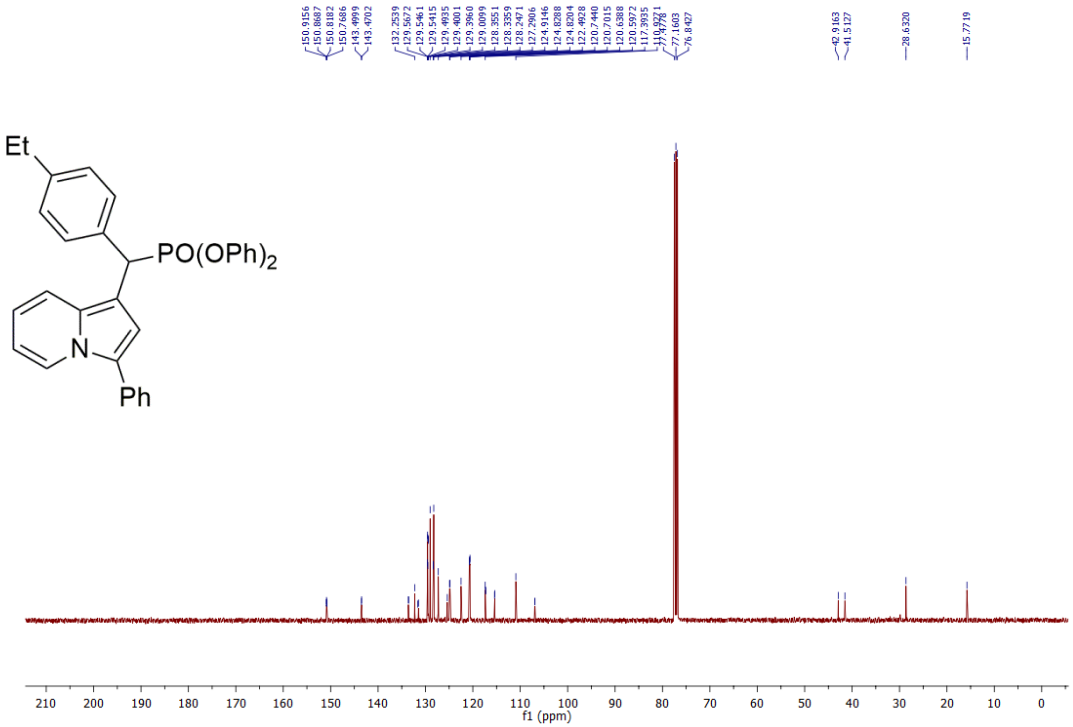
^{31}P NMR SPECTRUM OF 89o



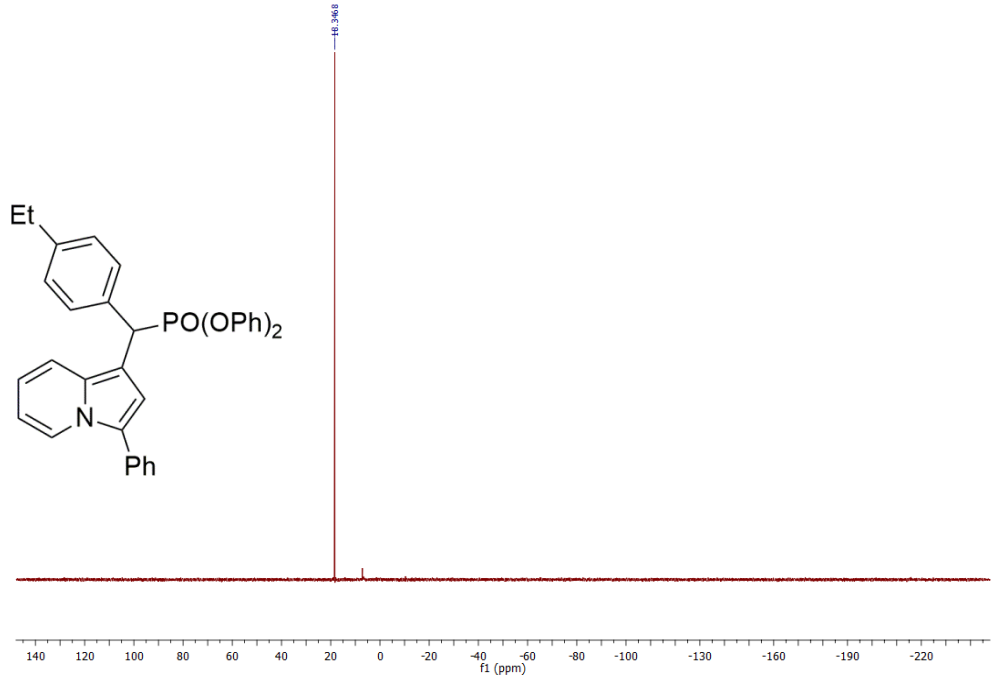
^{1}H NMR SPECTRUM OF 89p



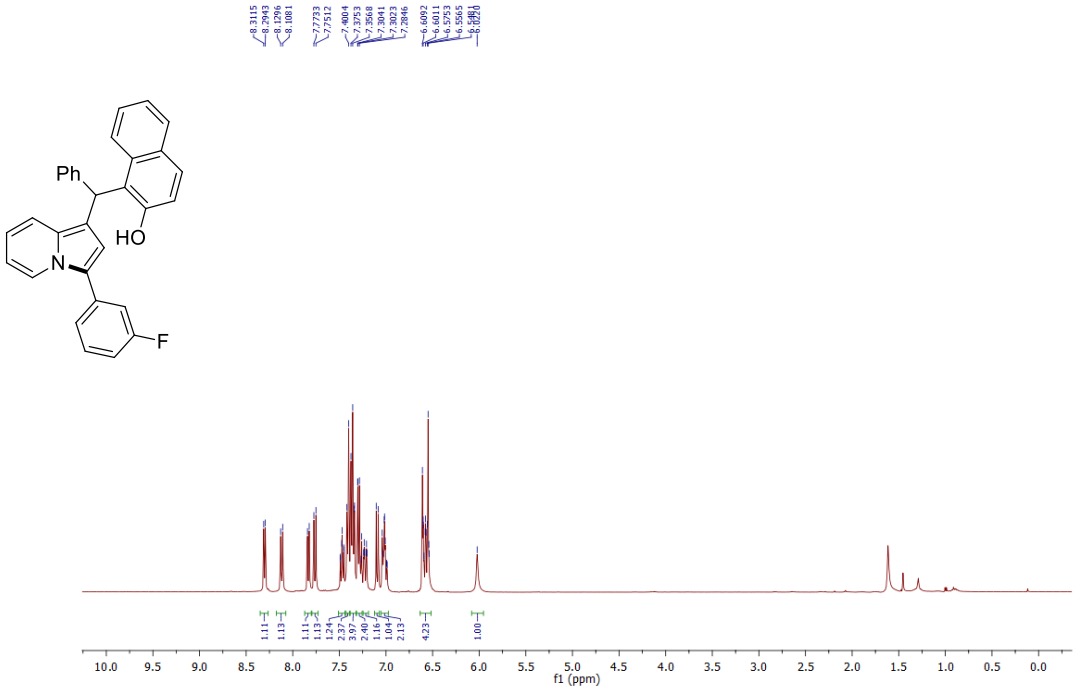
^{13}C NMR SPECTRUM OF 89p



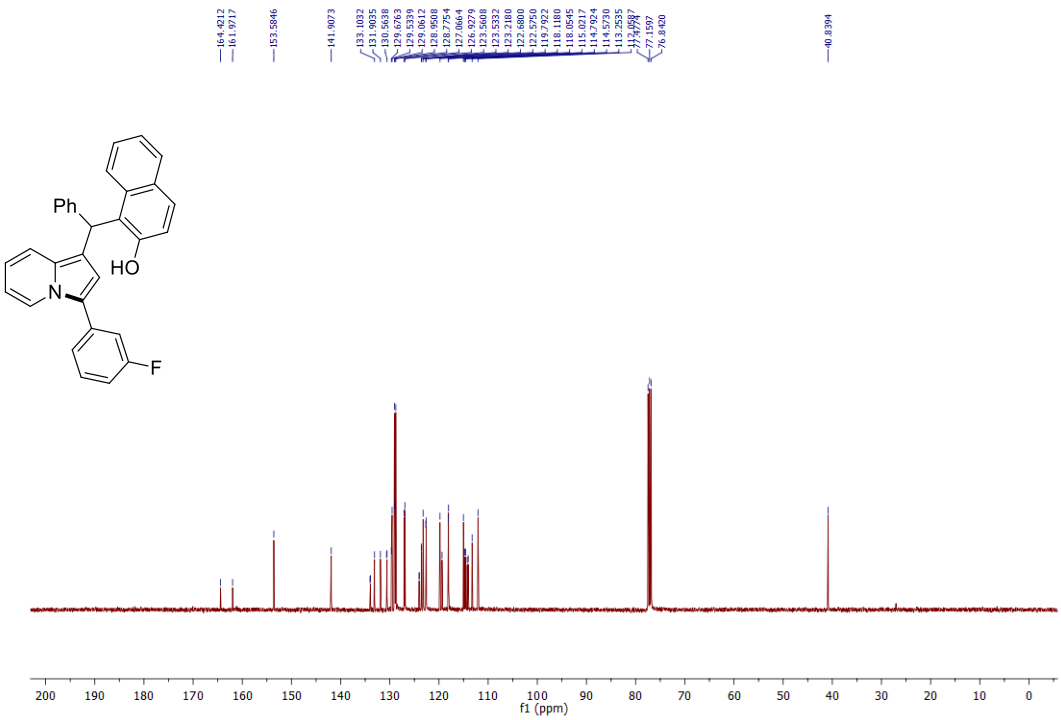
^{31}P NMR SPECTRUM OF 89p



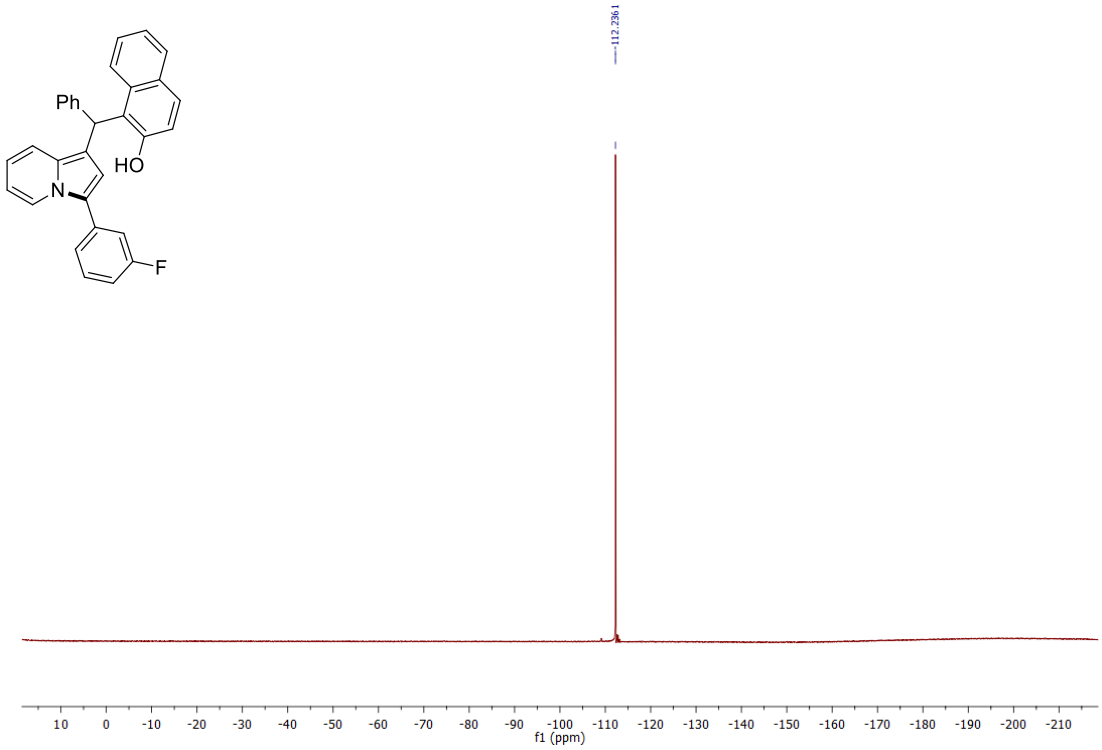
^{1}H Spectrum of 98g



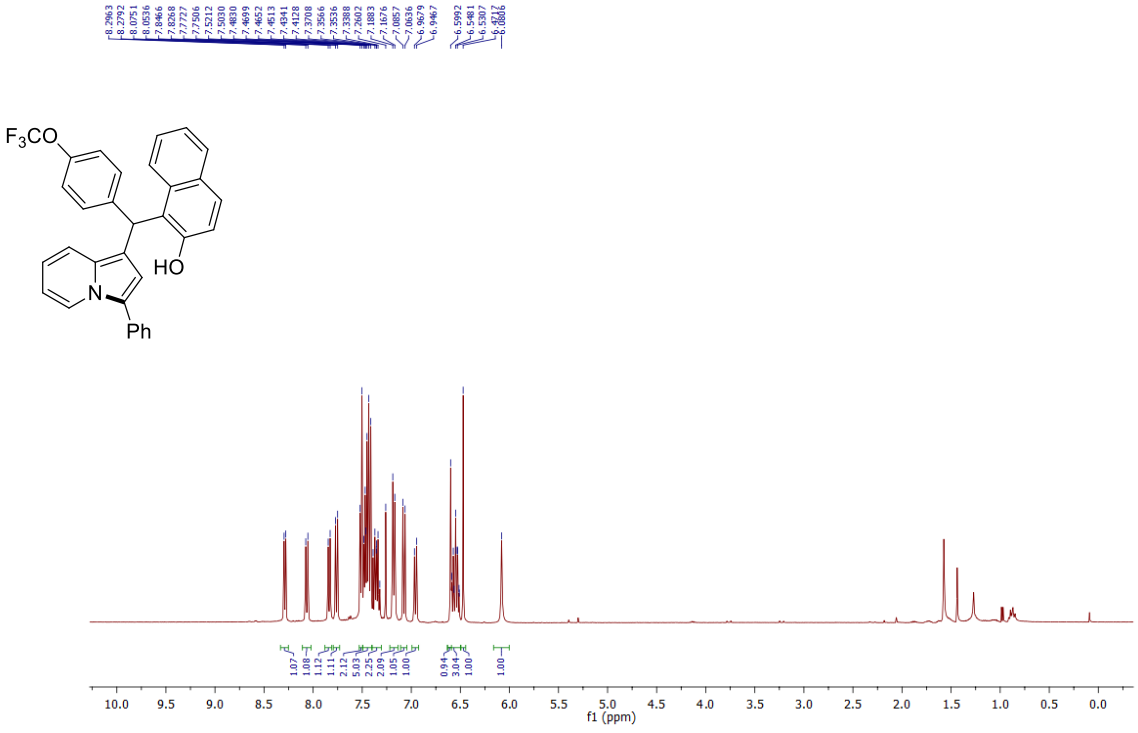
^{13}C Spectrum of 98g



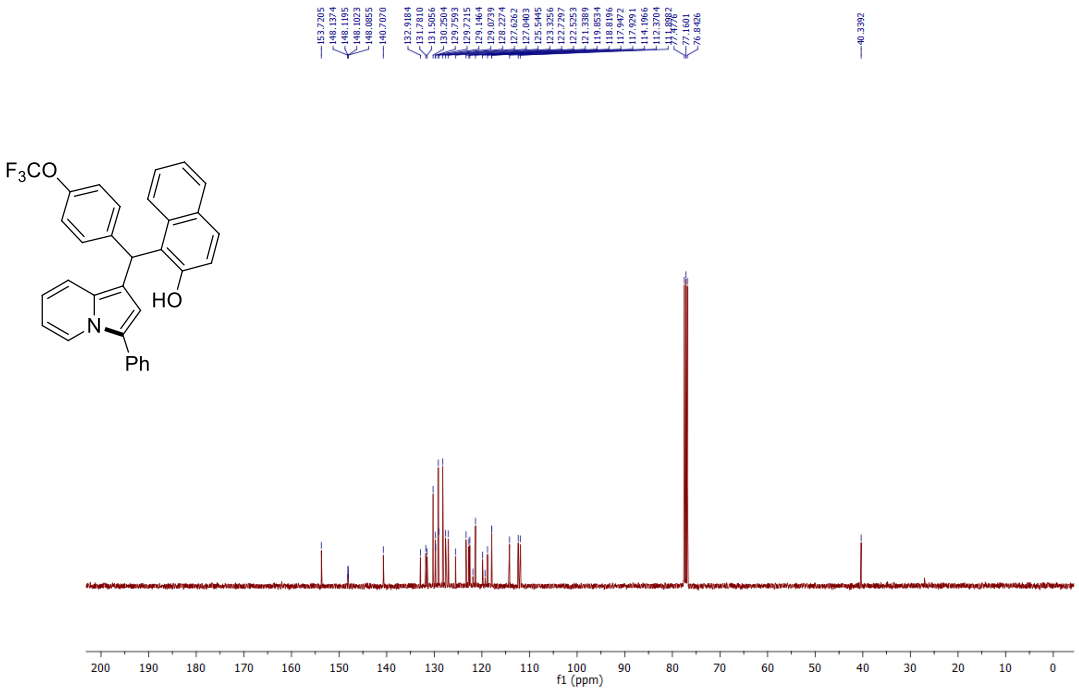
^{19}F Spectrum of 98g



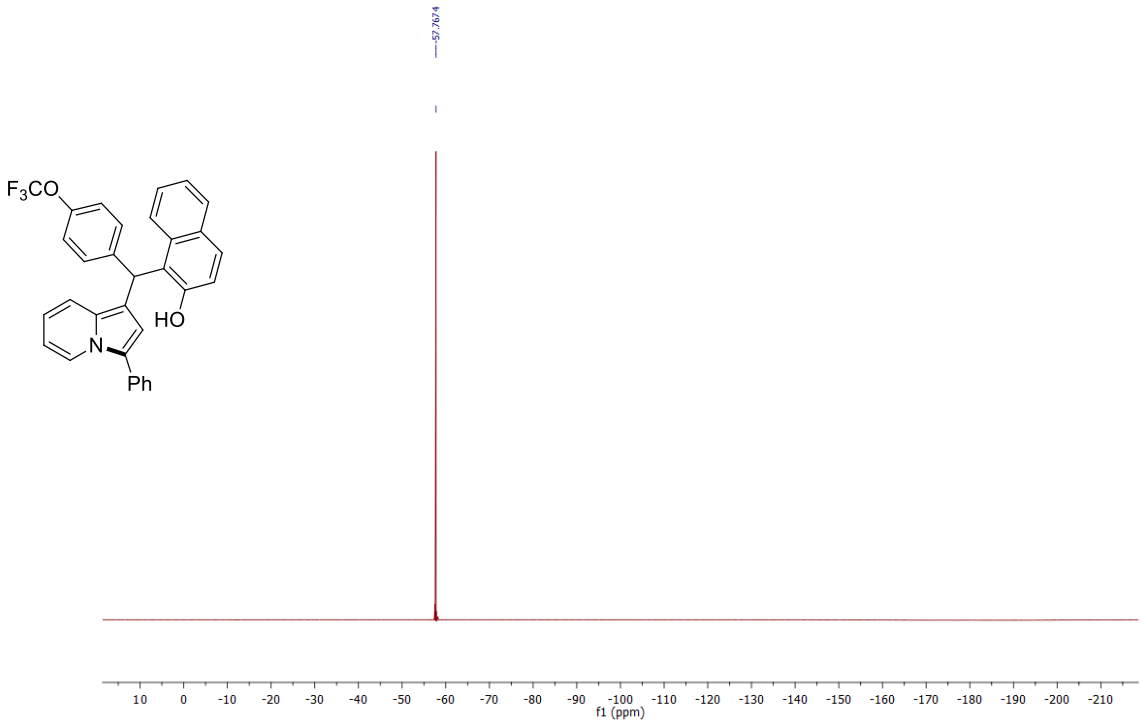
^{1}H Spectrum of 98m



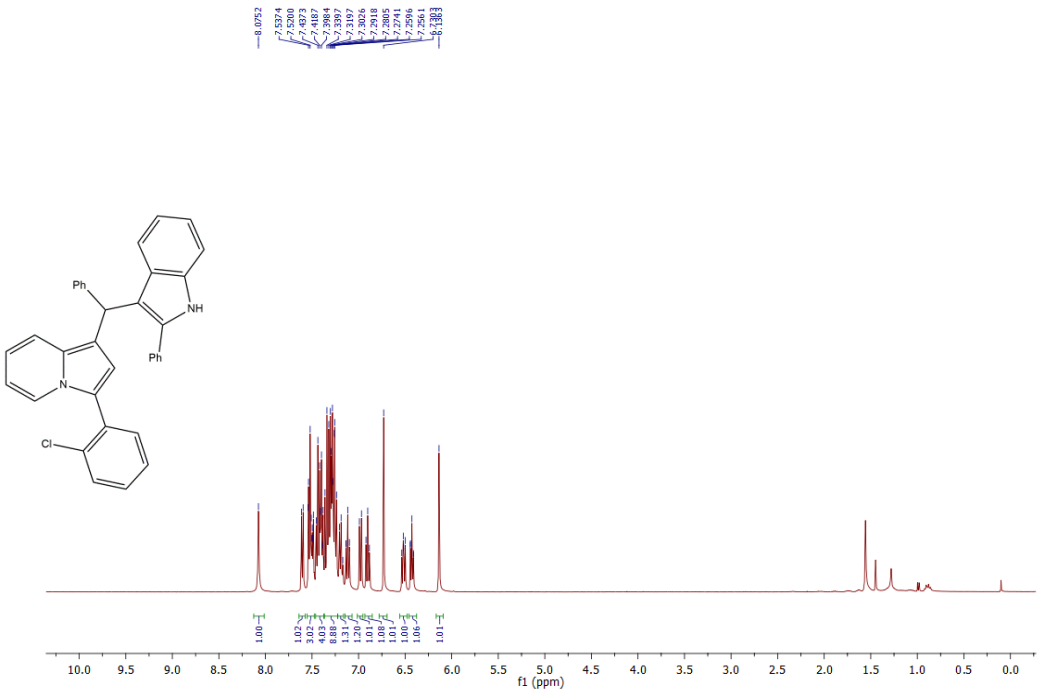
^{13}C Spectrum of 98m



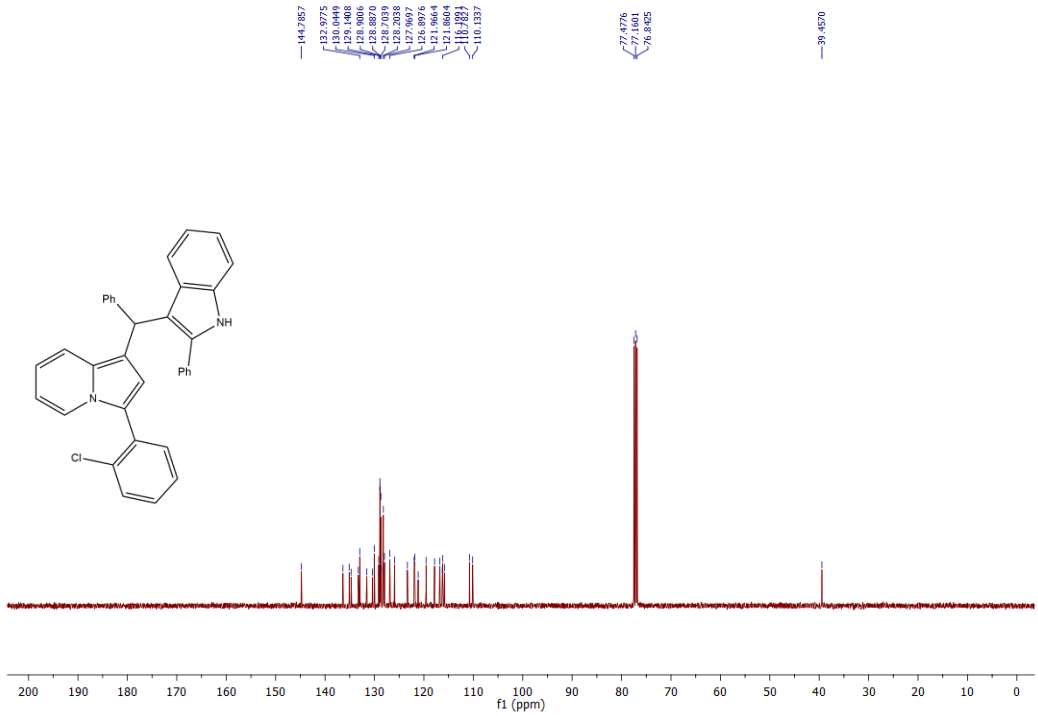
^{19}F Spectrum of 98m



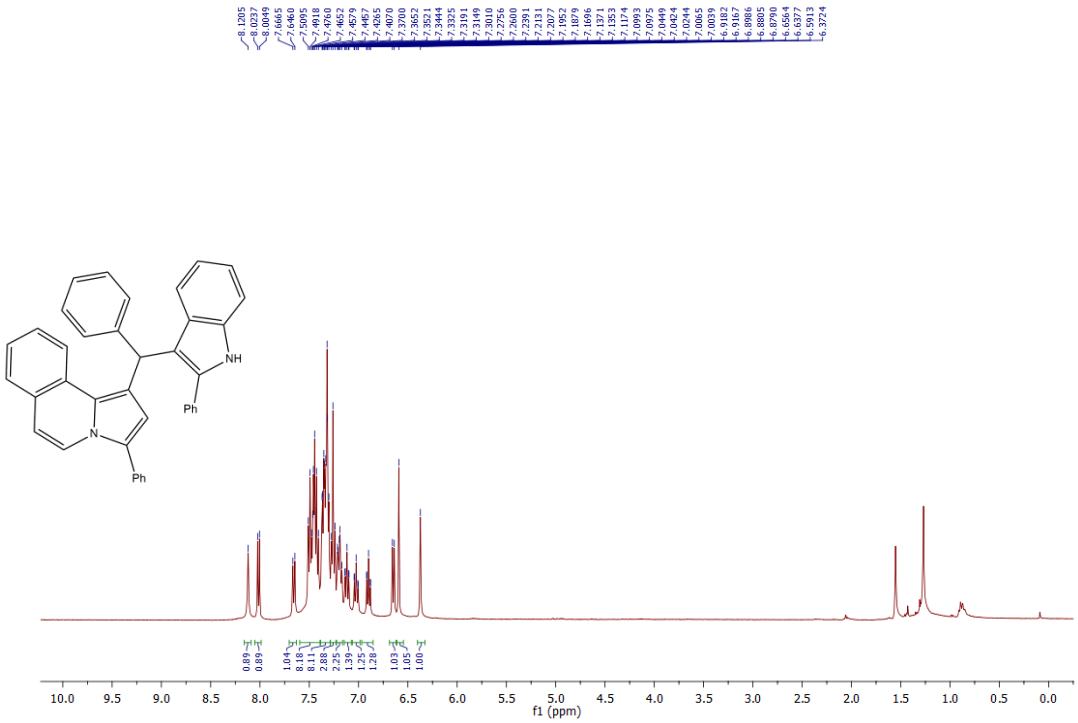
^{1}H Spectrum of **108g**



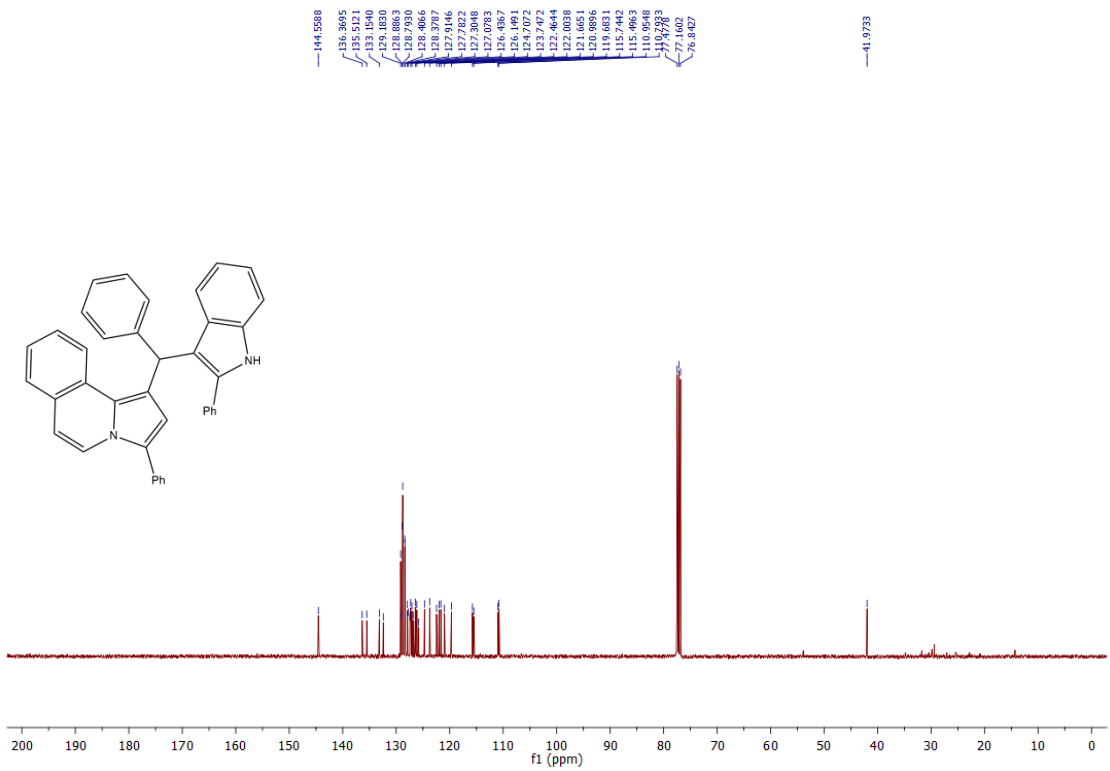
^{13}C Spectrum of **108g**



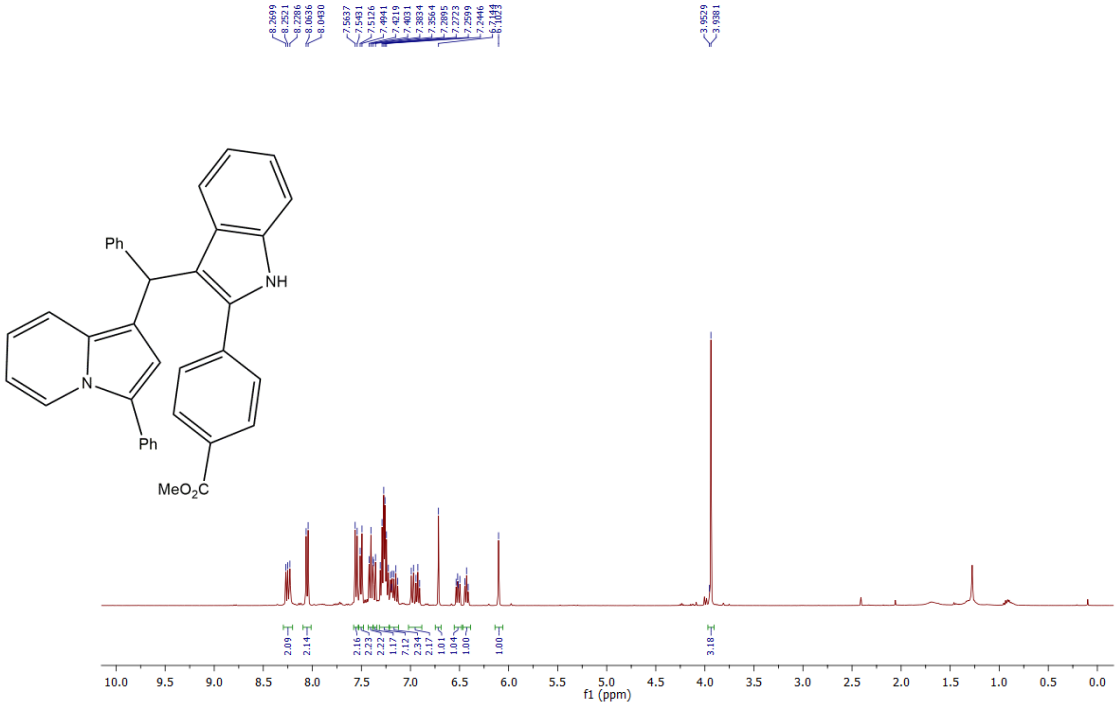
^{1}H Spectrum of **108w**



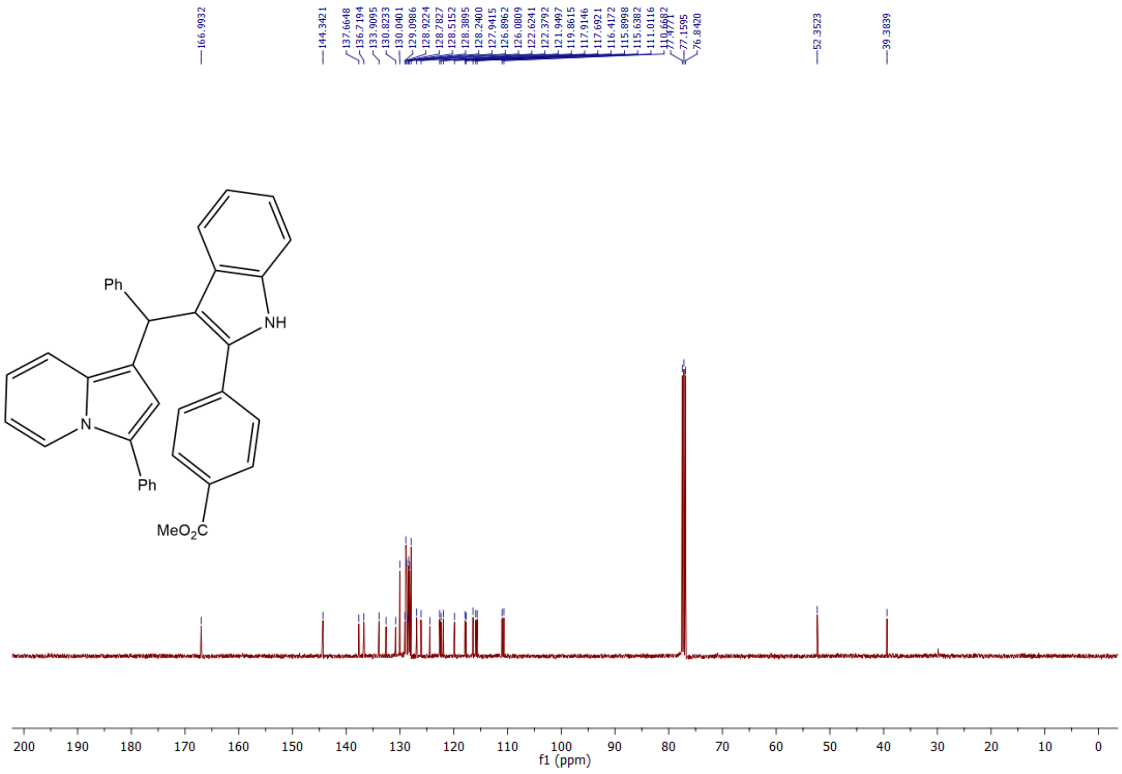
^{13}C Spectrum of **108w**



^{1}H Spectrum of **109f**



^{13}C Spectrum of **109f**



5. References:

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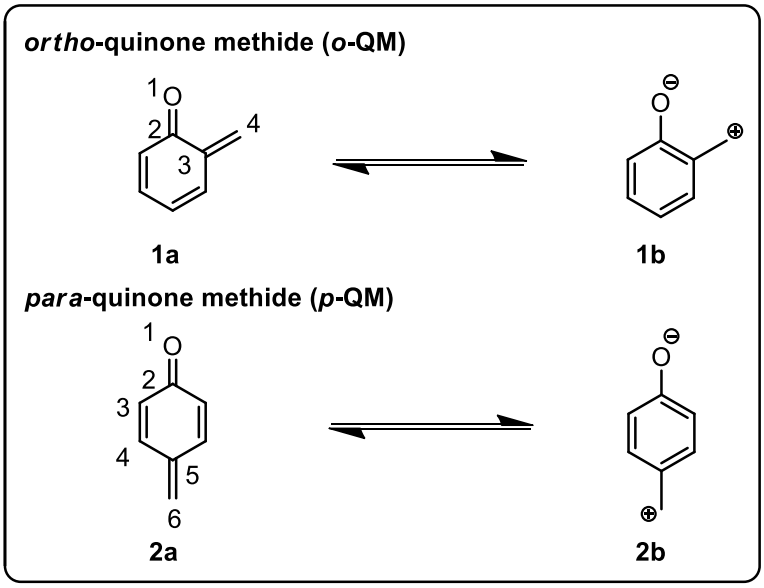
Chapter 3: Divergent approaches toward unsymmetrical diaryl- and triarylmethanes through 1,6-conjugate addition reactions of p-quinone methides

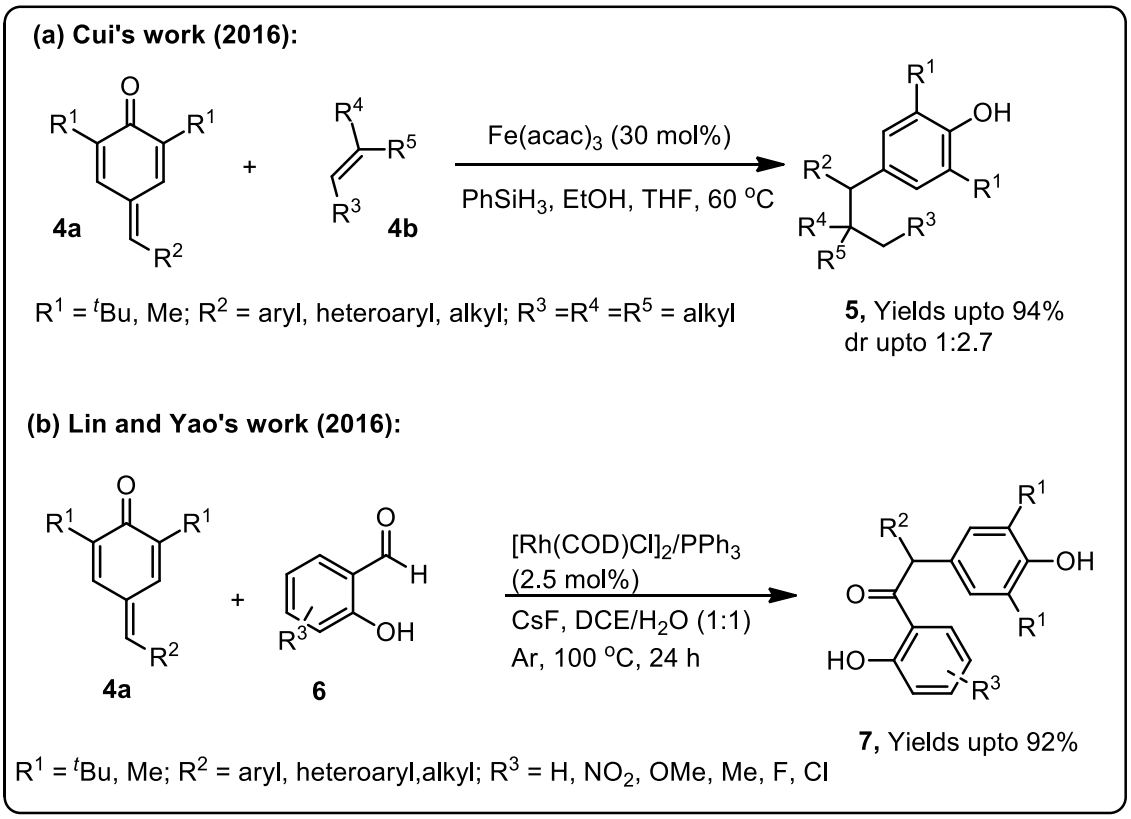
1. Introduction:

Quinone methides, also known as methylene quinones and quinone methines, are highly reactive Michael acceptors. These types of compounds are classified in to two types namely, 1,2-quinone methides (or *o*-quinone methides) and 1,4-quinone methides (or *p*-quinone methides). Basically, these quinone methides exist in its neutral (or) resonance stabilized zwitterionic forms (**Scheme 1**).[1] Due to their unique reactivity towards nucleophiles, these compounds are considered as building blocks of various important natural and unnatural organic molecules.[1b,2] Although, there is only one example of unsubstituted *p*-quinone methide (10-methyleneanthrone)[1b] reported to be moderately stable, a suitable substitution at C_6 or C_3 position imparts more stability to the quinone methide.[1h] The chemistry of *p*-quinone methides (*p*-QMs) is currently being explored for the construction of new C–C and C–X (X = hetero-atom) bonds through 1,6-conjugate addition of various nucleophiles. Moreover, *p*-QMs are revisiting as pro-chiral substrates for the synthesis of enantiomerically enriched diaryl- and triarylmethane derivatives.[3]



Scheme 1. Structure and reactivity of quinone methides

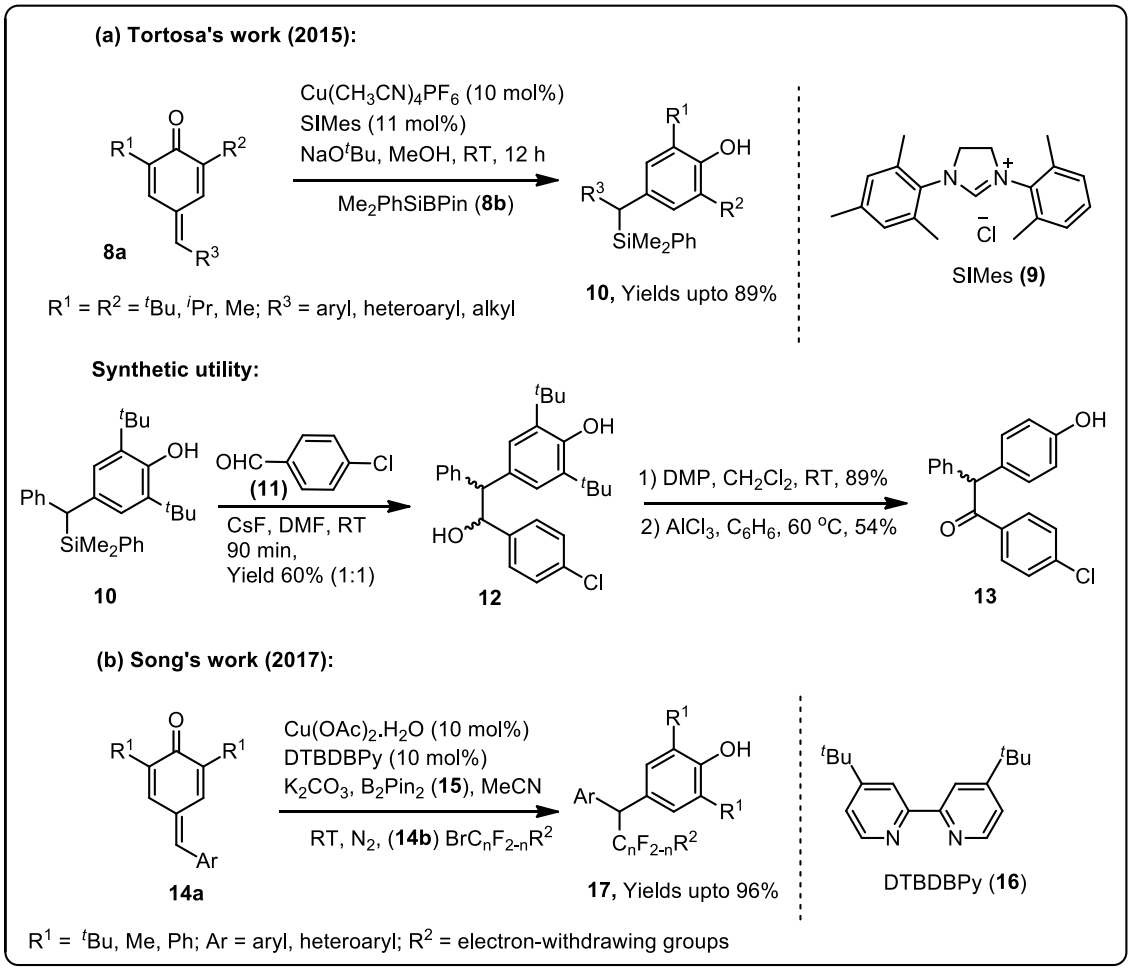
Cui and co-workers have developed a Fe-catalyzed olefin hydro-alkylation reaction with *para*-quinone methides (*p*-QMs) (**4a**) using substituted olefins (**4b**) and $PhSiH_3$ as a reducing agent (**a**, **Scheme 2**).[4a] Yao and Lin reported a Rh-catalyzed hydro-acylation of wide array of *p*-QMs (**4a**) with salicylaldehydes (**6**) for the synthesis of α,α′-diaryl-2-hydroxy acetophenones (**7**) *via* a tandem C−H activation/C−C bond formation/aromatization processes. High chemo-selectivity and good functional group tolerance are the salient features of this methodology (**b**, **Scheme 2**).[4b]



Scheme 2. Hydro-alkylation and hydro-acylation of *p*-quinone methides

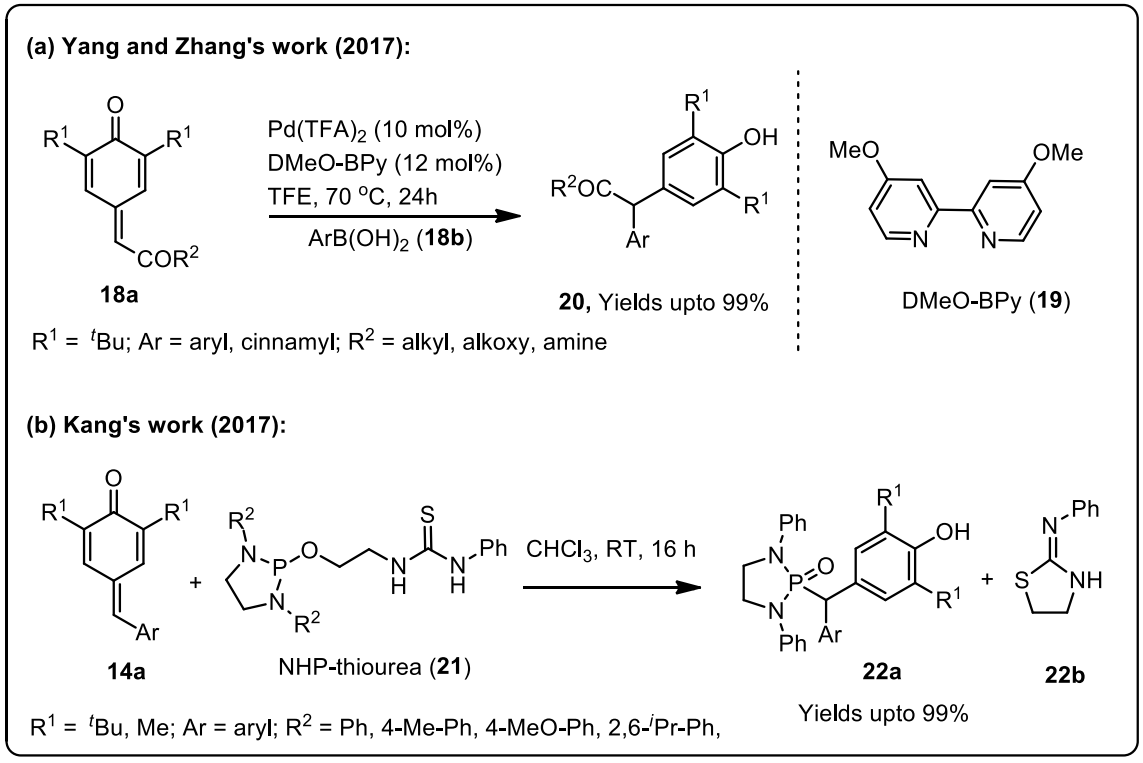
Tortosa and co-workers described a Cu(I)-catalyzed silylation of *p*-QM (**8a**) with silaborane (**8b**) in the presence of NHC (**9**) for the synthesis of unsymmetrical benzylic silanes (**10**). It was observed that under the optimal conditions, a variety of electron-donating/withdrawing aryl and hetero-aryl substituted *p*-QMs (**8a**) could be conveniently converted into their respective benzylic silanes (**10**) in good yields (**a**, **scheme 3**).[4c] Very recently, Song and co-workers realized the synthesis of broad range of fluorinated diarylmethanes (**17**) *via* an efficient Cu-catalyzed 1,6-

hydrodifluoroacetylation of *p*-QMs (**14a**) with difluoroalkyl bromides (**14b**) using [bis(pinacolato)diboron] (**15**) as a reductant (**b**, **scheme 3**).[4d]

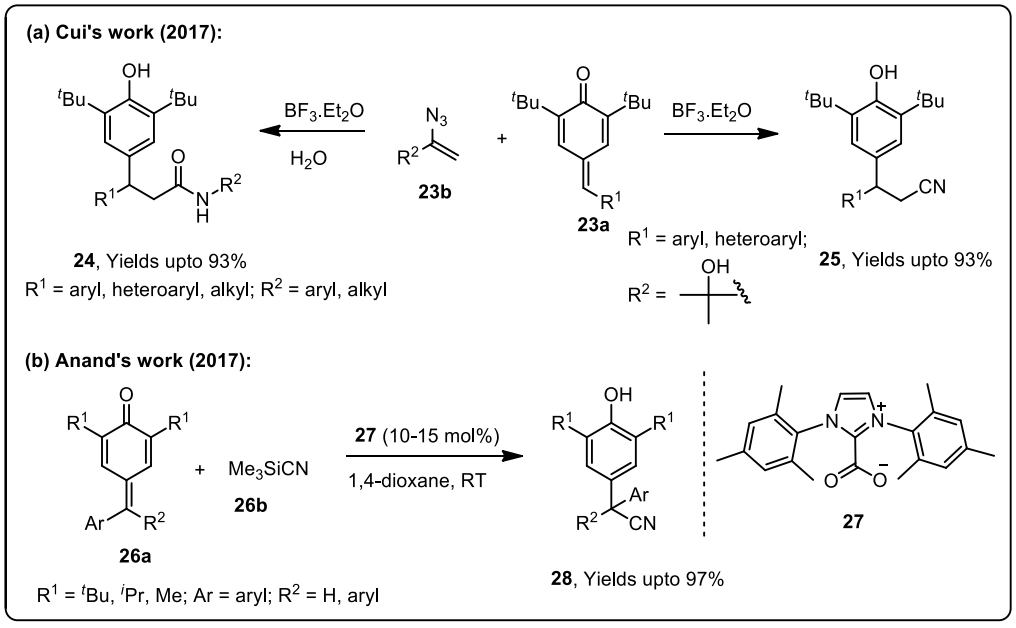


Scheme 3. Copper catalyzed derivatization of *p*-QMs

A Pd-catalyzed addition of arylboronic acids (**18b**) to *p*-QMs (**18a**) was developed by Yang and Zhang jointly. The present method delineates the vinylogous conjugate addition of arylboronic acids (**18b**) to ester/amide containing *p*-QMs (**18a**) to access unsymmetrical diaryl acetates (**20**) [**a**, **scheme 4**].[4e] Very recently, Kang and co-workers developed a catalyst and additive free 1,6-hydrophosphonylation of *p*-QMs (**14a**) with NHP-thioureas (**21**) for the preparation of diarylphosphonate derivatives (**22a**) in good to excellent yields. It was proposed that the reaction proceeds through the activation of *p*-QM by thiourea portion of **21**, through hydrogen bonding, followed by intramolecular nucleophilic attack of the diazaphosphium group (**b**, **scheme 4**).[4f]



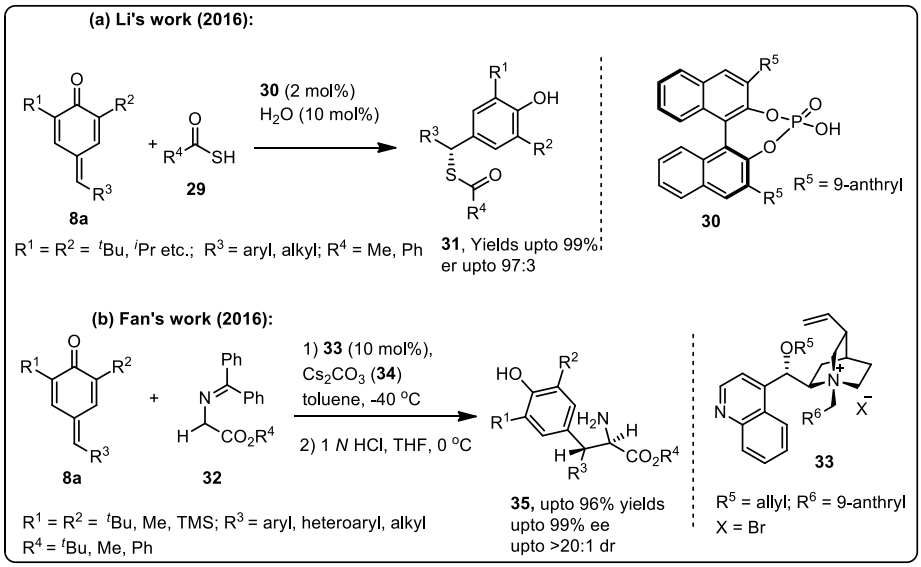
Scheme 4. Synthesis of diarylmethyl esters and phosphonates



Scheme 5. Synthesis of α- and β-arylated nitriles and amides

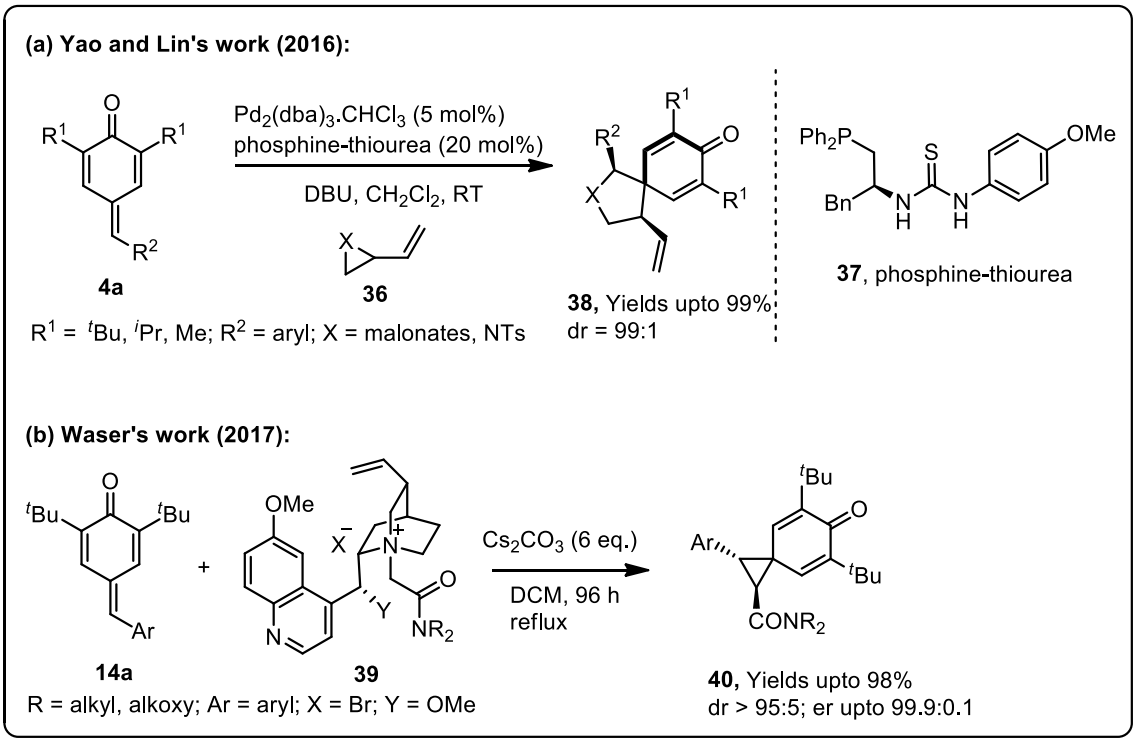
Cui and co-workers divulged another interesting approach for the synthesis of diverse range of β-aryl amide (**24**) and β-aryl nitrile (**25**) derivatives, through a $BF_3.OEt_2$ mediated 1,6-conjugate addition of vinyl azides (**23b**) to *p*-QM (**23a**). It was demonstrated that β-aryl amides (**24**) were obtained as a sole product in the presence of water and the β-aryl acetonitrile derivatives (**25**) could be accessed even in the absence of water (**a**, **scheme 5**).[4g] While continuing the derivatization of *p*-QMs through 1,6-conjugate addition of various nucleophiles, our research group developed an organocatalytic method for the synthesis of variety of α-diaryl- and α-triaryl nitriles (**28**) in good to excellent yields. The present work describes an *N*-heterocyclic carbene (**27**) catalyzed 1,6-conjugate addition of TMS-CN (**26b**) to *p*-quinone methides and fuchsones (**26a**) to generate α-diaryl- and α-triaryl nitriles (**28**) respectively, under mild reaction conditions (**b**, **scheme 5**).[4h]

Li and co-workers developed a chiral phosphoric acid (**30**) catalyzed strategy for an asymmetric 1,6-conjugate addition of thioacetic acid (**29**) with *p*-QM (**8a**). Through this method variety of enantiomerically enriched sulfur addition products (**31**) were accessed in the presence of water with high yields and excellent enantio-selectivity (**a**, **scheme 6**).[5a] Fan and co-workers have disclosed the synthesis of chiral β,β-diaryl-α-amino acid esters (**35**) in high yields and excellent stereo-selectivities, through 1,6-conjugate addition of glycine derivatives (**32**) to *p*-QM (**8a**) using chiral phase transfer catalysts (**b**, **scheme 6**).[5b]



Scheme 6. Asymmetric 1,6-conjugate addition reactions of *p*-QM

Yao and Lin developed a palladium and phosphine-thiourea co-operative catalytic system (**37**) for the annulation between *p*-QMs (**4a**) and vinylcyclopropanes (**36**). Through this method a vast array of spiro[4.5]deca-6,9-diene-8-ones (**38**) were accessed in high yields and with excellent diastereo-selectivities (**a**, **scheme 7**).[5c] Cinchona alkaloid-based chiral ammonium ylides (**39**) have been used by Waser and co-workers for the derivatization of *p*-QMs (**14a**) to chiral spiro[2.5]octa-4,7-dien-6-one (**40**) derivatives. Further, the products of the reaction were also used for the stereoselective ring opening reactions using simple alcohols (**b**, **scheme 7**).[5d]



Scheme 7. Synthesis of spirocyclic derivatives of *p*-QM

2. Objectives:

a. *To synthesize unsymmetrical allyl diarylmethanes through a Lewis acid catalyzed 1,6-conjugate allylation of p-quinone methides*
b. *To access unsymmetrical diaryl- and triarylmethanes via a Lewis acid catalyzed reduction of p-quinone methides and fuchsones*

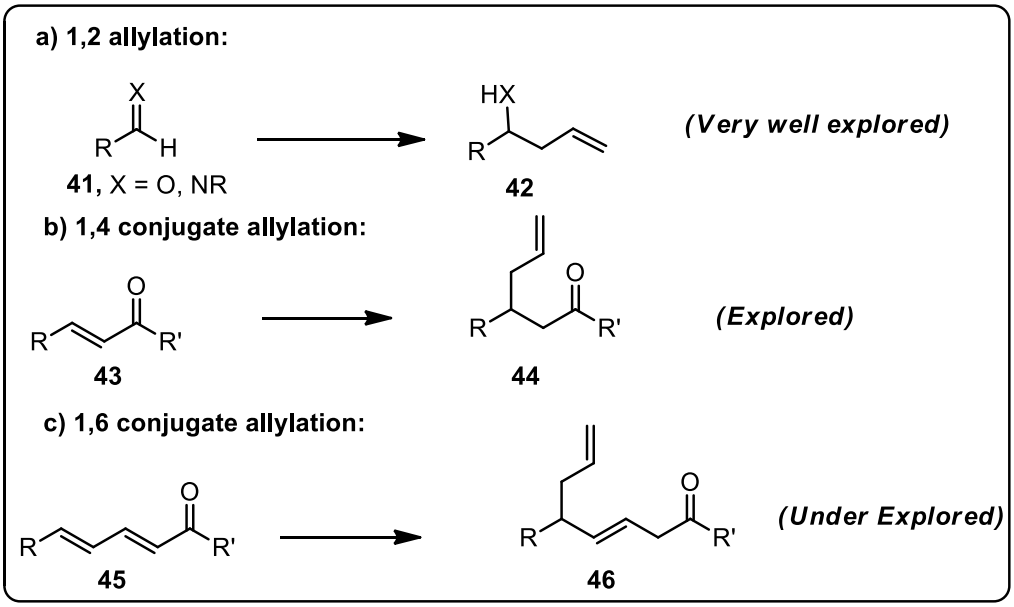
2a. Synthesis of allyldiarylmethanes through 1,6-conjugate allylation of p-QMs:

Allylation of carbon electrophiles is acknowledged to be one of the important methods in carbon–carbon bond forming transformations. Especially, the 1,2-allylation of carbonyl compounds and imines (**41**) leading to homoallyl derivatives (**42**) is very well explored as many of these derivatives serve as valuable synthons in natural product synthesis (**a**, **scheme 8**).[6] The 1,4-conjugate allylation of enones (**43**) is another well studied transformation that could be utilized to access γ-allylated carbonyl compounds (**43**) [**b**, **scheme 8**].[7] However, the vinylogous allylation *i.e.*, the 1,6-conjugate allylation of dienones (**44**) is under explored till date, though there are a very few reports available for the 1,6-conjugate addition of other alkylmetal reagents (**c**, **scheme 8**).[8]

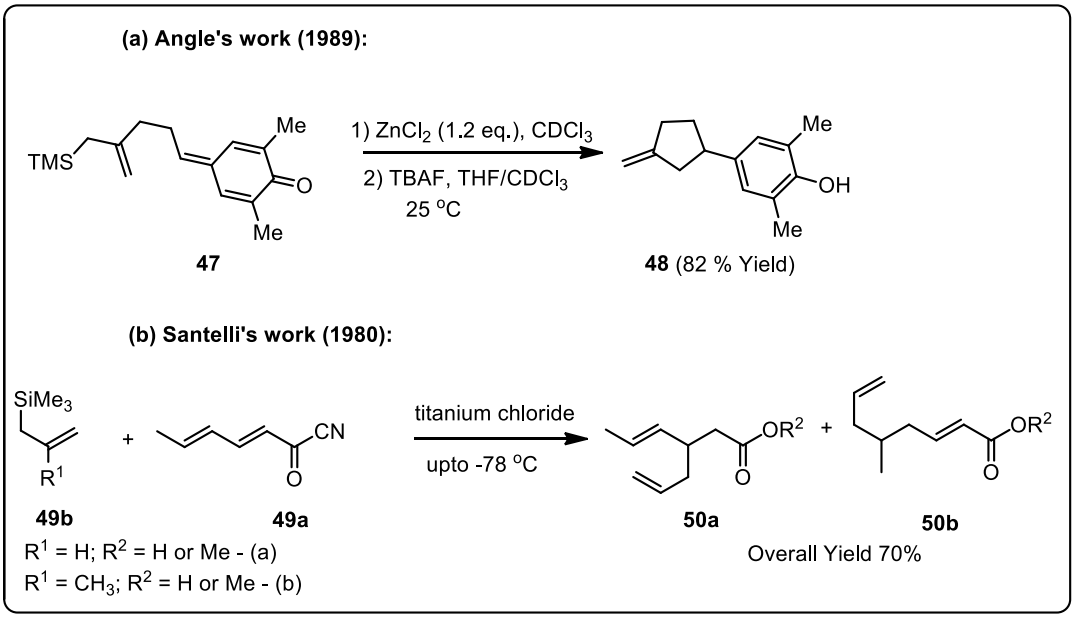
In fact, the regio-selective 1,6-conjugate addition of allyl-metal reagents to α,β,γ,δ-unsaturated Michael acceptors is a challenging task as this reaction would potentially generate 1,2- and 1,4-adducts as by-products along with 1,6-addition product. There are several parameters which affect the regio-selectivity in 1,6-conjugate addition reaction, which include the choice of the catalyst, nature of the nucleophilic reagent and the structure of the Michael acceptor.[8b] Due to these limiting parameters, the intermolecular 1,6-conjugate allylation of dienone system is under explored. In fact, only one example each is reported so far for the intramolecular[9a] as well as intermolecular (with very poor regio-selectivity)[9b] 1,6-conjugate allylation of the dienone systems (**Scheme 9**).

Of course, there are several other methods available in the literature for the synthesis of allyl diarylmethanes, which include Lewis acid catalyzed electrophilic substitution of diarylmethanol and its derivatives,[10] palladium[11] or nickel[12] catalyzed allylic substitution reactions, metal catalyzed direct arylation of homo-allyl arenes[13] and other miscellaneous reactions.[14] For instance, Walsh and co-workers disclosed a Tsuji-Trost allylation reaction, which demonstrates the Pd-catalyzed allylation of broad range of diarylmethane (**51a**) derivatives with protected allyl alcohols (**51b**) for the synthesis of allyl diarylmethanes (**52**) under mild reaction conditions (**a**, **Scheme 10**).[15a] Shintani and Hayashi jointly reported NHC-Cu (**54**) catalyzed asymmetric allylation of a variety of aryl and alkenyl boronates (**53b**) with allyl phosphates (**53a**). Through

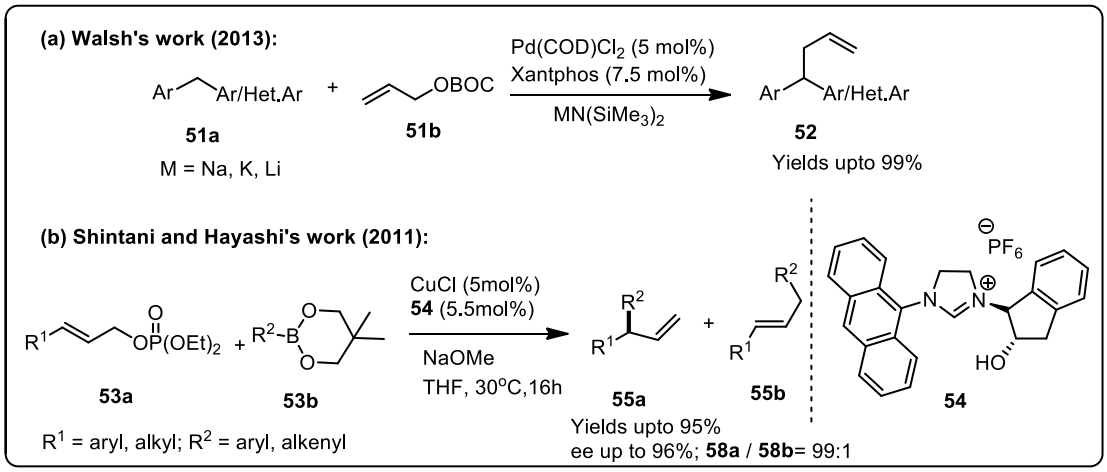
this method, a variety of allyl diarylmethanes (**55**) could be accessed in high yields and excellent enantio-selectivities (**b**, **Scheme 10**).[15b]



Scheme 8. 1,2-, 1,4- and 1,6-Allylation reactions



Scheme 9. 1,6-conjugate allylation of enones with allyl-$SiMe_3$



Scheme 10. Synthesis of allyl diarylmethanes

Results and discussion:

While working on the 1,6-conjugate addition of various nucleophiles to *p*-quinone methides (*p*-QMs),[16] we envisioned that it is possible to achieve the 1,6-conjugate allylation of *p*-QMs using an appropriate Lewis acid. The 1,6-conjugate allylation of *p*-QMs would generate allyl diarylmethanes, which have shown significant applications in medicinal chemistry. For example, allyl diarylmethanes (**56**-**58)** are found to possess distinct biological activities (**Figure 1**).[17] Since the synthesis of allyl diarylmethanes through a highly regio-selective intermolecular vinylogous allylation of *p*-QMs with allyl TMS reagents has not been reported so far, we have decided to investigate this challenging transformation in detail (**a**, **Scheme 11**).[16c] In this regard we have prepared a library of *p*-quinone methide derivatives (**59**) starting from a broad range arene-carbaldehydes (**59-II**) and 2,6-ditertiarybutyl phenol (**59-I**) [**b**, **Scheme 11**].[16a]

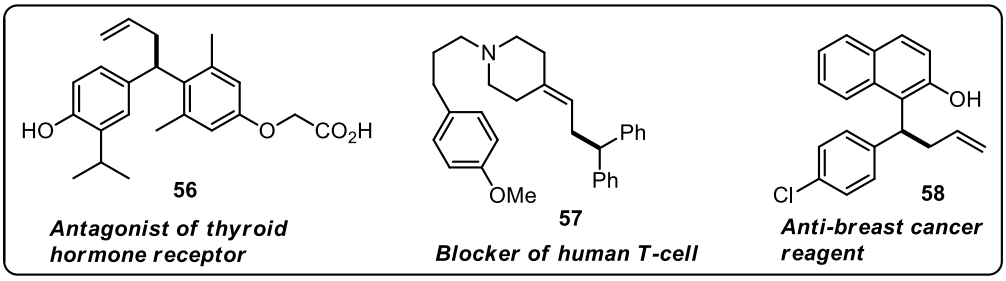
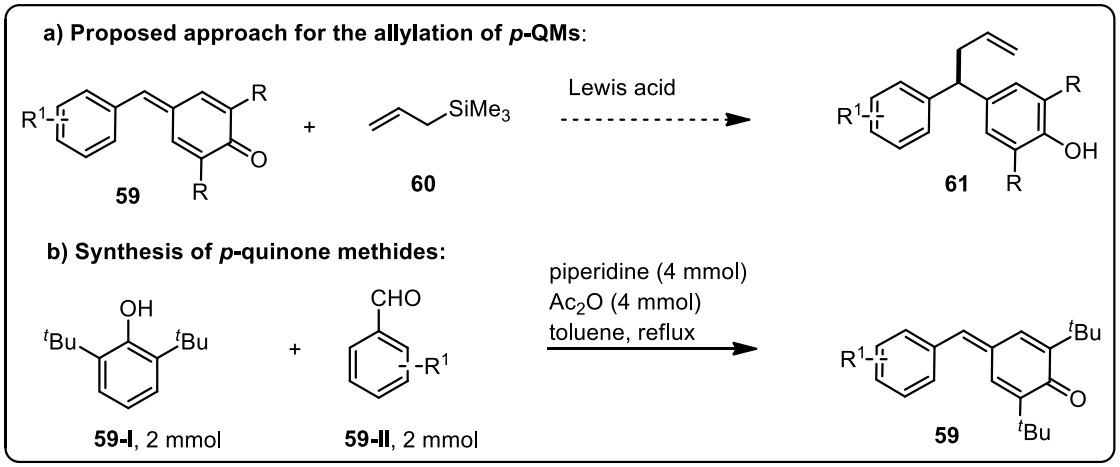


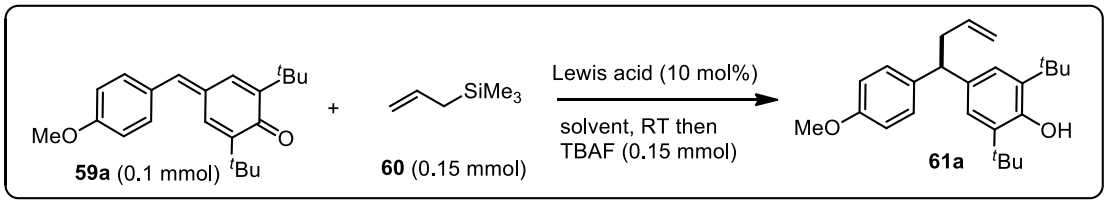
Figure 1. Biologically active allyl diarylmethanes



Scheme 11. Proposed approach to access allyl diarylmethanes

We began the optimization studies with *p*-quinone methide (**59a**) and allyl trimethylsilane (**60**) by employing a wide range of Lewis acids under various reaction conditions. Table 1 reveals the results of optimization studies. Our initial efforts toward the 1,6-allylation of **59a** was discouraging as the reaction did not generate the expected product **61** when the Lewis acids such as $Fe(OAc)_2$, $Fe(acac)_2$ and CuCl were used (Entries 1-3). Considering the initial unsuccessful attempts, we assumed that this transformation may require a strong Lewis acid. So, we shifted our attention towards boron based strong Lewis acids such as $B(C_6F_5)_3$. Although $B(C_6F_5)_3$ has been widely utilized in frustrated Lewis pair chemistry,[18] its catalytic property has also been explored in organic transformations[19] including allylation.[20] When 1 mol % $B(C_6F_5)_3$ was used as a catalyst in CH_2Cl_2, **60** was isolated in 5% yield after 24 h (Entry 4). Invigorated by this observation, the optimization study was extended with increased catalyst loading of $B(C_6F_5)_3$. To our delight, when 10 mol % of the $B(C_6F_5)_3$ was used, the allylated product **60** was obtained in 98% isolated yield within 5 minutes at room temperature after quenching the reaction with TBAF (Entry 5). The popular boron based Lewis acid, $BF_3.OEt_2$ also catalyzed this transformation, but found to be less effective when compared to $B(C_6F_5)_3$ (Entry 6). Other Lewis acids such as scandium triflate and aluminium chloride were found to be equally competent to effect this reaction. However, in both the cases, the reaction took a relatively longer period to complete (Entries 7 & 8).

Table 1. Optimization studies[a]

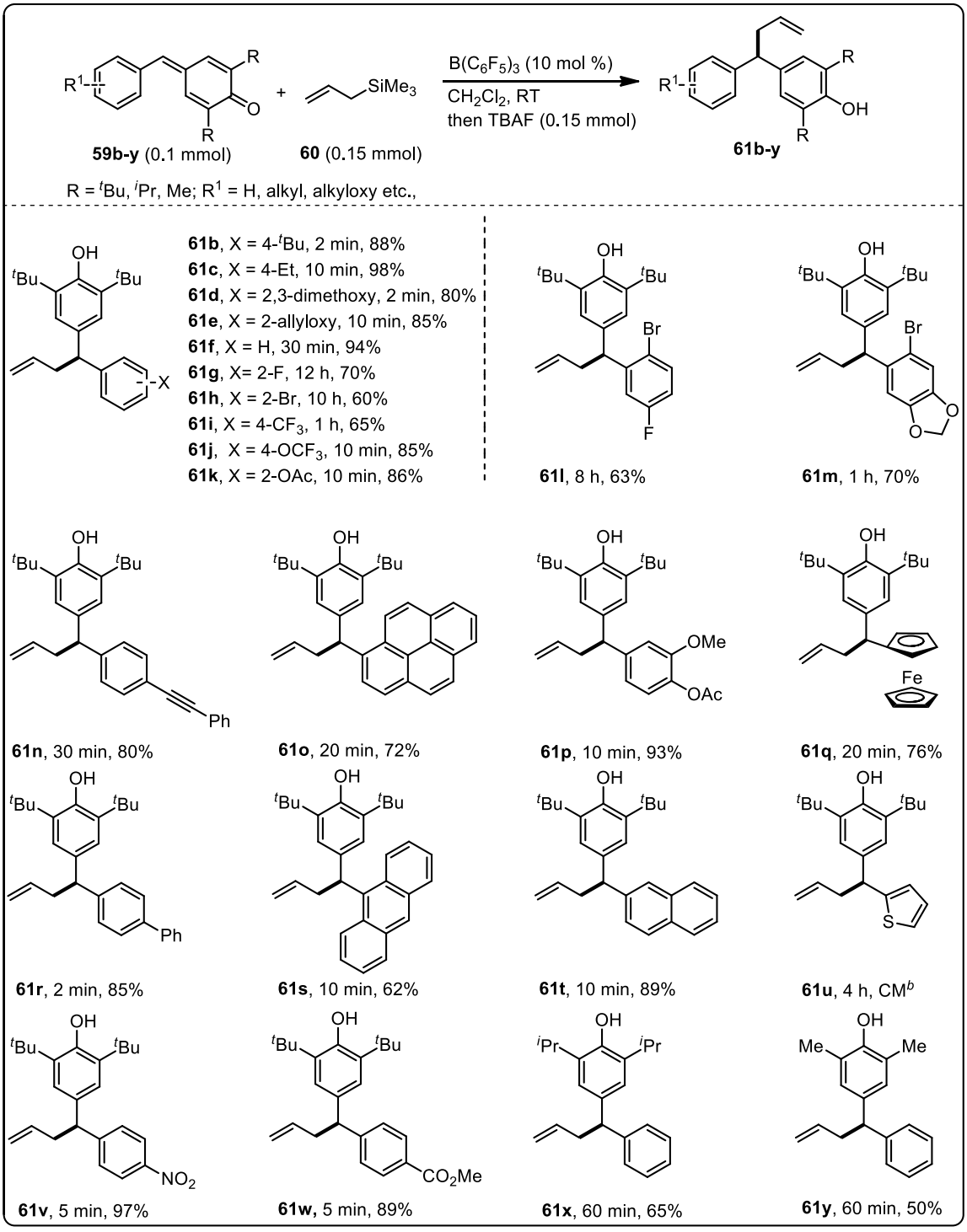


Entry	Lewis acid	Solvent	Time	Yield [%][b]
1	$Fe(OAc)_2$	CH_2Cl_2	24 h	0
2	$Fe(acac)_2$	CH_2Cl_2	24 h	0
3	CuCl	CH_2Cl_2	24 h	0
4[c]	$B(C_6F_5)_3$	CH_2Cl_2	24 h	5
5	**$B(C_6F_5)_3$**	**CH_2Cl_2**	**5 min**	**98**
6	$BF_3.OEt_2$	CH_2Cl_2	5 min	60
7	$Sc(OTf)_3$	CH_2Cl_2	30 min	97
8	$AlCl_3$	CH_2Cl_2	1 h	85
9	$B(C_6F_5)_3$	PhMe	1 h	88
10	$B(C_6F_5)_3$	$CHCl_3$	40 min	94
11	$B(C_6F_5)_3$	Et_2O	24 h	0
12	$B(C_6F_5)_3$	DMF	24 h	0
13	$B(C_6F_5)_3$	THF	24 h	CM[d]
14	---	CH_2Cl_2	24 h	0

[a]*Reaction conditions*: Unless otherwise mentioned all the reactions were carried out with 0.067 M of **59a** and 10 mol% of Lewis acid in solvent at room temperature (25–28 °C). [b]Isolated yield. [c]1 mol % of catalyst was used. [d]CM = Complex mixture. 1.5 Equivalents of **59b** with respect to **59a** was found to be optimal. The reaction was quenched with 1.5 equivalents of TBAF after completion.

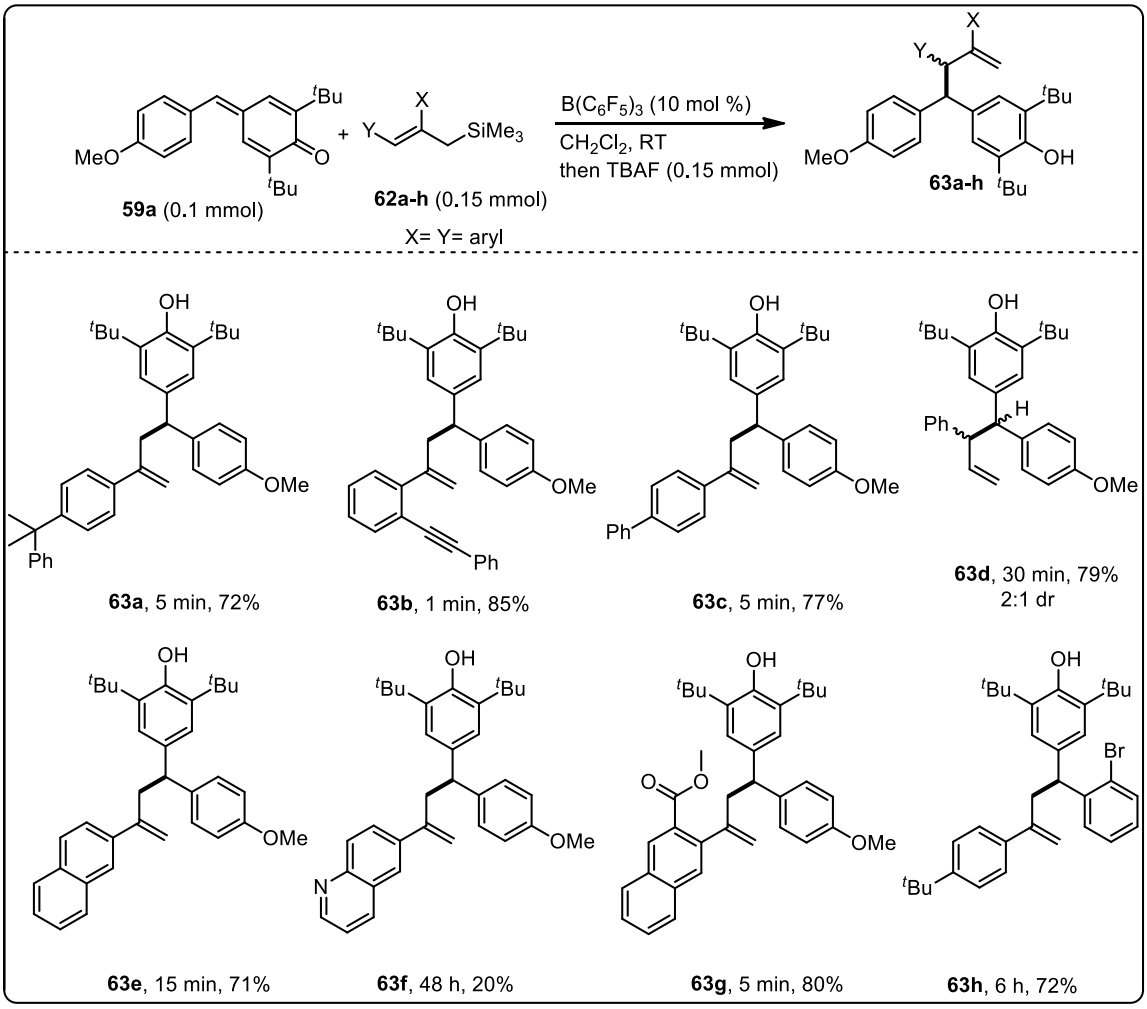
Further optimization studies were carried out using $B(C_6F_5)_3$ as a catalyst in other solvents such as toluene and chloroform, but the yield of the product **61** was found to be inferior when compared to Entry 5 (Entries 9 & 10). Surprisingly, the reaction did not work in solvents like diethylether and DMF (Entries 11 & 12). The formation of a complex mixture was observed when the reaction was carried out in THF (Entry 13). Notably, no product was observed when the reaction was carried out without any catalyst, which clearly indicates a Lewis acid catalyst is essential for this transformation (Entry 14).

Table 2. Substrate scope using different *p*-QMs



[a]*Reaction conditions:* 0.067 M of **59** in DCM, RT = 27-30 °C. Yields reported are isolated yields. [b]CM = complex mixture.

Table 3. Substrate scope with different allylating agents



[a]*Reaction conditions:* 0.067 M of **59a** in DCM, RT = 27-30 °C. Yields reported are isolated yields.

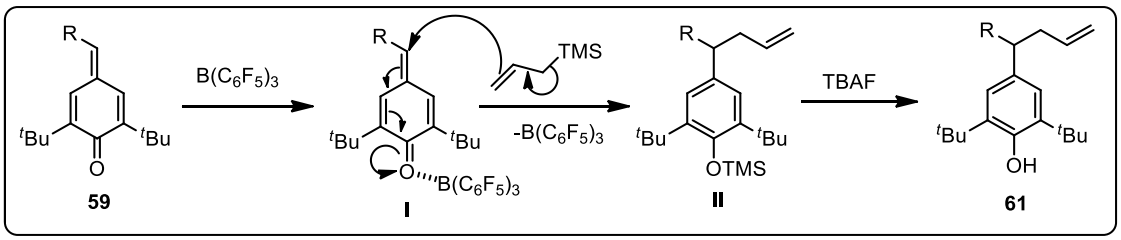
After finding an optimal condition for this transformation (Entry 6, Table 1), we focused on evaluating the substrate scope of *p*-QMs towards allylation. In this regard, a range of *p*-QMs were prepared and subjected to 1,6-conjugate allylation under standard conditions and the results are summarized in Table 2. In most of the cases, the reaction was completed within a few minutes. In general, this protocol worked well in cases of *p*-QMs derived from both electron-rich as well as electron-poor aromatic aldehydes, and the corresponding allyl diarylmethanes (**61b**-**61e**, **61p**, **61v,** and **61w**) were obtained in very good yields (80-98%). Halo-arene substituted *p*-QMs also underwent 1,6-allylation to yield the allyl diarylmethanes (**61g**, **61h**, **61l,** and **61m**) in moderate yields (60-70%). In cases of *p*-QMs (**59i** and **59j**), derived from 4-trifluoromethyl benzaldehyde and 4-

trifluoromethoxy benzaldehyde, the respective products **61i** and **61j** were obtained in 65 and 85% yields respectively. Under the optimal conditions, other allyl diarylmethanes (**61n**, **61o**, **61q**-**61t**) could be synthesized in moderate to good yields (62-89%) from their respective *p*-QM precursors. Unfortunately, the *p*-QM (**59u**), derived from thiophene-2-carboxaldehyde, resulted in the formation of complex mixture under the reaction conditions. On the other hand, the *p*-QMs derived from 2,6-diisopropyl phenol (**59x**) and 2,6-dimethyl phenol (**59y**) underwent 1,6-allylation and generated the allyl diarylmethanes **61x** and **61y** in 65 and 50% yields respectively.

To elaborate the substrate scope further we have prepared different allyl-TMS reagents by following a known literature procedure,[21] and subjected to 1,6-conjugate addition reaction with **59a** under optimized reaction conditions, and the results are summarized in Table 3. It is evident from Table 3 that this protocol worked well for all the allyl trimethylsilane derivatives tried. For instance, the reaction of **59a** with allyl trimethylsilane **62a** (X = 4-cumylphenyl, Y = H) provided the desired allyl diarylmethane **63a** in 72% yield within 5 min. Other allyl trimethylsilane derivatives such as **62b** (X = 4-alkynylphenyl, Y = H) and **62c** (X = 4-biphenyl, Y = H) reacted with **59a** and provided the products **63b** and **63c** in 85% and 77% yields respectively. Under the standard conditions, cinnamyl trimethylsilane **62d** (X = H, Y = Ph) gave the allylated product **63d** in 79% isolated yield as an inseparable diastereomeric mixture (dr = 2:1). The allyl diarylmethane **63e** was isolated in 71% yield when **59a** was treated with allyl trimethylsilane **62e** (X = 2-naphthyl, Y = H). Unfortunately, the reactivity of quinoline based allyl trimethylsilane **62f** (X = 6-quinolinyl, Y = H) toward **59a** was found to be less as the expected product **63f** was isolated only in 20% yield even after 2 days. On the other hand, the electron-poor aryl-substituted allyl trimethylsilane derivative **62g** (X = 3-naphthyl-2-carboxylic ester, Y = H) produced the allyl diarylmethane **63g** in 80% yield in 5 min. In the case of allylation of *p*-QM **59h** with **62h** (X = 4-*tert*-butylphenyl, Y = H), the desired product **63h** was isolated in 72% yield in 6h.

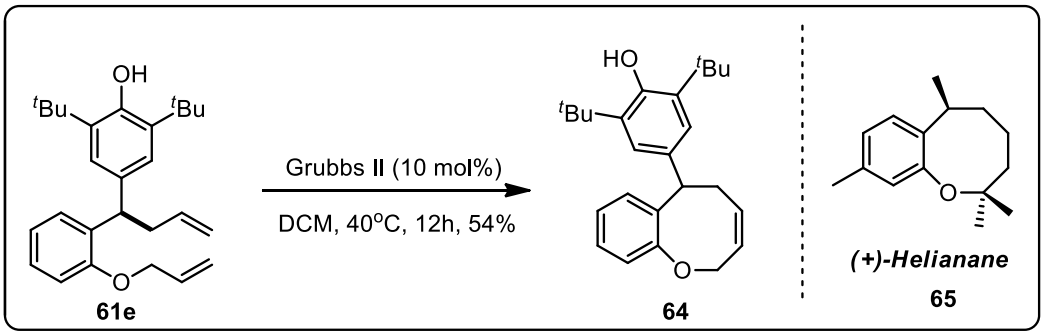
Based on the outcome of the reaction, we propose a plausible reaction mechanism (scheme 12). Initially, **59** is activated by $B(C_6F_5)_3$ and the subsequent allyl addition to *p*-

quinone methide through a 1,6-conjugate addition fashion leads to intermediate **II** with the extrusion of $B(C_6F_5)_3$. Furhter, deprotection of **II** using tetrabutylammonium fluoride (TBAF) delivers the desired product **61**.



Scheme 12: Plausible Mechanism for allylation of *p*-quinone methides

To depict the application potential of this transformation, one of the allyl diarylmethanes was elaborated to a natural product like core. In this experiment, the allyl diarylmethane **61e** was subjected to ring closing metathesis reaction with 10 mol % of the second generation Grubbs catalyst and, as expected, the 8-membered ring ether **64** was obtained in 54% yield after 12 h. This structure of **64** closely resembles a naturally occurring 8-membered ether (+)-helianane (**65**) (**Scheme 13**).[22]

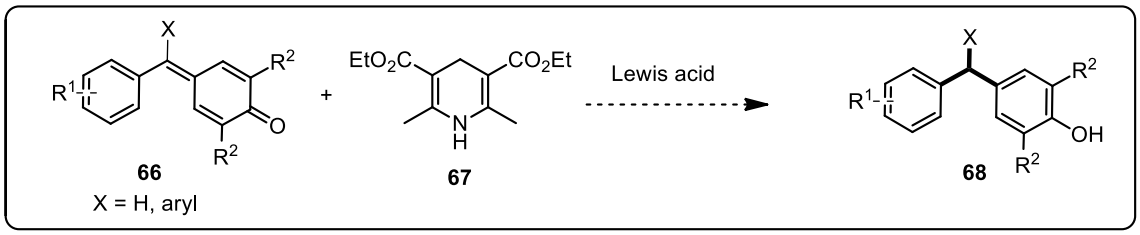


Scheme 13. Synthetic utility of allyl diarylmethane-**61e**

2b. Synthesis of unsymmetrical diaryl- and triarylmethanes methanes through reduction of p-QMs and fuchsones:

Organo-catalytic transfer hydrogenations using organic hydride donors has become a prevalent strategy to the synthetic community.[23] Of the various hydrogen sources, Hantzsch ester, a 1,4-dihydropyridine derivative, is found to be widely used for the transfer hydrogenation reactions. While developing a method for the synthesis of allyl

diarylmethanes, we anticipated that simple reduction of *p*-quinone methides (**66**, X = H) and fuchsones (**66**, X = Ar) using a reducing agent such as Hantzsch ester (**67**) would lead to unsymmetrical diaryl- and triarylmethanes (**68**) respectively (**Scheme 14**). Recently, Berionni and co-workers investigated the application of the frustrated Lewis pair concept for the reduction of electron-deficient olefins including *p*-quinone methides.[24b] However, their investigation was limited only to a couple of *p*-QMs. So far, there are no reports available for the Lewis acid catalyzed reduction of *p*-QMs, which triggered us to investigate this transformation in detail. Consequently, we have developed a Lewis acid catalyzed transfer hydrogenation protocol for the synthesis of diaryl- and triaryl methane derivatives using Hantzsch ester as a hydrogenating reagent and the results are discussed herein.[25]

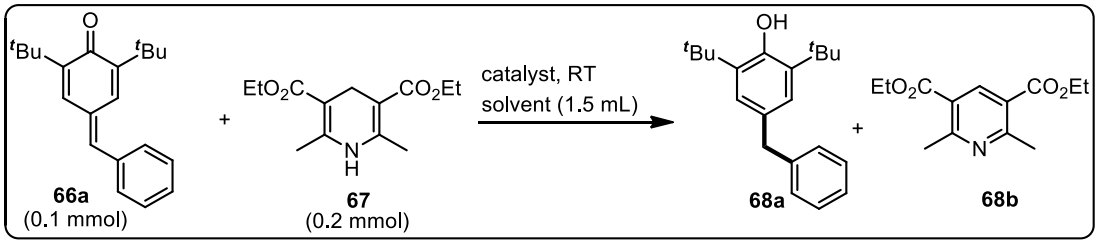


Scheme 14. Proposed synthetic approach toward diaryl- and triarylmethanes

The optimization studies were performed with a readily available *p*-QM **66a**, Hantzsch ester (**67**) and $B(C_6F_5)_3$ as a catalyst, and the results are shown in Table 4. To our pleasure, our initial attempt itself gave a fruitful result as the desired product **68a** was isolated in 70% yield in 12 h, when 1 mol% of $B(C_6F_5)_3$ and 1.1 equivalents of Hantzsch were used (Entry 1). When the number of equivalents of Hantzsch ester was increased to 2, there was a slight improvement in the yield (80%) of the product in CH_2Cl_2 (Entry 2). When the reaction was carried out using 5 mol% of $B(C_6F_5)_3$ and 2 equivalents of Hantzsch ester in CH_2Cl_2, the desired product **68a** was obtained in 93% yield after 12 h (Entry 3). Fortified by this observation, we extended the optimization studies in other solvents (Entries 4-8). Although the reaction was effectively progressing in all those solvents, the yield of **68a** was found to be inferior when compared to Entry 3. In the absence of catalyst, the desired product **68a** was observed only in trace amounts, which obviously indicates that a catalyst is necessary to drive this transformation (Entry 9). Other metal catalysts such as $Bi(OTf)_3$, $Sc(OTf)_3$, $Cu(OTf)_2$, and AgOTf were also found

to be suitable for this transformation; however, the yield of 68a was found to be moderate in all those cases (Entries 10-13).

Table 4. Optimization studies[a]



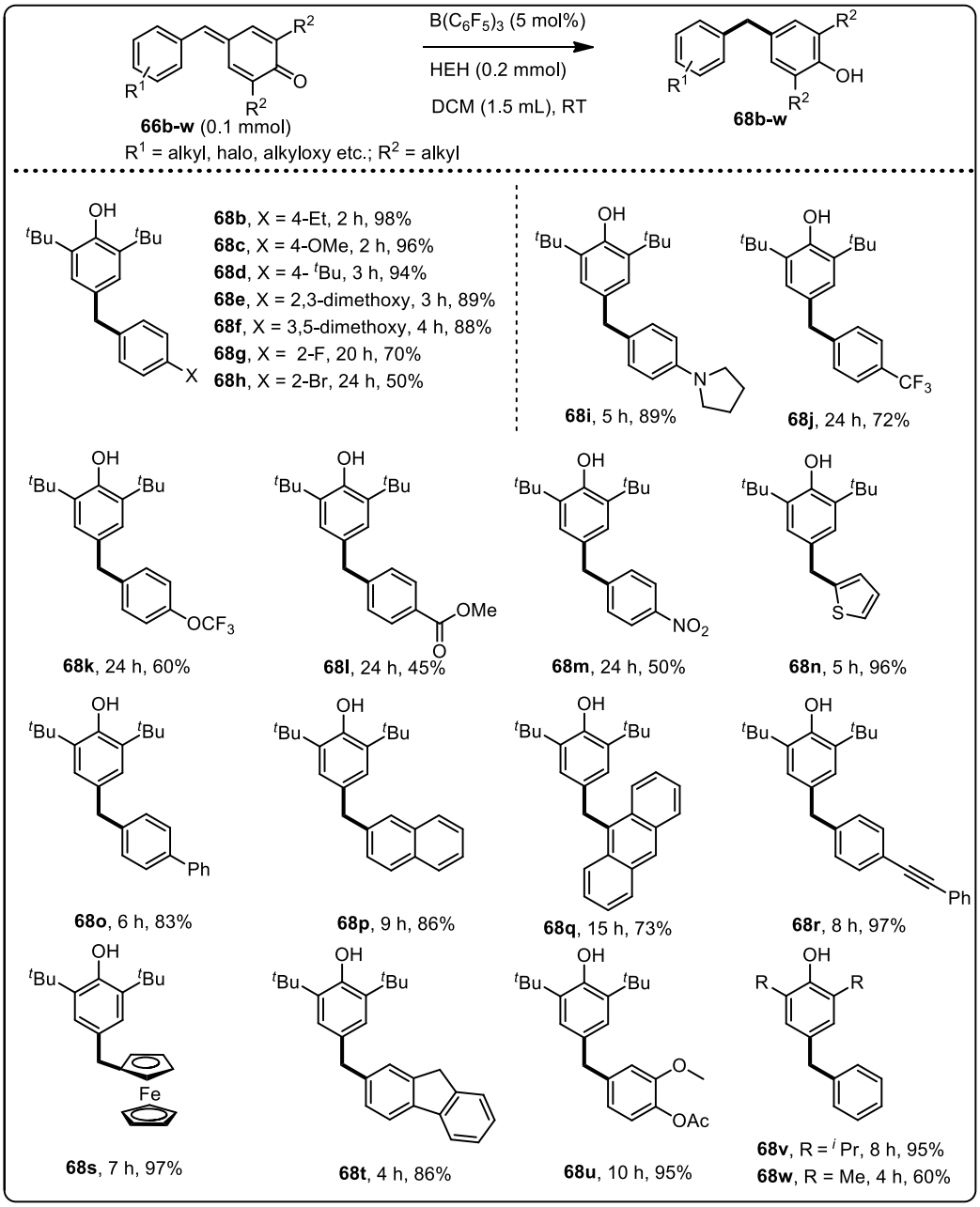
Entry	Lewis acid [mol %]	Solvent	Time [h]	Yield [%][b]
1[c]	$B(C_6F_5)_3$ [1]	CH_2Cl_2	12	70
2	$B(C_6F_5)_3$ [1]	CH_2Cl_2	12	80
3	**$B(C_6F_5)_3$ [5]**	**CH_2Cl_2**	**12**	**93**
4	$B(C_6F_5)_3$ [5]	$CHCl_3$	15	86
5	$B(C_6F_5)_3$ [5]	Toluene	24	40
6	$B(C_6F_5)_3$ [5]	Et_2O	24	trace
7	$B(C_6F_5)_3$ [5]	DCE	12	86
8	$B(C_6F_5)_3$ [5]	MeCN	24	77
9	----	CH_2Cl_2	24	trace
10	$Bi(OTf)_3$ [10]	CH_2Cl_2	24	85
11	$Sc(OTf)_3$ [10]	CH_2Cl_2	12	79
12	$Cu(OTf)_2$ [10]	CH_2Cl_2	12	40
13	Ag(OTf) [10]	CH_2Cl_2	24	70

[a]*Reaction conditions*: All reactions were performed with 0.067 M of **66a** in solvent and 2 equivalents of Hantzsch ester. RT = 27–30 °C. [b]Yields are isolated yield. [c]1.1 equiv. of Hantzsch ester used. DCE = 1,2-dicholoroethane

After identifying the optimal reaction conditions (Entry 3), the substrate scope was appraised using a variety of *p*-quinone methides (**66b-w**) and the results are unveiled in Table 5. This protocol generally worked well for all the *p*-QMs investigated and, in most of the cases, the desired diarylmethane derivatives (**68b-w**) were obtained in good to excellent yields. For instance, this method worked capably for the *p*-quinone methides

(**66b-f**, **66i**), derived from electron-rich aromatic aldehydes, and the desired products (**68b-f**, **68i**) were isolated in excellent yields (88-98%). However, the yield of diarylmethane derivatives (**68j-m**) in the cases of *p*-quinone methides (**66j-m**) bearing electron-withdrawing groups at the aryl group was found to be moderate (45-72%).

Table 5. Substrate scope with different *p*-QMs

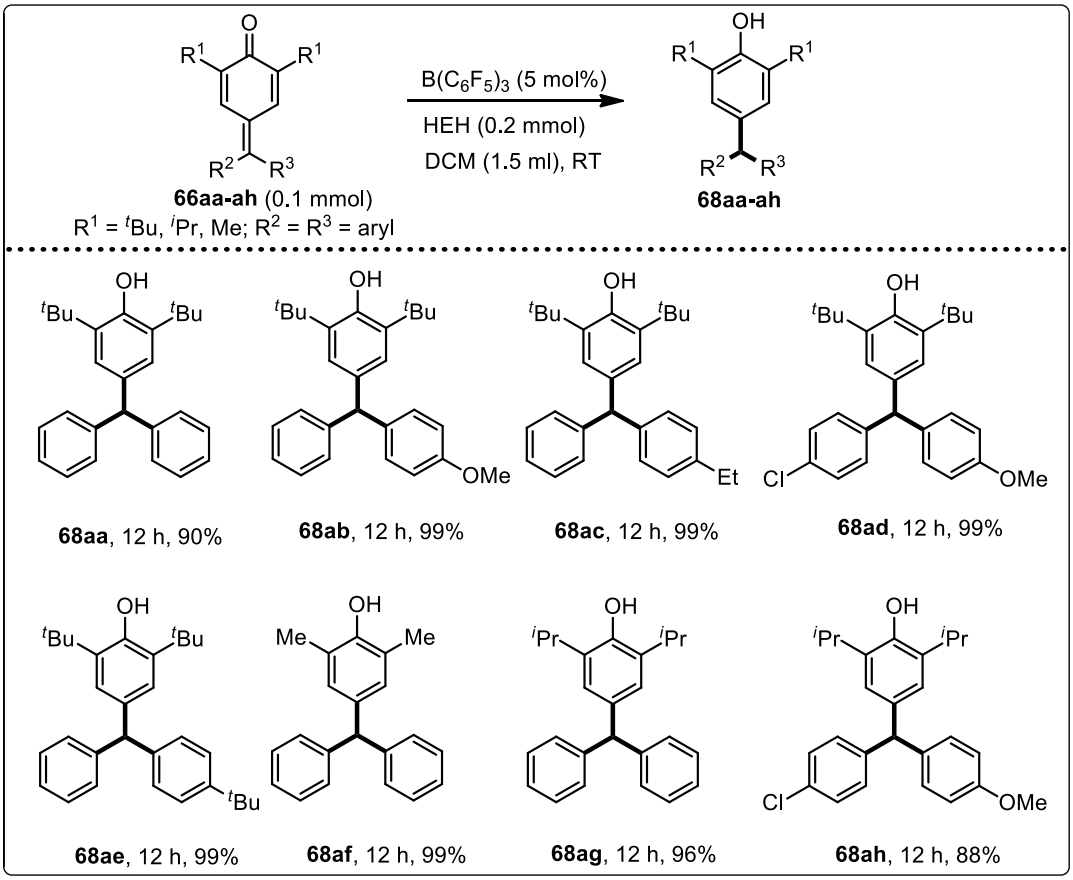


[a]*Reaction conditions:* 0.067 M of **66**(**b**-**w**) in CH_2Cl_2. RT = 27-30 °C. Yields reported are isolated yields.

Halo-substituted *p*-QMs (**66g** & **66h**) provided the respective diarylmethane derivatives **68g** and **68h** in 70 and 50% yields, respectively. The sterically hindered *p*-QM precursors

(**66o-q**), derived from 4-phenyl benzaldehyde, 2-naphthaldehyde, and 9-anthracene aldehyde underwent smooth conversion to their corresponding diarylmethane derivatives (**68o-q**) in the range of 73-83% yields. Furthermore, the *p*-quinone methide (**66n**), prepared from thiophene-2-carboxaldehyde aldehyde, was converted to its respective diarylmethane derivative (**68n**) in 96% yield. Under the optimal conditions, diarylmethanes **68r**-**68u** could be synthesized in the range of 86-97% yields from their corresponding precursors. Finally, this protocol was also extended to other *p*-QMs (**66v**, **66w**), derived from 2,6-diisopropyl phenol and 2,6-dimethyl phenol, and in both the cases, the expected products (**68v**, **68w**) were obtained in 95% and 60% respectively. It is worth mentioning that most of the reactive functional groups such as, nitro, ester and alkyne were well tolerated under the reaction conditions.[26]

Table 6. Substrate scope with different fuchsones

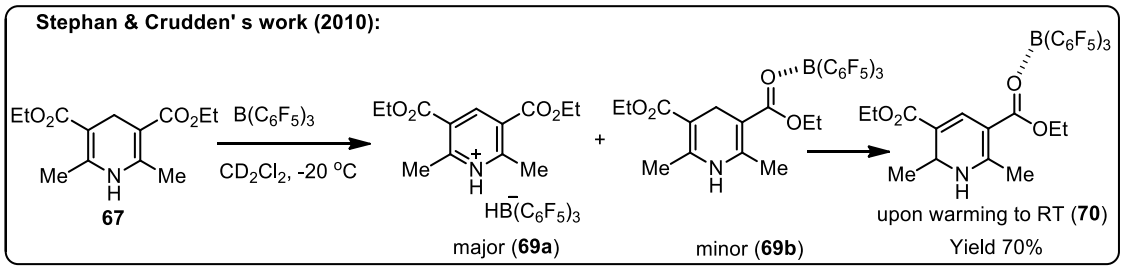


[a]*Reaction conditions:* 0.067 M of **66** in DCM, RT = 27-30 °C. Yields reported are isolated yields.

The feasibility of the present methodology was also elaborated for the synthesis of symmetrical as well as unsymmetrical triarymethanes using fuchsones instead of *p*-QMs. In this context,

many fuchsones (**66aa-ah**) were prepared using a known protocol[27] and subjected to $B(C_6F_5)_3$ catalyzed reduction with Hantzsch ester under the optimized conditions (Table 6). Remarkably, the optimized condition for the reduction of *p*-QMs was also found to be the well-suited condition for the reduction of fuchsones. Under this condition, a wide range of symmetrical and unsymmetrical triarylmethane derivatives (**68aa-ae**) were obtained in excellent yields (90-99%) from their respective fuchsone precursors (**66aa-ae**). Other fuchsones (**66af-ah**), derived from 2,6-disubstituted phenols such as, 2,6-diisopropylphenol and 2,6-dimethylphenol also underwent smooth transformation, and the products (**68af-ah**) were obtained in the range of 88-99% isolated yields.

After investigating the substrate scope for the synthesis of diaryl- and triarylmethanes, we shifted our attention to understand the mechanism of this transformation in detail. In fact, we were primarily interested in the mode of activation of Hantzsch ester by $B(C_6F_5)_3$. Recently, Stephan and Crudden jointly reported[24a] that the reaction of Hantzsch ester (**67**) with $B(C_6F_5)_3$ would generate a frustrated Lewis-pair (**69a**) as major product at -20 °C along with its Lewis acid-base adduct (**69b**). Interestingly, upon warming the reaction mixture to room temperature, they found that 1,2-dihydropyridine (**70**) could be isolated with maximum 70% yield in 24 h (**Scheme 15**).



Scheme 15. Frustrated Lewis pair Vs Lewis acid-base pair

Based on the above observation, we thought that both the activation modes are possible in the $B(C_6F_5)_3$ catalyzed reduction of *p*-QMs and fuchsones. To find out the actual mode of activation, a few experiments were performed. In one of the experiments, the reduction of **66a** was carried out at -20 °C; however, only traces of **68a** was observed (by TLC) after 12 h. Interestingly, when the same reaction mixture was warmed to room temperature, the conversion started taking place and the concentration of **68a** was gradually increasing with respect to time. This clearly indicates

that the frustrated Lewis-pair (**69a**) does not react with *p*-QMs at lower temperature even if we assume that it was formed during the progress of the reaction. Since the reduction of *p*-QMs (our protocol) is carried out at room temperature, it is less probable that the reaction is actually proceeding through frustrated Lewis-pair complex. In fact, the above experimental observation clearly supports our hypothesis. Moreover, it is reported in the literature that the frustrated Lewis-pair **69a** generally forms at lower temperature.[24a] Therefore, one can conclude that the reaction is actually proceeding through a Lewis acid-base pair. To further confirm this, an experiment was conducted in a NMR tube at room temperature using 1:1 ratio of Hantsch ester and $B(C_6F_5)_3$, and the progress of the reaction was monitored by ^{11}B NMR spectroscopy. In this case, a strong signal at δ -3.82 ppm was observed, which actually corresponds to the Lewis acid-base adduct (**69b**), according to the literature precedence.[24a] The peak that corresponds to the frustrated Lewis-pair complex [**69a**] (at -24.4 ppm) was not observed at all.[24a] Based on the above-mentioned observations, a plausible mechanism has been proposed (**Scheme 16**). Initially, *p*-quinone methide **66a** is activated by $B(C_6F_5)_3$ and the subsequent hydride migration from Hantzsch ester to *p*-quinone methide leads to intermediate **II**, which on protonation delivers the desired product **68a** with the extrusion of $B(C_6F_5)_3$.

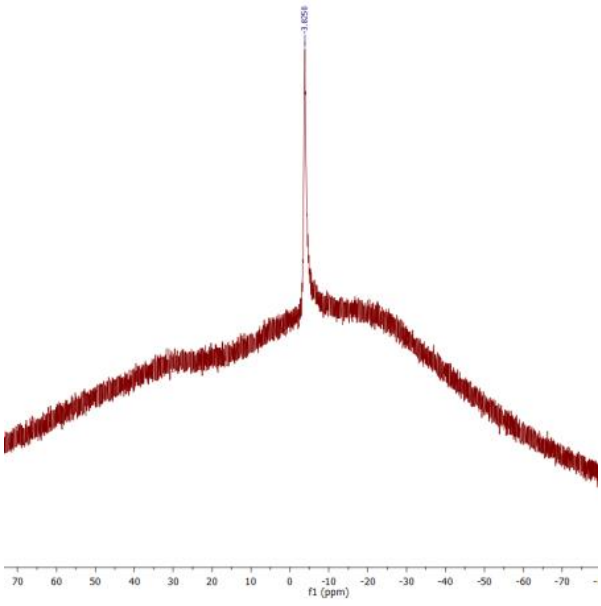
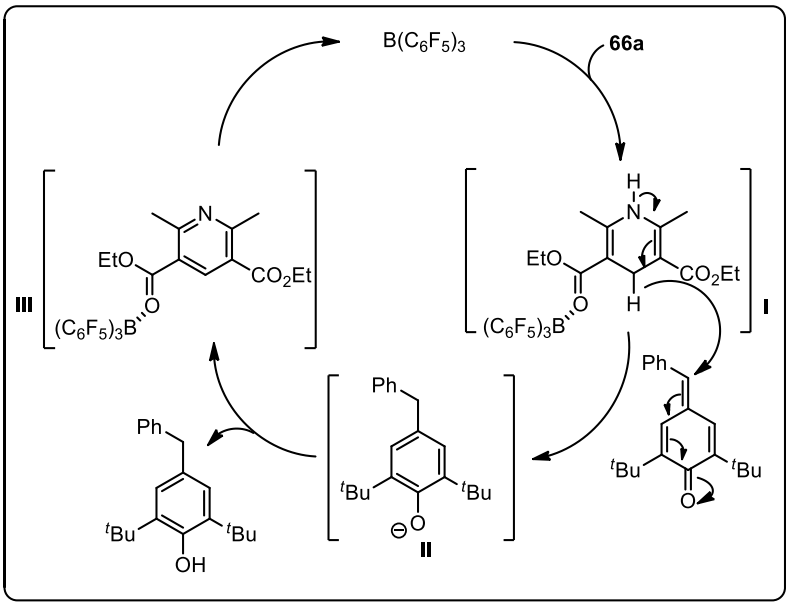
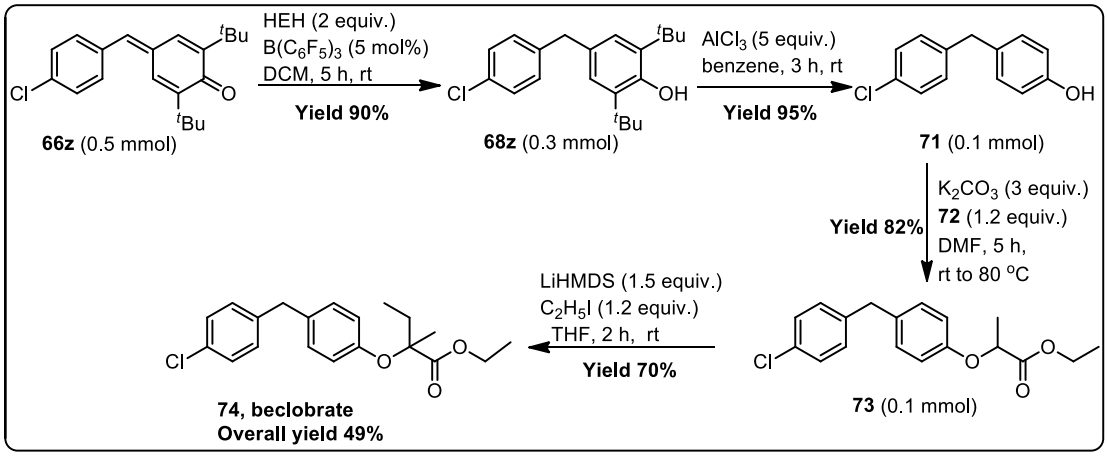


Figure 2: ^{11}B NMR of the reaction mixture



Scheme 16: Plausible reaction mechanism



Scheme 17: Synthetic elaboration to beclobrate preparation

To portray the synthetic utility, this protocol was elaborated to the synthesis of beclobrate, which is a potent cholesterol- and triglyceride lowering drug and is used for the treatment of hyperlipidemia.[28] A few divergent methods are available in the literature for the synthesis of beclobrate.[29] Our strategy for the synthesis of beclobrate is shown in Scheme 17. The reduction of *p*-QM **66z** using our standard reaction condition (Table 4, Entry 3) gave the respective diarylmethane **68z** in 90% yield. $AlCl_3$ Mediated de-*tert*-butylation of **68z** resulted the desired diarylmethane **71** in 95% yield. The conventional alkylation reaction between **71** and 2-bromoethylpropiolate (**72**) provided the beclobrate precursor

73 in 82% yield. Finally, a base mediated alkylation of **73** with iodoethane provided beclobrate (**74**) in 70% yield (49% overall yield from **66z**).

3. Conclusion:

In summary, we have shown the application of $B(C_6F_5)_3$ as a Lewis acid catalyst for the synthesis of unsymmetrical allyl diarylmethanes through 1,6-conjugate allylation of *p*-quinone methides. By taking the advantage of the unique reactivity of *p*-quinone methides, we could achieve this transformation in a highly regio-selective manner. This protocol worked generally well for all kinds of substituted *p*-QMs as well as substituted allyl trimethylsilanes. This protocol was also elaborated for the synthesis of core structure of Heliannane. In continuation of this methodology, we have also developed a general protocol to access unsymmetrical diaryl- and triarylmethanes through a $B(C_6F_5)_3$ catalyzed regio-selective reduction of *p*-QMs and fuchsones, respectively, using Hantzsch ester as a reducing agent under mild reaction conditions. In addition, this protocol was also elaborated to the total synthesis beclobrate, which is a potent cholesterol- and triglyceride lowering drug.

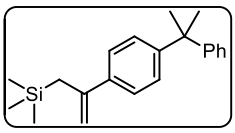
4. Experimental section:

General methods: Most of the reagents and starting materials used were purchased from commercial sources and used as such. All the *p*-Quinone methides were prepared by following a known literature procedure.[30] All the substituted allyltrimethylsilanes were prepared by following a literature method.[31] Melting points were recorded on SMP20 Melting point apparatus and are uncorrected. ^{1}H, ^{13}C and ^{19}F spectra were recorded in $CDCl_3$ (400, 100, 376 MHz respectively) on Brucker FT-NMR spectrometer. Chemical shifts values are reported in parts per million relative to TMS (for ^{1}H and ^{13}C), $BF_3.Et_2O$ (for ^{19}F). High resolution mass spectra were recorded on Waters Q-TOF Premier-HAB213 spectrometer. FT-IR spectra were recorded on a Perkin – Elmer FT-IR spectrometer. Thin layer chromatography was performed on Merck silica gel 60 F_{254} TLC plates using EtOAc/Haxane as an eluent. column chromatography was carried out through silica gel (100-200 mesh) using ethyl acetate/hexane mixture as an eluent.

General procedure for the synthesis of Allylsilane reagents: All the allyl reagents were prepared by following a literature method. A mixture of aryl triflate (1 mmol), palladium acetate (0.05 mmol), 1,1'-bis(diphenylphosphino)ferrocene (0.15 mmol), allyltrimethylsilane (5 mmol), trimethylamine (2 mmol), and dry acetonitrile (5 ml) was placed in an oven dried glass vial and the reaction mixture was heated to 60 °C, under stirring, for 12-15 hours. After the reaction was completed, as judged by T.L.C., acetonitrile was removed under reduced pressure and the crude product was directly subjected to column chromatography (hexane as an eluent) to yield desired allyl trimethylsilanes.

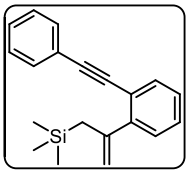
Characterization of products:

Trimethyl(2-(4-(2-phenylpropan-2-yl)phenyl)allyl)silane (62a):



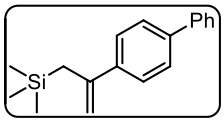
Colourless liquid; yield 65% (200 mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 (d, J = 8.5 Hz, 2H), 7.30-7.23 (m, 5H), 7.18 (d, J = 8.5 Hz, 2H), 5.15 (d, J = 1.7 Hz, 1H), 4.86 (d, J = 1.4 Hz, 1H), 2.02 (d, J = 0.7 Hz, 2H), 1.70 (s, 6H), -0.07 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9, 149.7, 146.3, 140.1, 128.1, 126.9, 126.6, 126.0, 125.7, 108.6, 42.9, 30.9, 26.2, -1.2 ppm.

Trimethyl(2-(2-(phenylethynyl)phenyl)allyl)silane (62b): Colourless liquid; yield 60%

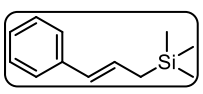


(175 mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56-7.21 (m, 9H), 5.10-5.08 (m, 2H), 2.20 (d, J = 0.6 Hz, 2H), -0.08 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.8, 133.0, 131.7, 131.5, 128.5, 128.48, 128.46, 128.4, 128.2, 126.8, 123.9, 113.6, 92.9, 89.5, 28.3, -1.4 ppm.

(2-([1,1'-Biphenyl]-4-yl)allyl)trimethylsilane (62c): White colour solid; yield 80% (212



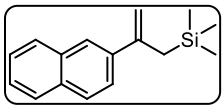
mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62 (d, J = 8.6 Hz, 2H), 7.56 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.46-7.43 (m, 2H), 7.36-7.32 (m, 1H), 5.21 (d, J = 1.5 Hz, 1H), 4.90 (s, 1H), 2.06 (s, 2H), -0.06 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.2, 141.7, 140.9, 140.0, 128.9, 127.3, 127.1, 126.9, 126.8, 110.2, 26.1, -1.2 ppm.



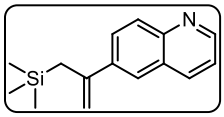
Cinnamyltrimethylsilane (62d): Colourless liquid; yield 60% (115 mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34-7.28 (m, 4H), 7.20-7.15 (m, 1H), 6.32-6.22 (m, 2H), 1.70-1.67 (m, 2H), 0.07 (s, 9H)

ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.6, 128.6, 128.4, 128.0, 126.3, 125.6, 24.1, -1.7 ppm.

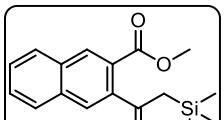
Trimethyl(2-(naphthalen-2-yl)allyl)silane (62e): Colourless liquid; yield 65% (156 mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.89-7.79 (m, 4H), 7.63 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.52-7.42 (m, 2H), 5.33 (d, *J* = 1.4 Hz, 1H), 5.01 (d, *J* = 0.8 Hz, 1H), 2.17 (s, 2H), -0.04 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.4, 140.0, 133.4, 132.9, 128.3, 127.7, 127.6, 126.1, 125.8, 125.03, 125.02, 110.8, 26.2, -1.2 ppm.



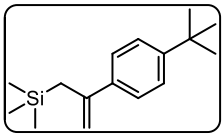
6-(3-(Trimethylsilyl)prop-1-en-2-yl)quinoline (62f): Colourless liquid; yield 80% (193 mg); R_f = 0.5 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.84 (d, *J* = 4.2 Hz, 1H), 8.10-8.01 (m, 2H), 7.81 (d, *J* = 8.9 Hz, 1H), 7.75 (s, 1H), 7.33 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.29 (s, 1H), 5.00 (s, 1H), 2.11 (s, 2H), -0.11 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.1, 147.7, 145.7, 140.7, 136.2, 129.1, 128.6, 128.1, 124.6, 121.3, 111.7, 26.1, -1.3 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{33}O_2$ $[M+H]^+$: 242.1366; found: 242.1356.



Methyl 3-(3-(trimethylsilyl)prop-1-en-2-yl)-2-naphthoate (62g): Colourless liquid; yield 65% (194 mg); R_f = 0.5 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.35 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.88-7.75 (m, 2H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.73 (s, 1H), 5.04-5.02 (m, 2H), 3.95 (s, 2H), 1.99 (d, *J* = 0.5 Hz, 2H), -0.09 (S, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.7, 148.3, 141.8, 134.6, 131.3, 128.7, 128.5, 128.2, 128.2, 127.7, 126.5, 125.3, 111.7, 52.3, 28.8, -1.3 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{33}O_2$ $[M+H]^+$: 299.1468; found: 242.1454.



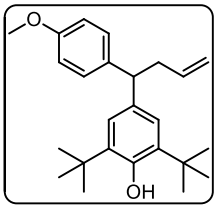
(2-(4-(*tert*-Butyl)phenyl)allyl)trimethylsilane (62h): Colourless liquid; yield 60% (148 mg); R_f = 0.7 (1% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40-7.30 (m, 4H), 5.16-5.15 (m, 1H), 4.89-4.85 (m, 1H), 2.50-2.02 (m, 1H), 1.34 (s, 9H), -0.06 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.3, 146.3, 139.8, 126.0, 125.9, 109.4, 34.6, 31.5, 26.1, -1.2 ppm.



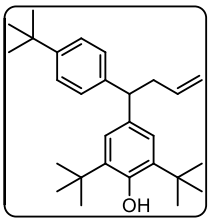
General procedure for the allylation of *p*-quinone methides: Allyltrimethisilane (0.15 mmol) was added to a solution of *p*-quinone methide (0.1 mmol) and $B(C_6F_5)_3$ (0.01 mmol) in 1.5 ml of CH_2Cl_2 and the resultant mixture was stirred at room temperature until the *p*-quinone methide was completely consumed (by T.L.C.). The reaction mixture was then quenched with tetrabutylammoniumfluoride (0.15 mmol) at rt. The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using 0.5-1% ethyl acetate/hexane mixture as an eluent to get the pure allyl diarymethane.

Characterization of products:

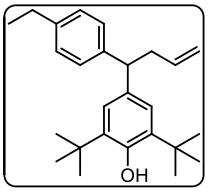
2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)but-3-en-1-yl)phenol (61a): Yellow oil; yield 98% (35.4 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3641, 2958, 2915, 2873 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.18 (d, *J* = 8.6 Hz, 2H), 7.03 (s, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.73 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.07-5.02(m, 1H), 5.05 (s, 1H), 4.97–4.94 (m, 1H), 3.91–3.87 (m, 1H), 3.79 (s, 3H), 2.79–2.75 (m, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 152.0, 137.6, 137.3, 135.7, 135.6, 129.0, 124.3, 116.0, 113.8, 55.3, 50.6, 41.0, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{33}O_2$ $[M-H]^+$: 365.2480; found: 365.2471.



2,6-Di-*tert*-butyl-4-(1-(4-(*tert*-butyl)phenyl)but-3-en-1-yl)phenol (61b): Yellow oil; yield 88% (34.5 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3646, 2958, 2911, 2873 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.04 (s, 2H), 5.72 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.06-5.01(m, 1H), 5.03 (s, 1H), 4.95–4.92 (m, 1H), 3.88 (t, *J* = 7.8 Hz, 1H), 2.80–2.75 (m, 2H), 1.41 (s, 18H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 148.7, 142.2, 137.7, 135.5, 135.4, 127.5, 125.3, 124.5, 115.9, 51.1, 41.0, 34.5, 34.4, 31.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{41}O$ $[M+H]^+$: 393.3158; found: 393.3150.

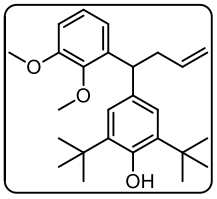


2,6-Di-*tert*-butyl-4-(1-(4-ethylphenyl)but-3-en-1-yl)phenol (61c): Yellow oil; yield 98% (35.7 mg); R_f = 0.8 (5% EtOAc in hexane); FT-IR 3644, 2961, 2927, 2872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.20 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.07 (s, 2H), 5.75 (ddt, *J* =17.0, 10.2, 6.9 Hz, 1H), 5.08-5.04 (m, 1H), 5.05 (s, 1H), 4.98–4.95 (m, 1H), 3.91 (t, *J* = 7.8 Hz, 1H), 2.86–2.76 (m, 2H),



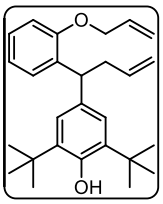
2.64 (q, *J* = 7.6 Hz, 2H), 1.44 (s, 18H), 1.24 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 142.4, 141.8, 137.7, 135.6, 135.5, 127.92, 127.90, 124.4, 115.9, 51.2, 40.9, 34.5, 30.5, 28.5, 15.7 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{35}O$ $[M-H]^+$: 363.2687; found: 363.2677.

2,6-Di-*tert*-butyl-4-(1-(2,3-dimethoxyphenyl)but-3-en-1-yl)phenol (61d): Yellow solid; yield



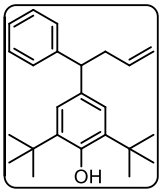
80% (31.7 mg); R_f = 0.2 (5% EtOAc in hexane); M.P. 88-90 °C; FT-IR 3642, 3077, 2958, 2915, 2877 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.08 (s, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.88 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.75 (dd, *J* = 8.1, 1.4 Hz, 1H), 5.72 (ddt, *J* = 17.0, 10.2, 6.8 Hz 1H), 5.04–4.99 (m, 1H), 5.00 (s, 1H), 4.93–4.90 (m, 1H), 4.43 (t, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.68 (s, 3H), 2.77–2.73 (m, 2H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.8, 152.0, 146.9, 139.1, 137.6, 135.5, 135.3, 124.6, 123.9, 120.1, 115.9, 109.9, 60.7, 55.7, 43.4, 40.2, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{35}O_3$ $[M-H]^+$: 395.2585; found: 395.2575.

4-(1-(2-(Allyloxy)phenyl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61e): Yellow oil; yield 85%



(33.3 mg); R_f = 0.3 (5% EtOAc in hexane); FT-IR 3646, 2965, 2915, 2877 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.14–7.10 (m, 1H), 7.08 (s, 2H), 6.91 (td, *J* = 7.4, 0.9 Hz, 1H), 6.82–6.80 (m, 1H), 6.02 (ddt, *J* = 17.2, 12.3, 3.2 Hz, 1H), 5.74 (ddt, 17.0, 10.2, 6.8 Hz, 1H), 5.38 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.24 (dq, *J* = 10.6, 1.5 Hz, 1H), 5.05–4.99 (m, 1H), 4.99 (s, 1H), 4.93–4.90 (m, 1H), 4.56–4.44 (m, 3H), 2.86–2.70 (m, 2H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.0, 151.9, 137.9, 135.3, 135.0, 134.0, 133.7, 128.1, 126.8, 124.8, 120.8, 116.9, 115.7, 112.0, 68.9, 43.3, 39.6, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{35}O_2$ $[M-H]^+$: 391.2636; found: 391.2623.

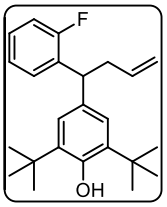
2,6-Di-*tert*-butyl-4-(1-phenylbut-3-en-1-yl)phenol (61f): Yellow semi solid; yield 94% (31.6



mg); R_f = 0.8 (5% EtOAc in hexane); FT-IR 3646, 2954, 2923, 2858 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31–7.25 (m, 4H), 7.20–7.15 (m, 1H), 7.04 (s, 2H), 5.76 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.06–5.01 (m, 1H), 5.04 (s, 1H), 4.96–4.93 (m, 1H), 3.93 (t, *J* = 7.8 Hz, 1H), 2.85–2.74 (m, 2H), 1.42 ppm (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 145.1, 137.5, 135.6, 135.3, 128.4, 128.1, 126.1, 124.5,

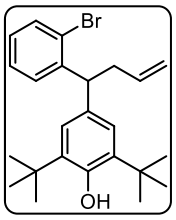
116.0, 51.4, 40.8, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{31}O$ $[M-H]^+$: 335.2374; found: 335.2362.

2,6-Di-*tert*-butyl-4-(1-(2-fluorophenyl)but-3-en-1-yl)phenol (61g): Yellow oil; yield 70%



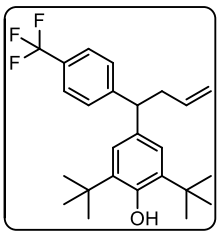
(24.8 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3646, 2958, 2919, 2873 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.26 (td, *J* = 7.5, 1.8 Hz, 1H), 7.18–7.13 (m, 1H), 7.10–7.06 (m, 1H), 7.08 (s, 2H), 7.03–6.98 (m, 1H), 5.74 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.07 (s, 1H), 5.07–5.02 (m, 1H), 4.97–4.94 (m, 2H), 4.31 (t, *J* = 7.9 Hz, 1H), 2.87–2.75 (m, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.8 (d, *J* = 244.0 Hz), 152.2, 137.0, 135.7, 134.0, 132.0 (d, *J* = 15.0 Hz), 129.1 (d, *J* = 5.0 Hz), 127.5 (d, *J* = 9.0 Hz), 124.6, 124.1 (d, *J* = 4.0 Hz), 116.3, 115.5 (d, *J* = 22.0 Hz), 43.6 (d, *J* = 2.0 Hz), 39.6, 34.5, 30.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$), δ = -117.7 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{30}FO$ $[M-H]^+$: 353.2280; found: 353.2272.

4-(1-(2-Bromophenyl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61h): Yellow oil; yield 60%



(24.8 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3638, 2958, 2931, 2869 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.53 (d, *J* = 7.8 Hz, 1H), 7.25–7.24 (m, 2H), 7.09 (s, 2H), 7.04–7.00 (m, 1H), 5.73 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.07-5.02(m, 1H), 5.05 (s, 1H), 4.96–4.93 (m, 1H), 4.52 (t, *J* = 7.8 Hz, 1H), 2.79–2.75 (m, 2H), 1.41 ppm (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 144.3, 136.8, 135.6, 133.7, 133.0, 129.0, 127.6, 127.5, 125.3, 124.8, 116.4, 48.9, 40.0, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{30}BrO$ $[M-H]^+$: 413.1479; found: 413.1470.

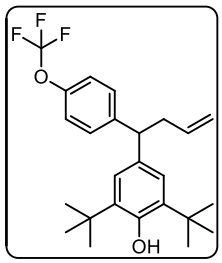
2,6-Di-*tert*-butyl-4-(1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)phenol (61i): Colourless oil;



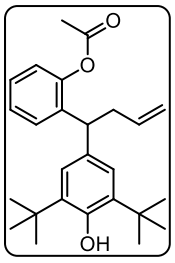
yield 65% (26.3 mg); R_f = 0.8 (5% EtOAc in hexane); FT-IR 3646, 2958, 2927, 2858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.54 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.02 (s, 2H), 5.70 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.09 (s, 1H), 5.06–5.02 (m, 1H), 4.98–4.95 (m, 1H), 3.99 (t, *J* = 7.9 Hz, 1H), 2.82–2.78 (m, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.4, 149.3 (q, *J* = 1.2 Hz), 136.8, 135.9, 134.2, 128.4, 128.3 (q, *J* = 32.0 Hz), 125.4 (q, *J* = 3.7 Hz), 124.5 (q, *J* = 270.0 Hz), 124.4, 116.6, 51.2, 40.4, 34.5, 30.4 ppm. ^{19}F NMR (376 MHz,

$CDCl_3$), δ = -62.3 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{30}F_3O$ $[M-H]^+$: 403.2248; found: 403.2234.

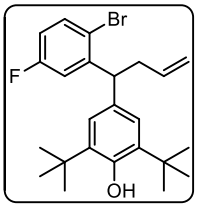
2,6-Di-*tert*-butyl-4-(1-(4-(trifluoromethoxy)phenyl)but-3-en-1-yl)phenol (61j): Yellow color semi solid; yield 85% (35.7 mg); R_f = 0.8 (5% EtOAc in hexane); FT-IR 3646, 2958, 2927, 2858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.26–7.23 (m, 2H), 7.14–7.11 (m, 2H), 7.0 (s, 2H), 5.69 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.1 (s, 1H), 5.06–5.00 (m, 1H), 4.97–4.94 (m, 1H), 3.93 (t, *J* = 8.0 Hz, 1H), 2.78–2.74 (m, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.3, 147.5 (q, *J* = 1.5 Hz), 143.9, 137.0, 135.8, 134.7, 129.3, 124.4, 120.9, 120.6 (q, *J* = 257.8 Hz,), 116.4, 50.7, 40.8, 34.5, 30.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.9 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{30}F_3O_2$ $[M-H]^+$: 419.2197; found: 419.2184.



2-(1-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)but-3-en-1-yl)phenyl acetate (61k): Yellow oil; yield 86% (33.9 mg); R_f = 0.4 (5% EtOAc in hexane); FT-IR 3642, 2961, 2923, 2873, 1761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.33–7.30 (m, 1H), 7.24–7.18 (m, 2H), 7.05–7.01 (m, 1H), 6.98 (s, 2H), 5.73 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.07–5.02 (m, 1H), 5.05 (s, 1H), 4.98–4.95 (m, 1H), 4.11 (t, *J* = 7.9 Hz, 1H), 2.76 (t, *J* = 7.1 Hz, 2H), 2.21 (s, 3H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.2, 152.1, 148.7, 137.1, 136.8, 135.6, 134.1, 128.7, 127.0, 126.1, 124.5, 122.8, 116.2, 44.3, 39.6, 34.5, 30.4, 21.1 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{33}O_3Na$ $[M + Na]^+$: 417.2408; found: 417.2400.

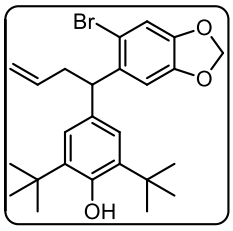


4-(1-(2-Bromo-5-fluorophenyl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61l): Yellow colour solid; yield 63% (27.2 mg); R_f = 0.6 (5% EtOAc in hexane); M.P. 83-85 °C; FT-IR 3646, 2958, 2927, 2858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.48 (dd, *J* = 8.8, 5.5 Hz, 1H), 7.07 (s, 2H), 6.94 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.78–6.74 (m, 1H), 5.71 (ddt, *J* = 16.9, 10.2, 6.8 Hz, 1H), 5.08 (s, 1H), 5.07–5.03 (m, 1H), 4.98–4.95 (m, 1H), 4.48 (t, *J* = 7.7 Hz, 1H), 2.76–2.72 (m, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (d, *J* = 245.0 Hz), 152.5, 146.7 (d, *J* = 6.0 Hz), 136.3, 135.8, 134.0 (d, *J* = 8.0 Hz), 132.9, 124.7, 119.1 (d, *J* = 3.0 Hz), 116.8, 116.0 (d, *J* = 23.0 Hz), 114.8 (d, *J* =



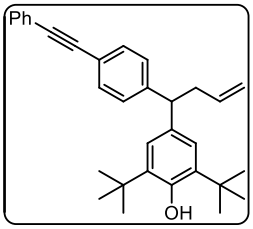
23.0 Hz), 49.1 (d, J = 1.0 Hz), 39.8, 34.5, 30.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -114.4 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{29}BrFO$ $[M-H]^+$: 431.1385; found: 431.1372.

4-(1-(6-Bromobenzo[d][1,3]dioxol-5-yl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61m): Yellow



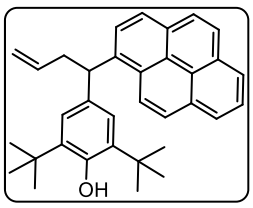
oil; yield 70% (32.2 mg); R_f = 0.4 (5% EtOAc in hexane); FT-IR 3641, 2957, 2914, 2872 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (s, 2H), 6.99 (s, 1H), 6.69 (s, 1H), 5.92 (dd, J = 10.6, 1.2 Hz, 2H), 5.73 (ddt, J = 16.9, 10.2, 6.8 Hz, 1H), 5.10 (s, 1H), 5.08–5.03 (m, 1H), 4.98–4.95 (m, 1H), 4.48 (t, J = 7.9 Hz, 1H), 2.78–2.66 (m, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.3, 147.6, 146.4, 137.9, 136.7, 135.7, 133.8, 124.5, 116.4, 114.9, 112.6, 108.5, 101.7, 48.6, 39.8, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{30}BrO_3$ $[M-H]^+$: 457.1378; found: 457.1369.

2,6-Di-*tert*-butyl-4-(1-(4-(phenylethynyl)phenyl)but-3-en-1-yl)phenol (61n): Yellow oil; yield



80% (35 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3634, 2958, 2923, 2873 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53–7.51 (m, 2H), 7.46 (d, J = 8.2 Hz, 2H), 7.37–7.31 (m, 3H), 7.23 (d, J = 8.2 Hz, 2H), 7.02 (s, 2H), 5.72 (ddt, J = 17.0, 10.2, 6.9 Hz, 1H), 5.06 (s, 1H), 5.06–5.01 (m, 1H), 4.97–4.94 (m, 1H), 3.94 (t, J = 7.8 Hz, 1H), 2.78 (t, J = 7.2 Hz, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 145.6, 137.2, 135.7, 134.8, 131.8, 131.7, 128.5, 128.3, 128.2, 124.4, 123.6, 120.9, 116.3, 89.7, 89.0, 51.2, 40.6, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{37}O$ $[M+H]^+$: 437.2845; found: 437.2829.

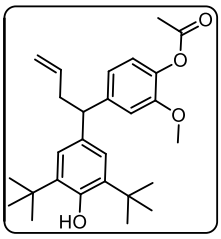
2,6-Di-*tert*-butyl-4-(1-(pyren-1-yl)but-3-en-1-yl)phenol (61o): Yellow soild; yield 72% (33.1



mg); R_f = 0.5 (5% EtOAc in hexane); M.P. 129-131 °C; FT-IR 3634, 2958, 2916, 2872 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (d, J = 9.4 Hz, 1H), 8.17 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 8.11 (d, J = 9.4 Hz, 1H), 8.03 (s, 2H), 8.00–7.97 (m, 2H), 7.18 (s, 2H), 5.81 (ddt, J = 16.9, 10.2, 6.8 Hz, 1H), 5.16–5.08 (m, 2H), 5.04 (s, 1H), 4.96–4.92 (m, 1H), 3.14–3.03 (m, 2H), 1.38 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 139.2, 137.4, 135.7, 135.2, 131.6, 130.9, 129.7, 128.9, 127.7, 127.4, 126.9, 125.9, 125.4, 125.3, 125.2, 125.1, 125.0, 124.8, 124.7, 123.4,

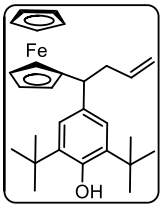
116.3, 46.0, 41.2, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{35}O$ $[M-H]^+$: 459.2687; found: 459.2681.

4-(1-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)but-3-en-1-yl)-2-methoxyphenyl acetate (61p):



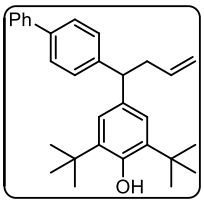
Yellow soild; yield 93% (39.4 mg); R_f = 0.2 (5% EtOAc in hexane); FT-IR 3638, 2958, 2915, 2873, 1765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.03 (s, 2H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.83 (s, 1H) 6.83–6.81 (m, 1H), 5.73 (ddt, *J* = 16.9, 10.2, 6.8 Hz, 1H), 5.06 (s, 1H), 5.06–5.02 (m, 1H), 4.97–4.94 (m, 1H), 3.89 (t, *J* = 7.8 Hz, 1H), 3.79 (s, 3H), 2.78–2.74 (m, 2H), 2.30 (s, 3H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.3, 152.2, 150.8, 144.1, 137.9, 137.3, 135.7, 134.7, 124.4, 122.5, 120.1, 116.2, 112.4, 55.9, 51.4, 41.0, 34.5, 30.5, 20.9 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{37}O_4$ $[M+H]^+$: 425.2693; found: 425.2680.

([1-{3,5-di-*tert*-butyl-4-hydroxyphenyl}but-3-en-1-yl]cyclopentadienyl)cyclopentadienyliron



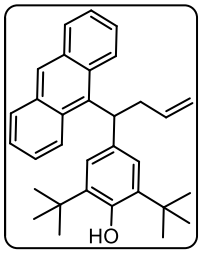
(61q): Yellow oil; yield 76% (33.7 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3642, 3084, 2958, 2915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 6.99 (s, 2H), 5.72 (ddt, *J* = 17.1, 9.8, 7.1 Hz, 1H), 5.03 (s, 1H), 5.02–4.97 (m, 1H), 4.94–4.91 (m, 1H), 4.11-4.03 (m, 3H), 4.0 (s, 5H), 3.92 (bs, 1H), 3.55 (dd, *J* = 9.3, 5.8 Hz, 1H), 2.75–2.69 (m, 1H), 2.63–2.55 (m,1H), 1.43 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 137.9, 135.4, 135.3, 124.6, 115.6, 94.9, 68.6, 67.54, 67.48, 67.4, 66.9, 46.0, 42.2, 34.5, 30.6 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{37}FeO$ $[M+H]^+$: 445.2195; found: 445.2180.

4-(1-([1,1'-Biphenyl]-4-yl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61r): Yellow semi soild;



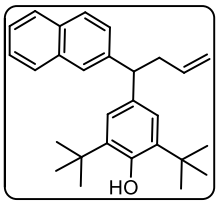
yield 85% (35 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3642, 2956, 2924, 2855 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.60–7.58 (m, 4H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.34–7.31 (m, 3H), 7.08 (s, 2H), 5.77 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.10–5.05 (m, 1H), 5.06 (s, 1H), 4.99–4.96 (m, 1H), 3.97 (t, *J* = 7.8 Hz, 1H), 2.89–2.77 (m, 2H), 1.43 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 144.3, 141.2, 138.9, 137.5, 135.7, 135.2, 128.8, 128.5, 127.2, 127.12, 127.10, 124.5, 116.2, 51.2, 40.8, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{30}H_{35}O$ $[M-H]^+$: 411.2687; found: 411.2676.

4-(1-(Anthracen-9-yl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (61s): Yellow semi soild; yield



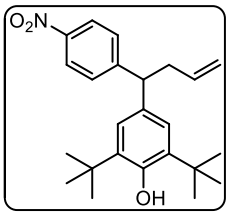
62% (27 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3627, 2958, 2931, 2865 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.74–7.72 (m, 1H), 7.43–7.41 (m, 1H), 7.31–7.19 (m, 8H), 7.17–7.13 (m, 1H), 6.99 (td, *J* = 7.6, 1.3 Hz, 1H), 6.94 (s, 1H), 5.78 (ddt, *J* = 17.2, 10.0, 7.0 Hz, 1H), 5.21 (s, 1H), 4.96–4.94 (m, 1H), 4.91–4.87 (m, 1H), 3.92 (t, *J* = 7.4 Hz, 1H), 2.50 (t, *J* = 7.2 Hz, 2H), 1.34 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.2, 141.1, 139.5, 139.4, 136.5, 135.5, 135.0, 133.8, 128.8, 128.4, 128.3, 127.4, 127.2, 126.8, 126.63, 126.59, 126.5, 125.2, 123.7, 116.8, 48.6, 43.6, 34.4, 30.3 ppm. HRMS (ESI): *m/z* calcd for $C_{32}H_{37}O$ $[M+H]^+$: 437.2845; found: 437.2831.

2,6-Di-*tert*-butyl-4-(1-(naphthalen-2-yl)but-3-en-1-yl)phenol (61t): Yellow oil; yield 89%

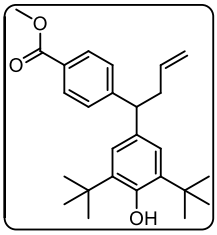


(34.3 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3640, 2957, 2925, 2872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 8.5 Hz, 1H); 7.86–7.84 (m, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.52–7.41 (m, 4H), 7.10 (s, 2H), 5.80 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.11–5.05 (m, 1H), 5.03 (s, 1H), 4.96–4.93 (m, 1H), 4.79 (t, *J* = 7.7 Hz, 1H), 2.99–2.84 (m, 2H), 1.39 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 140.9, 137.6, 135.6, 134.7, 134.2, 132.1, 129.0, 126.8, 125.9, 125.6, 125.3, 124.8, 124.7, 123.9, 116.1, 46.0, 41.0, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{33}O$ $[M-H]^+$: 385.2531; found: 385.2515.

2,6-Di-*tert*-butyl-4-(1-(4-nitrophenyl)but-3-en-1-yl)phenol (61v): Yellow oil; yield 97% (37



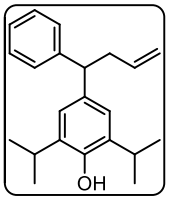
mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3642, 2954, 2927, 2854 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.15 (d, *J* = 8.7 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H), 6.99 (s, 2H), 5.68 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.11 (s, 1H), 5.05–5.01 (m, 1H), 4.99–4.96 (m, 1H), 4.04 (t, *J* = 8.2 Hz, 1H), 2.87–2.74 (m, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.0, 152.6, 146.4, 136.3, 136.1, 133.5, 129.0, 124.3, 123.8, 117.0, 51.2, 40.3, 34.5, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{30}NO_3$ $[M-H]^+$: 380.2225; found: 380.2218.



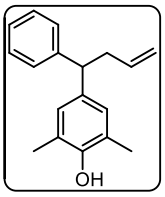
Methyl 4-(1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)but-3-en-1-yl)benzoate (61w): Yellow oil; yield 89% (35.1 mg); R_f = 0.4 (5% EtOAc in hexane); FT-IR 3642, 2954, 2923, 2873, 1723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ =

7.96 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.01 (s, 2H), 5.69 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.07 (s, 1H), 5.05–5.00 (m, 1H), 4.96–4.93 (m, 1H), 3.98 (t, *J* = 7.8 Hz, 1H), 3.89 (s, 3H), 2.79 (t, *J* = 7.0 Hz, 2H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.3, 152.3, 150.6, 136.9, 135.8, 134.4, 129.8, 128.2, 128.0, 124.4, 116.5, 52.1,51.3, 40,4, 34.5, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{35}O_3$ $[M+H]^+$: 395.2587; found: 395.2575.

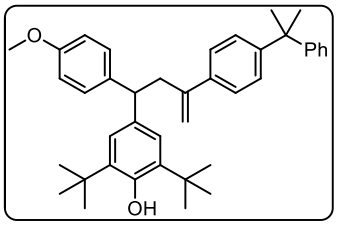
2,6-Diisopropyl-4-(1-phenylbut-3-en-1-yl)phenol (61x): Yellow oil; yield 65% (20 mg); R_f = 0.4 (10% EtOAc in hexane); FT-IR 3584, 2961, 2931, 2869 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29–7.22 (m, 4H), 7.18–7.14 (m,1H), 6.91 (s, 2H), 5.72 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.05–5.00 (m, 1H), 4.95-4.92 (m, 1H), 4.64 (s, 1H), 3.93 (t, *J* = 7.9 Hz, 1H), 3.11 (sept, *J* = 6.8 Hz, 2H), 2.80–2.76 (m, 2H), 1.24 (d, *J* = 2.9 Hz, 6H), 1.22 (d, *J* = 2.8 Hz, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 145.3, 137.4, 136.4, 133.5, 128.4, 128.0, 126.1, 123.0, 116.1, 51.2, 40.7, 27.5, 22.9 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{29}O$ $[M+H]^+$: 309.2219; found: 309.2207.



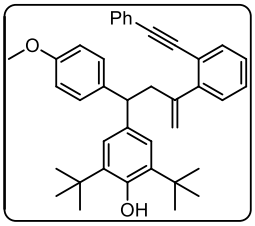
2,6-Dimethyl-4-(1-phenylbut-3-en-1-yl)phenol (61y): Yellow oil; yield 50% (12.6 mg); R_f = 0.2 (5% EtOAc in hexane); FT-IR 3569, 3027, 2923, 2854 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29–7.21 (m, 5H), 7.18–7.14 (m, 1H), 6.84 (s, 2H), 5.71 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.02 (dq, *J* = 17.1, 1.9 Hz, 1H), 4.95–4.92 (m, 1H), 4.47 (s, 1H), 3.89–3.85 (m , 1H), 2.78–2.74 (m, 2H), 2.2 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.6, 145.2, 137.3, 136.3, 128.5, 128.1, 127.9, 126.1, 122.9, 116.2, 50.7, 40.3, 16.2 ppm. HRMS (ESI): *m/z* calcd for $C_{18}H_{19}ONa$ $[M+Na]^+$: 275.1414; found: 275.1405.



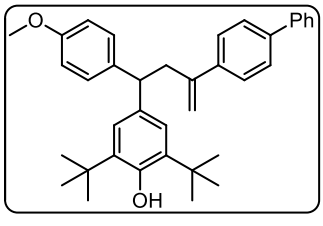
2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)-3-(4-(2-phenylpropan-2-yl)phenyl)but-3-en-1-yl)phenol (63a): Yellow oil; yield 72% (40.3 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3642, 2961, 2915, 2881 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32–7.17 (m, 9H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.94 (s, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.13 (s, 1H), 5.02 (s, 1H), 4.80 (s, 1H), 3.98 (t, *J* = 7.8 Hz, 1H), 3.78 (s, 3H), 3.18 (d, *J* = 7.8 Hz, 2H), 1.71 (s, 6H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 151.9, 150.7, 149.8, 146.5, 138.6, 137.3, 135.6, 135.4, 129.1, 128.1, 126.9, 126.8, 126.1, 125.8, 124.6, 114.2, 113.6, 55.3, 48.7, 42.9, 42.5, 34.5, 30.9, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{40}H_{47}O_2$ $[M-H]^+$: 559.3575; found: 559.3553.



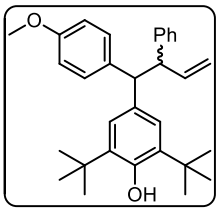
2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)-3-(2-(phenylethynyl)phenyl)but-3-en-1-yl)phenol (63b): Yellow oil; yield 85% (46.1 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3641, 2957, 2914, 2880 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.55–7.52 (m, 1H), 7.40–7.37 (m, 2H), 7.33–7.31 (m, 3H), 7.25–7.18 (m, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.95 (s, 2H), 6.91–6.89 (m, 1H), 6.76 (d, *J* = 8.6 Hz, 2H), 5.16 (s, 1H), 5.07 (s, 1H), 4.99 (s, 1H), 3.86 (t, *J* = 7.8 Hz, 1H), 3.73 (s, 3H), 3.50–3.37 (m, 2H), 1.36 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.7, 151.9, 148.0, 144.9, 137.2, 135.39, 135.36, 132.6, 131.6, 129.2, 129.1, 128.4, 128.2, 128.1, 126.8, 124.6, 123.7, 121.1, 117.4, 113.6, 92.8, 89.3, 55.2, 49.2, 43.7, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{39}H_{41}O_2$ $[M-H]^+$: 541.3106; found: 541.3120.



4-(3-([1,1'-Biphenyl]-4-yl)-1-(4-methoxyphenyl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (63c): Yellow oil; yield 77% (39.9 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3638, 2961, 2923, 2877 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.63–7.61 (m, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.47–7.44 (m, 2H), 7.39–7.33 (m, 3H), 7.11 (d, *J* = 8.6 Hz, 2H), 6.96 (s, 2H), 6.83–6.79 (m, 2H), 5.18 (d, *J* = 1.2 Hz, 1H), 5.02 (s, 1H), 4.86 (s, 1H), 3.96 (t, *J* = 8.0 Hz, 1H), 3.78 (s, 3H), 3.27–3.16 (m, 2H), 1.39 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 152.0, 146.5, 140.9, 140.4, 140.1, 137.3, 135.6, 135.5, 129.1, 128.9, 127.4, 127.1, 127.04, 127.02, 124.5, 114.9, 113.7, 55.3, 48.8, 42.6, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{41}O_2$ $[M-H]^+$: 517.3106; found: 517.3085.

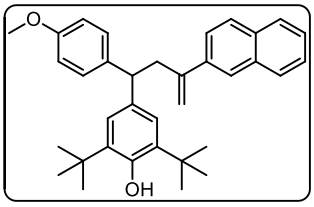


2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)-2-phenylbut-3-en-1-yl)phenol (63d): Yellow oil; yield 79% (34.9 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3642, 2961, 2919, 2873 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.27 (d, *J* = 9.2 Hz, 2H major), 7.18–6.98 (m, 9H major & minor), 6.86 (d, *J* = 8.7 Hz, 2H major), 6.74 (s, 2H major), 6.63 (d, *J* = 8.8 Hz, 1H minor), 6.02–5.88 (m, 1.5H major & minor), 5.01 (s, 0.5H minor), 4.97–4.89 (m, 2.5H major & minor), 4.86–4.81 (m, 0.5H minor), 4.85 (s, 1H major), 4.15–3.93 (m, 3H major & minor), 3.79 (s, 3H major), 3.68 (s, 1.5H minor), 1.42 (s, 9H minor), 1.27 (s, 18H major) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9 (major), 157.4 (minor), 152.0 (minor), 151.6 (major), 143.7 (major), 143.5 (minor), 141.5 (minor), 141.0 (major), 136.5 (minor), 135.9 (major), 135.4 (minor), 135.0 (major), 133.9 (major), 132.4



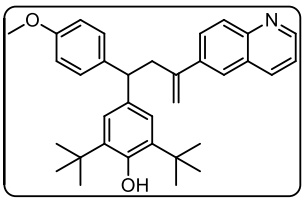
(minor), 129.8 (major), 129.2 (minor), 128.6 (minor) 128.5 (major), 128.2 (minor), 128.1 (major), 126.0 (minor), 125.9 (major), 125.3 (minor), 125.1 (major), 116.0 (major), 115.6 (minor), 113.7 (major), 113.4 (minor), 56.7 (major), 56.5 (minor), 55.8 (major), 55.5 (minor), 55.3 (major), 55.2 (minor), 34.5 (minor), 34.3 (major), 30.5 (minor), 30.3 (major) ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{37}O_2$ $[M-H]^+$: 441.2793; found: 441.2776.

2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)-3-(naphthalen-2-yl)but-3-en-1-yl)phenol (63e):

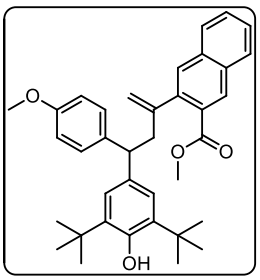


Yellow oil; yield 71% (36.9 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR 3638, 2961, 2873, 3061; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84–7.78 (m, 3H), 7.73 (s, 1H), 7.49–7.44 (m, 3H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.95 (s, 2H), 6.80 (d, *J* = 8.6 Hz), 5.24 (d, *J* = 1.1 Hz, 1H), 5.02 (s, 1H), 4.93 (s,1H), 3.96 (t, *J* = 8.2 Hz, 1H), 3.77 (s, 3H), 3.36–3.23 (m, 2H), 1.38 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 152.0, 146.9, 138.8, 137.2, 135.6, 135.5, 133.5, 132.9, 129.1, 128.3, 127.9, 127.7, 126.2, 125.9, 125.3, 125.2, 124.5, 115.5, 113.7, 55.3, 48.8, 42.8, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{35}H_{39}O_2$ $[M-H]^+$: 491.2949; found: 491.2932.

2,6-Di-*tert*-butyl-4-(1-(4-methoxyphenyl)-3-(quinolin-6-yl)but-3-en-1-yl)phenol (63f):



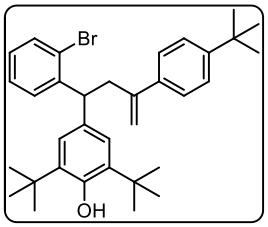
Yellow oil; yield 20% (9.8 mg); R_f = 0.2 (20% EtOAc in hexane); FT-IR 3638, 2961, 2927, 2858 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.89 (d, *J* = 3.0 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 7.70–7.67 (m, 2H), 7.40 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.94 (s, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 5.27 (s, 1H), 5.02 (s, 1H), 5.00 (s, 1H), 3.93 (t, *J* = 7.9 Hz, 1H), 3.77 (s, 3H), 3.35–3.24 (m, 2H), 1.36 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 152.1, 150.2, 147.7, 146.4, 139.7, 137.1, 136.5, 135.6, 135.4, 129.2, 129.0, 128.9, 128.3, 124.9, 124.5, 121.4, 116.4, 113.7, 55.3, 49.0, 42.7, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{40}NO_2$ $[M+H]^+$: 494.3060; found: 494.3042.



Methyl 3-(4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-4-(4-methoxyphenyl)but-1-en-2-yl)-2-naphthoate (63g): Yellow soild; yield 80% (43.8 mg); R_f = 0.2 (10% EtOAc in hexane); M.P. 148-150 °C; FT-IR 3634, 2955, 2873, 2834 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.41 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.56–7.48 (m,

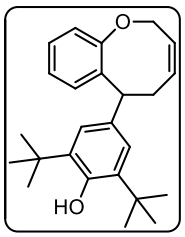
2H), 7.15 (s, 1H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.91 (s, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 5.13 (d, *J* = 1.2 Hz, 1H), 5.00 (d, *J* = 1.7 Hz, 1H), 4.96 (s, 1H), 3.89 (s, 3H), 3.78 (t, *J* = 8.0 Hz, 1H), 3.74 (s, 3H), 3.16 (d, *J* = 8.0 Hz, 2H), 1.34 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.2, 157.8, 151.9, 149.7, 140.4, 137.3, 135.4, 135.2, 134.6, 131.6, 131.4, 129.7, 129.0, 128.8, 128.2, 127.8, 127.4, 126.5, 124.5, 115.5, 113.7, 55.3, 52.3, 50.0, 44.2, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{37}H_{41}O_4$ $[M-H]^+$: 549.3004; found: 549.2984.

4-(1-(2-Bromophenyl)-3-(4-(*tert*-butyl)phenyl)but-3-en-1-yl)-2,6-di-*tert*-butylphenol (63h):



Yellow oil; yield 72% (39.3 mg); R_f = 0.6 (5% EtOAc in hexane); FT-IR 3641, 2961, 2911, 2872.0 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.36–7.29 (m, 3H), 7.26–7.22 (m, 3H), 7.04 (s, 2H), 7.04–6.99 (m, 1H), 5.17 (s, 1H), 5.03 (s, 1H), 4.90 (s, 1H), 4.66 (t, *J* = 7.8 Hz, 1H), 3.27–3.15 (m, 2H), 1.39 (s, 18H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 150.3, 146.4, 144.1, 138.7, 135.4, 133.7, 133.0, 128.9, 127.51, 127.50, 126.1, 125.4, 125.1, 125.0, 114.0, 47.7, 41.3, 34.6, 34.5, 31.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{42}BrO$ $[M-H]^+$: 545.2418; found: 545.2402.

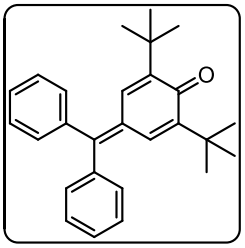
2,6-Di-*tert*-butyl-4-(5,6-dihydro-2H-benzo[b]oxocin-6-yl)phenol (64): The second generation



Grubbs catalyst (9 mg, 0.01 mmol) was added to a solution of **61e** (40 mg, 0.1 mmol) in CH_2Cl_2 (1.5 mL) under inert atmosphere and the resultant mixture was stirred at 40 °C until **61e** was completely consumed (by T.L.C.). The solvent was removed under reduced pressure and the residue was directly loaded on a silica gel column and purified using 0.5-1% ethyl acetate/hexane mixture as an eluent to get the pure product **64**. Yellow oil; yield 54% (19.7 mg); R_f = 0.2 (5% EtOAc in hexane); FT-IR 3638, 2958, 2926, 2873 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.20–7.15 (m, 1H), 7.08–7.05 (m, 2H), 7.07 (s, 2H), 7.03–6.99 (m, 1H), 5.92–5.84 (m, 1H), 5.42–5.38 (m, 1H), 5.05–5.01 (m, 1H), 5.02 (s, 1H), 4.45 (dd, *J* = 15.6, 4.6 Hz, 1H); 4.07 (dd, *J* = 12.3, 5.9 Hz, 1H), 3.56–3.47 (m, 1H), 2.49–2.43 (m, 1H), 1.39 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.0, 152.1, 137.5, 137.4, 135.8, 132.1, 131.9, 127.8, 126.8, 124.8, 124.4, 123.3, 73.5, 52.2, 37.0, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{31}O_2$ $[M-H]^+$: 363.2323; found: 363.2311.

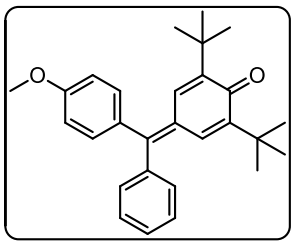
General Procedure of the $B(C_6F_5)_3$-Catalyzed Hydro aromatization of *p*-quinone methides :
p-Quinone methide (0.1 mmol) was added to a mixture of $B(C_6F_5)_3$ (0.05 mmol), Hantzsch ester (0.2 mmol) in 1.5 ml of DCM, and the resultant mixture was stirred at room temperature (27–30 °C) until the *p*-quinone methide completely consumed (by T.L.C). The solvent was removed under reduced pressure and the crude reaction mixture was directly loaded on silica gel column and purified using hexane/EtOAc mixture as an eluent to get the pure diaryl/triarylmethane.

Characterization data for fuchsones:



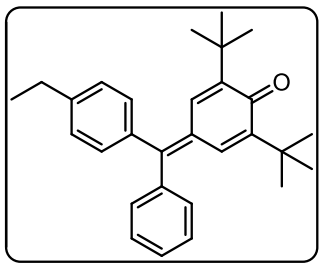
2,6-Di-*tert*-butyl-4-(diphenylmethylene)cyclohexa-2,5-dienone (66aa): Yellow solid; yield 70%; M.P. 184-186 °C; FT-IR: 2952, 2919, 1596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43 – 7.38 (m, 6H), 7.26 – 7.22 (m, 4H), 7.19 (s, 2H), 1.24 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.3, 156.2, 147.6, 140.9, 132.1, 132.05, 129.8, 129.3, 128.1, 35.4, 29.6 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{30}O$ [M+H]-: 371.2376; found: 371.2369.

2,6-Di-*tert*-butyl-4-[(4-methoxyphenyl)(phenyl)methylene]cyclohexa-2,5-dienone



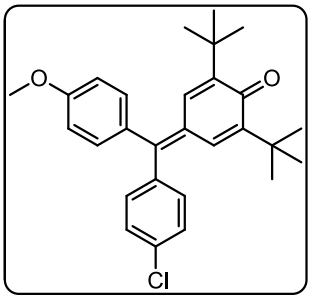
(66ab): Yellow solid; yield 76%; M.P. 206-208 °C; FT-IR: 2998, 2950, 1597, 1248 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.45 – 7.38 (m, 3H), 7.26 – 7.22 (m, 3H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.13 – 7.12 (m, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H), 1.27(s, 9H), 1.23(s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.2, 160.8, 156.4, 147.3, 147.1, 141.2, 134.0, 133.3, 132.4, 132.3, 132.26, 129.3, 129.25, 128.1, 113.6, 55.6, 35.4, 35.37, 29.7, 29.6 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{32}O_2$ [M+H]-: 401.2481; found: 401.2472.

2,6-Di-*tert*-butyl-4-[(4-ethylphenyl)(phenyl)methylene]cyclohexa-2,5-dienone (66ac):

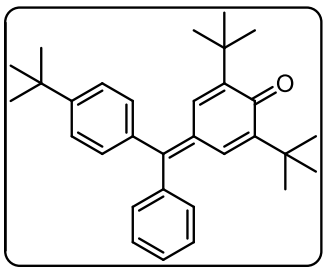


Yellow solid; yield 85%; M.P. 176-178 °C; FT-IR: 2996, 2961, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.44 - 7.37 (m, 3H), 7.26 - 7.22 (m, 5H), 7.16 – 7.14 (m, 3H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.31 - 1.24 (m, 21H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.3, 156.6, 147.4, 147.3, 145.8, 141.1, 138.2, 132.3, 132.3, 132.1, 129.6, 129.2, 128.0, 127.6, 126.2, 35.41, 35.4, 29.7, 29.6, 28.8, 15.3 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{34}O$ [M+H]-: 399.2689; found: 399.2675.

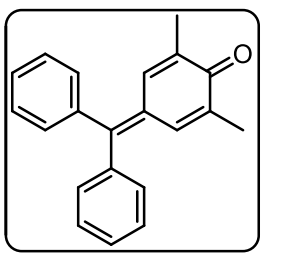
2,6-Di-*tert*-butyl-4-[(4-chlorophenyl)(4-methoxyphenyl)methylene]cyclohexa-2,5dienone (66ad): Yellow solid; yield 74%; M.P. 191-193 °C; FT-IR: 2989, 2956, 1599 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, J = 8.56 Hz, 2H), 7.21 (d, J = 2.6 Hz, 1H), 7.19 – 7.13 (m, 4H), 7.08 (d J = 2.6 Hz, 1H), 6.93 (d, J = 8.9 Hz, 2H), 3.88 (s, 3H), 1.25 (d, J = 6.6 Hz, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.2, 160.9, 154.6, 147.5, 147.455, 139.6, 135.5, 134.0, 133.5, 132.9, 132.2, 131.8, 129.5, 128.4, 113.7, 65.6, 35.4, 35.4, 29.7, 29.6 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{31}ClO_2$ [M+H]-: 435.2092; found: 435.2080**.**



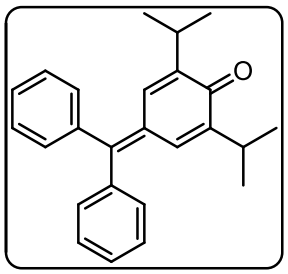
2,6-Di-*tert*-butyl-4-[(4-(*tert*-butyl)phenyl)(phenyl)methylene]cyclohexa-2,5-dienone (66ae): Yellow solid; yield 88%; M.P. 196-198 °C; FT-IR: 2951, 2901, 1599 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 - 7.38 (m, 5H), 7.26 – 7.23 (m, 3H), 7.18 – 7.14 (m, 3H), 1.36 (s, 9H), 1.26 (s, 9H), 1.23 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.3, 156.6, 152.7, 147.4, 147.2, 141.2, 137.9, 132.3, 132.28, 132.1, 132.07, 129.6, 129.2, 128.0, 125.0, 35.4, 35.38, 35.0, 31.4, 29.7, 29.6 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{38}O$ [M-H]-: 425.2844; found: 425.2846.



4-(Diphenylmethylene)-2,6-dimethylcyclohexa-2,5-dienone (66af): Yellow solid; yield 90%; M.P. 196-198 °C FT-IR: 3034, 2968, 1601 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 - 7.39 (m, 6H), 7.24 – 7.20 (m, 4H), 7.15 (s, 2H), 2.01 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 187.4, 156.8, 144.5, 140.8, 135.9, 135.7, 132.2, 129.5, 128.2, 16.9 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{18}O$ [M+H]-: 287.1437; found: 287.1429.

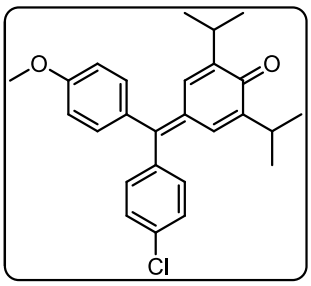


4-(Diphenylmethylene)-2,6-diisopropylcyclohexa-2,5-dienone (66ag): Yellow solid; yield 90%; M.P. 176-178°C; FT-IR: 2961, 2874, 1598 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 -7.39 (m, 6H), 7.26 – 7.22 (m, 4H), 7.12 (s, 2H), 3.18 (sept, J = 6.88 Hz, 2H), 1.05 (d, J = 6.88 Hz, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 185.2, 156.8, 145.7, 140.8, 140.3, 132.3, 131.9, 130.1, 129.5, 128.6, 128.1,



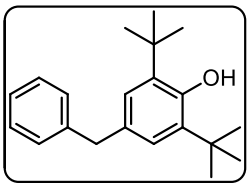
128.0, 127.2, 26.9, 22.1 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{26}O$ [M+H]-: 343.2063; found: 343.2055.

4-[(4-Chlorophenyl)(4-methoxyphenyl)methylene]-2,6-diisopropylcyclohexa-2,5-dienone (66ah): Yellow solid; yield 96%; M.P. 189-191 °C; FT-IR: 2958, 2901, 1597, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ = 7.40 (d, *J* = 8.52 Hz, 2H), 7.19 – 7.13 (m, 5H), 7.00 (d, *J* = 2.04 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H), 3.19 (sept., *J* = 6.56 Hz, 2H), 1.06 (t, *J* = 7Hz, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$); δ = 185.0, 161.1, 155.2, 145.6, 145.5, 139.5, 135.8, 134.3, 133.7, 132.8, 132.0, 131.6, 129.8, 128.5, 113.8, 55.6, 26.9, 26.9, 22.2, 22.2 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{27}ClO_2$ [M+H]-: 407.1779; found: 407.1770.

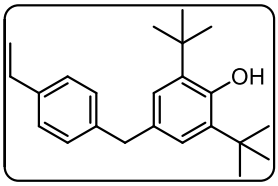


Characterization of products:

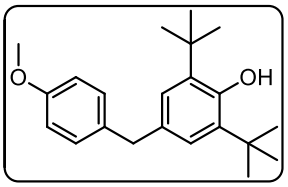
4-Benzyl-2,6-di-*tert*-butylphenol (68a): Colourless oil; yield 95% (28 mg); R_f = 0.6 (1% EtOAc in hexane); FT-IR (ATR) 3643, 2958, 2914 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.33 – 7.29 (m, 2H), 7.24 – 7.19 (m, 3H), 7.02 (s, 2H), 5.09 (s, 1H), 3.93 (s, 2H), 1.43 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 141.9, 135.9, 131.7, 129.0, 128.5, 125.9, 125.6, 41.9, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{28}O$ [M-H]-: 295.2062; found: 295.2068.



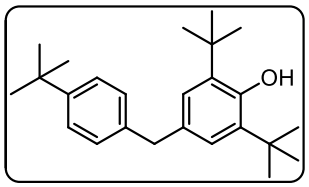
2,6-Di-*tert*-butyl-4-(4-ethylbenzyl)phenol (68b): Colourless oil; yield 98% (32 mg); R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR) 3642, 2959, 2911 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.13 (s, 4H), 7.01 (s, 2H), 5.07 (s, 1H), 3.88 (s, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.42 (s, 18H), 1.23 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 141.8, 139.2, 135.9, 131.9, 128.8, 128.0, 125.6, 41.6, 34.4, 30.4, 28.6, 15.8 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{32}O$ [M+H]-: 325.2531; found: 325.2541.



2,6-Di-*tert*-butyl-4-(4-methoxybenzyl)phenol (68c): Colourless solid; yield 96% (32 mg); M.P. 148–150 °C; R_f = 0.4 (1% EtOAc in hexane); FT-IR (ATR) 3618, 2999, 2952, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.12 (d, *J* = 8.6 Hz, 2H), 6.98 (s, 2H), 6.84 (d, *J* = 8.6 Hz, 2H),

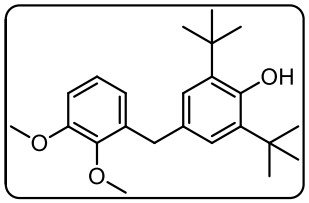


5.05 (s, 1H), 3.85 (s, 2H), 3.79 (s, 3H), 1.41(s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 152.1, 135.9, 134.0, 132.1, 129.9, 125.4, 113.9, 55.4, 41.0, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{30}O_2$ [M-H]-: 325.2168; found: 325.2158.



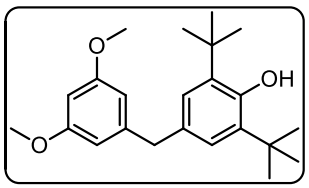
2,6-Di-*tert*-butyl-4-[4-(*tert*-butyl)benzyl]phenol (68d): Yellow solid; yield 94% (33 mg); M.P. 88–90 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3643, 2955, 2907 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 (d, *J* = 8.4Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 7.04 (s, 2H), 5.08 (s, 1H), 3.9 (s, 2H), 1.44 (s, 18H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 148.7, 139.0, 135.9, 131.7, 128.4, 125.7, 125.4, 41.4, 34.5, 34.4, 31.6, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{36}O$ [M-H]-: 351.2688; found: 351.2694.

2,6-Di-*tert*-butyl-4-(2,3-dimethoxybenzyl)phenol (68e): Colourless solid; yield 89% (31



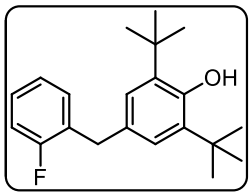
mg); M.P. 56–58 °C; R_f = 0.5 (5% EtOAc in hexane); FT-IR (ATR): 3639, 2954, 2910, 1230 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.05 (s, 2H), 6.99 (t, *J* = 7.9 Hz, 1H), 6.80 (dd, *J* = 1.44, 8.2 Hz, 1H), 6.76 (dd, *J* = 1.48, 7.7 Hz, 1H), 5.05 (s, 1H), 3.93 (s, 2H), 3.88 (s, 3H), 3.77 (s, 3H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.9, 152.0, 147.1, 136.0, 135.7, 131.6, 125.7, 123.9, 122.5, 110.4, 60.6, 55.8, 35.7, 34.4, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{32}O_3$ [M-H]-: 355.2273; found: 355.2268.

2,6-Di-*tert*-butyl-4-(3,5-dimethoxybenzyl)phenol (68f): Colourless oil; yield 88% (29



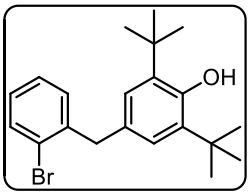
mg); R_f = 0.3 (1% EtOAc in hexane); FT-IR (ATR): 3636, 2998, 2953, 1149 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.00 (s, 2H), 6.37 (d, *J* = 2.1 Hz, 2H), 6.31 (t, *J* = 2.2 Hz, 1H), 5.07 (s, 1H), 3.84 (s, 2H), 3.77 (s, 6H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.8, 152.2, 144.4, 135.9, 131.2, 125.6, 107.1, 97.9, 55.4, 42.2, 34.4, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{32}O_3$ [M-H]-: 355.2273; found: 355.2279.

2,6-Di-*tert*-butyl-4-(2-fluorobenzyl)phenol (68g): Colourless oil; yield 70% (22 mg); R_f



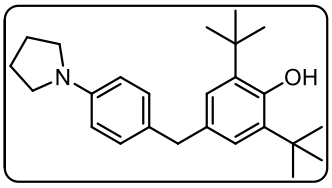
= 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3639, 2954, 2912 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.20 – 7.13 (m, 2H), 7.07 – 7.01 (m, 2H), 7.03 (s, 2H), 5.08 (s, 1H), 3.91 (s, 2H), 1.41 (s, 18H) ppm. ^{13}C

NMR (100 MHz, $CDCl_3$) δ = 161.1 (d, J_{C-F} = 243.4 Hz), 152.3, 136.0, 131.1 (d, J_{C-F} = 4.7 Hz), 130.4, 129.0 (d J_{C-F} = 15.9 Hz), 127.8 (d J_{C-F} = 8.0 Hz), 125.5, 124.1 (d, J_{C-F} = 3.6 Hz), 115.3 (d, J_{C-F} = 22.1 Hz), 34.7 (d, J_{C-F} = 2.8 Hz), 34.4, 30.4 ppm. ^{19}F NMR (376 MHz, CDCl3) δ = -118.0 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{27}FO$ [M-H]-: 313.1968; found: 313.1957.

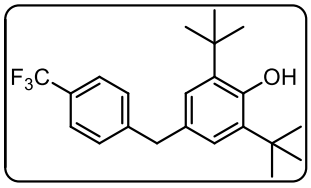


4-(2-Bromobenzyl)-2,6-di-*tert*-butylphenol (68h): Colourless solid; yield 50% (19 mg); M.P. 109–111 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3639, 2958, 2910 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.22 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.08 – 7.04 (m, 1H), 7.04 (s, 2H), 5.09 (s, 1H), 4.02 (s, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.3, 141.4, 136.0, 132.8, 131.0, 130.0, 127.7, 127.6, 125.8, 124.9, 41.7, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{27}BrO$ [M-H]-: 373.1167; found: 373.1154.

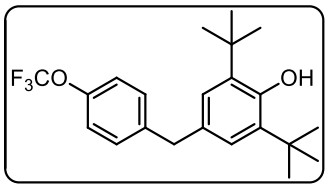
2,6-Di-*tert*-butyl-4-[4-(pyrrolidin-1-yl)benzyl]phenol (68i): Brown solid; yield 89% (18 mg); M.P. 108–110 °C; R_f = 0.3 (1% EtOAc in hexane); FT-IR (ATR): 3638, 2954, 2871 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.06 (d, *J* = 8.6 Hz, 2H), 7.01 (s, 2H), 6.52 (d, *J* = 8.6 Hz, 2H), 5.03 (s, 1H), 3.81 (s, 2H), 3.28 – 3.25 (m, 4H), 2.00 – 1.97 (m, 4H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.9, 146.5, 135.7, 132.8, 129.6, 128.8, 125.4, 111.8, 47.9, 41.0, 34.4, 30.5, 25.6 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{35}NO$ [M+H]-: 366.2798; found: 366.2789.



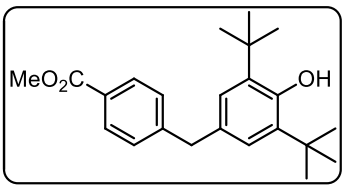
2,6-Di-*tert*-butyl-4-[4-(trifluoromethyl)benzyl]phenol (68j): Colourless solid; yield 72% (26 mg); M.P. 111–113 °C; R_f = 0.5 (1 % EtOAc in hexane); FT-IR (ATR): 3617, 2953, 2920 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.97 (s, 2H), 5.11 (s, 1H), 3.95 (s, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.5, 146.1 (J_{C-F} = 1.1 Hz), 136.2, 130.6, 129.2, 128.3 (q, J_{C-F} = 32 Hz), 125.6, 125.4 (q, J_{C-F} = 3.8 Hz), 124.5 (q, J_{C-F} = 270 Hz), 41.8, 34.5, 30.4 ppm. ^{19}F NMR (376 MHz, CDCl3) δ = -62.2 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{27}F_3O$ [M-H]-: 363.1926; found: 363.1929.



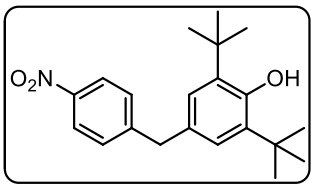
2,6-Di-*tert*-butyl-4-[4-(trifluoromethoxy)benzyl]phenol (68k): Colourless oil; yield 60% (22 mg); R_f = 0.1 (1% EtOAc in hexane); FT-IR (ATR): 3642, 2957, 2912, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.21 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.3 Hz, 2H), 6.97 (s, 2H), 5.10 (s, 1H), 3.90 (s, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.4, 147.5 (q, J_{C-F} = 1.7 Hz), 140.7, 136.1, 131.0, 130.1, 125.5, 121.1, 120.7 (q, J_{C-F} = 255 Hz), 41.2, 34.5, 30.4 ppm. ^{19}F NMR (376 MHz, CDCl3) δ = -57.9 ppm. HRMS (ESI): *m/z* calcd for $C_{22}H_{27}F_3O_2$ [M-H]-: 379.1885; found: 379.1884.



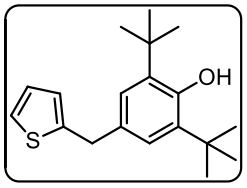
Methyl 4-(3,5-di-*tert*-butyl-4-hydroxybenzyl)benzoate (68l): Colourless solid; yield 45% (16 mg); M.P. 120–122 °C; R_f = 0.5 (5% EtOAc in hexane); FT-IR (ATR): 3642, 2957, 2911, 1721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.96 (d, J = 8.4 Hz, 2H), 7.28 – 7.26 (m, 2H), 6.96 (s, 2H), 5.10 (s, 1H), 3.95 (s, 2H), 3.90 (s, 3H), 1.40 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.4, 152.4, 147.4, 136.1, 130.8, 129.9, 129.0, 128.0, 125.6, 52.1, 42.0, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{23}H_{30}O_3$ [M-H]-: 353.2117; found: 353.2112.



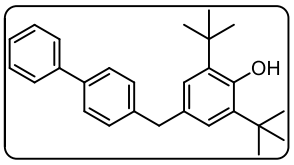
2,6-Di-*tert*-butyl-4-(4-nitrobenzyl)phenol (68m): Colourless solid; yield 50% (15 mg); M.P. 108–110 °C; R_f = 0.5 (5% EtOAc in hexane); FT-IR (ATR): 3618, 3008, 2957, 2916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.15 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 8.8 Hz, 2H), 6.95 (s, 2H), 5.14 (s, 1H), 3.99 (s, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.7, 149.9, 146.5, 136.4, 129.9, 129.7, 125.6, 123.8, 41.8, 34.5, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{27}NO_3$ [M-H]-: 340.1913; found: 340.1918.



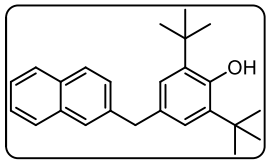
2,6-Di-*tert*-butyl-4-(thiophen-2-ylmethyl)phenol (68n): Yellow oil; yield 96% (29 mg); R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR) 3639, 2954, 2910, 2871 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.15 (dd, J = 5.1, 1.2 Hz, 1H), 7.08 (s, 2H), 6.96 – 6.93 (dd, J = 5.1, 3.4 Hz, 1H), 6.82 – 6.80 (m, 1H), 5.12 (s, 1H), 4.10 (s, 2H), 1.45 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.4, 145.2, 136.0, 131.0, 126.9, 125.3, 124.9, 123.7, 36.0, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}OS$ [M-H]-: 301.1626; found: 301.1629.



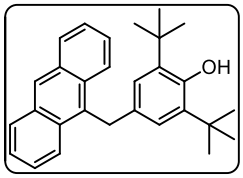
4-[(1,1'-Biphenyl)-4-ylmethyl]-2,6-di-*tert*-butylphenol (68o): Yellow solid; yield 83% (15 mg); M.P. 100 – 102 °C; R_f = 0.4 (1% EtOAc in hexane); FT-IR (ATR): 3631, 3005, 2954, 2909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.62 – 7.60 (m, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.36 – 7.32 (m, 1H), 7.30 (d, J = 8.1 Hz, 2H), 7.05 (s, 2H), 5.10 (s, 1H), 3.96 (s, 2H), 1.44 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 141.2, 141.1, 138.9, 136.0, 131.5, 129.3, 128.8, 127.2, 127.14, 127.12, 125.6, 41.6, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{32}O$ [M-H]-: 371.2375; found: 371.2369.



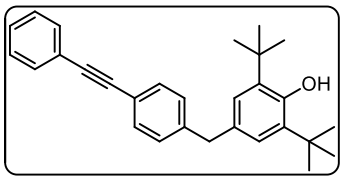
2,6-Di-*tert*-butyl-4-(naphthalen-2-ylmethyl)phenol (68p): Colourless solid; Yield 86% (29 mg); M.P. 93 – 95 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3622, 2952, 2913 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.13 – 8.09 (m, 1H), 7.89 – 7.85 (m, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.41 (dd, J = 8.1, 7.1 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.04 (s, 2H), 5.06 (s, 1H), 4.38 (s, 2H), 1.39 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 137.8, 135.9, 133.9, 132.3, 130.9, 128.7, 126.9, 126.89, 125.9, 125.7, 125.69, 125.6, 124.4, 38.7, 34.4, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{30}O$ [M-H]-: 345.2219; found: 345.2228.



4-(Anthracen-9-ylmethyl)-2,6-di-*tert*-butylphenol (68q): Yellow solid; yield 73% (22 mg); M.P. 152 – 154 °C; R_f = 0.3 (1% EtOAc in hexane); IR (cm^{-1}): 3632, 2955, 2911; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.41 (s, 1H), 8.33 – 8.29 (m, 2H), 8.03 – 8.00 (m, 2H), 7.50 – 7.43 (m, 4H), 6.99 (s, 2H), 4.99 (s, 1H), 4.91 (s, 2H), 1.28 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 135.8, 133.0, 131.8, 131.3, 130.6, 129.1, 126.3, 125.7, 125.3, 124.9, 124.89, 34.4, 33.4, 30.3 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{32}O$ [M+H]-: 397.2531; found: 397.2518.

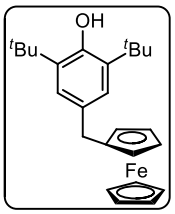


2,6-Di-*tert*-butyl-4-[4-(phenylethynyl)benzyl]phenol (68r): Colourless solid; yield 97% (38 mg); M.P. 139–141 °C; R_f = 0.3 (1% EtOAc in hexane); FT-IR (ATR): 3630, 3009, 2954, 2910, 2360 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.54 – 7.50 (m, 2H), 7.46 (d, J = 8.2 Hz, 2H), 7.37 – 7.31 (m, 3H), 7.18 (d, J = 8.4 Hz, 2H), 6.97 (s, 2H), 5.09 (s, 1H), 3.91 (s, 2H), 1.41 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.3, 142.4, 136.0, 131.8, 131.7, 131.2, 129.1, 128.5, 128.2, 125.6, 123.6, 120.8, 89.7, 89.0,



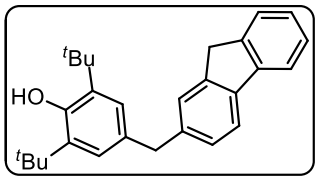
41.9, 34.5, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{32}O$ [M-H]-: 395.2375; found: 395.2385.

[(3,5-Di-*tert*-butyl-4-hydroxybenzyl)cyclopentadienyl] cyclopentadienyliron (68s):



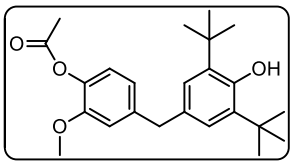
Brown solid; yield 97% (39 mg); M.P. 129–131 °C; R_f = 0.4 (1% EtOAc in hexane); FT-IR (ATR): 3620, 2951, 2908, 2871 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.00 (s, 2H), 5.05 (s, 1H), 4.11 (s, 5H), 4.08 – 4.07 (m, 4H), 3.59 (s, 2H), 1.43 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 135.7, 132.2, 125.2, 89.1, 68.7(2C), 67.5, 35.9, 34.4, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{32}FeO$ [M+H]-: 405.1881; found: 405.1880.

4-[(9H-Fluoren-2-yl)methyl]-2,6-di-*tert*-butylphenol (68t): Yellow solid; yield 86% (33



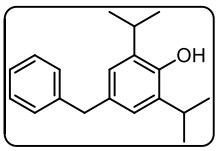
mg); M.P. 154–156 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3635, 2958, 2909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.29 – 7.25 (m, 1H), 7.24 – 7.22 (m, 1H), 7.03 (s, 2H), 5.08 (s, 1H), 3.98 (s, 2H), 3.87 (s, 2H), 1.42 (s, 18H) ppm. ^{13}C NMR (100 MHz,$CDCl_3$) δ = 152.2, 143.7, 143.4, 141.9, 140.6, 139.7, 135.9, 132.0, 127.7, 126.8, 126.4, 125.7, 125.6, 125.1, 119.8, 119.75, 42.1, 37.0, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{32}O$ [M-H]-: 383.2375; found: 383.2379.

4-(3,5-Di-*tert*-butyl-4-hydroxybenzyl)-2-methoxyphenyl acetate (68u): Colourless



solid; yield 95% (36 mg); M.P. 88–90 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3634, 2954, 2910, 1762, 1195 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.01 (s, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 1.8 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.9 Hz, 1H), 5.1 (s, 1H), 3.90 (s, 2H), 3.80 (s, 3H), 2.32 (s, 3H), 1.43 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.4, 152.3, 150.8, 140.9, 137.9, 136.0, 131.1, 125.6, 122.5, 121.0, 113.1, 55.9, 41.7, 34.4, 30.4, 20.8 ppm. HRMS (ESI): *m/z* calcd for $C_{24}H_{32}O_4$ [M-H]-: 383.2223; found: 383.2229.

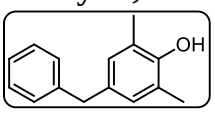
4-Benzyl-2,6-diisopropylphenol (68v): Yellow oil; yield 95% (22 mg); R_f = 0.5 (5%



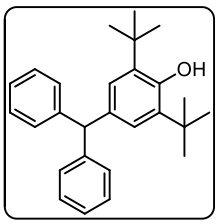
EtOAc in hexane); FT-IR (ATR): 3576, 2962, 2914 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32 – 7.26 (m, 2H), 7.21 – 7.18 (m, 3H), 6.89 (s, 2H), 4.68 (s, 1H), 3.93 (s, 2H), 3.13 (septet, *J* = 6.8 Hz, 2H), 1.25 (d, *J* =

6.9 Hz, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 142.0, 133.7, 132.9, 128.9, 128.5, 125.9, 124.2, 41.8, 27.4, 22.9 ppm. HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O$ [M+H]-: 269.1905; found: 269.1911.

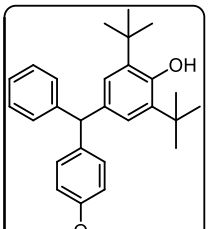
4-Benzyl-2,6-dimethylphenol (68w): Yellow oil; yield 60% (6 mg); R_f = 0.5 (5% EtOAc in hexane); FT-IR (ATR): 3471, 2967, 2919 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.26 (m, 2H), 7.20 – 7.17 (m, 3H), 6.80 (s, 2H), 4.49 (s, 1H), 3.85 (s, 2H), 2.20 (s, 6H) ppm. ^{13}C NMR (100 MHz,$CDCl_3$) δ = 150.6, 141.9, 132.9, 129.2, 128.9, 128.5, 126.0, 123.1, 41.2, 16.1 ppm.



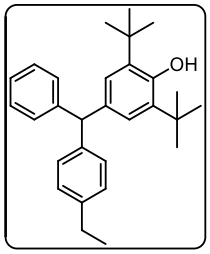
4-Benzhydryl-2,6-di-*tert*-butylphenol (68aa): Colourless solid; yield 90% (14 mg); M.P. 140–142 °C; R_f = 0.4 (1% EtOAc in hexane); FT-IR (ATR): 3579, 3021, 2952 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.26 (m, 4H), 7.22 – 7.17 (m, 2H), 7.14 – 7.11 (m, 4H), 6.91 (s, 2H), 5.45 (s, 1H), 5.09 (s, 1H), 1.36 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 144.9, 135.5, 134.2, 129.5, 128.2, 126.2, 126.1, 56.9, 34.5, 30.1 ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{32}O$ [M-H]-: 371.2375; found: 371.2380.



2,6-Di-*tert*-butyl-4-[(4-methoxyphenyl)(phenyl)methyl]phenol (68ab): Yellow solid; yield 99% (39 mg); M.P. 105–108 °C; R_f = 0.3 (1% EtOAc in hexane); FT-IR (ATR): 3637, 2998, 2954, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 – 7.26 (m, 2H), 7.22 – 7.18 (m, 1H), 7.15 – 7.13 (m, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.93 (s, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.42 (s, 1H), 5.1 (s 1H), 3.80 (s, 3H), 1.39 (s, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 152.1, 145.3, 137.2, 135.5, 134.6, 130.4, 129.4, 128.2, 126.1, 126.06, 113.6, 56.1, 55.3, 34.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{34}O_2$ [M-H]-: 401.2481; found: 401.2470.

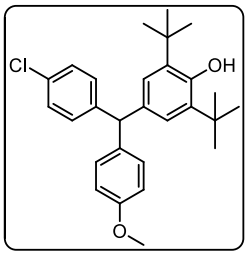


2,6-Di-*tert*-butyl-4-[(4-ethylphenyl)(phenyl)methyl]phenol (68ac): Colourless solid; yield 99% (40 mg); M.P. 94–96 °C; R_f = 0.4 (1% EtOAc in hexane); FT-IR (ATR): 3640, 3001, 2958 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 – 7.26 (m, 2H), 7.21 – 7.17 (m, 1H), 7.14 – 7.10 (m, 4H), 7.05 – 7.03 (m, 2H), 6.93 (s, 2H), 5.42 (s, 1H), 5.08 (s, 1H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.38 (s, 18 H), 1.23 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 145.2, 142.2, 141.9, 135.5, 134.4, 129.5, 129.4, 128.2, 127.7,



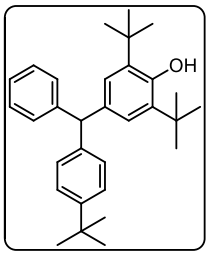
126.2, 126.0, 56.6, 34.5, 30.5, 28.5, 15.7 ppm. HRMS (ESI): *m/z* calcd for $C_{29}H_{36}O$ [M-H]-: 399.2688; found: 399.2683.

2,6-Di-*tert*-butyl-4-[(4-chlorophenyl)(4-methoxyphenyl)methyl]phenol (68ad):



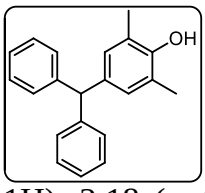
Yellow oil; yied 99% (46 mg); R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR): 3635, 3002, 2958, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.89 (s, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.38 (s, 1H), 5.12 (s, 1H), 3.80 (s, 3H), 1.38 (s. 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 152.3, 143.9, 136.6, 135.7, 134.1, 131.8, 130.8, 130.3, 128.3, 126.0, 113.7, 55.5, 55.3, 34.5, 30.4 ppm. HRMS (ESI): *m/z* calcd for $C_{28}H_{33}ClO_2$ [M-H]-: 435.2091; found: 435.2093.

2,6-Di-*tert*-butyl-4-[(4-*tert*-butyl-phenyl)(phenyl)methyl]phenol (68ae): Yellow solid; yield 99% (43 mg); M.P. 158–160 °C; R_f = 0.5 (1% EtOAc in hexane); FT-IR (ATR):



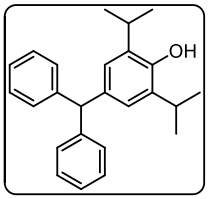
3641, 2956, 2904 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.25 (m, 4H), 7.20 – 7.16 (m, 1H), 7.14 – 7.12 (m, 2H), 7.04 (d, *J* = 8.2 Hz, 2H), 6.92 (s, 2H), 5.40 (s, 1H), 5.07 (s, 1H), 1.36 (s, 18H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$); δ = 152.1, 148.8, 145.3, 141.8, 135.5, 134.4, 129.5, 129.0, 128.2, 126.2, 126.0, 125.1, 56.6, 34.5, 34.47, 31.5, 30.5 ppm. HRMS (ESI): *m/z* calcd for $C_{31}H_{40}O$ [M-H]-: 427.3001; found: 427.3013.

4-Benzhydryl-2,6-dimethylphenol (68af): Light yellow solid; yield 99% (29 mg); M.P.



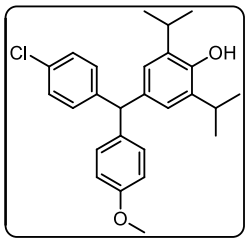
136–138 °C; R_f = 0.2 (5% EtOAc in hexane); FT-IR (ATR): 3573, 3025, 2958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.26 (m, 4H), 7.22 – 7.18 (m, 2H), 7.12 – 7.10 (m, 4H), 6.72 (s, 2H), 5.42 (s, 1H), 4.50 (s, 1H), 2.18 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.7, 144.5, 135.6, 129.7, 129.5, 128.4, 126.3, 122.9, 56.2, 16.2 ppm. HRMS (ESI): *m/z* calcd for $C_{21}H_{20}O$ [M-H]-: 287.1436; found: 287.1428.

4-Benzhydryl-2,6-diisopropylphenol (68ag): Light yellow solid; 96% (26 mg); R_f = 0.3



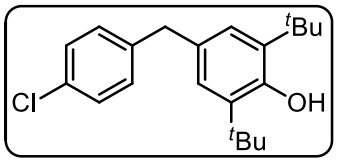
(5% EtOAc in hexane); FT-IR (ATR): 3586, 2962, 2870 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.26 (m, 4H), 7.22 – 7.19 (m, 2H), 7.14 – 7.12 (m, 4H), 6.81 (s, 2H), 5.49 (s, 1H), 4.70 (s, 1H), 3.1 (septet, *J* = 6.9 Hz, 2H), 1.19 (d, *J* = 6.9 Hz, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ

= 148.5, 144.8, 135.7, 133.4, 129.5, 128.3, 126.2, 124.7, 56.8, 27.5, 22.8 ppm. HRMS (ESI): *m/z* calcd for $C_{25}H_{28}O$ [M-H]-: 343.2062; found: 343.2049.



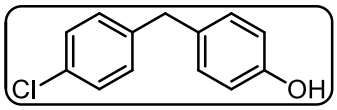
4-[(4-Chlorophenyl)(4-methoxyphenyl)methyl]-2,6-diisopropylphenol (68ah): Yellow oil; yield 88% (36 mg); R_f = 0.2 (5% EtOAc in hexane); FT-IR (ATR): 3497, 2962, 2902, 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.23 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.75 (s, 2H), 5.38 (s, 1H), 4.71 (s, 1H), 3.80 (s, 3H), 3.10 (septet, *J* = 6.9 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 148.6, 143.8, 136.4, 135.5, 133.5, 131.8, 130.8, 130.3, 128.4, 124.5, 113.7, 55.4, 55.3, 27.4, 22.8 ppm. HRMS (ESI): *m/z* calcd for $C_{26}H_{29}ClO_2$ [M+H]-: 409.1934; found: 409.1940.

2,6-Di-*tert*-butyl-4-(4-chlorobenzyl)phenol (68z): White solid; yield 90% (150 mg);



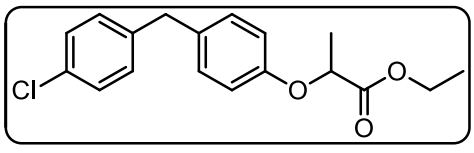
M.P. 108-110 °C; R_f = 0.6 (3% EtOAc in hexane); FT-IR (ATR): 3634, 2961, 1434, 1237 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.27 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.98 (s, 2H), 5.11 (s, 1H), 3.89 (s, 2H), 1.44 (s, 18H) ppm. ^{13}C NMR (10 MHz, $CDCl_3$) δ = 152.3, 140.4, 136.1, 131.7, 131.2, 130.3, 128.6, 125.5, 41.3, 34.4, 30.4 ppm.

4-(4-Chlorobenzyl)phenol (71): White solid; yield 95% (60 mg); R_f = 0.3 (10% EtOAc



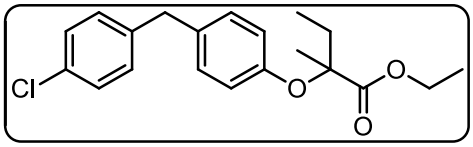
in hexane); M.P. 91-93 °C; FT-IR (ATR): 3541, 1613, 1513, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.27 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 2H), 5.57 (s, 1H), 3.89 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 140.1, 133.0, 131.8, 130.2, 130.1, 128.6, 115.5, 40.4 ppm.

Ethyl 2-[4-(4-chlorobenzyl)phenoxy]propanoate (73): Yellow oil; yield 82% (24 mg);



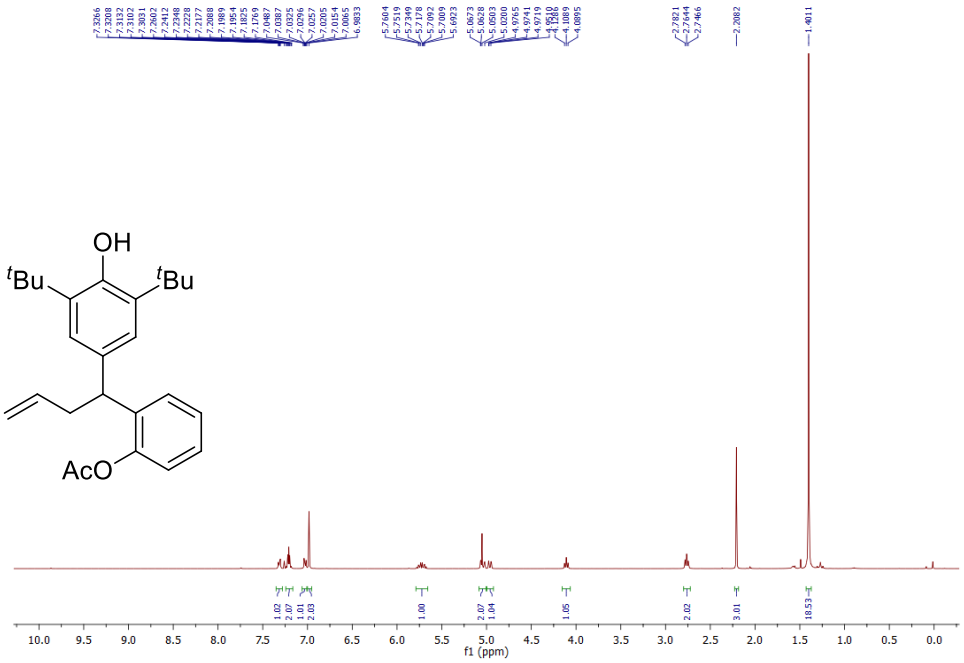
R_f = 0.5(10% EtOAc in hexane); FT-IR (ATR): 2987, 1754, 1510, 1241 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.24 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 4.70 (q, *J* = 6.8 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.4, 156.2, 139.9, 133.7, 131.9, 130.3, 130.0, 128.6, 115.3, 72.8, 61.4, 40.4, 18.7, 14.3 ppm.

Ethyl 2-[4-(4-chlorobenzyl)phenoxy]-2-methylbutanoate (74): Yellow oil; yield 70% (23 mg);

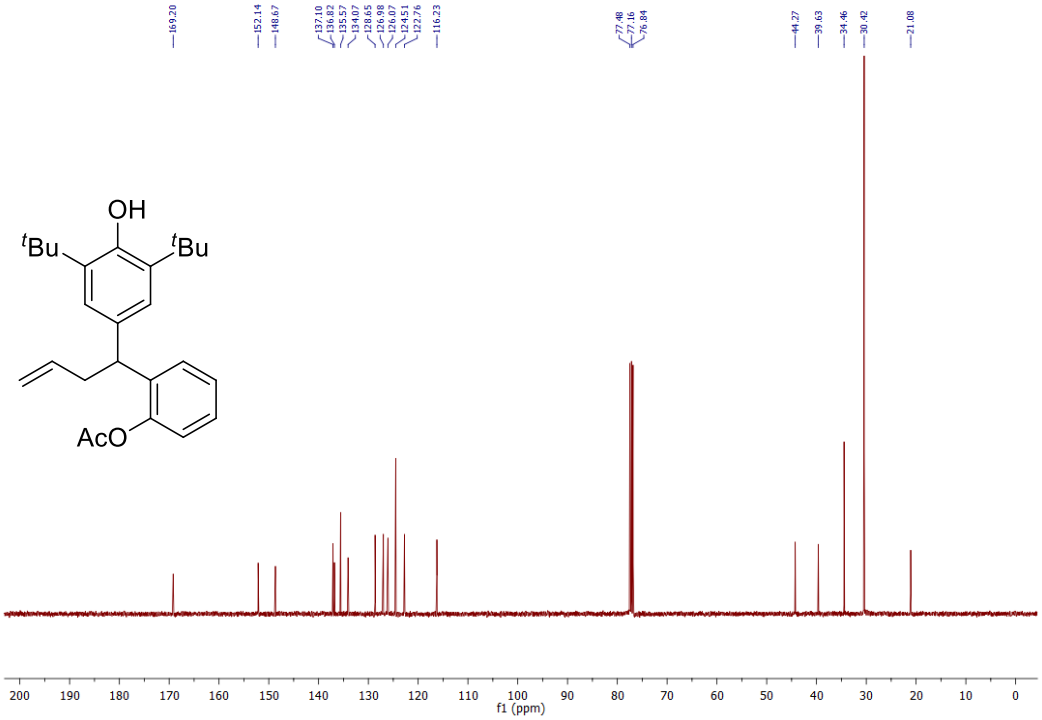


R_f = 0.5(10% EtOAc in hexane); FT-IR (ATR): 2980, 1732, 1508, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.24 (d, J = 7.7 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 7.01 (d, J = 8.1 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 4.24 (q, J = 7.1 Hz, 2H), 3.87 (s, 2H), 2.07 – 1.89 (m, 2H), 1.48 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.2, 154.0, 139.9, 134.2, 131.9, 130.3, 129.6, 128.6, 119.4, 82.0, 61.4, 40.5, 32.7, 20.9, 14.3, 8.0 ppm.

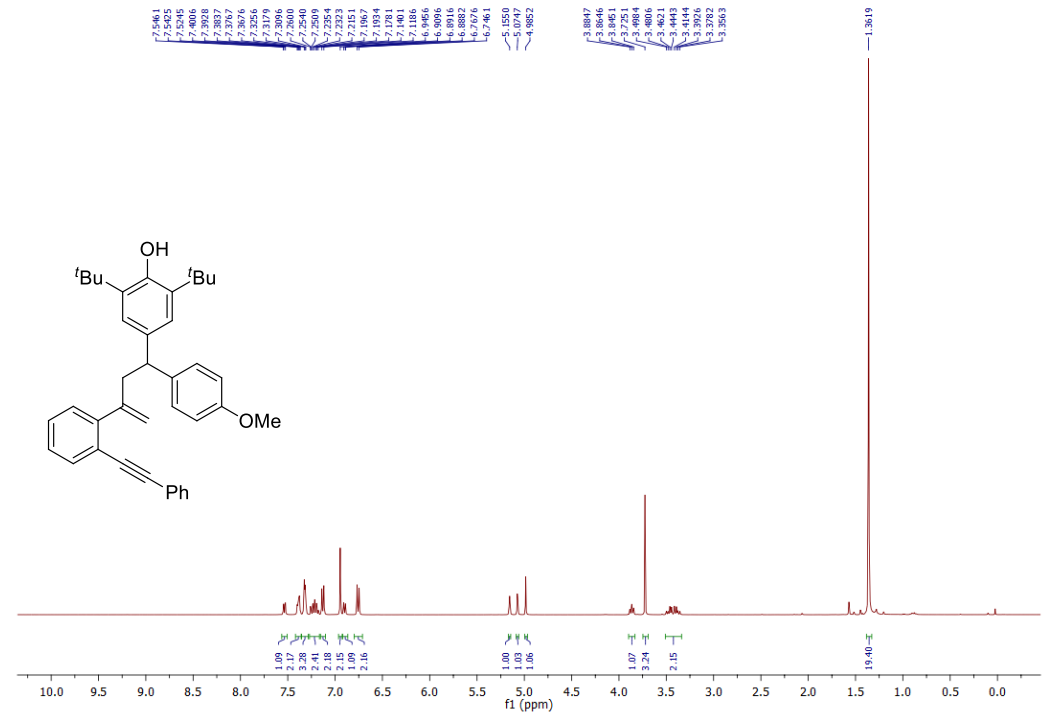
^{1}H NMR Spectrum of **61k**



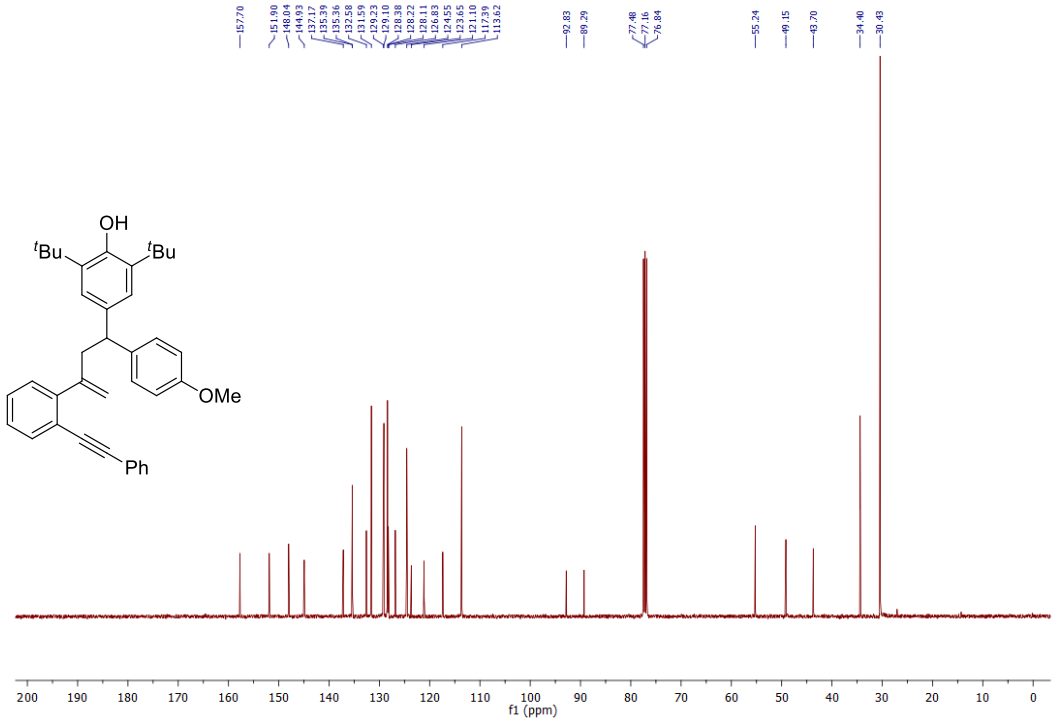
^{13}C NMR Spectrum of **61k**



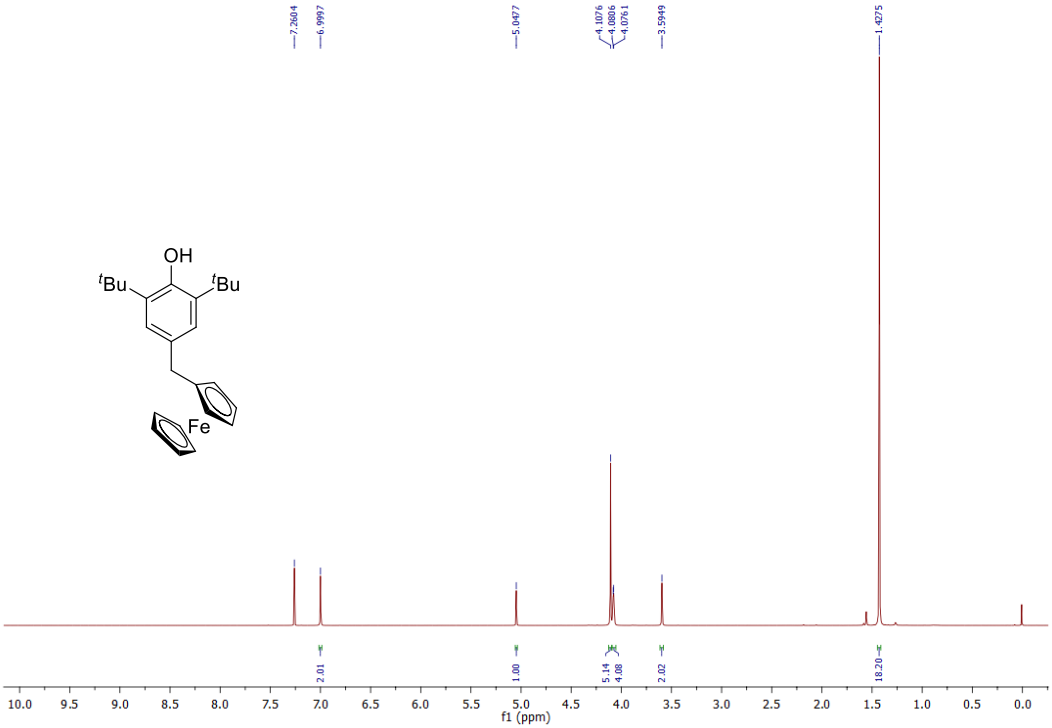
^{1}H NMR Spectrum of **63b**



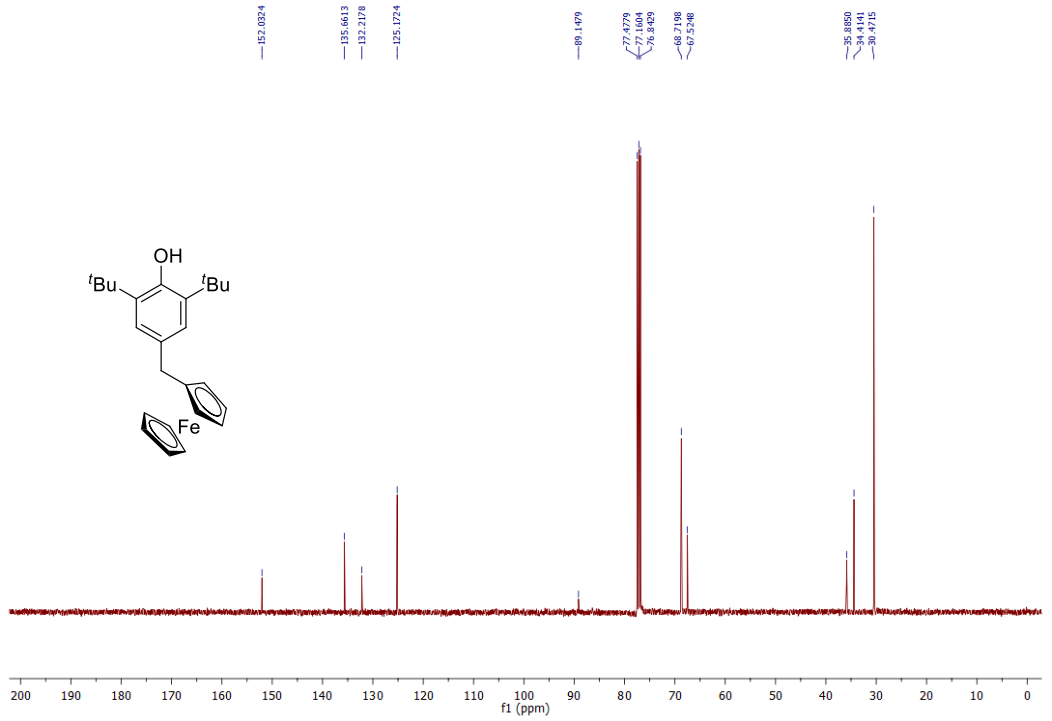
^{13}C NMR Spectrum of **63b**



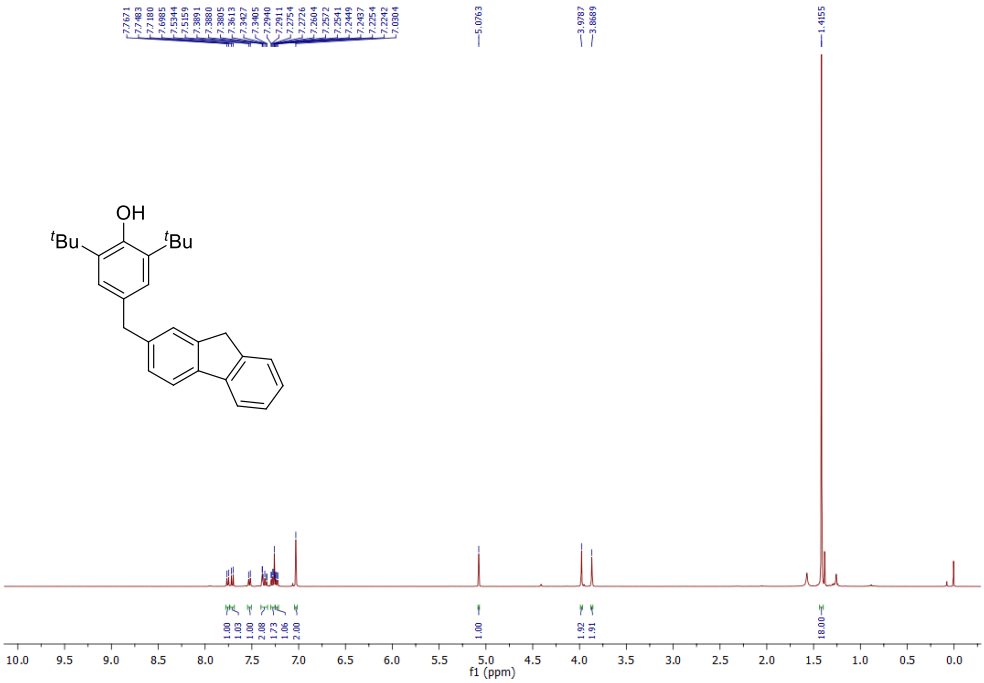
^{1}H NMR Spectrum of **68s**



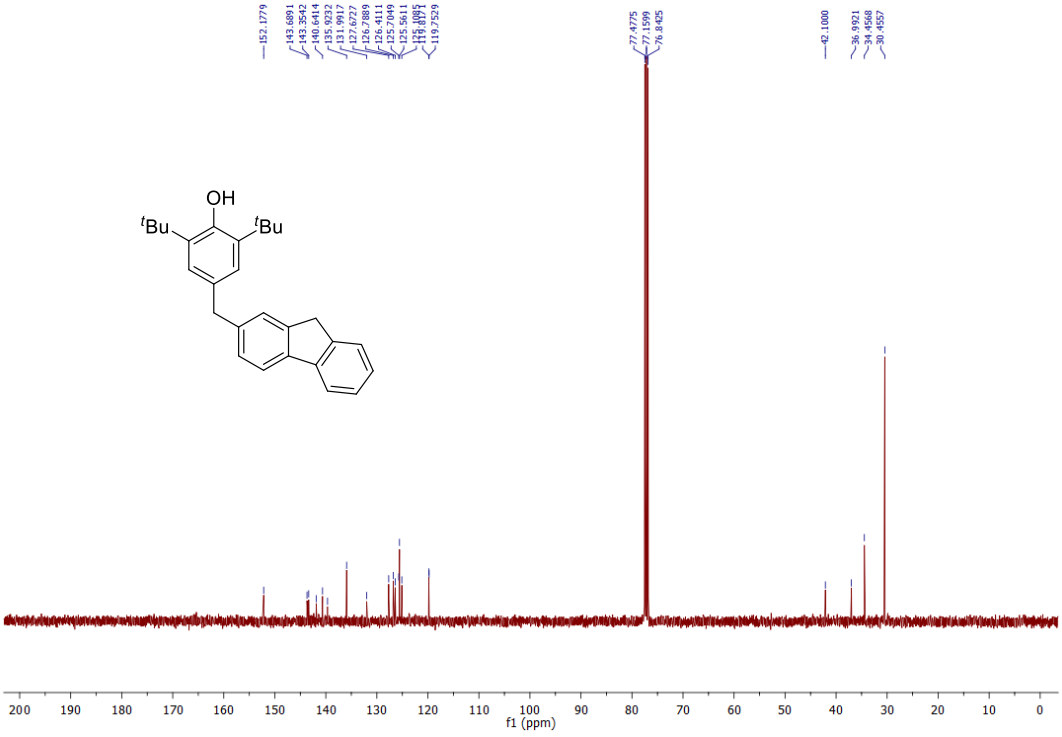
^{13}C NMR Spectrum of **68s**



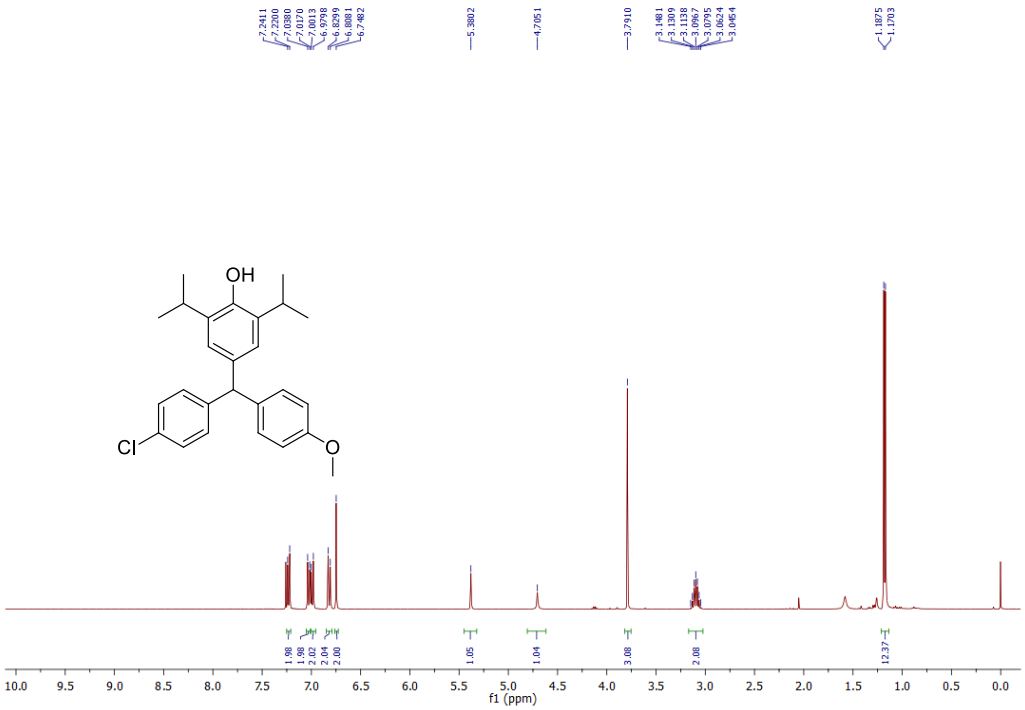
^{1}H NMR Spectrum of **68t**



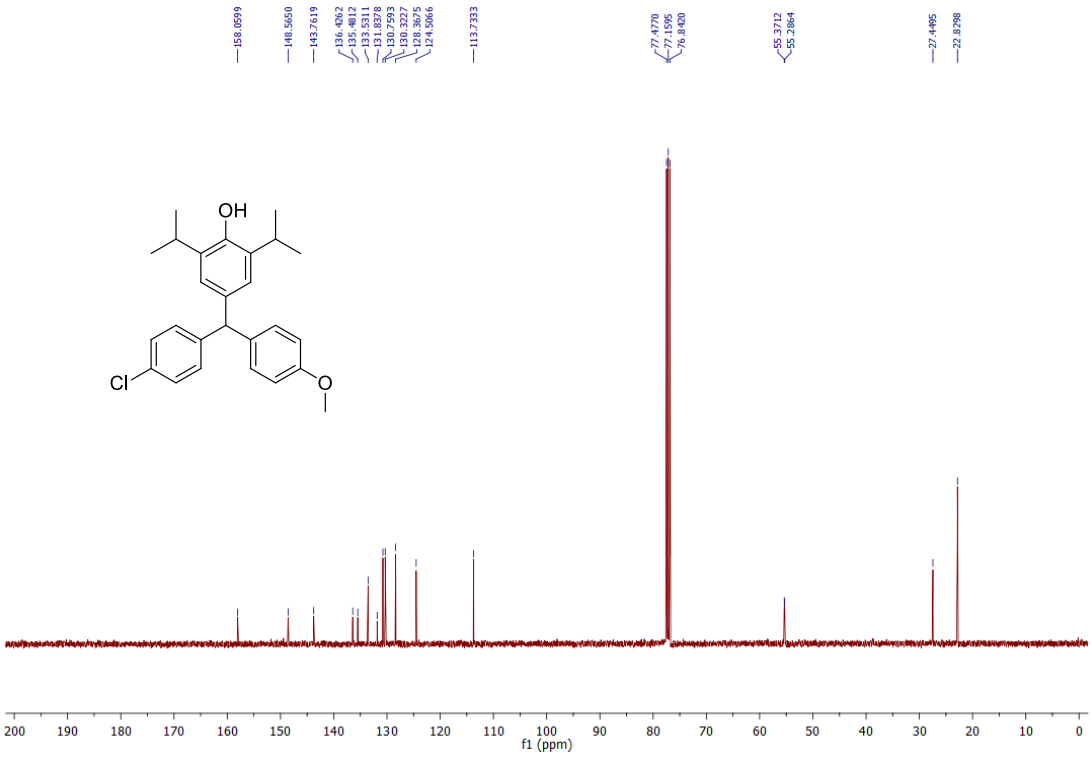
^{13}C NMR Spectrum of **68t**



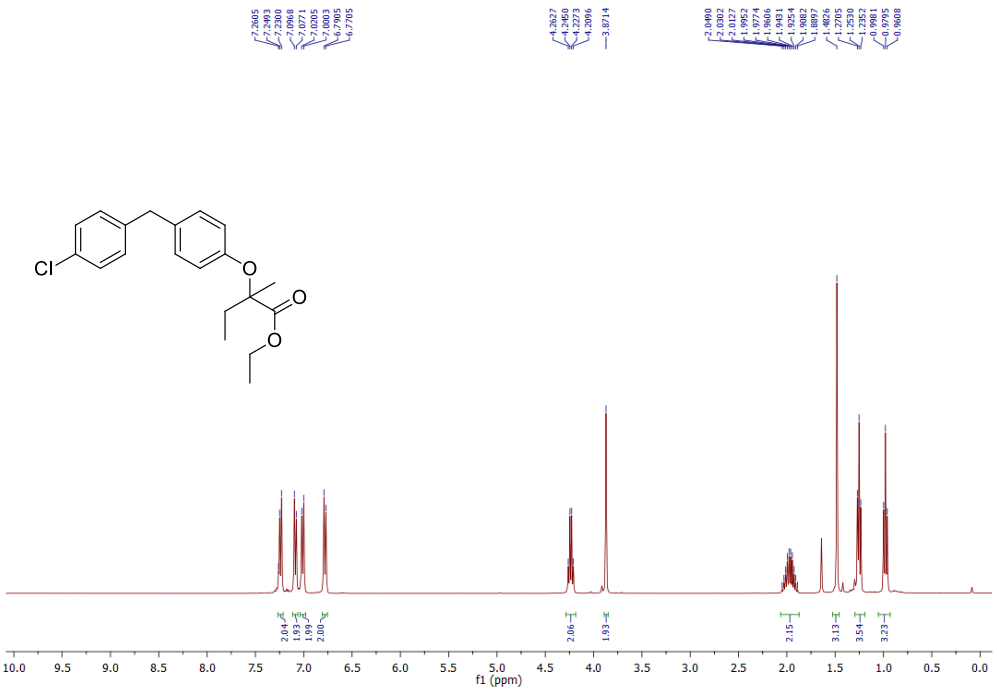
^{1}H NMR Spectrum of **68ah**



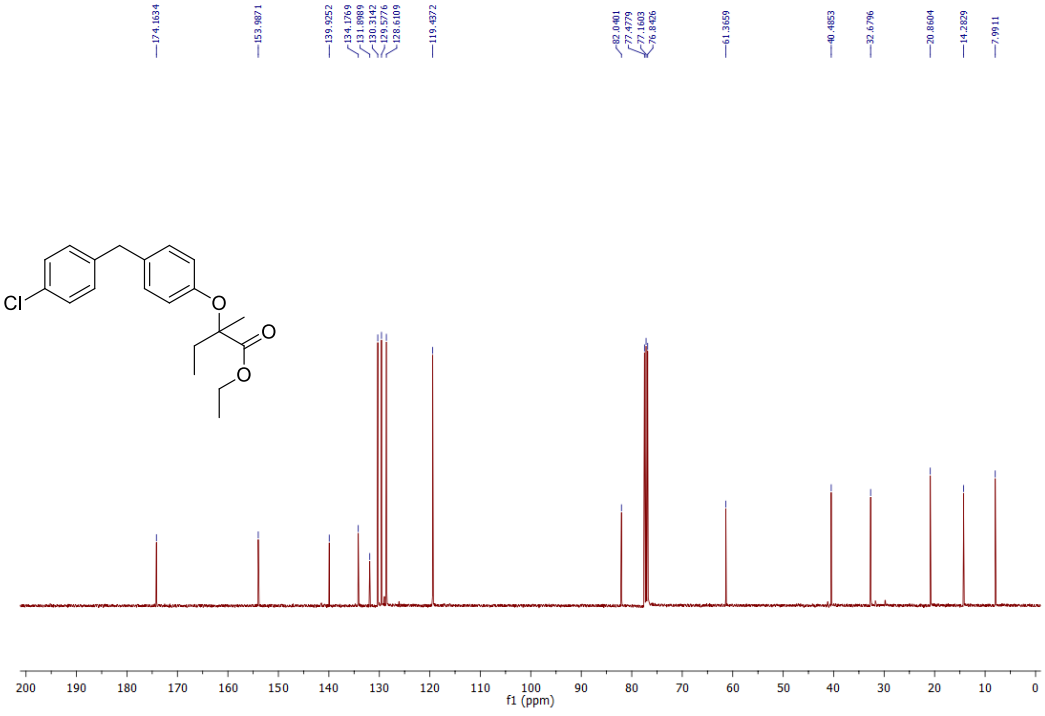
^{13}C NMR Spectrum of **68ah**



^{1}H NMR Spectrum of **74**



^{13}C NMR Spectrum of **74**



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Chapter 4: Base mediated 5-endo-dig cyclization of N-propargyl-L-proline ester derivatives: an expeditious entry into pyrrolizidine alkaloids

1. Introduction:

Owing to the remarkable biological activities, naturally occurring as well as the synthetic analogues of pyrrolizidine alkaloids (PAs) are important synthetic targets [Eg: supinidine (**1**), retronecine (**2**), heliotridine (**3**), crotanecine (**4**)] (**Figure 1**).[1] Pyrrolizidine alkaloids (PAs) possess cytotoxicity in domestic animals and humans.[1] In spite of having toxicity, quite a few have biological activity[2] such as anti-cancer, neuro-active properties and some of the PAs have applications in agricultural industry due to antifeedent activity against several insects.[3]

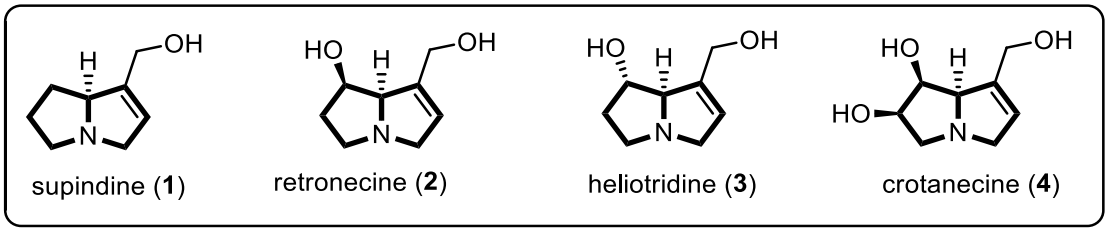
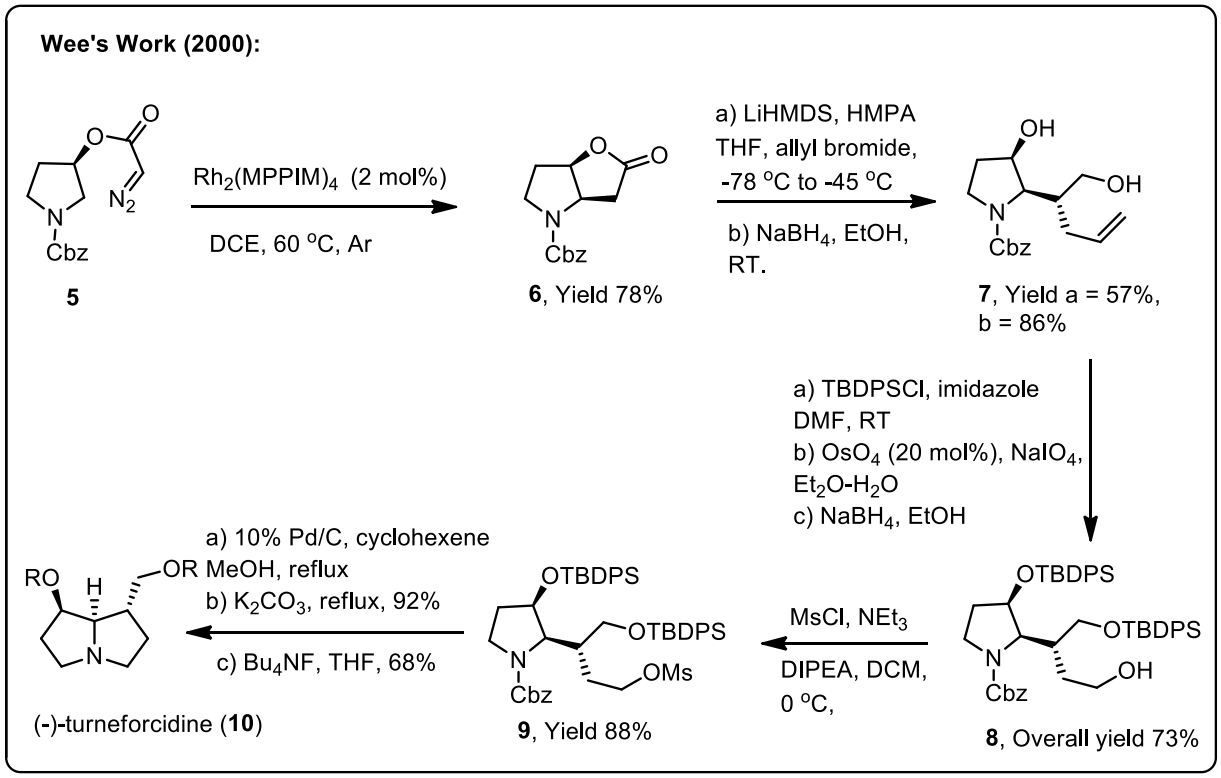
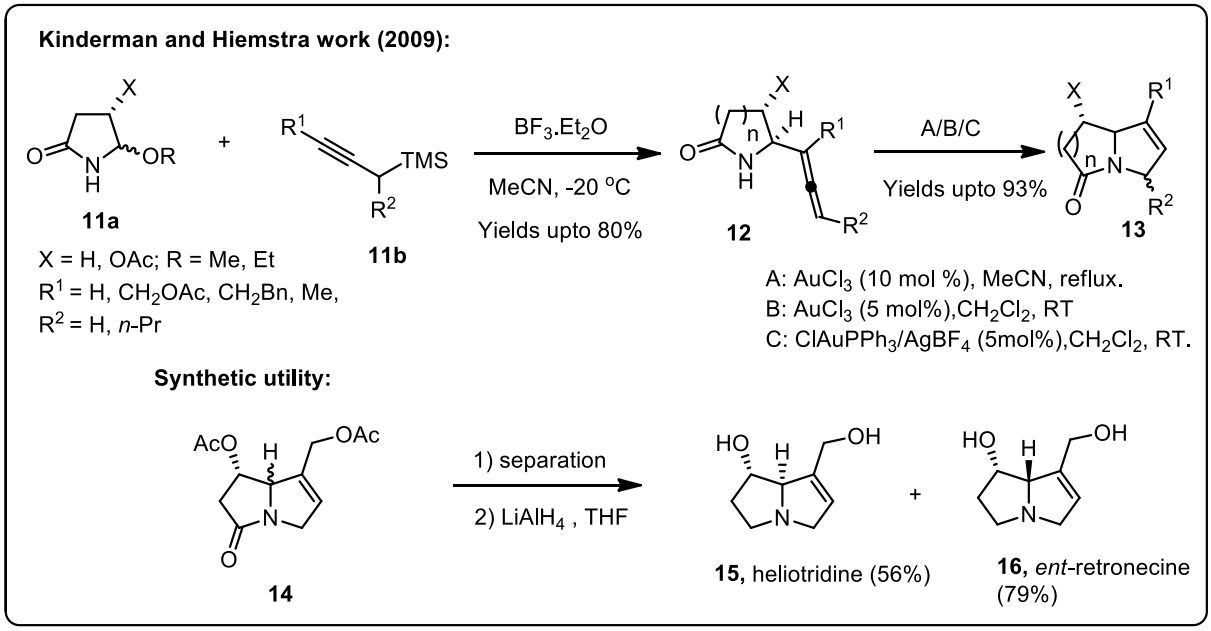


Figure 1: Biologically important pyrrolizidine alkaloids

Many groups have come up with different strategies for the construction of these alkaloids.[4] Most of the early approaches toward the synthesis of these bicyclic core moieties were based on the Geissman-Waiss lactone.[5] For instance, Wee reported the synthesis of (*1R*, *7R*, *8R*)-turneforcidine (**10**), which involves a Rh(II)-carbenoid mediated synthesis of (–)-Geissman-Waiss lactone (**6**) as a key step. An intramolecular C–H insertion reaction of chiral diazoacetates catalyzed by chiral $Rh_2(MPPIM)_4$ provided the *N*-cbz protected (-)-Geissman-Waiss lactone with excellent region-selectivity and *cis*-diastereo-selectivity. The (-)-Geissman-Waiss lactone (**6**) was then converted to **7** *via* allylation followed by reduction of lactone. Silylation of **7** followed by OsO_4 catalyzed oxidative cleavage led to an aldehyde, which on reduction with $NaBH_4$ delivered **8**. Finally, **8** was converted to (-)-turneforcidine (**10**) through a sequence of simple steps (**Scheme 1**).[5b,5c]



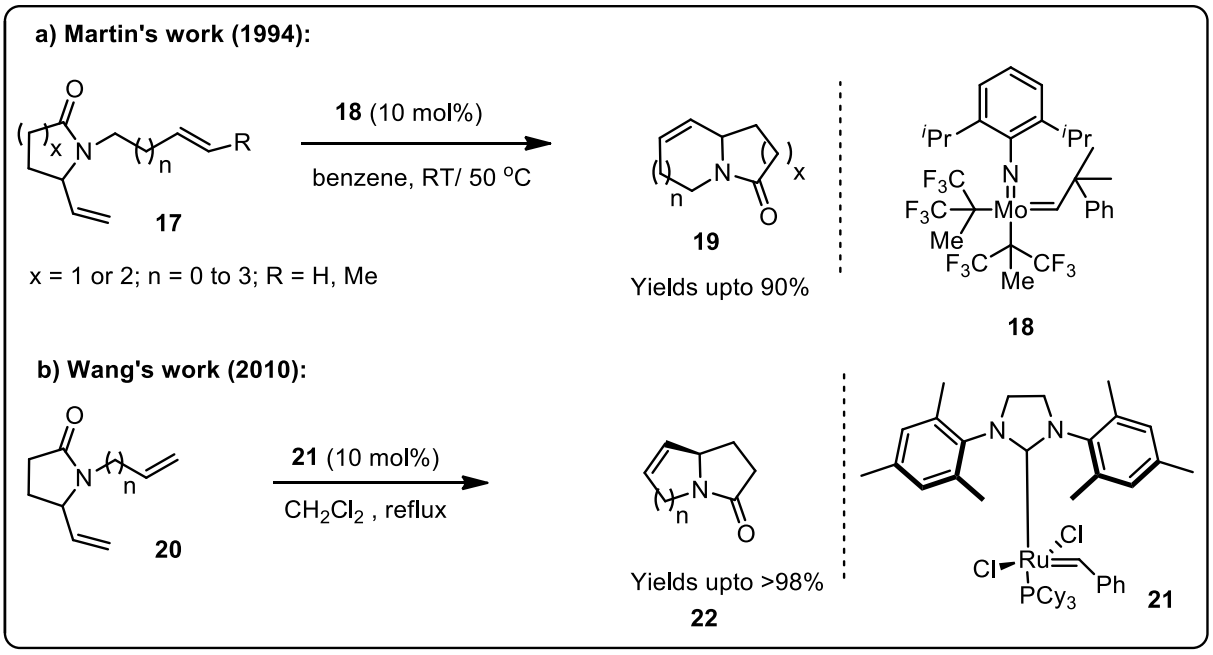
Scheme 1: Elaboration of Geissman-Waiss lactone to (-)-turneforcidine



Scheme 2: Gold catalyzed cyclization of α-allenyl amides

Kinderman and Hiemstra have jointly accounted a gold catalyzed α-allenyl amide cyclization (**12**) towards the synthesis of pyrrolizidine alkaloid core (**13**). Their strategy involves the addition of propargyl silanes (**11b**) to lactam-derived *N*-acyliminium ions (**11a**) followed by gold-catalyzed cyclization of the resulting α-allenyl amide (**12**), which led to a variety of pyrrolizidine alkaloid cores (**13**). Their protocol was also elaborated to the synthesis of pyrrolizidine alkaloids heliotridine **15** and *ent*-retronecine **16** (**Scheme 2**).[6]

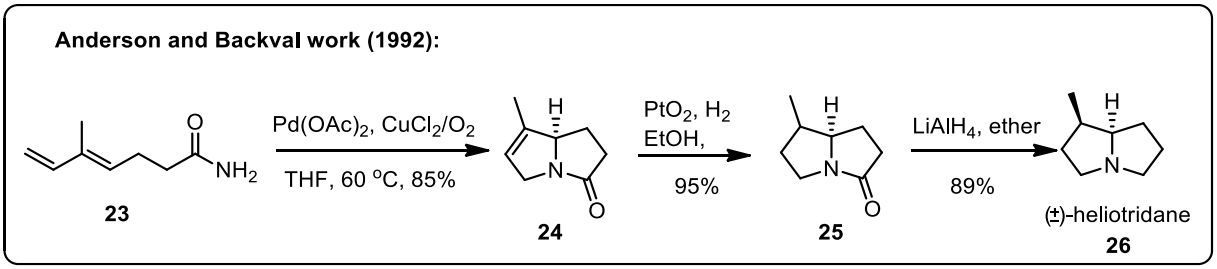
Molybdenum alkylidene (**18**) catalyzed ring-closing metathesis (RCM) of hetero-atom containing α,ε-dienes (**17**) was developed by Martin and co-workers in 1994. This protocol reveals a concise preparation of **17** in three steps, followed by a ring-closing metathesis of **17**, for the efficient synthesis of pyrrolizidine, indolizidine, and quinolizidine frame works with good yields (**a, scheme 3**).[7a] Later on, Wang and co-workers have reported an improved version of the RCM reaction using second generation Grubbs' catalyst (**21**) and, through this method, a wide range of *N*-bridged bicyclic systems (**22**) could be constructed in excellent yields (**b, scheme 3**).[7b]



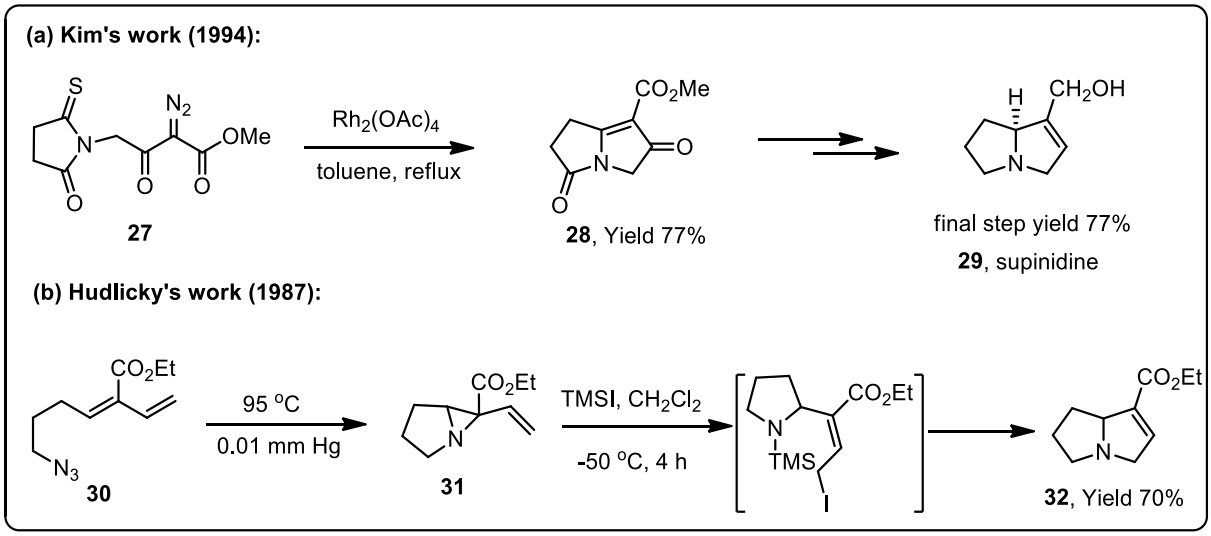
Scheme 3: Ring-closing metathesis based approaches to pyrrolizidine scaffold

A palladium catalyzed tandem cyclization approach to access the pyrrolizidine core was disclosed by Anderson and Backval in 1992. They described a combination of $Pd(OAc)_2$ and

diene-amide initially generates Pd-homoallyl complex intermediate, which on intramolecular nucleophilic addition of amide furnishes the desired *N*-bridged bicycle (**24**). Finally, (±)-heliotridane (**26**) was obtained through Pt-catalyzed hydrogenation of **24** followed by reduction (**scheme 4**).[8]



Scheme 4: Pd-catalyzed cyclization approach to (±)–heliotridane



Scheme 5: Carbene/Nitrene insertion reactions to access pyrrolizidine core

Kim and co-workers developed a concise synthetic sequence to (±)-supinidine (**29**) through an intramolecular carbenoid-thioimide (**27**) coupling reaction as a key step. The present work demonstrates a Rh-catalyzed intramolecular carbene-insertion reaction of **27** to construct pyrrolizidine skeleton (**28**). In addition, their studies were also extended for the efficient synthesis of (±)-supinidine (**29**) *via* simple synthetic sequence (**a, scheme 5**).[9] Hudlicky and co-workers have realized the synthesis of pyrrolizidine derivative (**32**) using flash vacuum pyrolysis technique. This work involves an intra molecular [4+1] type annulation of azido diene (**30**),

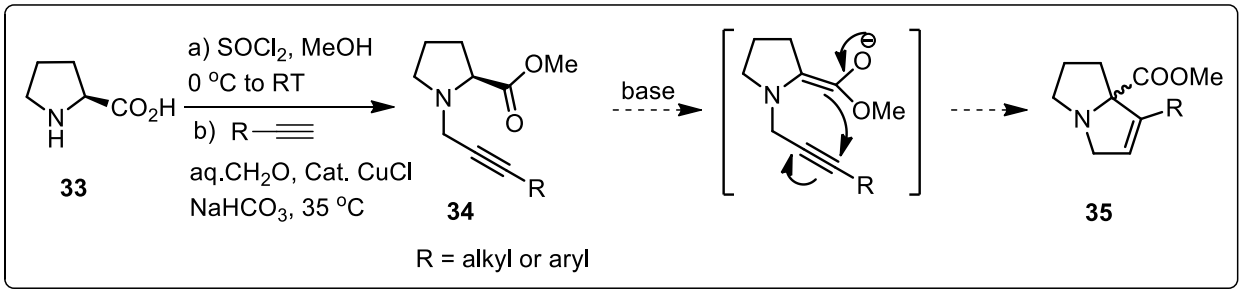
which leads to vinyl azide (**31**). TMS iodide mediated nucleophilic ring opening of **31** followed by ring closure provides the pyrrolizidine ester **32** (**b, scheme 5**).[10] Other interesting approaches toward the preparation of aza-bicyclic skeletons include [3+2] cycloaddition,[11] radical cyclization[12] and intramolecular lactamization.[13]

2. Objective:

- *To construct the bicyclic core of pyrrolizidine alkaloids through a base mediated 5-endo-dig cyclization of N-propargyl-L-proline esters.*

Results and discussion:

Since the *5-endo-dig* cyclization strategy has been proven to be a prevalent strategy for the assembly of cyclic or bicyclic core of many valuable molecules,[17] we became interested in employing this approach for the construction of the pyrrolizidine scaffold. Our proposed synthetic approach towards the pyrrolizidine skeleton is represented in **Scheme 6**. It is evident from **Scheme 6** that the bicyclic core of pyrrolizidine (**35**) could be easily assembled from *N*-propargyl-L-proline ester (**34**) through base facilitated *5-endo-dig* cyclization. The *N*-propargyl-L-proline ester (**34**) could be readily accessed from L-proline by adapting a precedented method.[14] To the best of our knowledge, this particular *5-endo-dig* cyclization strategy towards pyrrolizidine core remains unknown in the literature.

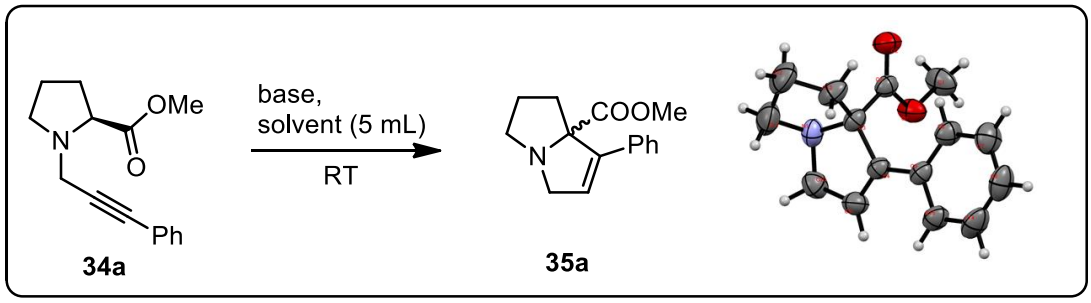


Scheme 6. Proposed approach towards pyrrolizidine scaffold

The optimization studies were carried out with **34a** under different conditions using various bases (**Table 1**). Initial efforts toward cyclization of **34a** were discouraging as it was decomposed when bases such as NaH or sodium *tert*-butoxide were used (Entries 1 & 2).

Organic bases such as DBU and Hünig's base also did not help the cyclization process (Entries 3 & 4).

Table 1. Optimization studies[a]

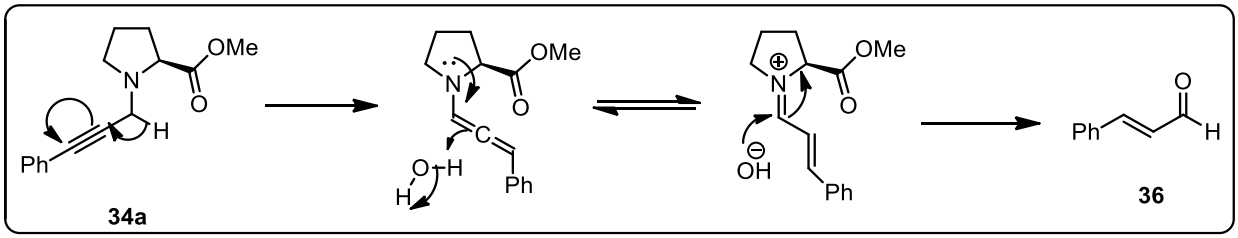


Entry	Base (equiv.)	Solvent	Time (h)	Yield [%][b]
1	NaH 1.5)	THF	2	Decomposed
2	NaO^{t}Bu (1.5)	THF	24	Decomposed
3	DBU (1.5)	THF	2	NR
4	DIPEA (1.5)	THF	24	NR
5	LDA (1.2)	THF	2	Decomposed
6[b]	NaH (1.2)	DMF	4	0
7	LiHMDS (1.5)	DMF	1	10
8	LiHMDS (1.5)	Toluene	1	50
9	LiHMDS (1.5)	CH_2Cl_2	1	10
10	**LiHMDS (1.5)**	**THF**	**1**	**70**
11	LiHMDS (1.5)	Et_2O	1	50

[a]*Reaction conditions:* All reactions were performed at 0.1M of **34a** in solvent. [b]Cinnamaldehyde was observed in 37% yield. RT = Room temperature. NR = No reaction

When the reaction was performed in DMF using NaH as a base, instead of **35a**, cinnamaldehyde (**36**) was obtained as the sole product in 37% yield (Entry 6). The formation of cinnamaldehyde (**36**) is probably due to isomerization of **34a** to allene enamine, which probably underwent hydrolysis during water work-up (**Scheme 7**). Surprisingly, the required product (**35a**) was obtained in 10% yield when a little excess of LiHMDS was used as a base (Entry 7). Encouraged

by this observation, we carried out further optimization studies using LiHMDS in different solvents (Entries 8-11). Of the solvents screened, satisfactory outcome was attained in THF (Entry 10, Table 1), and the product **35a** was isolated in 70% yield after chromatographic separation. Fortunately, cinnamaldehyde was detected only in trace quantities in most of the reactions, wherever LiHMDS was used as a base.

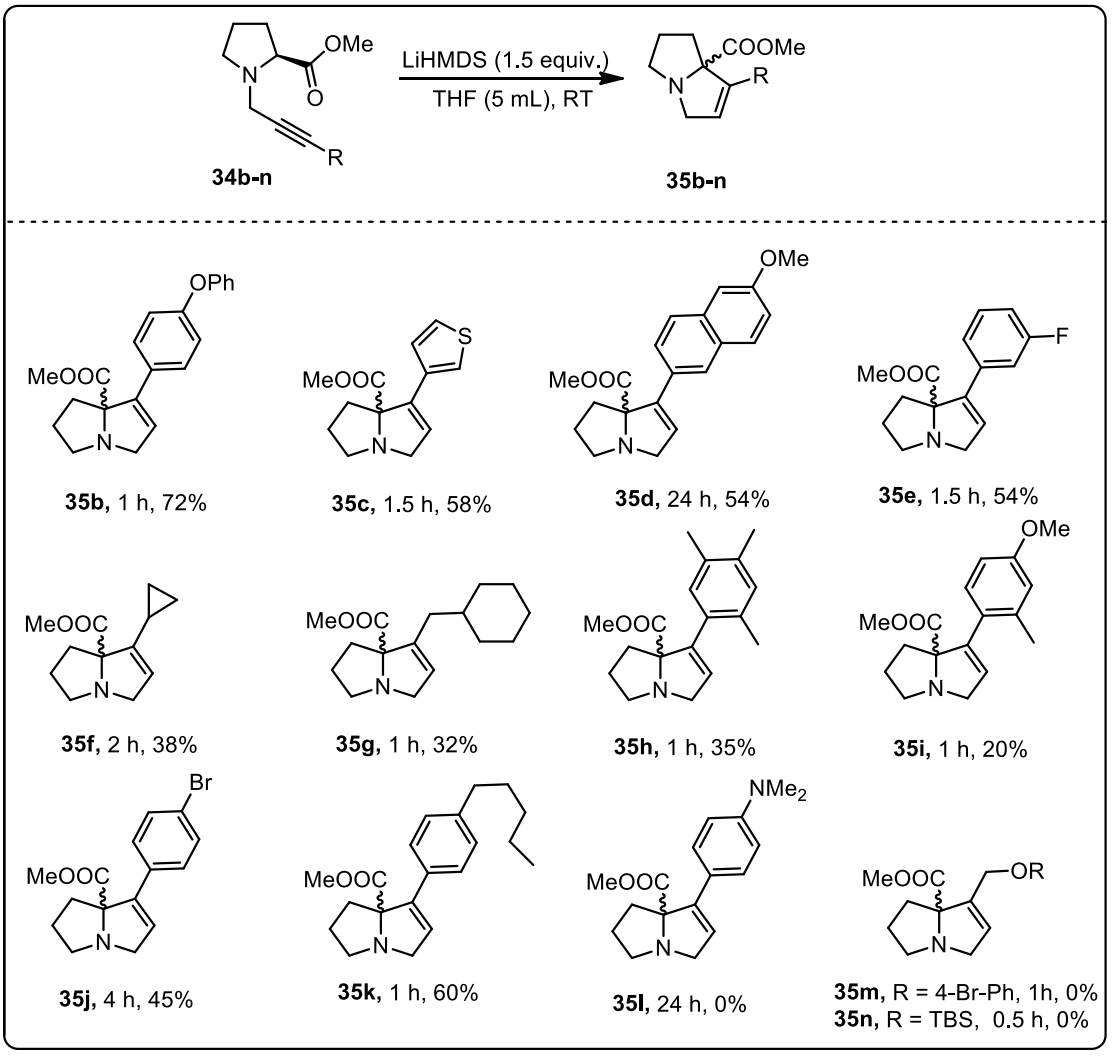


Scheme 7. Plausible mechanism for cinnamaldehyde formation

The structure of **35a** was confirmed by all the spectroscopic techniques (IR, NMR and HRMS). Further, the structure of **35a** was also characterized by X-ray crystallography. Since the concept of "memory of chirality"[15] is often observed in *α*-alkylation chemistry of amino acids, we expected transfer of chirality to the newly formed quaternary center of the product (**35a**). Unfortunately, the product was found to be racemic as it didn't show any specific rotation in polarimetry. It is documented in the literature that most of the transformations involving "memory of chirality" were performed at much lower temperatures (usually – 78 ^{o}C) to retain the chirality.[16] However in the present case, all reactions were carried out at room temperature, which is probably not suitable for retaining the chirality at the enolate stage, thus giving the racemic mixture.

To check the transfer of chirality at lower temperature in the present method, cyclization reaction of **34a** using LDA or LiHMDS in THF at – 78 ^{o}C was carried out. However, in both the cases no product was observed even after 12 h. This observation clearly indicates that the enolate did not react with alkyne at lower temperatures as the alkyne moiety is not a very good electrophile.

Table 2. Substrate scope with different *N*-propargyl-L-proline ester derivatives:



[a]*Reaction conditions:* All reactions were performed at 0.1M of **34b-n** in THF (RT = 27-30 °C). Yields reported are isolated yields.

Having optimized reaction condition (Entry 10, Table 1), our attention was shifted towards evaluating the substrate scope for this transformation. In this regard, a wide array of *N*-propargyl-L-proline ester derivatives (**34b**-**l**) were prepared using a variety of terminal acetylenes, and finally subjected to LiHMDS mediated *5-endo-dig* cyclization (Table 2). In most of the cases, the desired bicyclic derivatives were formed in moderate yields. Maximum yield of 72% was attained in the case of proline ester, derived from *p*-phenoxy phenylacetylene (**35b**). This methodology was also applied for the cyclization of proline ester derivatives prepared from substituted phenyl acetylenes with various electronic properties (electron-poor and electron-rich).

Even unactivated propargyl derivatives, synthesized from aliphatic and cycloalkyl acetylenes underwent smooth cyclization under the optimized conditions to lead to desired pyrrolizidine scaffolds (**35f**, **35g**). Unfortunately, the cyclization did not occur in the case of *N*-propargyl proline ester (**34l**), derived from highly electron-rich alkynes such as, 4-*N*, *N*-dimethylamino phenylacetylene even after 24 h. In the cases of propargyl alcohol derived substrates (**34m** and **34n**), complex mixtures were obtained under the standardized condition. Although, in most of the cases, the conversion was more than 90% (by TLC), the products were isolated only in moderate yields after purification through column chromatography. It is well documented in the literature that pyrrolizidine derivatives are prone to undergo decomposition during column chromatography.[10] This explains the lower yield of products after chromatographic purification.

3. Conclusion:

A mild, base promoted *5-endo-dig* cyclization strategy has been established for the synthesis of bicyclic core of pyrrolizidine alkaloids. A diverse range of *N*-propargy-L-proline esters, prepared from aliphatic and aryl substituted terminal alkynes, underwent smooth conversion to the respective pyrrolizidine derivatives under mild conditions.[18]

4. Experimental section:

General Methods: All the reactions of pyrrolizidine synthesis were carried out under inert atmosphere. All the reagents used were purchased from commercial sources and used as such. *N*-Propargyl-L-proline esters were prepared according to known literature procedure.[14] ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using 400 MHz Bruker FT-NMR spectrometer. Chemical shift values are reported in ppm relative to TMS. High resolution mass spectra (HRMS) were recorded on a Waters-Q-Tof spectrometer. IR spectra were recorded on a Brucker FT IR spectrometer. Thin layer chromatography was carried out on Merck silica gel 60 F254 TLC plates using EtOAc/hexane mixture as an eluent. Chromatographic separation was carried out through neutral alumina column (Pyrrolizidine derivatives) and silica gel column (*N*-propargyl proline ester derivatives).

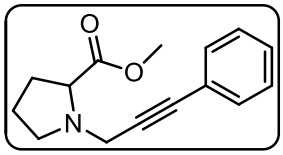
X-Ray Crystallography data of pyrrolizidine 35a:

Compound	**35a**
Emperical Formula	$C_{15}H_{17}N_1O_2$
Formula mass	243.3
T[K]	296K
Crystal system	Monoclinic
Space group	$P2_1/n$
a[Å]	8.0317(3)
b[Å]	10.8377(2)
c[Å]	15.2538(2)
α[°]	90
β[°]	102.930(1)
γ[°]	90
V[$Å^3$]	1294.10(2)
Z	4
D(Calcd.) [$g.cm^{-3}$]	1.25
μ(Mo-Kα) [mm–1]	0.083
F(000)	519.9
θ range [°]	2.3 to 25.0
Index range	$–9 \leq h \leq 9$
	$–12 \leq k \leq 12$
	$–18 \leq l \leq 18$
Reflections collected	8981
Independent reflections	2286
Data/restraints/parameters	2286/0/164
R1, wR2 [I>2σ(I)][a]	0.047,0.137
R1, wR2 (all data)[a]	0.058,0.140
GOF	1.056
Δρ(min), Δρ(max) [e•$Å^3$]	–0.163, 0.271

General procedure for the synthesis of *N*-propargyl-L-proline ester derivatives (34):

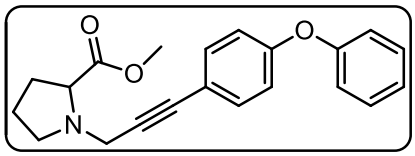
Formaldehyde (0.25 mmol), phenylacetylene (0.25 mmol), sodium bicarbonate (0.2 mmol), and CuCl (0.02 mmol) were stirred over night with proline methyl ester hydrochloride (0.2 mmol) at 35 °C under argon. After completion, the reaction mixture was directly loaded on a silica gel column and purified using Hexane/EtOAc mixture as an eluent.

Methyl-1-(3-phenylprop-2-yn-1-yl)pyrrolidine-2-carboxylate (34a):



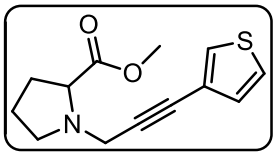
80% Yield; brown color liquid; FT-IR 2360, 1745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43-7.40 (m, 2H), 7.30-7.27 (m, 3H), 3.79 (d, *J* = 1.6 Hz, 2H), 3.73 (s, 3H), 3.50 (dd, *J* = 9.0 Hz, 6.4 Hz, 1H), 3.16-3.11 (m, 1H), 2.81-2.75 (m, 1H), 2.2-2.1 (m, 1H), 2.05-1.91 (m, 2H), 1.87-1.78 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.3, 131.8, 128.3, 128.2 123.0, 85.4, 84.1, 62.9, 52.6, 52.1, 42.2, 29.7, 23.4 ppm.

Methyl-1-[3-(4-phenoxyphenyl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34b):



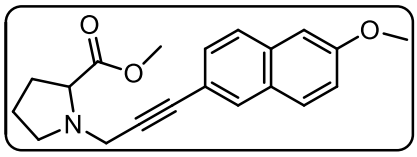
62% Yield; yellow liquid; FT-IR 2360, 1740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 8.8 Hz, 2H), 7.36-7.31 (m, 2H), 7.14-7.10 (m, 1H), 7.02-6.99 (m, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.78 (d, *J* = 1.20 Hz, 2H), 3.73 (s, 3H), 3.50 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.16-3.11 (m, 1H), 2.80-2.74 (m, 1H), 2.22-2.13 (m, 1H), 2.05-1.80 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.3, 157.5, 156.6, 133.4, 130.0, 123.9, 119.4, 118.4, 117.7, 85.0, 83.5, 63.1, 52.7, 52.1, 42.4, 29.8, 23.5 ppm. HRMS (ESI) calcd for $C_{21}H_{22}NO_3$ 336.1599, found 336.1590 $[M+H]^+$.

Methyl-1-[3-(thiophen-3-yl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34c):



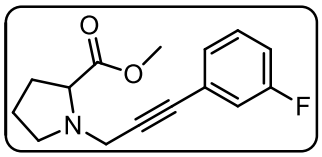
62% Yield; yellow liquid; FT-IR 2362, 1740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.39 (dd, *J* = 3.0 Hz, 1.0 Hz, 1H), 7.22 (dd, *J* = 5.0 Hz, 3.0 Hz, 1H), 7.07 (dd, *J* = 5.0 Hz, 1.1 Hz, 1H), 3.75 (s, 2H), 3.71 (s, 3H), 3.46 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.13-3.09 (m, 1H), 2.77-2.70 (m, 1H), 2.20-2.11 (m, 1H), 2.02-1.88 (m, 2H), 1.85-1.76 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.3, 130.1, 128.7, 125.3, 122.0, 83.7, 80.5, 63.0, 52.6, 52.1, 42.3, 29.7, 23.4 ppm. HRMS (ESI) calcd for $C_{13}H_{16}NO_2S$ 250.0901, found 250.0907 $[M+H]^+$.

Methyl-1-[3-(6-methoxynaphthalen-2-yl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34d):



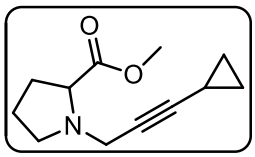
48.6% Yield; colorless solid; M.P. 66-68 °C; FT-IR 2330, 1745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86 (s, 1H), 7.66 (t, *J* = 9.3 Hz, 2H), 7.44 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H), 7.14 (dd, *J* = 8.9 Hz, 2.6 Hz, 1H), 7.09 (d, *J* = 2.3 Hz, 1H), 3.91 (s, 3H), 3.84 (d, *J* = 2.16, 2H), 3.74 (*s*, 3H), 3.55 (dd, *J* = 9.0 Hz, 6.4 Hz, 1H), 3.19-3.15 (m, 1H), 2.86-2.80 (m, 1H), 2.26-2.16 (m, 1H), 2.07-1.93 (m, 2H), 1.90-1.84 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.4, 158.3, 134.1, 131.5, 129.3, 129.3, 128.5, 126.9, 119.5, 180.0, 105.8, 86.0, 83.7, 63.1, 55.5, 52.7, 52.2, 42.5, 29.9, 23.5 ppm. HRMS (ESI) calcd for $C_{20}H_{22}NO_3$ 324.1599, found 324.1593 $[M+H]^+$.

Methyl-1-[3-(3-fluorophenyl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34e):



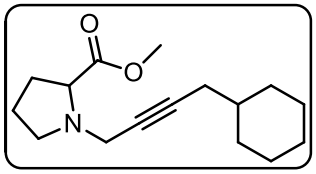
88% Yield; yellow liquid; FT-IR 2357, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.28-7.22 (m, 1H), 7.21-7.18 (m, 1H), 7.13-7.09 (m, 1H), 7.03-6.98 (m, 1H), 3.79 (d, *J* = 1.2 Hz, 2H), 3.73 (s, 3H), 3.48 (dd, J = 9.0 Hz, 6.5 Hz, 1H), 3.17-3.16 (m,1H), 2.79-2.73 (m, 1H), 2.23-2.13 (m, 1H), 2.06-1.91 (m, 2H), 1.88-1.80 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.2, 162.4 (d, J_{C-F} = 245 Hz), 129.9 (d, J_{C-F} = 8.8 Hz), 127.7 (d, J_{C-F} = 2.8 Hz), 124.9 (d, J_{C-F} = 9.6 Hz), 118.6 (d, J_{C-F} = 22.6 Hz), 115.6 (d, J_{C-F} = 20.5 Hz), 85.4, 84.2, 63.1, 52.7, 52.1, 42.3, 29.8, 23.4 ppm. HRMS (ESI) calcd for $C_{15}H_{17}FNO_2$ 262.1243, found 262.1241 $[M+H]^+$.

Methyl-1-(3-cyclopropylprop-2-yn-1-yl)pyrrolidine-2-carboxylate (34f):



67% Yield; light yellow liquid; FT-IR 2359, 1746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.70 (s, 3H), 3.47 (d, *J* = 1.9 Hz, 2H), 3.34 (dd, *J* = 9.1 Hz, 6.5 Hz, 1H), 3.03-2.99 (m, 1H), 2.65-2.59 (m, 1H), 2.16-2.07 (m, 1H), 1.98-1.83 (m, 2H), 1.81-1.73 (m, 1H), 1.23-1.15 (m, 1H), 0.73-0.69 (m, 2H), 0.64-0.59 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.4, 88.8, 69.7, 62.9, 52.5, 52.1, 41.9, 29.8, 23.4, 8.3, -0.5 ppm. HRMS (ESI) calcd for $C_{12}H_{18}NO_2$ 208.1337, found 208.1337 $[M+H]^+$.

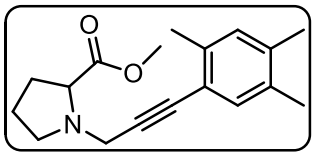
Methyl-1-(4-cyclohexylbut-2-yn-1-yl)pyrrolidine-2-carboxylate (34g):



63% Yield; colorless liquid; FT-IR 2309, 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.67 (s, 3H), 3.50 (t, *J* = 2.0 Hz, 2H), 3.38 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.02-2.97 (m, 1H), 2.7 (m, 1H), 2.13-2.06 (m,

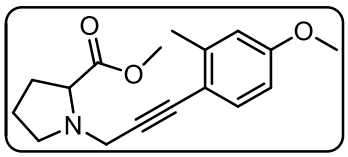
1H), 2.02 (td, *J* = 6.6 Hz, 2.1 Hz, 2H), 1.97-1.83 (m, 2H), 1.76-1.58 (m, 6H), 1.43-1.32 (m, 1H), 1.24-1.04 (m, 3H), 0.93 (dq, *J* = 12.2 Hz, 2.9 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.4, 84.4, 75.1, 62.7, 52.3, 52.0, 41.8, 37.4, 32.7, 29.7, 26.6, 26.3, 26.1, 23.4 ppm. HRMS (ESI) calcd for $C_{16}H_{26}NO_2$ 264.1963, found 264.1962 $[M+H]^+$.

Methyl-1-[3-(2,4,5-trimethylphenyl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34h):



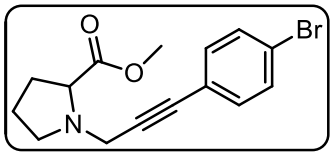
64% Yield; yellow solid; M.P. 60-62 °C; FT IR 2358, 1747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.16 (s, 1H), 6.95 (s, 1H), 3.84 (d, *J* = 4.24 Hz, 2H), 3.73 (s, 3H), 3.55 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.14-3.09 (m, 1H), 2.85-2.80 (m, 1H), 2.34 (s, 3H), 2.20 (s, 3H), 2.18 (s, 3H), 2.05-1.80 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.4, 137.3, 137.0, 133.7, 133.1, 130.9, 120.0, 86.7, 84.6, 62.7, 52.4, 52.1, 42.3, 29.8, 23.5, 20.3, 19.7, 19.1 ppm. HRMS (ESI) calcd for $C_{18}H_{24}NO_2$ 286.1807, found 286.1808 $[M+H]^+$.

Methyl-1-(3-(4-methoxy-2-methylphenyl)prop-2-yn-1-yl)pyrrolidine-2-carboxylate (34i):



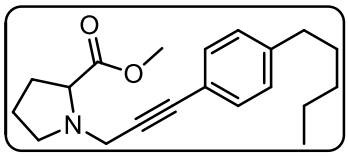
66% Yield; yellow liquid; FT-IR 2358, 1738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 2.5 Hz, 1H), 6.65 (dd, *J* = 8.5 Hz, 2.6 Hz, 1H), 3.82 (d, *J* = 4.0 Hz, 2H), 3.77 (s, 3H), 3.71 (s, 3H), 3.53 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.14-3.09 (m, 1H), 2.83-2.77 (m, 1H), 2.38 (s, 3H), 2.20-2.11 (m, 1H), 2.04-1.89 (m, 2H), 1.85-1.79 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.4, 159.4, 141.9, 133.5, 115.2, 115.1, 111.2, 86.3, 84.2, 62.8, 55.3, 52.5, 52.1, 42.4, 29.8, 23.5, 21.2 ppm. HRMS (ESI) calcd for $C_{17}H_{22}NO_3$ 288.1599, found 288.1596 $[M+H]^+$.

Methyl-1-(3-(4-bromophenyl)prop-2-yn-1-yl)pyrrolidine-2-carboxylate (34j):



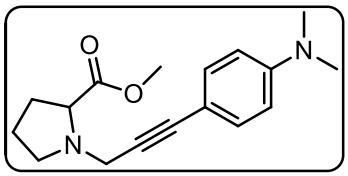
71% Yield; light yellow liquid; FT-IR 2358, 1743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 2H), 3.73 (s, 3H), 3.46 (dd, *J* = 9.0 Hz, 6.4 Hz, 1H), 3.20-3.12 (m, 1H), 2.78-2.71 (m, 1H), 2.23-2.12 (m, 1H), 2.05-1.90 (m, 2H), 1.87-1.79 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.1, 133.2, 131.5, 122.3, 121.9, 85.5, 84.3, 63.0, 52.6, 52.1, 42.3, 29.7, 23.3 ppm. HRMS (ESI) calcd for $C_{15}H_{17}BrNO_2$ 322.0442, found 322.0441 $[M+H]^+$.

Methyl-1-[3-(4-pentylphenyl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34k):



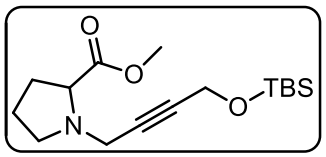
50% Yield; light yellow liquid; FT-IR 2364, 1746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 3.78 (d, *J* = 2.1, 2H), 3.72 (s, 3H), 3.50 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.14-3.10 (m, 1H), 2.81-2.74 (m, 1H), 2.57 (t, *J* = 7.9 Hz, 2H), 2.20-2.12 (m, 1H), 2.04-1.90 (m, 2H), 1.85-1.77 (m,1H), 1.61-1.53 (m, 2H), 1.36-1.23 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.3, 143.4, 131.7, 128.5, 120.2, 85.6, 83.3, 62.9, 52.6, 52.1, 42.3, 35.9, 31.5, 31.0, 29.8, 23.5, 22.6, 14.1 ppm. HRMS (ESI) calcd for $C_{20}H_{28}NO_2$ 314.2120, found 314.2123 $[M+H]^+$.

Methyl-1-[3-(4-(dimethylamino)phenyl)prop-2-yn-1-yl]pyrrolidine-2-carboxylate (34l):



46% Yield; brown liquid; FT-IR 2358, 1747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.9 Hz, 2H), 6.59 (d, *J* = 8.9 Hz, 2H), 3.77 (d, *J* = 2.9 Hz, 2H), 3.72 (s, 3H), 3.51 (dd, *J* = 9.0 Hz, 6.5 Hz, 1H), 3.13-3.10 (m, 1H), 2.90 (s, 6H), 2.81-2.74 (m, 1H), 2.21-2.11 (m, 1H), 2.03-1.88 (m, 2H), 1.84-1.76 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.5, 150.1, 132.8, 111.8, 110.0, 86.2, 81.5, 63.0, 52.6, 52.1, 42.5, 40.3, 29.8, 23.5 ppm. HRMS (ESI) calcd for $C_{17}H_{23}N_2O_2$ 287.1759, found 287.1751 $[M+H]^+$.

Methyl-1-(4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-yl)pyrrolidine-2-carboxylate (34n):

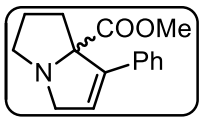


71% Yield; colorless liquid; FT-IR 2370, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 4.28 (s, 2H), 3.68 (s, 3H), 3.57 (s, 2H), 3.39 (dd, *J* = 8.9 Hz, 6.6 Hz, 1Hz), 3.02-2.9 (m, 1H), 2.70-2.63 (m, 1H), 2.15-2.05 (m, 1H), 1.97-1.72 (m, 3H), 0.86 (s, 9H), 0.06 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.2, 84.0, 79.3, 62.5, 52.3, 52.0, 51.8, 41.5, 29.6, 25.8, 23.3, 18.3, -5.1 ppm.

General procedure for synthesis of pyrrolizidine scaffold (35):

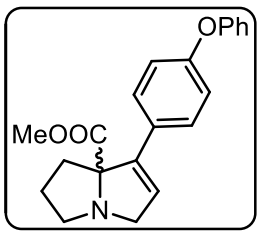
A solution of LiHMDS (0.75 mmol) in hexane was added in a drop-wise manner to a solution of *N*-Propargyl proline ester (0.5 mmol) in dry THF (5 mL) at RT under inert atmosphere and the resulting solution was stirred vigorously until the starting material was completely consumed. The solvent was evaporated under reduced pressure and the residue was purified through neutral alumina column using EtOAc/Hexane mixture as an eluent.

Methyl-7-phenyl-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35a):



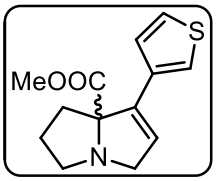
70% Yield; light yellow solid; M.P. 97-99 °C; FT IR: 2930, 1724, 1497 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.36 (m, 2H), 7.33-7.29 (m, 2H), 7.26-7.22 (m, 1H), 6.26 (t, *J* = 2.2 Hz, 1H), 4.14 (dd, *J* = 16.6 Hz, 2.2 Hz, 1H), 3.68 (s, 3H), 3.54 (dd, *J* = 16.6 Hz, 2.4 Hz, 1H), 3.32-3.29 (m, 1H), 2.92 (ddd, *J* = 12.2 Hz, 6.8 Hz, 2.4 Hz, 1H), 2.56 (m, 1H), 2.02-1.91 (m, 1H), 1.90-1.81 (m, 1H), 1.80-1.69 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 142.3, 133.1, 128.7, 127.8, 126.4, 124.3, 83.1, 61.4, 57.7, 52.8, 33.4, 26.5 ppm. HRMS (ESI): Calcd for $C_{15}H_{18}NO_2$ 244.1337; found 244.1333 $[M+H]^+$.

Methyl-7-(4-phenoxyphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35b):

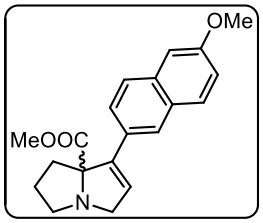


72% Yield; yellow gel; FT-IR: 2949, 1730, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.31 (m, 4H), 7.14-7.10 (m, 1H), 7.03-7.00 (m, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.16 (t, *J* = 2.2 Hz, 1H), 4.13 (dd, *J* = 16.8 Hz, 2.0 Hz, 1H), 3.69 (s, 3H), 3.53 (dd, *J* = 16.8 Hz, 2.4 Hz, 1H), 3.33-3.29 (m, 1H), 2.89 (ddd, *J* = 12.3 Hz, 6.9 Hz, 2.5 Hz, 1H), 2.56-2.50 (m, 1H), 1.99-1.90 (m, 1H), 1.88-1.82 (m, 1H), 1.74-1.69 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1, 157.1, 156.9, 141.6, 129.9, 128.2, 127.8, 123.7, 123.3, 119.3, 118.7, 83.2, 61.4, 57.7, 52.8, 33.4, 26.5 ppm. HRMS (ESI): Calcd for $C_{21}H_{22}NO_3$ 336.1599; found 336.1601 $[M+H]^+$.

Methyl-7-(thiophen-3-yl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35c):



58% Yield; yellow semi solid; FT IR: 2938, 1728, 1432 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.27 (m, 1H), 7.22 (dd, *J* = 5.1 Hz, 1.4 Hz, 1H), 7.19-7.18 (m, 1H), 6.06 (t, *J* = 2.2 Hz, 1H), 4.13 (dd, *J* = 16.5 Hz, 1.9 Hz, 1H), 3.67 (s, 3H), 3.54 (dd, *J* = 16.5 Hz, 2.4 Hz, 1H), 3.34-3.30 (m, 1H), 2.94-2.89 (m, 1H), 2.55-2.49 (m, 1H), 1.97-1.77 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 138.0, 134.6, 126.6, 125.9, 123.3, 121.4, 83.5, 61.5, 57.7, 52.9, 33.4, 26.4 ppm. HRMS (ESI): Calcd for $C_{13}H_{16}NO_2S$ 250.0901;found 250.0903 $[M+H]^+$.

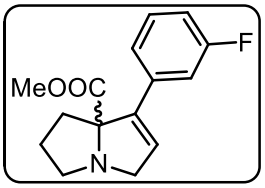


Methyl-7-(6-methoxynaphthalen-2-yl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35d):

54% Yield; light red solid; M.P. 126-128 °C; FT IR: 2950, 1731, 1487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.75-7.68 (m, 2H), 7.65 (bs, 1H), 7.60

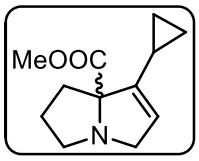
(dd, J = 8.6 Hz, 1.9 Hz, 1H), 7.15 (dd, J = 8.6 Hz, 2.6 Hz, 1H), 7.12 (d, J = 2.6 Hz, 1H), 6.35 (t, J = 2.2 Hz, 1H), 4.20 (dd, J = 16.6 Hz, 1.9 Hz, 1H), 3.94 (s, 3H), 3.71 (s, 3H), 3.61 (dd, J = 16.6 Hz, 2.5 Hz, 1H), 3.38-3.34 (m, 1H), 3.06 (ddd, J = 11.8 Hz, 6.4 Hz, 1.8 Hz, 1H), 2.62-2.55 (m, 1H), 2.08-1.97 (m, 1H), 1.94-1.86 (m, 1H), 1.86-1.78 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 158.1, 142.4, 134.0, 130.0, 128.8, 128.4, 127.1, 125.3, 124.9, 123.9, 119.1, 105.8, 83.2, 61.5, 57.7, 55.5, 52.8, 33.6, 26.6 ppm. HRMS (ESI): Calcd for $C_{20}H_{22}NO_3$ 324.1599; found 324.1592 $[M+H]^+$.

Methyl-7-(3-fluorophenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35e):



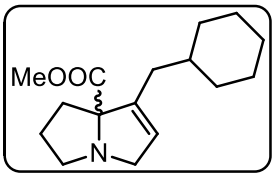
54% Yield; yellow gel; FT-IR: 2949, 1730, 1488 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.28 (m, 1H), 7.16-7.10 (m, 2H), 6.99-6.94 (m, 1H), 6.27 (t, J = 2.2 Hz, 1H), 4.12 (dd, J = 16.9 Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, J = 16.8 Hz, 2.4 Hz, 1H), 3.33-3.28 (m, 1H), 2.89 (ddd, J = 12.4 Hz, 6.9 Hz, 2.5 Hz, 1H), 2.55-2.49 (m, 1H), 2.02-1.92 (m, 1H), 1.89-1.81 (m, 1H), 1.74-1.66 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 163.0 (d, J_{C-F} = 243.5 Hz), 141.5 (d, J_{C-F} = 3 Hz), 135.4 (d, J_{C-F} = 8 Hz), 130.2 (d, J_{C-F} = 8.7 Hz), 125.9, 122.0 (d, J_{C-F} = 2.3 Hz), 114.6 (d, J_{C-F} = 21.2 Hz), 113.3 (d, J_{C-F} = 21.8 Hz), 83.1, 61.3, 57.6, 52.8, 33.4, 26.5 ppm. HRMS (ESI): Calcd for $C_{15}H_{17}FNO_2$ 262.1243; found 262.1240 $[M+H]^+$.

Methyl-7-cyclopropyl-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35f):



38% Yield; light yellow liquid; FT-IR: 2949, 1730, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.18 (bq, J = 1.8 Hz, 1H), 3.92 (td, J = 15.4 Hz, 1.6 Hz, 1H), 3.71 (s, 3H), 3.31-3.27 (m, 1H), 3.26-3.21 (m, 1H), 2.59-2.45 (m, 2H), 1.86-1.74 (m, 3H), 1.25-1.21 (m, 1H), 0.76-0.66 (m, 2H), 0.48-0.37 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.5, 145.7, 118.5, 85.1, 61.5, 57.9, 52.5, 33.1, 25.7, 8.2, 7.0 ppm. HRMS (ESI): Calcd for $C_{12}H_{18}NO_2$ 208.1337; found 208.1331 $[M+H]^+$.

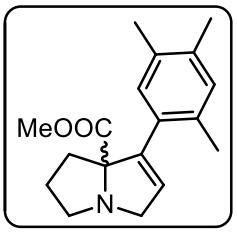
Methyl-7-(cyclohexylmethyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35g):



32% Yield; color less oil; FT-IR: 2921, 1731, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 (t, J = 1.6 Hz, 1H), 3.95 (dd, J = 15.3 Hz, 2.0 Hz, 1H), 3.67 (s, 3H), 3.33 (dd, J = 15.3 Hz, 2.0 Hz, 1H), 3.26-3.22 (m, 1H), 2.52-2.41 (m, 2H), 1.93-1.82 (m, 2H), 1.79-1.56 (m, 8H), 1.49-1.37 (m, 1H), 1.26-1.14 (m, 3H), 0.88-0.78 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.4, 141.3,

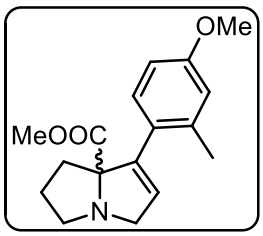
122.2, 85.3, 61.8, 57.9, 52.5, 36.1, 35.1, 33.7, 33.4, 33.0, 26.4, 25.8 ppm. HRMS (ESI): Calcd for $C_{16}H_{26}NO_2$ 264.1963; found 264.1965 $[M+H]^+$.

Methyl-7-(2,4,5-trimethylphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35h):



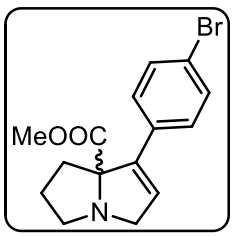
35% Yield; yellow gel; FT-IR: 2946, 1732, 1455 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.98 (s, 1H), 6.73 (s, 1H), 5.76 (t, *J* = 2.0 Hz, 1H), 4.16 (dd, *J* = 16.0 Hz, 1.7 Hz, 1H), 3.72 (s, 3H), 3.55 (dd, *J* = 16.0 Hz, 2.2 Hz, 1H), 3.33-3.29 (m, 1H), 2.63-2.52 (m, 2H), 2.23 (s, 3H), 2.20 (s, 3H), 2.18 (s, 3H), 1.86-1.81 (m, 1H), 1.76-1.73 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 141.1, 135.8, 133.9, 133.6, 132.2, 131.6, 129.2, 128.0, 85.9, 62.0, 57.9, 52.6, 32.6, 26.1, 20.3, 19.5, 19.5 ppm. HRMS (ESI): Calcd for $C_{18}H_{24}NO_2$ 286.1807; found 286.1809 $[M+H]^+$.

Methyl-7-(4-methoxy-2-methylphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35i):



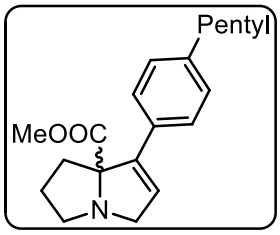
20% Yield; yellow gel; FT-IR: 2949, 1731, 1500 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, *J* = 8.6 Hz, 1H), 6.75 (d, *J* = 2.7 Hz, 1H), 6.68 (dd, *J* = 8.6 Hz, 2.7 Hz, 1H), 5.77 (t, *J* = 2.0 Hz, 1H), 4.16 (dd, *J* = 16.0 Hz, 1.7 Hz, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.56 (dd, *J* = 16.0 Hz, 2.3 Hz, 1H), 3.33-3.29 (m, 1H), 2.62-2.53 (m, 2H), 2.29 (s, 3H), 1.89-1.81 (m, 2H), 1.73-1.67 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 158.6, 140.7, 138.4, 129.0, 127.8, 126.6, 116.4, 111.0, 85.8, 62.0, 57.9, 55.3, 52.6, 32.6, 26.1, 21.4 ppm. HRMS (ESI): Calcd for $C_{17}H_{22}NO_3$ 288.1599; found 288.1596 $[M+H]^+$.

Methyl-7-(4-bromophenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35j):



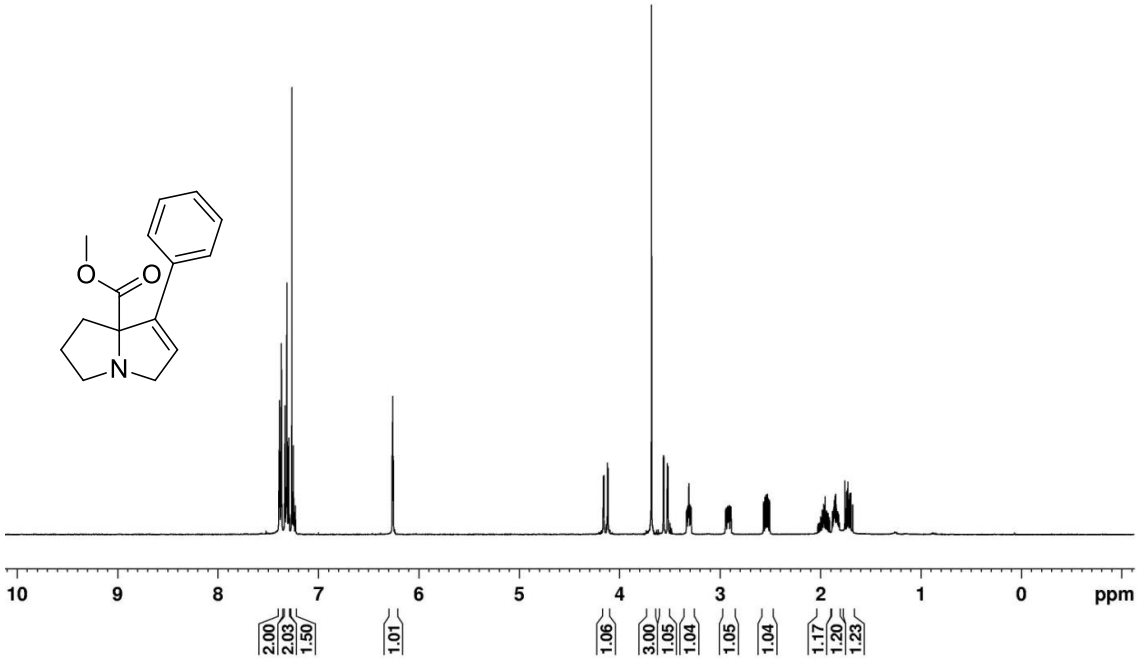
45% Yield; color less semi solid; FT-IR: 2968, 1729, 1488 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44-7.41 (m, 2H), 7.26-7.23 (m, 2H), 6.26 (t, *J* = 2.2 Hz, 1H), 4.11 (dd, *J* = 16.8 Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, *J* = 16.8 Hz, 2.5 Hz, 1H), 3.33-3.29 (m, 1H), 2.90 (ddd, *J* =12.4 Hz, 6.8 Hz, 2.5 Hz, 1H), 2.56-2.49 (m, 1H), 2.01-1.92 (m, 1H), 1.89-1.81 (m,1H), 1.72-1.65 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 141.4, 132.1, 131.8, 128.0, 125.2, 121.8, 83.1, 61.4, 57.6, 52.9, 33.4, 26.5 ppm. HRMS (ESI): Calcd for $C_{15}H_{17}BrNO_2$ 322.0442; found 322.0442 $[M+H]^+$.

Methyl-7-(4-pentylphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (35k):

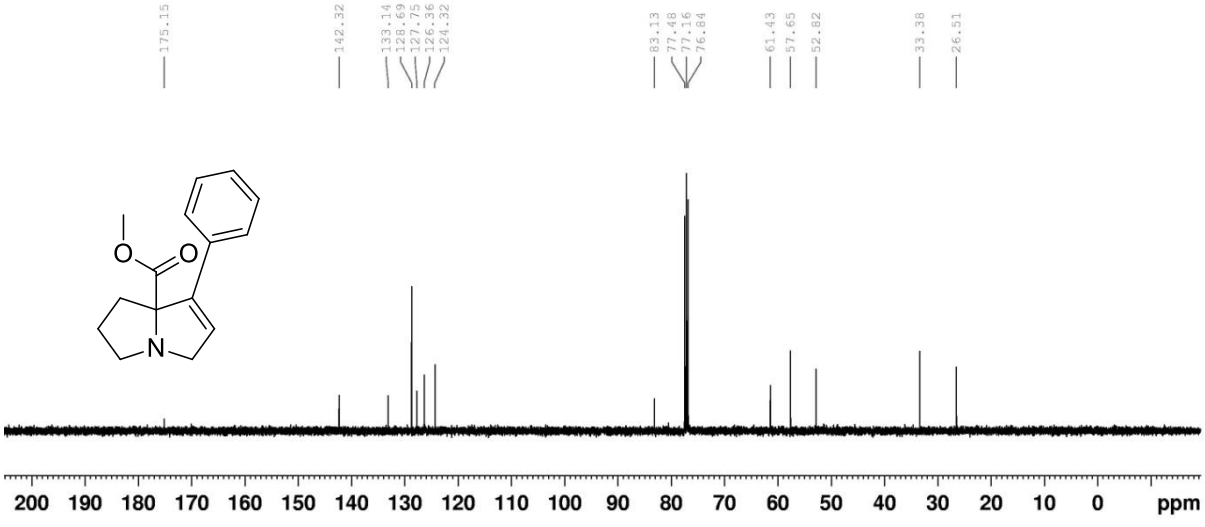


60% Yield; yellow liquid; FT-IR: 2953, 1731, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.20 (t, *J* = 2.2 Hz, 1H), 4.12 (dd, *J* = 16.5 Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.52 (dd, *J* = 16.5 Hz, 2.5 Hz, 1H), 3.32-3.27 (m, 1H), 2.91 (ddd, *J* = 12.2 Hz, 6.8 Hz, 2.4 Hz, 1H), 2.59-2.49 (m, 3H)**,** 2.00-1.89 (m, 1H), 1.87-1.80 (m, 1H), 1.73-1.67 (m, 1H), 1.63-1.55 (m, 2H), 1.35-1.26 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 142.7, 142.2, 130.4, 128.7, 126.2, 123.2, 83.1, 61.4, 57.7, 52.8, 35.7, 33.4, 31.6, 31.2, 26.5, 22.7, 14.2 ppm. HRMS (ESI): Calcd for $C_{20}H_{28}NO_2$ 314.2120; found 314.2120 $[M+H]^+$.

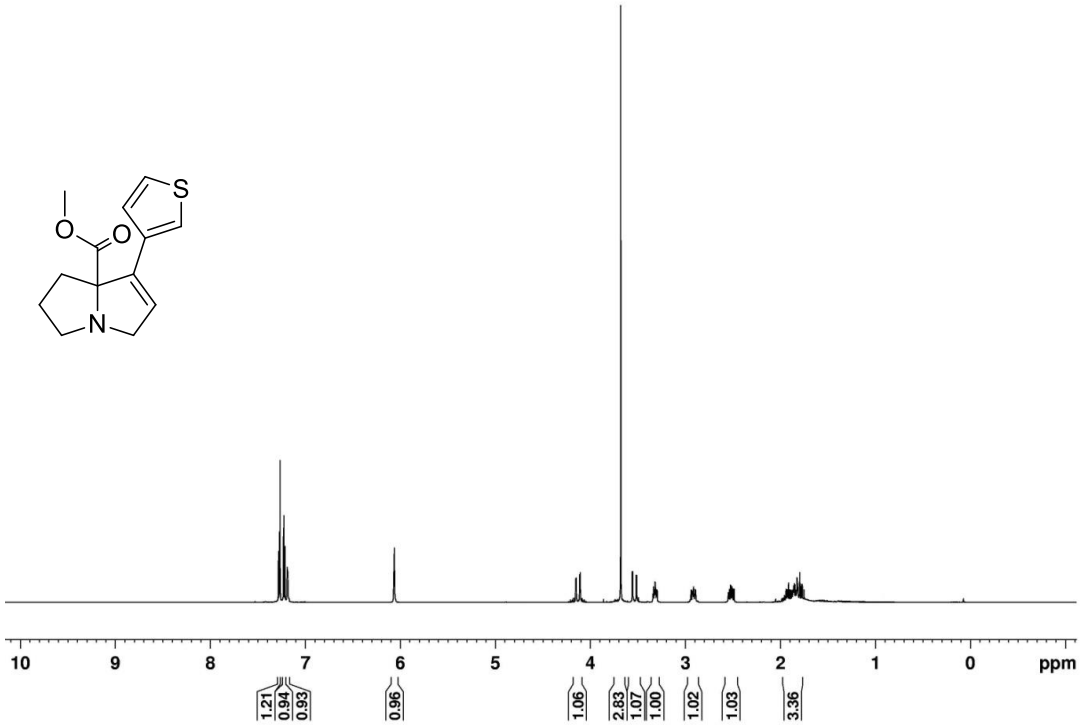
^{1}H spectrum of **35a**



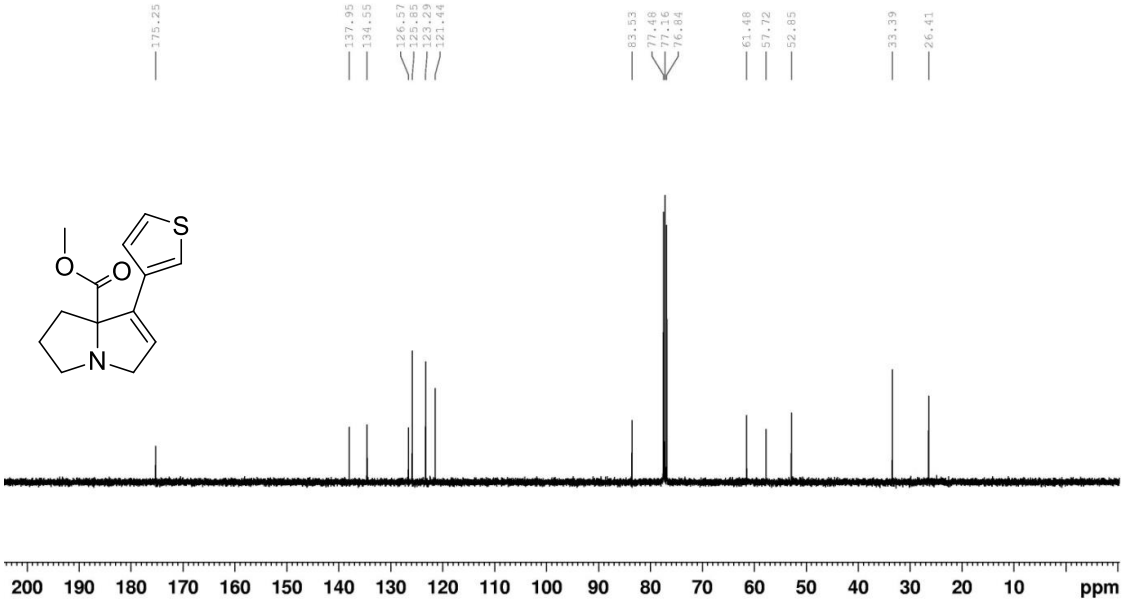
^{13}C spectrum of **35a**



^{1}H spectrum of **35c**



^{13}C spectrum of **35c**



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List of publications

1. "$B(C_6F_5)_3$ catalysed reduction of *para*-quinone methides and fuchsones to access unsymmetrical diaryl- and triarylmethanes: elaboration to beclobrate" **Mahesh, S.**; Anand, R. V. *Org. Biomol.Chem.***2017**, *15,* 8393.
2. "Synthesis of Indolizine Containing Diaryl- and Triarylmethanes through a Cu-Catalyzed Domino Cyclization of 2-(2-Enynyl)pyridines" **Mahesh, S.**; Paluru, D. K.; Ahmad, F.; Patil, S.; Kant, G.; Anand, R. V. *Asian. J. Org. Chem.* doi:10.1002/ajoc.201700419.
3. "Cu-Catalyzed Hydrophosphonylation of 2-(2-Enynyl)pyridines: Easy Access to Indolizine-Containing Diarylmethylphosphonates" **Mahesh, S.**; Anand, R. V. *Eur. J. Org. Chem*. **2017**, 2698.
4. "$B(C_6F_5)_3$ catalysed 1,6-conjugate allylation of *para*-quinone methides: expedient access to allyldiarylmethanes" **Mahesh, S.**; Kant, G.; Anand, R. V. *RSC Adv.* **2016**, *6,* 80718.
5. "Bis(amino)cyclopropenylidene-Catalyzed 1,6-Conjugate Addition of Aromatic Aldehydes to *para*-Quinone Methides: Expedient Access to α,α′-Diarylated Ketones" Ramanjaneyulu, B. T.; **Mahesh, S.**; Anand, R. V. *Org. Lett*. **2015**, *17*, 3952.
6. "*N*-Heterocyclic Carbene Catalyzed Highly Chemoselective Intermolecular Crossed Acyloin Condensation of Aromatic Aldehydes with Trifluoroacetaldehyde Ethyl Hemiacetal" Ramanjaneyulu, B. T.; **Mahesh, S.**; Anand, R. V. *Org. Lett*. **2015**, *17*, 6.
7. "Combining Oxidative *N*-Heterocyclic Carbene Catalysis with Click Chemistry: A Facile One-Pot Approach to 1,2,3-Triazole Derivatives" Ramanjaneyulu, B. T.; Reddy, V.; Arde, P.; **Mahesh, S.**; Anand, R. V. *Chem. Asian J.* 2013, *8*, 1489.
8. "Base mediated 5-*endo*-dig cyclization of *N*-propargyl proline derivatives: A facile entry to pyrrolizidine scaffolds" **Mahesh, S.**; Pareek, M.; Ramanjaneyulu, B. T.; Kaur, G.; Anand, R. V. *Indian. J. Chem., Sec. A* **2013**, *52A,* 1086 (Invited Article for a Special Issue "Complex Chemical Systems").
9. "Silver Catalyzed Double 5-*endo*-dig Cyclization Cascade: A One pot Access to Hetero-arylated Unsymmetrical Triarylmethanes" Paluru, D. K.; Karthik, E.; **Mahesh, S.**; Anand, R. V.; Gautam, U. K. **(manuscript under preparation).**

Conferences/Symposia

- Base Mediated *5-endo*-dig Cyclization of *N*-Propargyl-*L*-Proline Derivatives: A Facile Entry to Pyrrolizidine Scaffolds" **Mahesh, S**. and Anand, R. V.
  Poster presented in *9th Junior National Organic Symposium (J-NOST)* held at the Department of Chemistry, Indian Institute of Science Education and Research (IISER) Bhopal, India (4-6th December, 2013).

- *5-endo*-dig Cyclization of pyridine derivatives *via* Cu-catalyzed hydrophosphonylation : An Expeditious access to indolizine derivatives **Mahesh, S**. and Anand, R. V.
  Poster presented in *Inter IISER-Chem Meet* held at the Department of Chemistry, Indian Institute of Science Education and Research (IISER) Bhopal, India (20-22nd Jan, 2017).

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Education and Work Experience

Jan 2012−Till date	**Ph. D. Student** (Supervisor: Dr. R. Vijaya Anand)	IISER Mohali.
Apr 2011 - Dec 2011	**Trainee Scientist** Anthem Bio-Sciences Pvt. Ltd., Bangalore	Bangalore
2007 – 2009	**M. Sc.** Organic Chemistry	Sai-Sudhir P.G. College, Osmania University, Hyderabad, Telangana, India.
2004 - 2007	**B. Sc.** Maths, Physics, Chemistry	Girraj Govt. College, Telangana University, Nizamabad, Telangana, India.

Research Experience

Ph. D. Details

Thesis Title: **"*Lewis acid catalyzed synthetic approaches toward unsymmetrical diaryl- and triarylmethanes*"**

Thesis Supervisor: Dr. R. Vijaya Anand, Associate Professor, IISER Mohali, India.

Technical Skills

- Handling of phyrophoric and air/moisture sensitive compounds
- Hands-on experience in multinuclear NMR measurements and data interpretation
- HPLC Separation
- Chromatographic purification

Awards and Honors

- Qualified CSIR-UGC (Council of Scientific and Industrial Research-University Grants Commission) test for Junior Research Fellow with 74th rank in 2011.