New Approaches Toward the Synthesis of Furotropones, Benzofurans, Triazoles and Axially Chiral Styrenes

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the degree of Doctor of Philosophy

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Dedicated to…

Aai, Bapu, & Aba

…for their unconditional love, support & encouragement

Declaration

The work presented in this thesis has been carried out by me under the guidance of **Dr. Sripada S. V. Rama Sastry** at the Indian Institute of Science Education and Research Mohali. This work has not been submitted in part or in full for a degree, a 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 acknowledgement of collaborative research and discussions. This thesis is a bona fide record of original work done by me and all sources listed within have been detailed in the bibliography.

Rajendra Pratap Shirke

Place:

Date:

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:

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CONTENTS

Summary

Heterocyclic compounds are widely distributed in nature and they play a vital role in the metabolism of all living cells. Among them, furanoids and triazoles represent one of the most privileged classes of naturally occurring versatile building blocks in synthetic organic chemistry due to their wealth of unique functional, conformational, and stereochemical information. These compounds possess a distinct place in the field of medicinal and pharmaceutical chemistry with diverse biological activities and plays pivotal roles in organic transformation. However, development of general and efficient methods from readily available starting material remains an emerging research area.

The thesis entitled "*New Approaches Toward the Synthesis of Furotropones, Benzofurans, Triazole and Axially Chiral Styrenes*" describes the efforts taken towards the development of novel heterocyclic compounds and synthesis of axially chiral styrene. The content of the thesis has been divided into four chapters. In all the chapters, a brief introduction is provided, the compounds are sequentially numbered (bold), and references are marked sequentially as superscript and listed at the end of the thesis.

This thesis mainly described the design and development of new strategies towards the synthesis of furotropones, benzofurans, triazole and axially chiral styrenes. In this regard, chapter 1 and 2 will highlight the utilization of readily available starting material 3-furancarboxaldehyde towards the synthesis of furotropones and benzofuran.

Tropones are commonly known as non-benzenoid aromatic compounds. Tropones are mainly found in natural products or they can be isolated from plants and fungi. They can be also used significantly against antibiotic-resistant bacteria. In addition, troponoids manifest several different biological activities like antiviral, antitumor, to mention a few. Moreover, tropone derivatives were studying widely from a synthetic, theoretical, photophysical and biological point of view. Among troponoids, furotropones were representing a significant class. Towards this, chapter 1 describes an efficient diversity oriented approach towards the synthesis of functionalized furotropone and benzofurotropones via mild base-mediated cyclization followed by oxidative aerobic aromatization. Further, various photophysical studies like UV-Vis, fluorescence, lifetime, and quantum yields were recorded. In addition, it found was that furotropones show selective fluorogenic sensing properties towards Fe^{3+} ion.

N-Heterocyclic carbenes (NHCs) have been playing an important role in organocatalytic transformations, mainly in carbon-carbon, carbon-heteroatom bond formation and annulation reactions. The synthetic utilities of NHCs have explored in various organic transformations. The importance of NHC catalysis in the area of pharmaceutical sciences and material chemistry holds the key for the ever-growing interest to develop more efficient synthetic protocols. The chapter 2 discusses a NHC catalyzed efficient approach for the synthesis of highly functionalized dihydrobenzofuranones. After the successful development of intramolecular NHC catalyzed cross-benzoin reaction, the synthetic utility of this methodology was demonstrating a one-step elaboration towards benzofurans. The $POCl_3$-mediated reaction of dihydrobenzofuranone furnished the benzofurans in good yields.

Over the past few decades, versatile methodologies to employ azide as an aminating agent for the synthesis of nitrogen containing compounds such as azoles, nitriles, amides, quinolone, pyrrole, pyridine, etc. have been developed. The importance and unique chemical reactivity of azides have attracted the attention of modern chemists toward the development of novel methodologies. Herein, chapter 3 describes the development of efficient organocatalytic radical β-azidation reaction of enone via electron acceptor-donor-complex with Zhdankin reagent. Subsequently, a series of one-step elaboration of the azides have demonstrated to access tricyclic triazoles and 1,4-disubstituted triazoles.

On the other hand, axially chiral compounds are widespread in biologically active or medicinally important compounds and being used as a chiral ligands or organocatalysts in asymmetric catalysis. With respect to other alkenes, styrenes are one of the most abundant and important building block for the chemical synthesis and their enantiomers exist due to the restricted rotation around a single bond between a substituted alkene and an aromatic ring. Therefore, the establishment of new approaches towards the atroposelective synthesis of styrenes is an important task in organic chemistry. Here, in chapter 4 describes the effort taken towards the efficient synthesis of axially chiral styrenes via Suzuki-Miyaura cross coupling reaction. In an attempt to develop atropselective Suzuki coupling reaction various combinations of bases, ligands, solvent and Pd catalyst evaluated. An excellent enantioselectivity observed with the combination of $Pd_2(dba)_3$ and BOX catalyst.

LIST OF ABBREVIATIONS

λabs	absorption maxima
Aq	aqueous
Atm	atmospheric
Brs	broad singlet
Calcd	calculated
Cod	cyclooctadiene
°C	degree celsius
d	doublet
d	day(s)
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DCM	dichloromethane
dd	doublet of a doublet
ddd	doublet of a doublet of doublet
DMAP	4-dimethylaminopyridine
DMF	*N*,*N'*-dimethyl formamide
DMSO	dimethyl sulfoxide
dq	doublet of a quartet
dr	diastereomeric ratio
dt	doublet of a triplet
λemi	Emission maxima
ee	enantiomeric excess
eq	equivalents
ESI	electron spray ionization
FT-IR	Fourier-transform infrared spectroscopy
H	hour(s)
HRMS	high-resolution mass spectrum
Hz	Hertz

IBX	2-iodoxybenzoic acid
Ipc	diisopinocamphenyl
J	coupling constant
M	multiplet
Mg	milligram(s)
MHz	megahertz
Min	minute(s)
mL	milliliter(s)
mmol	millimole(s)
mp	melting point
MS	molecular sieves
m/z	mass/charge
µL	Microliter (s)
µm	Micrometre (s)
NMF	N-methylformamide
ppm	parts per million
*n*Pr	*n*-propyl
p-TSA	*para*-toluenesulfonic acid
q	quartet
qd	quartet of doublet
rt	room temperature
s	singlet
sept	septet
t	triplet
*t*Bu	*tert*-butyl
td	triplet of a doublet
tert	tertiary
THF	tetrahydrofuran
TMS	trimethylsilyl
TMS	tetramethylsilane
TLC	thin layer chromatography

UV	Ultraviolet
Vis	Visible
Φ_f	Quantum yield
τ_f	lifetime of fluorescence

Chapter 1

Modular assembly of furotropones, benzofurotropones and study of their physicochemical properties

In the middle of the nineteenth century, many advances were made in chemical sciences concerning the new invention, breakthrough, evaluation or synthesis of many new compounds, and non-benzenoid aromatic compound were among them. Tropones belong to the class of non-benzenoid aromatic compounds they are also known as troponoids or tropolonoids, Fig 1.[1] Tropones are mainly found in natural products or they can be easily isolated from plants and fungi. There has been much consideration towards the synthesis of tropones and screening of their different pharmacological activities. Although the simplest tropone is not naturally

available (R=H), Fig 1.[1] However, tropones having numerous facet side chains on the 7-membered ring, such as hydroxyl, isopropyl, acetyl or even different bulky teams, like alkaloid, terpenoid, flavonoid etc, are widely found in nature.[2] These derivatives have been frequently used as a building block for several functional transformations. Still, there a few studies on them, most likely owing to their limited occurring quantity, distribution, or diversity of troponoids as compared with different natural products.

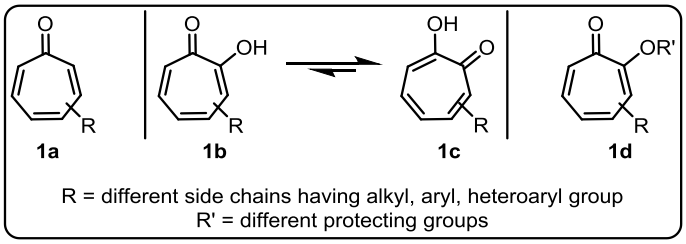


Fig 1: Tropone, tropolone and its derivative

Troponoids have attracted in-depth studies for various important biological activities. They significantly were used against antibiotic-resistant bacteria. They are also used as anticancer and antifungal agent. Troponoids manifest several different biological activities like antiviral, antitumor, inhibitor, insecticidal or accelerator substance activities, to mention a few.[3] In addition, they have monumental potential to be lead structures for the planning of vital medicinal compounds. In 1960s, the studies of troponoid compounds concerning the identification of its chemical structure, biological activity, photochemistry or biosynthesis were studied. These studies have a guide to a deep understanding of troponoids properties with respect to the structure-activity relationship. Further, phytochemistry and medicinal study on troponoid compounds again started from the early 1990s, once scientists started a large-scale screening of natural products for anticancer drugs.

Troponoids are chiefly distributed in plant species, such as needle tree *gymnosperm* and grass *liliaceae* family, Fig. 2.[4] Moreover, tropolone itself isolated from *Pseudomonas*. On the other hand, simple and complex tropones, possessing completely different biological activities are also rife in various types of plants. Like, bicyclic tropone Cordytropolone was isolated from a fungal insect pathogen *Cordyceps* showing antifungal activity. Tricyclic, tetracyclic or pentacyclic troponoids containing heteroatoms exist in nature. Malettinins E isolated from an

unidentified, non-sporulating fungal colonist, *Mycelia sterilia* as an antibacterial agent. Utahin is the only tricyclic troponoids or ditropolonofuran isolated from the tree *juniperus utahensis*.

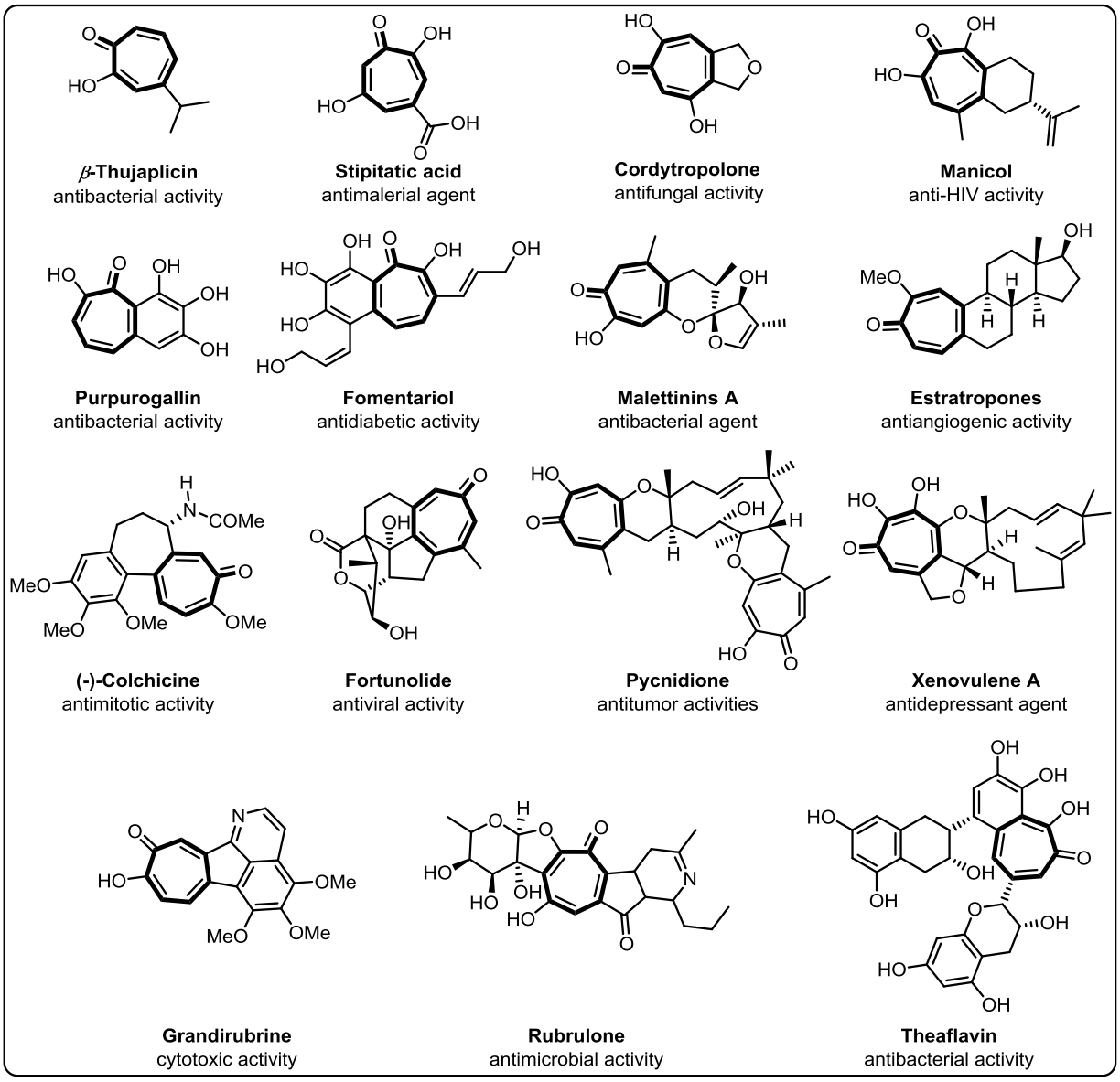


Figure 2: Natural products and pharmaceutically important molecules possessing tropone

Xenovulene A was isolated as co-metabolite from *Acremonium strictum* as an antidepressant agent. The complex molecular structure possessing two fused seven-membered rings colchicine and its derivative are found in *colcicum species* as well as the plant of other species like *lilliaceae* showing antimalarial and anti-mitotic activities. Hexacyclic diterpenoid tropone Hainanolidol and Fortunolide were isolated from the plants *Cephalotaxus hainanensis*

and C. fortune, which possess antineoplastic and antiviral activities. Manicol is simple sesquiterpene troponoid isolated from the *guyanan* tree exhibit anti-HIV activity. Polyphenolic compound theaflavin is an antibacterial agent.

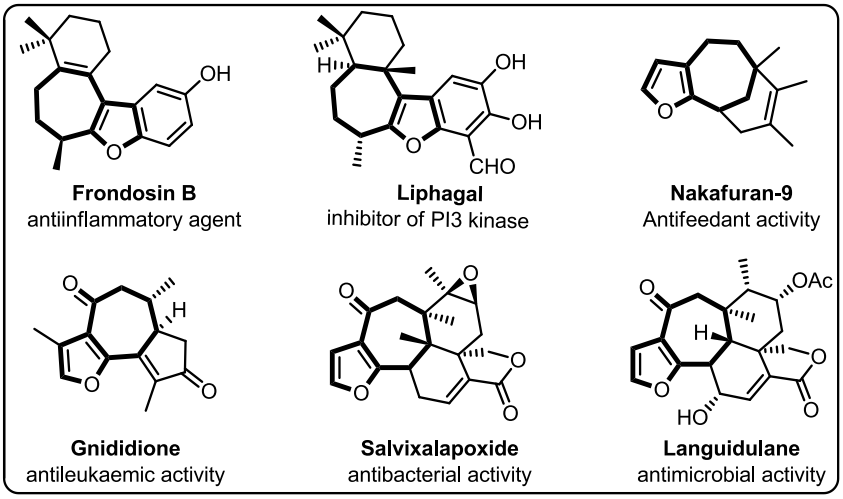


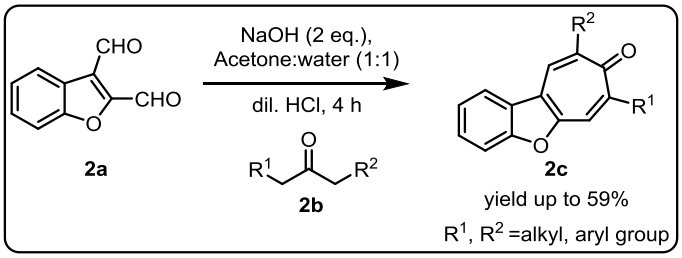
Figure 3: Natural products accessible from furotropone and benzofurotropones

Several cyclohepta[*b*]furans are well known in the literature having various biological activities, Fig. 3.[5] For example, Frondosin B isolated from *dysidea frondosa* along with its five important derivatives are anti-inflammatory agents. Liphagal isolated from the sponge *aka coralliphaga* has selective inhibitor of PI3 kinase activity. Medicinally important salvixalapoxide secluded from the leaves of *salvia xalapensis* exhibit antibacterial activity. New classes of diterpene languidulane were isolated from *salvia tonalensis*. Furanosesterterpene nakafuran-9 was isolated from the South African nudibranch *hypselodoris capensis* and dictyoceratida sponges along with other derivatives as antifeedant agents.

Tropones are notable topic of interest and continue to be one of the most active research areas in organic chemistry. Towards this, various methods have been developed for the synthesis of tropones.[6] Few important methods leading to the synthesis of furotropones and benzofurotropones is discussed in the next subsection.

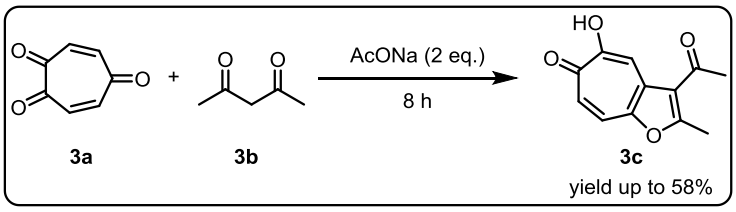
1.1: Novel approaches for the synthesis of furotropones and benzofurotropones

In 1975, Shafiee[7] independently reported the synthesis of 7,9-disubstituted-8*H*-cyclohepta[*b*]benzo[*d*]furan-8-ones **2c,** Scheme 1. The reaction between diformylbenzofuran **2a** and ketone **2b** under basic condition resulted in the formation of substituted benzofurotropone **2c** in moderate yield. This reaction opened a new avenue in the area of furotropone synthesis.



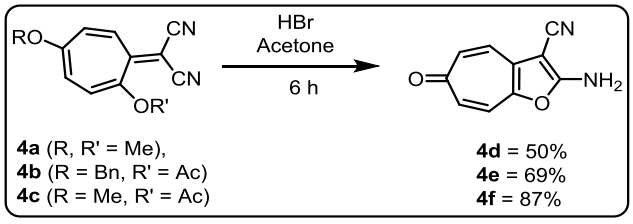
Scheme 1: Shafiee's synthesis of benzofurotropones

In 1976, Ito *et al.*[8] described an easy method for the synthesis of hydroxyfurotropone **3c**, Scheme 2. The cyclization reaction of cyclohepta-3,6-diene-1,2,5-triones **3a** with acetyl acetone **3b** in presence of sodium acetate afforded substituted furotropones **3c** in moderate yield.



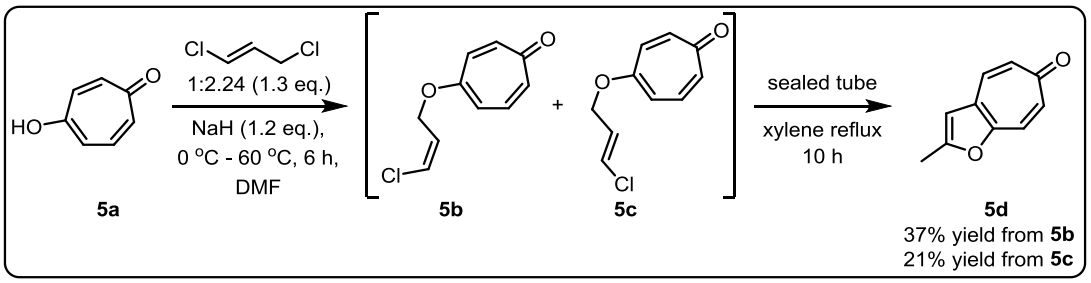
Scheme 2: Ito's hydroxyfurotropones synthesis

In 1991, Takeshita *et al.*[9] have reported the synthesis of functionalized furotropones, Scheme 3. The acid hydrolysis reaction of 8,8-dicyanoheptafulvene **4a-4c** delivered the cyclized product, 2-amino-3-cyano-6[*H*]-cyclohepta[*b*]furan-6-one **4d-4f** in moderate yields.



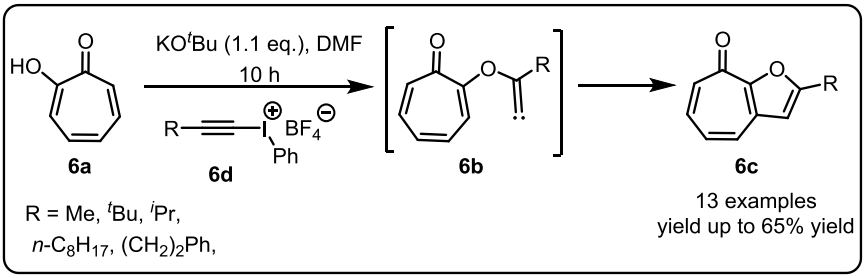
Scheme 3: Takeshita's synthesis of functionalized furotropones

In 1994, Takeshita *et al.*[10] described a novel Claisen rearrangement pathway for the synthesis of furotropones by employing hydroxytropone **5a**, Scheme 4. The process involves initial substitution reaction of 4-hydroxy tropone **5a** with allyl bromide in the presence of NaH (60% dispersion in oil) led to the formation of two different isomers **5b** and **5c**. Further, heating of **5b** and **5c** in the sealed tubes were resulted in the formation of furotropone **5d** in 37% from (*E*)-isomer **5b** and 27% in (*Z*)-isomer **5e** via cascade Claisen rearrangement and cyclization reaction.



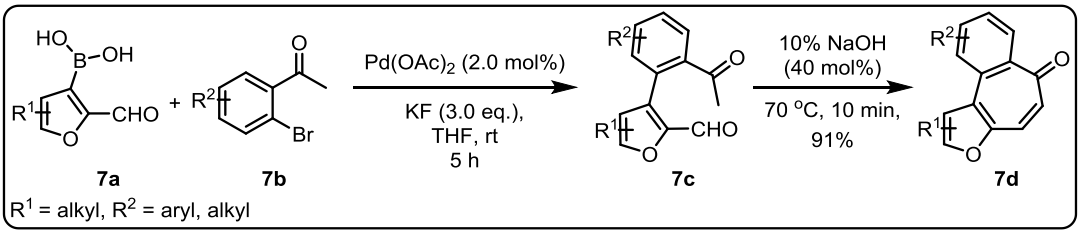
Scheme 4: Takeshita's Claisen rearrangement pathway for furotropone

In 1996, Ochiai *et al.*[11] reported simple tandem-Michael carbene insertion reaction pathway to synthesize substituted furotropones **6c**, Scheme 5. The base-mediated cyclization reaction between aIkynyl(phenyl)iodonium salts and tropolone **6a** afforded furotropones **6c** in moderate to good yield.



Scheme 5: Ochiai's tandem Michael carbene insertion reaction

In 2009, Heo *et al.*[12] described an efficient synthesis of fused furotropones via sequential Suzuki-Miyaura cross-coupling reaction followed by aldol condensation, Scheme 6. The coupling reaction between (3-formylfuran-2-yl)boronic acid **7a** with reactive 2'-bromoacetophenone **7b** resulted in the formation of coupled product **7c** and subsequent intramolecular base-mediated aldol condensation reaction furnished furotropone **7d** in high yield.

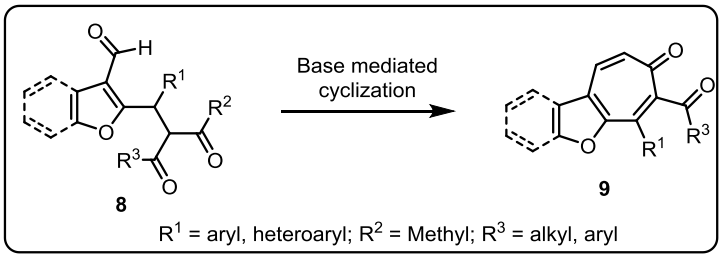


Scheme 6: Heo's synthesis of fused furotropone

Among annulated tropone derivatives, heteroaromatic tropones are not well explored concerning to their synthesis and photophysical properties and have been attracted the interest of scientists in the modern era.[13] Among troponoids, furotropone represents a significant class. Further, there are few unresolved challenges for the synthesis, for example (i) The instability of furan moiety which leads to various side reaction during the process (ii) Difficult to access starting material as it involves construction of five and seven membered rings (iii) The synthesis requires harsh reaction condition leading to different side reactions, and (iv) it requires multistep synthesis. Consequently, the development of a general and efficient protocol for highly functionalized furotropones remains challenging.

1.2: Results and discussion

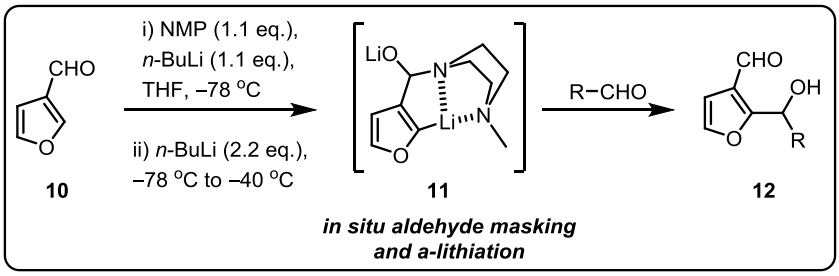
Detailed literature surveys were revealed that there is no general and straightforward strategy for the synthesis of furotropones and benzofurotropones. Toward this, we have initiated analysis to ascertain a brief, economical and ascendible approach for the synthesis of previously unknown furo[2,3-*d*]tropones, Scheme 7.[14] In addition, to address the synthetic challenges related to furotropones we have designed a model substrate **8** starting from easily available furan/benzofuran-3-carboxaldehyde.



Scheme 7: Our design for the synthesis of furotropones and benzofurotropones

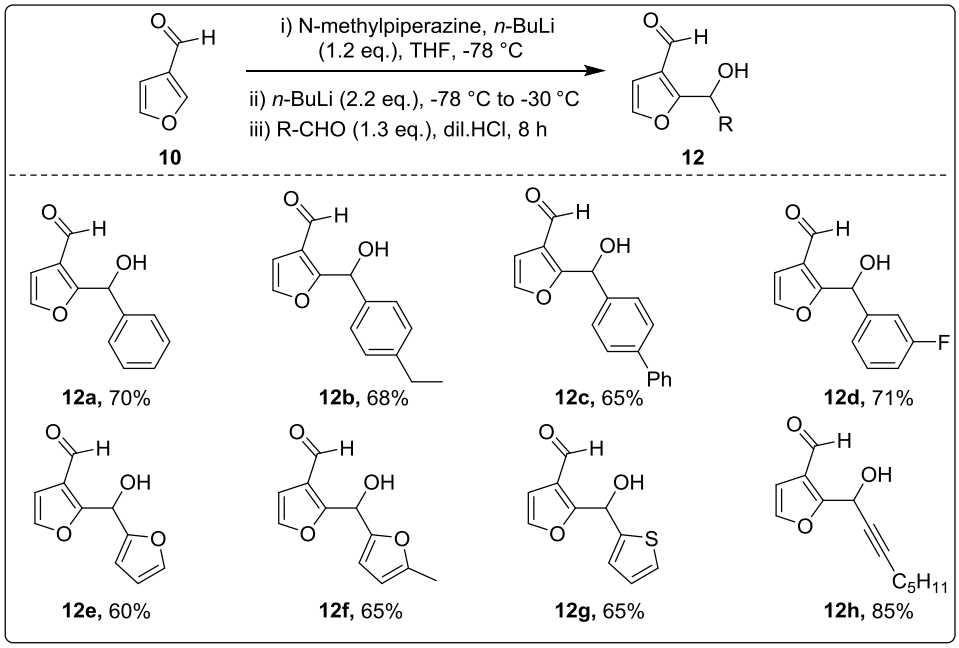
1.2.1: Synthesis of furotropones and benzofurotropones

For the synthesis of functionalized furotropones, we have relied on a synthesis of the two-step starting material as reported on literature, Scheme 8.[15] A modular synthesis of 3-formyl-2-furylcarbinols **12** was easily achieved by regioselectivity directed chelation controlled α-lithiation strategy. In situ masking of aldehyde functionality in 3-furancarboxaldyde **10** by lithium N-methylpiperazide (generated from NMP and *n*-BuLi) and subsequent chelation controlled C-2 (α-lithiation) alkylation **11** with commercially available aldehyde led to the formation of enol **12**. This reaction was found to be optimal with THF solvent in lower temperature and working well for alkyl, aryl, and heteroaryl aldehyde in moderate to good yield of the respective product, result is summarized in Table 1.

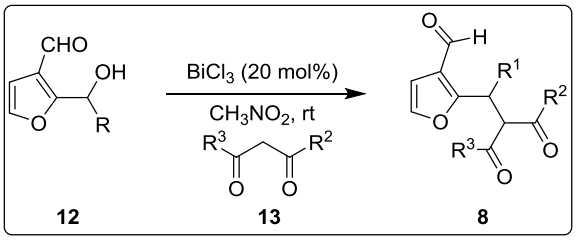


Scheme 8: Synthesis of 3-formyl-2-furylcarbinols **12** by following our earlier report

Table 1: Synthesis of 3-formyl-2-furylcarbinols **12**

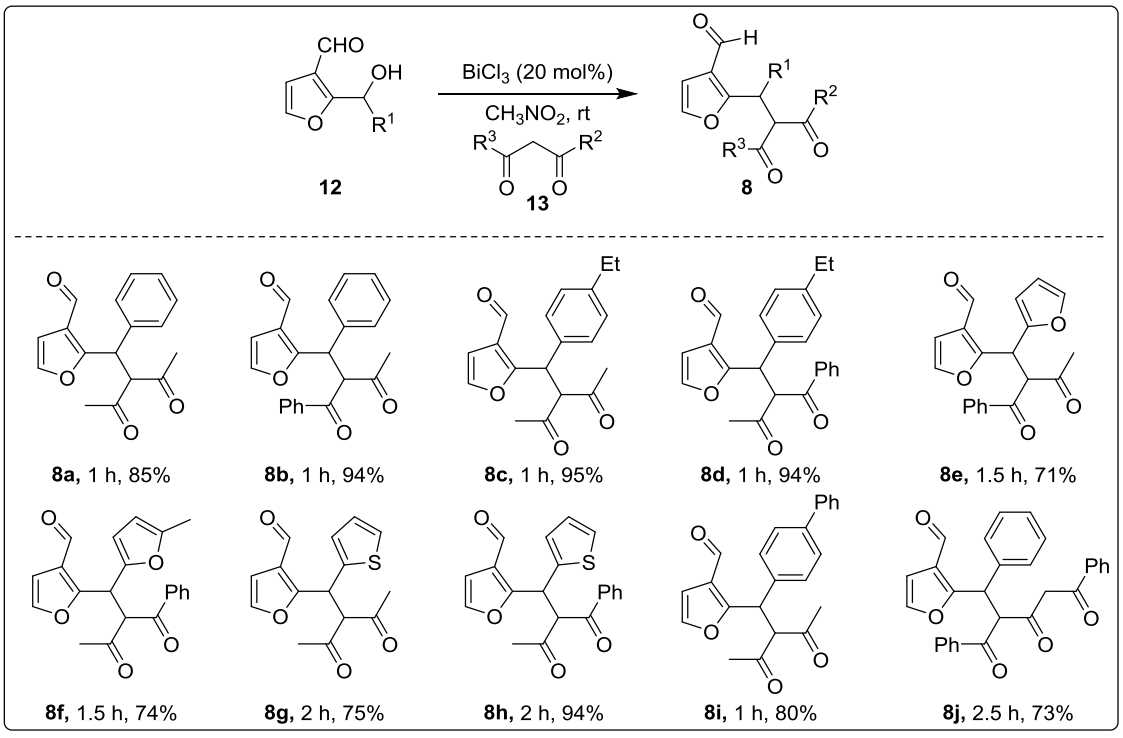


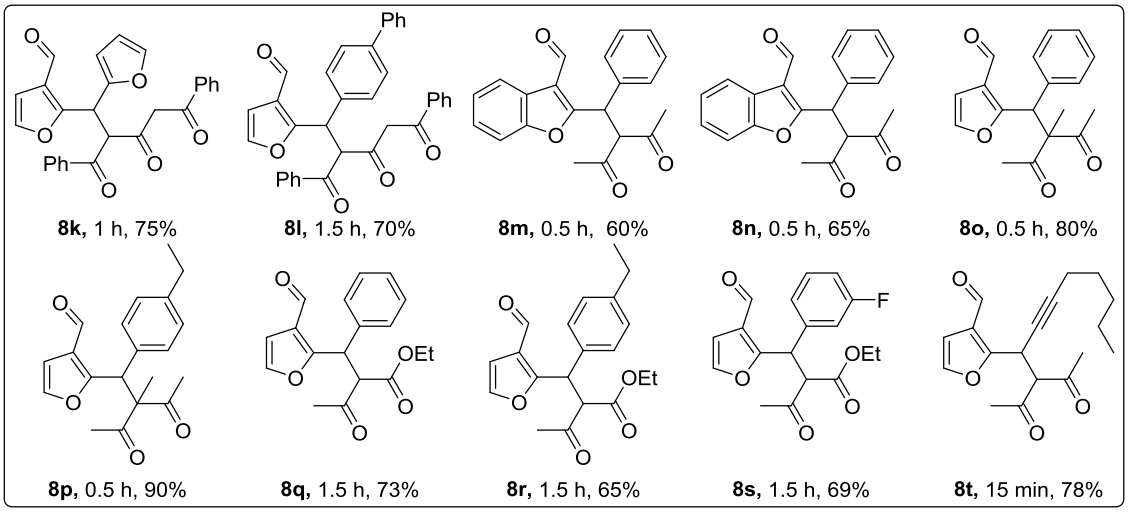
Subsequently, the required starting material was prepared according to the strategy described in the literature, Scheme 9.[16] The $BiCl_3$ catalyzed substitution reaction of furylcarbinols **12** and 1,3-dicarbonyl **13** furnished **8** in good to excellent yields. Various Lewis acid, Brønsted acid catalysts were screened for this reaction. Delightfully, Bi(III) found to be the best catalyst and delivered the desired product in good to excellent yield. Different 1,3-dicarbonyl or 1,3,5-tricarbonyl compounds were utilized as an active nucleophilic source and found to be very excellent in selectivity and product formation, Table 2.



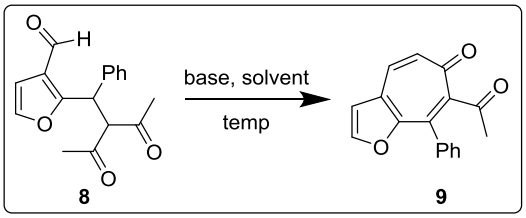
Scheme 9: Synthesis of diketoaldehyde **8** by following our earlier report

Table 2: Synthesis of diketoaldehyde **8**





After successfully achieving two-step synthesis of starting material, we have turned our attention to investigate the entropically advantageous intramolecular reaction for the synthesis of functionalized furotropones, Scheme 10. Towards this, diverse range diketoaldehyde substrates were subjected to optimized condition, Table 3.

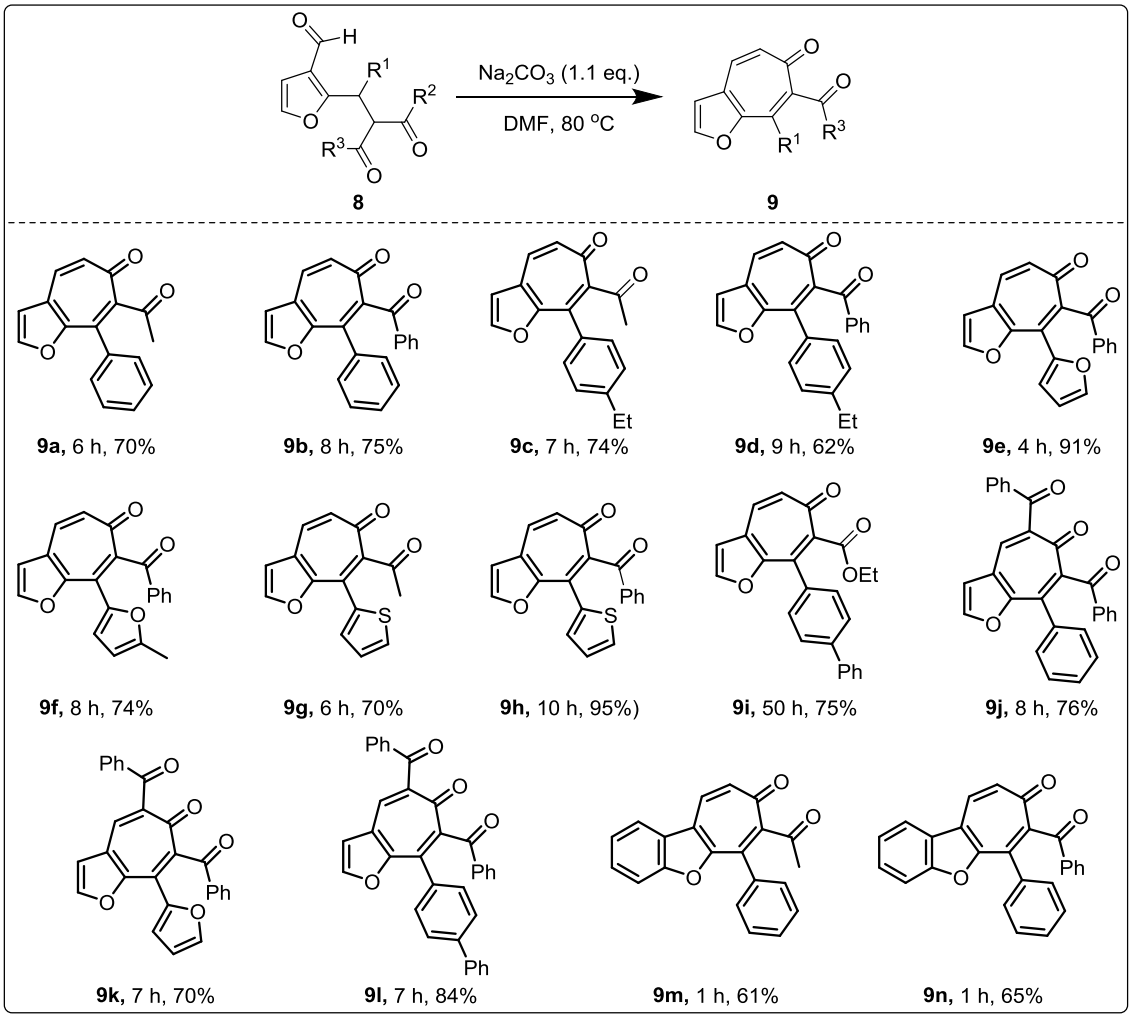


Scheme 10: Synthesis of functionalized furotropones and benzofurotropones

The reaction of various substituted and unsubstituted dicarbonyls with base furnished respective products in good to excellent yields. The diketoaldehyde adduct of acetyl acetone having substituted aryl or heteroaryl appended to furan **8a, 8c, 8g** and **8i** delivered the tropone **9a, 9c, 9g** and **9i** in good yield, while in case of benzofuran **8m** furnished the tropone **9m** in a moderate yield in short reaction time. On the other hand, diketoaldehyde adducts of benzyl acetone appended furan **8b, 8d, 8e, 8f** and **8h** delivered the respective tropone **9b, 9d, 9e, 9f** and **9h** in good to excellent yields, while in case of benzofuran **8n** furnished the tropone **9n** in moderate yield. The triketoaldehyde adduct of 1,3,5-triketone appended furan **8j-8l** delivered the respective furotropone **9j-9l** in good yields. The intramolecular aldol reaction with

diketoaldehyde or triketoaldehyde adducts were realized to be general, efficient, and a diverse range of tropones assessed in good to excellent yields.

Table 3: Substrate scope of functionalized furotropone



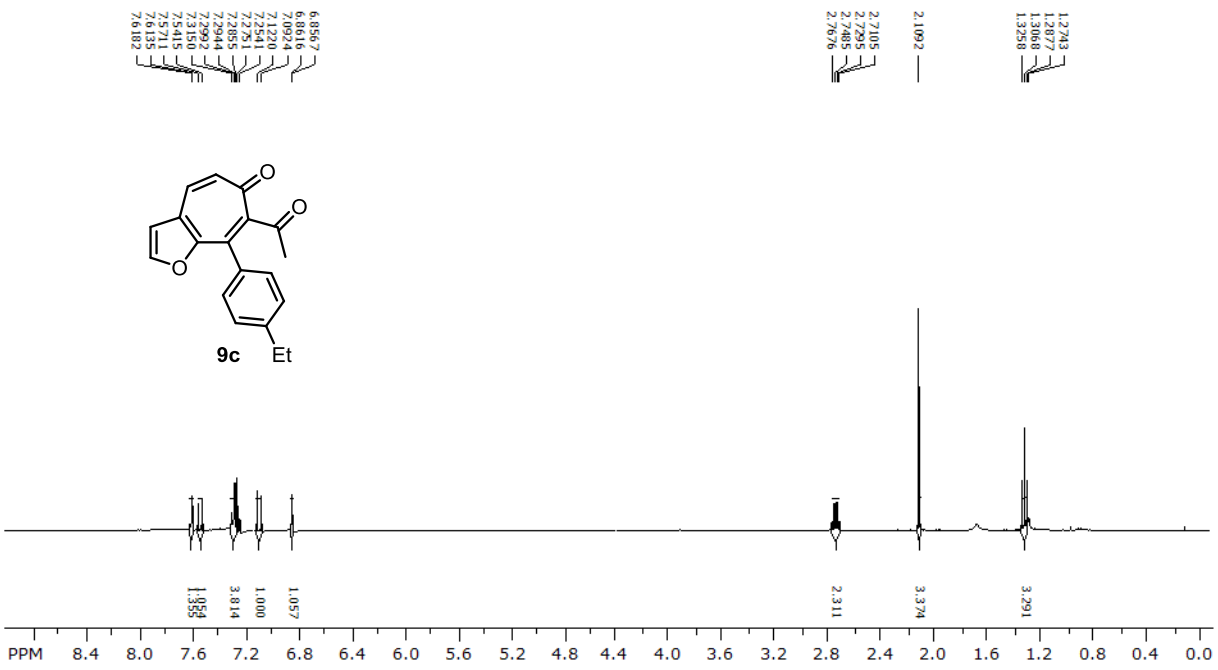


Figure 4: ^{1}H-NMR spectrum of **9c**

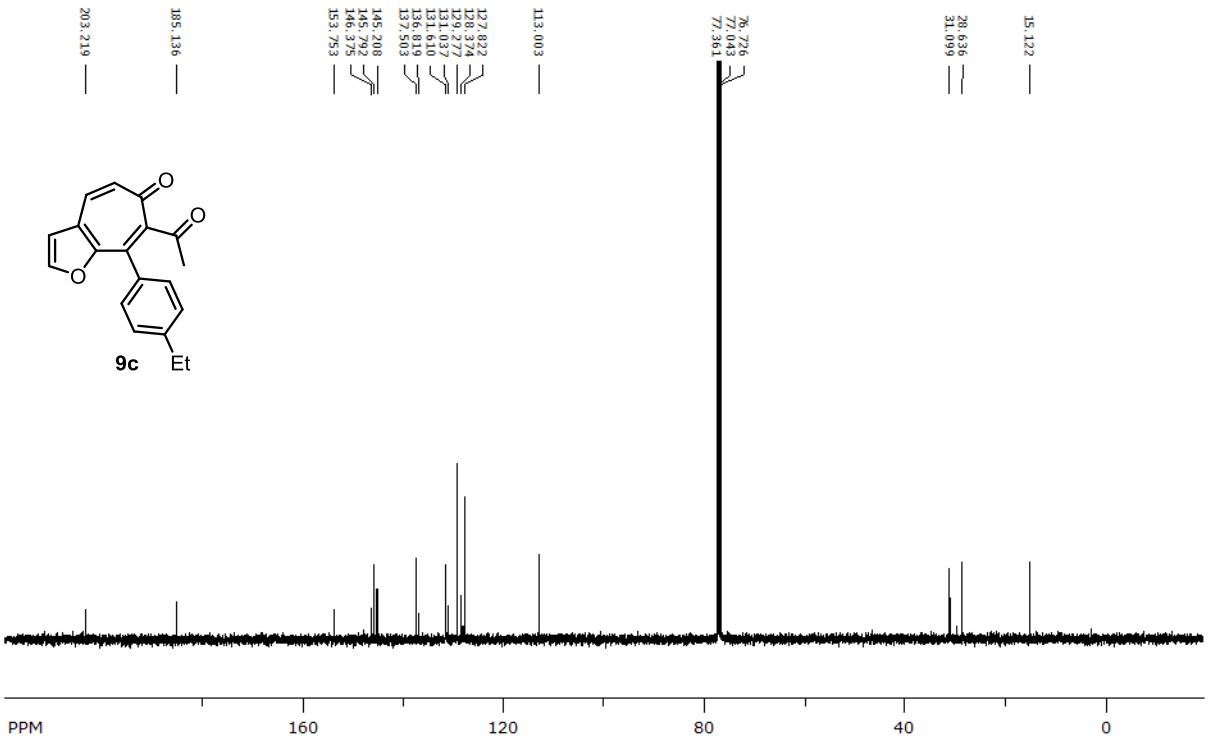
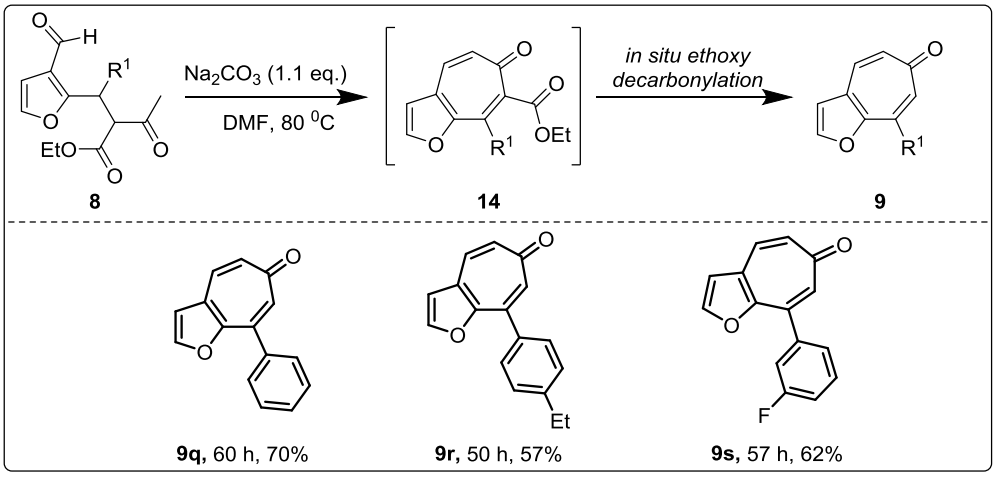
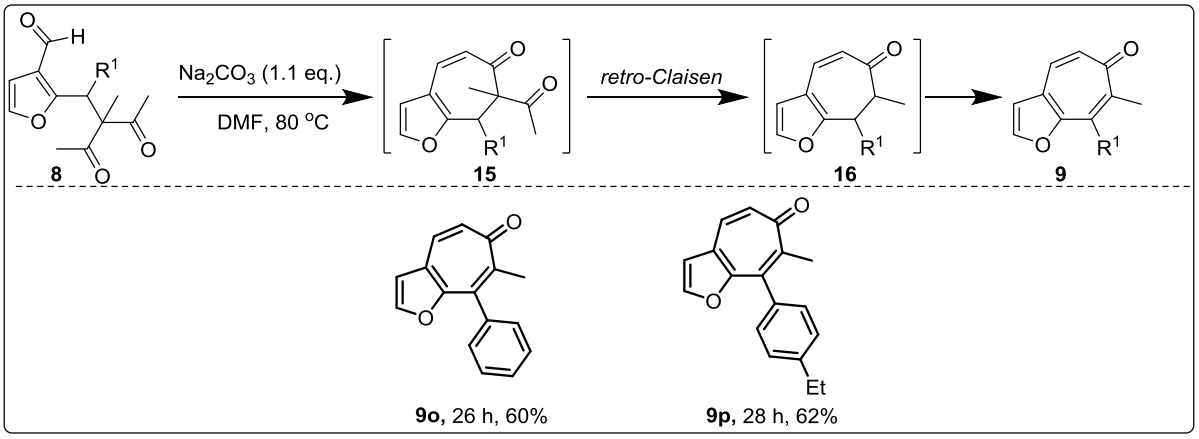


Figure 5: ^{13}C-NMR spectrum of **9c**



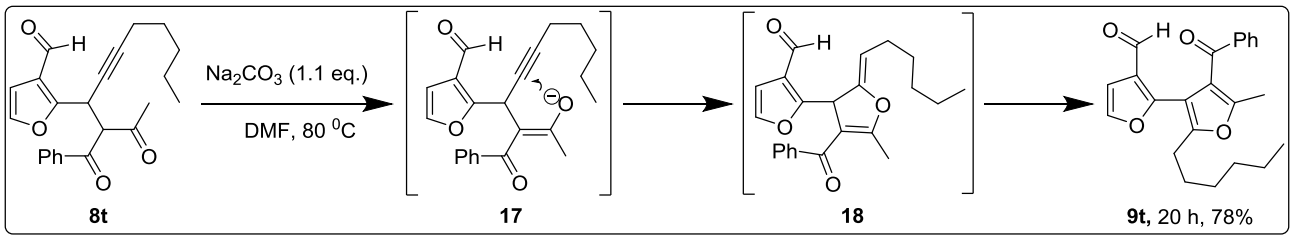
Scheme 11: Synthesis of mono substituted furotropones via in situ ethoxy decarbonylation

After exploring the substrate scope of furotropones having various aryl and heteroaryl substituents, we have also evaluated the scope and limitation of this transformation by varying ketoester and the results are summarized in, Scheme 11. Treatment of diketoaldehyde adduct of ethyl acetoacetate **8q-8s** appended to furan was subjected under the optimized condition, delivered the decarboxylated furotropone **9q-9s** in moderate yield. On the other hand, ketoester adduct of ethyl acetoacetate having biphenyl **8i** delivered esterfurotropone **9i** in good yield. Here, we didn't observe the decarboxylated product formation even though the reaction was continued for a prolonged time.



Scheme 12: Synthesis of disubstituted furotropones via retro-Claisen condensation

After realizing a facile transformation of the diketoaldehyde and ketoesteraldehyde under the optimized condition, we have thought to expand the substrate scope of furotropone possessing different functionality. Interestingly, when we treated diketoaldehyde adduct of 3-methyl-2,4-pentadione having arenes appended to furan **8o, 8p** under the optimized condition delivered the unexpected α-methyl furotropone **9o, 9p** via in situ retro-Claisen followed by aromatization reaction in moderate yield, Scheme 12.



Scheme 13: Synthesis of 2,3-bifuran derivatives

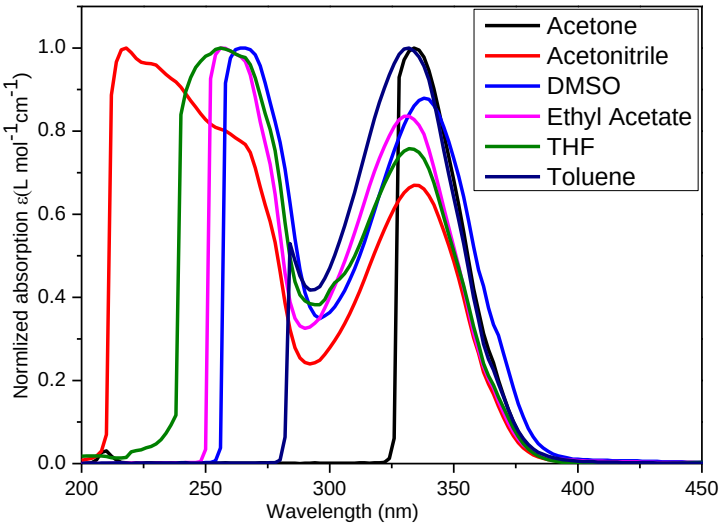
Surprisingly, when we subjected diketoaldehyde possessing alkyne functionality **8t** under the standard optimized condition delivered the unexpected 4'-benzoyl-2'-hexyl-5'-methyl-[2,3'-bifuran]-3-carbaldehyde **9t** unlike expected furotropone in 78% yield, Scheme 13. A general and straightforward mechanism was proposed that rationalizes the transformation of diketoaldehyde into furotropone under basic conditions. Synthesis of bifuran **9t** involves a subtle rearrangement of diketone and alkyne leading to cyclization and subsequent aromatization leading to 2,3'-bifuran.[17] This method involves the simple and useful approach for the synthesis of substituted difuran derivatives, which are otherwise difficult to access.

1.3: Photophysical properties of functionalized furotropones

In the last few decades, principle photophysical properties of tropones like circular dichroism, electroluminescence, molecular and electronics study were documented in the literature.[18] However, no attempt was made to understand the photophysical properties of furotropones. Thus, we intended to analyze the photophysical properties of furotropones. Eight different functional furotropones were chosen for analyzing the photophysical study. UV-Vis and emission spectra were recorded at 10μM concentration with a different combination of solvents. Therefore, we began our study by initially recording the UV-Vis properties of **9r** under the

different solvent (non-polar to polar). Among the solvents screened, the absorption band due to *n*-π* transition was observed in the range of 332-338 nm. A non-polar solvent like toluene exhibited an absorption maximum at 332 nm while the polar solvent exhibited the absorption maximum at 338 nm indicating the bathochromic shift (red shift) of about 6 nm. On the other hand, the absorption band due to π-π* transition was observed in the range of 266-284 nm showing the hypsochromic shift (blue shift) of about 18 nm from toluene to DMSO Fig. 6 (I). Additionally, UV-Vis absorption spectra of few other di- and triketofurotropones were recorded and the results are summarized in Fig. 6 (II).

(I)



(II)

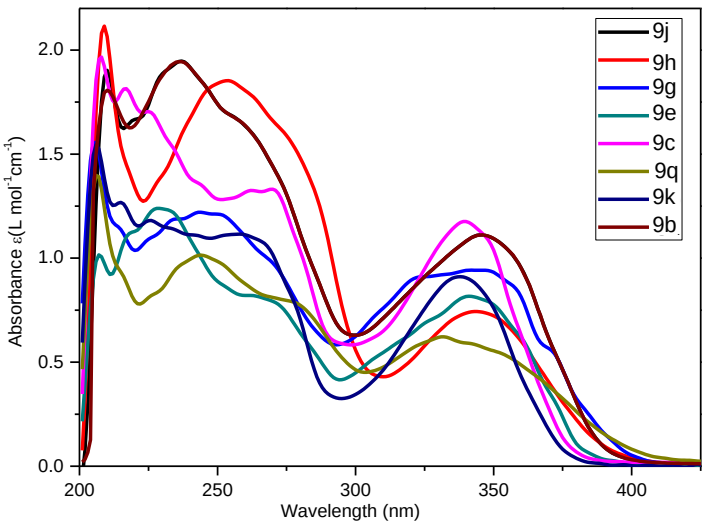
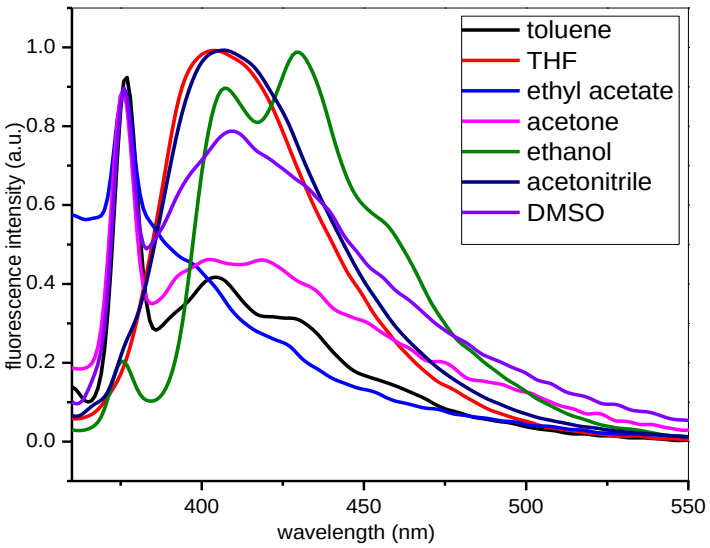


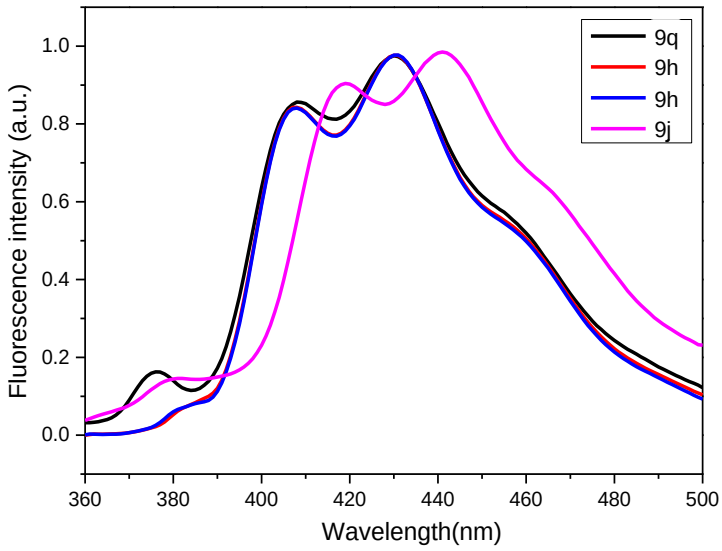
Figure 6: (I) UV-vis absorption spectra of **9q** (10 μM) in different solvents. (II) UV-vis absorption spectra of **9b, 9c, 9e, 9g, 9h, 9j, 9k** and **9q** in ethanol (10 μM)

Next, we have focused on the fluorescence emission for these compounds. The emission spectra of all compounds were recorded at the same concentration by exciting the respective solutions at their absorption maxima (longer wavelength). Fluorescence emissions of **9q** were recorded in different solvents at 10 µM concentration by exciting the molecule at 340 nm. The fluorescence was found to be strongly dependent on solvent and concentration of respective compounds and the result are summarized in Fig. 7 (III). Single Strong emission was observed for THF and ACN at 402, 410 nm respectively. Fluorescence emission band for DMSO solvent observed with less intensity, whereas EtOH showing the highest emission value at 376 nm. Further, fluorescence emissions were recorded for the different compounds **9b, 9c, 9e, 9g, 9h, 9j, 9k** and **9q** at the same concentration by exciting the respective solution at their absorption maxima, Fig. 7 (IV) and (V).

(III)



(IV)



(V)

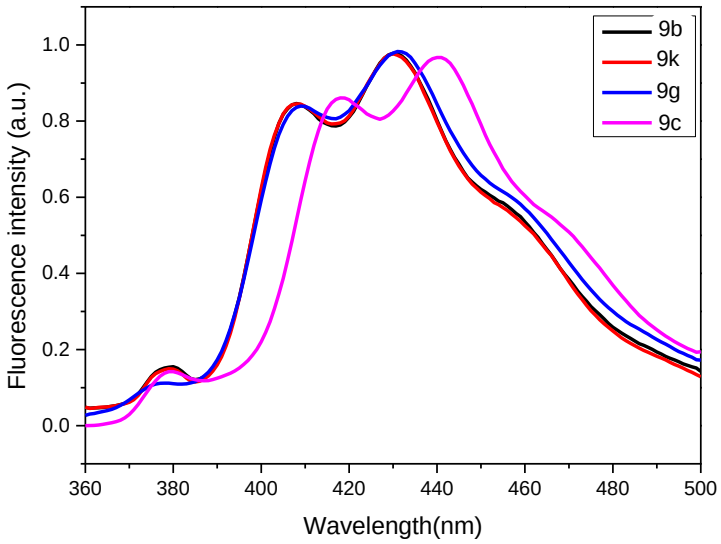


Figure 7: (III) Fluorescence emission spectra of **9q** (10 μM) in different solvents (IV) Fluorescence emission spectra of **9q, 9h,9, 9j** (10 μM) in EtOH (V) Fluorescence emission spectra of **9b, 9g, 9c, 9k** (10 μM) in EtOH

With the fascinating electronic structure and fluorescence emission result, we were interested to find out the fluorescence lifetime as it gives detailed information regarding actual time spent by fluorophore in the excited state before it coming back to the ground state. Initially, fluorescence lifetime was recorded for **9r** in different solvent and found to be maximum in THF (5.89 ns) and least in ethanol (1.34 ns), Table 4. Further, the fluorescence lifetimes of eight different compounds were also measured in EtOH and it lies within 1.08 to 1.44 ns. These results perhaps indicate inherently rigid electronic nature and thus least solvent polarity dependency of furotropones. These results further point to their strong nonpolar character and possible absence of push-pull electronic effects in the excited state. On the other hand, stokes shift and molar absorptivity calculated for functional furotropone. Interestingly, maximum stokes shift (97 nm) observed in DMSO while minimum stokes shift observed in acetone (41 nm) for **9r,** Table 4. Meanwhile, stokes shifts for different compounds were recorded and found to be maximum in (95 nm) for **9j**. Molar absorptivity was recorded for **9r** in different solvent and all eight different compounds were recorded with EtOH solvent. For **9r** molar absorptivity was found to the

maximum in THF solvent (10.84) and minimum in toluene (4.17) and all results summarized in Table **4** and **5**).

Table 4. Photophysical data of **9q** in different solvents.

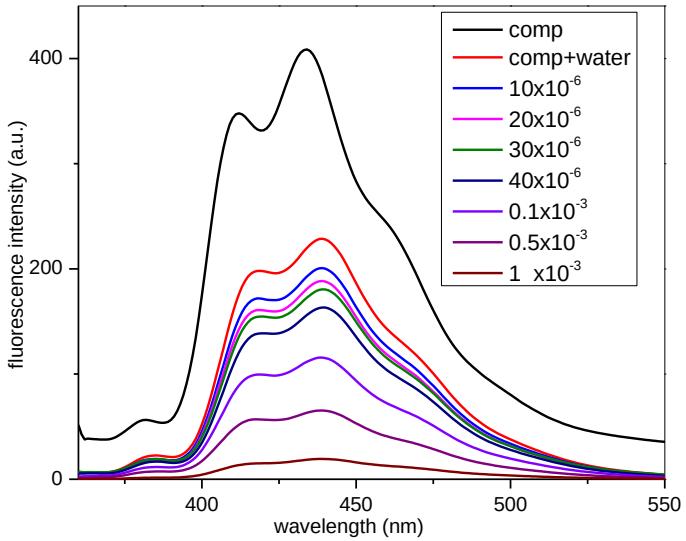
Solvents	λ_{abs} **(nm)**	**ε**	**log ε**	λ_{emi}**(nm)**	$D\lambda_{stokes}$**(nm)**	τ_f **(ns)**	Φ_f
THF	256, 330	10.84	1.035	402	72	5.89	0.0048
ACN	260, 334	8.72	0.940	410	76	3.13	0.0145
Toluene	284, 332	4.17	0.620	406	74	2.38	0.0011
DMSO	266, 338	5.09	0.706	435	97	3.31	0.0017
Acetone	210, 334	8.34	0.921	375	41	1.41	0.0036
EtOAc	256, 332	7.90	0.897	376	44	1.47	0.0083
Ethanol	244, 337	9.48	0.977	431	94	1.34	0.0081

Table 5. Photophysical data of few other furotropones **9b, 9c, 9e, 9g, 9h, 9j, 9k** and **9q**.

Compounds	λ_{abs} **(nm)**	**ε**	**log ε**	λ_{emi}**(nm)**	$D\lambda_{stokes}$**(nm)**	τ_f **(ns)**	Φ_f
9b	339, 258	7.59	0.88	431	91	1.32	0.0065
9c	340, 268	7.59	0.88	431	91	1.41	0.0017
9e	341, 229	16.75	1.22	431	90	1.08	0.0039
9g	342, 242	9.99	0.99	430	88	1.44	0.0011
9h	343, 251	10.68	1.02	430	87	1.43	0.0098
9j	345, 237	2.70	0.43	440	95	1.42	0.0092
9k	347, 237	6.66	0.82	441	94	1.44	0.0174
9q	337, 244	9.48	0.97	430	93	1.34	0.0081

Fluorescence emission intensity and electronic properties of the furotropones were found to be sensitive in different solvent environment. Molecular architecture of furotropone with the presence of 1,3-di or 1,3,5,-triketo group inspired us to explore the novelty in chemosensor probe for a different metal ions with the potential to coordinate this functionality. For fluorescent quenching study, **9b** was chosen as model substrate and different metal ions such as Hg^{2+}, Pb^{2+}, Cr^{2+}, Cd^{2+}, Ag^{+}, Zn^{2+}, Cu^{2+}, Co^{2+}, Fe^{2+}, Ni^{2+} were subjected to various conditions. Initially, fluorescence emission for **9b** was recorded from higher concentration of 100 µm to lower concentration 10 µm in EtOH, Fig 8 (VII). Almost no change in fluorescence intensity was observed when the solution of these metal ions tested. Furotropone **9b** was found to exhibit an interesting and highly selective fluorescent molecular sensing property for Fe^{3+}, Fig. 8 (VI).[19] As decreasing the concentration of metal ion the fluorescence intensity increases while no additional quenching observed by further decreasing the concentration or varying the metal and ligand variation. From this study, we have realized that furotropones could function as a probe for the detection of Fe^{3+} up to 10 µM concentration.

(VI)



(VII)

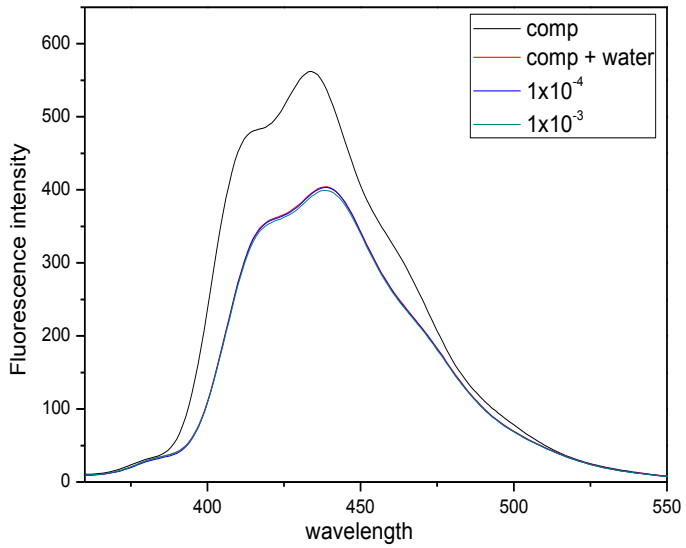


Figure 8: (VI) Fluorescence emission spectra of **9b** in ethanol solvent with different concentration of Fe^{3+} (VII) Fluorescence emission spectra of **9b** in ethanol solvent with different concentration of Co^{2+}.

In conclusion, we have demonstrated the modular approach to rapidly access functionalized and polysubstituted furotropones and benzofurotropones starting from readily accessible materials. The three-step protocol features directed α-alkylation of 3-furancarboxaldehydes, Bi(III)-mediated furfurylation and an unusual base-mediated intramolecular aldol condensation reaction. This protocol is suitable to construct Mono substituted furotropones via in situ alkoxy decarbonylation, disubstituted furotropones via retro-Claisen-aromatization, and trisubstituted furotropones through base-mediated intramolecular aldol reaction of 1,3,5-triketones. We have identified that these new chromophores, with their unique structural features, have potential to be highly sensitive and selective sensors for the detection of hard cations such as Fe^{3+}, with the detection limit as low as 10 μM.

Chapter 2

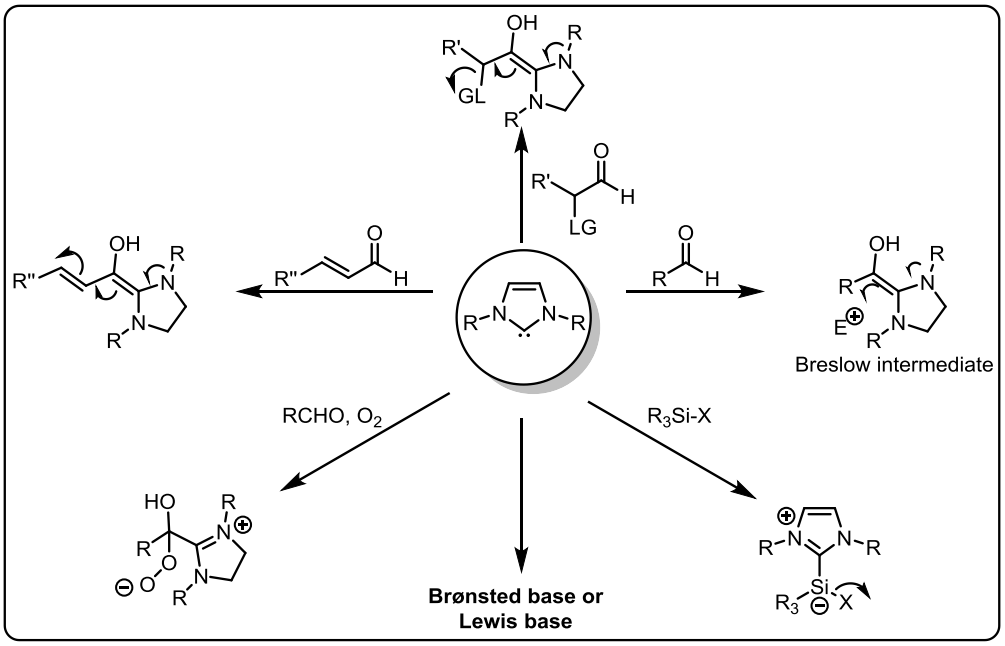
Synthesis of benzofurans from furans via intramolecular cross benzoin reaction catalyzed by N-heterocyclic carbenes

In recent years, organocatalysis has become one of the most fascinating areas in organic synthesis. Organocatalysis has proven synthetic utility in accessing complex molecular frameworks with high selectivity in a more economical and environmentally friendly manner.[20] Organocatalysis has received tremendous attention from the synthetic community due to easy handling, and most often being moisture insensitive. Further, it leads to building the synthesis of biologically active frameworks with high efficiency and stereoselectivity.[21] In recent years, organocatalysis has widened in many different directions. Among them, N-heterocyclic carbenes

(NHCs),[22] amines,[23] chiral Brønsted acids,[24] organo-phosphines[25] and hydrogen bonding catalysts[26] are most often employed in catalysis. The NHCs facilitated enormous growth in chiral and cascade reactions.

2.1: General introduction about NHCs

In recent years, carbene chemistry has become an interesting area in organic chemistry.[26] NHC catalysis has revamped the chemistry of aldehydes by reversing their native polarity (umpolung).[27] Ever since the first report of Ukai *et al.* on the NHC-catalyzed cross-benzoin reaction in 1943,[29] significant advancements have been witnessed in the chemo- and enantioselective intermolecular variants. NHC catalysis has emerged as a powerful tool in organocatalytic transformations, mainly in carbon-carbon, carbon-heteroatom bond formation and allowing access for catalytically generated acyl anions, homoenolates, enolates, and α-acyl vinyl anion equivalents, Scheme 14.[30] The synthetic utility of NHCs has also been explored in other organic transformations such as oxidation reactions,[31] trans esterifications,[32] Morita-Baylis-Hillman reactions,[33] Michael addition reactions,[34] and silyl activation.[35]

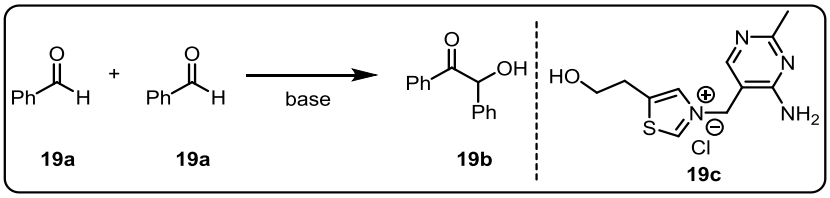


Scheme 14: Different modes of activation of NHC toward various functional groups

The versatility of NHCs is due to their different modes of activation towards different functional groups. The applications of NHC as an organocatalyst for various types of organic reactions are highlighted in Scheme 14. These reactive intermediates have been added to a wide range of electrophiles, there by assembling complex and biologically active structural motifs. This catalytic process can be limited with respect to the stereoselectivity, regioselectivity or versatility of electrophilic and nucleophilic species involved.

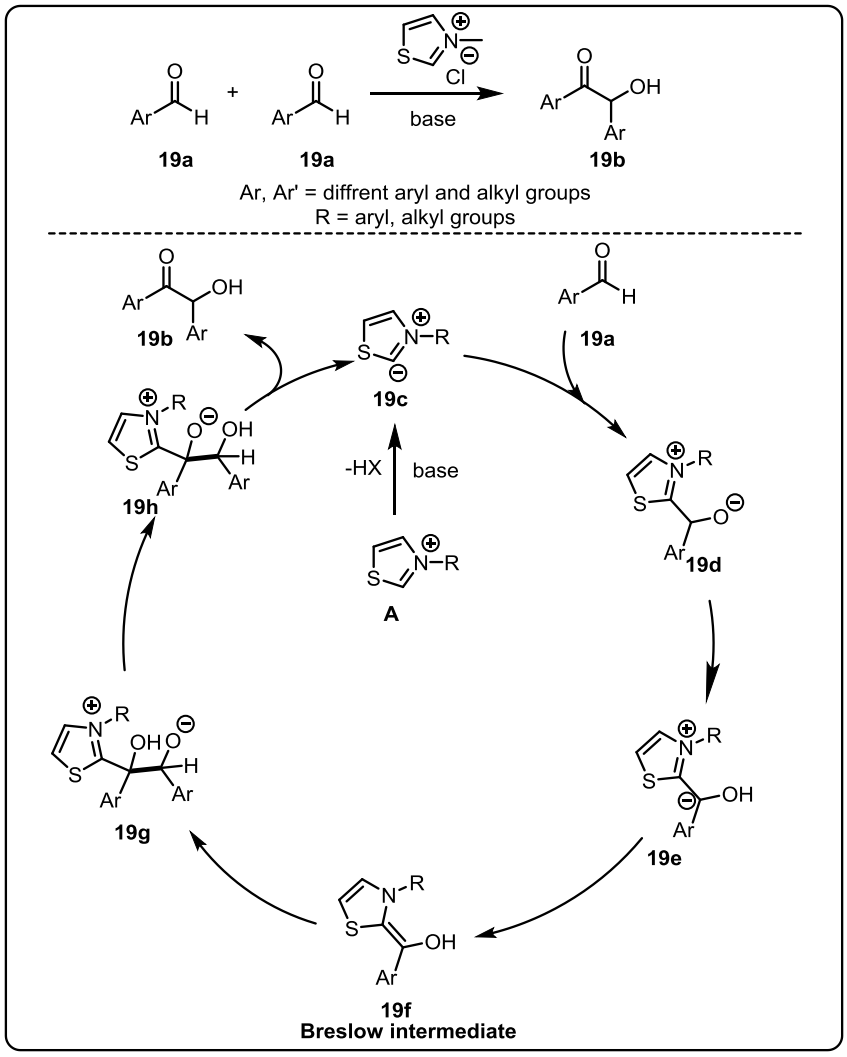
2.2. NHC-catalyzed benzoin reaction

In the last two decades, N-heterocyclic carbene catalysis has made astonishing contributions in the field of organocatalysis through its umpolung or non-umpolung reactivity. Ukai and co-workers reported their earliest revolutionary that the thiazolium salts **19c** can also furnish the homodimerized benzoin product **19b** of aldehydes **19a** in the presence of a base, Scheme 15.[36a]



Scheme 15: Thiazolium salt catalyzed benzoin condensation

Based on Ukai's and Lapworth's work, Breslow proposed the mechanism for benzoin-condensation catalyzed by thiazolium NHC, Scheme 16.[36b] He anticipated that the active carbene catalytic species for this transformation is thiazolin-2-ylidene **19c**, generated from deprotonation of the thiazolium salt **A**. This thiazolin-2-ylidene **19c** reacts with the aldehyde **19a** to produce an intermediate commonly known as Breslow intermediate **19f**. The plausible catalytic cycle for this transformation is shown in, Scheme 16.

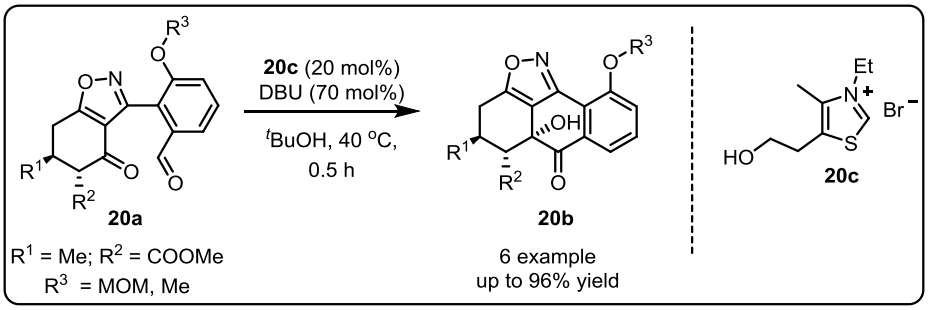


Scheme 16: Plausible mechanism for benzoin condensation proposed by Breslow

The benzoin reaction of same aldehyde led to the formation of homocoupling product, while two different aldehyde leads to cross-coupling product. The reaction between two different aldehyde and ketone opens the access to a wide variety of benzoin products.[37] Many attempts have been made to improve the chemoselectivity and regioselectivity of homocoupling and cross-coupling intermolecular benzoin reaction. But surprisingly, there have been limited successes in the intramolecular cross-benzoin reaction. In the next subsection, a pioneering contribution of some of the few groups towards intramolecular cross-benzoin reaction is described.

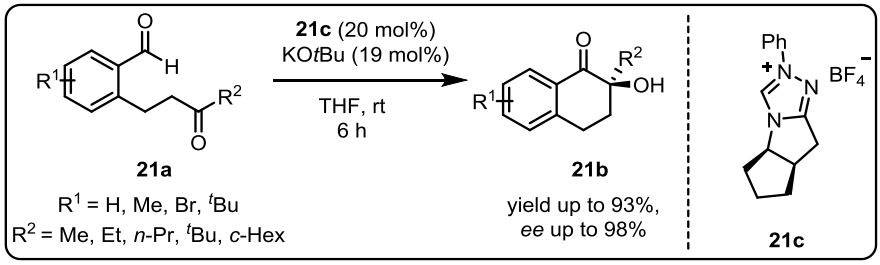
2.3: NHC-catalyzed intramolecular benzoin condensation reaction

In 2003, Suzuki *et al.*[38] developed the first intramolecular NHC-catalyzed reaction of conjugated ketone-aldehyde **20a**, which led to the formation of tetracyclic isoxazole **20b**, Scheme 17. Excellent diastereoselective was observed with substrates possessing additional stereogenic centers. This reaction efficiently delivered a wide variety substituted isoxazole derivatives in up to 96% yields by using DBU and thiazolium **20c** catalyst.



Scheme 17: First intramolecular crossed benzoin condensation

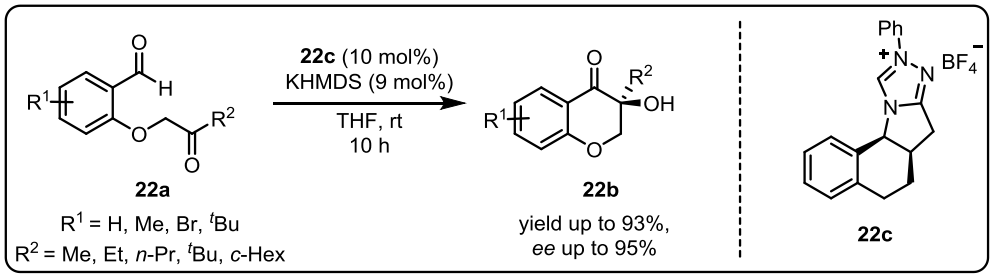
In 2006, Balensiefer *et al.*[39] described an enantioselective intramolecular crossed benzoin reaction of **21a** with the NHC **21c**, Scheme 18. The in situ generated carbene catalyzes the cyclization reaction by creating a quaternary stereocenter **21b** in high yield and excellent enantioselectivity. This protocol provides an extended scope for cyclic acyloin derivatives in high yield and good enantiomeric excess.



Scheme 18: Balensiefer's enantioselective intramolecular crossed benzoin condensation

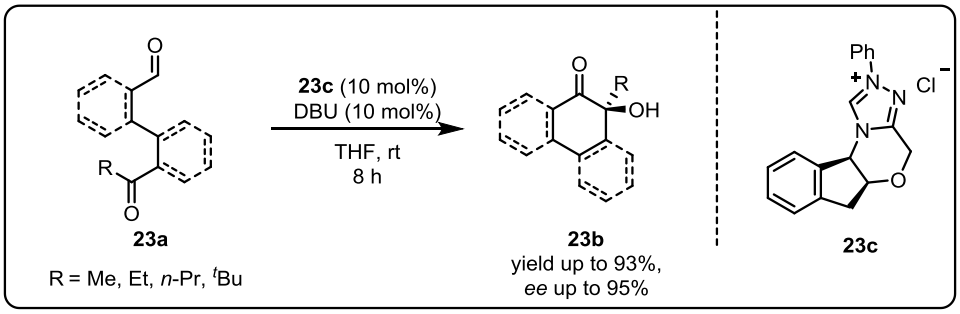
In 2006, Raabe *et al.*[40] disclosed the NHC-catalyzed asymmetric synthesis of chromanone **22b** via intramolecular crossed benzoin condensation reaction between aldehyde and ketone **22a** with sterically hindered catalyst **22c,** by using KHMDS as base in THF solvent in good to excellent yield with high enantioselectivity, Scheme 19. The sterically different

catalysts **22c** were chosen in order to adjust the steric and electronic properties of substrates. Wide ranges of substituted chromanone derivative were efficiently prepared.



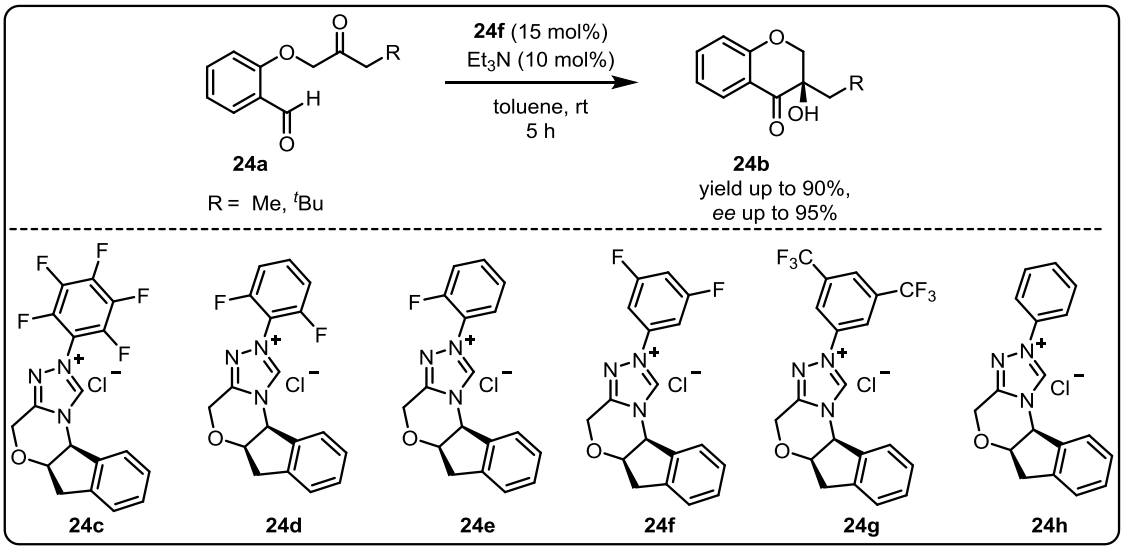
Scheme 19: Raabe's synthesis of chiral chromanone

In 2006, Suzuki *et al.*[41] demonstrated a catalytic enantioselective intramolecular crossed benzoin reaction, Scheme 20. The enantioselective cyclization of **23a** with NHC **23c** in presence DBU furnished the corresponding cyclic product **23b** in good to excellent yield with high enantiomeric excess. Wide substrate scope involving aliphatic, alkyl and aryl ketoaldehyde proved to be good substrates in this transformation and yielded the bicyclic, tricyclic and tetracyclic acyloin products in high enantioselectivity. In addition, it provides a concise entry to the natural product eucomol.



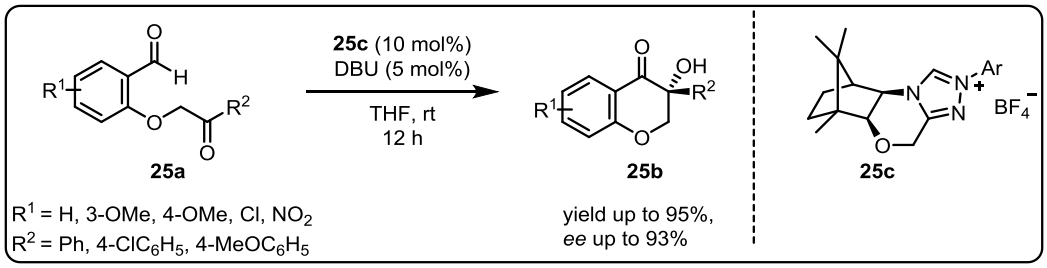
Scheme 20: Suzuki's NHC-catalyzed enantioselective benzoin reaction

In 2007, Suzuki *et al.*[42] developed a chiral triazolium salt for the enantioselective benzoin reaction of enolizable ketoaldehyde **24a**, Scheme 21. The reaction between ketoaldehyde **24a** and modified NHC **24f** with Et_3N furnished the corresponding chromanone **24b** in moderate to good yield with high enantioselectivity. This reaction was screened by modifying Rovis catalyst **24h** to different derivatives **(24c-24g)**. This reaction gives access for the synthesis of natural product like (+) sappanone B.



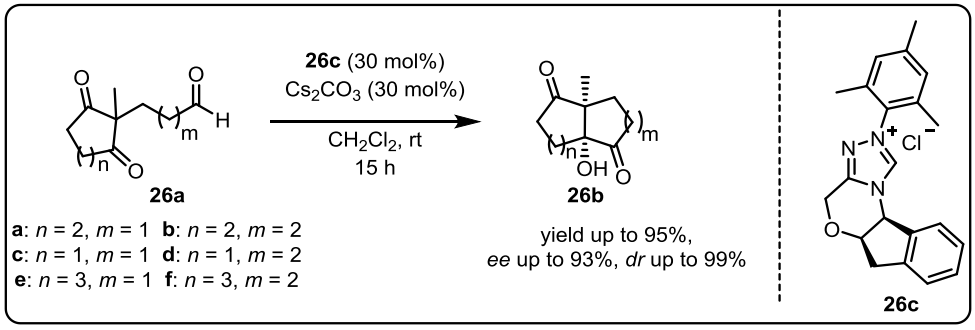
Scheme 21: Suzuki's modified NHC catalysts for intramolecular reaction

In 2008, You *et al.*[43] reported the modified D-Camphor derived triazolium NHC for intramolecular cross benzoin reaction, Scheme 22. Treatment of ketoaldehyde **25a** with modified NHC **25c** in presence of DBU furnished the chromanone **25b** in high yield with excellent enantioselectivity. A variety of Camphor based triazolium NHC derivative were prepared and screened for this reaction



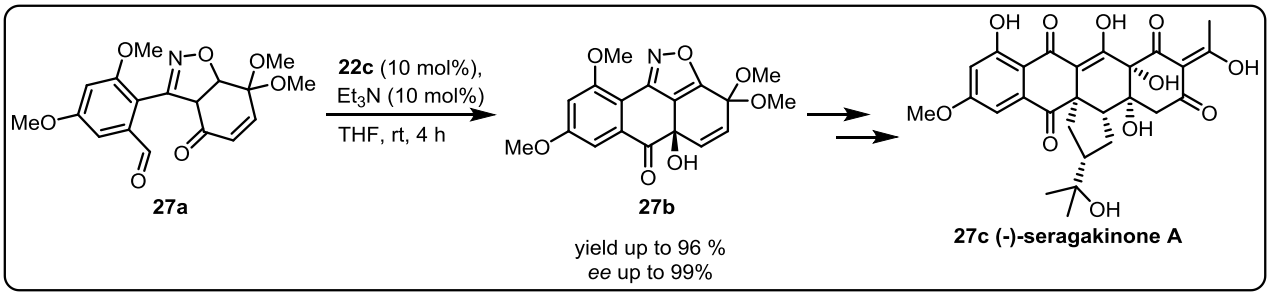
Scheme 22: You's D-camphor NHC catalyzed intramolecular benzoin condensation

In 2009, Sakai *et al.*[44] constructed the enantioselective bicyclic quaternary alcohol **26b** via an intramolecular NHC-catalyzed benzoin reaction, Scheme 23. The reaction of cyclic diketone **26a** with NHC **26c** in presence of Et_3N delivered bicyclic compound **26b** in good yield with excellent enantioselectivity. A diversity of cyclic acyloin compounds have been synthesized easily with high enantiopurity.



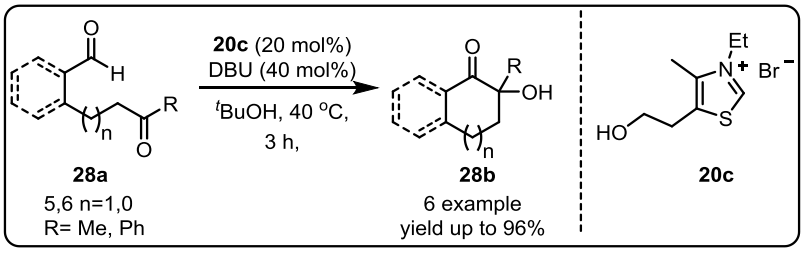
Scheme 23: Sakai's intramolecular NHC-catalyzed reaction

In 2011, Suzuki *et al.*[45] developed novel strategy for the total synthesis of (-)-Seragakinone A **27c**, Scheme 24. An advanced ketone-aldehyde intermediate **27a** was subjected to modified NHC catalysis in THF solvent delivered highly functional tetracyclic acyloin product **27b** with excellent yield, which was further elaborated to natural product **27c**.



Scheme 24: Suzuki's total synthesis of (-)-Seragakinone A

In 2004, Niemeier *et al*,[46] demonstrated an intramolecular variant of crossed benzoin reaction of **28a** with moderately basic thiazolium derived NHC catalyst in ^{t}BuOH solvent for the synthesis of bicyclic acyloin **28b**, Scheme 25.



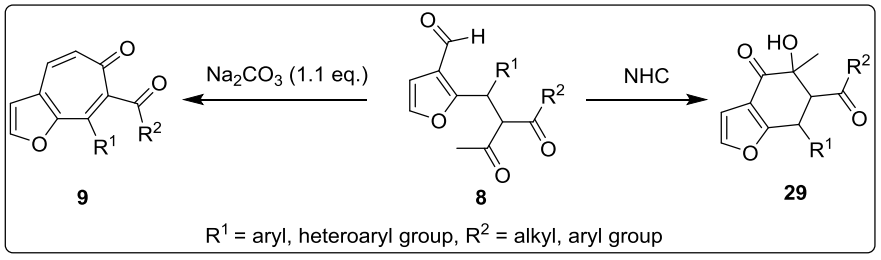
Scheme 25: Niemeier's intramolecular crossed benzoin condensation

Despite tremendous advancements in intramolecular NHC-catalyzed reactions, the aforementioned reaction strategies and brief literature survey revealed that most of the strategies are limited to build cyclopentanones, tetralones, chromanones, dihydroisoquinolones and phenanthraquinones. But there is no NHC based efforts for the synthesis of benzofurans that have been reported. The development of general and efficient protocols to synthesize the highly functionalized benzofurans via this strategy remains challenging. Most often benzofurans assembled in a multi-step manner due to lack of efficient strategies and it has encouraged us to develop new advancement towards this reaction.

2.4: NHC-Catalyzed synthesis of dihydrofuranones from furans

Benzofurans are considered privileged structures from the drug discovery point of view, because of their widespread occurrence in an array of bioactive natural products and multifarious therapeutically relevant compounds.[47] Thus, the significance of benzofurans demands efficient synthetic methodologies to rapidly access the functionalized core. Consequently, several noteworthy protocols have been developed for the synthesis of benzofuran derivatives.[48]

Initially we have demonstrated that, when the reaction of diketoaldehyde **8** was carried out under basic condition led to the formation of functionalized furotropone **9** in excellent yield. While working on the synthesis of functionalized furotropones and benzofurotropones, we envisioned that these diketoaldehyde **8** utilized for the synthesis of functionalized benzofurans. Here, we have developed an NHC-catalyzed approach for the synthesis of dihydrobenzofuranone **29** and the results are discussed below, Scheme 26.[49]

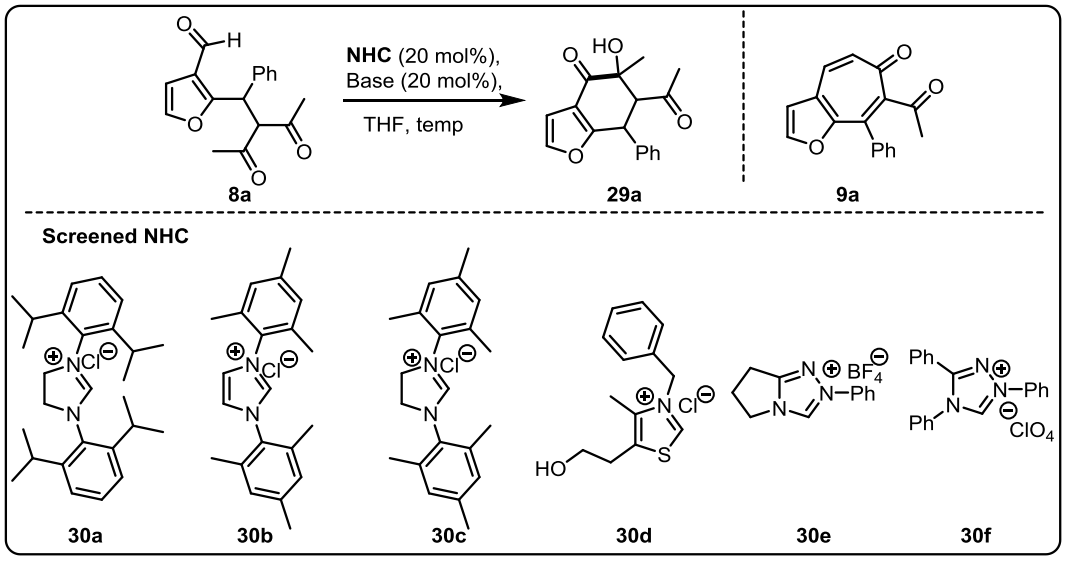


Scheme 26: Our design for the synthesis of dihydrobenzofuranones via intramolecular NHC-catalyzed reaction

2.5: Results and discussion

In order to validate our hypothesis, the optimization studies are carried out by treating **8a** with various reaction conditions and the results are disclosed in Table 6. Our initial attempt was to employ catalysts **30a-30c** with DBU in THF solvent at room temperature, which was not encouraging as no product formed in that reaction (Table 6, entries 1-2). Further, when we used **30c** catalyst in the reaction, the formation of furotropone **9a** was observed (Table 6, entry 3). Surprisingly, when the reaction was performed by using **30d** catalysts the expected dihydrobenzofuranone **29a** was obtained in moderate yield (Table 6, entry 4). The structure of dihydrobenzofuranone **29a** deduced from spectral data. The presence of one absorption band in the IR spectrum at 3461 cm^{-1} due to tertiary alcohol and at 1707 cm^{-1} and 1686 cm^{-1} due to ketone indicated the formation of product **29a**. In ^{1}H-NMR spectrum (see Fig. 10) the absence of aldehyde peak and the presence of a singlet at δ 1.40 ppm due to tertiary methyl and a singlet at 4.06 ppm due to alcohol, and in the ^{13}C-NMR spectrum (see Fig. 11) the presence of δ 206.5 ppm and δ 195.3 ppm signal due to two carbonyl groups and δ 21.9 ppm due to methyl group confirmed the formation of **29a**. In the high-resolution mass spectrum, the presence of molecular ion peak at *m/z* 302.1146 $(M+H_2O)^+$ further supports the product formation. The X-ray diffraction analysis of **29a** confirmed the product formation, Fig. 9.

Table 6: Optimization of reaction parameter for intramolecular NHC reaction

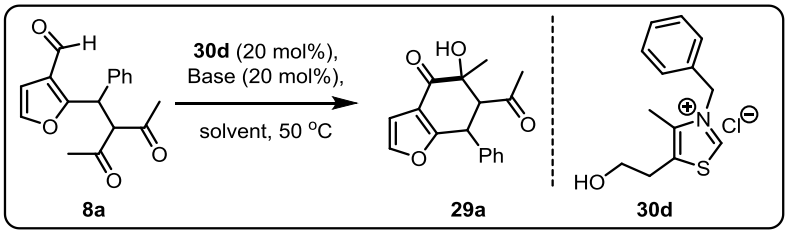


Sr. No.	NHC (20 mol%)	Base (20 mol%)	Temp	% Yield[a]
1	**30a**	DBU	rt	No reaction
2	**30b**	DBU	rt	No reaction
3	**30c**	DBU	rt	Furotropone
4	**30d**	DBU	rt	65
5	**30e**	DBU	rt	63
6	**30e**	Et_3N	rt	10
7	**30e**	Cs_2CO_3	rt	40
8	**30e**	K_2CO_3	rt	30
9	**30e**	K_3PO_4	rt	60
10	**30e**	DBU	20 ^oC	20
11	**30d**	DBU	50 ^oC	85
12	**30e**	DBU	50 ^oC	60
13	**30d**	DBU	70 ^oC	60
14	**30e**	DBU	70 ^oC	65

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yields after silica gel column chromatography.

Further, standardization studies were performed with **30e** catalyst in presence of different bases (Et_3N, DBU, Cs_2CO_3, K_2CO_3 and K_3PO_4) but no significant improvement in the yield of product was observed. Further, decreasing the temperature of reaction was not encouraging (Table 6, entries 5-10). Delightfully, when the reaction of **13b** was performed with **30d** catalyst in DBU at 50 ^oC, **29a** was isolated in 85% yield (Table 6, entry 11). Meanwhile, when Cs_2CO_3 was employed as a base yield of desired product **29a** improved to 89% (Table 7, entry 19). To find out best solvent for this transformation, optimization studies were performed with the solvents such as 1,4-dioxane, acetonitrile, toluene, and DMF using **30d** catalyst at 50 ^oC (Table 7, entries 20-23). However, the isolated yields of **29a** in all those cases were found to be low when compared to the reaction in THF.

Table 7: Optimization of reaction parameters



Sr. No.	NHC (20mol%)	Base (20 mol %)	Solvent	Temp	% Yield[a]
15	**30d**	KO*t*Bu	THF	50 °C	70
16	**30d**	Et_3N	THF	50 °C	10
17	**30d**	K_3PO_4	THF	50 °C	30
18	**30d**	K_2CO_3	THF	50 °C	10
19	**30d**	**Cs_2CO_3**	**THF**	**50 °C**	**89**
20	**30d**	Cs_2CO_3	1,4-Dioxane	50 °C	70
21	**30d**	Cs_2CO_3	ACN	50 °C	20
22	**30d**	Cs_2CO_3	Toluene	50 °C	20
23	**30d**	Cs_2CO_3	DMF	50 °C	20

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yields after silica gel column chromatography

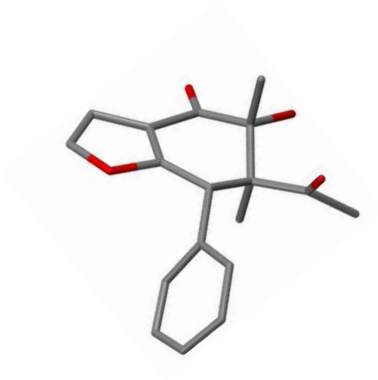
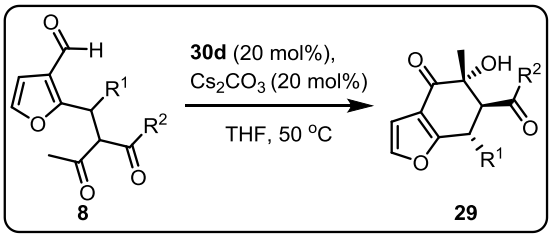
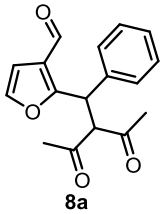
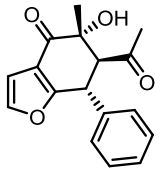
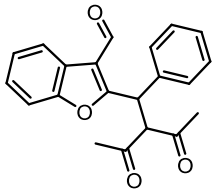
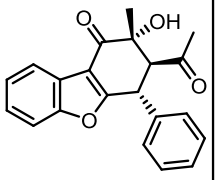
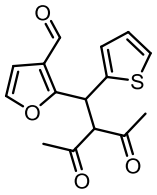
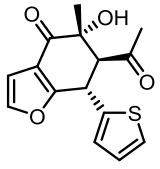
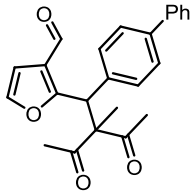
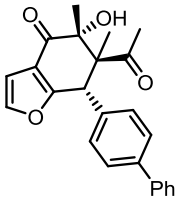
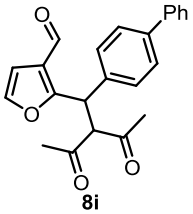
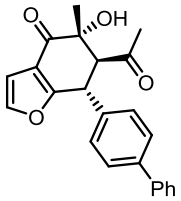
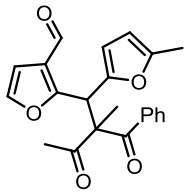
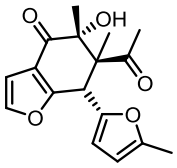
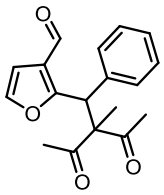
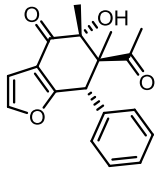
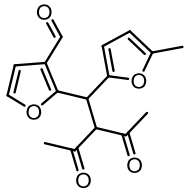
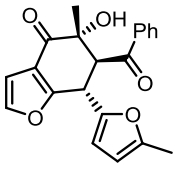
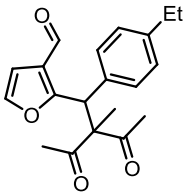
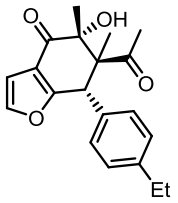


Figure 9: ORTEP diagram of Dihydrobenzofuranone **29o**

With the optimal condition in hand, limitation and scope of this reaction were examined, Table 8. The acetyl acetone adducts of diketoaldehyde having aryl or heteroaryl appended to furan **8a, 8b, 8i and 8m** delivered the dihydrobenzofuranone in excellent yields **29a, 29b, 29i** and **29m**. While, benzyl acetone adducts of diketoaldehyde **8w** furnished the dihydrobenzofuranone **29w** in poor yield may be due to steric reasons, otherwise a variety aryl/heteroaryl substituent were well tolerated. Delightfully, when acetyl acetone adduct of diketoaldehyde appended benzofuran **8m** treated under optimized condition the respective product yielded **29m** was obtained in 82% yield.

Table 8: Substrate Scope: dihydrobenzofuranone



Sr. No.	Substrate	product	Sr. No.	Substrate	product
1	 **8a**	 **29a,** 18 h, 85%	6	 **8m**	 **29m,** 9.5 h, 82%
2	 **8g**	 **29g,** 10 h, 85%	7	 **8u**	 **29u,** 10 h, 81%
3	 **8i**	 **29i,** 8 h, 83%	8	 **8v**	 **29v,** 30 h, 76%
4	 **80**	 **29o,** 13 h, 78%	9	 **8w**	 **29w,** 34 h, 30%
5	 **8p**	 **29p,** 12 h, 82%			

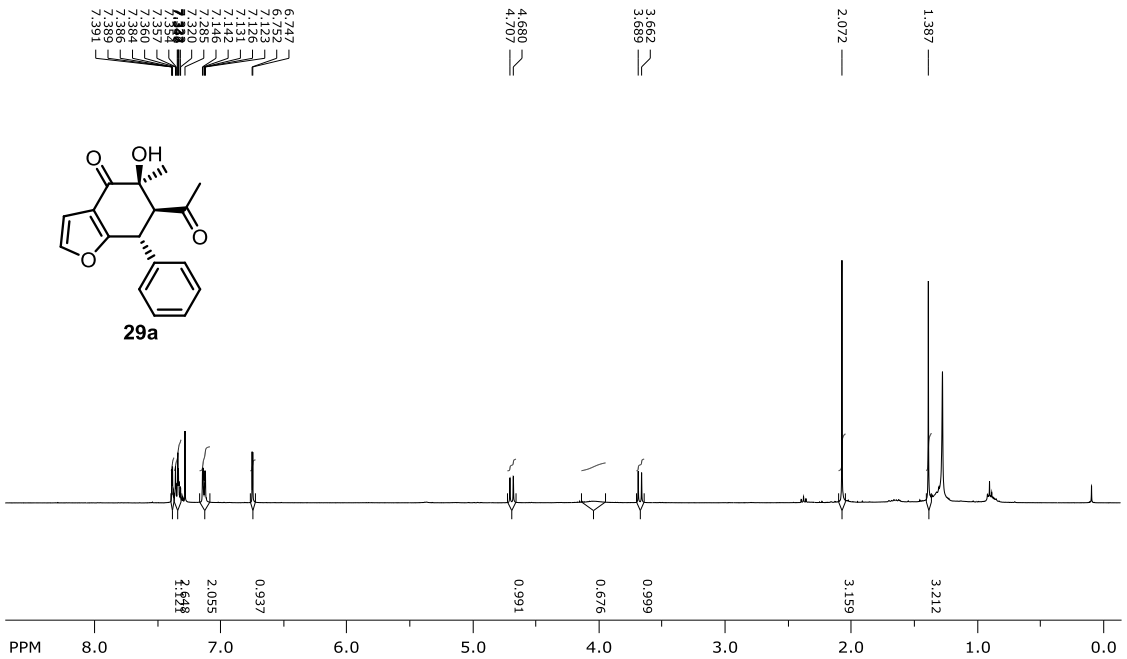


Figure 10: ^{1}H-NMR spectrum of **29a**

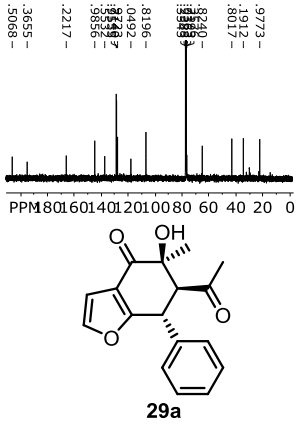
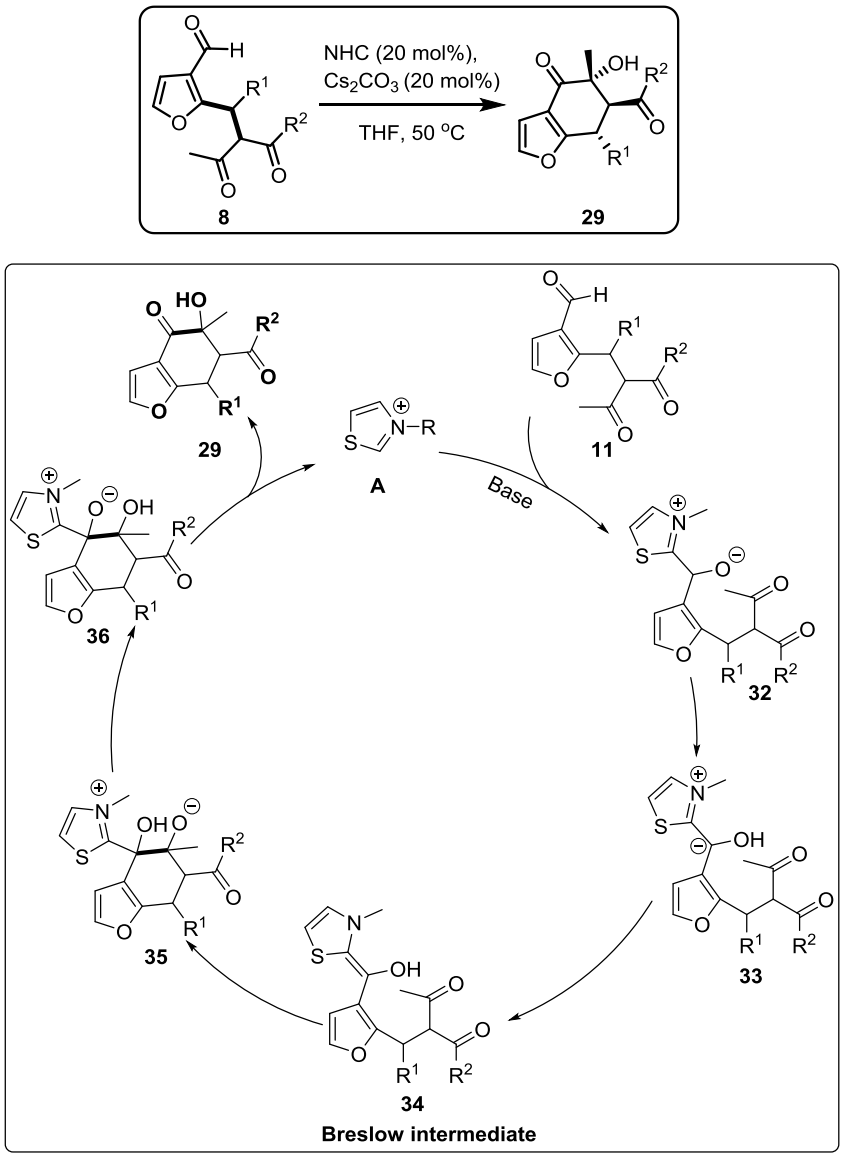


Figure 11: ^{13}C-NMR spectrum of **29a**

2.6: Plausible mechanism for the cyclization reaction

Based on literature reports, we propose a plausible mechanism for this transformation, Scheme 27. The reaction between thiazolium salt and base, generated carbene **B**, which reacts with aldehyde from **8** and subsequent proton shift, generates the Breslow intermediate **33.** Further intramolecular cyclization with ketone of **8** and deprotonation leads to the desired product **29**.

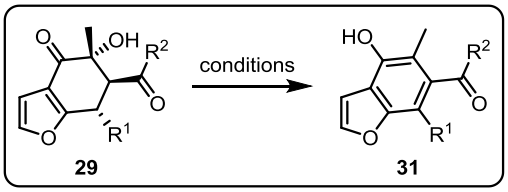


Scheme 27: Plausible mechanism for NHC reaction

2.7: Elaboration towards the functionalized benzofurans

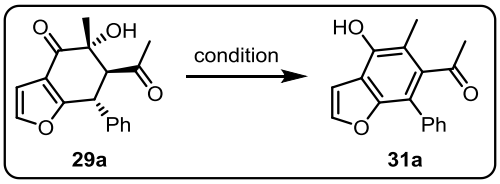
Next, we have shifted our attention to illustrate generality and synthetic utility towards benzofuran synthesis, Scheme 28. It was presumed that the elimination of tertiary alcohol could provide benzofurans, but dihydrobenzofuranone **29** was found to be resistant to several conditions, Table 9. When we treated **29** with $POCl_3$, the substituted benzofuran **30** was obtained in good yield.[50]

This reaction opens the access for the synthesis of substituted benzene appended furan or polysubstituted benzofuran scaffold.[51]



Scheme 28: Elaboration towards benzofuran synthesis

Table 9: Screening of reaction parameter

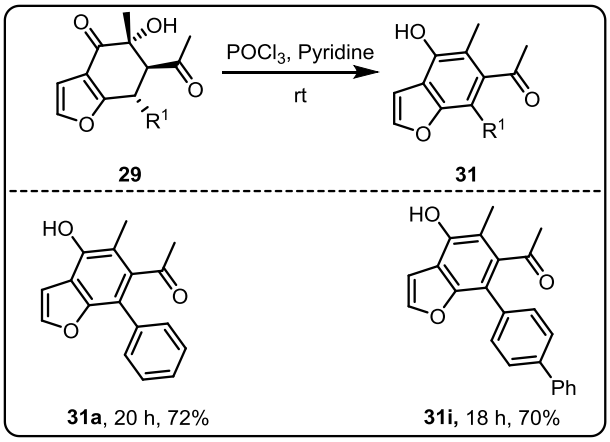


Entry	Conditions	Comments
1	conc. HCl, (THF:H_2O) (1:1), rt to 100 ^oC, 50 h	Decomposed the starting material
2	conc. H_2SO_4, (THF:H_2O) (1:1), rt to 100 ^oC, 50 h	Decomposed the starting material
3	conc. HCl, (MeOH:H_2O) (1:1), rt to 100 ^oC, 60 h	Decomposed the starting material
4	conc. H_2SO_4, (MeOH:H_2O) (1:1), rt to 100 ^oC, 60 h	Decomposed the starting material
5	DDQ (5 eq.), Toluene 130 ^oC, 30 h	Starting material as it is
6	*p*-TSA (20 mol%), Toluene, 140 ^oC, 48 h	Starting material as it is
7	*p*-TSA (1.0 eq.), Toluene, 140 ^oC	Starting material as it is
8	*p*-TSA (20 mol%), Toluene, Dean-stark apparatus, 140 ^oC, 24 h	Starting material as it is

9	Triflic unhydride (1.1 eq.), Py (4 eq),1,4-dioxane, rt, 48 h	Starting material as it is
10	TfOH (20 mol%), Dry DCM, rt, 72 h	Starting material as it is
11	DMAP (20 mol%), $MeSO_2Cl$ (1.1 eq.), Py (5 eq.), DCM, rt, 48 h	Complex TLC
12	KO*t*Bu (1eq.), $MeSO_2Cl$ (1.1 eq.) THF, rt, 24 h	Starting material as it is
13	NaH (1eq.), $MeSO_2Cl$ (1.1eq.), THF, rt, 24 h	Starting material as it is
14	DBU (1 eq.), $MeSO_2Cl$ (1.1 eq.) THF, rt, 24 h	Starting material as it is
15	NaH (1 eq.), CDI (1 eq.), Py, rt, 24 h	Complex TLC
16	$POCl_3$(30 eq.), Py, rt, 48 h	72 % of **31a**

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yields after silica gel column chromatography.

Scheme 29: Substrate scope: Benzofuran



In conclusion, we have disclosed here an atom-economical method for the synthesis of highly functionalized substituted derivative of dihydrobenzofuranone. We have shown that the product can be efficiently utilized to generation of substituted benzofuran derivative. This method can be used efficiently for making substituted benzofuran in natural product synthesis or pharmaceutical.

Chapter 3

Organocatalytic β-azidation of enones initiated by an electron-donor-acceptor complex

Since the discovery of organic azide by Peter Griess,[52] numerous novel transformation of azide derivative have emerged and widely used as an important intermediate in organic synthesis.[53] Over the past few decades, versatile synthetic methodologies to employ azide as an aminating agent for the construction of nitrogen containing compounds such as azoles, nitriles, amides, quinolones, pyrroles, pyridines, etc. have been developed.[54] In modern chemistry, these are the important scaffold found in various natural products and widely present in biologically or pharmaceutically active compounds.[55] In more recent times, completely new perspectives were developed for their use in peptide chemistry,[56] combinatorial chemistry.[57] Industrial interest in organic azide began with the synthesis of heterocyclic compounds such as triazoles and

tetrazoles. The heavy-metal azides are also used as detonators in explosive devices or blowing agent in industry.[58]

On the other hand, hypervalent iodine compounds have always fascinated chemists, due to their non-classical bond character and exceptional reactivity.[59] Among them benziodoxole reagent has witnessed the significant advancement in the field of chemical sciences, due to strong electrophilic and valuable oxidizing properties.[60] For example, the Dess-Martin periodinane **37** (DMP) as a mild and non-toxic reagent is now one of the most often used oxidant in organic synthesis, Fig 12.[61] Whereas, the formation of C-C bonds using non-cyclic iodonium reagents have also been very successful in the last decades.[62] It is only in 2006, that Togni reported the benziodoxole derived reagents **39** for CF_3 transfer.[63] Further Waser group introduced ethynylbenziodoxolone (EBX) reagents **40** for acetylene transfer reactions.[64] Uses of hypervalent benziodoxole reagents **41-44** in various synthetic transformations such as halogenation, C−R_f (R_f = perfluoroalkyl), C-N bond formation, amination reaction are well explored.[58]

Realizing the reactivity in benziodoxoles reagent and importance of azide, Zhdankin and co-workers developed the first cyclic hypervalent iodine reagent **38**, which can be stable up to 100 ^oC.[65] This reagent is a preliminary source for electrophilic and radical azide. With the advent of the Zhdankin azidoiodane reagent **38** electrophilic and radical azidation modes have been received tremendous attention.[66] Among them, the strategy to introduce azide via the *β*-azidation of activated alkenes has emerged only recently. Radical reactions of azides are less documented, but the reported studies have clearly revealed that these reactions also provide useful synthetic routes to N-heterocycles.[67]

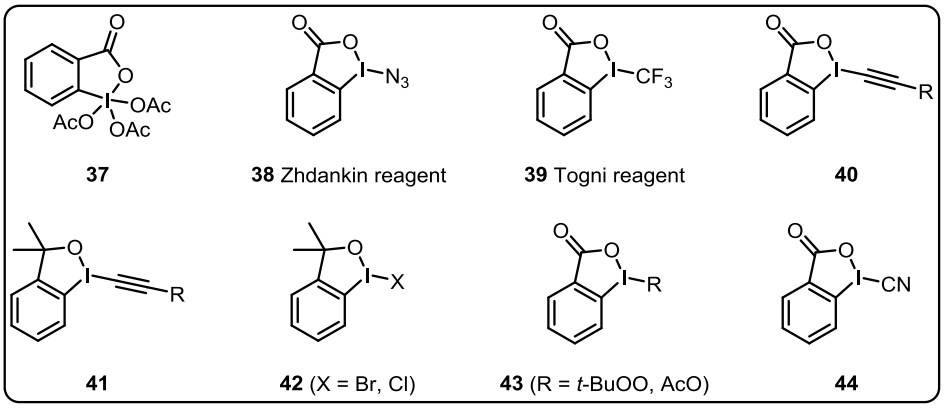
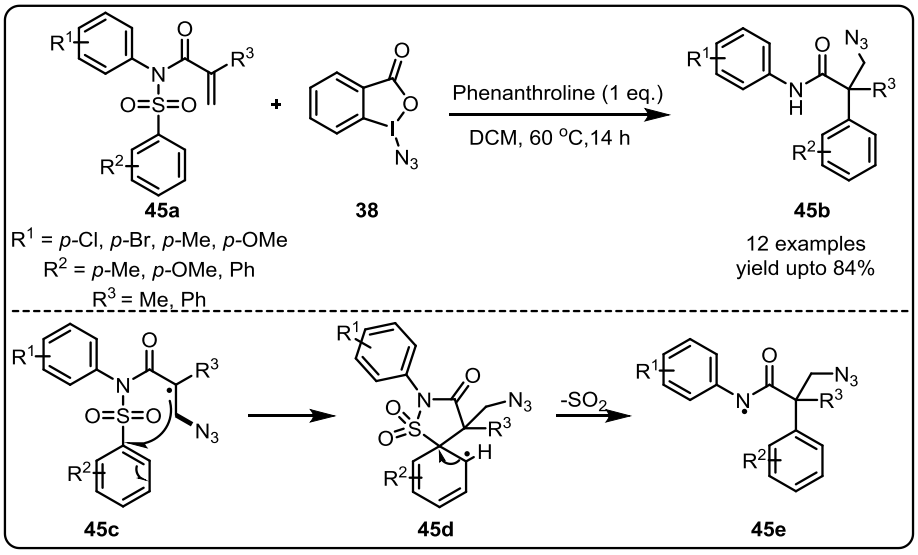


Figure 12: Hypervalent iodine (III) reagents

The aforementioned importances of azide and hypervalent iodine reagent in the area of synthetic organic and pharmaceutical chemistry hold the key to develop new strategy for functional transformation. Recently azide radical mediated *β*-azidation received the attention due to its less toxic, ecofriendly and atom-economical properties. In the next subsection, a few important methods related to *β*-azidation of activated olefins via azide radical are described.

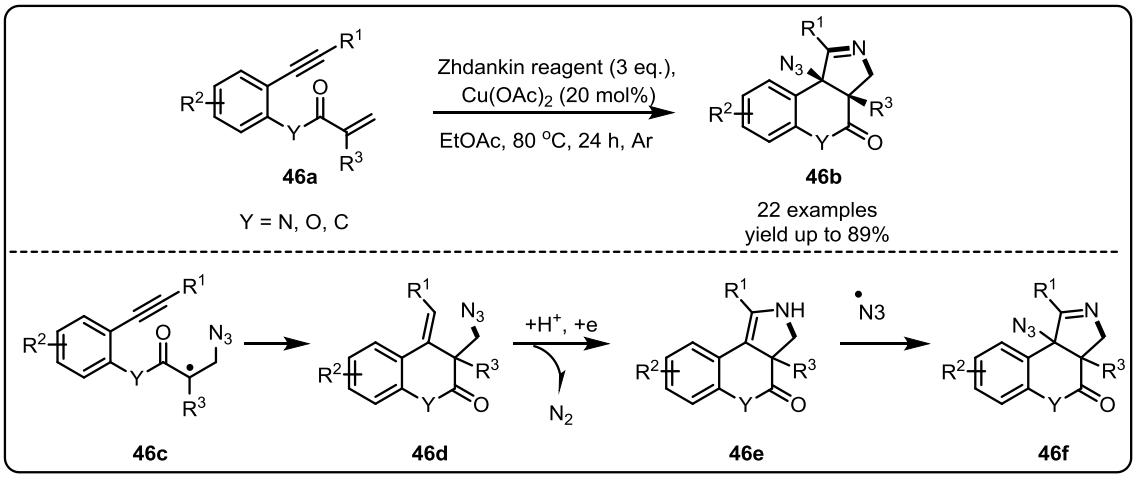
3.1: β-Azidation of activated olefins employing Zhdankin reagent

In 2014, Nevado *et al.*[68] described the radical azidation of activated alkene **45a**, Scheme 30. The radical mediated *β*-azidation of *α*-substituted acryl sulfonamide **45a** with Zhdankin reagent **38** in presence of stoichiometric amount of 1,10-phenanthroline was developed. A wide variety of arylazidation products **45b** were synthesized in high yields. However, the role of 1,10-phenanthroline was not understood.



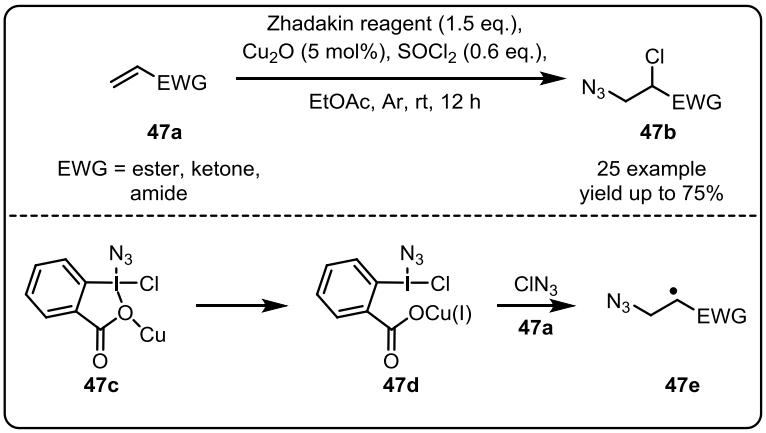
Scheme 30: Nevado's *β*-azidation of *α*-substituted acryl sulfonamides

In 2015, Li *et al.*[69] demonstrated cascade copper-catalyzed azide radical [2+2+1] annulation of benzene-linked 1,*n*-enynes **46a** with Zhdankin reagent **38**, Scheme 31. The intramolecular radical cyclization provided wide variety functionalized quinolones, chromones and indenones derivatives in a good to excellent yield.



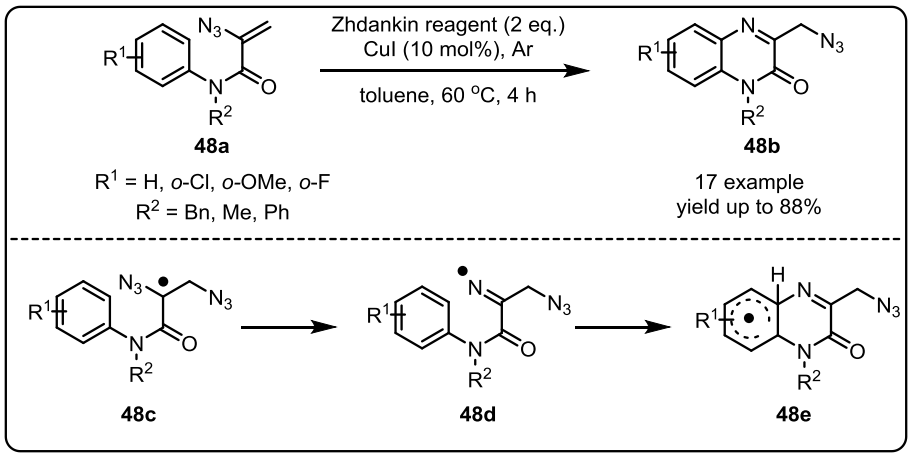
Scheme 31: Li's cascade copper-catalyzed azide radical annulation reaction

In 2016, Yang *et al.*[70] developed an efficient and practical approach for copper-catalyzed intermolecular chloroazidation of activated olefins **47a**, Scheme 32. The reaction between *α,β*-unsaturated amide **47a**, Zhdankin reagent **38** and $SOCl_2$ in presence of copper catalyst delivered the chloroazide product **47b** in excellent yield. A wide variety of functionalized azide derivatives can be accessed in one step.



Scheme 32: Yang's intermolecular chloroazidation of activated olefin

In 2016, Yu *et al.*[71] demonstrated that activated olefins **48a** undergo tandem Michael addition-cyclization reaction to afford quinoxalins **48b**, Scheme 33. Under the copper catalysis, Zhdankin reagent provides azide radical which then reacts with 2-azido-N-arylacrylamides to afford the corresponding α-(arylaminocarbonyl)iminyl radical **48d**. Subsequent, cyclization of iminyl radical delivered quinoxalin-2(1*H*)-ones **48b** in moderate yields.

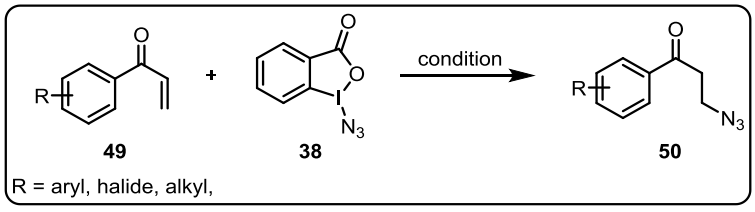


Scheme 33: Yu's copper-catalyzed azide radical reaction

3.2: Organocatalytic β-azidation of enones with Zhdankin reagent

Despite tremendous advancements in azide chemistry, the aforementioned studies are restricted mostly to α-substituted acrylamides.[68-71] The lack of efficient process for the catalytic azidation of enones has encouraged us to envision new advancement in th free radical chemistry.

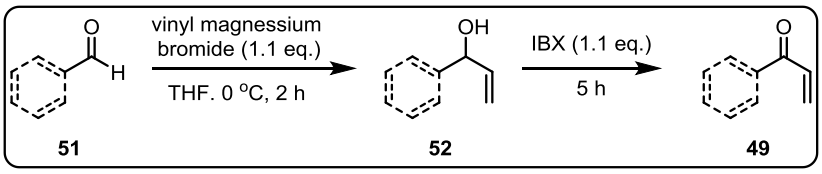
In an attempt to address these concerns, we commenced our efforts for the development of an organocatalytic β-azidation of ubiquitous α,β-unsaturated ketones under practical and straightforward conditions, Scheme 34.[72] It was envisioned that activated olefin **49** utilized for the transformation to β-azidoketones **50** with Zhdankin reagent **38** via electron-donor-acceptor complex formation.



Scheme 34: General reaction for β-azidation of activated enone

3.3: Results and discussion

The proposed starting material **49** was synthesized by using a two-step protocol, Scheme 35.[73] A variety of vinyl ketone can be achieved from the addition of vinyl Grignard reagent to respective aldehydes **51** and subsequent IBX oxidation.

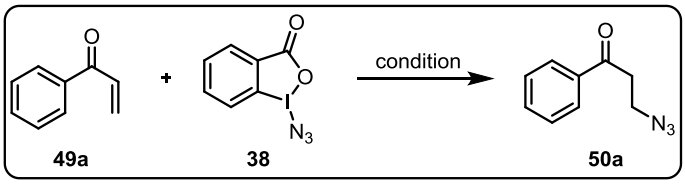


Scheme 35: Synthesis of enones

We have commenced the optimization studies by considering **50a** as the model substrate, Table 10. Our initial attempt by employing Zhdankin reagent **38** in toluene in the absence of external additives was discouraging even after reaction continued for four days (Table 10, entry 1). [74] Further to our delight, when the reaction performed by using imidazole as a catalyst, the expected product **50a** was formed in moderate yield (Table 10, entry 2). The structure of *β*-azidation product confirmed from spectral data. In the IR spectrum, the presence of an absorption band at 2104 cm^{-1} due to azide and 1696 cm^{-1} due to ketone indicated the **50a** product formation. In ^{1}H-NMR spectrum (see Fig. 13), the absence of vinyl proton peak and the presence of a triplet at δ 3.76 ppm and δ 3.27 ppm due to aliphatic methyl confirm the azide addition, and in the ^{13}C-NMR spectrum (see Fig. 14), the presence of δ 197.1 ppm signal established the product formation **52a**. In the high-resolution mass spectrum presence of molecular ion peak at *m/z* 176.0824 $(M+H)^{+}$ further support the product formation.

Encouraged by this result, further to improve the efficiency of the reaction, different amine bases (DABCO, DBU and DMAP) were screened (Table 10, entries 3-5). Gratifyingly, when the reaction performed in presence of DABCO (20 mol%) at room temperature, **50a** was obtained in 94% yield (Table 10, entry 5). While, the reaction was carried out with decreasing catalyst loading to 10 mol% the expected product **50a** obtained in 96% yield (Table 10, entry 13). Solvents such as DCM, THF, CH_3CN, DMSO were screened with DABCO catalyst, but result were discouraging (Table 10, entries 6-9). Additionally, the reaction at 50 °C considerably diminished the yield of the product **50a** (Table 10, entry 11). When the reaction was carried out in absence of light, formation of excellent yield product indicated that the reaction is not triggered by light source (Table 10, entry 12).

Table 10: Optimization of the reaction parameters

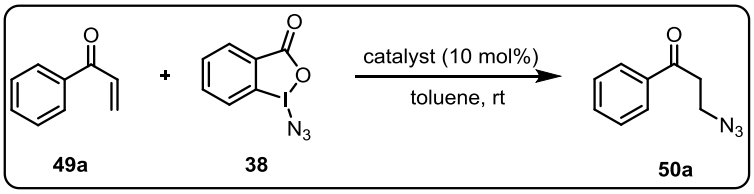


Sr. No.	Additive/Catalyst (20 mol%)	Solvent	Time (h)	Yield (%)[a]
1	-	Toluene	96	-
2	Imidazole	Toluene	18	51
3	DBU	Toluene	13	85
4	DMAP	Toluene	13	63
5	DABCO	Toluene	8	94
6	DABCO	DCM	12	83
7	DABCO	THF	12	73
8	DABCO	ACN	17	71
9	DABCO	DMSO	20	47
11[b]	DABCO	Toluene	2	35
12[c]	DABCO	Toluene	9	90
13[d]	**DABCO**	**Toluene**	**8**	**96**

All reactions were performed on 0.1 mmol scales. [a]Yields were calculated after silica gel column chromatography, [b]reaction at 50 °C. [c]reaction in the absence of light. [d]10 mol % of DABCO .

To validate the generalization of reaction, the some of the reported methods were attempted for this transformation but interestingly poor yield of the product **50a** was observed (Table 11, entries 1-4). As expected, when the reaction was carried out with *o*-iodobenzoic acid no product formation was observed (Table 11, entry 5). Subsequently, different bases such as pyridine, TMEDA, quinidine, 3-quinuclidinol, 4-methylmorpholine, guanyl thiourea, guanidinium chloride were tried but yield of reaction did not improve (Table 11, entries 6-13).

Table 11: Optimization of the reaction condition



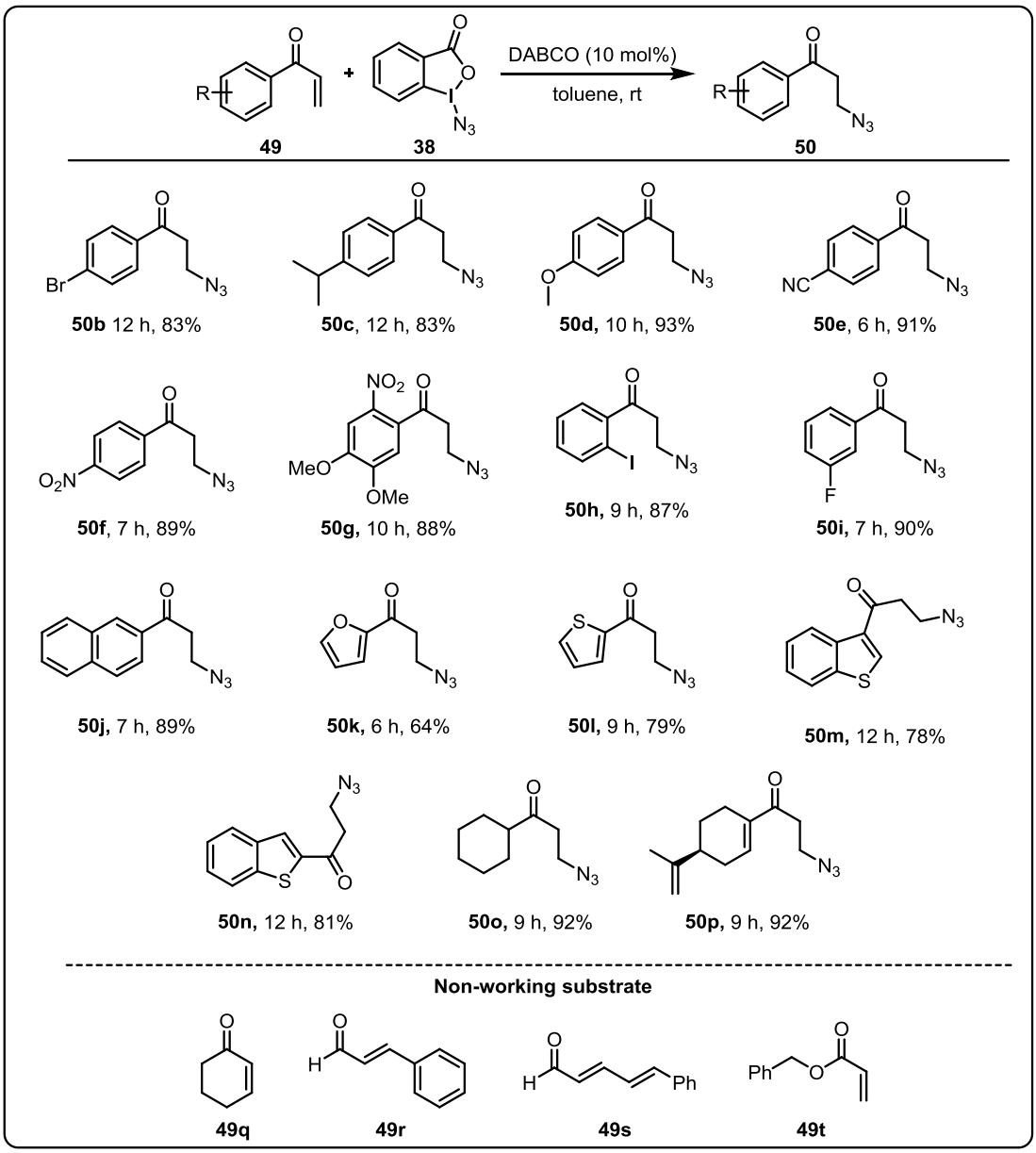
Sr. no	Additive/Catalyst (20 mol%)	Time (h)	Yield (%)[a]
1	1,10-Phenanthroline	48	40
2	2,6-di-*tert*-butyl-4-methylpyridine	48	5
3	CuI	48	11
4	Cu(OAc)2	48	34
5[e]	-	48	-
6	Pyridine	25	33
7	TMEDA	11	51
8	Quinidine	48	-
9	3-Quinuclidinol	10	73
11	4-Methymorpholine	14	66
12	Guanyl thiourea	30	31
13	Guanidinium chloride	30	26

All reactions were performed on 0.1 mmol scales. [a]Yields were calculated after silica gel column chromatography. [e]In the presence of 1.1 eq. of *o*-iodobenzoic acid.

With the optimized reaction conditions in hand, the scope, generality and limitation of the reaction were investigated and results are summarized in Table 12. A diverse range of electron rich and electron poor vinyl aryl ketones **49a-49j** were prepared and subjected to optimize reaction condition yielded respective products **50a-50j** in good to excellent yields. A wide range of heteroaryl vinyl ketones were subjected to optimized condition and delivered *β*-azidoketones **50l-50n** in good yields. When furan vinyl ketone was subjected to optimized reaction condition, moderate yield of the product **50k** observed due unstable nature of furan. Subsequently, when alkyl vinyl ketones **49o** was treated under the optimized condition, the product **50o** formed in excellent yield. The reaction of **49p**, where *β*-mono substituted, *β*-unsubstituted and isolated olefin was present in the system. However, when **49p** was treated under optimized condition, **50p** formed exclusively. The result shows that azide addition occurred only from unsubstituted

double bond. This result was eventually verified with other activated *β*-substituted alkenes, Such as enones **49q** monosubstituted enones **49r**, dienones **49s**, acrylates **49t**, where failed to generate desired product.

Table 12: Substrate scope for *β*-azidation compounds



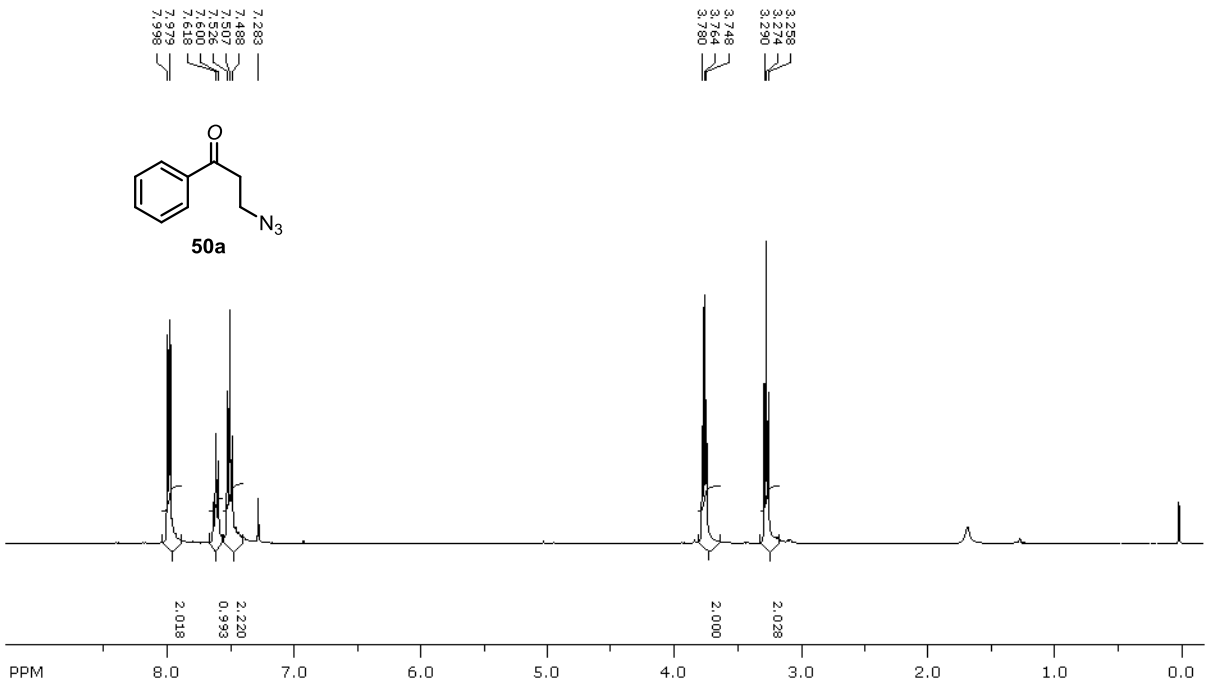


Figure 13: ^{1}H-NMR spectrum of **50a**

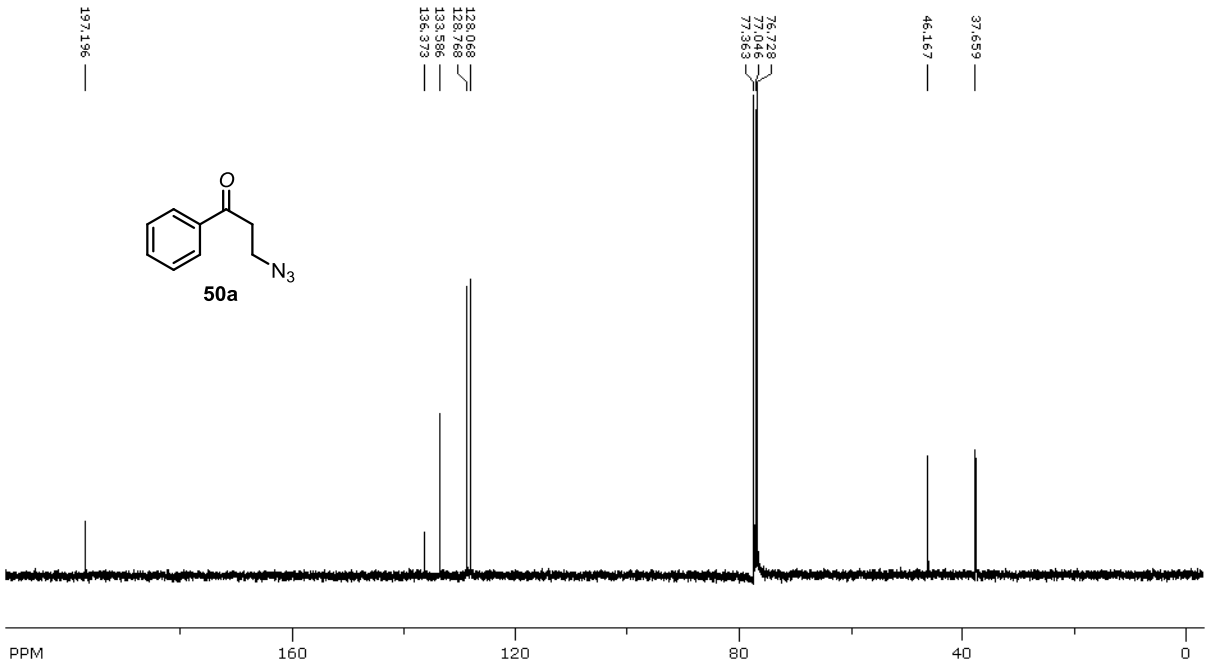


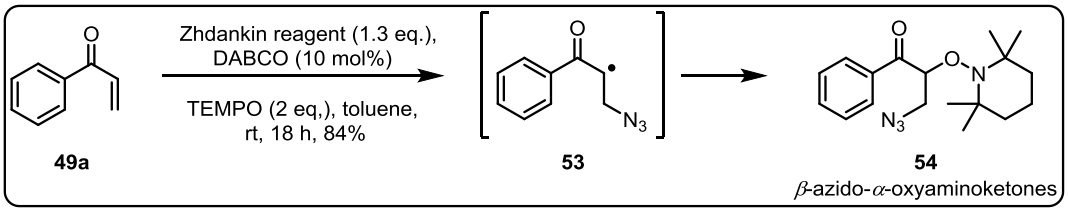
Figure 14: ^{13}C-NMR spectrum of **50a**

3.4: Mechanistic insights

In an attempt to gain mechanistic insight, following control experiments were performed.

3.4.1: Radical entrapment by TEMPO

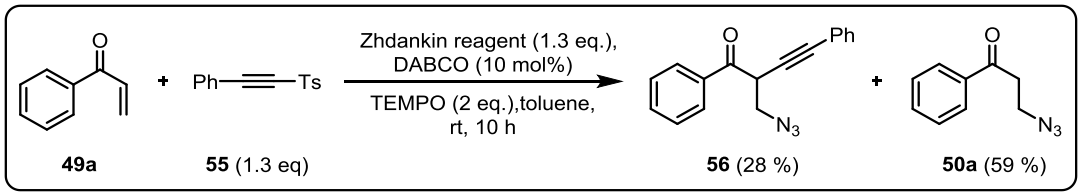
TEMPO is used as a radical marker in organic radical reactions. The reaction of **49a** and Zhdankin reagent **38** with TEMPO provided the TEMPO adduct **54** in 84% yield, Scheme 36. This indicates that the reaction follows the free radical pathway. The *β*-azido-*α*-oxyaminoketone **53** further gives access for elaboration to *β*-amino-*α*-hydroxyketones.[75]



Scheme 36: Synthesis of *β*-azido-*α*-oxyaminoketones

3.4.2: Radical trapping experiment: one-pot azidoalkynylation

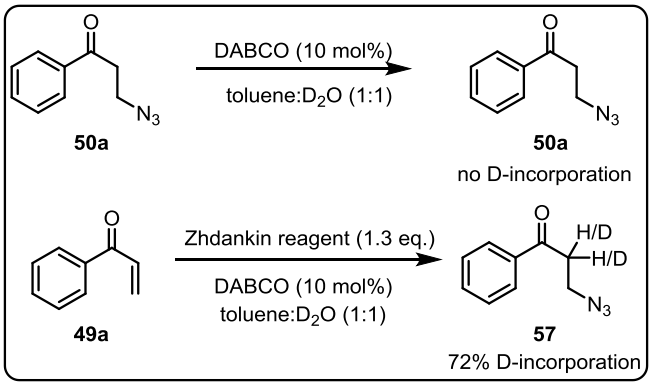
The reaction of **49a** with phenylethynyl-*p*-tolyl sulfone **55** under the optimized condition furnished **56** by undergoing a tandem azidoalkynylation, Scheme 37.[76] As expected, this result additionally suggests the potential involvement of a radical species **53** in the transformation.



Scheme 37: Reaction of phenylethynyl *p*-tolyl sulfone and activated enone

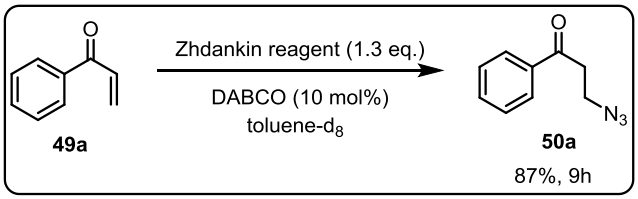
3.4.3: β-Azidation reaction with D_2O

To identify the role of water, moisture or solvent in quenching the radical intermediate **53** formed during the reaction, *β*-azidation reaction was carried out with **49a** and Zhdankin reagent in touene:D_2O (1:1), Scheme 38. The product **57** was isolated with 72% D-incorporation. On the other hand, when reaction was performed with **50a** in toluene:D_2O (1:1), no D-incorporation was observed, indicating that intermediate radical species abstract H-radical from moisture/water present in the solvent medium.



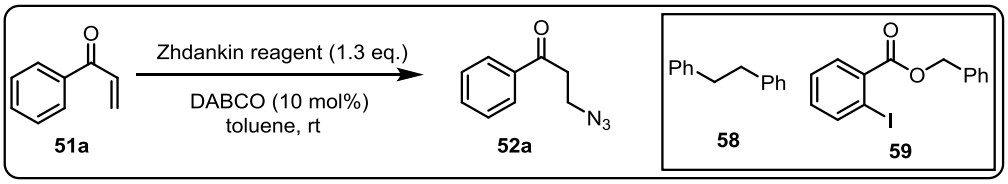
Scheme 38: *β*-azidation reaction with D_2O

To confirm this hypothesis, we have performed the reaction of **49a** in presence of toluene-d_8 were no D-incorporation was observed, Scheme 39. This result further confirms that, the radical species **53** formed in the reaction medium quenched by solvent or traces of water present in the reaction medium.



Scheme 39: Reaction with toluene-d_8

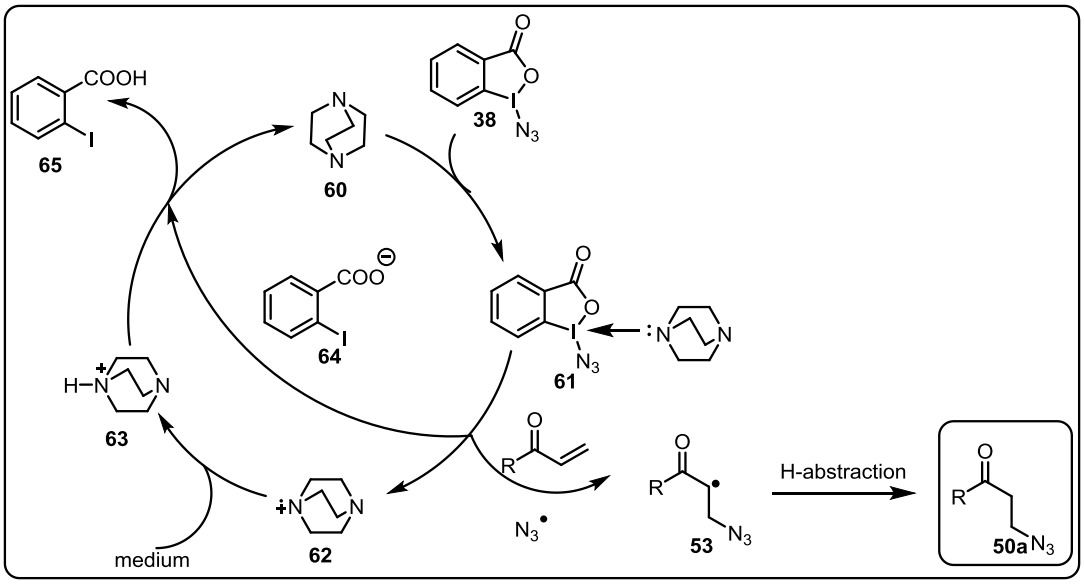
In an effort to prove whether the intermediate radical **53** is taking up H-atom from the solvent toluene, Scheme 40. We have recorded the ^{1}H-NMR and mass data of the crude reaction mixture of **49a** converting to **50a**. Our intention is to find either i) **58** formed via dimerization of benzyl radical or ii) the DABCO radical cation might also SET oxidize the benzyl radical to give the corresponding benzyl cation that will react with *ortho*-iodobenzoate to the corresponding ester **59**. However, we could not be able to detect either 1,2-diphenylethane **58** or *ortho*-iodobenzoate **59** from NMR and mass data of the crude reaction mixture. Further, confirm the process that intermediate **53** quenched through the taking proton from moisture or traces of moisture present in the reaction medium.



Scheme 40: *β*-Azidation reaction of phenyl vinyl ketone

3.5: Plausible mechanism for β-azidation reaction

Based on the control experiments and literature reports,[77] a plausible mechanism for *β*-azidation reaction is outlined below, Scheme 41. Charge transfer complex[78] (CT) or electron-donor-acceptor (EDA) complex **61** formed between DABCO **60** and Zhdankin reagent **38** leads to the generation of azide radical. The reaction of activated olefin **49a** with azide radical forms radical intermediate **53**, which subsequent abstract proton from traces of moisture in the medium to form product **50a**. Further, so formed DABCO radical cation **62** can abstract proton from the medium leads to **63**. The so formed protonated DABCO can then protonate o-iodobenzoate **64** leads to regeneration of DABCO in the reaction medium.

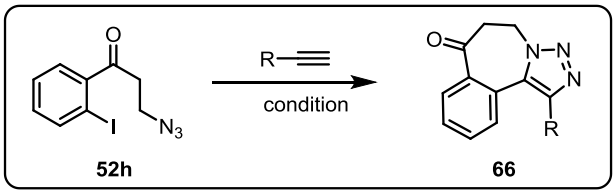


Scheme 41: Plausible mechanism for *β*-azidation of activated olefin

3.6: Synthesis of a new class of fused tricyclic 1,2,3-triazoles

1,2,3-Triazoles has gained considerable attention due to their extensive applications in medicinal chemistry[79] and material sciences.[80] Especially, a large number of triazole derivatives possesses a diverse range of pharmacological activities such as antituberculosis, anti-HIV, anti-cancer, antiviral, antibacterial, antifungal, etc.[79] Owing to the large dipole moment and hydrogen bond acceptor capability, 1,2,3-triazoles could act as effective amide surrogates in biologically significant molecules.[81] Apart from bioactivity its applications can also be found in industrial sector, agrochemicals, polymer industry, pigments and optical brighteners.[82]

The emerging field of click chemistry offers a unique approach to the synthesis of simple or fused 1,2,3-triazole-containing molecules. Fused 1,2,3-triazoles are another interesting set of compounds because of their presence in variety of biologically active natural products and drugs.[83] Considering significance and application of the triazole compound, the development of new strategy to access them is of great importance. In an attempt to illustrate the generality and synthetic utility of this method, we have considered the synthetic strategy for fused tricyclic triazole **66**, Scheme 42.[72] With the presence of well positioned iodo and azide group in **52h**, we have planned cascade Sonogashira reaction followed by an intramolecular Cu-catalyzed azide-alkyne cycloaddition (CuAAC).[84]

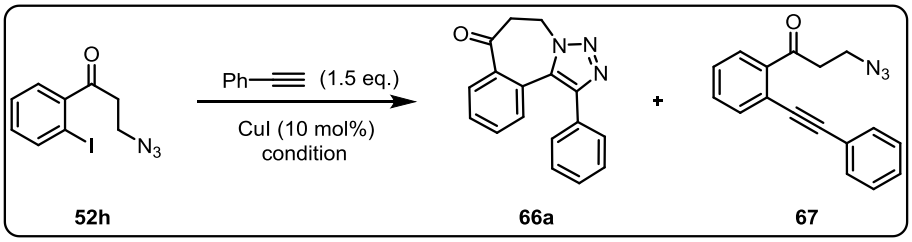


Scheme 42: General reaction for the synthesis of tricyclic triazole

Initially we have applied the reported procedure for the synthesis of tricyclic 1,2,3-triazole,[85] however, this result in the poor formation of the expected product **66a**. Further, to improve yield of the reaction various condition have screened, and we were pleased to identify suitable condition for the product **66a**. The tricyclic triazole product **66a** confirmed from spectral data. In the absorption spectrum the absence of azide peak and presence of ketone 1683 cm^{-1} indicate the product formation. In ^{1}H-NMR spectrum (see Fig. 16) the shifting the proton value at δ 4.80 ppm due to aliphatic CH_2, and in the ^{13}C-NMR (see Fig. 17) cyclic carbonyl at δ 200.1 ppm further established the product formation. Moreover, crystal structure confirms the product

formation Fig. 15. Few other tricyclic triazole **66b-66f** analogs were synthesized by employing the same optimized protocol. To confirm the mechanism pathway, reaction was stoped after 10 h and isolate the intermediate **67**, which indicate that the reaction first undergoes Sonogashira reaction and subsequently, the azide-alkyne [3+2]-cycloaddition to generate **66a.**

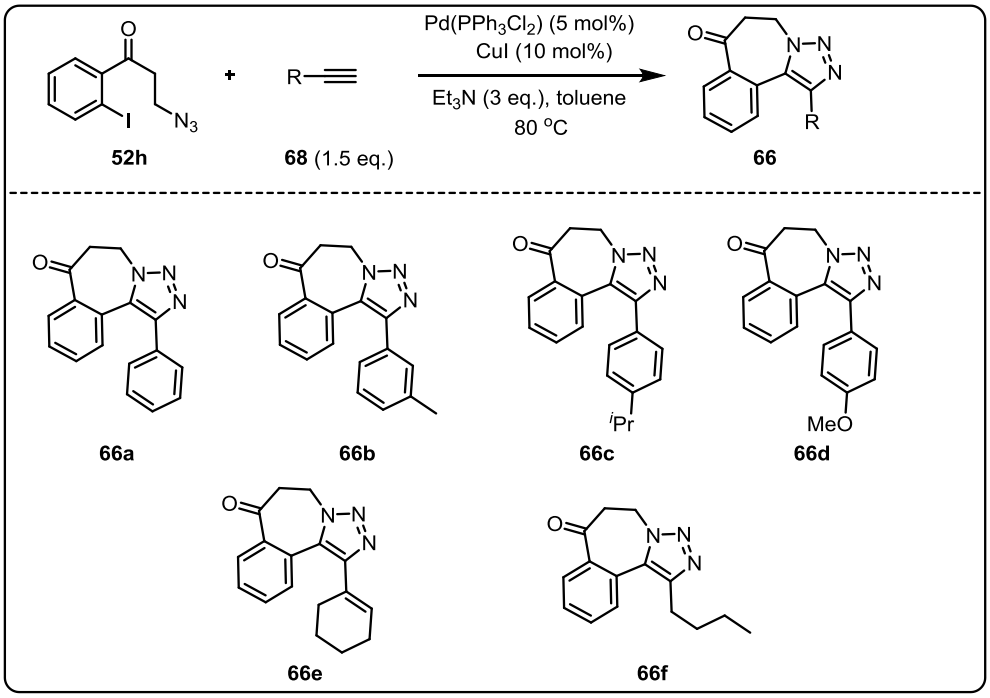
Table 13: Optimization of the reaction parameters



Sr. No.	Pd catalyst (5 mol%)	Base	Solvent	Temp (^{o}C)	Time (h)	Yield (%)[a] 66a/67
1	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	DMF	120	31	14/37
2	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	THF	120	40	Trace/0
3	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	ACN	120	20	25
4	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	Toluene	120	20	33
5	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	Toluene:DMF (1:1)	80	13	23
6	$Pd(PPh_3)_2Cl_2$	Et_3N (10 eq.)	Toluene:THF (1:1)	80	13	27
7	**$Pd(PPh_3)_2Cl_2$**	**Et_3N (3 eq.)**	**Toluene**	**80**	**26**	**49**
8	$Pd(PPh_3)_2Cl_2$	K_2CO_3 (3 eq.)	Toluene	120	-	-
9	$Pd(PPh_3)_2Cl_2$	Na_2CO_3 (3 eq.)	Toluene	120	18	Trace
10	$Pd(PPh_3)_2Cl_2$	KOAc (3 eq.)	Toluene	120	-	-
11	$PdCl_2$	Et_3N (10 eq.)	Toluene	120	-	-
12	$Pd(OAc)_2$	Et_3N (10 eq.)	Toluene	120	-	-
13	$Pd_2(dba)_3$	Et_3N (10 eq.)	Toluene	120	-	-
14	$Pd(PPh_3)_2Cl_2$	Et_3N (3 eq.)	Toluene	80	10	25/51

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

Table 14: Synthesis of new class of tricyclic 1,2,3-triazole



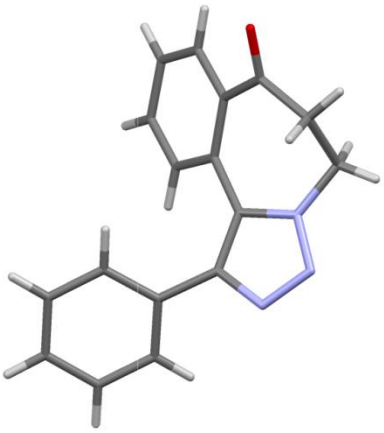


Fig. 15: ORTEP diagram of **66a** with 50% ellipsoidal probability.

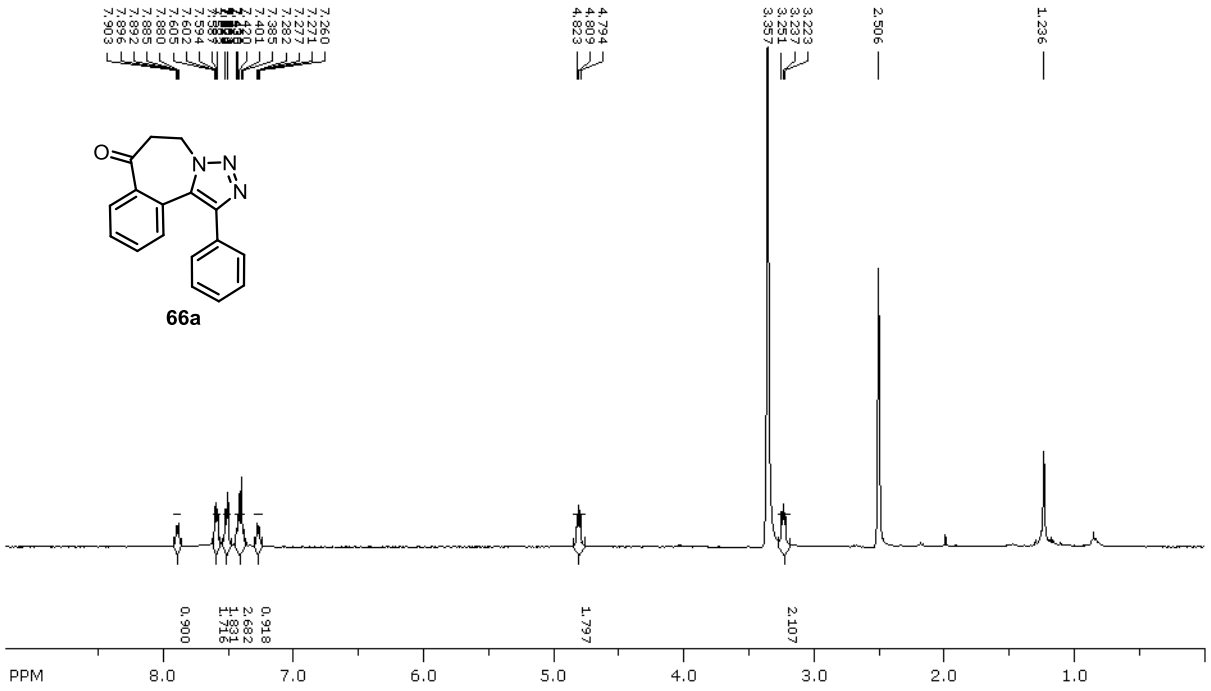


Figure 16: ^{1}H-NMR spectrum of **66a**

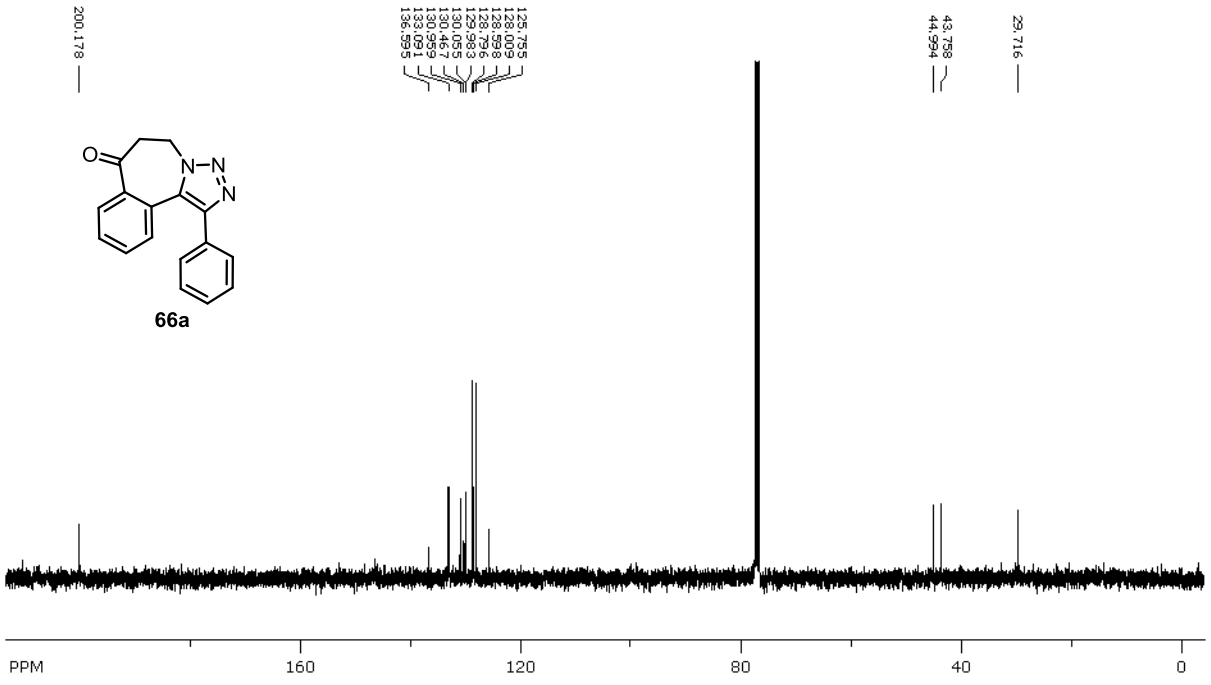
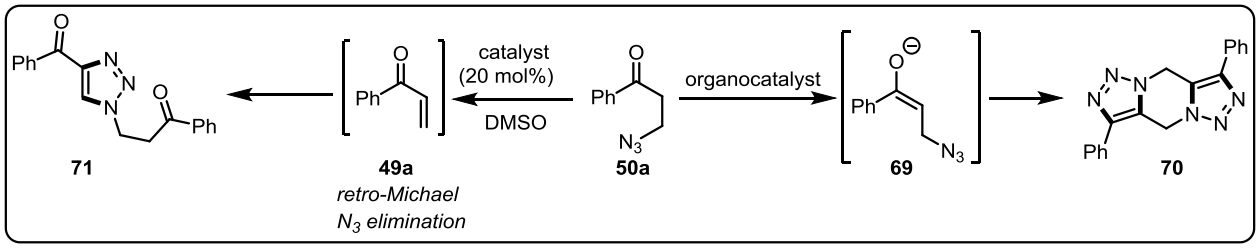


Figure 17: ^{13}C-NMR spectrum of **66a**

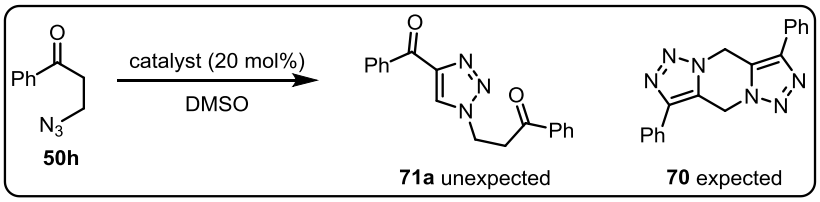
3.7: Synthesis of 1,4-disubstituted 1,2,3-triazoles

Organocatalytic [3+2] reaction between azide and enolisable ketone/aldehyde has gained tremendous attention owing to their high reaction rate, mild reaction conditions and wide substrates scope. [86] This is an alternative approach for well-known metal (Cu, Ru, Ir) catalysed azide alkyne cycloaddition reaction.[84] While working on the synthesis of tricyclic triazole, we envisioned that this chemistry could be utilized for the synthesis of tricyclic bis-1,2,3-triazole **70** via base-mediated enolate **69** generation could undergo azide-enolate[3+2]cycloaddition followed by intramolecular click reaction, Scheme 43. The reaction of **52a** with catalytic DABCO resulted in the formation of unexpected 1,4-disubstituted-1,2,3-triazole **71a** product via a [3+2]-cycloaddition of the in situ generated enone **51a** and the azide **52a**, followed by aromatization. Formation of enones from *β*-azidoketones, which occurs via a retro-Michael process, is rare since azide is a poor leaving group.[87] The triazole product **71** confirmed from spectral data. In the IR spectrum, the absence of azide peak and presence of two ketones at 1657 cm^{-1} and 1651 cm^{-1} indicate the product formation. In ^{1}H-NMR spectrum the shifting the proton value at δ 4.95 ppm and δ 3.75 ppm due to aliphatic CH_2, and in the ^{13}C-NMR presence carbonyl peak at δ 196.1 ppm and δ 185.7 ppm further establish the product formation. Further, HRMS data confirm the product formation.



Scheme 43: General approach for *1,4-disubstituted 1,2,3-triazoles*

Table 15: Optimization of the reaction parameters

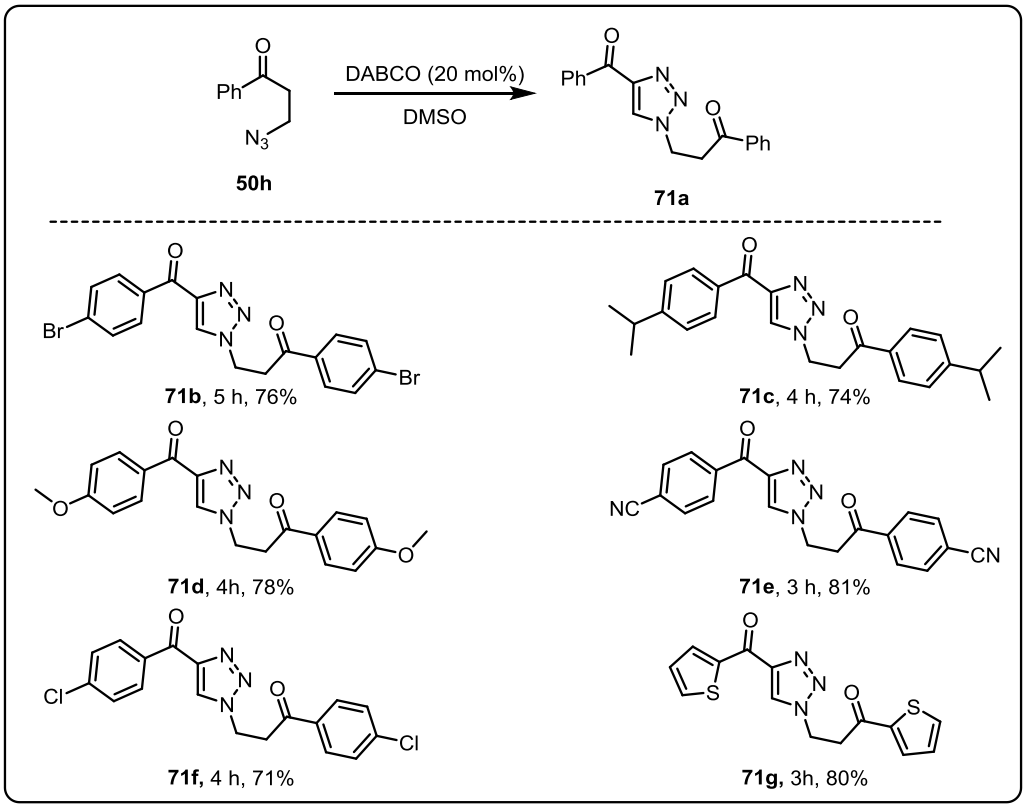


Sr. No.	Catalyst (20 mol%)	Temp (^{o}C)	Time (h)	Yield (%)[a] 71
1	Et_3N	rt	13	45
2	DBU	rt	10	53
3	K_2CO_3	rt	-	-
4	Proline	rt	-	-
5	Pyrrolidine	rt	-	-
6	Piperidine	rt	-	-
7	Benzylamine	rt	-	-
8	DABCO	rt	15	73
9	**DABCO**	**60**	**4**	**75**
10	DABCO (10 mol%)	60	6.5	65

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

The brief optimization studies were carried out by varying the catalysts in the synthesis. Among them, the reaction of **52h** with Et_3N and DBU furnished **71a** in moderate yield (Table15, entries 1-2), while the other catalyst such as (K_2CO_3, proline, pyrrolidine, piperidine, benzylamine,) were failed to give the product (Table 15, entries 3-7). When the reaction was performed in presence of 10 mol% DABCO at 60 ^{o}C delivered **71a** in good yield. With the optimized reaction condition in hand and realizing the significance of reaction few more derivatives were synthesized in good yield Table 16.

Table 16: Synthesis of triazole

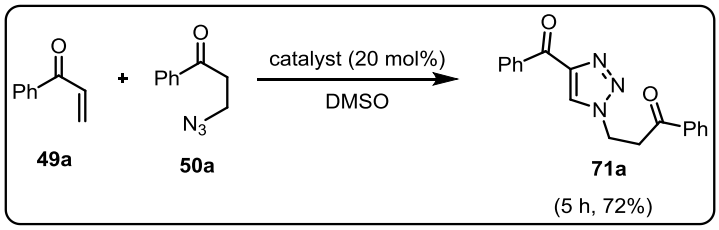


3.8: Mechanistic insights

We then moved our attention to understand the mechanism and identify the intermediate formed in the reaction. The reaction, which proceeds under simple and mild conditions, also represents a metal-free azide-alkene click reaction.[88]

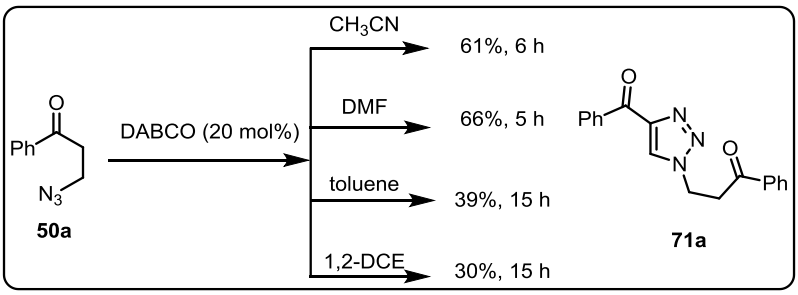
To confirm the hypothesis and gain insight the mechanism few control experiment were conducted.

A) When the reaction was carried out with activated olefin **51a** and azide **52a** under the optimized condition, the expected product **71a** was obtained in 72%. This result indicated that the reaction going through formation of enone **51a** intermediate, Scheme 44.



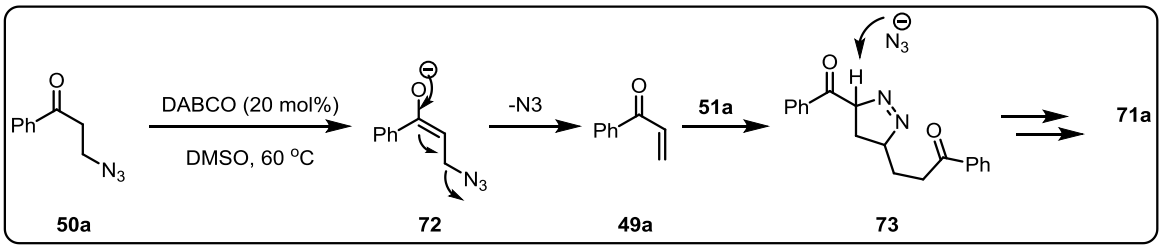
Scheme 44: Reaction with external activated olefin

B) To check the role of solvent in aromatization, various solvents were screened for this reaction Scheme 45. This result shows that DMSO solvent has no role in aromatization.



Scheme 45: Solvent screening for 1,4-disubstituted 1,2,3-triazoles

C) The reaction of **52a** was performed under the optimized reaction condition in inert atmosphere the resultant product **71a** obtained in 77%, indicate that the generated azide anion **73** may responsible for the hydrogen abstraction and subsequent aromatization, Scheme 46.



Scheme 46: Reaction of *β*-azidoketone under inert atmosphere

In conclusion, we have developed an efficient organocatalytic *β*-azidation of enones under practical and scalable conditions and further proved that reaction going through electron-donor-acceptor pathway. In addition, a new method for the rapid assemblage of functionalized fused triazoles and disubstituted triazole has been established. Functionalized tricyclic triazoles have been synthesized in moderate yields, whereas 1,4,-disubstituted-1,2,3-triazoles synthesized in good yield.

Chapter 4

Synthesis of axially chiral styrenes via Suzuki-Miyaura cross coupling reaction

Chirality plays a vital role in biological and life-sustaining processes.[89] It is a geometric property of a molecule that controls the spatial arrangement of substituents within a molecular framework and retaining its intrinsic properties. Chirality belongs to a single chiral center is known as point chirality. Whereas, axial chirality originates from highly sterically hindered rotation of a chiral axis.[90] It has received tremendous attention from chemists because of its widespread appearance in biologically active compounds and medicinal important compounds.[91] Axially chiral compounds have found common usage as chiral ligands in asymmetric catalysis.[92]

Various biologically active compounds which are widely present in nature exhibit an axis of chirality, Fig. 18.[93] Vancomycin was first isolated by Edmund Kornfeld from a soil sample collected from the interior jungles of Borneo and shows promising antibiotic activity. Steganacin is a parent member of *Steganotaenia Araliacea* dibenzocyclooctadiene ligand showing antileukemia activity. Knipholone was isolated from the *Kniphofia foliosa* exhibits antimalarial activity and Korupensamines, was isolated from *Ancistrocladus korupensis*, as a potent anti-HIV agent.

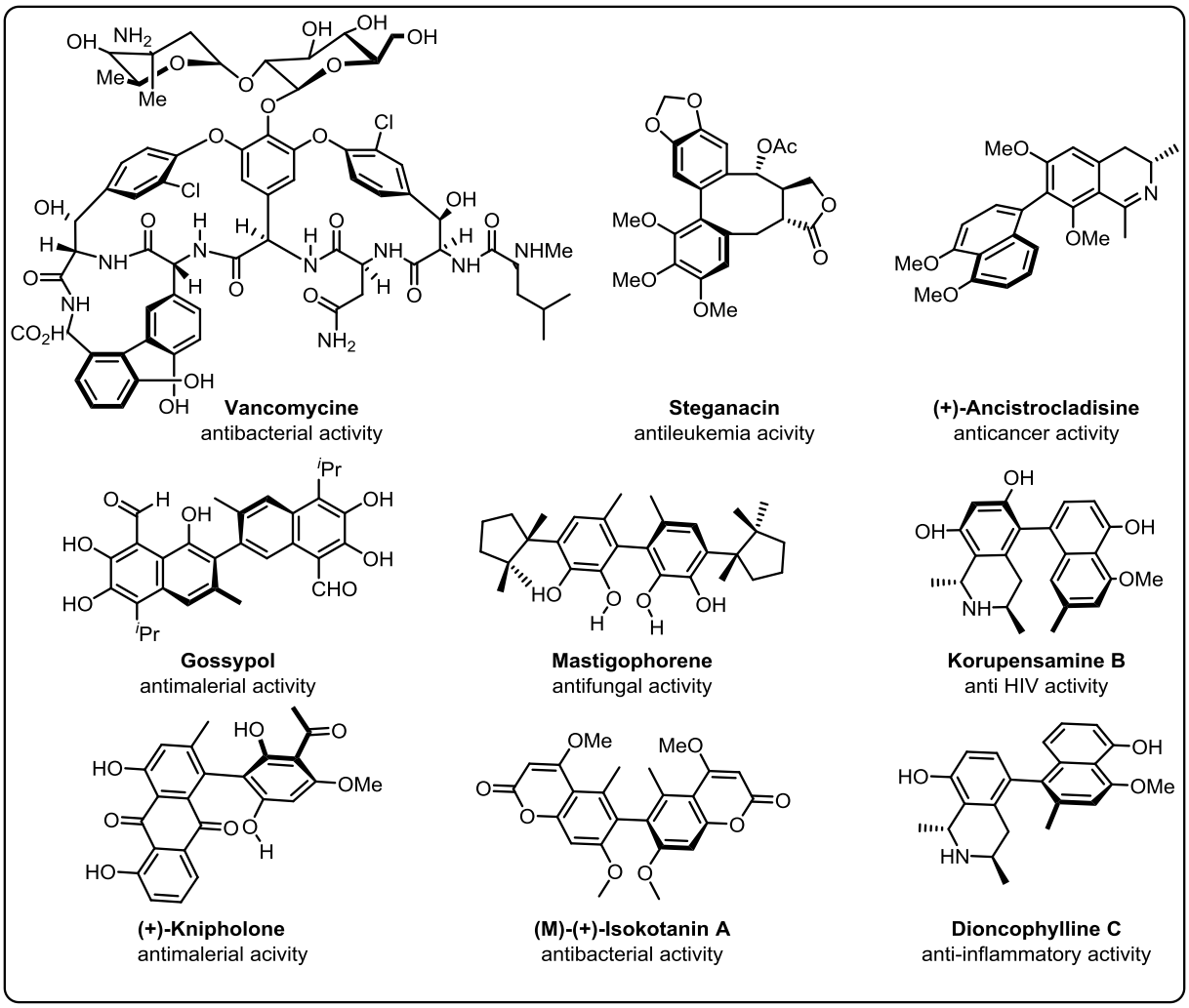


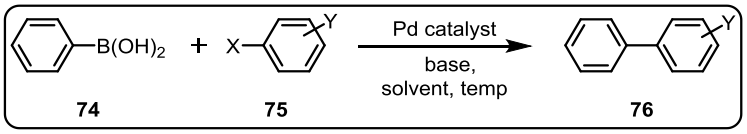
Figure 18: Representative examples of bioactive axially chiral biaryl compounds

These aforementioned axially chiral compounds represent an important class in the area of pharmaceuticals and materials sciences.[94] It holds the key to the ever-growing research interest for the development of an efficient synthetic protocol. Different strategies to arrange

isomerically enriched atropisomers by stereoselective chemical processes are still restricted to selected structural entities. Synthesis of axially chiral compounds based on various challenging approaches such as coupling reaction, de-novo construction of arenes, desymmetrization, atropselective photoreaction, and cycloaddition reaction are well known.[95] Among all these synthetic methods Suzuki-Miyaura cross-coupling reaction is well explored and its advantage and mechanism are mentioned in the next subsection.

4.1: Suzuki-Miyaura cross coupling reaction

From the last three decades, transition-metal catalyzed cross-coupling reactions have an important role in synthetic transformation.[96] A huge development in the area of various coupling reactions has been done especially in the Suzuki cross-coupling reaction.[97] Suzuki and Miyaura have first developed a cross-coupling reaction by using boronic acid **74** and organohalide **75** as a coupling partner in presence of base and palladium catalyst for the formation of biaryl compound **76**, Scheme 47.[98]



Scheme 47: General Suzuki-Miyaura cross-coupling reaction for the synthesis of biaryls

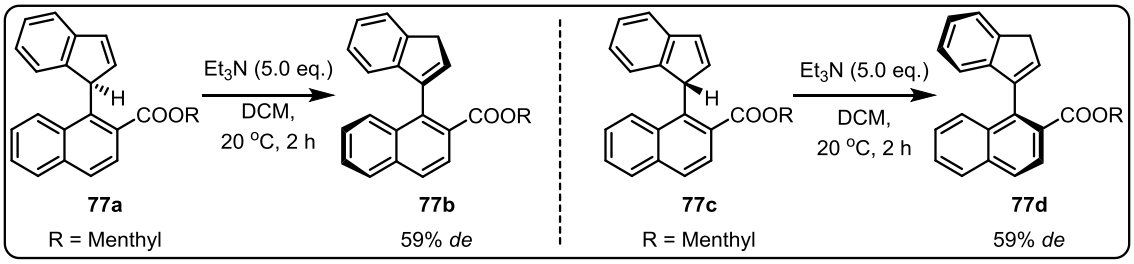
Suzuki-Miyaura cross-coupling reaction holds many advantages,[99] such as i) demonstrates good reproducibility together with high yield and selectivity[100] ii) symmetrical and unsymmetrical substrates work well for this reaction iii) mild reaction conditions can be employed[101] iv) low quantity of palladium catalyst or heterogeneous palladium catalyst can be employed for this transformation v) high stability of organoborane reagent[102] and vi) water may be used as solvent in the reaction.[103] Few disadvantages are also associated with this reaction, for example, i) highly hindered partners bearing three or four *ortho* substituents is often problematic[104] ii) The boronic acid can be difficult to purify, containing mixtures of trimeric anhydrides boroxines.[105]

This Suzuki coupling reaction is efficiently used for the synthesis of the racemic or axially chiral biaryl compound. Numerous synthetic methods are known to control the axial chirality in biaryl compounds. Despite this, the axially chiral alkenes were rarely prepared using

Suzuki coupling reaction. In the next subsection, some of the pioneering contributions towards the synthesis of axially chiral alkenes are described.

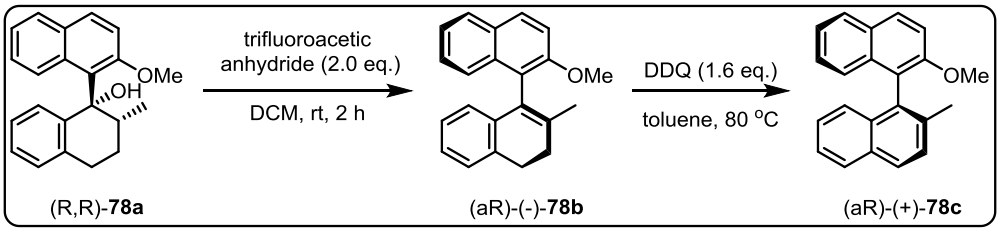
4.2: Different methods to access axially chiral alkenes

In 1996, Wallace *et al.*[106] developed the synthesis of axially chiral indenes through molecular rearrangement, Scheme 48. The reaction of an optically active indenyl naphthalene-2-carboxylates **77a, 77c** with triethylamine furnished the axially chiral indene **77b, 77d**. This reaction has opened a new domain towards the synthesis of several other types of axially chiral vinyl arene.



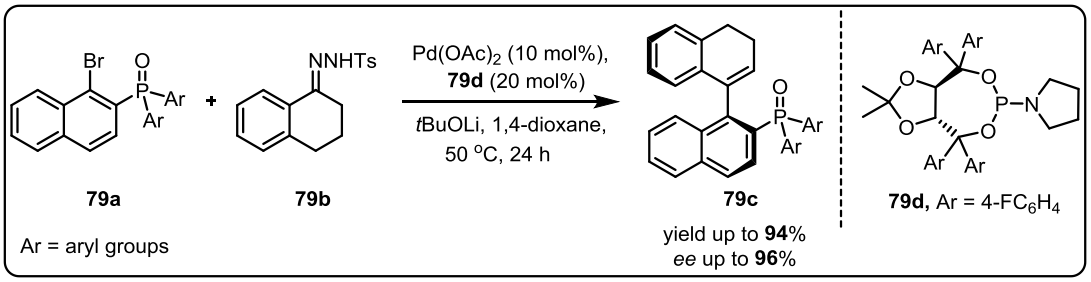
Scheme 48: Wallce's synthesis of axially chiral indenes

In 2001, Miyano *et al.*[107] described the highly stereospecific conversion of central to axial chirality, Scheme 49. Dehydration of **78a** led to the stereospecific conversion of its **78b** with high yield and excellent enantioselectivity. Further, DDQ aromatization led to the formation of biaryl **78c** without losing its chirality.



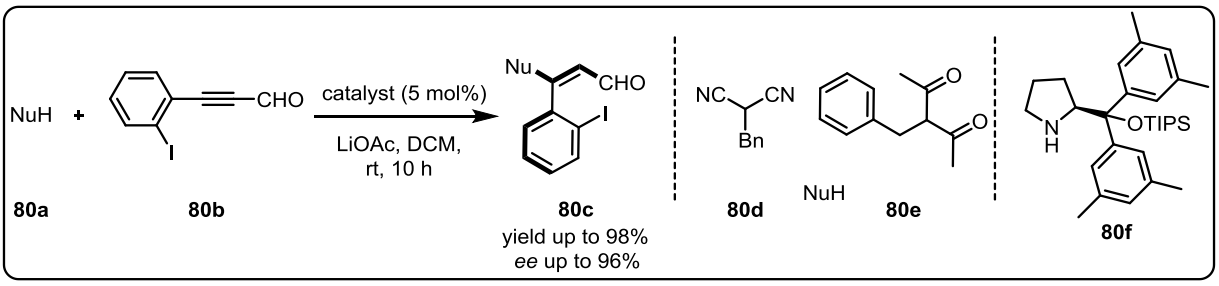
Scheme 49: Miyano's synthesis for vinyl arenes

In 2016, Gu *et al.*[108] demonstrated an efficient enantioselective synthesis of vinyl arenes **79c**, Scheme 50. The reaction of aryl bromide **79a** and hydrazones **79b** with palladium acetate and ligand **79d** delivered the axially chiral dihydrobinaphthalene phosphine oxide **79c** with high yield and excellent enantioselectivity.



Scheme 50: Gu's synthesis of axially chiral alkene

In 2017, Tan *et al.*[109] developed the first organocatalytic atropselective synthesis of styrene **80c**, Scheme 51. The reaction between alkynal **80b**, catalyst **80f** and activayed methylene compound **80d, 80e** delivered the axially chiral styrene **80c** with high yield and excellent enantioselectivity. The reaction preceded *via* secondary amine-catalyzed iminium activation under mild reaction conditions.



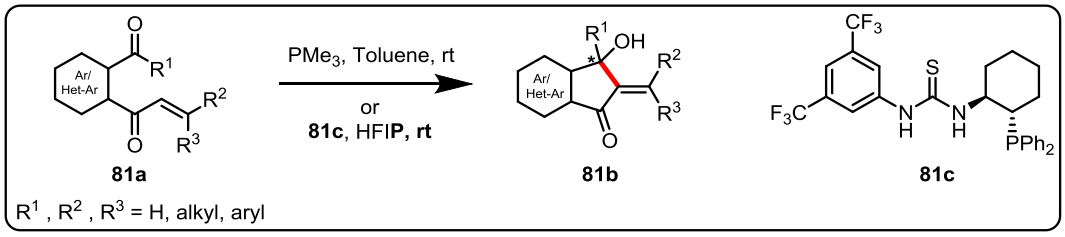
Scheme 51: Tan's synthesis of axially chiral styrenes

Despite tremendous advancement in the Suzuki-Miyaura cross-coupling reaction, these aforementioned strategies and a brief literature survey revealed that most of the reactions mainly focused on the axially chiral biaryl coupling or aryl/heteroaryl coupling reactions.[110] The lack of general strategies for the synthesis of axially chiral styrenes encouraged us to envision new advancements in coupling chemistry.

4.3: Atropselective synthesis of alkenes

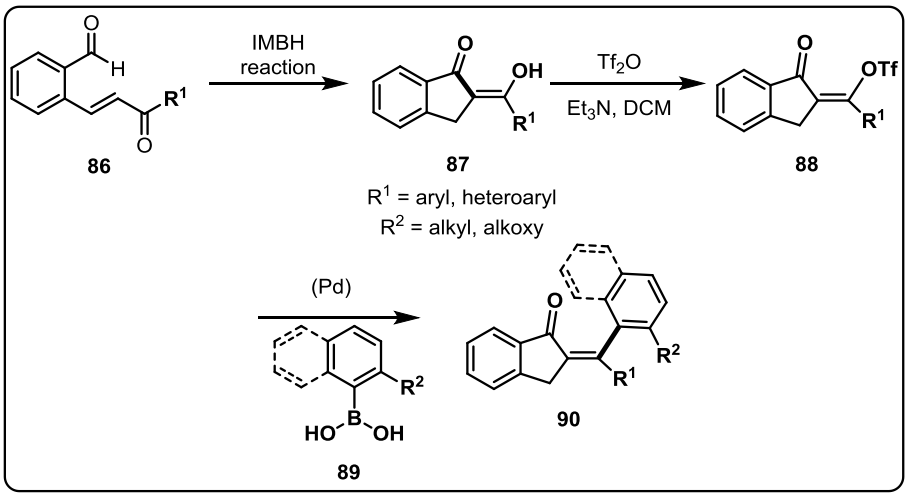
Alkenes are widely studied in organic synthesis.[111] There are various reports known for the synthesis of alkenes and their subsequent transformation to a variety of important compounds. However, only a handful reports are known for the asymmetric synthesis and application of the axially chiral alkene.[112] However, Kawabata first illustrated this type of atropisomer which described the new concept in memory of chirality.[113] There are mainly two reasons for the axially chiral alkenes remaining underexplored,[114] i) relatively low-rotation energy to racemization and ii) the difficulty to control the enantioselectivity.

Our current research is focused on the efficient synthesis of cyclopentanes owing to their importance in natural products and pharmaceuticals.[115] Earlier, we have developed an enantioselective intramolecular Morita-Baylis-Hillman (IMBH) reaction-based approach for enantioselective synthesis of cyclopent[*b*]annulated arenes or heteroarenes, Scheme 52.[116] This study prompted us to new design new substrate that is amenable for the synthesis of axially chiral styrenes.



Scheme 52: Enantioselective IMBH reaction for cyclopentanes

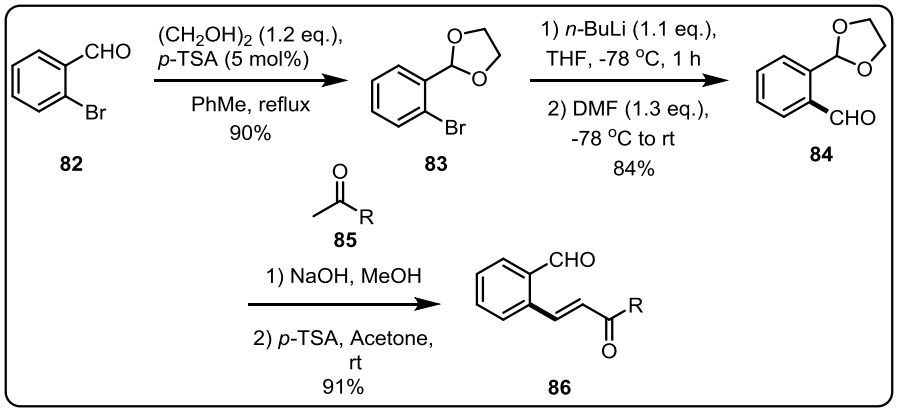
To address the challenge to synthesize axially chiral alkene, **88** was considered as a model substrate, Scheme 53. A few crucial aspects were considered regarding the substrate design before performing the coupling reaction, such as (i) The steric hindrance of indenone and adjacent aryl moiety, (ii) the electronic nature and steric hindrance of boronic acid. The required starting material **87** was accessed by the IMBH reaction of **86** and subsequent triflate protection of **88**.



Scheme 53: Our design for the synthesis of axially chiral styrene

4.4: Results and discussion:

With the desire to access the axially chiral styrenes, we have initiated the synthesis of the proposed starting material **87** through the IMBH reaction of enone-aldehyde **86**, Scheme 54.[117] A modular access of enone-aldehyde **86** can be easily achieved from bromobenzaldehyde **82** by following a four-step protocol. The protection of the aldehyde with ethylene glycol followed by formylation with *n*-Buli/DMF led to the formation of **84**. Further, condensation of **84** with respective ketone **85** and smooth deprotection of aldehyde resulted in the formation of enone-aldehyde **86** in excellent yield.

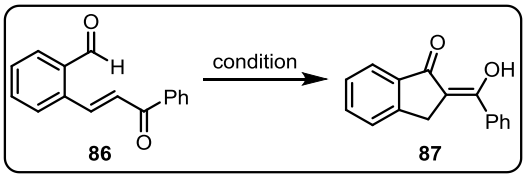


Scheme 54: General procedure for the synthesis of enone-aldehyde **86**

We have started optimization studies by considering **86a** as a model substrate, Table 17. A wide variety of phosphine and amine catalysts were screened for the IMBH reaction. The

reaction with phosphine catalysts (PMe_3, PCy_3, and PPh_3) in toluene was discouraging as no product formed in that reaction (Table 17, entries 1-3). But, when the reaction was carried out with PBu_3 expected IMBH product **87a** was obtained in good yield (Table 17, entry 4). The structure of IMBH product **87a** was carefully deduced from the IR, NMR, and HRMS data. In the IR spectrum, the presence of a broad absorption band at 3400 cm^{-1} due to alcohol and a sharp band at 1690 cm^{-1} due to the unsaturated cyclic ketone was indicate the formation of product **87a**. In the ^{1}H-NMR spectrum (see Fig. 19), presence of a broad singlet at a δ 14.0 ppm due to the OH proton, and a singlet at δ 4.01 ppm due to the methylene, and in ^{13}C-NMR spectrum (see Fig. 20), presence of a peak at δ 190.1 ppm due to unsaturated ketone and a peak at δ 40.8 ppm due to methylene carbon, confirmed the formation of product **87a**. The presence of a molecular ion peak at *m/z* 236.0838 due to $(M+H)^+$ further supported the product formation.

Table 17: Optimization of reaction parameters



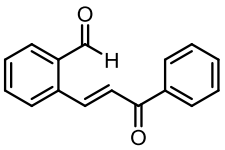
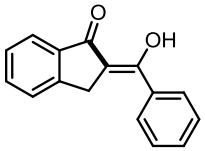
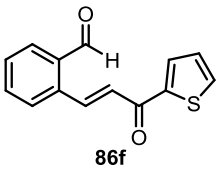
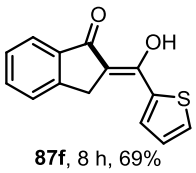
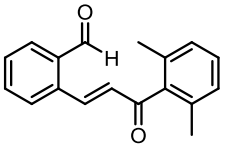
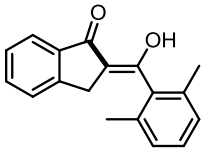
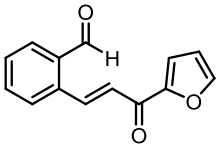
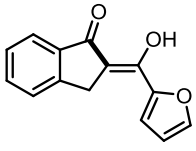
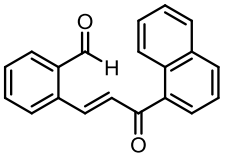
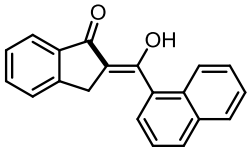
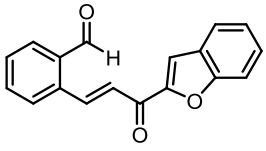
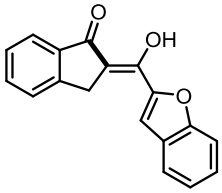
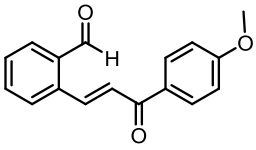
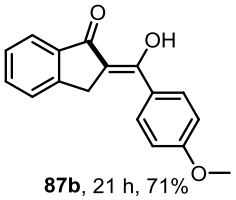
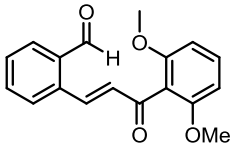
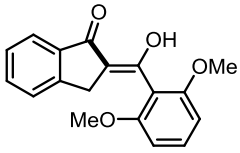
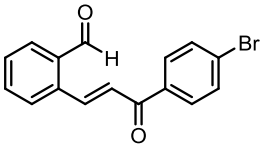
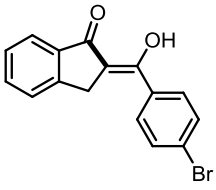
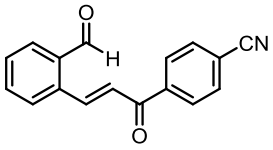
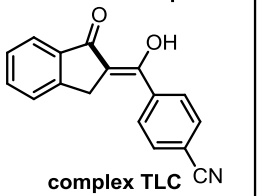
Sr. No.	Catalyst (20 mol%)	Solvent	Time (h)	Yield (%)[a]
1	PMe_3	Toluene	48	Multiple spot
2	PCy_3	Toluene	64	-
3	PPh_3	Toluene	64	-
4	**PBu_3**	**Toluene**	**20**	**74**
5	DABCO	Toluene	18	66
6	DBU	Toluene	10	69
7	Imidazole	Toluene	16	51
8	*β*-ICD	Toluene	64	-
9	PBu_3	DCE	25	65
10	PBu_3	CH_3NO_2	40	15
11	PBu_3	Trifluoroethanol	48	61
12	PBu_3	THF	48	50
13	PBu_3	DMF	48	57
14	PBu_3 (10 mol%)	Toluene	31	69

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yields after silica gel column chromatography.

Further, standardization studies were performed with different amines (DBU, DABCO, *β*-ICD, imidazole), but no significant improvement in the yield of the product was observed (Table 17, entries 5-8). To find optimalsolvent for the suitable transformation, optimization studies were performed with solvents such as CH_3NO_2, DCE, trifluoroethanol, THF, DMF. However the isolated yield of the **87a** in all those cases found to be low when compared to the reaction in toluene (Table 17, entries 9-12).

With the optimized reaction condition in hand, the limitation and scope of the reaction were examined, Table 18. A diverse range of aryl-substituted enones were synthesized and subjected to the optimized reaction condition, which led to the formation of respective products in good yields. Aryl enones with electron donating groups (-OMe, -Me) **86b-86d** or substituted halogens (Br, Cl) **86b-86d** were treated under the optimized condition delivered the respective products **87b-87d** in good yields. The heteroaryl substituted enones **86f-86h** were treated under the optimized condition, delivered the respective cyclized products **87f-87h** within the optimal reaction time. The IMBH reaction was realized to be general and efficient, and a diverse range of products were accessed in good yields.

Table 18: Substrate Scope: IMBH products

Entry	substrate	product	Entry	substrate	product
1	 **86a**	 **87a**, 20 h, 74%	6	 **86f**	 **87f**, 8 h, 69%
2	 **86b**	 **87c**, 17 h, 75%	7	 **86g**	 **87g**, 16 h, 71%
3	 **86c**	 **87d**, 17 h, 81%	8	 **86h**	 **87h**, 19 h, 73%
4	 **86d**	 **87b**, 21 h, 71%	9	 **86i**	 **didn't observe the product**
5	 **86e**	 **87f**, 15 h, 78%	10	 **86j**	 **complex TLC**

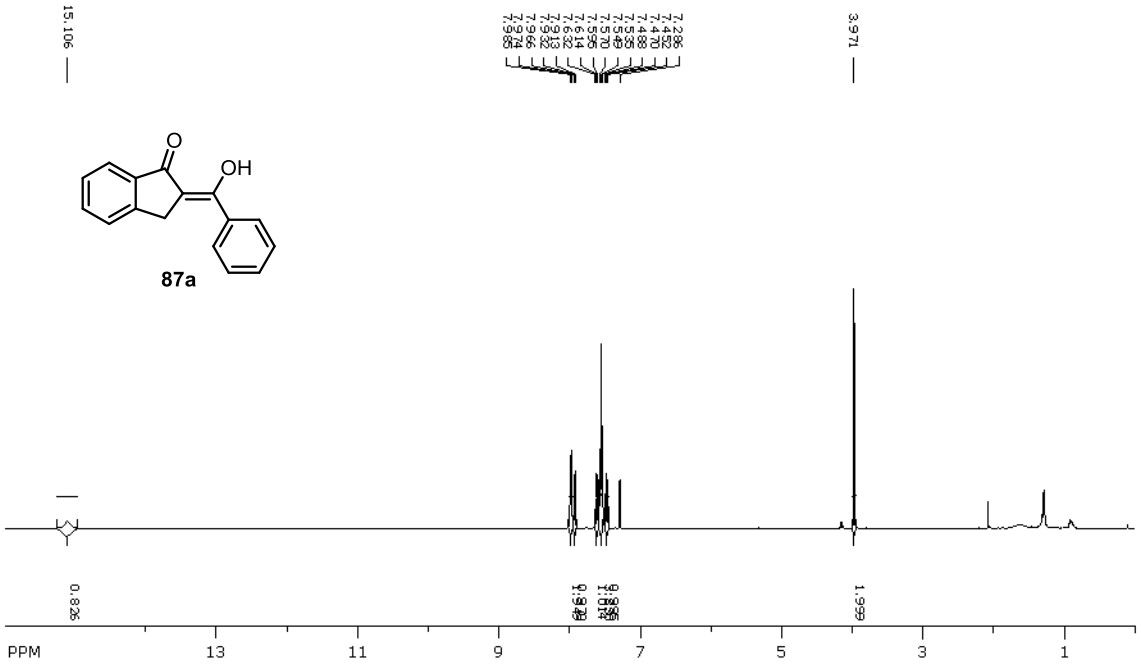


Figure 19: ^{1}H-NMR spectrum of **87a**

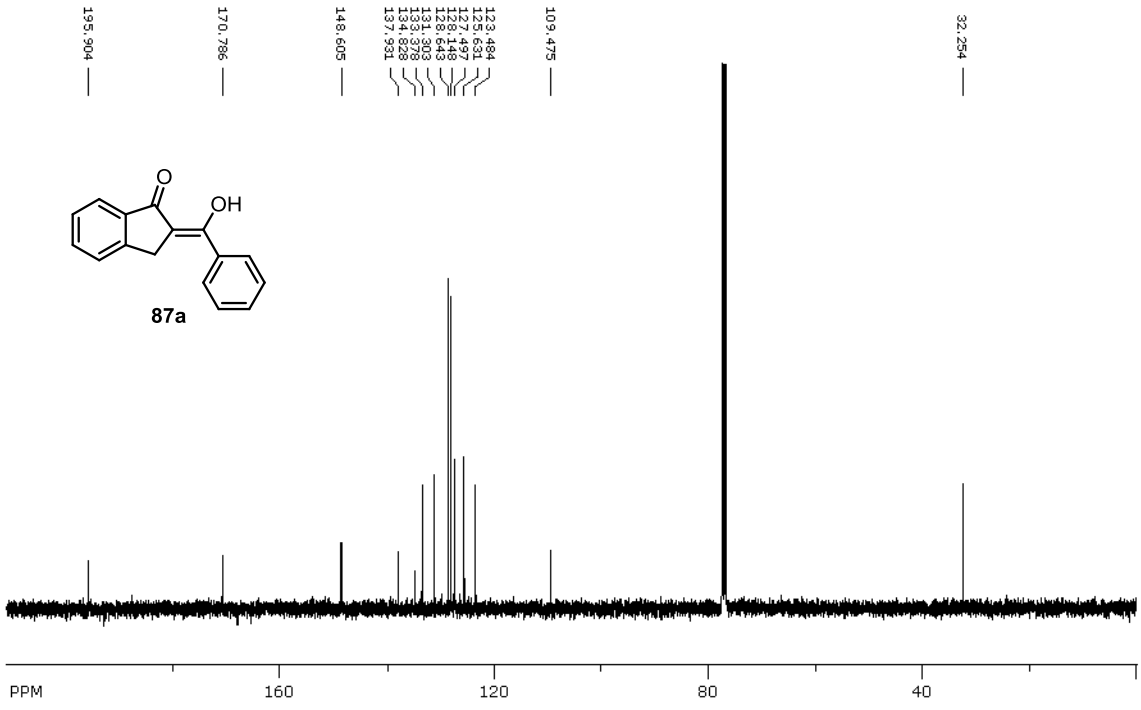
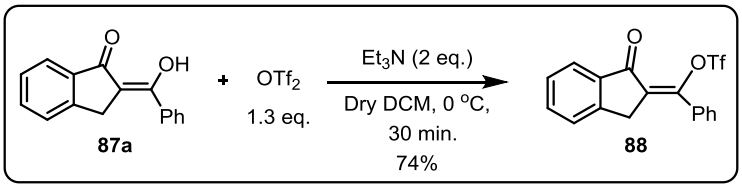


Figure 20: ^{13}C-NMR spectrum of **87a**

4.4.1: Synthesis of triflates

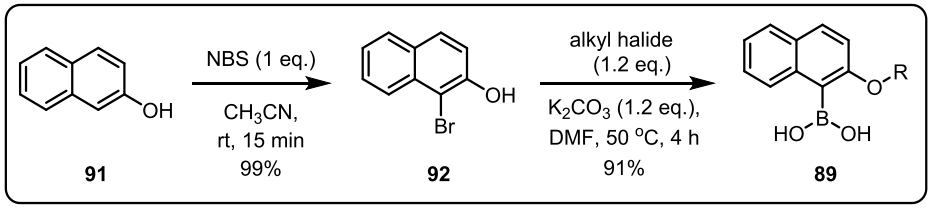
After the development of the IMBH reaction in a highly practical and scalable manner, we next focused on the development of Suzuki-Miyaura cross-coupling reaction. Towards this, we have initiated a study by considering **88** as the model substrate, Scheme 55.[118] The respective substrate was synthesized *via* simple protection of IMBH product **87a** by triflic anhydride.



Scheme 55: General approach for the synthesis of triflates

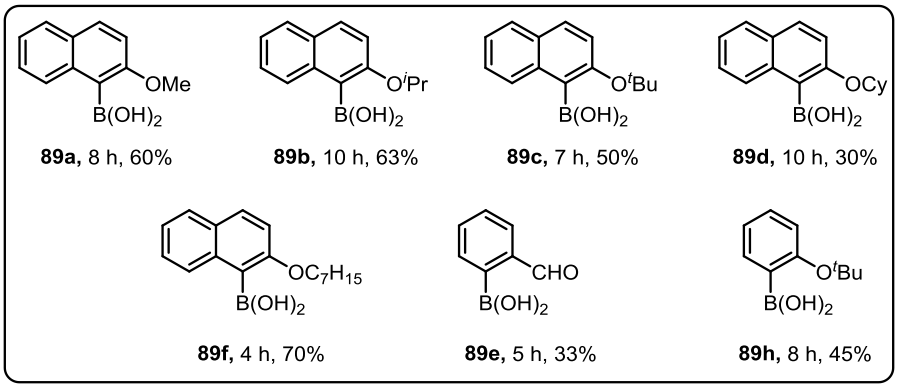
4.4.2: Synthesis of boronic acids

Boronic acids were prepared by following a three-step protocol, Scheme 56.[119] Bromination of 2-naphthols **91** with NBS and subsequent protection of alcohol with respective alkyl halide led to the formation of **92** in excellent yield. Further, direct *n*-butyllithium mediated metal-halogen exchange in **92** followed by borylation with trimethyl borate and treatment with dil. HCl generated boronic acids **89**.

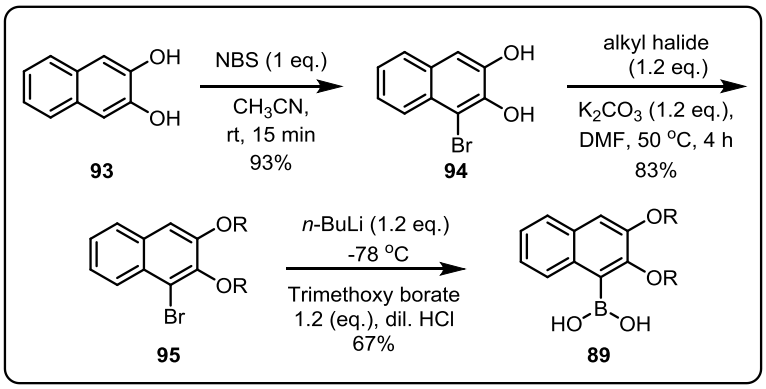


Scheme 56: Synthesis of boronic acids

Table 19: Substrate scope: 2-substituted boronic acids

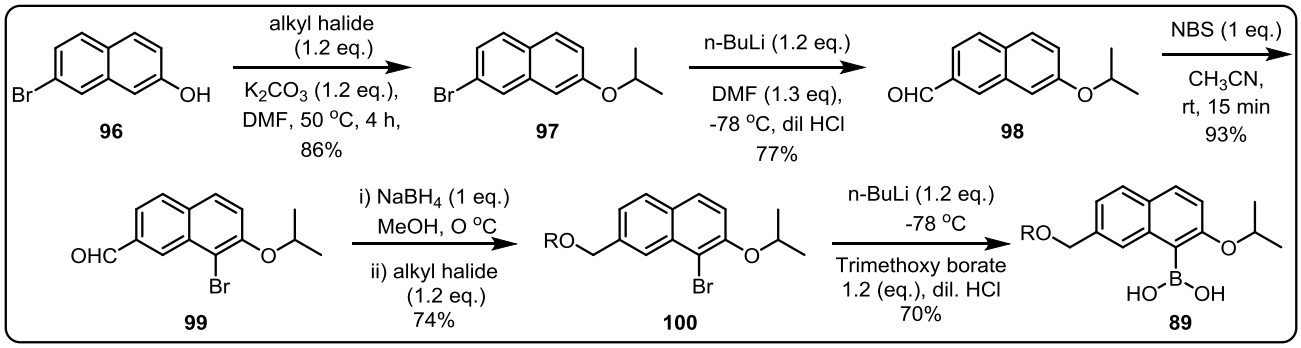


Symmetrically substituted naphthalene boronic acids were easily accessed by following a three-step protocol, Scheme 57. Dihydroxynaphthalene **93** underwent bromination with NBS which upon subsequent alcohol protection delivered bromonaphthalene **95**. Further, *n*-butyllithium reaction of bromonaphthalene followed by borylation with trimethyl borate and treatment with dil. HCl generated boronic acids **89**.



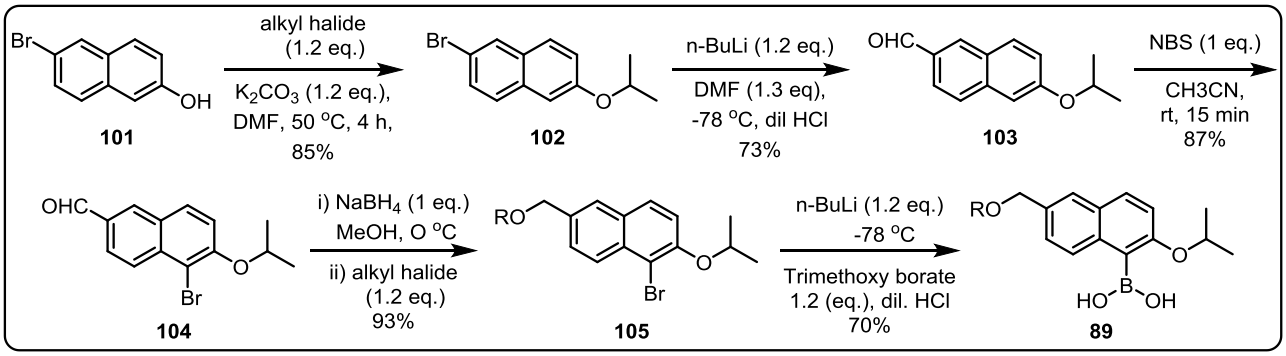
Scheme 57: Synthesis of 2,3-disubstituted boronic acids

6-Substituted naphthalene boronic acid derivatives was easily synthesized from 6-bromonaphthalen, Scheme 58. Protection phenol moiety in of 6-bromonaphthol **96** with an alkyl halide and subsequent formylation furnished **98**. Bromination of **98** with NBS delivered bromonaphthalene **99** in excellent yield. Further, reduction of aldehyde and protection of alcohol with respective alkyl halide provided **100**. Direct *n*-butyllithium mediated metal-halogen exchange of naphthalene **100** followed by borylation with a trimethyl borate and treatment with dil. HCl generated delivered the boronic acids **89**.



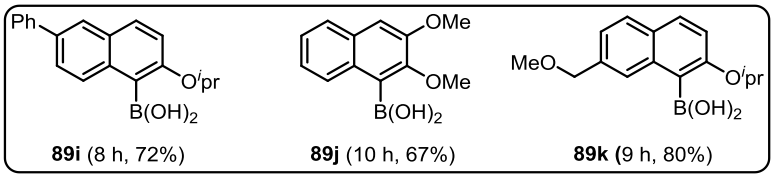
Scheme 58: Synthesis of 2,7-disubstituted boronic acid

7-Substituted naphthalene boronic acid derivatives were easily synthesized by following the strategies described in, Scheme 59.



Scheme 59: Synthesis of 2,6-disubstituted boronic acids

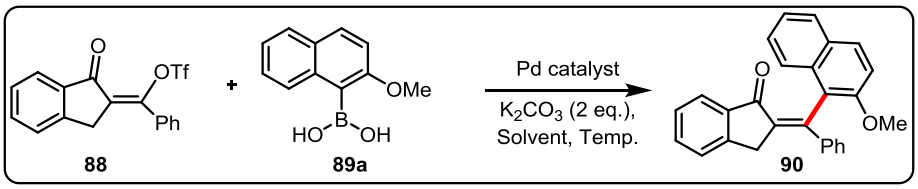
Table 20: Substrate scope: substituted boronic acids



After achieving the successful synthesis of the starting materials, we have initiated the synthesis of Suzuki coupling by considering triflate **88** and naphthalene boronic acid **89a** as a model substrate, Table 21. Our initial attempt by employing $Pd(PPh_3)_4$ catalyst was discouraging as a very low yield of coupling product **89a** was observed (Table 21, entry 1). Interestingly, when the reaction was performed by using $PdCl_2$(dppf), the expected product **89a** formed in good yield (Table 21, entry 2). The structure of the coupling product was confirmed from spectral data. In the IR spectrum, the presence of absorption band at 1680 cm^{-1} due to *α,β*-unsaturated carbonyl group, and absence of alcohol peak was indicated the formation of coupling product **89a**. In ^{1}H-NMR spectrum (see, fig. 22), presence of a doublet at δ 4.15 due to CH_2 and presence of singlet at δ 3.88 ppm due to methoxy group, and in ^{13}C-NMR spectrum (see Fig. 23), presence of δ 192.4 ppm due to the *α,β*-unsaturated carbonyl carbon and signal at δ 56.6 ppm due to methoxy group established the product formation **89a**. In the high-resolution mass spectrum, the presence of molecular ion peak at *m/z* 376.1545 $(M+H)^+$ further confirmed the formation of product **89a**.

Further, to improve the efficiency of reaction, various solvent were screened (DMF, THF, Dioxane, and DMSO), but failed to improve the yield (Table 21, entries 7-10). On the other hand, the reaction in toluene:water (9:1) led to the formation of product in 88% (Table 21, entry 11). When the reaction was carried out in $PdCl_2(PPh_3)_2$, the formation of product was observed in excellent yield. When the reaction was carried out with other palladium catalysts (PdI_2, $PdCl_2$, $Pd(OAc)_2$), only moderate yield of the product observed (Table 21, entries 4-6). Thus we identified that the combination of toluene:water (9:1), $PdCl_2(dppf)_2$, K_2CO_3 as optimal condition for the coupling reaction.

Table 21: Optimizing reaction parameters

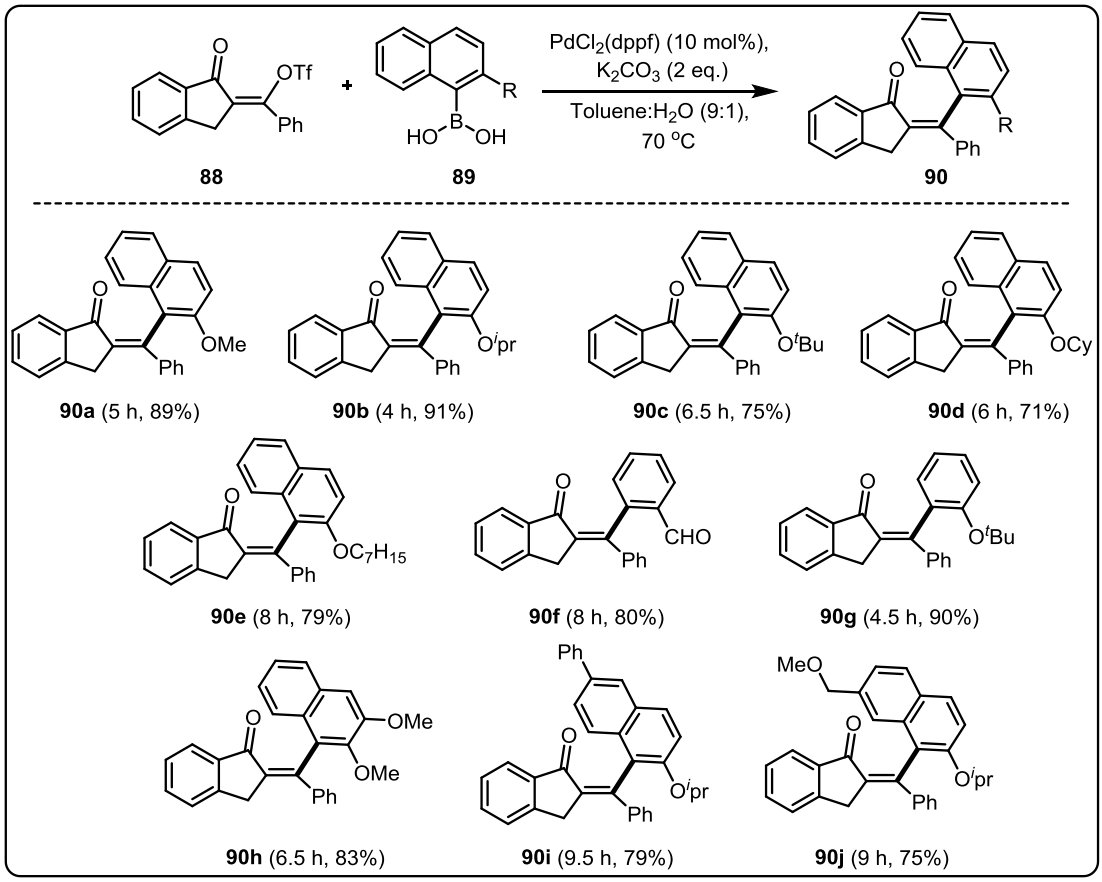


Sr. No.	Catalyst (10 mol%)	Solvent	Temp	Time (h)	Yield (%)
1	$Pd(PPh_3)_4$	Toluene	70	8.5	15
2	$PdCl_2(dppf)$	Toluene	70	9	71
3	$PdCl_2(PPh_3)_2$	Toluene	70	10	65
4	PdI_2	Toluene	70	6.5	45
5	$PdCl_2$	Toluene	70	7	40
6	$Pd(OAc)_2$	Toluene	70	9	55
7	$PdCl_2(dppf)$	DMF	70	13	55
8	$PdCl_2(dppf)$	THF	70	13.5	65
9	$PdCl_2(dppf)$	DCE	70	20	19
10	$PdCl_2(dppf)$	Dioxane	70	17	37
11	**$PdCl_2(dppf)$**	**Toluene:H_2O (9:1)**	**70**	**6.5**	**90**
12	$PdCl_2(dppf)$	DMF:H_2O (9:1)	70	11	55
13	$PdCl_2(dppf)$	THF:H_2O (9:1)	70	11	65
14	$PdCl_2(dppf)$	Dioxane:H_2O (9:1)	70	16	40
15	$PdCl_2(dppf)$	Toluene:H_2O (9:1)	90	17	67
16	$PdCl_2(dppf)$	Toluene:H_2O (9:1)	50	19	60

All reactions were done on 0.1 mmol scales in 1 mL of solvent. [a]Isolated yields after silica gel column chromatography.

With the optimized reaction conditions in hand, limitation and scope of this reaction were investigated, Table 22. Diverse ranges of o-substituted boronic acids **89a-89g** were subjected to the optimized reaction condition, which led to the formation of respective products **90a-90g** in excellent yield. 2,3-Disubstituted naphthalene boronic acids **89h-89k** were also effective in this reaction and provided good to excellent yield of the product. When the reaction carried out with 2,6- and 2,7-disubstituted naphthalene boronic acids, the resulted respective products were obtained in good to excellent yields. Simple phenyl substituted boronic acids also works well with this optimized reaction condition.

Table 22: Substrate scope



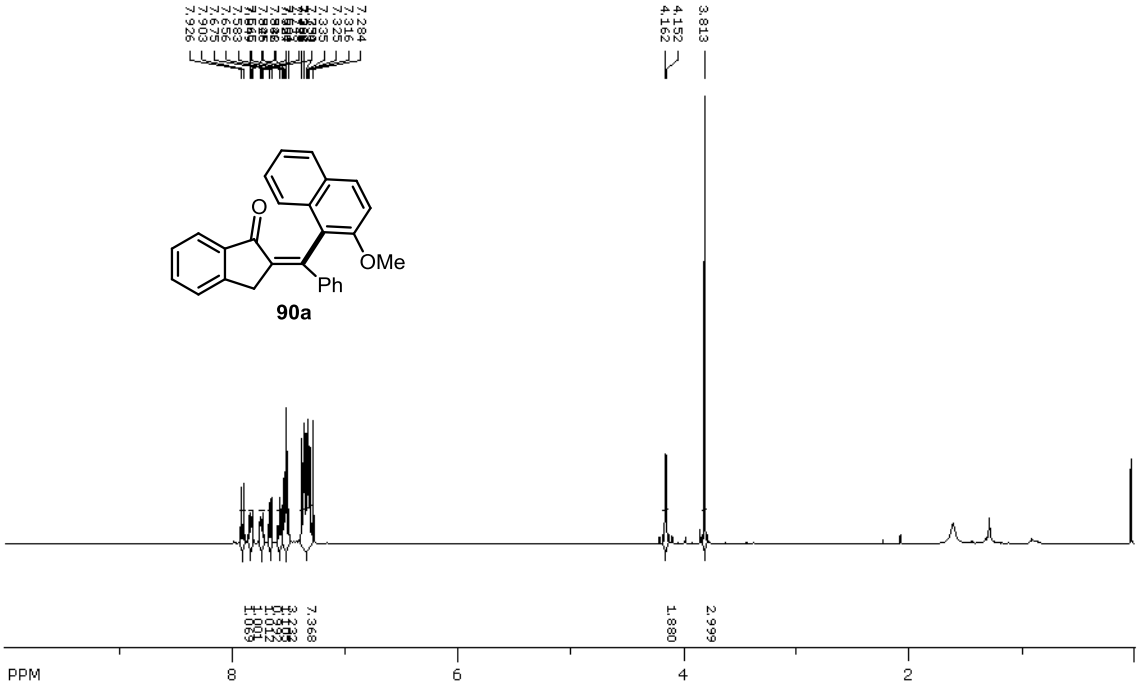


Figure 22: ^{1}H-NMR spectrum of **90a**

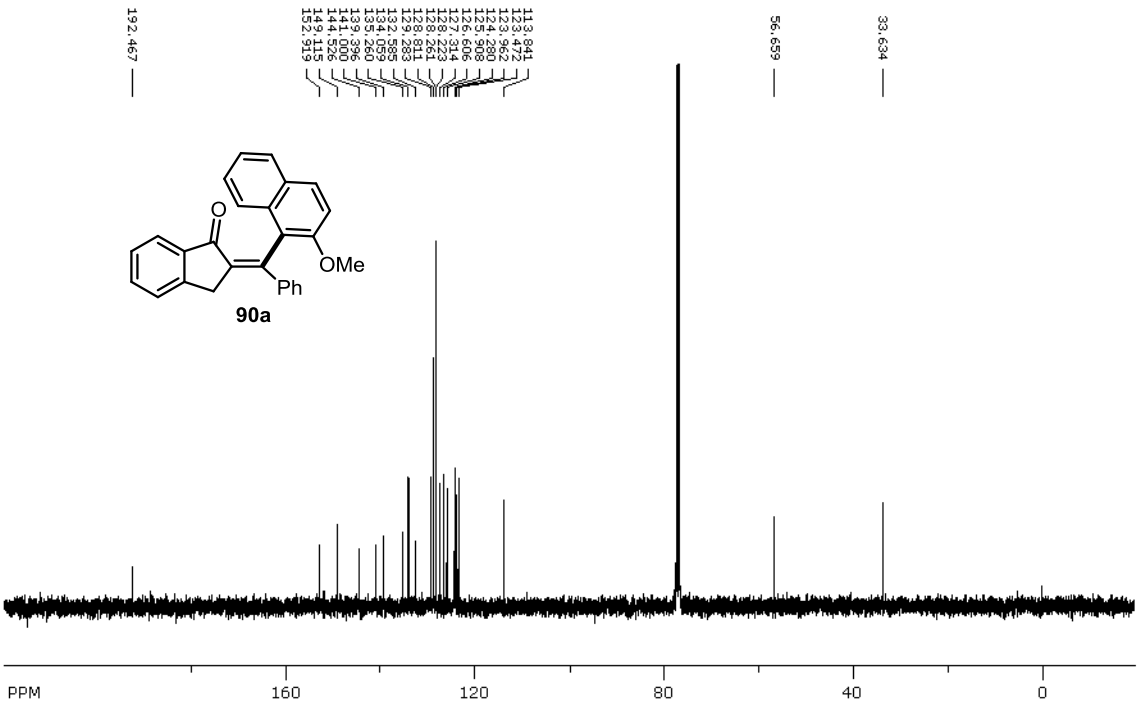


Figure 22: ^{13}C-NMR spectrum of **90a**

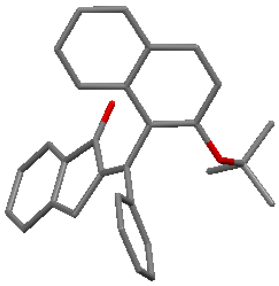
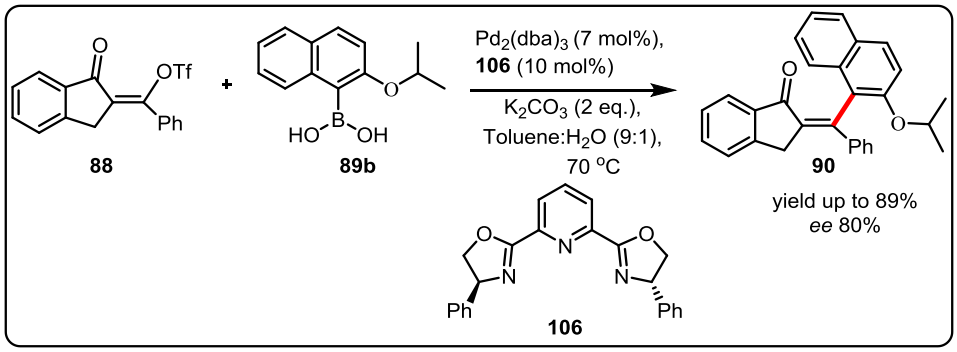


Figure 21: Crystal structure of **90g**.

4.5: Development of atropselective Suzuki-Miyaura cross-coupling reaction

After successfully achieving a practical, scalable and highly efficient synthesis of Suzuki-Miyaura cross-coupling reaction, we next focused on the development of the synthesis of axially chiral styrenes. With the racemic condition in hand, we began to seek an efficient asymmetric catalytic system that could be used to achieve the efficient synthesis of axially chiral styrene. Towards this, we have initiated the study by considering **88** and **89c** as a model substrate. Various catalysts, ligands, and solvents combinations were evaluated for atroposelective reaction. When the reaction was carried out with $Pd_2(dba)_3$ and box ligand **106,** the coupling product was obtained **90c** in an excellent yield with high enantioselectivity.



Scheme 60: Axially chiral synthesis of styrene

In conclusion, we have demonstrated the first synthesis of axially chiral styrene via Suzuki-Miyaura cross-coupling reaction. An enantiomerically enriched coupling product was synthesized from easily accessible starting materials in excellent yields.

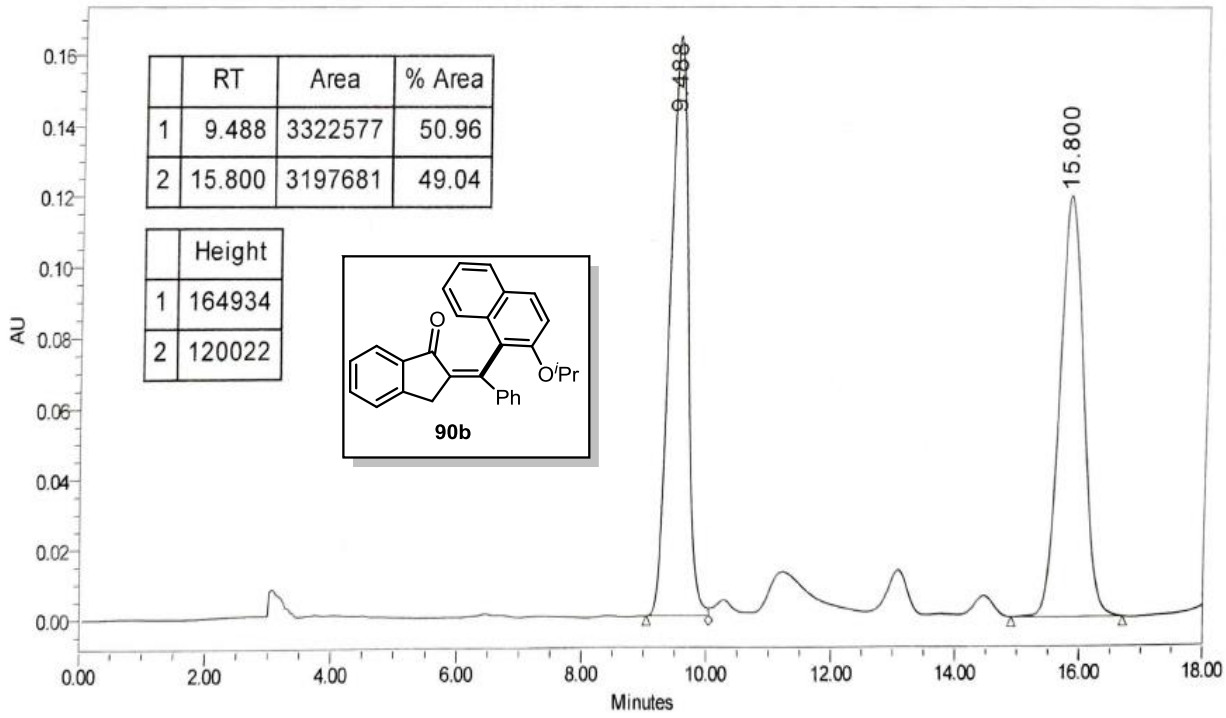


Figure 22: HPLC chromatogram of racemic **90b**

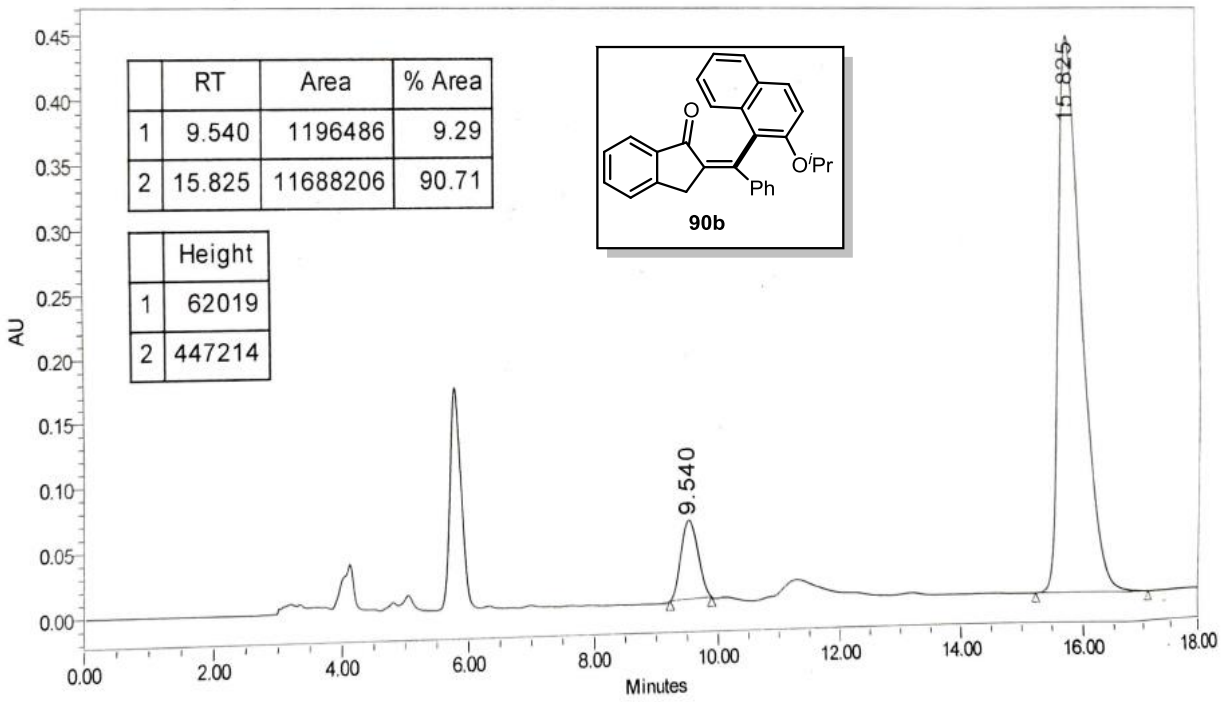


Figure 23: HPLC chromatogram of chiral **90b**

CONCLUSION

In conclusion, we have demonstrated the modular approach to rapidly access functionalized and polysubstituted furotropones and benzofurotropones starting from readily accessible materials. Further, we have identified that these new chromophores, with their unique structural features, have potential to be highly sensitive and selective sensors for the detection of hard cations such as Fe^{3+}, with the detection limit as low as 10 μM. Further, exploring the advancement in furan chemistry we have described the NHC catalyzed efficient approach for the synthesis of dihydrobenzofuranones and their subsequent conversion into functionalized benzofuran. This method can be used efficiently for making substituted benzofuran in natural product synthesis or pharmaceutical.

Continued research interest in developing new strategies to achieve heterocycles led us to develop an efficient synthesis of triazoles. We have described organocatalytic β- azidation of enones initiated by an electron-donor-acceptor complex. The synthetic utility of the β-azide product was shown towards one-step elaboration to access triazoles. A diverse range of β- azidoketone and triazlole synthesized from good to excellent yield.

Further, we have developed the synthesis of axially chiral vinyl arene via Suzuki-Miyaura cross-coupling reaction. The excellent enantioselectivity was successfully achieved by combination of box catalyst with $Pd_2(dba)_3$.

EXPERIMENTAL SECTION

General experimental methods: All the starting compounds and catalysts employed in this study were procured from Sigma-Aldrich, TCI chemicals, Avra Synthesis and were used without further purification. For thin layer chromatography (TLC), silica aluminium foils with fluorescent indicator 254 nm (from Aldrich) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using SD Merck silica gel 60-120 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and stored over sodium wire. IR spectra were recorded on a Perkin–Elmer FT IR spectrometer as thin films or KBr pellet, as indicated, with νmax in inverse centimetres. Melting points were recorded on a digital melting point apparatus Stuart SMP30. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a 400 MHz Bruker Biospin Avance III FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet and m=multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$ or in $(CD_3)_2SO$ (δ 2.50 ppm) or in $(CD_3)_2CO$ (δ 2.05 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm) or in $(CD_3)_2SO$ (δ 39.5 ppm) or in $(CD_3)_2CO$ at δ 29.9 and 206.7. Single crystal X-ray analysis was carried on a Bruker AXS KAPPA APEX II system or Rigaku XtaLAB mini X-ray diffractometer. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. Optical rotations were recorded on Rudolph APIII/2W. HPLC data was acquired from a Waters 515 using normal phase chiral columns.

General Procedure-1: Synthesis of 3-formyl-2-furylcarbinols starting 12 from 3 furancarboxaldehyes.

To a solution of N-methylpiperazine (NMP, 0.66 mmol, 1.3 equiv) in THF (2 mL) at -78 °C was added n-BuLi (0.66 mmol, 1.3 equiv). After 15 min, 3-furaldehyde (0.045 mL, 0.52 mmol) was added, and then the reaction mixture was stirred for an additional 30 min. A cyclohexane solution of n-BuLi (1.32 mmol, 2 equiv) was added, and the mixture was stirred for an additional

15 min, and then the mixture was warmed to -30 °C in 2 h. The solution was again cooled to -78 °C and an aldehyde (1.02 mmol, 1.6 equiv) was added dropwise over 5 min. The mixture was warmed to room temperature over 30 min. The reaction progress was monitored by TLC. Reaction mixture was quenched with saturated aq. Ammonium chloride solution and extracted with ethyl acetate. The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography on silica gel (ethyl acetate−hexanes) to afford 3-formyl-2-furylcarbinols in 60-80% yields.

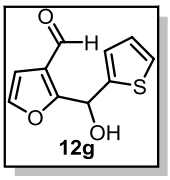
General Procedure-2: Reaction of 3-formyl-2-furylcarbinols with various 1,3-dicarbonyls.

To a solution of furfuryl alcohol (0.1 mmol, 1 equiv) in nitromethane (1 mL), were added acetylacetone (0.11 mmol, 1.1 equiv) followed by $BiCl_3$ (0.02 mmol, 0.2 equiv) at room temperature. The reaction was stirred at room temperature until the alcohol was consumed as monitored by TLC, and the reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1−2 mL). The reaction mixture was diluted with ethyl acetate (1-2 mL), and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1-2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (ethyl acetate-hexanes) to afford 1,3-dicarbonyl adducts in 60-95% yields.

General Procedure 3: Base-mediated intramolecular aldol condensation of the 1,3-dicarbonyl adducts for the synthesis of furotropones 9.

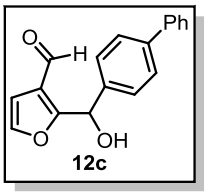
To a solution of the 1,3-dicarbonyl adduct (0.06 mmol, 1 equiv) in 1 mL DMF, sodium carbonate (5 mg, 1 equiv) was added under nitrogen atmosphere. The flask was placed in an oil bath (80 °C) and stirring was continued for 3 h. The reaction mixture was washed with water and extracted with ethyl acetate. The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography on silica gel (ethyl acetate-hexanes) to afford furotropone.

2-(Hydroxy(thiophen-2-yl)methyl)furan-3-carbaldehyde (12g).



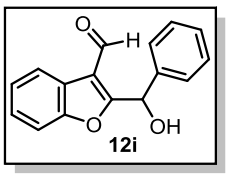
This compound was prepared by following the general procedure **1** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3372, 2872, 1672, 1580, 1516, 1422, 1237, 1127, 1024, 805. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.98 (s, 1H), 7.42 (d, *J* = 1.9 Hz, 1H), 7.32 (m, 1H), 6.98 (m, 2H), 6.83 (d, *J* = 1.9 Hz, 1H), 6.30 (d, *J* = 7.0 Hz, 1H), 4.69 (d, *J* = 7.0 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 187.0, 162.1, 143.7, 142.5, 126.9, 126.1, 125.2, 122.5, 110.2, 66.6. **HRMS (ESI):** *m/z* calcd for $C_{10}H_9O_3S$ $(M+H)^+$ 209.0272, found 209.0277.

2-([1,1′-Biphenyl]-4-yl(hydroxy)methyl)furan-3-carbaldehyde (12c).



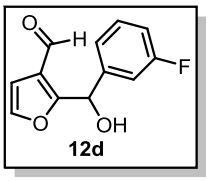
This compound was prepared by following the general procedure **1** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3370, 2870, 1670, 1578, 1514, 1418, 1235, 1022, 703. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.0 (s, 1H), 7.63-7.58 (m, 4H), 7.51-7.44 (m, 4H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.37 (tt, *J* = 8.5 and 1.2 Hz, 1H), 6.83 (d, *J* = 2.0 Hz, 1H), 6.15 (d, *J* = 7.3 Hz, 1H), 4.49 (d, *J* = 7.3 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 187.2, 163.2, 142.4, 141.3, 140.5, 139.1, 128.8 (2C), 127.5 (2C), 127.3, 127.1 (2C), 126.6 (2C), 122.6, 110.2, 70.3. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{15}O_3$ $(M+H)^+$ 279.1021, found 279.1026.

2-(Hydroxy(phenyl)methyl)benzofuran-3-carbaldehyde (12i).



This compound was prepared by following the general procedure **1** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3313, 3031, 1661, 1575, 1495, 1479, 1452, 1176, 1011, 748. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.48 (s, 1H), 8.12 (dd, *J* = 6.8 and 3.3 Hz, 1H), 7.53-7.51 (m, 3H), 7.43-7.36 (m, 5H), 6.29 (d, *J* = 5.5 Hz, 1H), 4.03 (d, *J* = 5.6 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 186.6, 166.7, 139.6, 128.9 (2CH), 128.7, 126.4 (2CH), 125.8, 125.0, 124.8, 121.4, 117.5, 111.5, 101.9, 65.4. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{13}O_3$ $(M+H)^+$ 253.0865, found 253.0839.

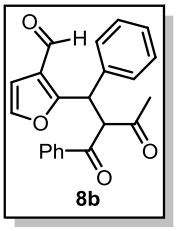
2-((3-Fluorophenyl)(hydroxy)methyl)furan-3-carbaldehyde (12d).



12d

This compound was prepared by following the general procedure **1** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3363, 2927, 1673, 1615, 1592, 1488, 1451, 1250, 1129, 1024, 787. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.96 (s, 1H), 7.41 (d, *J* = 1.8 Hz, 1H), 7.37-7.34 (m, 1H), 7.18 (dd, *J* = 13.2 and 8.9, 2H), 7.02 (td, *J* = 8.4 and 2.5 Hz, 1H), 6.82 (d, *J* = 2.0 Hz, 1H), 6.08 (d, *J* = 5.3 Hz, 1H), 4.73 (d, *J* = 6.8 Hz,1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 187.3, 162.9 (d, *J* = 245.06 Hz), 162.6, 142.6, 142.5, 130.1 (d, *J* = 8.05 Hz), 122.6, 121.7, 115.2 (d, *J* = 20.9 Hz), 113.2 (d, *J* = 22.51 Hz), 110.4, 69.8. **^{19}F-NMR (376.4 MHz, $CDCl_3$):** δ -112.15. **HRMS (ESI):** *m/z* calcd for $C_{12}H_8FO_2$ $(M\text{-}OH)^+$ 203.0509, found 203.0498.

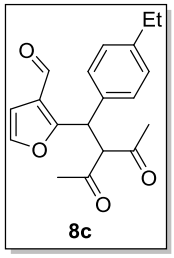
2-(2-Benzoyl-3-oxo-1-phenylbutyl)furan-3-carbaldehyde (8b).



8b

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1722, 1673, 1600, 1546, 1443, 1325, 752. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.10 (s, 1H), 8.05 (m, 2H), 7.62 (tt, *J* = 7.4 and 1.7 Hz, 1H), 7.52 (m, 4H), 7.38 (m, 2H), 7.31 (m, 1H), 7.18 (d, *J* = 1.9 Hz, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 5.78 (d, *J* = 11.5 Hz, 1H), 5.63 (d, *J* = 11.6 Hz, 1H), 2.02 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 200.9, 193.1, 184.7, 161.9, 142.4, 137.1, 135.9, 134.1, 129.2 (2CH), 128.9 (2CH), 128.8 (2CH), 128.4 (2CH), 128.1, 122.3, 108.7, 66.3, 43.6, 29.1. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{18}O_4Na$ $(M+Na)^+$ 369.1103, found 369.1104.

2-(2-Acetyl-1-(4-ethylphenyl)-3-oxobutyl)furan-3-carbaldehyde (8c).

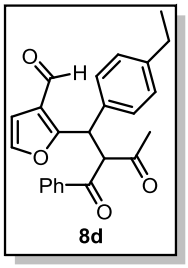


8c

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2965, 1733, 1702, 1681, 1574, 1514, 1471, 1358, 1124, 746. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.05 (s, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.27 (m, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.68 (d, *J* = 2.0 Hz, 1H), 5.38 (d, *J* = 11.8 Hz, 1H), 4.92 (d, *J* = 12.0 Hz, 1H), 2.60 (q, *J* = 7.0 Hz, 2H), 2.17 (s, 3H), 2.03 (s, 3H), 1.20 (t, *J* = 7.7 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.1, 200.9, 184.7, 161.9, 144.0, 142.5, 134.2, 128.7 (2C), 128.0

(2C), 122.0, 109.7, 71.7, 42.8, 30.2, 29.4, 28.3, 15.2. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{20}O_4Li$ $(M+Li)^+$ 319.1522, found 319.1565.

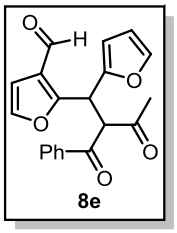
2-(2-Benzoyl-1-(4-ethylphenyl)-3-oxobutyl)furan-3-carbaldehyde (8d).



8d

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max} /cm^{-1} 2922, 1725, 1680, 1448, 1358, 1267, 1125, 1023, 748. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.12 (s, 1H), 8.03 (dd, *J* = 8.5 and 1.3 Hz, 2H), 7.62 (tt, *J* = 7.4 and 1.3 Hz, 1H), 7.51 (m, 2H), 7.39 (tt, *J* = 10.1 and 1.7 Hz, 2H), 7.20 (m, 3H), 6.58 (d, *J* = 2.0 Hz, 1H), 5.76 (d, *J* = 11.5 Hz, 1H), 5.60 (d, *J* = 11.5 Hz, 1H), 2.63 (q, *J* = 7.6 Hz, 2H), 2.04 (s, 3H), 1.22 (t, *J* = 7.6 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 201.1, 193.2, 184.7, 162.3, 144.1, 142.3, 135.9, 134.1, 134.0, 128.9 (2C), 128.8 (2C), 128.7 (2C), 128.3 (2C), 122.2, 66.4, 43.2, 29.0, 28.4, 18.6, 15.3. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{22}O_4Na$ $(M+Na)^+$ 397.1416, found 397.1432.

2-(2-Benzoyl-1-(furan-2-yl)-3-oxobutyl)furan-3-carbaldehyde (8e).

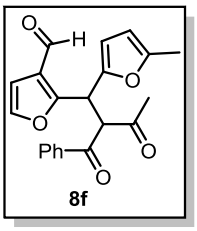


8e

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 1725, 1680, 1594, 1417, 1269, 1012, 744. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.11 (s, 1H), 8.05 (m, 2H), 7.54 (m, 4H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.16 (dd, *J* = 1.8 and 0.7 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.14 (dd, *J* = 3.0 and 1.8 Hz, 1H), 6.11 (d, *J* = 3.2 Hz, 1H), 5.81 (d, *J* = 10.3 Hz, 1H), 2.11 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 199.7, 192.9, 184.8, 159.6, 49.7, 142.8, 142.4, 136.1, 134.1, 128.9 (2C), 128.8 (2C), 122.9, 110.6, 108.9, 108.0, 63.2, 37.3, 29.0. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}O_5Na$ $(M+Na)^+$ 359.0895, found 359.0898.

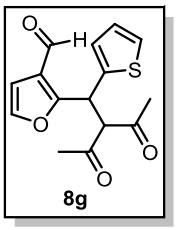
2-(2-Benzoyl-1-(5-methylfuran-2-yl)-3-oxobutyl)furan-3-carbaldehyde (8f).

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 1725, 1680, 1448, 1358, 1267, 1125, 1023, 748, 695. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.11 (s, 1H), 8.06 (m, 2H), 7.54-7.47 (m, 4H), 7.39 (d, *J* = 1.9 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 5.97 (d, *J* = 11.3 Hz, 1H),



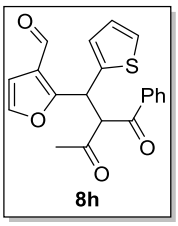
5.94 (d, *J* = 3.0 Hz, 1H), 5.79 (d, *J* = 11.3 Hz, 1H), 2.12 (s, 3H), 2.04 (d, *J* = 0.8 Hz, 3H). **^{13}C-NMR (100 MHz, CDCl$_3$):** δ 199.9, 192.7, 184.8, 159.8, 152.5, 147.7, 142.6, 136.6, 134.1, 128.9 (2C), 128.8 (2C), 122.8, 109.1, 108.8, 106.7, 64.3, 37.3, 28.4, 13.5. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{18}O_5Na$ $(M+Na)^+$ 373.1052, found 373.1073.

2-(2-Acetyl-3-oxo-1-(thiophen-2-yl)butyl)furan-3-carbaldehyde (8g).



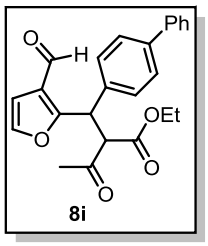
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2997, 2866, 1721, 1698, 1680, 1610, 1512, 1394, 1360, 1250, 1182, 1088, 1045, 744. **^{1}H-NMR (400 MHz, CDCl$_3$**): δ 10.07 (s, 1H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.22 (dd, *J* = 5.2 and 1.0 Hz, 1H), 7.01 (dd, *J* = 3.5 and 0.6 Hz, 1H), 6.94 (m, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 5.75 (d, *J* = 5.8 Hz, 1H), 4.91 (d, *J* = 5.8 Hz, 1H), 2.16 (s, 3H), 2.14 (s, 3H). **^{13}C-NMR (100 MHz, CDCl$_3$):** δ 200.7, 200.2, 184.7, 160.2, 142.6, 139.3, 127.1, 126.5, 125.7, 122.1, 109.1, 72.3, 38.1, 30.1, 29.4. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{14}O_4SNa$ $(M+Na)^+$ 313.0510, found 313.0520.

2-(2-Benzoyl-3-oxo-1-(thiophen-2-yl)butyl)furan-3-carbaldehyde (8h).



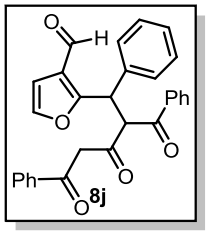
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2956, 2870, 1721, 1698, 1682, 1573, 1519, 1418, 1366, 1124, 759. **^{1}H-NMR (400 MHz, CDCl$_3$):** δ 10.13 (s, 1H), 8.01 (dd, *J* = 0.9 Hz, 3H), 7.51-7.47 (m, 2H), 7.43 (d, *J* = 2.0 Hz, 1H), 7.07 (d, *J* = 1.0 Hz, 1H), 6.95 (m, 1H), 6.79 (m, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.02 (d, *J* = 11.3 Hz, 1H), 5.79 (d, *J* = 11.3 Hz, 1H), 2.10 (s, 3H). **^{13}C-NMR (100 MHz, CDCl$_3$)** δ 199.9, 192.7, 184.7, 160.8, 142.7, 139.6, 136.4, 134.1, 128.9 (2C), 128.8 (2C), 126.9, 126.6, 125.3, 122.3, 109.1, 66.6, 38.6, 28.8. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{16}O_4SNa$ $(M+Na)^+$ 375.0667, found 375.0663.

Ethyl 2-([1,1′-biphenyl]-4-yl(3-formylfuran-2-yl)methyl)-3-oxobutanoate (8i).



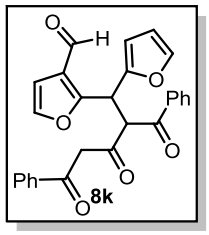
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2957, 2870, 1722, 1697, 1680, 1570, 1514, 1413, 1370, 1124, 766. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.11 (s, 1H), 7.62 (m, 1H), 7.54 (m, 3H), 7.44 (m, 4H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.36 (m, 1H), 6.71 (d, *J* = 2.0 Hz, 1H), 5.38 (d, *J* = 5.3 Hz, 1H), 4.76 (d, *J* = 3.3 Hz, 1H), 4.04 (qd, *J* = 7.1 and 1.8 Hz, 2H), 2.29 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.0, 184.5, 166.7, 161.9, 142.6, 140.7, 140.2, 139.8, 136.4, 128.8 (2C), 128.7 (2C), 127.7 (2C), 127.5 (2C), 127.3, 109.6, 64.1, 63.1, 61.9, 42.3, 29.0. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{22}O_5Na$ $(M+Na)^+$ 413.1365, found 413.1373.

2-(2-Benzoyl-3,5-dioxo-1,5-diphenylpentyl)furan-3-carbaldehyde (8j).



This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2924, 2852, 1681, 1597, 1493, 1448, 1278, 1026, 744, 695. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.10 (s, 1H), 8.03-8.00 (m, 2H), 7.80 (m, 1H), 7.63 (m, 1H), 7.61 (m, 2H), 7.54 (m, 1H), 7.52 (m, 1H), 7.50 (m, 2H), 7.48 (m, 2H), 7.34 (m, 1H), 7.21 (s, 2H), 7.17 (m, 1H), 7.13 (m, 1H), 6.38 (m, 1H), 5.65 (d, *J* = 11.5 Hz, 1H), 5.55 (d, *J* = 11.5 Hz, 1H), 5.03 (dd, *J* = 10.7 and 4.7 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 193.6, 193.6, 193.0, 182.0, 159.0, 142.4, 137.9, 137.3, 135.9, 133.9, 133.5, 132.4, 129.3 (2C), 128.9 (2C), 128.8 (2C), 128.7 (2C), 128.1 (2C), 127.1 (2C), 122.2, 112.6, 62.3, 53.4, 44.4. **HRMS (ESI)** *m/z* calcd for $C_{29}H_{22}O_5Na$ $(M+Na)^+$ 473.1365, found 473.1384.

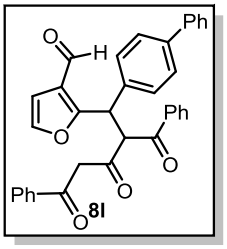
2-(2-Benzoyl-1-(furan-2-yl)-3,5-dioxo-5-phenylpentyl)furan-3-carbaldehyde (8k).



This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2926, 1682, 1597, 1448, 1274, 1250, 1181, 1013, 742. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.10 (s, 1H), 8.07 (m, 2H), 7.82 (m, 2H), 7.55 (m, 2H), 7.51 (m, 2H), 7.45 (s, 1H), 7.49 (m, 2H), 7.43 (m, 1H), 7.37 (dd, *J* = 1.7 and 0.6 Hz, 1H), 7.24 (d, *J* = 1.9 Hz, 1H), 6.67 (d, *J* = 1.9 Hz, 1H), 6.36 (d, *J* = 3.1 Hz, 1H),

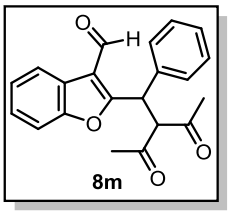
6.30 (m, 1H), 5.79 (d, *J* = 11.4 Hz, 1H), 5.60 (d, *J* = 11.4 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 193.0, 190.5, 184.8, 182.1, 159.9, 156.2, 149.7, 143.0, 142.7, 142.6, 134.1, 132.9, 129.0, 128.95, 128.91 (2CH), 128.7 (2CH), 127.1 (2CH), 122.7, 110.8, 108.4, 107.8, 96.2, 60.2, 37.9. **HRMS (ESI)** m/z calcd for $C_{27}H_{20}O_6Na$ $(M+Na)^+$ 463.1168, found 463.1158.

2-(1-([1,1′-Biphenyl]-4-yl)-2-benzoyl-3,5-dioxo-5-phenylpentyl)-furan-3-carbaldehyde (8l).



This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 2853, 1734, 1681, 1597, 1487, 1448, 1123, 1077, 821, 738. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.18 (s, 1H), 8.07 (m, 2H), 7.82 (m, 2H), 7.51 (m, 7H), 7.45 (m, 6H), 7.37 (m, 1H), 7.24 (d, *J* = 1.9 Hz, 1H), 6.67 (d, *J* = 2.0 Hz, 1H), 6.35 (d, *J* = 3.6 Hz, 1H), 6.31 (s, 1H), 6.30 (m, 1H), 6.20 (d, *J* = 3.6 Hz, 1H), 5.60 (d, *J* = 11.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 193.0, 190.5, 184.9, 182.1, 159.8, 149.7, 142.7, 142.3, 135.7, 135.7, 134.0, 134.6, 134.0, 133.5, 132.9, 129.0 (2C), 128.9 (2C), 128.8 (3C), 128.7 (3C), 128.1, 127.1 (2C), 122.7, 110.8, 108.6, 108.4, 96.2, 60.2, 37.9. **HRMS (ESI)** m/z calcd for $C_{35}H_{26}O_5Na$ $(M+Na)^+$ 549.1678, found 549.1661.

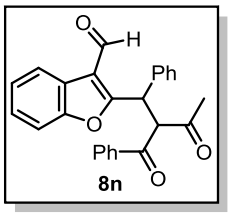
2-(2-Acetyl-3-oxo-1-phenylbutyl)benzofuran-3-carbaldehyde (8m).



This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat)** ν_{max}/cm^{-1} 2947, 2868, 1720, 1697, 1681, 1487, 1451, 1124, 760. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.45 (s, 1H), 8.11 (m, 1H), 7.52 (m, 1H), 7.46 (m, 2H), 7.40 (d, *J* = 4.8 Hz, 1H), 7.37 (m, 3H), 5.55 (d, *J* = 11.8 Hz, 1H), 5.10 (q, *J* = 11.8 Hz, 2H), 2.23 (s, 3H), 2.08 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 200.9, 200.3, 184.7, 166.0, 153.8, 136.6, 129.4 (2CH), 128.6, 128.2 (2CH), 125.6, 124.9, 124.6, 121.9, 117.1, 111.0, 71.2, 43.2, 30.3, 29.7. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{18}O_4Na$ $(M+Na)^+$ 357.1103, found 357.1103.

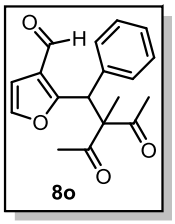
2-(2-Benzoyl-3-oxo-1-phenylbutyl)benzofuran-3-carbaldehyde (8n).

This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2962, 2929, 1738, 1704,



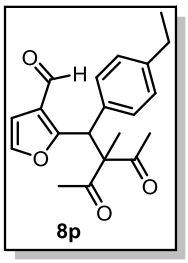
1681, 1575, 1487, 1125, 765, 747. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.49 (s, 1H), 8.06 (m, 2H), 7.97 (m, 2H), 7.49 (m, 2H), 7.42 (m, 3H), 7.38 (m, 3H), 7.22 (m, 2H), 5.97 (d, *J* = 11.5 Hz, 1H), 5.80 (d, *J* = 11.3 Hz, 1H), 2.18 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.0, 193.1, 184.8, 166.7, 153.9, 137.0, 134.1, 129.0 (2C), 128.9 (2C), 128.8 (2C), 128.5, 128.3 (2C), 127.0, 125.5, 124.9, 124.6, 122.07, 117.2, 110.0, 65.3, 43.7, 29.3. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{20}O_4Na$ $(M+Na)^+$ 419.1259, found 419.1250.

2-(2-Acetyl-2-methyl-3-oxo-1-phenylbutyl)furan-3-carbaldehyde (8o).



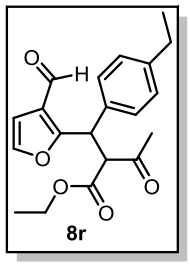
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2925, 1738, 1716, 1682, 1580, 1494, 1454, 1369, 1246, 1145, 1045, 758. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.0 (s, 1H), 7.40 (d, *J* = 1.9 Hz, 1H), 7.29-7.27 (m, 5H), 6.7 (d, *J* = 1.9 Hz, 1H), 5.98 (s, 1H), 2.05 (s, 3H), 2.06 (s, 3H), 1.74 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 205.2, 204.0, 185.0, 162.2, 142.2, 136.8, 129.8 (2CH), 128.6 (2CH), 127.8, 122.9, 108.8, 71.4, 45.5, 27.2, 26.5, 16.5. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{19}O_4$ $(M+H)^+$ 299.1283, found 299.1249.

2-(2-Acetyl-1-(4-ethylphenyl)-2-methyl-3-oxobutyl)furan-3-carbaldehyde (8p).



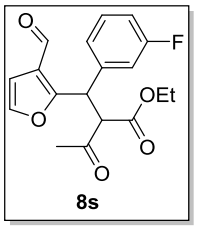
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3363, 1673, 1583, 1503, 1418, 1274, 1145, 1128, 1012. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.99 (s, 1H), 7.39 (d, *J* = 1.9 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 6.72 (d, *J* = 1.9 Hz, 1H), 5.90 (s, 1H), 2.60 (q, *J* = 7.6 Hz, 2H), 2.04 (s, 3H), 2.01 (s, 3H), 1.73 (s, 3H), 1.20 (t, *J* = 7.6 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 205.2, 204.2, 185.1, 162.5, 143.8, 142.5, 133.9, 129.7 (2C), 128.1 (2C), 122.9, 108.7, 71.5, 45.2, 28.3, 27.2, 26.6, 16.5, 15.2. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{22}O_4Na$ $(M+Na)^+$ 349.1416, found 349.1417.

Ethyl 2-((4-ethylphenyl)(3-formylfuran-2-yl)methyl)-3-oxobutanoate (8r).



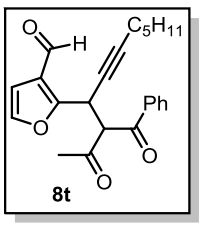
This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2966, 1743, 1720, 1681, 1514, 1245, 1124, 750. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.01 (s, 1H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.30-7.28 (m, 2H), 7.16-7.14 (m, 2H), 6.69 (d, *J* = 2.0 Hz, 1H), 5.32 (d, *J* = 4.0 Hz, 1H), 4.70 (d, *J* = 3.7 Hz, 1H), 4.10 (m, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 2.26 (s, 3H), 1.20 (td, *J* = 7.6 and 2.6 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.5, 184.7, 166.6, 162.5, 143.9, 142.5, 134.6, 128.6 (2C), 128.3 (2C), 122.1, 108.8, 82.6, 61.9, 42.2, 29.4, 28.4, 15.4, 13.7. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{22}O_5Na$ $(M+Na)^+$ 365.1365, found 365.1356.

Ethyl 2-((3-fluorophenyl)(3-formylfuran-2-yl)methyl)-3-oxobutanoate (8s).



This compound was prepared by following the general procedure **2** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max} $/cm^{-1}$ 2958, 2927, 1733, 1681, 1521, 1418, 1359, 1131, 1046, 888. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.07 (s, 1H), 7.35 (d, *J* = 2.0 Hz, 1H), 7.19 (m, 2H), 6.99 (m, 2H), 6.70 (d, *J* = 2.0 Hz, 1H), 5.37 (d, *J* = 6.3 Hz, 1H), 5.34 (d, *J* = 6.3 Hz, 1H), 4.00-4.10 (m, 2H), 2.28 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 199.9, 184.6, 166.4, 162.8 (d, *J* = 245.86 Hz), 161.4, 142.7, 139.8 (d, *J* = 7.00 Hz), 130.6 (d, *J* = 8.15 Hz), 124.1, 122.5, 115.3 (d, *J* = 22.23 Hz), 115.0 (d, *J* = 20.7 Hz), 109.2, 62.9, 62.1, 42.2, 30.9, 13.9. **^{19}F-NMR (376.4 MHz, CDCl3):** δ -111.8. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{17}O_5FNa$ $(M+Na)^+$ 355.0958, found 355.0967.

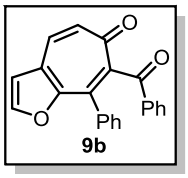
2-(1-Phenyloct-2-yn-1-yl)furan-3-carbaldehyde (8t)



This compound was prepared by following the general procedure **2** and isolated as a colorless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3363, 2123, 1705, 1673, 1583, 1503, 1418, 1274, 1145, 1128, 1012, 896, 785. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.20 (s, 1H), 7.94 (dd, *J* = 8.5 and 1.3 Hz, 2H), 7.60 (m, 3H), 7.23 (dd, *J* = 2.0 and 0.5 Hz, 1H), 6.62 (d, *J* = 2.0 Hz, 1H), 5.40 (d, *J* = 10.4 Hz, 1H), 5.23 (td, *J* = 10.4 and 2.3 Hz, 1H), 2.35 (s, 3H) 2.19 (td, *J* = 7.2 and 1.8 Hz, 2H), 1.35-1.29 (m, 4H), 1.11-1.06 (s, 2H), 0.77 (t, *J* = 6.4 Hz,

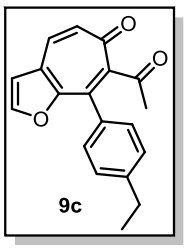
3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.0, 192.3, 184.4, 158.6, 142.7, 135.6, 134.2, 129.1 (2C), 128.9 (2C), 122.8, 108.3, 86.6, 74.4, 66.3, 30.9, 29.9, 28.3, 28.0, 22.1, 18.6, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{25}O_4$ $(M+H)^+$ 365.1753, found 365.1755.

7-Benzoyl-8-phenyl-6H-cyclohepta[b]furan-6-one (9b).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 266-269 °C. R_f = 0.4 (EtOAc/Hexane= 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 1711, 1673, 1535, 1497, 1454, 1343, 1260, 1096, 734. **^{1}H-NMR (400 MHz, CDCl3):** δ 7.73 (m, 2H), 7.62 (d, *J* = 11.8 Hz, 1H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.46 (tt, *J* = 7.3 and 1.2 Hz, 1H), 7.34 (m, 3H), 7.30 (m, 4H), 7.14 (d, *J* = 11.8 Hz, 1H), 6.90 (d, *J* = 1.9 Hz, 1H). **^{13}C-NMR (100 MHz, CDCl3):** δ 195.3, 185.6, 153.6, 145.8, 144.1, 138.4, 137.4, 136.7, 133.7, 133.0, 131.5, 129.4, 129.3, 129.3, 128.7 (2C), 128.7, 128.6, 128.3 (2C), 127.8, 113.0. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{15}O_3$ $(M+H)^+$ 327.1000, found 327.0990.

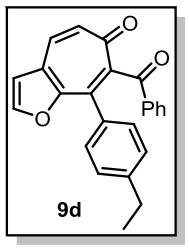
7-Acetyl-8-(4-ethylphenyl)-6H-cyclohepta[b]furan-6-one (9c).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 250-253 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2963, 2925, 2854, 1711, 1621, 1578, 1538, 1496, 1454, 1340, 1136, 1091, 816. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.61 (d, *J* = 1.8 Hz, 1H), 7.55 (d, *J* = 11.8 Hz, 1H), 7.28 (m, 4H), 7.10 (d, *J* = 11.8 Hz, 1H), 6.85 (d, *J* = 1.8 Hz, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 2.10 (s, 3H), 1.30 (t, *J* = 7.6 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ.203.2, 185.1, 153.7, 146.3, 145.7, 145.2, 137.5, 136.8, 131.6, 131.0, 129.2 (2C), 128.3, 127.8 (2C), 113.0, 31.0, 28.6, 15.1. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{17}O_3$ $(M+H)^+$ 293.1178, found 293.1176.

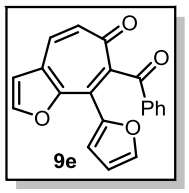
7-Benzoyl-8-(4-ethylphenyl)-6*H*-cyclohepta[*b*]furan-6-one (9d).

This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 260-262 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max} $/cm^{-1}$ 2960, 2926, 1671, 1636, 1536, 1494, 813. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.72 (dd, *J* = 6.4 and 1.3 Hz, 2H), 7.63 (d, *J* = 2.0 Hz, 1H), 7.61 (d, *J* = 11.8, 1H), 7.46 (tt, *J* = 8.6, 2.4, and 1.2 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 11.8 Hz, 2H), 7.08 (brs, 3H), 6.90 (d, *J* = 2.0 Hz, 1H), 2.60



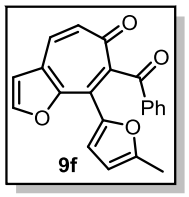
(q, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.7 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.5, 185.6, 153.7, 145.7, 145.7, 144.7, 144.2, 138.7, 137.4, 136.8, 132.9, 131.5, 130.9, 128.7 (2C), 128.6, 128.3 (2C), 127.4, 127.3, 127.3, 113.0, 28.5, 15.0. **HRMS (ESI):** m/z calcd for $C_{24}H_{19}O_3$ $(M+H)^+$ 355.1334, found 355.1337.

7-Benzoyl-8-(furan-2-yl)-6*H*-cyclohepta[*b*]furan-6-one (9e).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 252-255 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3145, 2924, 2853, 1675, 1574, 1544, 1498, 1449, 1336, 1255, 831, 693. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.90 (m, 2H), 7.75 (d, *J* = 1.9 Hz, 1H), 7.55 (m, 2H), 7.42 (m, 2H), 7.32 (dd, *J* = 1.7 and 0.7, 1H), 7.05 (d, *J* = 11.7 Hz, 1H), 6.93 (dd, *J* = 3.4 and 0.6 Hz, 1H), 6.90 (d, *J* = 1.9 Hz, 1H). 6.42 (q, *J* = 1.8 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.3, 185.5, 151.8, 145.4, 145.2, 144.2, 142.5, 137.2, 136.7, 132.9, 131.1, 128.7, 128.6 (2C), 128.4 (2C), 127.4, 116.8, 113.1, 111.8. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{13}O_4$ $(M+H)^+$ 317.0814, found 317.0823.

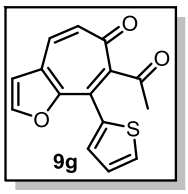
7-Benzoyl-8-(5-methylfuran-2-yl)-6*H*-cyclohepta[*b*]furan-6-one (9f).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 255-258 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 2852, 1678, 1623, 1535, 1497, 1448, 1361, 1249, 1096, 833. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.95 (m, 2H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.53 (m, 2H), 7.44 (m, 2H), 7.04 (m, 2H), 6.88 (d, *J* = 1.9 Hz, 1H), 6.06 (m, 1H), 1.96 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.6, 185.8, 155.0, 151.5, 144.9, 143.7, 141.1, 137.3, 137.2, 132.6, 130.8, 128.5 (3C), 128.3 (2C), 127.2, 119.0, 113.1, 108.6, 13.1. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{15}O_4$ $(M+H)^+$ 331.0970, found 331.0953.

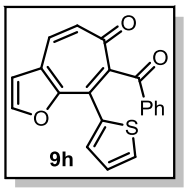
7-Acetyl-8-(thiophen-2-yl)-6*H*-cyclohepta[*b*]furan-6-one (9g).

This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 250-253 °C; R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3132, 2922, 1708, 1616, 1573, 1537, 1496, 1452, 1325, 1165, 1089, 830, 794. **^{1}H-NMR (400 MHz,**



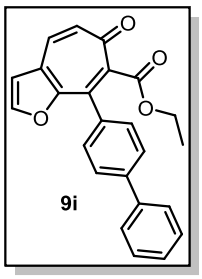
CDCl3): δ 7.66 (d, J = 1.9 Hz, 1H), 7.57 (dd, J = 4.9 and 1.4 Hz, 1H), 7.57 (d, J = 11.8 Hz, 1H), 7.14 (m, 2H), 7.08 (d, J = 11.8 Hz, 1H), 6.87 (d, J = 1.9 Hz, 1H), 2.17 (s, 3H). **^{13}C-NMR (100 MHz, CDCl3):** δ 202.7, 184.6, 147.2, 145.6, 137.4, 137.1, 132.9, 131.6, 131.3, 130.1, 128.5, 128.1, 127.0, 113.1, 30.6; **HRMS (ESI):** *m/z* calcd for $C_{15}H_{11}O_3S$ $(M+H)^+$ 271.0429, found 271.0440.

7-Benzoyl-8-(thiophen-2-yl)-6*H*-cyclohepta[*b*]furan-6-one (9h).



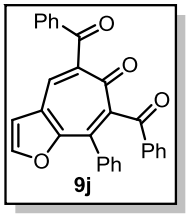
This compound was isolated as a pale yellow solid (18 mg, 95%): mp = 260-263 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat)** ν_{max}/cm^{-1} 3112, 2954, 2853, 1673, 1537, 1494, 1452, 1356, 1328, 1258, 1092, 823. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (m, 2H), 7.68 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 11.8 Hz, 1H), 7.48 (tt, *J* = 7.4 and 1.7 Hz, 1H), 7.35 (m, 3H), 7.11 (d, *J* = 11.8 Hz, 1H), 7.01 (dd, *J* = 3.6 and 1.2 Hz, 1H), 6.91 (m, 2H). **^{13}C-NMR (100 MHz, CDCl3):** δ 195.0, 185.1, 153.2, 145.7, 145.2, 137.3, 136.3, 133.2, 133.1, 132.1, 131.5, 131.2, 128.8 (2C), 128.5, 128.4 (2C), 128.41, 126.5, 113.2. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{13}O_3S$ $(M+H)^+$ 333.0585, found 333.0598.

Ethyl 8-([1,1′-biphenyl]-4-yl)-6-oxo-6*H*-cyclohepta[*b*]furan-7-carboxylate (9i).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 273-276 °C.; R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3031, 2925, 2854, 1730, 1620, 1590, 1539, 1496, 1043, 758. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.73 (tt, J = 5.3 and 1.9 Hz, 1H), 7.69 (t, *J* = 1.9 Hz, 1H), 7.67 (m, 1H), 7.65 (m, 2H), 7.55 (d, *J* = 11.9 Hz, 1H), 7.51 (m, 4H), 7.43 (m, 1H), 7.15 (d, *J* = 11.9 Hz, 1H), 6.87 (d, *J* = 1.8 Hz, 1H), 4.05 (q, *J* = 7.1 Hz, 2H), 0.97 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 183.8, 166.6, 146.0, 141.8, 140.2, 137.4, 133.4, 131.3, 129.6, 129.4 (2C), 128.9 (2C), 128.8 (2C), 127.7, 127.2, 127.17 (2C), 127.11, 126.7, 113.1, 61.3, 13.6. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{19}O_4$ $(M+H)^+$ 371.1283, found 371.1287.

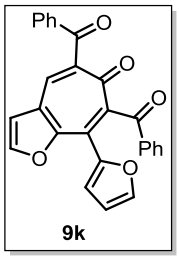
6-Oxo-8-phenyl-6*H*-cyclohepta[*b*]furan-5,7-diy-l)bis-(phenylmethanone) (9j).



9j

This compound was prepared by following the general procedure **3** and isolated isolated as a pale yellow solid. mp = 290-293 °C; R_f = 0.4 (EtOAc/Hexane = 2/ 3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 2924, 2853, 1674, 1597, 1540, 1448, 1286, 1208, 872. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.94 (m, 1H), 7.92 (t, *J* = 4.0 and 2.0 Hz, 2H), 7.71 (m, 1H), 7.69 (t, *J* = 4.0 Hz, 2H), 7.54 (tt, *J* = 8.0 and 4.0 Hz, 1H), 7.46 (m, 3H), 7.32 (m, 7H), 6.98 (d, *J* = 4.0 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.8, 194.7, 183.9, 154.0, 146.6, 146.2, 145.3, 138.4, 136.7, 135.8, 133.4, 133.2, 133.2, 131.7, 129.3, 129.2 (2C), 128.9 (2C), 128.8 (2C), 128.5 (2C), 128.3 (2C), 128.0 (2C), 127.7, 113.7. **HRMS (ESI):** *m/z* calcd for $C_{29}H_{19}O_4$ $(M+H)^+$ 431.1283, found 431.1267.

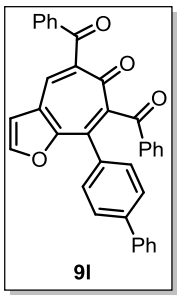
8-(Furan-2-yl)-6-oxo-6*H*-cyclohepta[*b*]furan-5,7-diyl)bis-(phenylmethanone) (9k).



9k

This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 285-288 °C; R_f = 0.4 (EtOAc/ Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2923, 2853, 1690, 1674, 1542, 1498, 1261, 835. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.89 (m, 4H), 7.83 (d, *J* = 2.0 Hz, 1H), 7.50 (tt, *J* = 8.0 and 1.2 Hz, 2H), 7.42 (m, 4H), 7.35 (dd, *J* = 2.0 and 0.8 Hz, 1H), 7.07 (dd, *J* = 3.6 and 0.6 Hz, 2H), 6.99 (d, *J* = 2.0 Hz, 1H), 6.47 (dd, *J* = 2.0 and 1.3 Hz, 1H). **^{13}C-NMR (100 MHz, CDCl3):** δ 195.4, 184.0, 180.5, 152.1, 146.3, 145.5, 144.6, 143.1, 136.9, 135.7, 133.3, 133.0, 131.2, 129.2 (2CH), 128.7 (2CH), 128.56, 128.54 (2CH), 128.50, 128.4 (2CH), 127.6, 117.5, 113.8, 112.1. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{17}O_5$ $(M+H)^+$ 421.1076, found 421.1072.

8-([1,1′-Biphenyl]-4-yl)-6-oxo-6*H*-cyclohepta[*b*]furan-5,7-diyl)bis-(phenylmethanone) (9l).

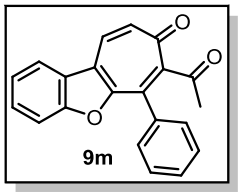


9l

This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 297-300 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2925, 1673, 1597, 1579, 1538, 1494, 1337, 1286, 1006. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 1.0 Hz, 1H), 7.93−7.92 (m, 2H), 7.73 (d, *J* = 1.0 Hz, 1H), 7.72 (m, 2H), 7.57 (m, 1H), 7.54 (s, 2H), 7.52 (t, *J* = 1.2 Hz, 1H), 7.50 (s, 1H), 7.45 (d, *J* = 1.8 Hz, 1H), 7.44 (m, 2H), 7.42 (m, 2H), 7.38 (t, *J* = 1.2 Hz, 1H), 7.36 (t, *J* = 2.2 Hz, 1H), 7.35 (t, *J* = 1.2 Hz, 1H), 7.32

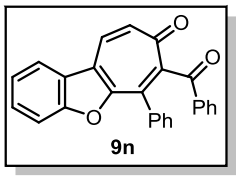
(s, 1H), 7.30 (s, 1H), 6.99 (d, *J* = 1.8 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.8, 194.8, 183.9, 154.0, 146.7, 146.2, 145.4, 141.6, 140.0, 138.2, 136.8, 135.8, 133.4, 133.2, 132.1, 131.7, 129.8, 129.8, 129.2 (2C), 128.9 (2C), 128.8 (2C), 128.6 (2C), 128.3 (2C), 127.78, 127.74, 127.1 (2C), 126.6 (2C), 113.7. **HRMS (ESI):** *m/z* calcd for $C_{35}H_{23}O_4$ $(M+H)^+$ 507.1596, found 507.1608.

7-Acetyl-6-phenyl-8*H*-cyclohepta[*b*]benzofuran-8-one (9m).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 201−202 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2919, 2852, 1716, 1668, 1635, 1480, 1385, 1284, 819. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 11.9 Hz, 1H), 7.96 (m, 1H), 7.53 (m, 3H), 7.49 (m, 2H), 7.47 (m, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 6.70 (s, 1H), 2.14 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 202.8, 185.0, 154.5, 149.2, 137.6, 133.8, 129.4 (2C), 129.3, 129.1, 128.5, 128.4, 128.4 (2C), 125.8, 124.5, 123.5, 120.1, 116.1, 112.3, 30.9. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{15}O_3$ $(M+H)^+$ 315.1021, found 315.1026.

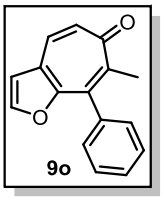
7-Benzoyl-6-phenyl-8*H*-cyclohepta[*b*]benzofuran-8-one (9n).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 207-210 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2852, 1709, 1668, 1635, 1557, 1480, 1446, 1281, 883, 819. **^{1}H-NMR (400 MHz, CDCl3):** δ 8.03 (d, *J* = 11.8 Hz, 1H), 7.99 (m, 1H), 7.74 (m, 2H), 7.54 (m, 1H), 7.50 (m, 4H), 7.35 (t, *J* = 1.5 Hz, 1H), 7.33 (m, 6H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.1, 185.4, 155.1, 154.5, 147.6, 147.3, 146.3, 139.0, 137.5, 136.5, 133.7, 133.1, 129.1, 128.7 (2C), 128.6, 128.5, 128.4 (2C), 127.9, 127.9, 125.9, 124.5, 123.7, 120.1, 112.3. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{17}O_3$ $(M+H)^+$ 377.1178, found 377.1179.

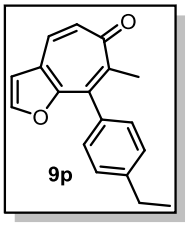
7-Methyl-8-phenyl-6*H*-cyclohepta[*b*]furan-6-one (9o).

This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 261-263 °C. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 1710, 1620, 1575, 1536, 1452, 1356, 1352, 1326, 830, 716. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.55



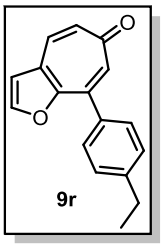
(m, 5H), 7.26 (m, 2H), 7.10 (d, *J* = 11.9 Hz, 1H), 6.79 (d, *J* = 1.9 Hz, 1H), 2.03 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 187.3, 154.2, 144.3, 142.3, 139.1, 138.3, 134.5, 129.8, 128.5 (2C), 128.2 (2C), 127.9, 126.6, 112.0, 19.5. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{13}O_2$ $(M+H)^+$ 237.0900, found 237.0909.

7-Benzoyl-8-(4-ethylphenyl)-6*H*-cyclohepta[*b*]furan-6-one (9p).



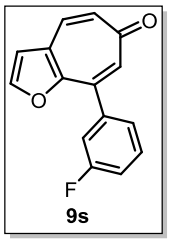
This compound was prepared by following the general procedure **3** and isolated as a pale yellow solid. mp = 268-271 °C. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat)** ν_{max}/cm^{-1} 2900, 1715, 1690, 1620, 1470, 1430, 1356, 1351, 1315, 1270, 830. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.50 (d, *J* = 1.9 Hz, 1H), 7.47 (d, *J* = 11.8 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 11.8 Hz, 1H), 6.78 (d, *J* = 1.9 Hz, 1H), 2.78 (q, *J* = 7.6 Hz, 2H), 2.04 (s, 3H), 1.34 (t, *J* = 7.6 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 187.3, 144.3, 143.8, 142.9, 139.3, 135.5, 134.5, 130.2, 129.8, 128.1 (2C), 128.0 (2C), 126.5, 112.0, 28.6, 19.6, 15.3. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{17}O_2$ $(M+H)^+$ 265.1229, found 265.1227.

8-(4-Ethylphenyl)-6*H*-cyclohepta[*b*]furan-6-one (9r).



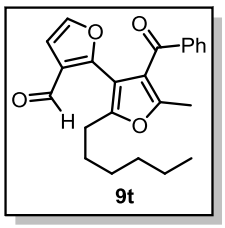
This compound was prepared by following the general procedure **3** and isolated as a pale yellow liquid. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2963, 2926, 2854, 1710, 1620, 1590, 1540, 1496, 1460, 1350, 1090, 847. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.64 (d, *J* = 2.0 Hz, 1H), 7.52 (m, 3H), 7.36 (m, 2H), 7.06 (m, 2H), 6.85 (d, *J* = 1.8 Hz, 1H), 2.76 (q, *J* = 7.7 Hz, 2H), 1.33 (t, *J* = 7.5 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 186.9, 153.4, 145.5, 144.6, 140.7, 136.3, 136.0, 134.8, 131.4, 129.1 (2C), 128.4, 127.9 (2C), 113.0, 28.6, 15.3. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{15}O_2$ $(M+H)^+$ 251.1072, found 251.1071.

8-(3-Fluorophenyl)-6*H*-cyclohepta[*b*]furan-6-one (9s).



This compound was prepared by following the general procedure **3** and isolated as a pale yellow liquid. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2924, 2853, 1730, 1621, 1545, 1498, 1455, 1343, 1259, 1092, 1041, 867, 789. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.65 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 11.5 Hz, 1H), 7.49 (m, 1H), 7.34-7.29 (m, 2H), 7.21 (dt, *J* = 8.4 and 1.9, 1H), 7.04 (dd, *J* = 11.7 and 2.3 Hz, 2H), 6.87 (d, *J* = 2.0 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 186.7, 156.2 (d, *J* = 226.96 Hz), 144.8, 139.4, 136.5, 136.1, 131.5, 130.9, 130.0 (d, *J* = 8.16 Hz), 128.6, 126.3, 124.8, 116.4 (d, *J* = 22.77 Hz), 116.1 (d, *J* = 20.71 Hz), 113.1. **^{19}F-NMR** (**376.4 MHz, $CDCl_3$):** δ -112.6. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{10}FO_2$ $(M+H)^+$ 241.0665, found 241.0667.

4′-Acetyl-2′-hexyl-5′-methyl-[2,3′-bifuran]-3-carbaldehyde (9t).



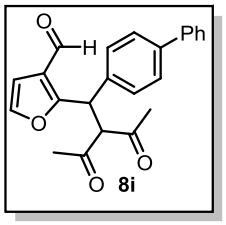
This compound was prepared by following the general procedure **3** and isolated as a colorless liquid. R_f = 0.3 (EtOAc/Hexane = 1/5). **IR (thin film, neat):** ν_{max}/cm^{-1} 3059, 2925, 1673, 1597, 1579, 1538, 1494, 1337, 1286, 1006, 739. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.74 (s, 1H), 7.66-7.64 (m, 2H), 7.46 (tt, *J* = 7.4 and 1.2 Hz, 1H), 7.34 (m, 2H), 7.23 (dd, *J* = 2.0 and 0.5 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 2.67 (t, *J* = 7.7 Hz, 2H), 2.42 (s, 3H), 1.71 (m, 2H), 1.32 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 191.0, 184.9, 156.6, 155.8, 155.0, 143.2, 138.2, 132.5, 128.8 (2C), 128.2 (2C), 124.1, 121.3, 109.8, 108.0, 31.3, 28.7, 27.9, 26.7, 22.4, 14.0, 13.8. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{25}O_4$ $(M+H)^+$ 365.1753, found 365.1766.

General procedure 4: Synthesis of diketone 8i, 8u, 8v

The Substrates bearing diketone backbone **8i, 8u, 8v** also can be readily synthesized from 3-formyl-2-furyl carbinol **12c, 12f** by following the general procedure **1** and **2**.

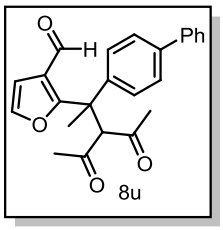
2-(1-([1,1'-Biphenyl]-4-yl)-2-acetyl-3-oxobutyl)furan-3-carbaldehyde (8i).

This compound was prepared by following the general procedure **4** and isolated as a colourless liquid. R_f = 0.5 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 1725, 1699, 1681, 1570, 1357, 1123, 1206. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.09 (s, 1H), 7.55 (m, 4H), 7.42 (m,



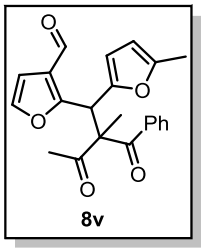
4H), 7.36 (m, 2H), 6.71 (d, *J* = 1.6 Hz, 1H), 5.48 (d, *J* = 11.8 Hz, 1H), 4.98 (d, *J* = 11.8 Hz, 1H), 2.19 (s, 3H), 2.08 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 201.1, 200.8, 184.7, 161.4, 142.6, 140.9, 140.1, 136.1, 128.8 (2C), 128.6 (2C), 127.8 (2C), 127.5, 127.0 (2C), 122.1, 109.2, 71.6, 42.7, 30.3, 29.4. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{20}O_4Na$ $(M+Na)^+$: 383.1255, Found: 383.1259.

2-(2-([1,1'-biphenyl]-4-yl)-3-acetyl-4-oxopentan-2-yl)furan-3-carbaldehyde (8u).



This compound was prepared by following the general procedure **4** and isolated as a colourless liquid. R_f = 0.5 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 1725, 1699, 1681, 1570, 1357, 1123, 1206. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.05 (s, 1H), 7.54 (m, 4H), 7.44 (m, 3H), 7.37 (m, 3H), 6.76 (d, *J* = 1.4 Hz, 1H), 6.05 (s, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.70 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 205.1, 204.0, 185.0, 162.0, 142.7, 140.6, 140.1, 135.7, 130.3 (2C), 128.8 (2C), 127.5, 127.2 (2C), 127.0 (2C), 122.9, 108.9, 71.5, 45.2, 27.3, 26.5, 16.6. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{22}O_4Na$ $(M+Na)^+$: 397.1416, Found. 397.1421.

2-(2-acetyl-2-methyl-1-(5-methylfuran-2-yl)-3-oxobutyl)furan-3-carbaldehyde (8v).



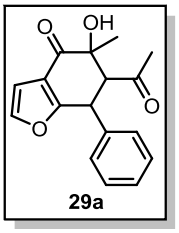
This compound was prepared by following the general procedure **4** and isolated as a colourless liquid. R_f = 0.5 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2924, 1725, 1702, 1681, 1555, 1404, 1352, 1123, 1099. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.9 (s, 1H), 7.38 (dd, *J* = 0.3, 2.0 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.00 (d, *J* = 3.1 Hz, 1H), 5.90 (s, 1H), 5.88 (m, 1H), 2.22 (s, 3H), 2.18 (s, 3H), 2.07 (s, 3H), 1.65 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 204.6, 204.0, 185.4, 159.0, 152.1, 147.7, 142.7, 124.0, 110.6, 108.5, 106.6, 71.0, 40.6, 26.7, 26.5, 16.2, 13.5. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{18}O_5Na$ $(M+Na)^+$: 325.1052, Found. 325.1053.

General Procedure-5: Synthesis of dihydrobenzofuranone

To a flame-dried, round-bottom flask, equipped with magnetic stir bar were added 1,3-dicarbonyl adduct **8** (0.1 mmol), catalyst **30d** (0.02 mmol), and Cs_2CO_3 (0.02 mmol) under N_2 atmosphere at r.t. The reaction mixture was dissolved in anhydrous THF (1 mL) and the resultant

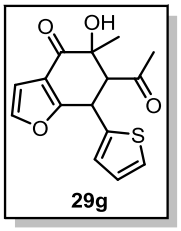
reaction mixture was stirred at 50 °C until the starting material was consumed, as monitored by TLC. Upon completion, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (hexane/EtOAc) to afford **29**.

6-Acetyl-5-hydroxy-5,6-dimethyl-7-phenyl-6,7-dihydrobenzofuran-4(5*H*)-one (29a).



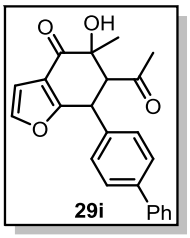
This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3461, 2923, 2854, 1707, 1686, 1364, 1264, 1118. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.43 (dd, *J* = 0.6, 2.0 Hz, 1H), 7.30 (m, 3H), 7.08 (m, 2H), 6.76 (d, *J* = 2.0 Hz, 1H), 5.42 (s, 1H), 4.18 (s, 1H), 2.15 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 208.6, 195.1, 165.9, 144.4, 136.0 (2C), 128.0 (2C), 127.6, 117.8, 106.7, 79.1, 63.6, 45.7, 29.9, 23.5, 23.5, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{18}O_4$ $(M+H_2O)^+$: 302.1154, Found: 302.1146.

6-Acetyl-5-hydroxy-5-methyl-7-(thiophen-2-yl)-6,7-dihydrobenzofuran-4(5*H*)-one (29g).



This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3463, 2963, 2963, 1692, 1514, 1457, 1355, 1120, 1097. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.41 (s, 1H), 7.27 (s, 1H), 7.00 (s, 2H), 6.74 (s, 1H), 5.06 (d, *J* = 10.8 Hz, 1H), 4.03 (s, 1H), 3.75 (d, *J* = 10.8 Hz, 1H), 2.22 (s, 3H), 1.35 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 206.2, 195.0, 164.9, 145.1, 139.4, 127.4, 127.0, 125.4, 117.2, 106.9, 76.3, 65.1, 37.9, 34.0, 21.8. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}O_4S$ $(M+H)^+$: 291.0691, Found: 291.0680.

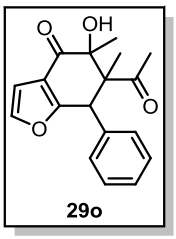
7-([1,1'-Biphenyl]-4-yl)-6-acetyl-5-hydroxy-5-methyl-6,7-dihydrobenzofuran-4(5*H*)-one (29i).



This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3466, 2922, 1688, 1360, 1260, 1120, 945. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.60 (m, 4H), 7.41 (m, 4H), 7.21 (m, 2H), 6.77 (d, *J* = 1.0 Hz, 1H), 4.75 (d, *J* = 10.7 Hz, 1H), 4.06 (s, 1H), 3.71 (d, *J* = 10.7 Hz, 1H), 2.12 (s, 3H),

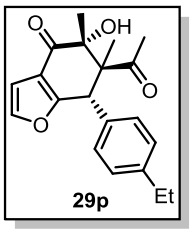
1.40 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 206.5, 195.3, 166.1, 145.0, 140.8, 140.3, 136.5, 129.1 (2C), 128.8 (2C), 127.6 (2C), 127.5, 127.0 (2C), 118.0, 106.8, 76.3, 64.8, 42.4, 34.2, 22.0. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{21}O_4$ $(M+H)^+$: 361.1440; Found: 361.1455.

6-Acetyl-5-hydroxy-5,6-dimethyl-7-phenyl-6,7-dihydrobenzofuran-4(5*H*)-one (29o).



This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3461, 2923, 2854, 1707, 1686, 1364, 1264, 1118**. ^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.43 (dd, *J* = 0.6, 2.0 Hz, 1H), 7.30 (m, 3H), 7.08 (m, 2H), 6.76 (d, *J* = 2.0 Hz, 1H), 5.42 (s, 1H), 4.18 (s, 1H), 2.15 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 208.6, 195.1, 165.9, 144.4, 136.0 (2C), 128.0 (2C), 127.6, 117.8, 106.7, 79.1, 63.6, 45.7, 29.9, 23.5, 23.5, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{18}O_4$ $(M-H)^+$: 297.1127; Found: 297.1118.

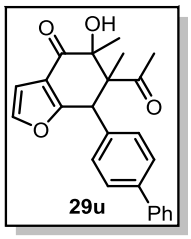
6-Acetyl-7-(4-ethylphenyl)-5-hydroxy-5,6-dimethyl-6,7-dihydrobenzofuran-4(5*H*)-one (29p).



This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3461, 2923, 2854, 1714, 1687, 1454, 1368, 1260, 1126, 1088. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.42 (d, *J* = 1.5 Hz,1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.76 (d, *J* = 1.9 Hz, 1H), 5.39 (s, 1H), 4.17 (s, 1H), 2.66 (q, *J* = 7.6, 15.2 Hz, 2H), 2.15 (s, 3H), 1.59 (s, 3H), 1.35 (s, 3H), 1.23(s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 208.6, 195.2, 166.3, 144.4, 143.5, 133.1, 130.9 (2C), 127.5 (2C), 117.7, 106.6, 79.1, 63.7, 45.4, 29.9, 28.4, 23.5, 15.2, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{22}O_4Na$ (M+Na): 349.1416, Found: 349.1403.

7-([1,1'-Biphenyl]-4-yl)-6-acetyl-5-hydroxy-5,6-dimethyl-6,7-dihydrobenzofuran-4(5*H*)-one (29u).

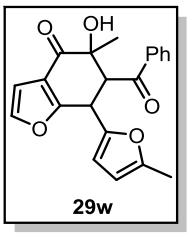
This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3462, 2925, 1703, 1488, 1376, 1355, 1178, 1096, 1008, 905. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.60 (d, *J* = 7.8 Hz, 2H),



29u

7.55 (d, *J* = 7.9 Hz, 2H), 7.46 (m, 3H), 7.34 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.79 (s, 1H), 5.47 (s, 1H), 4.20 (s, 1H), 2.19 (s, 3H), 1.38 (s, 3H), 1.28 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 208.6, 195.1, 165.9, 144.5, 140.45, 140.44, 135.0, 131.4 (2C), 128.8 (2C), 127.4, 127.0 (2C), 126.7 (2C), 117.9, 106.7, 79.1, 63.8, 45.4, 29.9, 23.5, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{23}O_4$ $(M+H)^+$: 375.1596; Found: 375.1603.

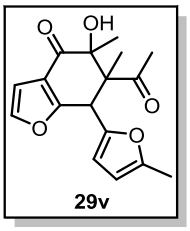
6-Benzoyl-5-hydroxy-5,6-dimethyl-7-(5-methylfuran-2-yl)-6,7-dihydrobenzofuran-4(5*H*)-one (29w).



29w

This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3466, 2922, 1688, 1360, 1260, 1120, 945. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.97 (m, 2H), 7.54 (m, 1H), 7.43 (m, 3H), 6.78 (d, *J* = 2.0 Hz, 1H), 6.12 (d, *J* = 3.0 Hz, 1H), 5.97 (dd, *J* = 1.0 and 3.1 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.76 (d, *J* = 10.9 Hz, 1H), 3.90 (s, 1H), 2.11 (s, 3H), 1.46 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.9, 195.2, 164.2, 152.3, 147.0, 144.9, 133.2, 128.9 (2C), 128.2 (2C), 117.4, 109.7, 107.0, 106.3, 67.9, 55.4, 25.6, 21.9, 13.6. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{18}O_5K$ $(M+K)^+$: 389.0791; Found: 389.0778.

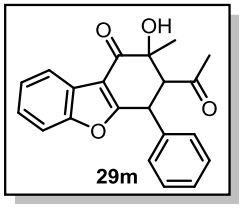
6-Acetyl-5-hydroxy-5,6-dimethyl-7-(5-methylfuran-2-yl)-6,7-dihydrobenzofuran-4(5*H*)-one (29v).



29v

This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3466, 2922, 1688, 1360, 1260, 1120, 945. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.46 (dd, *J* = 0.6, 2.0 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.16 (d, *J* = 3.0 Hz, 1H), 5.92 (dd, *J* = 0.9 and 2.2 Hz, 1H), 5.42 (d, 1H), 4.16 (s, 1H), 2.26 (s, 3H), 2.23 (s, 3H), 1.28 (s, 3H), 1.24 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 208.3, 194.8, 163.8, 152.0, 147.4, 144.6, 117.1, 111.3, 106.7, 106.2, 78.2, 63.8, 40.3, 29.3, 23.5, 14.0, 13.6. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{18}O_5Na$ $(M+Na)^+$: 325.1052; Found: 325.1040.

3-Acetyl-2-hydroxy-2-methyl-4-phenyl-3,4-dihydrodibenzo[*b,d*]furan-1(2*H*)-one (29m).

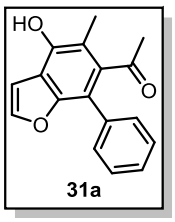


This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3463, 2926, 2963, 1703, 1514, 1457, 1376, 1355, 1244, 1120, 1097. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.07 (d, *J* = 7.3 Hz, 1H), 7.41 (m, 2H), 7.36 (m, 4H), 7.19 (d, *J* = 7.3 Hz, 2H), 4.87 (d, *J* = 10.7 Hz), 4.12 (s, 1H), 3.78 (d, *J* = 10.8 Hz, 1H), 2.11 (s, 3H), 1.44 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 206.3, 195.4, 169.8, 155.7, 137.3, 129.0 (2C), 128.8 (2C), 128.0, 125.8, 124.9, 123.1, 121.6, 113.6, 111.7, 76.0, 64.8, 43.1, 34.1, 22.1. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{18}O_4$ $(M)^+$: 334.1205; Found: 334.1195.

General procedure-6: Synthesis of benzofuran

To a solution of alcohol **29** (10 mg, 0.08 mmol) in pyridine (0.5 mL) at 0 °C was added $POCl_3$ (362 μL, 2.4 mmol). The resulting reaction mixture was stirred at r.t. until starting material was consumed, as monitored by TLC. The reaction mixture was quenched by addition of sat. aq NaHCO3 and extracted with EtOAc (3×5 mL). The organic extracts were combined and dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (hexane/EtOAc) to afford **31**.

1-(4-Hydroxy-5-methyl-7-phenylbenzofuran-6-yl)ethanone (31a).

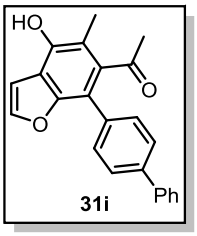


This compound was prepared by following the general procedure **6** and isolated as colourless liquid colourless oil. R_f = 0.4 (EtOAc/hexane = 3/7). **IR (neat):** ν_{max}/cm^{-1} 3428, 2929, 2854, 1698, 1643, 1450, 1349, 1260, 1040. **^{1}H-NMR (400 MHz, DMSO-d_6):** δ 8.16 (d, *J* = 2.4 Hz, 1 H), 7.51 (m, 3 H), 7.41 (m, 2 H), 7.09 (d, *J* = 2.1 Hz, 1 H), 2.34 (s, 3 H), 2.03 (s, 3 H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 206.4, 150.5, 146.8, 139.0, 133.4, 130.0 (2C), 128.7 (2C), 128.4, 127.5, 126.0, 125.9, 121.1, 105.9, 32.6, 16.3**. HRMS (ESI):** *m/z* $(M-H)^+$ calcd for $C_{17}H_{13}O_3$: 265.0865; found: 265.0857.

1-(4-Hydroxy-5-methyl-7-phenylbenzofuran-6-yl)ethanone (31i).

This compound was prepared by following the general procedure **5** and isolated as a colourless liquid. R_f = 0.4 (EtOAc/hexane = 3/7). **IR (neat):** ν_{max}/cm^{-1} 3430, 2927, 2850, 1700, 1650, 1445,

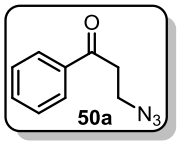
1350, 1265, 1044 . **^{1}H-NMR (400 MHz, DMSO-d_6):** δ 8.19 (d, *J* = 2.0 Hz, 1 H), 7.84 (m, 2 H), 7.78 (m, 2 H), 7.52 (m, 4 H), 7.42 (m, 1 H), 7.11 (d, *J* = 2.3 Hz, 1 H), 2.35 (s, 3 H), 2.10 (s, 3 H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 206.4, 150.5, 146.9, 141.3, 139.0, 132.3, 130.4 (2C), 128.9 (2C), 127.6, 127.5, 127.4 (2C), 127.1 (2C), 126.08, 126.06, 120.7, 105.7, 32.8, 16.3. **HRMS (ESI):** *m/z* $(M–H)^+$ calcd for $C_{23}H_{17}O_3$ 341.1178, found: 341.1166.



General procedure-7: Synthesis of *β*-azidoketone

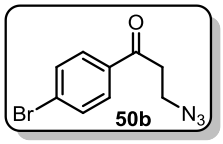
An oven-dried 5 mL glass vial was charged with an enone **49** (0.2 mmol, 1.0 equiv), Zhdankin reagent **38** (0.26 mmol, 1.3 equiv), toluene (1 mL) and DABCO (0.02 mmol, 0.1 equiv) at room temperature (rt) and continued stirring at rt until starting material disappeared as monitored by TLC. The reaction mixture was quenched with aqueous ammonium chloride solution, diluted with ethyl acetate and the layers were separated. The aqueous layer further extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **50.**

3-Azido-1-phenylpropan-1-one (50a).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2853, 2104, 1696, 1585, 1281, 763. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.00 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 2H), 3.27 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.1, 136.3, 133.5, 128.7 (2C), 128.0 (2C), 46.1, 37.6. **HRMS (ESI):** *m/z* calcd for $C_9H_{10}N_3O$ $(M+H)^+$: 176.0824, Found: 176.0819.

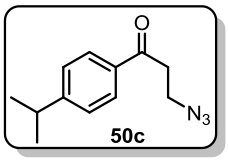
3-Azido-1-(4-bromophenyl)propan-1-one (50b).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2088, 1700, 1584, 1431, 1288. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.23 (d, *J* =

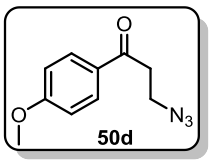
6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 196.2, 135.0, 132.1 (2C), 129.5 (2C), 128.8, 46.0, 37.6. **HRMS (ESI):** *m/z* calcd for $C_9H_7N_3OBr$ $(M-H)^+$: 251.9773, Found: 251.9760.

3-Azido-1-(4-isopropylphenyl)propan-1-one (50c).



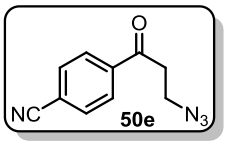
This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2100, 1700, 1585, 1431, 1289. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.24 (t, *J* = 6.4 Hz, 2H), 2.99 (m, 1H), 1.30 (s, 3H), 1.29 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 196.8, 155.1, 134.2 (2C), 128.3 (2C), 126.8, 46.2, 37.5, 34.3, 23.68, 23.64. **HRMS (ESI):** *m/z* calcd for $C_{12}H_{16}N_3O$ $(M+H)^+$: 218.1293; Found: 218.1282.

3-Azido-1-(4-methoxyphenyl)propan-1-one (50d).



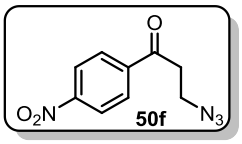
This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2103, 1685, 1497, 1281, 1205, 756. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H), 3.74 (t, *J* = 6.1 Hz, 2H), 3.22 (t, *J* = 6.1 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.6, 163.8, 130.3 (2C), 129.5, 113.8 (2C), 55.5, 46.3, 37.2. **HRMS (ESI):** *m/z* calcd for $C_{10}H_{10}N_3O_2$ $(M-H)^+$: 204.0773; Found: 204.0764.

4-(3-Azidopropanoyl)benzonitrile (50e).



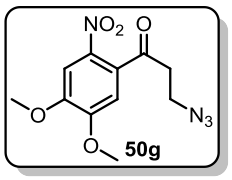
This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 2/3). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2224, 2102, 1681, 1591, 1267, 760. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 2H), 3.78 (t, *J* = 6.3 Hz, 2H), 3.27 (t, *J* = 6.3 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.9, 139.1, 132.6 (2C), 128.4 (2C), 117.8, 116.8, 45.8, 38.0. **HRMS (ESI):** *m/z* calcd for $C_{10}H_8N_4ONa$ $(M+Na)^+$: 223.0596; Found: 223.0588.

3-Azido-1-(4-nitrophenyl)propan-1-one (50f).



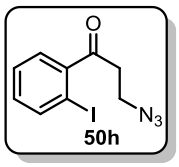
This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2935, 2102, 1698, 1580, 1280, 1017, 758. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.36 (d, *J* = 8.6 Hz, 2H), 8.15 (d, *J* = 8.6 Hz, 2H), 3.80 (t, *J* = 6.3 Hz, 2H), 3.31 (t, *J* = 6.3 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.7, 150.2, 140.6, 129.1 (2C), 124.0 (2C), 45.8, 38.3. **HRMS (ESI):** *m/z* calcd for $C_9H_9N_4O_3$ $(M+H)^+$: 221.0675, Found: 221.0663.

3-Azido-1-(4,5-dimethoxy-2-nitrophenyl)propan-1-one (50g).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2937, 2103, 1685, 1493, 1443, 1285. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.67 (s, 1H), 6.77 (s, 1H), 4.0 (s, 6H), 3.76 (t, *J* = 6.4 Hz, 2H), 3.01 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.0, 154.2, 149.7, 138.1, 132.0, 108.5, 106.8, 56.8, 56.6, 46.3, 42.1. **HRMS (ESI):** *m/z* calcd for $C_{11}H_{12}N_4O_5Na$ $(M+Na)^+$: 303.0705, Found: 303.0691.

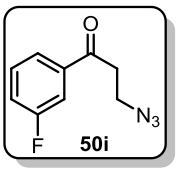
3-Azido-1-(2-iodophenyl)propan-1-one (50h).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2849, 2107, 1692, 1585, 1427, 1208, 743. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.45 (m, 2H), 7.10 (m, 1H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.20 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 201.5, 143.5, 140.8, 132.1, 128.2, 128.0, 90.9, 46.1, 40.9. **HRMS (ESI):** *m/z* calcd for $C_9H_9N_3OI$ $(M+H)^+$: 301.9790, Found: 301.9775.

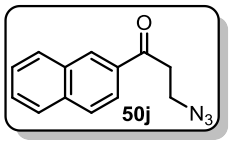
3-Azido-1-(3-fluorophenyl)propan-1-one (50i).

This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2962, 2125, 1700, 1598, 1289, 751. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.66 (dt, *J* = 2.0 and 9.2



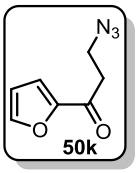
Hz, 1H), 7.48 (m, 1H), 7.64 (m, 1H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.24 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 196.0 (d, *J* = 2.0 Hz), 162.8 (d, *J* = 246.9), 138.4 (d, *J* = 5.8 Hz), 130.5 (d, *J* = 7.5 Hz), 123.8 (d, *J* = 3.0 Hz), 120.8 (d, *J* = 21.3 Hz), 114.7 (d, *J* = 22.1 Hz), 45.9, 37.8. **^{19}F-NMR (376.4 MHz, $CDCl_3$):** δ −111.4. **HRMS (ESI):** *m/z* calcd for $C_9H_8N_3OFNa$ $(M+Na)^+$: 216.0549; Found: 216.0540.

3-Azido-1-(3-fluorophenyl)propan-1-one (50j).



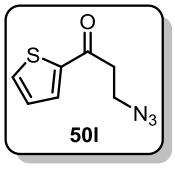
This compound was prepared by following the general procedure **7** and isolated as pale yellow viscous oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 2103, 1681, 1627, 1469, 1373, 1276, 864. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.47 (s, 1H), 8.03 (dd, *J* = 1.6 and 8.4 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.90 (m, 2H), 7.61 (m, 2H), 3.80 (t, *J* = 6.8 Hz, 2H), 3.37 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.1, 135.7, 133.7, 132.4, 129.9, 129.6, 128.7, 128.6, 127.8, 126.9, 123.5, 46.2, 37.7. **HRMS (ESI):** *m/z* calcd for $C_{13}H_{10}N_3O$ $(M-H)^+$: 224.0824; Found: 224.0813.

3-Azido-1-(furan-2-yl)propan-1-one (50k).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2928, 2097, 1695, 1630, 1257, 1092, 836. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.08 (s, 1H), 7.48 (s, 1H), 6.80 (m, 1H), 4.01 (t, *J* = 5.2 Hz, 2H), 3.04 (t, *J* = 5.2 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 205.0, 147.6, 144.4, 127.6, 108.3, 58.0, 42.0. **HRMS (ESI):** *m/z* calcd for $C_7H_7N_3O_2Na$ $(M+Na)^+$: 188.0436, Found: 188.0430.

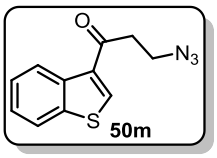
3-Azido-1-(thiophen-2-yl)propan-1-one (50l).



This compound was prepared by following the general procedure **7** and isolated as pale yellow oil. R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2849, 2104, 1692, 1585, 1424, 1266, 743. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 3.8 Hz, 1H), 7.70 (d, *J* = 4.9 Hz, 1H), 7.17 (t, *J* = 4.4 Hz,

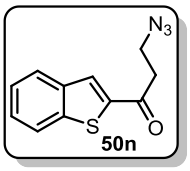
1H), 3.74 (t, *J* = 6.4 Hz, 2H), 3.20 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 189.9, 143.6, 134.3, 132.3, 128.2, 46.1, 38.3. **HRMS (ESI):** *m/z* calcd for $C_7H_8N_3OS$ $(M+H)^+$: 182.0388, Found: 182.0380.

3-Azido-1-(benzo[*b*]thiophen-3-yl)propan-1-one (50m).



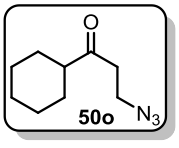
This compound was prepared by following the general procedure **7** and isolated as pale yellow solid. mp = 65-67 °C. R_f = 0.3 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2124, 1662, 1599, 1481, 1292, 1020, 753. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.01 (s, 1H), 7.92 (t, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.3 Hz, 1H), 3.79 (t, *J* = 6.4 Hz, 2H), 3.31 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 191.5, 142.9, 142.6, 138.9, 129.5, 127.7, 126.0, 125.1, 123.0, 46.2, 38.2. **HRMS (ESI):** *m/z* calcd for $C_{11}H_9N_3OSNa$ $(M+Na)^+$: 254.0364, Found: 254.0372.

3-Azido-1-(benzo[*b*]thiophen-2-yl)propan-1-one (50n).



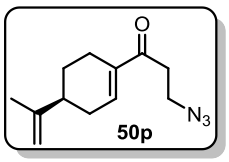
This compound was prepared by following the general procedure **7** and isolated as pale yellow solid. mp = 63-65 °C. R_f = 0.3 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2926, 2103, 1658, 1592, 1427, 1454, 1367, 1301, 1249. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.79 (d, *J* = 8.1 Hz, 1H), 8.32 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.53 (t, *J* = 7.1 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 3.80 (t, *J* = 6.4 Hz, 2H), 3.29 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.1, 139.7, 137.3, 136.3, 134.8, 126.6, 125.68, 126.65, 122.0, 46.2, 39.0.

3-Azido-1-cyclohexylpropan-1-one (50o).



This compound was prepared by following the general procedure **7** and isolated as colourless oil. R_f = 0.6 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2933, 2103, 1704, 1585, 1278, 1208, 1016. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 3.56 (t, *J* = 6.3 Hz, 2H), 2.74 (t, *J* = 6.3 Hz, 2H), 2.37 (m, 1H), 1.80 (m, 5H), 1.28 (m, 5H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 211.1, 51.0, 45.8, 39.2, 28.2 (2C), 25.7, 25.5 (2C). **HRMS (ESI):** *m/z* calcd for $C_9H_{16}N_3O$ $(M+H)^+$: 182.1293, Found: 182.1285.

3-Azido-1-(4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)propan-1-one (50p).

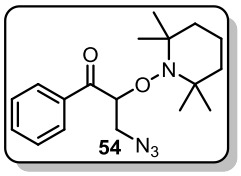


This compound was prepared by following the general procedure **7** and isolated as colourless oil. R_f = 0.6 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2934, 2102, 1696, 1585, 1281, 1020, 763. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 6.96 (d, *J* = 4.8 Hz, 1H), 4.79 (s, 1H), 4.74 (s, 1H), 3.62 (t, *J* = 6.5 Hz, 2H), 2.93 (t, *J* = 6.5 Hz, 2H), 2.50 (m, 1H), 2.42 (m, 1H), 2.18 (m, 3H), 1.94 (m, 1H), 1.77 (s, 3H), 1.45 (m, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.7, 148.6, 140.3, 138.8, 109.3, 46.4, 40.1, 36.0, 26.8, 31.4, 23.4, 20.7. **HRMS (ESI):** *m/z* calcd for $C_{12}H_{18}N_3O$ $(M+H)^+$: 220.1450; Found: 220.1440.

General procedure-8: Radical entrapment by TEMPO

An oven-dried 5 mL glass vial was charged with enone **49a** (0.22 mmol, 1.0 equiv), Zhdankin reagent **38** (0.29 mmol, 1.3 equiv), TEMPO (0.44 mmol, 2.0 equiv). Toluene (1.5 mL) and DABCO (0.02 mmol, 0.1 equiv) were then introduced at room temperature (rt) and continued stirring at rt until starting material disappeared as monitored by TLC. The reaction mixture was quenched with aqueous ammonium chloride solution, diluted with ethyl acetate and the layers were separated. The aqueous layer further extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **54**.

3-Azido-1-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (54).

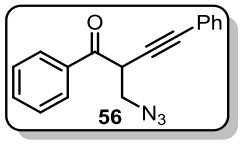


This compound was prepared by following the general procedure **8** and isolated as pale yellow oil. R_f = 0.5 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2926, 2104, 1696, 1585, 1281, 1208, 763. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.09 (m, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 5.17 (dd, *J* = 4.9 and 6.6 Hz, 1H), 3.83 (dq, *J* = 6.9, 12.6 and 19.2 Hz, 2H), 1.53 (s, 2H), 1.39 (m, 2H), 1.35 (s, 3H), 1.28 (m, 2H), 1.21 (s, 3H), 1.06 (s, 3H), 0.9 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 199.9, 136.3, 133.4, 129.2 (2C), 128.5 (2C), 85.4, 60.28, 60.21, 52.0, 40.3, 40.2, 34.1, 33.6, 20.3, 20.2, 17.0. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{27}N_4O_2$ $(M+H)^+$: 331.2134; Found: 331.2120.

General procedure-9: One-pot azidoalkynylation

An oven-dried 5 mL glass vial was charged with enone **49a** (0.22 mmol, 1.0 equiv), Zhdankin reagent **38** (0.29 mmol, 1.3 equiv), **55** (0.33 mmol, 1.5 equiv). Toluene (1.5 mL) and DABCO (0.02 mmol, 0.1 equiv) were then introduced at room temperature (rt) and continued stirring at rt until starting material disappeared as monitored by TLC. The reaction mixture was quenched with aqueous ammonium chloride solution, diluted with ethyl acetate and the layers were separated. The aqueous layer further extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **56**.

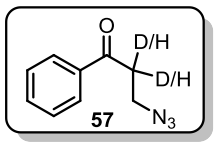
3-Azido-1-(2-(phenylethynyl)phenyl)propan-1-one (56).



This compound was prepared by following the general procedure **9** and isolated as pale yellow viscous oil. R_f = 0.5 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2936, 2231, 2107, 1693, 1607, 1567, 1445, 1405, 1371, 1240, 1210. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.05 (d, *J* = 8.0 Hz, 1H), 7.84 (m, 1H), 7.77 (m, 1H), 7.65 (m, 1H), 7.50 (m, 3H), 7.29 (m, 3H), 5.05 (d, *J* = 2.4 Hz, 1H), 2.43 (m, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.1, 136.3, 133.5, 132.1 (2C), 128.8 (2C), 128.7, 128.3 (2C), 128.0 (2C), 122.1, 83.6, 77.2, 46.1, 37.6. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}N_3O$ $(M+H)^+$: 276.1137, Found: 276.1124.

General procedure-10: Deuterium labeling experiment

An oven-dried 5 mL glass vial was charged with enone **49a** (0.22 mmol, 1.0 equiv), Zhdankin reagent **38** (0.29 mmol, 1.3 equiv), toluene:MeOD (1:1, 1 mL) and DABCO (0.02 mmol, 0.1 equiv) at room temperature (rt) and continued stirring at rt until starting material disappeared as monitored by TLC. The reaction mixture was quenched with aqueous ammonium chloride solution, diluted with ethyl acetate and the layers were separated. The aqueous layer further extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **57.**

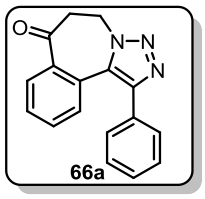


This compound was prepared by following the general procedure **10** and isolated as pale yellow oil. (~74% D-incorporation by ^{1}H-NMR). R_f = 0.4 (EtOAc/Hexane = 1/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 2922, 2853, 2103, 1695, 1585, 1281, 763. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.00 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.25 (t, *J* = 6.4 Hz, 0.52H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 197.2 (d, *J* = 17.0 Hz), 136.3, 133.5, 128.7 (2C), 128.0 (2C), 46.1 (d, *J* = 4.3 Hz), 37.3 (t, *J* = 19.0 Hz). **HRMS (ESI):** *m/z* calcd for $C_9H_7N_3OD_2Na$ $(M+Na)^+$: 200.0769, Found: 200.0774.

General procedure-11: Synthesis of tricyclic triazoles

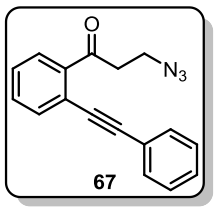
To a solution of **50h** (0.10 mmol, 1 equiv) in anhydrous toluene (1 mL) the reagents $Pd(PPh_3)_2Cl_2$ (0.005 mmol, 0.05 equiv), CuI (0.01 mmol, 0.1 equiv) and Et_3N (0.3 mmol, 3.0 equiv) were sequentially added and the mixture was stirred at rt under an argon atmosphere for 20 min. Acetylenic compound (0.15 mmol, 1.5 equiv) dissolved in anhydrous toluene (1 mL) was added dropwise under argon atmosphere. The reaction mixture was then heated at 80 °C until starting material disappeared as monitored by TLC. After completion of the reaction, the solvent was removed *in vacuo*, the residue was extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **66**.

1-Phenyl-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66a).



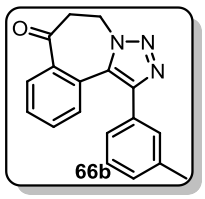
This compound was prepared by following the general procedure **11** and isolated as a pale yellow solid. mp = 133-135 °C. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2991, 1683, 1653, 1236, 1450, 1253, 760. **^{1}H-NMR (400 MHz, $(CD_3)_2SO$):** δ 7.88 (m, 1H), 7.59 (m, 2H), 7.51 (m, 2H), 7.41 (m, 3H), 7.27 (m, 1H), 4.80 (t, *J* = 6.0 Hz, 2H), 3.23 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.1, 146.4, 136.5, 133.0, 131.0, 130.4, 130.9, 130.0, 129.9, 128.7 (2C), 128.5, 128.0 (2C), 125.7, 44.9, 43.7. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}N_3O$ $(M+H)^+$: 276.1137; Found: 276.1124.

3-Azido-1-(2-(phenylethynyl)phenyl)propan-1-one (67).



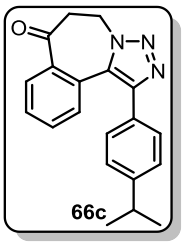
This compound was prepared by following the general procedure **11** and isolated as colourless viscous oil. R_f = 0.5 (EtOAc/Hexane = 1/4**). IR (thin film, neat):** ν_{max}/cm^{-1} 2930, 2230, 2105, 1693, 1445, 1370, 1205, 1139, 914. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.59 (m, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.43 (m, 4H), 3.77 (t, *J* = 6.8 Hz, 2H), 3.52 (t, *J* = 6.8 Hz, 2H).**^{13}C-NMR (100 MHz, $CDCl_3$):** δ 199.7, 139.8, 134.0, 131.6, 131.5 (2C), 128.9, 128.6, 128.5 (2C), 128.4, 122.6, 121.6, 95.3, 88.1, 46.4, 41.1. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}N_3O$ $(M+H)^+$: 276.1137; Found: 276.1124.

1-(*m*-Tolyl)-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66b).



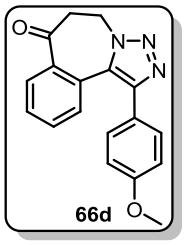
This compound was prepared by following the general procedure **11** and isolated as yellow solid. mp = 135-137 °C. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2956, 2929, 1684, 1598, 1371, 1279, 1239, 1012, 771. **^{1}H-NMR (400 MHz, $(CD_3)_2SO$):** δ 7.89 (m, 1H), 7.59 (m, 2H), 7.38 (s, 1H), 7.23 (m, 4H), 4.80 (t, *J* = 5.6 Hz, 2H), 3.23 (t, *J* = 5.6 Hz, 2H), 2.29 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.3, 146.5, 138.6, 136.5, 133.0, 130.97, 130.91, 130.3, 130.1, 129.9, 129.3, 128.69, 128.61, 125.8, 125.0, 44.9, 43.7, 21.4. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{16}N_3O$ $(M+H)^+$: 290.1293, Found: 290.1280.

1-(4-Isopropylphenyl)-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66c).



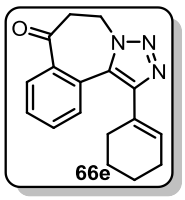
This compound was prepared by following the general procedure **11** and isolated as yellow solid. mp = 150-152 °C. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2959, 2925, 1679, 1596, 1446, 1368, 1239, 981. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.99 (m, 1H), 7.53 (m, 4H), 7.45 (m, 1H), 7.25 (m, 2H), 4.85 (t, *J* = 5.6 Hz, 2H), 3.29 (t, *J* = 5.6 Hz, 2H), 2.95 (m, 1H), 1.30 (s, 3H), 1.28 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.3, 149.4, 140.9, 136.5, 133.1, 132.0, 130.9, 130.1, 130.0, 129.8, 127.8 (2C), 126.8 (2C), 125.9, 44.9, 43.7, 33.9, 23.9 (2C). **HRMS (ESI):** *m/z* calcd for $C_{20}H_{20}N_3O$ $(M+H)^+$: 318.1606; Found: 318.1621.

1-(4-Methoxyphenyl)-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66d).



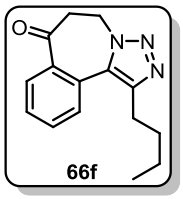
This compound was prepared by following the general procedure **11** and isolated as yellow solid. mp = 141-142 ^{o}C. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2930, 2857, 1680, 1446, 1279, 1139, 914. **^{1}H-NMR (400 MHz, $(CD_3)_2SO$):** δ 7.88 (m, 1H), 7.58 (m, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.28 (m, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.79 (t, *J* = 5.2 Hz, 2H), 3.78 (s, 3H), 3.22 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.3, 159.8, 146.3, 136.5, 133.0, 130.9, 130.3, 129.9, 129.8, 129.3 (2C), 126.0, 122.9, 114.2 (2C), 55.3, 44.9, 43.7. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{16}N_3O_2$ $(M+H)^+$: 306.1243; Found: 306.1228.

1-(Cyclohex-1-en-1-yl)-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66e).



This compound was prepared by following the general procedure **11** and isolated as viscous oil. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2930, 2859, 1681, 1595, 1445, 1340, 1279, 1139, 914. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.63 (m, 2H), 7.53 (m, 1H), 6.11 (s, 1H), 4.76 (t, *J* = 6.0 Hz, 2H), 3.21 (t, *J* = 6.0 Hz, 2H), 2.34 (m, 2H), 2.16 (m, 2H), 1.70 (m, 4H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.3, 143.4, 136.3, 132.9, 130.7, 129.8, 129.5 (2C), 128.24, 128.21, 126.4, 44.9, 43.6, 27.3, 25.5, 22.6, 21.9. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{18}N_3O$ $(M+H)^+$: 280.1450, Found: 280.1437.

1-Butyl-5*H*-benzo[*c*][1,2,3]triazolo[1,5-*a*]azepin-7(6*H*)-one (66f).

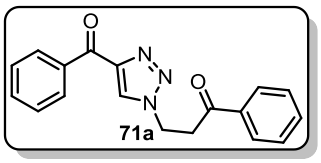


This compound was prepared by following the general procedure **11** and isolated as colourless viscous oil. R_f = 0.4 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2956, 2929, 1689, 1597, 1468, 1371, 1213, 771. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.2 Hz, 1H), 7.54 (m, 2H), 4.79 (t, *J* = 5.6 Hz, 2H), 3.19 (t, *J* = 5.6 Hz, 2H), 2.84 (t, *J* = 7.6 Hz, 2H), 1.78 (m, 2H), 1.47 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.2, 147.1, 136.4, 133.2, 131.2, 131.1, 129.4, 128.8, 126.1, 44.9, 43.5, 31.3, 25.4, 22.6, 13.8. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{18}N_3O$ $(M+H)^+$: 256.1450; Found: 256.1437.

General procedure-12: Synthesis 1,4-disubstituted-1,2,3-triazoles.

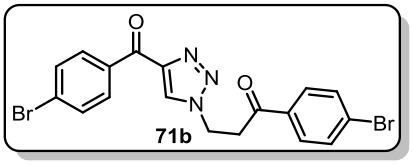
An oven-dried 5 mL glass vial was charged with azide **50** (0.2 mmol, 1.0 equiv), DMSO (1 mL) at room temperature. DABCO (0.04 mmol, 0.2 equiv) was then introduced at room temperature (rt) and continued stirring at 60 °C until starting material disappeared as monitored by TLC. The reaction mixture was quenched with aqueous ammonium chloride solution, diluted with ethyl acetate and the layers were separated. The aqueous layer further extracted with ethyl acetate. The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexane/ethyl acetate) to afford the respective product **71.**

3-(4-Benzoyl-1*H*-1,2,3-triazol-1-yl)-1-phenylpropan-1-one (71a).



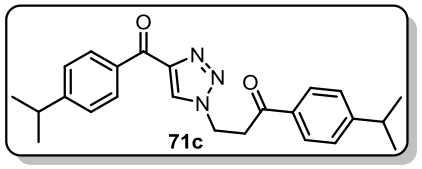
This compound was prepared by following the general procedure **12** and isolated as yellow solid. mp = 133-135 ^oC. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3098, 1657, 1651, 1691, 1411, 1354, 1051, 855. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.47 (s, 1H), 8.39 (m, 2H), 7.98 (m, 2H), 7.60 (m, 2H), 7.51 (m, 4H), 4.95 (t, *J* = 6.0 Hz, 2H), 3.75 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 196.1, 185.7, 136.6, 135.7, 134.0, 133.2, 130.5, 128.7 (2C), 129.8, 128.8 (2C), 128.3 (2C), 128.1 (2C), 45.1, 38.4. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{15}N_3O_2Na$ $(M+Na)^+$: 328.1062, Found: 328.1046.

3-(4-(4-Bromobenzoyl)-1*H*-1,2,3-triazol-1-yl)-1-(4-bromophenyl)propan-1-one (71b).



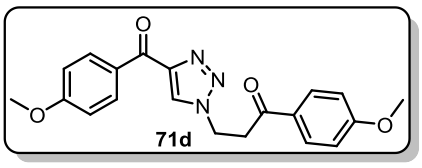
This compound was prepared by following the general procedure **12** and isolated as yellow solid. mp = 151-153 ^oC. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3100, 1660, 1650, 1410, 1352, 1051, 855. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.47 (s, 1H), 8.33 (m, 2H), 7.83 (m, 2H), 7.66 (m, 4H), 4.93 (t, *J* = 6.0 Hz, 2H), 3.72 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.0, 184.4, 147.6, 135.1, 134.4, 132.2 (2C), 132.1 (2C), 131.7 (2C), 129.9, 129.5 (2C), 129.4, 128.6, 45.0, 38.2. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{14}Br_2N_3O_2$ $(M+H)^+$: 461.9453, Found: 461.9435.

3-(4-(4-Isopropylbenzoyl)-1*H*-1,2,3-triazol-1-yl)-1-(4-isopropylphenyl)propan-1-one (71c).



This compound was prepared by following the general procedure **12** and isolated as yellow solid. mp = 140-142 ^{o}C. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3098, 1657, 1651, 1619, 1530, 1411, 1354, 1242, 1051, 856. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.43 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 4.94 (t, *J* = 6.0 Hz, 2H), 3.72 (t, *J* = 6.0 Hz, 2H), 3.00 (m, 2H), 131 (s, 3H), 1.29 (s, 6H), 1.27 (s, 3H).**^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.7, 185.4, 155.7, 154.7, 147.9, 134.4, 133.6, 130.7 (2C), 129.6, 128.3 (2C), 126.9 (2C), 126.5 (2C), 45.1, 38.3, 34.6, 34.3, 23.7 (2C), 23.6 (2C). **HRMS (ESI):** *m/z* calcd for $C_{24}H_{28}N_3O_2$ $(M+H)^+$: 390.2182, Found: 390.2164.

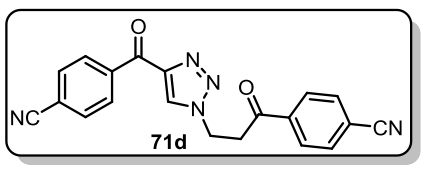
3-(4-(4-Methoxybenzoyl)-1*H*-1,2,3-triazol-1-yl)-1-(4-methoxyphenyl)propan-1-one (71d).



This compound was prepared by following the general procedure **12** and isolated as yellow solid. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 1674, 1640, 1597, 1369, 1253, 1119, 1044, 907. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.48 (d, *J* = 8.8 Hz, 2H), 8.42 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 9.2 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.92 (t, *J* = 6.4 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.68 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 194.5, 184.0, 164.1, 163.7, 148.1, 133.0 (2C), 130.4 (2C), 129.58, 129.54, 128.9, 114.0 (2C), 113.6 (2C), 55.6, 55.5, 45.2, 38.0. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{20}N_3O_4$ $(M+H)^+$: 366.1454, Found: 366.1438.

3-(4-(4-Methoxybenzoyl)-1*H*-1,2,3-triazol-1-yl)-1-(4-methoxyphenyl)propan-1-one (71e).

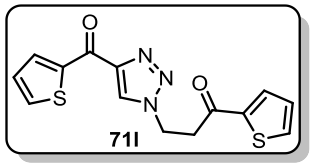
This compound was prepared by following the general procedure **12** and isolated as yellow solid.



mp = 157-160 ^{o}C. R_f = 0.3 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 1674, 1640, 1597, 1369, 1253, 1119, 1044, 907. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.55 (s, 1H), 8.53 (s, 2H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 4H), 4.97 (t, *J* = 5.6 Hz, 2H), 3.79 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 194.8, 183.9, 147.3, 139.5, 138.4, 133.1, 132.7 (2C), 132.1 (2C), 131.0, 130.9 (2C), 130.3, 128.5 (2C),

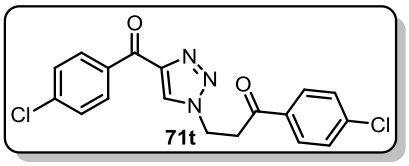
117.3, 116.4, 44.9, 38.4. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{14}N_5O_2$ $(M+H)^+$: 356.1147; Found, 356.1131.

1-(Thiophen-2-yl)-3-(4-(thiophene-2-carbonyl)-1*H*-1,2,3-triazol-1-yl)propan-1-one (71l).



This compound was prepared by following the general procedure **12** and isolated as yellow solid. mp = 146-149 ^oC. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3098, 1657, 1651, 1619, 1530, 1411, 1354, 1242, 1051, 856. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.70 (d, *J* = 2.8 Hz, 1H), 8.43 (s, 1H), 7.76 (d, *J* = 4.0 Hz, 2H), 7.71 (d, *J* = 4.8 Hz, 1H), 7.29 (t, *J* = 4.8 Hz, 1H), 7.16 (t, *J* = 4.0 Hz, 1H), 4.92 (t, *J* = 6.4 Hz, 2H), 3.68 (t, *J* = 6.4 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 188.7, 177.1, 147.4, 142.7, 142.3, 136.1, 135.0, 134.8, 132.7, 129.1, 128.43, 128.41, 45.0, 38.8. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{11}S_2N_3O_2Na$ $(M+Na)^+$: 340.0190, Found: 340.0184.

3-(4-(4-Chlorobenzoyl)-1*H*-1,2,3-triazol-1-yl)-1-(4-chlorophenyl)propan-1-one (71t).

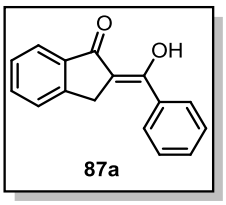


This compound was prepared by following the general procedure **12** and isolated as yellow solid. R_f = 0.5 (EtOAc/Hexane = 1/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2990, 1672, 1643, 1595, 1361, 1254, 1119, 1041, 907. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.48 (s, 1H), 8.42 (m, 2H), 7.92 (m, 2H), 7.49 (m, 4H), 4.94 (t, *J* = 6.0 Hz, 2H), 3.73 (t, *J* = 6.0 Hz, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 194.8, 184.2, 147.7, 140.6, 139.8, 134.7, 134.0, 132.0 (2C), 129.9, 129.4 (2C), 129.2 (2C), 128.7 (2C), 45.0, 38.2. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{14}Cl_2N_3O_2$ $(M+H)^+$: 374.0463; Found: 374.0446.

General procedure-13: Intramolecular MBH reaction

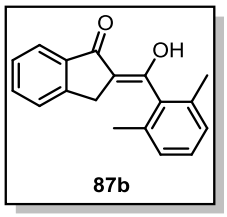
An oven dried 5 mL glass vial was charged with **86** (30 mg, 0.15 mmol). Toluene (1 mL) and PBu_3 (1 M solution in toluene, 0.1 mL, 0.015 mmol) were introduced at room temperature (rt) under nitrogen atmosphere and stirring continued at rt until **86** disappeared as monitored by TLC. All the volatiles were removed under reduced pressure. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **87**.

(Z)-2-(Hydroxy(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (87a).



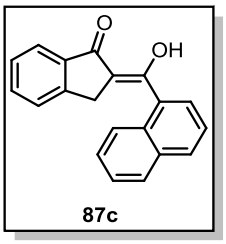
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3061, 2833, 1650, 1603, 1570, 1487, 1103. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 15.1 (s, 1H), 7.97 (m, 2H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.54 (m, 5H), 7.47 (t, *J* = 7.2 Hz, 1H), 3.97 (s, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 195.9, 177.1, 148.6, 137.9, 134.8, 128.6 (2C), 128.1 (2C), 127.4, 125.6, 123.4, 109.4, 69.3. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{13}O_2$ $(M+H)^+$ 237.0916, found 237.0914.

(Z)-2-((2,6-Dimethylphenyl)(hydroxy)methylene)-2,3-dihydro-1*H*-inden-1-one (87b).



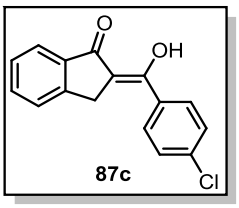
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3061, 3834, 1652, 1579, 1376, 1276, 770. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.46 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 3.33 (s, 2H), 2.34 (s, 6H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 194.8, 173.4, 148.7, 138.5, 135.0, 134.1, 133.4, 129.3, 127.5 (2C), 127.4 (2C), 125.9, 123.5, 111.9, 34.2 (2C). **HRMS (ESI):** *m/z* calcd for $C_{18}H_{17}O_2$ $(M+H)^+$ 265.1229, found 265.1221.

(Z)-2-(Hydroxy(naphthalen-1-yl)methylene)-2,3-dihydro-1*H*-inden-1-one (87c).



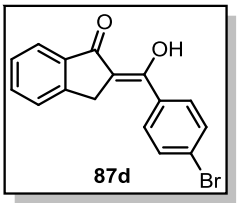
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3100, 2866, 1648, 1578, 1378, 1279, 1142, 1102, 669. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 14.85 (s, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 3.6 Hz, 1H), 7.66 (d, *J* = 4.8 Hz, 1H),7.55 (m, 4H) 7.59 (m, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.22 (t, *J* = 4.0 Hz, 1H), 3.87 (s, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 194.6, 173.65, 148.88, 138.25, 133.7, 133.4, 132.5, 130.7, 130.0, 128.5, 127.4, 127.0, 126.6, 126.4, 125.8, 125.5, 124.9, 123.5, 112.3, 31.0. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{15}O_2$ $(M+H)^+$ 287.1072, found 287.1076.

(Z)-2-((4-Chlorophenyl)(hydroxy)methylene)-2,3-dihydro-1*H*-inden-1-one (87d).



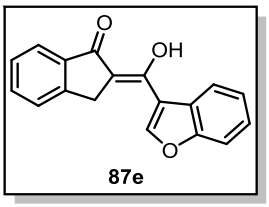
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** vmax/cm^{-1} 3080, 2835, 1658, 1570, 1370, 1140, 778. **^{1}H-NMR (400 MHz, CDCl$_3$):** δ 15.06 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 3H), 7.60 (m, 1H), 7.55 (m, 1H), 7.50 (m, 3H), 3.94 (s, 2H). **^{13}C-NMR (100 MHz, CDCl$_3$):** δ 195.9, 169.3, 148.4, 137.7, 137.4, 133.5, 129.4 (2C), 128.3 (2C), 127.6, 126.3, 125.6, 123.5, 109.5, 32.2. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{12}O_2Cl$ $(M+H)^+$ 271.0526, found 271.0531.

(Z)-2-((4-Bromophenyl)(hydroxy)methylene)-2,3-dihydro-1*H*-inden-1-one (87e).



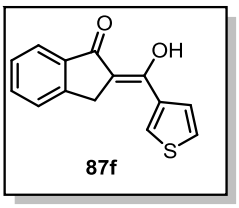
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** vmax/cm^{-1} 3066, 2900, 1660, 1590, 1278, 1232, 1026, 778. **^{1}H-NMR (400 MHz, CDCl$_3$):** δ 15.06 (s, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.8 Hz, 2H), 7.61 (m, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 3.93 (s, 2H). **^{13}C-NMR (100 MHz, CDCl$_3$):** δ 196.0, 169.3, 148.4, 137.7, 133.6, 133.6, 131.9 (2C), 126.9 (2C), 127.6, 126.0, 125.6, 123.5, 109.5, 32.1. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{12}O_2Br$ $(M+H)^+$ 315.0021, found 315.0017.

(Z)-2-(Benzofuran-3-yl(hydroxy)methylene)-2,3-dihydro-1*H*-inden-1-one (87e).



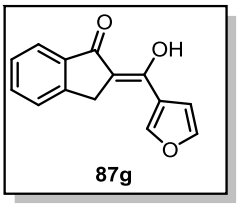
This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3100, 2900, 1665, 1603, 1560, 12765, 1235, 1124, 1026.**^{1}H-NMR (400 MHz, CDCl$_3$):** δ 14.32 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.63 (m, 3H), 7.54 (s, 1H), 7.46 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 4.13 (s, 2H). **^{13}C-NMR (100 MHz, CDCl$_3$):** δ 196.2, 159.7, 156.0, 150.6, 149.4, 138.0, 133.6, 127.5, 127.4, 126.9, 125.8, 123.8, 123.4, 122.5, 111.8, 111.5, 109.5, 31.5. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{13}O_3$ $(M+H)^+$ 277.0865, found 277.0860.

(Z)-2-(Hydroxy(thiophen-3-yl)methylene)-2,3-dihydro-1*H*-inden-1-one (87f).



This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3100, 2910, 1665, 1578, 1425, 1328, 1269, 1190, 998. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 14.85 (s, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 4.0 Hz, 1H), 7.83 (m, 1H), 7.68 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.58 (m, 2H), 7.45 (m, 1H), 3.93 (s, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ, 194.1, 166.0, 14.8, 138.6, 138.0, 133.2, 131.6, 130.7, 128.3, 127.5, 125.6, 123.1, 108.5, 32.1. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{11}O_2S$ $(M + H)^+$ 243.0480, found 243.0486.

(Z)-2-(Furan-3-yl(hydroxy)methylene)-2,3-dihydro-1*H*-inden-1-one (87g).



This compound was prepared by following the general procedure **13** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3089, 2905, 1661, 1579, 1455, 1396, 1260, 1190, 998. **^{1}H -NMR (400 MHz, $CDCl_3$)** δ 14.25 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.67 (s, 1H), 7.53 (m, 2H), 7.40 (t, *J* = 3.60 Hz, 1H), 7.17 (d, *J* = 3.60 Hz, 1H), 6.60 (m, 2H), 3.90 (s, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 194.5, 161.2, 149.5, 148.8, 146.1, 138.0, 133.1, 127.2, 125.6, 123.0, 115.8, 112.4, 107.9, 31.5. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{11}O$ $(M+H)^+$ 227.0708, found 227.0700.

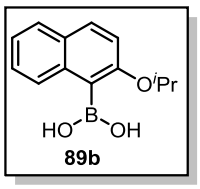
General procedure-14: Synthesis of triflate

A solution of **87a** (2.50 mmol, 1equiv) and triethylamine (3.75 mmol, 1.5 equiv) in dry dichloromethane (12 mL) under argon was cooled to 0 °C and triflic anhydride (3.75 mmol, 1.5 equiv) was then added dropwise at the same temperature. After 30 min stirring, the solution was carefully poured onto a saturated aqueous solution of $NaHCO_3$ The organic layer was separated and the aqueous one extracted with dichloromethane (3×20 mL). The combined organic layers were washed with brine (20 mL) then water (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford orange oil. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **88.**

General procedure-15: Synthesis of boronic acids

To a solution of 1-bromonaphthalene derivative (4.2 mmol, 1.0 equiv) in anhydrous THF (5 mL) at -78 °C was added dropwise, *n*-BuLi (4.6 mmol, 1.2 equiv). The reaction solution was stirred for 45 min at -78 °C, then trimethyl borate (5.06 mmol, 1.5 equiv) was added dropwise and the mixture allowed warming to rt over a 6 h period. Aqueous 10% HCl (40 mL) was added and the mixture stirred at rt for another 30 min. After the solvent was evaporated, the slurry was diluted with ethyl acetate (100 mL), washed with saturated aqueous NH_4Cl, brine and dried over $MgSO_4$ and filtered. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **89.**

(2-Isopropoxynaphthalen-1-yl)boronic acid (89b).

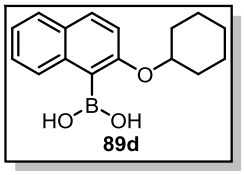


89b

This compound was prepared by following the general procedure **15** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3205, 2978, 1598, 1378, 1188, 1105, 947, 886. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.45 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.42 (m, 3H), 4.68 (m, 1H), 1.30 (s, 3H), 1.30 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 157.7, 146.1, 135.1, 130.1, 129.0, 129.1, 128.1, 127.6, 125.6, 117.3, 71.3, 22.7 (2C). **HRMS (ESI):** *m/z* calcd for $C_{13}H_{15}O_3BNa$ $(M+Na)^+$ 253.1012, found 253.0813.

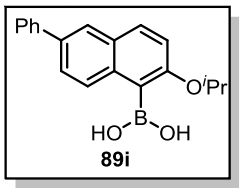
(2-(Cyclohexyloxy)naphthalen-1-yl)boronic acid (89d).

This compound was prepared by following the general procedure **15** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3215, 2990, 1578, 1368, 1190, 1155, 988, 889. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.45 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.42 (m, 3H), 4.32 (m, 1H) 1.85 (m, 1H), 1.41 (m, 3H), 1.19 (m, 2H), 1.07 (m, 2H), 0.89 (m, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 157.1, 145.9, 136.1, 130.1, 129.6, 129.1, 128.5, 127.4, 125.8, 117.1, 75.8, 33.6, 32.1, 31.5, 25.5, 23.4. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{19}O_3BNa$ $(M+Na)^+$ 293.1325, found 293.1336.



89d

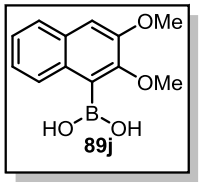
(2-Isopropoxy-6-phenylnaphthalen-1-yl)boronic acid (89i).



89i

This compound was prepared by following the general procedure **15** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3210, 2970, 1460, 1387, 1333, 1110, 957. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.27 (s, 2H), 8.15 (s, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.78 (m, 4H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.36 (m, 2H), 6.59 (s, 1H), 4.67 (m, 1H), 1.31 (s, 3H), 1.29 (s, 1H), 1.30 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 157.9, 146.5, 135.6, 135.1, 130.1, 129.4, 129.10 (2C), 128.6 (2C), 127.6, 127.0, 125.2, 117.5, 71.6, 22.9 (2C). **HRMS (ESI):** *m/z* calcd for $C_{19}H_{19}O_3BNa$ $(M+Na)^+$ 297.1274, found 297.1280.

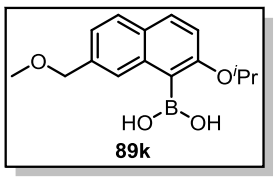
(2,3-Dimethoxynaphthalen-1-yl)boronic acid (89j).



89j

This compound was prepared by following the general procedure **15** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3301, 2990, 1468, 1353, 1348, 1115, 973. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.41 (s, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.32 (m, 3H), 3.92 (s, 3H), 3.89 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 151.9, 146.6, 131.5, 129.5, 126.7, 126.7, 125.8, 125.0, 116.6, 107.6, 69.3, 64.3. **HRMS (ESI):** *m/z* calcd for $C_{12}H_{13}O_4BNa$ $(M + Na)^+$ 255.0805, found 255.0813.

Dihydroxy(2-isopropoxy-7-(methoxymethyl)naphthalen-1-yl)-l3-bromane (89k).



89k

This compound was prepared by following the general procedure **15** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3204, 2975, 1447, 1373, 1332, 1102, 949. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.25 (d, *J* = 8.8 Hz, 1H), 7.75 (m, 2H), 7.55 (d, *J* = 8.8, 1.2 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 4.69 (m, 1H), 4.63 (s, 2H), 3.45 (s, 3H), 1.46 (s, 3H), 1.44 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 152.6, 134.4, 132.9, 129.9, 128.6, 127.6, 127.4, 126.4, 117.9, 111.4, 74.3, 73.4, 58.1, 22.4 (2C). **HRMS (ESI)** *m/z* calcd for $C_{15}H_{19}O_4BNa$ $(M+Na)^+$ 297.1274, found 297.1280.

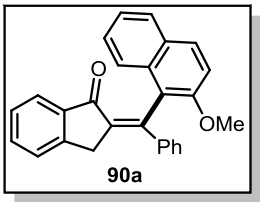
General procedure 16: Suzuki-Miyaura cross-coupling reaction

Indenone triflate **88** (20 mg, 1.0 equiv), $Pd_2(dba)_3$ (2.3 mg, 0.1 equiv), Boronic acid **89** (19 mg, 1.0 equiv), and K_2CO_3 (24.0 mg, 3.0 equiv) were placed in a flame dried sealed tube under a N_2 atmosphere, then degassed 1.0 mL THF/water (9:1) was added. The sealed tube was stirred at 70 ^oC for 5 h. After cooling to room temperature, the reaction was quenched with saturated NH_4Cl and was extracted three times with 3 mL of EtOAc and the combined organic layer was washed with brine and dried over Na_2SO_4. Volatiles were removed under reduced pressure. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **90**.

General procedure 17: Atropselective Suzuki-Miyaura cross-coupling reaction

Indenone triflate **88** (20 mg, 1.0 equiv), $Pd_2(dba)_3$ (2.3 mg, 0.1 equiv), ligand (3.2 mg, 0.15 equiv), Boronic acid **89** (19 mg, 1.0 equiv), and K_2CO_3 (24.0 mg, 3 equiv) were placed in a flame dried sealed tube under a N_2 atmosphere, then degassed 1.0 mL THF/water (9:1) was added. The sealed tube was stirred at 70 ^oC for 5 h. After cooling to room temperature, the reaction was quenched with saturated NH_4Cl and was extracted three times with 3 mL of EtOAc and the combined organic layer was washed with brine and dried over Na_2SO_4. Volatiles were removed under reduced pressure. The crude product was purified by silica gel flash chromatography using hexane/ethyl acetate as eluent, to afford **90**.

(Z)-2-((2-Methoxynaphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90a).

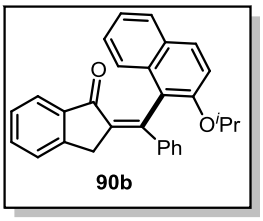


90a

This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3056, 1693, 1602, 1462, 1419, 1393, 1250, 1116, 1101, 976. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 9.20 Hz, 1H), 7.83 (m, 1H), 7.74 (m, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.52 (m, 4H), 7.35 (m, 7H), 4.16 (d, *J* = 4.0 Hz, 1H), 3.81 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.4, 152.9, 149.1, 144.5, 140.9, 139.3, 135.2, 134.0, 132.5, 129.6, 129.2 (2C), 128.8 (2C), 128.26, 128.22 (2C), 127.3, 126.6, 125.9, 124.4, 124.2, 123.9, 123.4, 113.8, 56.6, 33.3. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{20}ONa$ $(M+Na)^+$ 399.1361, found 399.1358.

(Z)-2-((2-Isopropoxynaphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90b).

This compound was prepared by following the general procedure **17** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** νmax/cm^{-1} 3057, 1690, 1596, 1443, 1410, 1303, 1235, 1115, 1095, 987. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.86 (d, *J* = 9.2 Hz, 1H), 7.83 (m, 1H), 7.75 (m, 1H), 7.66 (d, *J* =7.6 Hz, 1H), 7.56 (t, *J* = 6.8 Hz, 1H), 7.50 (m, 3H), 7.33 (m, 7H), 4.61 (m, 1H), 4.29 (d, *J* = 20.8 Hz, 1H), 4.03 (d, *J* = 20.8, 1H), 1.20 (d, *J* = 6.0 Hz, 3H), 0.90 (d, *J* = 6.0 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.3, 151.4, 149.1, 145.0, 141.5, 139.4, 135.0, 133.9, 132.9, 129.0 (2C), 129.03, 129.00, 128.9, 128.2, 128.07, 128.0 (2C), 127.2, 126.5, 125.8, 124.2, 123.8, 123.4, 116.1, 70.7, 33.5, 22.5, 21.6. **HRMS (ESI):** *m/z* calcd for $C_{29}H_{24}O_2Na$ $(M + Na)^+$ 404.1776, found 404.1780.

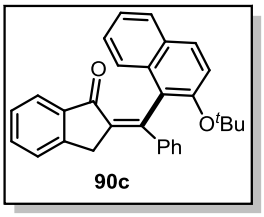


90b

Optical rotation: $[\alpha]^{22}_{D}$ +105.6 (*c* 0.10, $CHCl_3$) for a sample with *ee* 80%. The enantiomeric excess was determined by HPLC analysis using Daicel Chiralcel IB Column (90:10 *n*- Hexane/2-Propanol, 1.0 mL/min, 254 nm, τ_{major} = 15.5 min, τ_{minor} = 9.8 min).

(Z)-2-((2-(Tert-butyl)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90c).

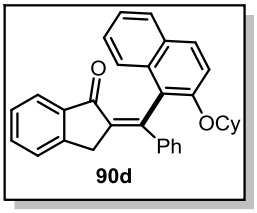
This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3062, 1699, 1609, 1460, 1409, 1360, 1245, 1115, 1080, 970. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.84 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 6.8 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.47 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.39 (d, *J* = 9.2 Hz, 1H), 7.33 (m, 6H), 4.33 (d, *J* = 20.8 Hz, 1H), 4.00 (d, *J* = 20.8 Hz, 1H), 1.29 (s, 9H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.1, 150.8, 149.0, 145.6, 141.3, 139.4, 135.0, 133.9, 133.0, 129.6, 129.4, 129.1 (2C), 128.26, 128.2, 128.1, 128.0 (2C), 127.3, 126.4, 125.8, 124.3, 124.2, 123.8, 122.0, 79.6, 33.6, 29.7 (3C). **HRMS (ESI):** *m/z* calcd for $C_{30}H_{26}ONa$ $(M+Na)^+$ 425.1881, found 425.1889.



90c

(Z)-2-((2-(Cyclohexyloxy)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90d).

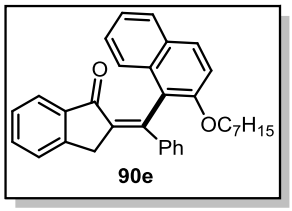
This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3000, 1689, 1598, 1441, 1390, 1320, 1290, 1110, 1015, 978. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.894 (d, *J* = 8.8 Hz, 1H), 7.81 (m, 1H), 7.73 (m, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.58 (m, 1H), 7.50 (m, 3H), 7.32 (m, 7H), 4.32 (m, 1H), 4.25 (d, *J* = 20.4 Hz, 1H), 4.06 (d, *J* = 20.4 Hz, 1H), 1.85 (m, 1H), 1.41 (m, 3H), 1.19 (m, 2H), 1.07 (m, 2H), 0.89 (m, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 192.3, 151.3, 149.1, 145.0, 141.4, 139.4, 135.1, 133.9, 133.0, 130.5, 131.6, 13.9 (2C), 129.9, 129.31 (2C), 129.2, 128.9 (2C), 128.91, 125.8, 125.3, 124.2, 123.8, 123.2, 115.8, 75.8, 32.1, 31.5, 25.5, 23.4, 23.4. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{29}O_2Na$ $(M + H)^+$ 445.2168, found 445.2173.



90d

(Z)-2-((2-(Cyclohexyloxy)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90e).

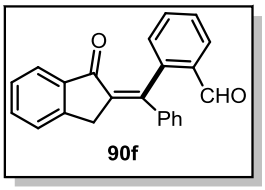
This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3089, 1696, 1601, 1541, 1490, 1320, 1290, 1105, 988, 878. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.89 (d, *J* = 8.8 Hz, 1H), 7.83 (m, 1H), 7.74 (m, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.61 (m, 2H) 7.54 (m, 4H), 7.33 (m, 5H), 4.41 (d, *J* = 3.2 Hz, 1H), 4.16 (d, *J* = 3.2 Hz, 1H), 4.01 (m, 1H), 1.54 (m, 2H), 1.15 (m, 7H), 1.03 (m, 2H), 0.81 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.4, 152.5, 149.0, 144.8, 141.2, 139.4, 135.1, 133.9, 132.7, 129.1, 129.3, 128.9 (2C), 128.42, 128.2, 128.1, 128.14 (2C), 127.3, 126.5, 125.8, 124.5, 124.2, 123.9, 123.3, 114.7, 69.1, 33.6, 29.5, 28.9, 25.9, 25.5, 14.0. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{32}O_2$ $(M+H)^+$ 460.2402, found 460.2413.



90e

(Z)-2-((2-(Tert-butyl)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90f).

This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 2960, 1691, 1670, 1571,

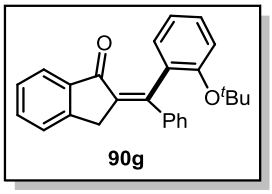


90f

1430, 1319, 1120, 1280, 1041, 846, 789. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 10.1 (s, 1H), 8.01 (dd, *J* =7.6 and 1.2 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.67 (td, *J* = 14.8, 7.6, 0.6, 1H), 7.59 (m, 2H), 7.49 (dt, *J* = 7.6 , 0.6 Hz, 1H), 7.39 (m, 6H), 7.32 (dd, *J* =7.6 and 0.8 HZ, 1H), 4.15 (d, *J* =18.0 Hz, 1H), 3.97 (d, *J* = 18.0 Hz, 1H). **^{13}C-HNMR (100 MHz, $CDCl_3$):** δ 192.8, 191.3, 149.0, 146.3, 143.6, 140.2, 139.0, 134.8, 134.5, 133.8, 133.7, 129.77, 129.74, 129.0 (2C), 128.8, 128.5 (2C), 128.1, 127.5, 125.9, 124.3, 33.5. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{17}O_2$ $(M+Na)^+$ 325.1229, found 325.1233.

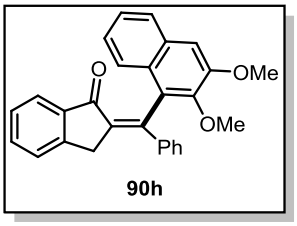
(Z)-2-((2-(Tert-butyl)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90g).

This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3090, 1691, 1589, 1481, 1390, 1320, 1270, 1065, 889, 898. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 11.6 Hz, 1H), 7.65 (m, 1H), 7.57 (dt, *J* =14.8, 7.6 and 1.2 Hz, 1H), 7.45 (m, 2H), 7.37 (m, 5H), 7.24 (d, *J* =7.6 , 1.6 Hz,1H), 7.1 (m, 2H), 4.17 (d, *J* = 20.0, 1H), 3.74 (d, *J* = 20.0 Hz, 1H), 1.29 (s, 9H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.8, 153.6, 149.0, 143.3, 141.6, 139.8, 136.3, 135.6, 133.9, 133.4, 131.0, 129.1 (2C), 128.9, 128.6, 128.4, 128.1, 127.9 (2C), 127.3, 125.7, 124.2, 121.7, 79.3, 33.8, 29.0. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{25}O$ $(M + Na)^+$ 353.1905, found 353.1909.



90g

(Z)-2-((2-Methoxynaphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90h).

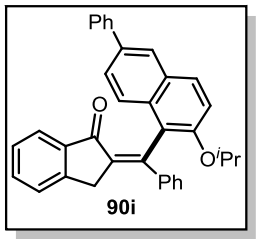


90h

This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3060, 1691, 1590, 1425, 1320, 1169, 1278, 1065, 889, 778. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.88 (d, *J* = 9.20 Hz, 1H), 7.82 (m, 1H), 7.70 (m, 1H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.50 (m, 3H), 7.31 (m, 5H), 3.98 (d, *J* = 4.0 Hz, 1H), 4.15 (d, *J* =18.0 Hz, 1H), 3.97 (d, *J* = 18.0 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.4, 152.9, 149.1, 144.5, 140.9, 139.3, 135.2, 134.0, 133.2, 132.5, 129.2 (2C), 128.8 (2C),

128.26, 128.22 (2C), 127.3, 126.6, 125.9, 124.4, 124.2, 123.9, 123.4, 113.8, 58.9, 56.6, 33.3. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{23}O_3$ $(M+H)^+$ 407.1647, found 407.1660.

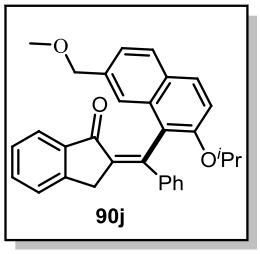
(Z)-2-((2-Methoxynaphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90i).



This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3015, 1685, 1549, 1489, 1306, 1145, 1268, 1036, 828, 769. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.93 (d, *J* = 8.8 Hz, 1H), 7.82 (m, 1H), 7.70 (m, 2H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.58 (m, 4H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.50 (m, 3H), 7.31 (m, 6H), 4.10 (d, *J* =18.0 Hz, 1H), 3.97 (d, *J* = 18.0 Hz, 1H), 3.98 (d, *J* = 4.0 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.1, 152.7, 148.9, 144.4, 140.1, 139.1, 137.6, 136.1, 135.1, 134.3, 133.2, 132.1, 129.1 (2C), 128.9, 128.7 (2C), 128.9 (2C), 128.1 (2C), 128.21, 128.20 (2C), 126.9, 126.1, 125.5, 124.3, 124.0, 123.8, 123.1, 113.5, 58.0, 56.0, 33.9. **HRMS (ESI):** *m/z* calcd for $C_{35}H_{29}O_2$ $(M+H)^+$ 481.2168, found 481.2170.

(Z)-2-((2-Isopropoxy-7-(methoxymethyl)naphthalen-1-yl)(phenyl)methylene)-2,3-dihydro-1*H*-inden-1-one (90j).

This compound was prepared by following the general procedure **16** and isolated as colorless liquid. R_f = 0.4 (EtOAc/ Hexane = 3/7). **IR (thin film, neat):** ν_{max}/cm^{-1} 3009, 1688, 1569, 1436, 1356, 1135, 1268, 1026, 859, 789. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.90 (d, *J* = 8.8 Hz, 1H), 7.79 (m, 1H), 7.67 (m, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.55 (m, 4H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.43 (m, 3H), 7.28 (m, 2H), 4.42 (s, 2H), 4.00 (d, *J* =18.0 Hz, 1H), 3.98 (d, *J* = 18.0 Hz, 1H), 3.88 (d, J = 4.0 Hz, 1H), 3.76 (s, 3H), 3.80 (s, 3H), 3.30 (s, 3H). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 192.8, 153.1, 149.6, 144.9, 141.3, 139.9, 135.8, 134.6, 132.9, 129.5, 129.3, 129.0, 128.8, 128.5, 128.4, 128.3, 128.26, 128.22, 127.8, 127.9, 126.9, 126.1, 125.3, 124.8, 124.1, 123.9, 113.9, 70.9, 58.7, 56.6, 33.9. **HRMS (ESI):** m/z calcd for $C_{21}H_{29}O_3$ $(M+H)^+$ 449.2117, found 449.2120.



Crystal structure of furotropone 9j (CCDC 1046548): A single crystal of **9j** suitable for X-ray diffraction was obtained by slow evaporation of its solution in ethanol and cyclohexane. The compounds **9j** was crystallized in the monoclinic centrosymmetric $P2_1/c$ space group with 4 molecules in the unit cell (Z = 4). In the crystal lattice of **9j**, one dimensional chain of molecules was observed along the *a*-axis (Figure 5c). The ORTEP (drawn at 50% probability level) of the compound **9j** is shown in Figure 5a. The compound display significant twisted structure. The torsion angle between the tropone unit and furan unit is about 178° (C_6-C_{22}-C_{21}-C_{20}), which is an indication of the approximately planar structure of the furotropone core.

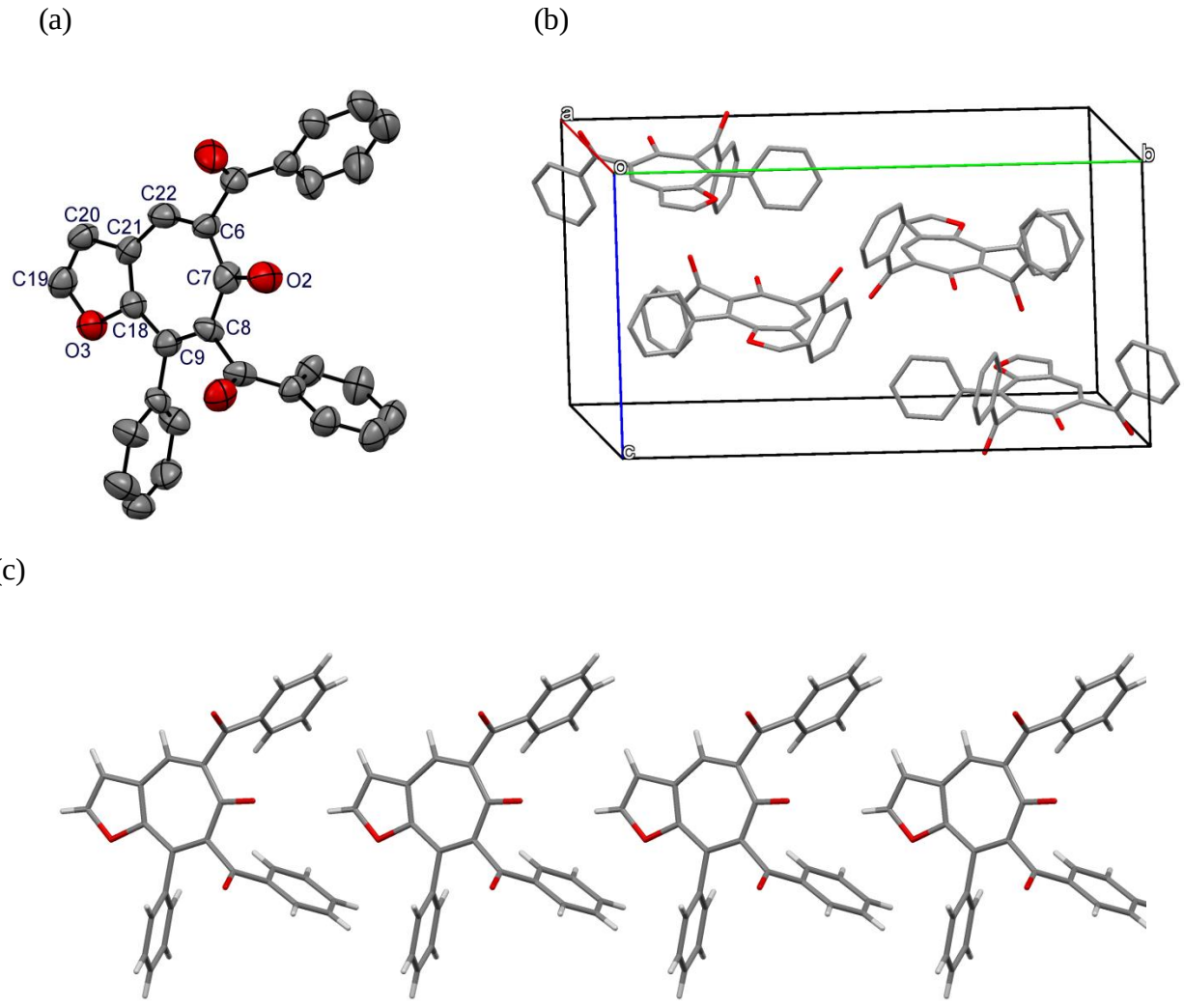


Figure 24. (a) ORTEP of the structure of **9j (**Hydrogen atom are omitted for clarity); (b) Tetramer of molecule in the unit cell, (c) One dimensional packing of **9j** molecules along *a* direction.

Table 22: Crystal data and structure refinement for **9j**

Empirical formula	$C_{29}O_4H_{18}$
Formula weight	280.43
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.63(3)
b/Å	9.940(11)
c/Å	17.23(4)
α/°	90
β/°	108.27(9)
γ/°	90
Volume/Å^3	2217(7)
Z	4
ρ_{calc}g/cm^3	0.840
μ/mm^{-1}	0.061
F(000)	561.0
Radiation	MoKα (λ = 0.71075)
2Θ range for data collection/°	6.15 to 39.67
Index ranges	$-12 \leq h \leq 12$, $-9 \leq k \leq 9$, $-16 \leq l \leq 16$
Reflections collected	10735
Independent reflections	1973 [R_{int} = 0.1736, R_{sigma} = 0.0959]
Data/restraints/parameters	1973/0/97
Goodness-of-fit on F^2	1.705
Final R indexes [I>=2σ (I)]	R_1 = 0.2728, wR_2 = 0.5551
Final R indexes [all data]	R_1 = 0.3435, wR_2 = 0.6158
Largest diff. peak/hole / e Å^{-3}	0.67/-0.39

Crystal structure of furotropone 29o (CCDC 1454583**):** Structure of the dihydrobenzofuranone **29o** was confirmed by single crystal X-ray diffraction analysis.

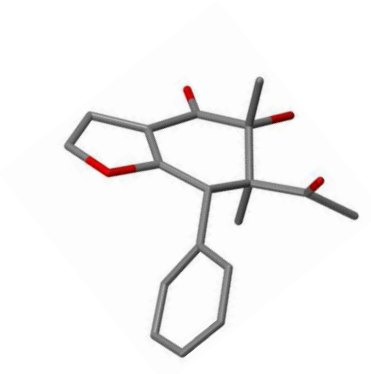


Fig. 25: ORTEP diagram of **29o** with 50% ellipsoidal probability.

Table 23: Crystal data and structure refinement for **29o**

Empirical formula	$C_{18}O_4H_{18}$
Formula weight	280.43
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.63(3)
b/Å	9.940(11)
c/Å	17.23(4)
α/°	90
β/°	108.27(9)
γ/°	90
Volume/Å^3	2217(7)
Z	4
ρ_{calc}g/cm^3	0.840
μ/mm^{-1}	0.061
F(000)	561.0
Radiation	MoKα (λ = 0.71075)
2Θ range for data collection/°	6.15 to 39.67
Index ranges	$-12 \leq h \leq 12$, $-9 \leq k \leq 9$, $-16 \leq l \leq 16$
Reflections collected	10735
Independent reflections	1973 [R_{int} = 0.1736, R_{sigma} = 0.0959]
Data/restraints/parameters	1973/0/97
Goodness-of-fit on F^2	1.705
Final R indexes [I>=2σ (I)]	R_1 = 0.2728, wR_2 = 0.5551
Final R indexes [all data]	R_1 = 0.3435, wR_2 = 0.6158
Largest diff. peak/hole / e Å^{-3}	0.67/-0.39

Crystal structure of 66a (CCDC 1548395): Structure of the tricyclic triazole **66a** was confirmed by single crystal X-ray diffraction analysis.

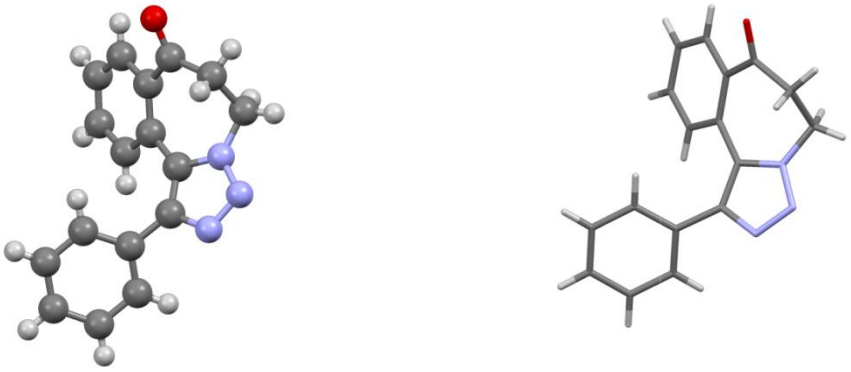


Fig. 26: ORTEP diagram of **66a** with 50% ellipsoidal probability.

Table 24: Crystal data and structure refinement for 66a.

Empirical formula	**$C_{17}H_{13}N_3O$**
Formula weight	275.30
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	7.8532(17)
b/Å	8.5948(2)
c/Å	11.0694(18)
α/°	69.43(4)
β/°	89.34(4)
γ/°	77.22(3)
Volume/Å^3	680.4(3)
Z	2
ρ_{calc}g/cm^3	1.344
μ/mm^{-1}	0.087
F(000)	288.0
Crystal size/mm^3	0.3 × 0.24 × 0.24
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.398 to 50.054
Index ranges	$-9 \leq h \leq 8$, $-6 \leq k \leq 10$, $-9 \leq l \leq 13$
Reflections collected	2291
Independent reflections	2012 [R_{int} = 0.0359, R_{sigma} = 0.0218]
Data/restraints/parameters	2012/0/190

Goodness-of-fit on F^2	1.253
Final R indexes [I>=2σ (I)]	R_1 = 0.0535, wR_2 = 0.1495
Final R indexes [all data]	R_1 = 0.0689, wR_2 = 0.1831
Largest diff. peak/hole / e $Å^{-3}$	0.19/-0.22

Crystal structure of coupling product 90c (CCDC 1454583**):** Structure of the dihydrobenzofuranone **90c** was confirmed by single crystal X-ray diffraction analysis.

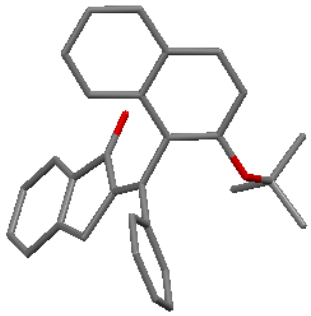


Fig. 27: ORTEP diagram of **90c** with 50% ellipsoidal probability.

Table 25: Crystal data and structure refinement for **90c**

Empirical formula	$C_{30}H_{26}O_2$
Formula weight	837.01
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	12.239(5)
b/Å	12.334(5)
c/Å	16.152(7)
α/°	78.511(10)
β/°	73.425(10)
γ/°	89.573(10)
Volume/$Å^3$	2286.8(16)
Z	2
ρ_{calc}g/cm^3	1.216
μ/mm^{-1}	0.075
F(000)	888.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.688 to 50.954
Index ranges	$-14 \leq h \leq 14$, $-14 \leq k \leq 14$, $-19 \leq l \leq 19$
Reflections collected	32270
Independent reflections	8241 [R_{int} = 0.0453, R_{sigma} = 0.0459]

Data/restraints/parameters	8241/0/583
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0559, wR_2 = 0.1442
Final R indexes [all data]	R_1 = 0.0984, wR_2 = 0.1727
Largest diff. peak/hole / e $Å^{-3}$	0.55/-0.31

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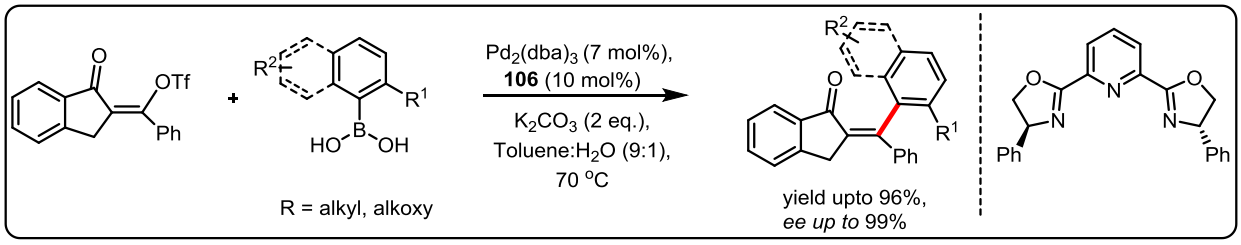
LIST OF PUBLICATIONS

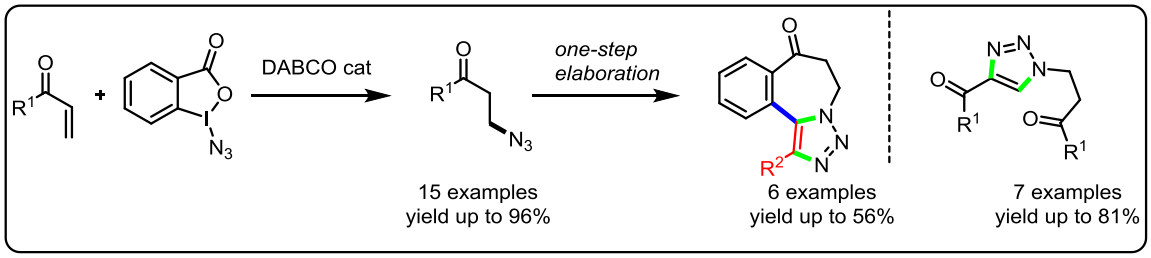
(1) *"Synthesis of axially chiral styrenes via Suzuki-Miyaura cross coupling reaction"*

Shirke, R. P.; Kumar, P.; Ramasastry, S. S. V. '**Manuscript under preparation**'



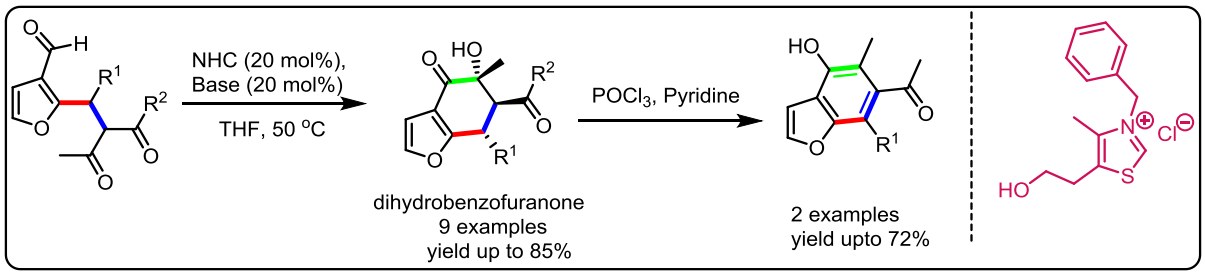
(2) *"Organocatalytic β-azidation of enones initiated by an electron-donor-acceptor complex"*

Shirke, R. P.; Ramasastry, S. S. V. *Org. Lett.* **2017**, 19, 5482.



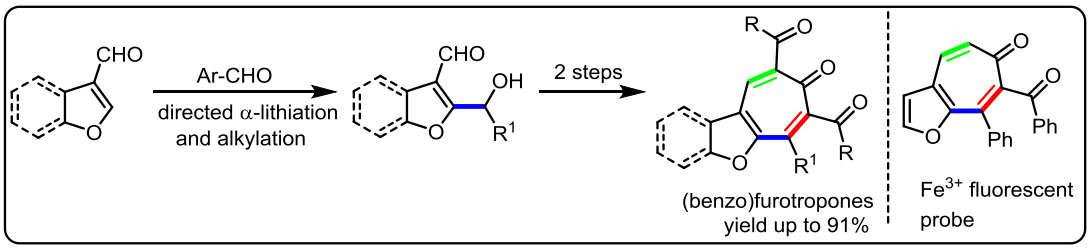
(3) *"Synthesis of benzofurans from furans via intramolecular cross benzoin reactions catalyzed by N-heterocyclic carbenes"*

Shirke, R. P*.; Reddy, V.*; Anand, R. V.; Ramasastry, S. S. V. *Synthesis* **2016**, *48*, 1865. (Authors contributed equally) [Invited for the special issue 'Cyclization tactics and strategies']



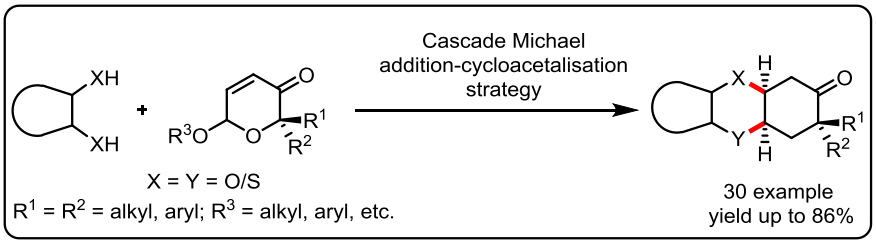
(4) *"Modular assembly of furotropones and benzofurotropones, and study of their physicochemical properties"*

Shirke, R. P.; Ramasastry, S. S. V. *J. Org. Chem.* **2015**, *80*, 4893.



(5) *"Synthesis of O,S-containing polycycles via one-pot Michael addition cycloacetalisation Cascade"*

Bankar, S. K.; Shirke, R. P.; Ramasastry, S. S. V. *Adv. Synth. Catal.* **2015**, *357*, 3284.



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The author, Mr. Rajendra Pratap Shirke was born at Wangi, Maharashtra. After his initial schooling at Wangi, he received a B.Sc. degree in Chemistry from Balwant college vita, Shivaji University in 2009. After obtaining a Masters degree from the Yashavantrao Chavan Institute of Science, Satara in 2011, he joined the research group of Dr. Ramasastry at the Indian Institute of Science Education and Research (IISER) Mohali, as a Ph.D. student in August 2013. He passed the comprehensive examination in August 2014. Presently, he is working as a Senior Research Fellow of IISER Mohali in the Department of Chemical Sciences.

CONFERENCES ATTENDED

- Presented a poster at the **Emerging Trends in Drug Developments and Natural Products (ETDDNP-2018)** held at University of Delhi, India during January 2018. Title of the presentation: *Synthesis of furotropones, Benzofurotropones and benzofurans (Elsevier award for one of the best poster presentations).*
- Presented a poster at the **XII JNOST-Organic Chemistry Conference (JNOST-OCC)** held at CDRI-Lucknow, India during December 2016. Title of the presentation: *Modular assembly of furotropones, Benzofurotropones and study of their physicochemical properties.*
- Presented a poster at the **10th CRSI-RSC Symposium** held at Punjab University Chandigarh, India during February 2016. Title of the presentation: *Modular assembly of furotropones, Benzofurotropones and study of their physicochemical properties.*