Annulation reactions of heterocyclic chlorovinyl-aldehydes. Synthesis of functionalized *6H*-benzo[*c*]chromen-6-ones (biaryl lactones), *6H*-benzo[*c*]chromenes and heteroannulated pyridines

Dissertation

Zur

Erlangung des akademischen Grades

Doctor rerum naturalium (Dr. rer. nat.)

Der Mathematisch-Naturwissenschaftlichen Fakultät

des Universität Rostock

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Geb. 09-04-1975 Haripur, Pakistan

Rostock, 2015

urn:nbn:de:gbv:28-diss2015-0086-0

Die vorliegende Arbeit wurde am Institut für Chemie der Universität Rostock unter der Leitung von Prof. Dr. Dr. h.c. mult. Peter Langer angefertigt.

The present thesis was completed at the University of Rostock under the guidance of Prof. Dr. Dr. h.c Peter Langer.

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Datum der Einreichnung: 20.08.2014

Datum der Verteidigung: 21.04.2015

DECLARATION/ERKLÄRUNG

I hereby declare that this work has so far neither been submitted to the Faculty of mathematics and natural science of the University of Rostock nor to any other scientific organization or institute for the purpose of doctorate. Furthermore, I declare that I have written this dissertation myself and did not use any other source, other than mentioned earlier in this work.

Hier erkläre ich, dass diese Arbeit zuvor weder an der Fakultat fur Mathematik und Naturwissenschaften der Universität Rostock noch an einem anderen wissenschaftlichen Institut zum Zweck der Promotion vorgelegt wurde. Desweiteren erklare ich, dass ich diese Arbeit selbst geschrieben und keine Quellen verwendet habe, die nicht in diesen Werk erwähnt wurden.

ABSTRACT/KURZBESCHREIBUNG

The present work is based on the synthesis of novel oxygen containing and nitrogen containing heterocycles. A simple and convenient domino cycloaromatization approach towards the synthesis of novel benzo[*c*]chromen-6-ones and benzo[*c*]chromenes by treatment of heterocyclic chlorovinyl-aldehydes with active methylene compounds has been developed. In another strategy novel biaryl lactones were prepared by Sonogashira cross-coupling and base catalyzed reactions of 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde with terminal alkynes and 1, 3-dicarbonyl compounds. Finally some heterocyclic chlorovinyl-aldehydes were treated with electron rich heterocyclic amines to afford novel heteroannulated pyrrolo and pyrazolo pyridines.

Die vorliegende Arbeit basiert auf der Synthese neuer Sauerstoff- und Stickstoffheterozyklen. Ein einfacher und zugleich praktischer Ansatz zur Synthese bisher unbekannter benzo[*c*]chromen-6-onen und Benzo[*c*]Chromenen wurde entwickelt. Die Umsetzung von heterozyklischen Chlorvinyl-Aldehyden mit CH-aziden Verbindungen führte in einer Domino-Zyklisierungs-Aromatisierungs Sequenz zu den entsprechenden Produkten.

Weiterhin wurden neue Biaryllaktone mittels Sonogashira-Reaktion und anschließender basenkatalysierter Reaktion von 4-Chlor-2-oxo-*2H*-Chromene-3-Carbaldehyd, terminalen Alkinen und 1,3-Dicarbonylverbindungen synthetisiert.

Abschließend gelang die Synthese bisher unbekannter heterozyklisch verknüpfter Pyrrolpyridine und Pyrazolpyridine durch Umsetzung heterozyklischer Chlorvinyl-aldehyde mit elektronenreichen, heterozyklischen Aminen.

AKNOWLEDGEMENTS

All praises due to ALLAH (SWT). The most beneficent and the most merciful. Lord of the heavens and the earth. Creator of all things. From whom we came and to whom we return back. He is the only one who shows the straight path to all human beings. Because of His blessings and help I was able to accomplish this onerous task.

All respects and regards due to the last Prophet MUHAMMAD (Peace be upon Him). Mercy and blessing to all mankind. I always feel proud to be a member of HIS UMMAH. He is the last one who guides truly all human beings. I forever feel thirsty of his love, kindness and blissfulness in this world and Hereafter.

I would like to express my sincere gratitude and appreciation to Prof. Dr. Dr. h.c., multi Peter Langer for inviting me to carry out Ph.d research in his group. I am thankful to him for arrangement of funds from DAAD and DFG and provision of work place in his labs. I have learned a lot the way he encouraged and supported me and other students of his group. He is an enthusiastic organic chemist.

I am especially thankful to Dr. Peter Ehlers, Dr. A. Villinger, Dr. M. Hein, Dr. H, Feist, Dr. D, Michalik, Dr. Kristine Fischer and Assistant Staff for their academic and technical support during my Ph.D study.

I owe a great debt of gratitude to my M.Phil supervisor Prof. Dr. Naghmana Rashid and Dr. Muhammad Sher for their initiatives regarding pursuance of my Ph.d studies abroad. I am also thankful to all my friends, fellows and well-wishers, who always pray for my success. All my complements go to my family especially to my parents Abu Jan and Ami Jan who always comprehend my feelings and pains in their heart and fervently remember me in their prayers. I pay special thanks to my Sisters Baji Farhat, Guria, Tabinda and Brother Zakir, Jamil, and children of my family for their overwhelming love and kind support.

Lastly, I would like to thank my wife Nosheen Gul, We have endured a lot together in our life-long relationship. She has been a very loving companion of my life. Surely, I would not be able to complete my higher education without her cooperation, patience and support. She deserves a lot more than what I have written in her appreciation.

PREFACE

Parts of this thesis have been adapted from following publications

1. Viktor O. Iaroshenko,* **Muhammad S. A. Abbasi**, Alexander Villinger, Peter Langer.* *Tetrahedron Lett*. **2011**, 52, 5910. Synthesis of *6H*-Benzo[*c*]chromen-6-ones by Cyclocondensation of 1, 3-dicarbonyl compounds with 4-Chloro-3-formylcoumarin.

http://www.sciencedirect.com/science/article/pii/S0040403911012780

2.Viktor O. Iaroshenko,* **Muhammad S. A. Abbasi**, Alexander Villinger, Peter Langer.* *Adv. Synth. Catal.* **2012**, 803–806. One-Pot Synthesis of Biaryl lactones by Sonogashira Cross-Coupling Reactions of 4-Chloro-3-formyl coumarin and Subsequent Domino [5+1] Cyclization/Deacetylation Reactions with 1,3-dicarbonyl compounds.

http://onlinelibrary.wiley.com/doi/10.1002/adsc.201100621/abstract

Highlighted in *Synafacts* **2012**, 8 (6), 0603, as "Sonogashira-Mediated route to Benzo[*c*]chromen-6-ones".

https://www.thieme-connect.com/ejournals/html/10.1055/s-0031-1291071

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1. Heterocyclic chlorovinyl-aldehydes

1.1 General introduction and synthesis

Heterocyclic chlorovinyl-aldehydes are important and versatile molecular building blocks for the synthesis of variety of organic compounds with interesting biological and physico-organic properties. These building blocks were appeared first in the scientific literature following the advent of famous Vilsmeier-Haack reagent ($POCl_3$+DMF) in 1927[1]. One key aspect of this reagent is that depending on the nature of reacting substrates, it could introduce chloro-formyl functionality in the product skeleton. In 1958 Arnold and Zemlicka first reported the synthesis of β-chloro-acroleins when they treated $POCl_3$ and DMF with enolizable ketones.[2] Later on the Vilsmeier-Haack chloro-formylation reactions were employed to cyclic substrates bearing keto methylene functionality, which resulted heteocyclic chlorovinyl-aldehydes successfully.[3-6] A general mechanistic scheme of the reaction is given in figure 1.

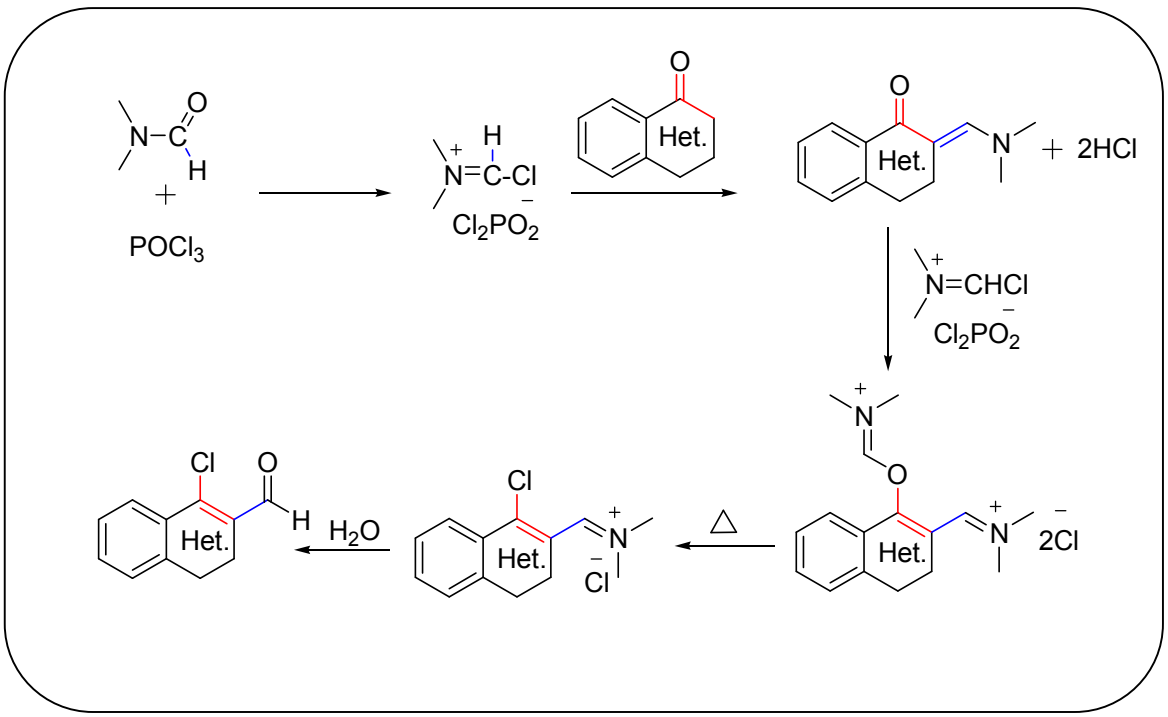


Figure 1. A general mechanism for the synthesis of heterocyclic chlorovinyl-aldehydes

1.2 Synthetic scope of heterocyclic chlorovinyl-aldehydes

Heterocylic chlorovinyl-aldehydes act as ambident elecrophiles because of the presence of formyl functionality and an activated chloro group, therefore easily undergo variety of cyclization reactions with compounds possessing bis-nucleophilic properties. A graphical overview of heterocyclization reactions of chlorovinyl-aldehydes is given in figure 2.[7-14]

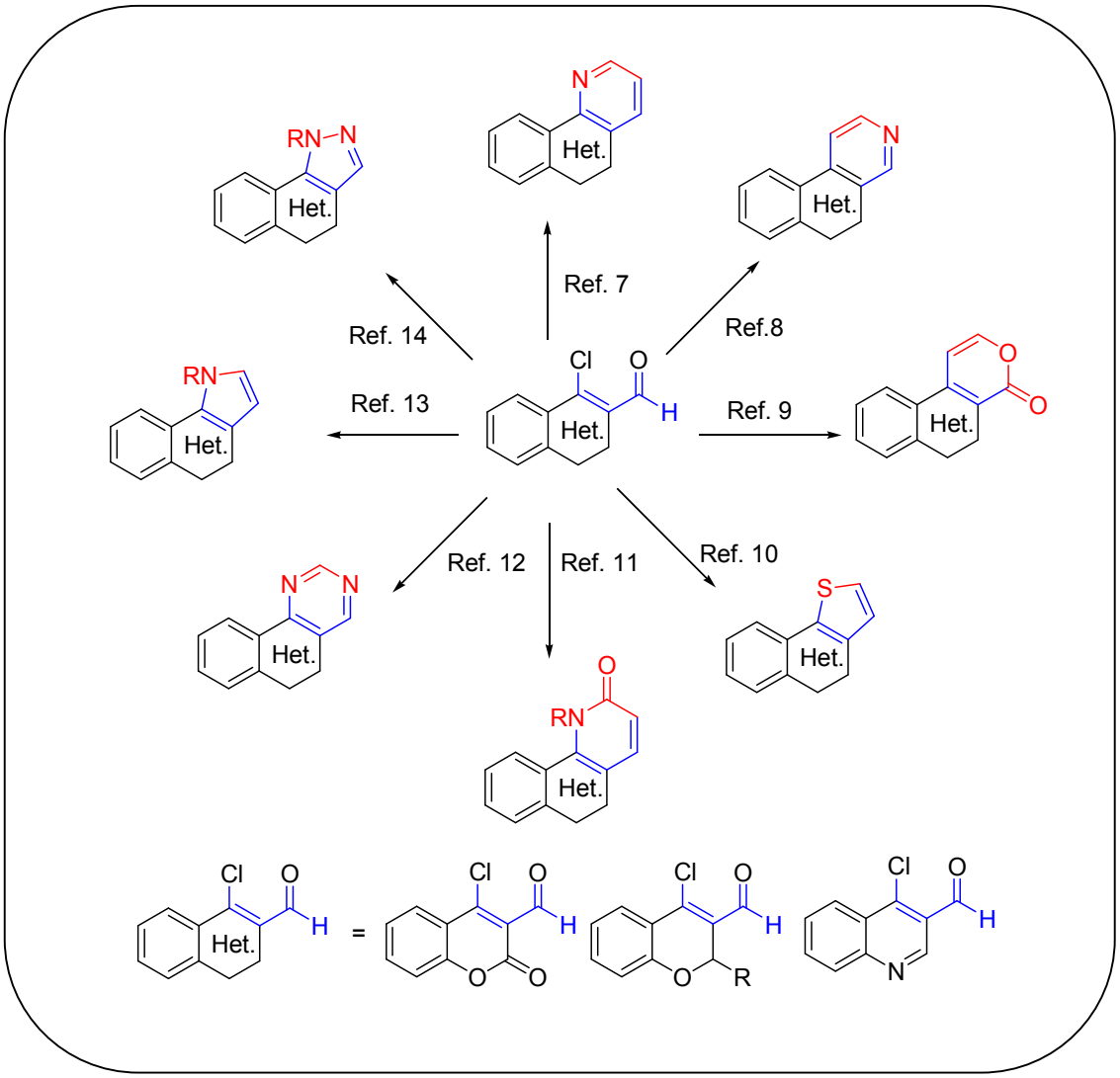


Figure 2. Synthetic utility of some selected heterocyclic chlorovinyl-aldehydes.

The heterocyclized products obtained from chlorovinyl-aldehydes have been evaluated against variety of biological protocols and are known to possess anti-bacterial, anti-oxidant and anticancer activities. Literature survey revealed that many researchers have employed different synthetic strategies on these organic substrates and have constructed interesting heterocylic systems with remarkable pharmaceutical and photo-physical properties. These methodologies involved, multistep synthesis based on function group transformations, metal catalyzed cross-coupling reactions and subsequent annulations reactions, multi-component reactions and domino-cyclization reactions etc. Ray et al.[15] have described a multistep synthesis of antitumor poly cyclic oxa-coumarins from chloroaldehyde derivatives. Stephanie Hesse and Gilbert Krisch have studied Suzuki cross-coupling reactions with β-chloroacroleins, subsequent ring closure of Suzuki products to δ-lactone gave heterocycles bearing a coumarinic moiety.[9]In another report Ding-Yah Yang and co-workers have synthesized two light sensitive pyranocoumarins via multicomponent condensation of chloro-aldehyde coumarin and 4-methyl quinolines.[16]

1.3 Annulation reactions of heterocyclic chlorovinyl-aldehydes: Present work

As we have seen that hetero-annulation reactions of heterocyclic chlorovinyl-aldehydes are quite common in scientific literature. Nonetheless, there is a domain of carbocylcoaromatization reactions of these building blocks that still requires attention of synthetic chemists. Efficient protocols for the benzoannulation of heterocyclic chlorovinyl-aldehydes are relatively rare. Only few reports related to benzoannulation reactions of cyclic β-bromovinyl-aldehydes are available. Ray et al[17] have synthesized substituted benzene derivatives employing base-catalyzed and water mediated cycloaromatization reactions of cyclic β-bromovinyl-aldehydes with β-ketoesters. The mechanism involved classical Knoevenagel type cyclocondensation reaction. In another synthetic approach transition metal catalyzed aromatization using tendem Heck and aldol reactions were employed for the construction of carbocylic skeleton on the simple aromatic β-bromovinyl-aldehydes.[18] These findings could instigate one to employ similar benzoannulation approaches to heterocyclic chlorovinyl-aldehydes substrates that may finally lead to the synthesis of novel biologically active

benzoannulated heterocycles. In view of above literary findings a general layout of the current work on heterocylic chlorovinyl-aldehydes is given in figure 3.

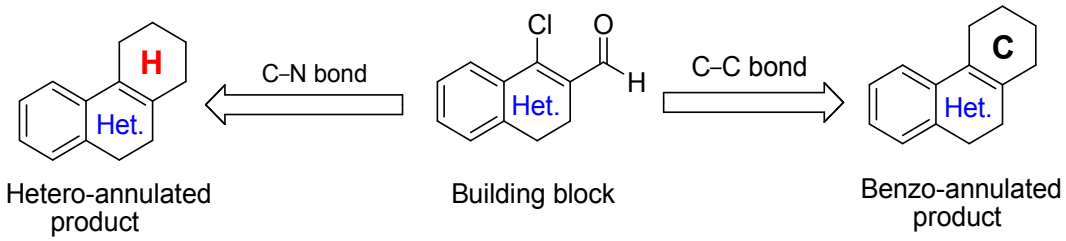


Figure 3. Layout for the synthesis of benzoannulated and heteroannulated heterocycles

In the present work four heterocyclic chlorovinyl-aldehyde building blocks were selected for their further reactions with nucleophilic reagents.

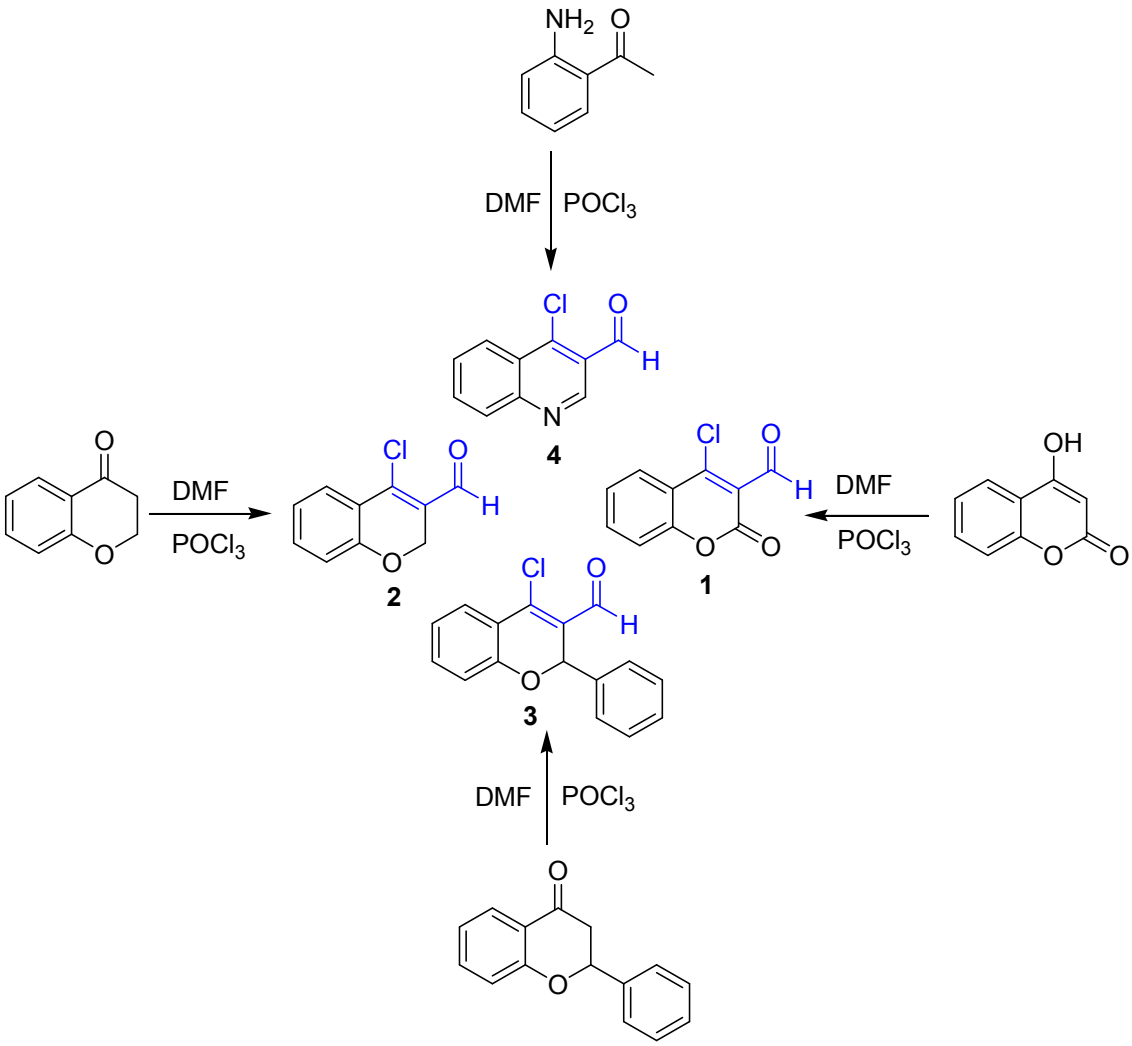


Figure 4. Synthesis of some heterocyclic cholorvinyl-aldehyde building blocks.

These molecular building blocks namely 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde (**1**), 4-chloro-2*H*-chromene-3-carbaldehyde (**2**), 4-chloro-2-phenyl-2*H*-chromene-3-carbaldehyde (**3**) and 4-chloroquiniline-3-carbaldehyde (**4**) were synthesized from their corresponding substrates by well-known Vilsmeier-Haack reactions.[19-22] (Figure 4).

2. One pot synthesis of *6H*-benzo[*c*]chromen-6-ones by cyclocondensation of 1, 3-dicarbonyl compounds with 4-chloro-3-formylcoumarin.

2.1 Introduction

Functionalized biaryl lactones(*6H*-benzo[*c*]chromen-6-ones or 6*H*-dibenzo [*b,d*] pyran-6-ones) are found in a variety of important natural productswith considerable pharmacological relevance such asfasciculiferol alternariol, autmnariol, autumnariniol and altenuisol etc.[23,24] Some of their structural analogues with variety of ring extensions and functional group substitutions are known to possess enzyme and cell growth inhibition, bactericidal and antitumor activities e.g. ellagic acid, gilvocarcins, ravidomycins, chrysomycins and arnottin I.[25-29]

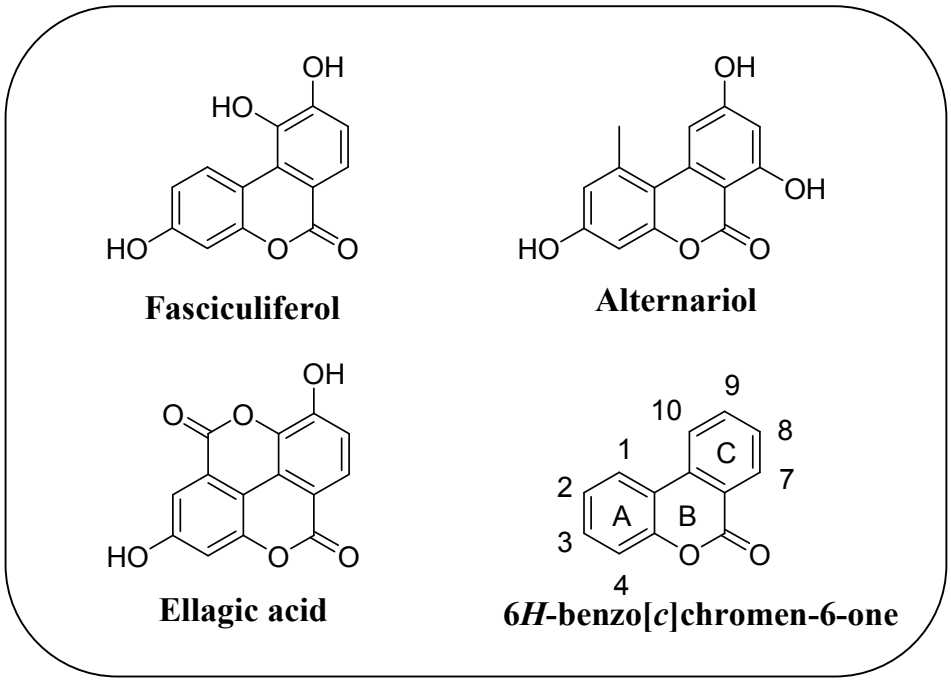


Figure 5. Biaryl lactones natural products and *6H*-benzo[*c*] chromen-6-one nucleus).

Several strategies for the syntheses of substituted *6H*-benzo[*c*]chromen-6-ones have been appeared in the scientific literature. Some of the important approaches include cyclization of o-bromobenzoic acid with phenols,[30]intramolecular Pd (II)-catalyzed coupling reactions of aryl benzoates,[31]combination of directed ortho-

metalations (DOM) with subsequent Suzuki cross-coupling reactions etc.[26] Few years ago, Chan et al. reported salicylates based approach for the synthesis of biaryl lactones by formal [3+3] cyclization of 1,3-bis (silyl enol ethers) with 3-siloxy-2-en-1-ones.[32] In recent years, many cyclization reaction's strategies were developed for the synthesis of novel *6H*-benzo[*c*]chromen-6-ones (**7**) in the group of Prof. Langer (Figure 6) (for clarity reasons substitution pattern is omitted). In one case, treatment of activated chromones **5** with 1, 3-bis (silyl enol ethers) gave functionalized 2, 3-dihydrogen benzopyrans which on treatment with NEt_3 or BBr_3 underwent retro-Michael-aldol-lactonization reactions to give variety of 7-hydroxy *6H*-benzo[*c*]chromen-6-ones.[33]

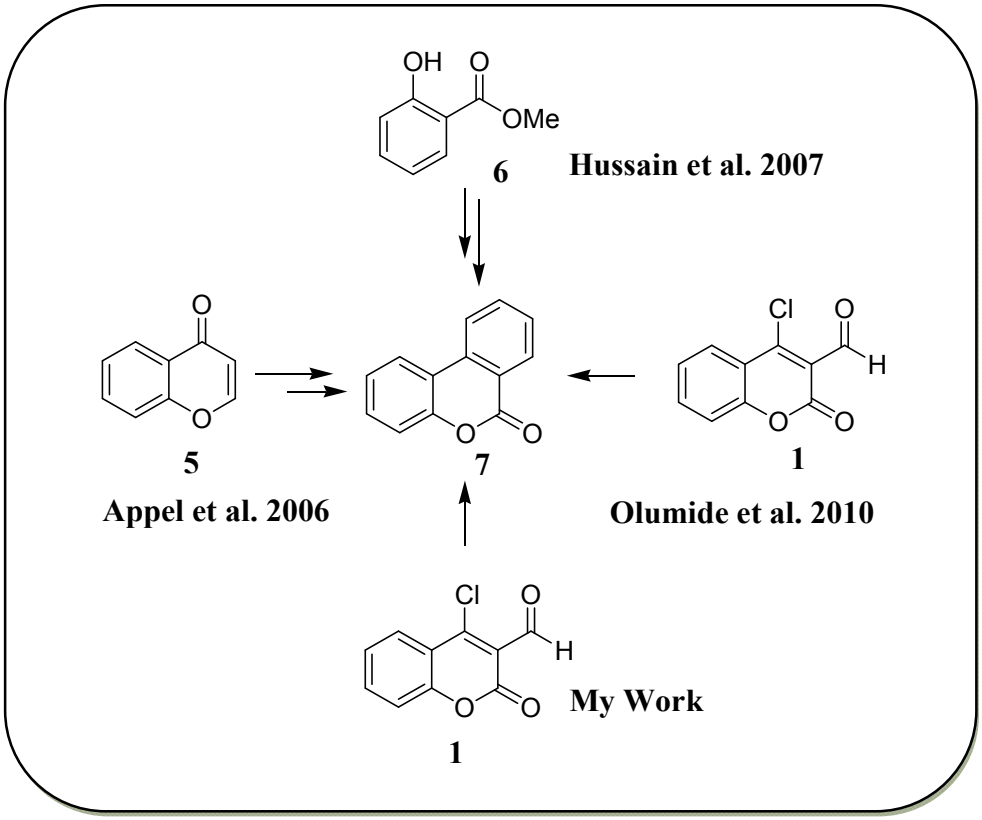


Figure 6. Synthesis of *6H*-benzo[*c*]chromen-6-ones (**7**) (Langer's group)

In another strategy, variety of salicylates **6** have been prepared by formal [3+3] cyclization of 1,3-bis (silyl enol ethers) with 3-siloxy-2-en-1-ones, suzuki coupling of their triflates with o-methoxy boronic acids and subsequent BBr_3-mediated lactonization afforded flora of novel *6H*-benzo[*c*]chromen-6-ones .[34] Moving forward on the same lines in Langer's lab, functionalized 9-hydroxy-6H-benzo[c]chromen-6-

ones have been prepared by cyclization of 1,3-bis (silyloxy)-1,3-butadienes with easily synthesized 4-cholor-3-formylcoumarin (4-chloro-2-oxo-2H-chromene-3-carbaldehyde) (**1**).[35] Recently Bodwell et al. employed an efficient multicomponent (MCR) technique for the synthesis of *6H*-benzo[*c*]chromen-6-ones.[36]

A critical study of above mentioned synthesis however reveals the fact that more or less each reported synthetic strategy is associated with some synthetic drawbacks such as harsh temperature conditions, longer reaction times, lower products yield, use of expensive catalyst and difficult purification procedures etc. Presence of these short comings may however let down some of the important reported synthetic methodologies and if ever be considered by an industry for large scale production of these pharmaceutically interesting compounds, an alternatively easier, environmentally friendly and direct approach free from any synthetic upheaval will be welcomed indubitably.

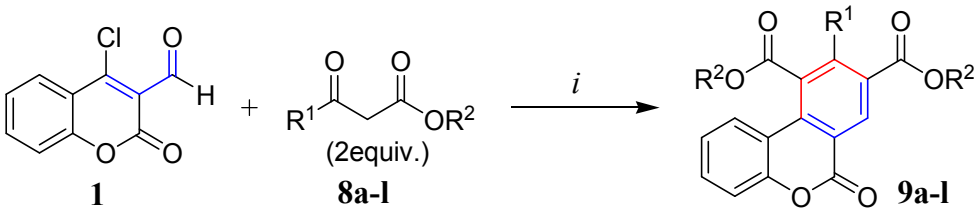
Here in I wish to report a facile one pot synthesis of highly functionalized *6H*-benzo[*c*]chromen-6-ones by cyclocondensation of 1, 3-dicarbonyl compounds with 4-chloro-3-formylcoumarin.

2.2 Results and Discussions

The substrate 4-chloro-3-formylcoumarin (**1**) was easily prepared from commercially available 4-hydroxycoumarin by employing well-known Vilsmeier-Haack reaction.[19]

I treated substrate **1** with 2 equivalent of β-ketoesters **8a-l** which underwent domino cyclizations to give cyclized products **9a-l** in fairly good yields (Scheme 1)**.**

Initially I started my work by using K_2CO_3 as base and DMF as solvent. These conditions were successfully employed by Ray and co-workers for the cyclization reactions of β-ketoesters with cyclic β-bromovinylaldehydes to achieve the synthesis of substituted benzene derivatives.[17]Unfortunately, with these conditions; I met with limited success and got low product yields. I also experienced difficult extraction workup because of high boiling point of DMF solvent and its highly polar nature. However, changing the solvent to THF gave me highly acceptable results.



Scheme 1. Synthesis of **9a-l.** Reagents and conditions: (i) **1** (0.5 mmol), **8a-l** (1 mmol) K_2CO_3 (2.0 equiv.), THF 7-8 mL, 50 °C, 4-8 hrs.

When I treated substrate **1** with methylacetoacetate (**8a**) by employing THF as solvent and K_2CO_3as base, i got the desired product **9a** in 75% yield. The structure of **9a** was independently confirmed by X-ray crystal structure analysis (Figure 7)**.**

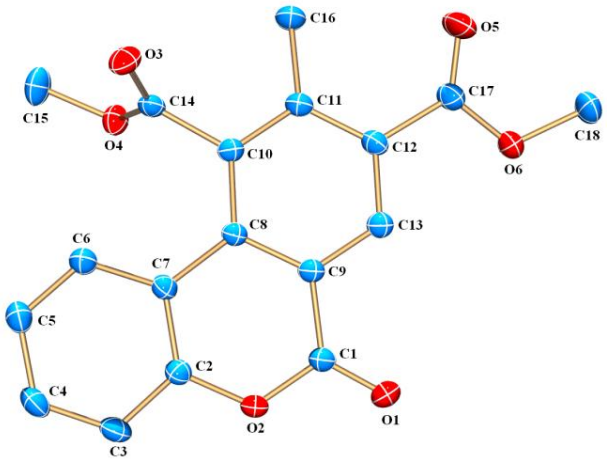


Figure 7. Ortep plot of compound **9a**

No results were obtained when triethylamine was used as base. Following these conditions, products **9a-l** were prepared in 45-77% yield by cyclization of **1** with β-ketoesters **8a-l** (Table 1). The reaction times had to be adjusted for each individual reaction and were monitored by TLC after regular intervals.

Table 1. Synthesis of products **9a-l**

8,9	R^1	R^2	Time (hrs)	Yield (%)[a]
a	Me	Me	4	75
b	Me	*i*Pr	6	72
c	Me	Et	6	71
d	Me	$(CH_2)_2OMe$	8	60
e	Me	Allyl	8	76
f	Me	CH_2Ph	4	62
g	Et	Me	4	45
h	CH_2Cl	Me	4	72
i	CH_2Cl	Et	4	73
j	Pr	Et	5	66
k	Ph	Et	8	62
l	CH_2OMe	Me	6	77

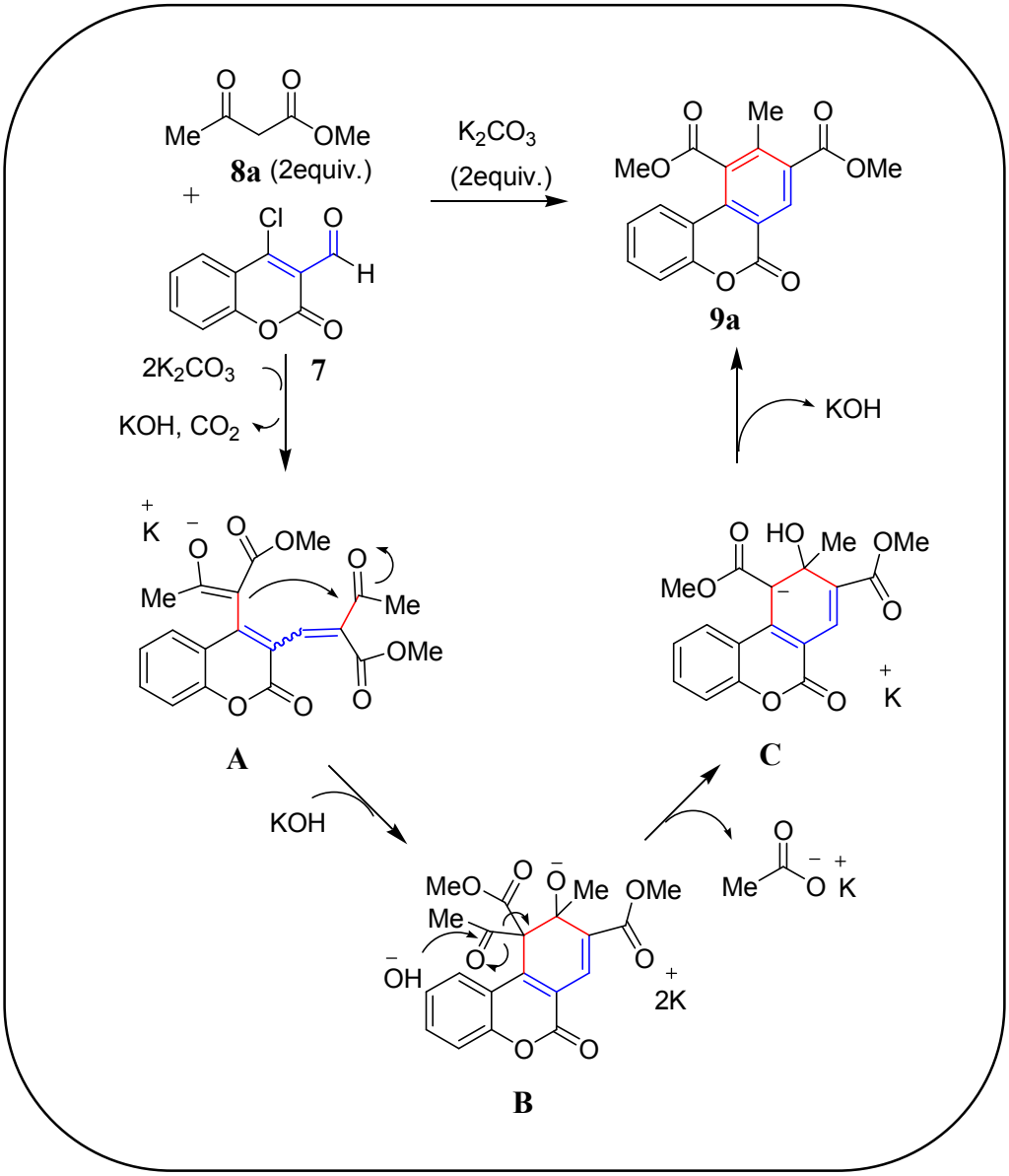
[a]Yields of isolated products.

2.2.1 Proposed Mechanism

The formation of products **9a-l** can be explicated as follows (Scheme 2): the Knoevenagel-type reaction[37,38]of 1 equiv of β-ketoester **8a** with4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde **(1)** followed by nucleophilic substitution of the chlorine atom by a second equivalent of β-ketoester **8a** gave intermediate **A**.

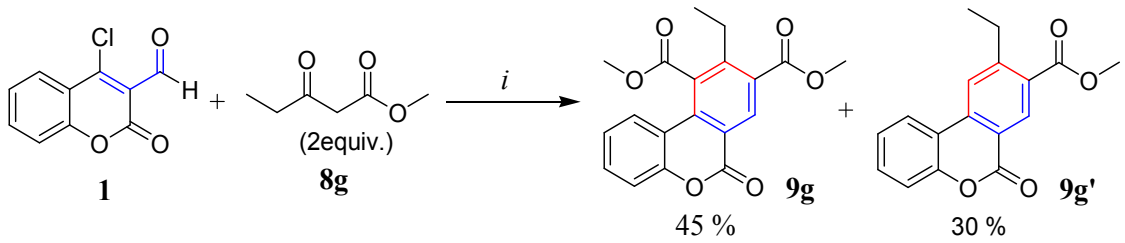
A base mediated cyclization afforded intermediate **B** which subsequently underwent cleavage of the acetate (intermediate **C**) and aromatization. The cyclization proceeds by regioselective attack onto the keto group which is more electrophilic than the ester group.

In literature the Suzuki reaction of β-bromovinylaldehyde with alkenylboronic acids and subsequent Harner-Wadsworth-Emmons reaction and 6π-electrocyclization has been reported to give annulated ring systems.[39]However, such electrocyclization reactions require high temperatures and presumably do not account for the formation of products **9a-l**.



Scheme 2. Possible reaction mechanism for the formation of **9a**

Some important deviations in products formation have also been noted e.g. when substrate **1** was treated with β-ketoester methyl-3-oxopentanoate (**8g**), I got the desired product **9g** in 45%, and a by-product **9g'** in 30% yield (Scheme 3).



Scheme 3. Synthesis of **9g and 9g'.**Reagents and conditions: (i) **1** (0.5 mmol), **8g** (1 mmol), K_2CO_3 (2.0 equiv.), THF 7-8 mL, 50 °C, 4 hrs.

The formation of side product **9g'** is observed because of decarboxylation of one ester side arm during the reaction. The ortep plot of side product **9g'** (Figure 8).

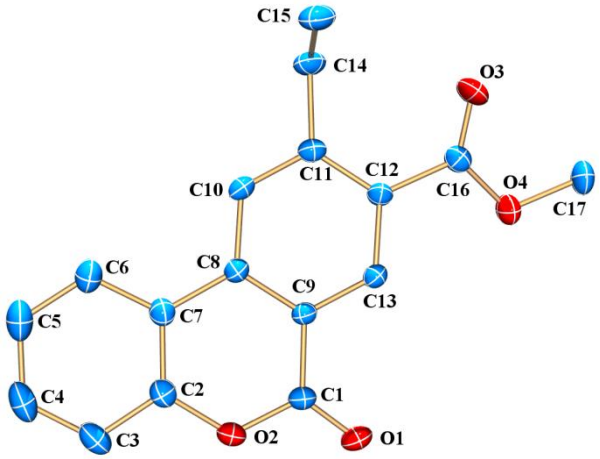
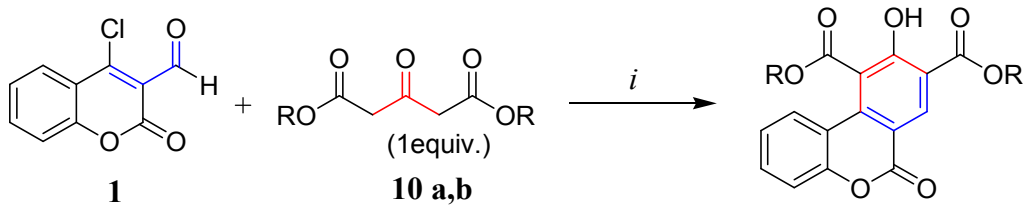


Figure 8. Ortep plot of compound **9g'**

I have further studied the scope of reaction by treating dimethyl-3-oxopentanedioate (**10a**) and diethyl-3-oxopentanedioate (**10b**) with substrate **1** (Scheme 4).



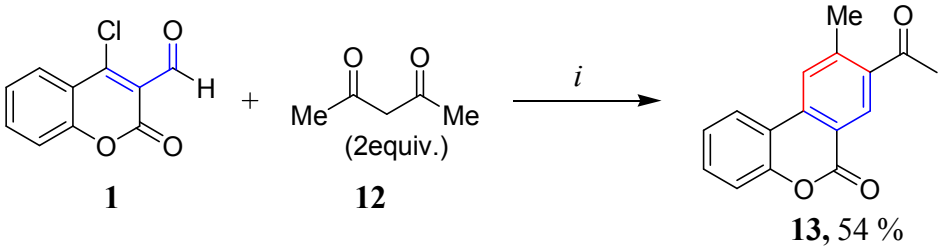
11a (R = Me), 79 %; **11b** (R = Et), 81 %

Scheme 4. Synthesis of **11a and 11b.** Reagents and conditions: (i) **1** (0.5 mmol), **10a, b** (1 mmol) K_2CO_3 (2.0 equiv.), THF 7-8 mL, 50 °C, 2 hrs.

The reaction successfully afforded *6H*-benzo[*c*]chromen-6-ones **11a** and **11b** bearing hydroxyl functionality on the **C** ring.

The formation of products follows a 1:1 stoichiometry. The reagents **10a** and **10b** bear two nucleophilic parts each bearing acidic protons. The first part may condense with the aldehyde group and the other part replaced the chloro group leading to an aromatized product.

The K_2CO_3 mediated reaction of **1** with acetylacetone (**12**) followed a 2:1 stoichiometry and afforded novel *6H*-benzo[*c*]chromen-6-ones **13** (Scheme 5).



1 **12** **13,** 54 %

Scheme 5. Synthesis of **13.** Reagents and conditions: (i) **1** (0.5 mmol), **12** (1 mmol), K_2CO_3 (2.0 equiv.), THF 7-8 mL, 50 °C, 4hrs.

The structure of **13** was independently confirmed by X-ray crystal structure analysis (Figure 9). The formation of product **13** can be explained by mechanism similar to the one discussed for the formation of **9g'.**

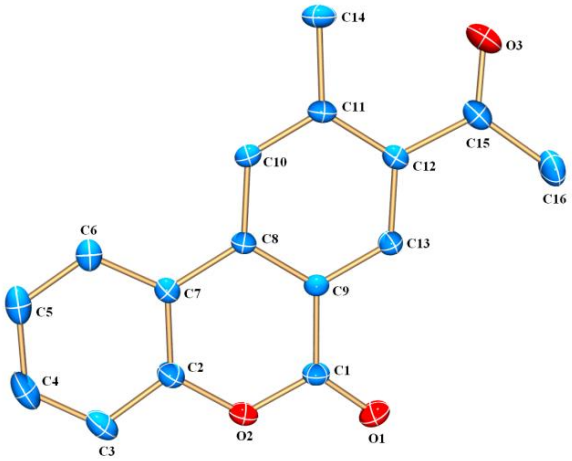
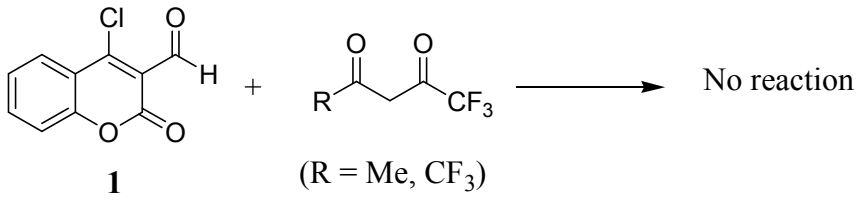


Figure 9. Ortep plot of compound **13**

2.2.2 Limitations

In order to extend the scope of the methodology for the preparation of fluorine substituted *6H*-benzo[*c*]chromen-6-ones. I treated substrate **1** with fluorinated diketones such as 1, 1, 1-trifluoro-pentane 2, 4-dione and 1, 1, 1 ,5, 5, 5-hexafluoro-pentane 2,4-dione, but unfortunately, I could not get any desired cyclized product (Scheme 6). The reason for unsuccessful reactions of fluorinated β-diketones lies in the high electronegativity of fluorine atoms, which make fluorinated β-diketones highly reactive nucleophilic species prone to hydration or cleavage in alkaline medium.[40]



Scheme 6. Unsuccessful reactions of substrate **1** with fluorinated diketones.

2.3 Conclusion

In conclusion i have developed a simple and convenient one pot synthesis of novel*6H*-benzo[*c*]chromen-6-ones by base mediated cyclocondensation of 4-chloro-3-formyl coumarin with 1, 3-dicarbonyl compounds. Utilizing variety of 1, 3-diketones the synthetic scope and limitations were studied in detail. In a nut shell construction of **C** ring of *6H*-benzo[*c*]chromen-6-ones with novel functional group substitution pattern has been achieved in a domino fashion. Bio-evaluation of synthesized compounds is in progress.

3. Base-mediated one pot domino synthesis of *6H*-benzo[*c*]chromenes. Study of some structural and physico-organic aspects of newly synthesized products.

3.1 Introduction.

The benzochromene nucleus is found in many heterocyclic biological molecules.[41]In particular, the *6H*-benzo[*c*]chromene is an important molecular scaffold of a natural product cannabinol,[42]whose analogues are known to possess antiemetic, analgesic and anticonvulsant properties and may act as selective progesterone receptor modulators (SPRM).[43-46] (Figure10).

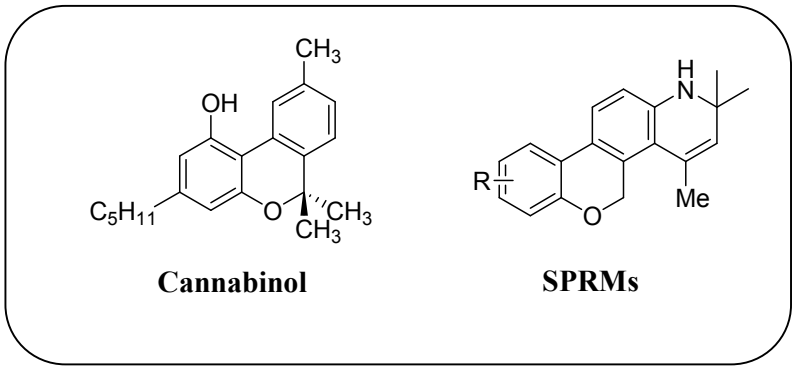
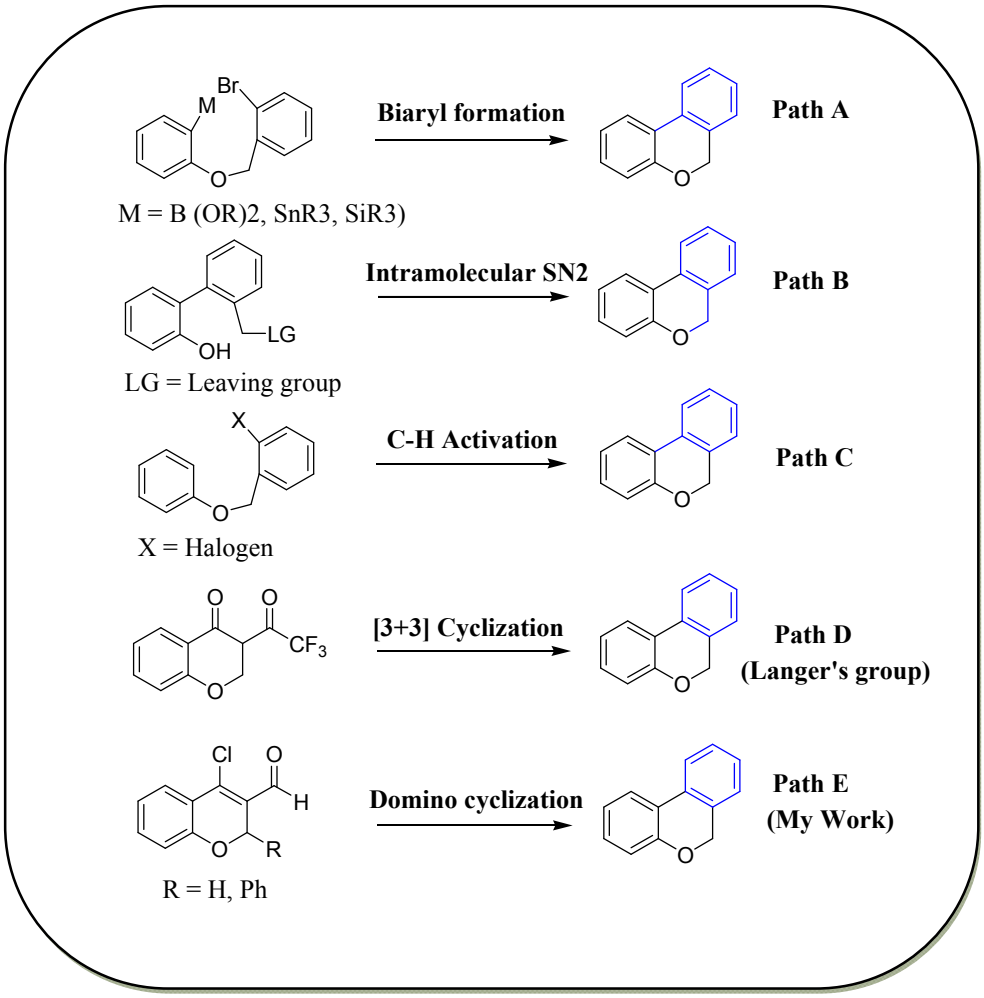


Figure 10. Important examples of *6H*-benzo[*c*]chromenes.

In literature, different methodologies have been reported for the synthesis of substituted *6H*-benzo[*c*]chromenes. Some selected pathways based on underlying reaction's principle are summarized in (Scheme 7). These strategies include metal catalyzed coupling reactions,[47, 48] intermolecular SN_2 reactions,[49] and direct C-H functionalization[50]etc. In the group of Prof. Langer a substrate based strategy has been successfully applied for the synthesis of novel *6H*-benzo[*c*]chromenes.[51] In this methodology an activated chromanone have been treated with substituted 1, 3-bis(silyloxy)-1,3-butadienes, that underwent [3+3] cyclization to give desired novel *6H*-benzo[*c*]chromenes. However, despite literary importance these methodologies have evolved few synthetic lacking as use of relatively expensive catalysts (comparative to inorganic bases), non-benign temperature conditions and worth noting

is the non-availability of desired collar of functionalization surrounding basicbenzo[*c*]chromene nucleus that may be required for essential structure-activity relationship among other similar classes of heterocyclic compounds.



Scheme 7. Strategies towards the synthesis of *6H*-benzo[*c*]chromenes core

3.2 Results and Discussions

My previous successful findings related to the synthesis of *6H*-benzo[*c*]chromen-6-ones led me to design a similar series of heterocyclic compounds bearing same functionalization onto the C ring. To do this, I have selected substrates 4-chloro-*2H*-chromene-3-carbaldehyde (**2**) and 4-chloro-2-phenyl-*2H*-chromene-3-carbaldehyde (**3**). (Figure 11). I have synthesized these substrates from their corresponding precursors by

famous Vilsmeier-Haack reactions.[20, 21] For expediency, the chemistry of each substrate will be discussed separately.

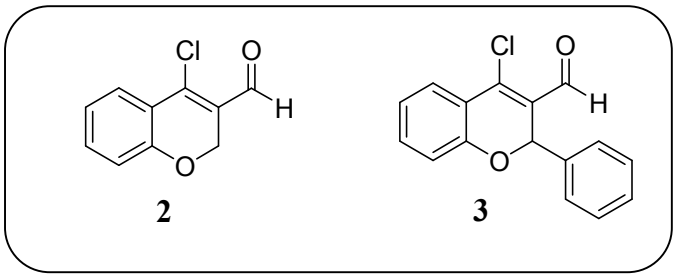
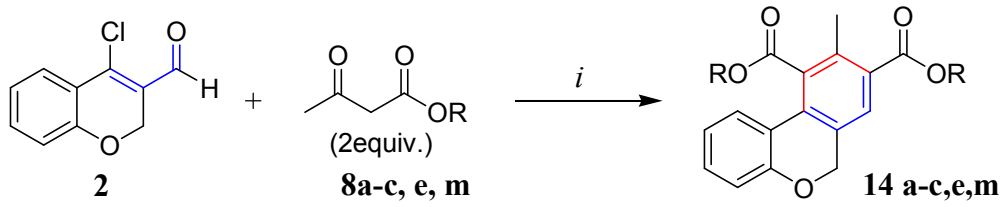


Figure 11. Chloro substituted chromene-3-carbaldehydes.

When I treated substrate **2** with methyl acetoacetate (**8a**) using K_2CO_3 as base and THF as solvent at room temperature, I could not get the desired cyclized product. Although a yellow bright spot was observed on TLC plate, which I could not purify even by column chromatography. However on maintaining the moisture free conditions and heating the reaction mixture between 50-60 °C for about 2 hrs, I observed the appearance of another blue spot that allow me to alter the reaction partners i.e. base and the solvent. I started trying base K_2CO_3 with set of solvents such as DMF, CH_3CN and toluene but could not observe any appreciable change. However on changing the base from K_2CO_3 to Cs_2CO_3 and using solvent DMF, I was able to isolate the desired cyclized product in only 2% yield (Scheme 8).



Scheme 8. Synthesis of **14a-c, e, m.** Reagents and conditions: (i) **2** (1 mmol), **8a-c, e, m** (2 mmol), Cs_2CO_3 (2.0 equiv.), DMF 7-8 mL, 50 °C, 2-4 hrs.

No reaction was observed, when organic bases such as triethyl amine, Pepperidine and morpholine were used. Fortunately, using the β-ketoester **8c** instead of **8a** and applying Cs_2CO_3-DMF base-solvent conditions, I have been successfully able to isolate

the desired cyclized product in 20 % yield (Table 2). I found purification of desired products a bit difficult; therefore repeated column chromatography was done in most of the cases. A significant role of nature of ester-linkage on the cyclization process has been observed e.g. more electron-donating ester part was found to have a positive effect on the product yield. Because of experiencing a limiting trend in the products yield, I could not reach to manage a certain set of optimized conditions. Rather, I twisted my attention to explore the structural and physico-organic aspects of the formed products.

Fortunately, I was able to grow the crystal of product **14c**. A highly strained structural frame work of cyclized product was obtained as is revealed by its X-ray analysis. Inspite of the fact, that one could guess easily theoretically the strained skeletal features of the cyclized product by keeping in view the sp3 carbon of *6H*-benzo[*c*]chromene in middle ring, it is worth mentioning that results of the physical parameters of this newly cyclized product along with their role in comparison with a base as decisive factors on the success of reactions have not been communicated earlier. The detailed discussion will be made in structural description section separately later on.

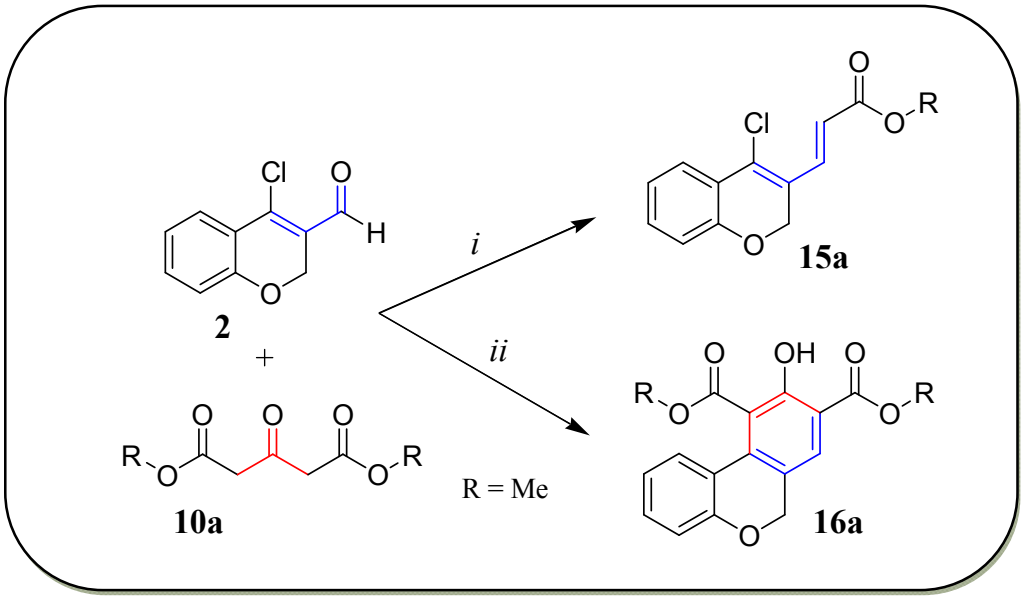
Table 2. Synthesis of *6H*-benzo[*c*] chromenes **14a-c, e, m**

8,18	R^1	R^2	Time(hrs)	Yield **14a-c, e, m** (%)[a]
a	Me	Me	4	< 2
b	Me	*i*Pr	4	31
c	Me	Et	4	22
e	Me	Allyl	4	38
m	Me	*t* butyl	4	35

a Yields of isolated products.

I have noticed some interesting observations. When I treated substrate **2** with dimethyl acetone-1, 3-dicaroboxylate (**10a**) in the presence of CS_2CO_3 and DMF, I got **15a** as a major product in 60 % yield instead of expected cyclized product. By

switching over back to conditions using K_2CO_3 and THF, I got the desired cyclized product **16a** in 52 % yield along with uncyclized product **15a** as minor product in 28 % yield (Scheme 9)**.**



Scheme 9. Synthesis of **15** and **16.** Reagents and conditions: (i) **2** (1 mmol), **10a** (2 mmol), Cs_2CO_3 (2.0 equiv.), DMF 7-8 mL, 50 °C, 6 hrs. (ii) **2** (1 mmol), **10a** (2 mmol), K_2CO_3 (2.0 equiv.), THF 7-8 mL, 50 °C, 6 hrs.

I have selected the right conditions suitable for the formation of cyclized products with OH functionality on ring C and prepared three examples in fairly good yields**.** (Table 3).

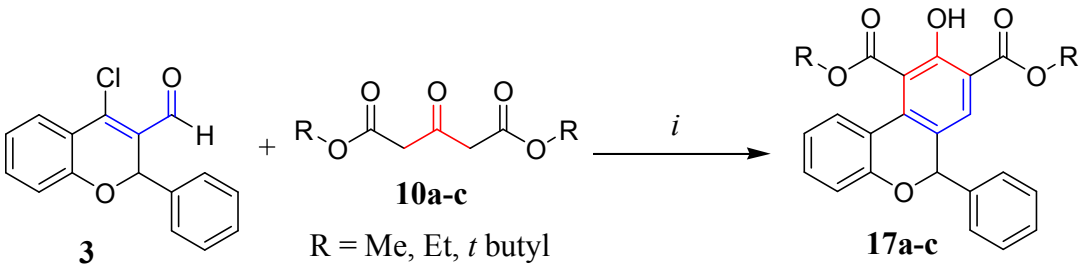
Table 3. Synthesis of*6H*-benzo[*c*]chromenes **16a-c**

8,18	R^1	Time(hrs)	Yield **16a-c** (%)[a]
a	Me	6	52
b	Et	6	65
c	*t*butyl	6	62

[a] Yields of isolated products.

Nevertheless, both K_2CO_3 and Cs_2CO_3 are relatively strong bases; they behave quite differently in organic reactions. The size and softness of cesium cation confer

peculiar characteristic to Cs_2CO_3 thus render it more soluble and reactive in polar solvents[52]. I myself at this stage considered it too early to ascertain the role of two different base-solvent systems K_2CO_3-THF and Cs_2CO_3-DMF which were found to be operated successfully so far. Interestingly when I carried out the reaction of 4-chloro-2-phenyl-2*H*-chromene-3-carbaldehyde (**3**) with dilalkyl-3-oxo-pentanedioates (**10a-c**) using K_2CO_3 as base and DMF as solvent, i got desirable results **(**Scheme 10).



Scheme 10. Synthesis of **17a-c.**Reagents and conditions: (i) **3** (1mmol), **10a-c** (2 mmol), K_2CO_3 (2.0 equiv.), DMF 7-8 mL, 50 °C, 4 hrs.

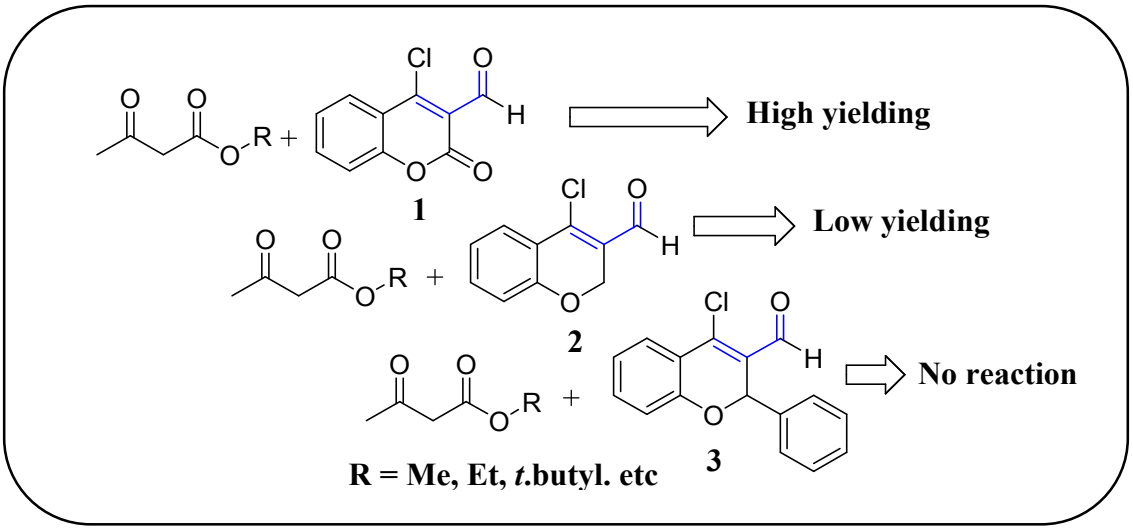
The yields of the products are given in table 4. Uptill now from my study on the reaction of some heterocyclic chlorovinyl-aldehyes with 1, 3-dicarbonyl compounds and 1, 3, 5-tricarbonyl compounds, I sorted out three different reaction conditions which gave me satisfactory results. The most effective parameters were type of base, nature of solvents and nature of substrates. The details of products yield are given in (Table 4).

Table 4. Synthesis of *6H*-benzo[*c*]chromenes **17a-c**

10, 17	R	Time (hrs)	Yield **17a-c** (%)[a]
a	Me	4	54
b	Et	4	60
c	*t*- butyl	4	66

[a]Yields of isolated products.

Unexpectedly, 4-chloro-2-phenyl-2*H*-chromene-3-carbaldehyde (**3**) did not show any desired reaction with β-ketoesters under any set of reaction conditions I employed so far. These findings have finally revealed a decreasing reactivity trend of reactions of β-ketoesters with some oxygen containing heterocylic chlorovinyl-aldehydes (Scheme 11).



Scheme11. Reactivity trend of reactions of chloroformyl benzochromenones and benzochromenes with β-ketoesters.

3.2.1 Structural Description of compound 9c

Inorder to discuss X-ray structural aspects of cyclized products, I selected the compounds with similar functional group patterns. For that purpose, I first grow the crystal of compound **9c** (Figure 12).

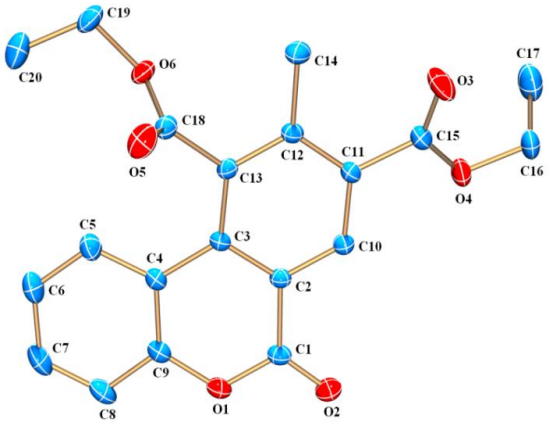


Figure 12. Ortep plot of compound **9c**

It serves as standard model for rest of analogous compound possessing similar functional group pattern and differ only at one or two position in the rest of skeleton.

The X-ray structural information shows that over all molecular frame work is planar, general parameters includes single bonds between C1-C2 and C3-C4 with corresponding bond lengths 1.471 Å and 1.468 Å respectively. Because of aromatic character the bond lengths between C2-C3 and C4-C9 are about 1.40 Å. Though ring B is almost planar compare to the rest of molecule, however the torsional angle < C1-O1-C9 is 121.84 which shows slight deviation from planarity. The bond length between C1-O1 is 1.356 Å which is slightly shorter than the bond length between O1-C9 i.e. 1.381 Å. The bond length between C1-O2 is 1.20 Å that corresponds to double bond. The ester side arm attached to C-11 is out of the plane with dihedral angle of 21.02°, whereas the other ester side arm attached to C13 shows a higher order of deviation from molecular planarity that results a dihedral angle of 81.6°.

3.2.2 Structural Description of compound 14c

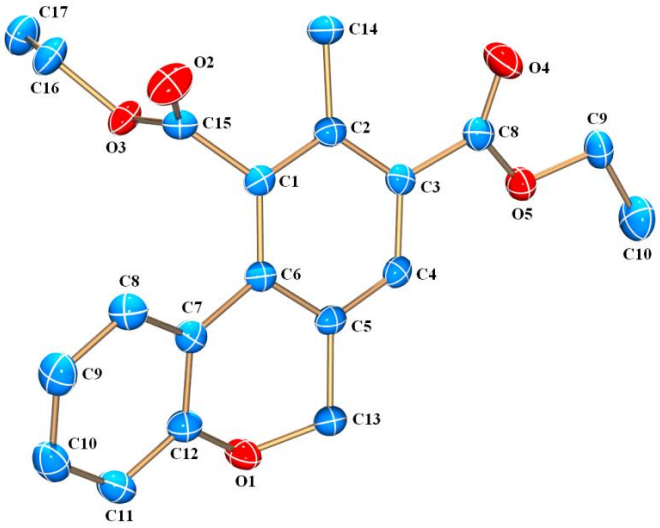


Figure 13. Ortep plot of compound **14c**

The X-ray crystal structure of compound **14c** reveals a highly strained molecular framework having all the three fused rings which shows no planarity with respect to each other and this is because of the sp3 C-13 of ring B. It gave the ring B a half-chair conformation (Figure 13).

The bond length between C13-O1 is 1.4367 Å whereas the bond length between O1-C12 is relatively shorter i.e 1.376 Å which justifies half-chair conformation of ring B. The bond length between C13-C5 and C6-C7 are 1.498 Å and 1.477 Å respectively. The information for the non-linearity of three rings with respect to each other comes from the dihedral angles between C5-C6-C7-C12 which 21.74° which slightly have more value than the dihedral angle between C1-C6-C7-C8 which is 24.66°. The torsional angle between C3-C4-C5-C13 is 175°. The ester side arm attached to C-3 is out of the plane with dihedral angle of 21.76°, whereas the other ester side arm attached to C1 shows a higher order of deviation from molecular planarity signified by a dihedral angle of 86.6°.

3.2.3 Structural Description of compound 17b.

In order to evaluate the effect of substitution on carbon 13 of ring B on structural parameter. I need the same compound bearing similar set of functionality pattern, but unfortunately I could not get the desired compound. However I was able to get another analogue with a hydroxyl functional group on ring C instead of methyl group and a phenyl group on carbon atom C9 (Figure 14).

The molecule appears to have an overall strained skeleton like that of compound **14c**. The dihedral angle between C1-C6-C7-C8 is 23.54° and between C5-C6-C7-C8 is 26.37° which are relatively higher than its structural analogue **14c**. Likewise the torsional angle between C18-C19-C8-C9 is 179.07° which is also slightly higher. The single bond lengths between C8-C9 and are found to be 1.51 Å and 1.474 Å respectively. The bond-length between C1-O1 is 1.375 which is shorter than the single bond length between O1-C9 which is 1.4754 Å. This longer arm makes the C9 out of the plane of ring B and confers a strained half-chair conformation. The ester side arm attached to carbon16 is found to be out of plane by a dihedral angle of 75.12°. On contrary the ester side arm attached to carbon18 is almost planar to main frame by an angle of just 1.05 Å and this is because of hydrogen bonding between hydroxyl group and neighboring carbonyl functional group i.e C=O·····H-O5 is 1.719 Å. The phenyl ring attached to C9 attains a pseudo-perpendicular geometry because of half-chair

conformation of C9. The torsional angle between O1-C9-C10-C11 is found to be 51.86 Å, whereas the dihedral angle between C8-C9-C10-C11 is found to be 168.9 Å.

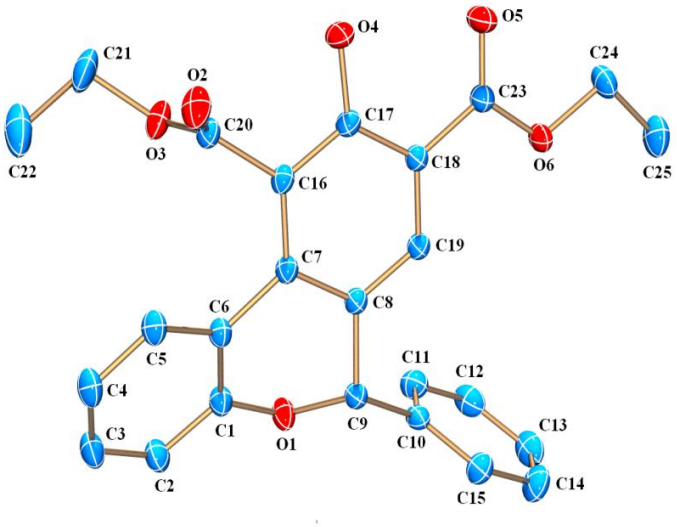


Figure 14. Ortep plot of compound **17b**

3.2.4 Mass spectral studies of compound17c

Apart from the fact that factors affecting lower yields, like structural strain in the newly synthesized *6H*-benzo[*c*]chromenes and the base. I noticed another effect of temperature also. The compound **71c** is found to be thermally labile as proved by its different GC-MS spectrograph from the rest of series of analogous compounds (Figure 15).

The Gas Chromatogram shows two peaks which were appeared later in the mass spectrum as molecular ions of masses 274 and 374 respectively that matched exactly of the fragments formed after losing ester-side arms of parent molecules while passing through gas column (Scheme 12).

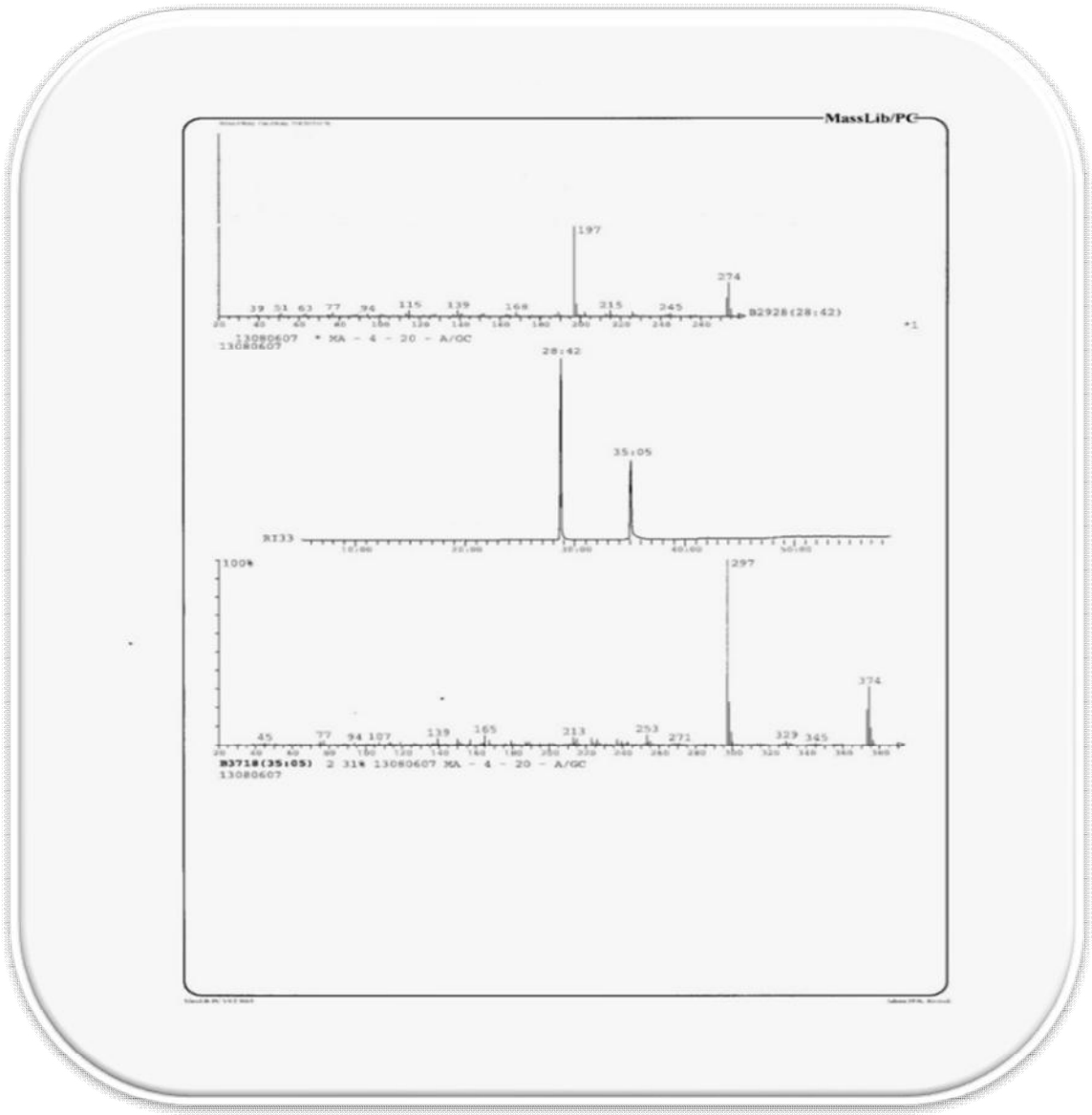
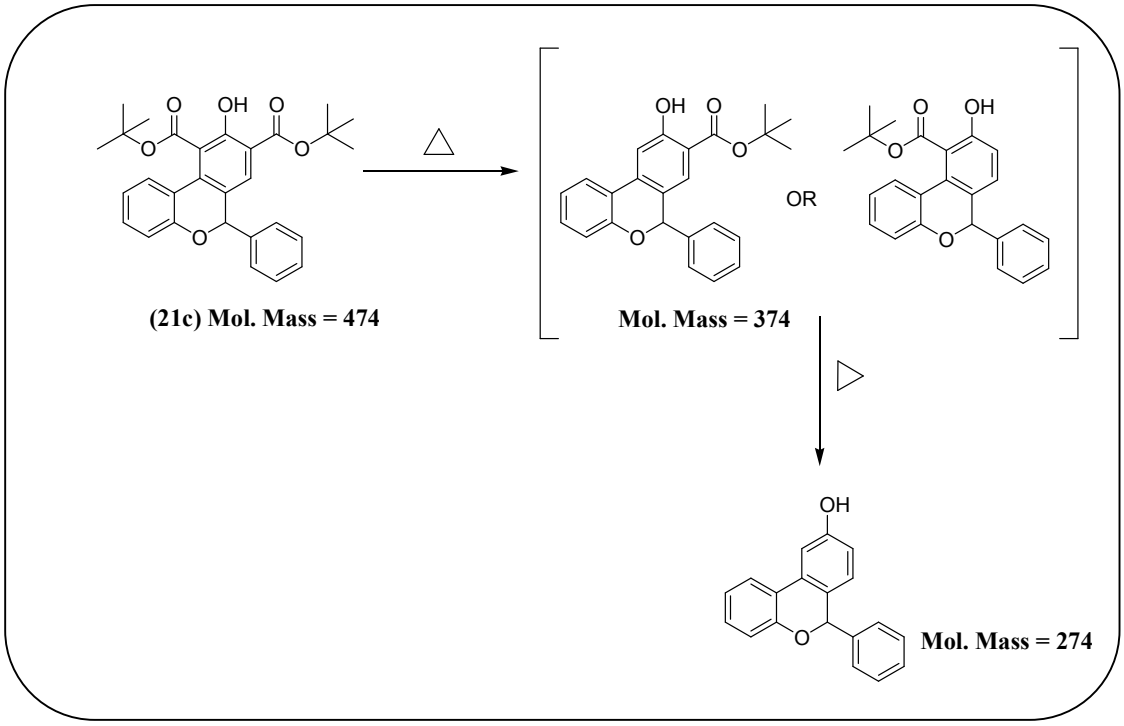


Figure 15. Gas Chromatogram alongwith Mass spectrum of compound **17c**.

Nevertheless, for compound **17c**, appearance of quasi-molecular ion peak at 497 m/z $(M+Na)^+$which was observed in ESI-TOF/MassSpectrum that gave another structural proof that finally compliment the chain of other structural analyses such as IR, ^{1}HNMR and ^{13}CNMR etc.



Scheme 12. Thermal disintegration of compound **17c**

3.2.5 Photophysical studies of selected *6H*-benzo[*c*]chromenes and*6H*-benzo[*c*]chromen-6-ones

Interestingly, *6H*-benzo[*c*]chromenes were found to exhibit UV/Vis and fluorescent properties contrary to *6H*-benzo[*c*]chromenes-6-ones which could not exhibit fluorescent behavior, so I got the opportunity to measure the UV/VIS and fluorescentactivities of some selected *6H*-benzo[*c*]chromenes. The UV/VIS and fluorescent spectra are shown in figure 16.

The fluorescence measurements were done using established protocols[53]. The UV/VIS spectra have shown that compounds **11a** and **11b** have same patterns ofmain absorption peaks and shoulders because of common biaryl lactone moiety.Similarly compounds **14c** and **14e** possess similar spectral behavior. Compound **16b** was found to absorb at longer wavelength than rest of the compounds, but its emission spectrum lies in between the emission spectra of **11**(**a**,**b**) and **14** (**c,e**). The analytical details related to UV/VIS and fluorescent properties of *6H*-benzo[*c*]chromenes and *6H*-benzo[*c*]chromenes-6-ones is summarized in table 5.

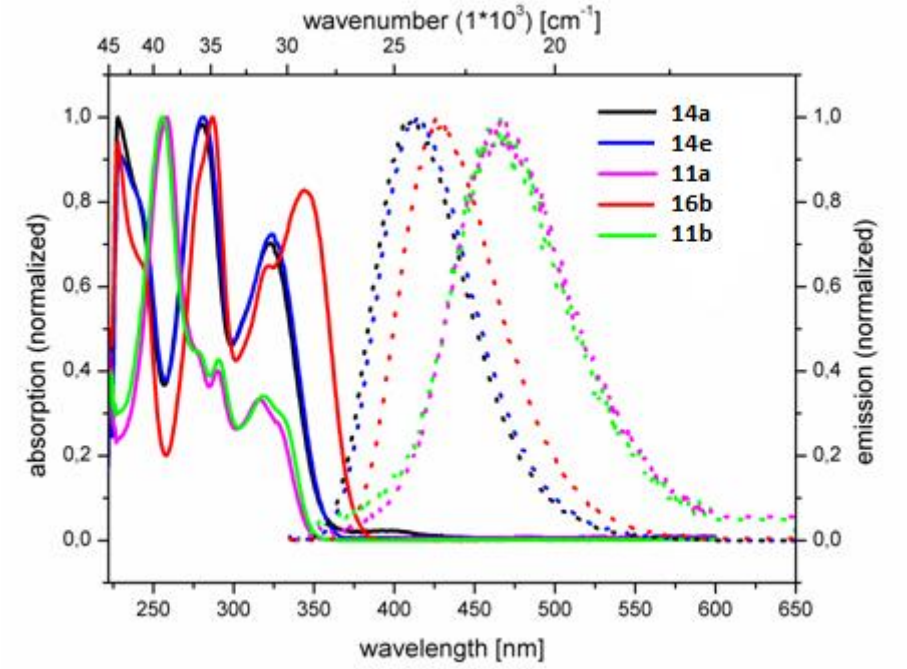


Figure 16. UV/VIS and fluorescent spectra of **11(a, b), 14** (**c, e**), **16b**.

Table 5. The UV/VIS and fluorescent measurement data of **11** (**a, b**), **14** (**c, e**), **16b**.

compound	λ_{abs} [nm], ε_{max} ([10^5 M^{-1} cm^{-1}])	λ_{flu}[nm]	Quantum Yield (Φ_{flu})
14c	228(20140), 280(19800), 323(14230)	412	0.489
14e	230(14260), 281(16390), 324(11870)	414	0.511
11a	258(47030), 290(18770), 316(15550)	470	0.081
16b	228(20500), 287(21640), 344(17820)	426	0.411
11b	256(54790), 319(18700)	466	0.063

The UV/VIS and fluorescent data in table 5 shows that compound **14c**, **14e** and compound **16b** exhibit strong UV-fluorescence as depicted by their relatively high

quantum yield values. Comparison of spectral studies between benzo[*c*]chromenes and benzo[*c*]chromenones with similar substitution patterns surrounding basic nucleus revealed a fact that presence of keto group in the ring **B** overall inhibits the fluorescence activity and it is the biaryl moiety in both kind of compounds that is somehow responsible for the fluorescence emission activity. A detailed study of effect of ring **C** substituents onthe fluorescence emission of benzo[*c*]chromenes and benzo[*c*]chromenones, one could draw out a meaningful statistical correlation at some later stage.

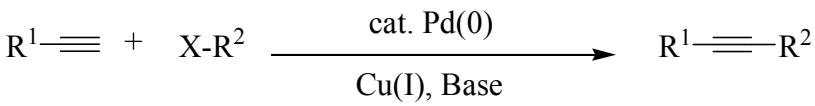
3.3 Conclusion

In conclusion, I synthesized highly functionalized novel *6H*-benzo[*c*]chromenes by base mediated cyclocondensation of chloro substituted chromene-3-carbaldehydes with β-ketoesters and alkyl-3-oxo-pentanedioates. Owing to possess highly strained structures, the physical parameters of their molecular frameworks were discussed. UV/VIS and fluorescent measurements of some selected photo physically active compounds were carried out. A simplified justification for structure-fluorescence activity relationship was established. Biological assay studies of newly synthesized compounds are underway.

4. One-Pot synthesis of biaryl lactones by Sonogashira cross-coupling reactions of 4-Chloro-3-formylcoumarin and subsequent domino [5+1] cyclization/deacetylation reactions with 1, 3-dicarbonyl compounds.

4.1 Introduction

Sonogashira cross-coupling reaction is one of the important class of Palladium catalyzed C-C bond formation processes which involve coupling of a terminal sp hybridized carbon from an alkyne with a sp^2 carbon of an aryl or vinyl halide (or triflate) (Scheme. 13). The reaction was discovered in 1975 by Sonogashira, Tohda and Hagihara. The reaction is usually carried out at room temperature and under basic conditions using a palladium source such as $PdCl_2$ $(PPh_3)_2$ with CuI as co-catalyst.[54]



R^1 = Aryl, Hetaryl, Alkyl, SiR_3
R^2 = Aryl, Hetaryl, Vinyl
X = I, Br, Cl, OTf

Scheme 13. Typical Sonogashira reaction

A complete mechanism of Sonogashira reaction is not well understood mainly because of the involvement of two catalytic species, which are generally supposed to participate in two different but associated catalytic cycles **A** and **B** (Figure 13).[55]

Based on various mechanistic studies however a general compromise states that cycle **A** starts with an active Palladium specie Pd(0) that undergo an oxidative-addition with an Aryl, hetaryl or vinyl halide etc. The next step is transmetallation by copper(I)acetylide which is generated parallel during cycle B. Reductive elimination of the transmetallaed specie affords the coupled product and regenerates the Pd(0) catalyst.[56]

The alkynylation of halogenated aryl systems and halogentated heterocycles under typical sonogashira cross-coupling conditions led to the synthesis of variety of natural products,[57-64] bioactive molecules,[65,66]molecular electronics,[67] conjugated polymers[68]and dendrimers[69] etc.

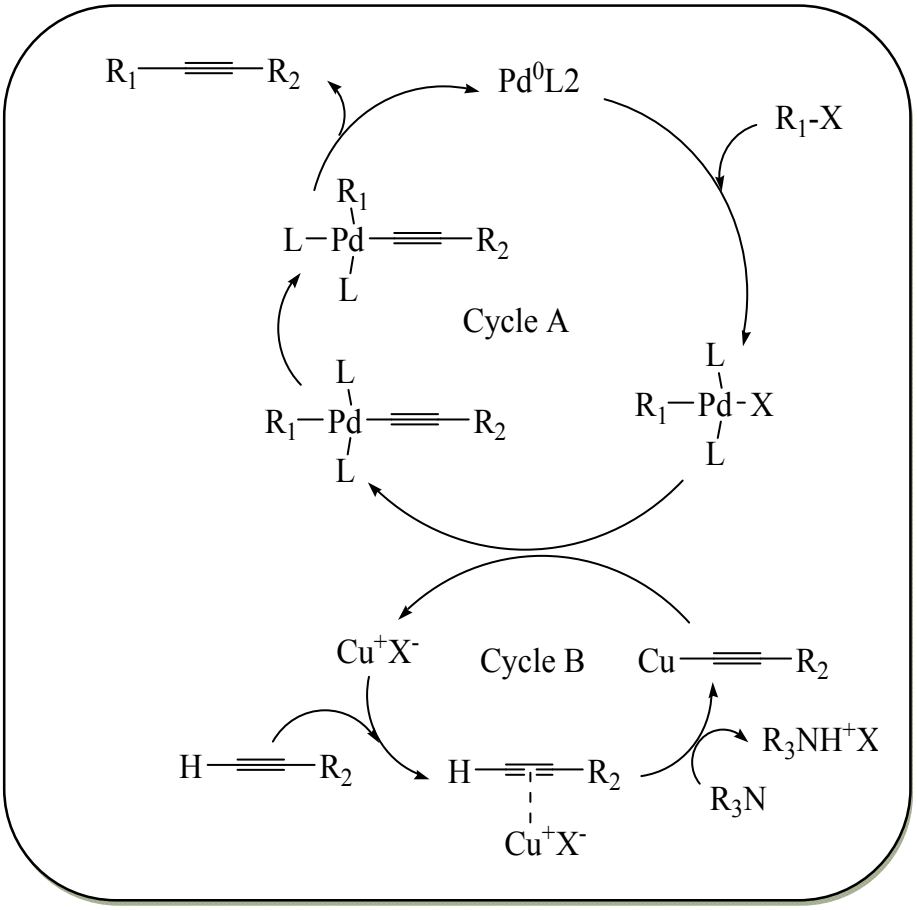


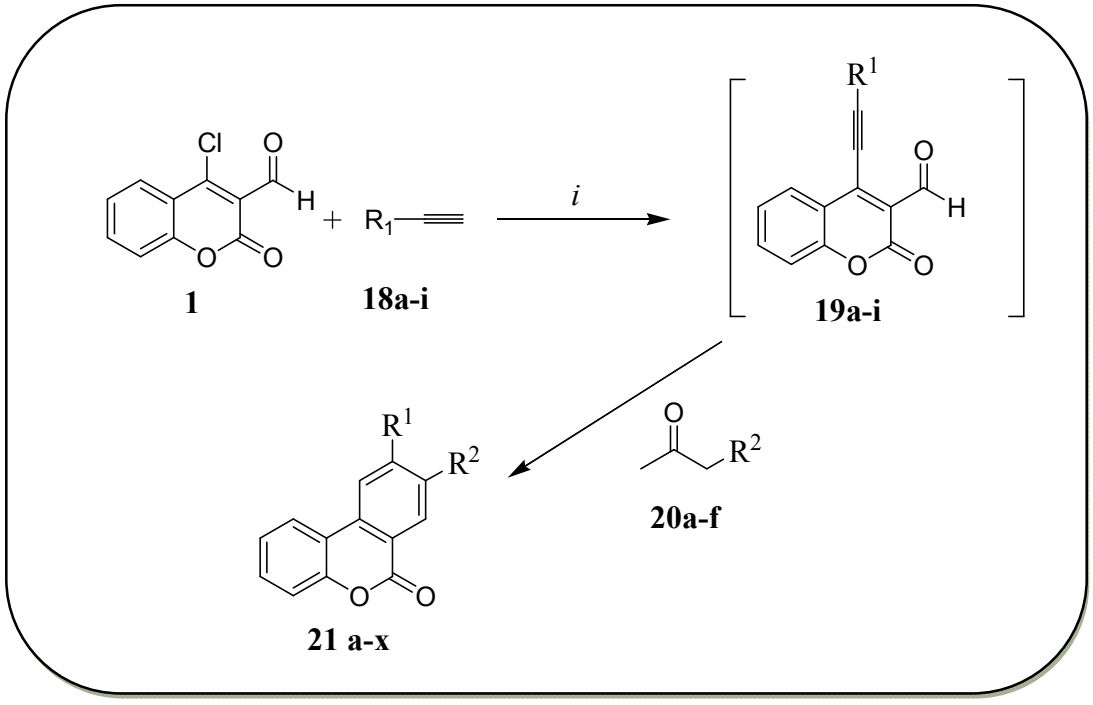
Figure 17. Supposed mechanism of copper co-catalyzed Sonogashira Reactions.[56]

In the group of Prof. Langer Sonogashira cross-coupling strategy have been successfully employed for the syntheses of Polyalkynylated Arenes and Polyalkynylated Heterocycles.[70-76] Moreover within our group Ghazwan *et al* have adapted an advanced and efficient approach employing Sonogashira reactions for the synthesis of fused heterocyles.[77]Muller and co-workers reported the syntheses of variety of Heterocycles by consecutive multicomponent reactions initiated by Sonogashira cross-coupling reactions.[77]However despite these successful findings a step a head in Sonogashira chemistry is to use such reactions as a tool in benzoannulation of a heterocylic substratewas still a dream that needs to be fulfilled.

Literature search revealed that Larock group has done comprehensive work on heterocyclic synthesesby using Sonogashira cross-coupling reactions and subsequent electrophilic and Palladium aided cyclizations.[79]Among these strategies Larock *et al* utilized halo-formyl substituted Arenes and heterocycles as their initial substrates. Sonogashira coupling reactions followed by imination with *t*-butyl amine afforded variety of isoquinoline and Carbolines derivatives.[80]With these positive literary findings; I decided to apply Palladium/Copper co-catalysis on my substrates of interests.

4.2 Results and Discussion

The Sonogashira reactions of substrate **1** with aryl acetylenes and subsequent addition of 1, 3 dicarbonyl compounds afforded the biaryl lactones in one pot fashion (Scheme 14).



Scheme 14. Reagents and Conditions: (i) **1** (1 mmol) **18a-i** (1.5 mmol), $PdCl_2(PPh_3)_2$ (4 mol %), CuI (7 mol %), THF 7-8 mL, K_2CO_3 (1.5 equiv.), 20 °C, 8-10 hrs; (ii) **20a-f** (1.5 mmol)**,** 50 °C, 5-6 hrs.

In the first step I reacted substrate **1** with terminal alkynes **18a-i**, the4-alkynyl-2-oxo-2H-crhomene-3-carbaldehydes **19a-e** intermediate species were formed which

Table 6. Synthesis of biaryl lactones **21a-x**

18	20	21	R^1	R^2	Time (hrs) [a]	Yield (%)[b]
a	**a**	**a**	4-MeC_6H_4	CO_2Me	8+5	48
a	**b**	**b**	4-MeC_6H_4	CO_2Et	8+5	47
a	**c**	**c**	4-MeC_6H_4	COMe	8+5	43
b	**c**	**d**	Ph	COMe	8+5	42
b	**b**	**e**	Ph	CO_2Et	8+5	46
b	**a**	**f**	Ph	CO_2Me	8+5	47
b	**d**	**g**	Ph	CO_2-*i*Pr	8+5	44
c	**d**	**h**	*n*Pr	CO_2-*i*Pr	10+6	41
c	**a**	**i**	*n*Pr	CO_2Me	10+6	38
c	**b**	**j**	*n*Pr	CO_2Et	10+6	43
c	**c**	**k**	*n*Pr	COMe	10+6	41
d	**c**	**l**	*n*Pent	COMe	10+6	43
d	**a**	**m**	*n*Pent	CO_2Me	10+6	45
d	**b**	**n**	*n*Pent	CO_2Et	10+6	44
e	**a**	**o**	*t*BuC_6H_4	CO_2Me	8+5	50
e	**b**	**p**	*t*BuC_6H_4	CO_2Et	8+5	47
e	**e**	**q**	*t*BuC_6H_4	CO_2-*t*Bu	8+5	45
e	**f**	**r**	*t*BuC_6H_4	CO_2.allyl	8+5	44
f	**a**	**s**	2-MeC_6H_4	CO_2Me	8+5	44
g	**a**	**t**	4-*n*Pr-C_6H_4	CO_2Me	8+5	46
h	**a**	**u**	4-FC_6H_4	CO_2Me	8+5	54
h	**b**	**v**	4-FC_6H_4	CO_2Et	8+5	52

i	**a**	**w**	4-(MeO)C_6H_4	CO_2Me	8+5	55
i	**b**	**x**	4-(MeO)C_6H_4	CO_2Et	8+5	54

[a]The first step involves room temp reaction for about 8 to 10 hrs. After addition of 1, 3-dicarbonyl compounds the reaction mixture was heated to 50 °C for 5 to 6 hrs

[b]Yields of isolated products.

were, without isolation, directly transformed to products **21 a-x** by the addition of 1, 3-dicarbonyl compounds **20a-f** into the reaction mixture (Table 6). The formation of one of the intermediates **19a** was proven by its isolation and characterization and then its subsequent transformation into corresponding product **21a**.The structure of compound **21f** was confirmed by X-ray crystallographic analysis (Figure 18).

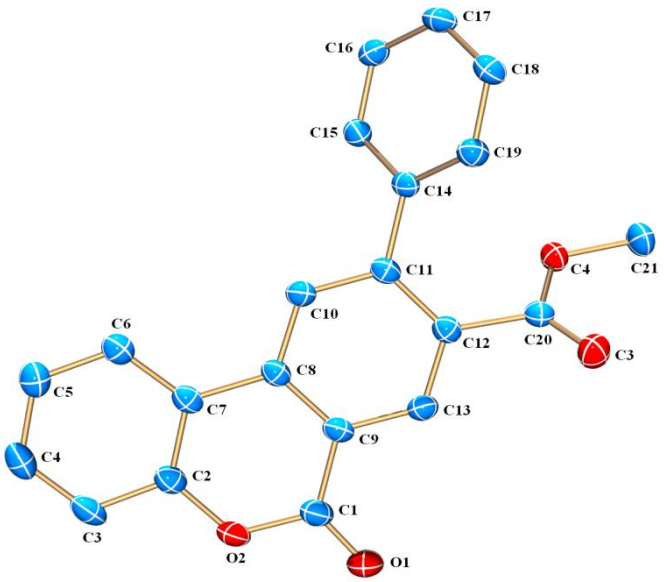


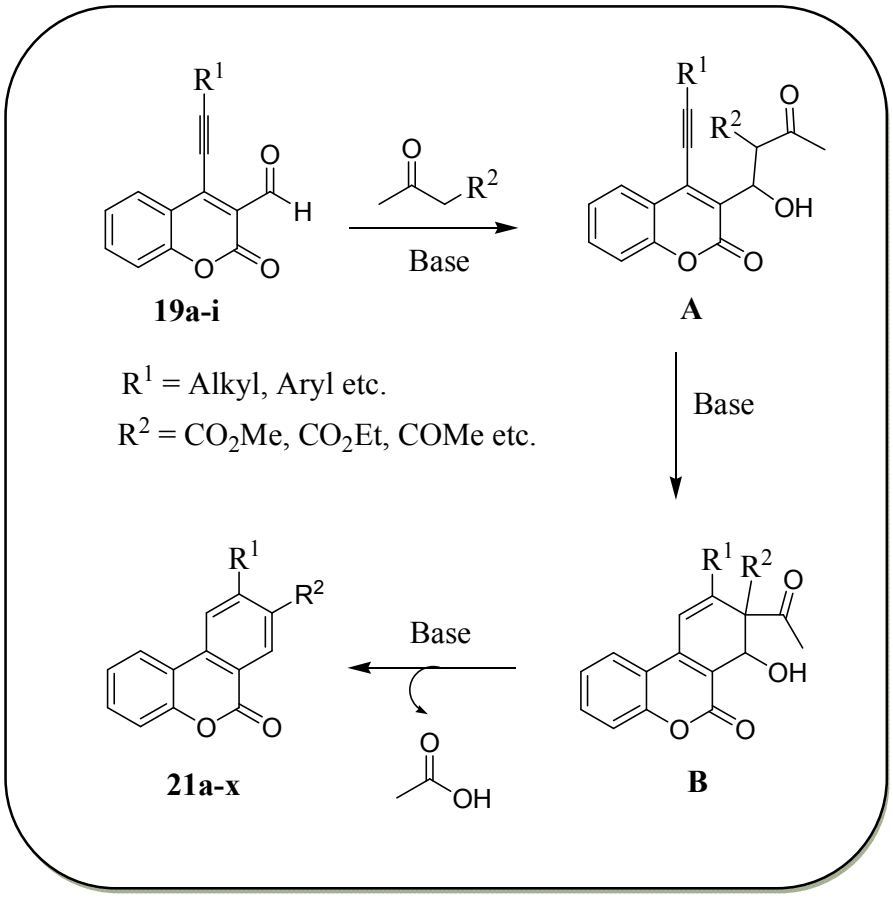
Figure 18. Ortep plot of compound **21f**

The best yields were obtained when $PdCl_2(PPh_3)_2$ was used as the catalyst. The use of other catalyst such as $Pd(PPh_3)_4$ or $Pd(OAc)_2$ were found to be less effective. The real problem i faced was the isolation of intermediate specie especially because of formation of soluble copper acetylide impurity got entangled with alkynl intermediate during column chromatography. Inspired by knoevenagel type deacetylation mechanism of previous successful work (see chapter. 2), I have decided to add directly

a 1, 3-dicarbonyl compound into the reaction vessel. On heating the reaction mixture a cyclization reaction leading to the formation of substituting ring **C** of biaryl lactone accomplished successfully.

4.2.1 Proposed Mechanism

The formation of the products can be explained by base-mediated attack of the 1, 3-dicarobonyl compound on the aldehyde group in knoevenagel fashion to give intermediate **A**, which underwent further a base-mediated cyclization to give intermediate **B**, which subsequently converted to aromatized product by deactylation (Scheme 15). The overall process can be envisaged as a formal [5+1] cyclization. 1, 3-dicaronyl compounds of type such as β-ketoesters and acetylacetone have shown successful reactions whereas both aryl and alkyl substituted alkynes were employed successfully.



Scheme 15. Possible mechanism for the formation of compounds **21a-x**

In the year 2011, a base-catalyzed cyclocondensations of methyl mercaptoacetate with heteroarenes, bearing a formyl and an alkynyl group located in a 1, 2-relationship, have been reported.[81]This reaction may also be presumed as a formal [5+1] cyclization, which proceeds by extrusion of H_2S. Unfortunately, due to the mandatory use of methyl thioacetate, the preparative scope of the reaction is restricted.

4.3 Conclusion

In conclusion, I have reported the one pot synthesis of biaryl lactones by Sonogashira cross-coupling reaction of 4-chloro-2-oxo-*2H*-chromene-3-carbaledehyde and subsequent cyclocondensation with 1, 3-dicarbonyl compounds. The cyclization proceeds by a novel domino [5+1] cyclization/deacytylation reaction. Though from a preparative viewpoint, the substitution pattern of the products is reported somewhere else. However from methodology viewpoint, the domino process reported has, to the best of our knowledge, not been reported so far and might be of general interest. The biological evaluation of synthesized products and the scope of reaction are under investigation.

5. Cyclocondensation reactions of electron rich heterocyclic enamines with heterocyclic chlorovinyl-aldehydes. Synthesis of novel heteroannulatedpyridines.

5.1 Introduction

Heteroannulated pyridines are known to possess anticipated pharmacological activities.[82] Recently pyrrolo [2,3-*b*] pyridines derivatives are evaluatedas effective small molecular inhibitors of tumor necrosis factor alpha, P38 and Cdc7 Kinases. [83,84,85]One important synthetic route to achieve heteroannulated pyridines is the reaction of electorn rich enamines with carbonyl or Halo-carbonyl containing substrates. In the group of Prof. Langer an extensive work has been done on the reaction of electron rich enamines with bis-electrophilic substrates that afforded synthesis of novel benzochromones and benzochromenones heterocycles bearing an extended heteroannulated pyridine ring system.

In one strategy 4-Chloro-3-(trifluoroacetyl)coumarin and 4-chloro-3(methoxalyl)coumarins were treated with electron rich amino heterocycles to afford coumarin fused heteroannulated pyridines.[86] In another approach 3-methoxalylchromone was treated with heterocyclic enamines to give a set of heteroannulated pyridines bearing CO_2Me functionality attached at the alpha position of pyridine ring.[87]Iaroshenko et al[88] have synthesized functionalized heteroannulated 3-nitropyridines by [3+3] cyclocondenation of 3-nitrochromone with electron-rich aminohetrocycles.[88] In another methodology the reaction of heterocyclic enamines with 3-acyl and 3-formyl indoles afforded heteroannulated pyridines. The transformation involved nucleophilic attack of aminoheterocycles on carbonyl functionality of indole that follows indole ring cleavage and subsequent cyclocondenstion to achieve a heteroannulated pyridine ring system in a less common domino style reaction.[89]A general schematic overview of such reactions is given in figure 19.

One important field in the modern drug design is the synthesis of DNA-intercalating agents. These agents bind to DNA via intercalation and exert their action through Topoisomerase II inhibition, an enzyme responsible to control changes in

DNA replication and transcription. Such compounds more or less share common structural characteristics, such as having poly aromatic planar rings, overall linear molecular skeleton and presence of heterocyclic core.[90]

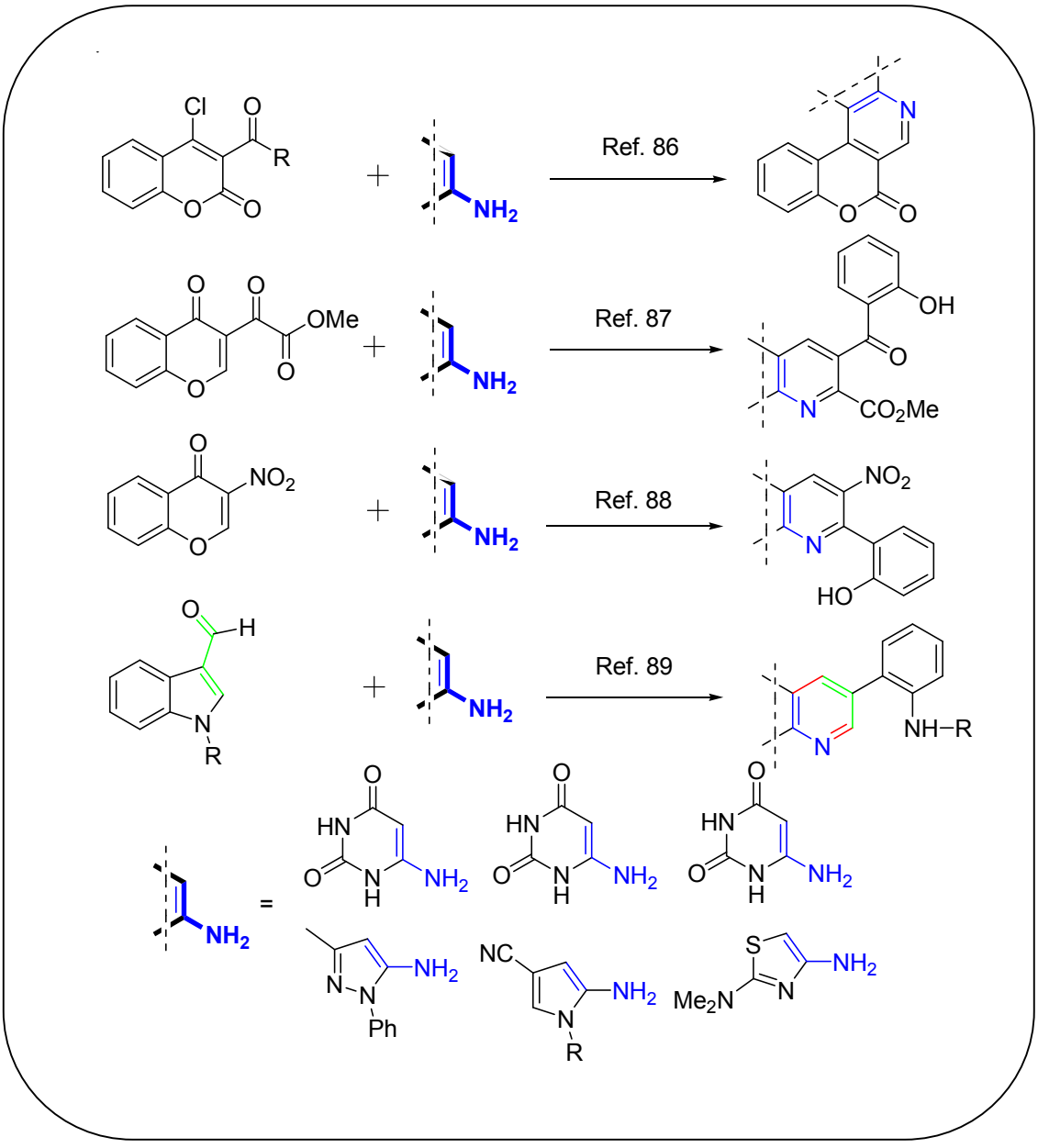


Figure 19. Synthesis of heteroannulated pyridines based on electron rich amino heterochycles

Heterocyclic electron rich enamines bear two different nucleophilic sites. Due to this peculiar nature, their cyclocondenstion reactions with bis-electrophilic

substrates like heterocyclic chlolrovinyl-aledehydes may result two different regiomeric products, which have different forms either linear or non-linear relative to each other (Figure 20).

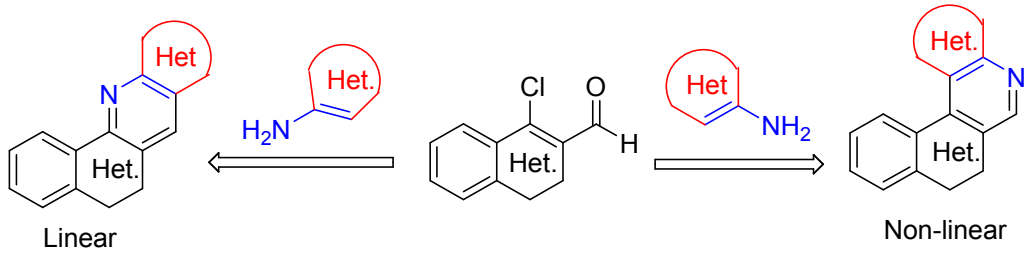
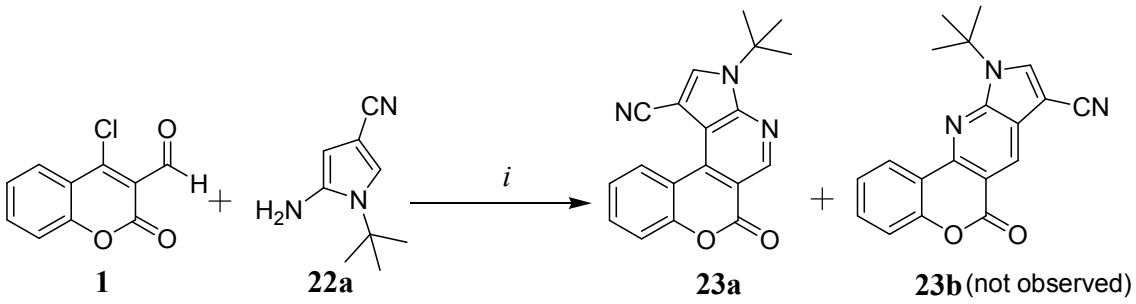


Figure 20. Regiomeric outcome of reactions of electron rich enamines with heterocyclic chlorovinyl-aldehydes

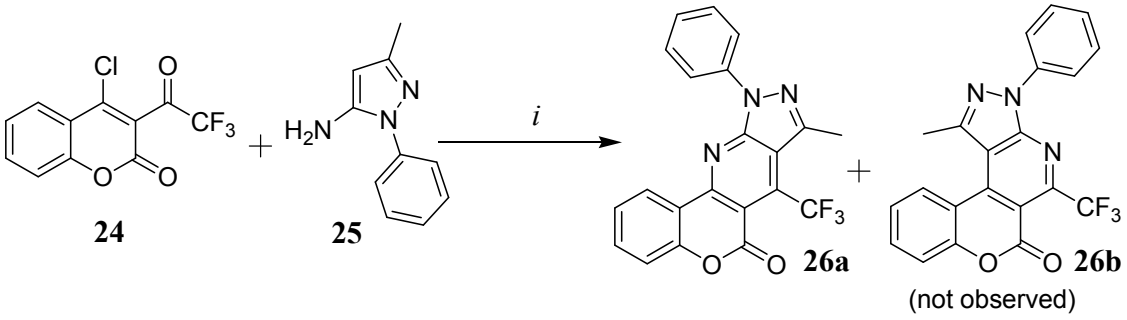
While working on the chemistry of Halo-carbonyl containing compounds laroshenko and co-workers, when treated a heterocyclic chlorovinyl-aldehyde (4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde) (**1**) with a heterocyclic enamine (5-amino-1-tert-butyl-1*H*-pyrrole-3-carbonitrile) (**22a**), they got regioselectively pure non-linear tetracyclic compound **23a** in 40% yield[86](Scheme 16).



Scheme 16. Synthesis of **23a.**Reagents and Conditions: (i), **1** (2 mmol) **22** (2 mmol),TMSCl 1mL, DMF 10 mL, 100-120 °C, 2-10 hrs.

The researchers did not claim to observe the formation of linear regiomer **23b** under given set of reaction conditions. However in another similar study they observed a completely different regiochemistry. When they treated4-chloro-3-(2, 2, 2-trifluoroacetyl-2*H*-chromen-2-one (**24**) with electron rich enamine (3-mehtyl-1-phenyl-

1*H*-pyrazol-5-amine) (**25**), interestingly they got a linear tetracyclic compound **26a** instead of its expected non-linear counterpart **26b**.[86] (Scheme 17).



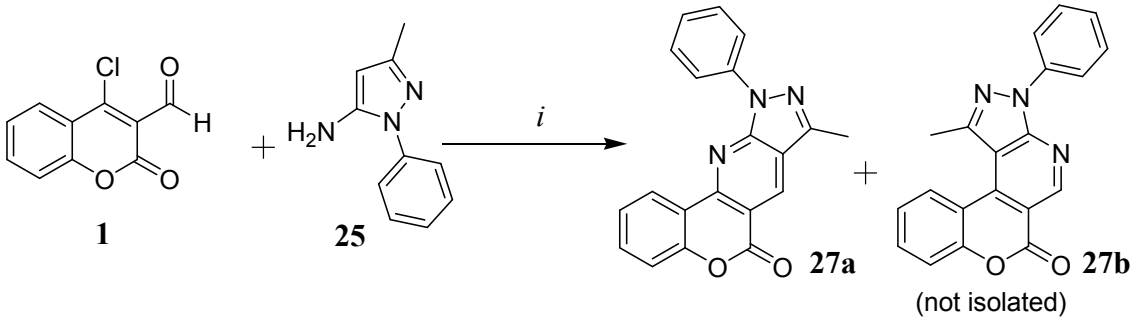
Scheme 17. Synthesis of **26a.**Reagents and Conditions: (i), **1** (2 mmol) **22** (2 mmol),TMSCl 1mL, DMF 10 mL, 100-120 °C, 2-10 hrs.

The successful appearance of such linear tetracyclic compound inspired me to extend the chemistry of electron rich enamines towards chlorovinyl-aldehydes substrates of interests and enlightened my hope to look for tetracyclic heterocyclic compounds with linear configuration relative to their non-linear regiomeric analogues.

5.2 Result and Discussions

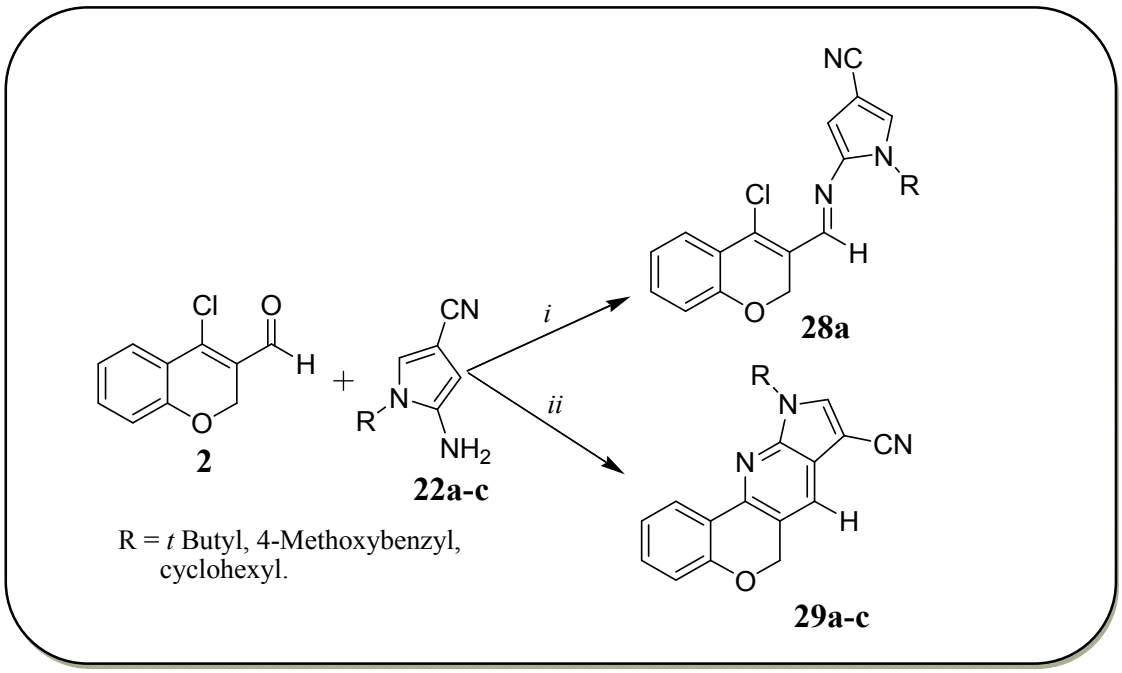
In order to look for the possibility of formation of compound **23b**, I repeated the procedure of Iaroshenko *et al*.[86]and got same results, however i found purification of product **23a** bit difficult because of highly polar nature of DMF and its high boiling point. I carried out the reaction using $AlCl_3$ and MeOH; the conditions successfully applied previously for the synthesis of variety of heteroannulated pyridines. [89]I again observed compound **23a** as major component formed, however I noticed the formation of two more compounds as indicated by TLC, I tried to separate the components but unfortunately could not do so. I changed my strategy and set another reaction of substrate **1** with 3-mehtyl-1-phenyl-1*H*-pyrazol-5-amine **(25)** under similar reaction conditions. Fortunately, I got the desired linear tetracyclic product **27a** in 58% yield (Scheme 18). Indeed, the formation of regiomer **27b** was also observed as indicated by the GC spectra of reaction mixture, which gave two similar molecular ion peaks. Momentarily, taking it out of the scope of current subject, the isolation of regiomer **27b**

was not proceeded further. The structure of linear tetracyclic compound **27a** was confirmed using 1D and 2D NMR techniques.



Scheme 18. Syntheis of **27a.** Reagents and conditions (i), **1** (1 mmol), **25** (1.2 mmol), $AlCl_3$ (3.0 equiv.), MeOH 10 ml, Reflux 8 - 10 hrs.

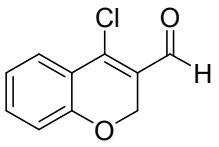
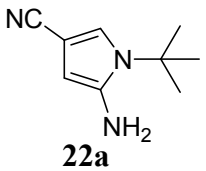
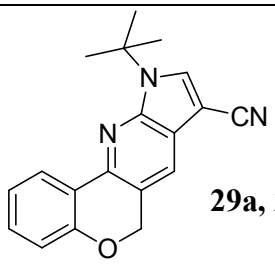
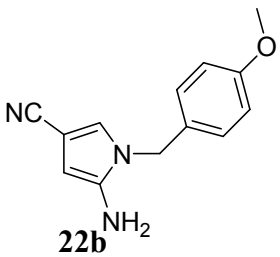
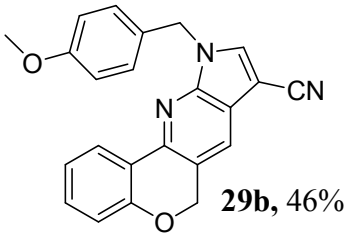
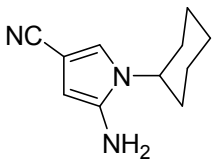
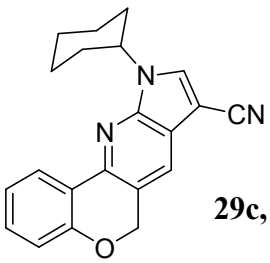
Working on the same line when i treated 4-chloro-2*H*-chromene-3-carbaldehyde **(2)** with 5-amino-1-tert-butyl-1*H*-pyrrole-3-carbonitrile **(22a)** in the presence of TMSCl and DMF, unexpectedly, I got a schiff base **28a** as the only product in a very good yield.



Scheme 19. Reagents and Conditions: (i) **2** (1 mmol) **22a** (1.2 mmol), TMSCl 1mL, DMF 10 mL, 100-120˚C, 2-10 hrs. (ii) **2** (1mmol) **22a-c** (1.2 mmol), $AlCl_3$ (3.0 equiv.), MeOH 10 mL, Reflux 8-10 hrs.

However when the reactions was carried out in $AlCl_3$/MeOH, i got desired cyclic products **29a-c** in affordable yields. A completely different behavior of reaction of 4-chloro-*2H*-chromene-3-carbaldehyde **(2)** and N-substituted α-amino pyrroles under two different set of conditions is shown in (Scheme 19) (Table 7).

Table7. Synthesis of **29a-c**

2	22	Yield (%) (29)[a]
	 **22a**	 **29a,** 28%
	 **22b**	 **29b,** 46%
	 **22c**	 **29c,** 43%

[a]yields of isolated product.

The crystalline nature of schiff base allows me to grow crystals in appropriate solvents. The Ortep plot of schiff base **28a** is given in figure 21.

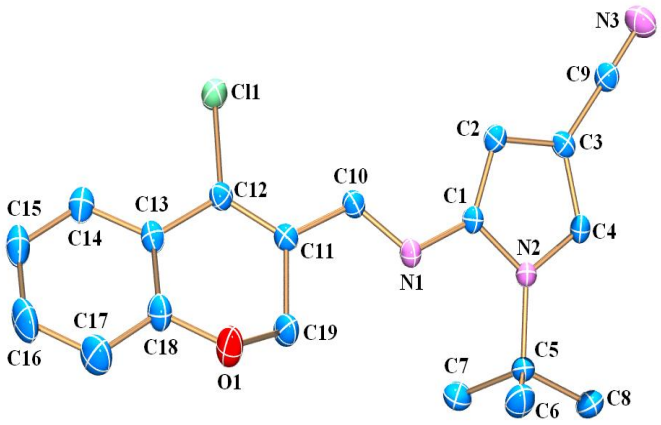
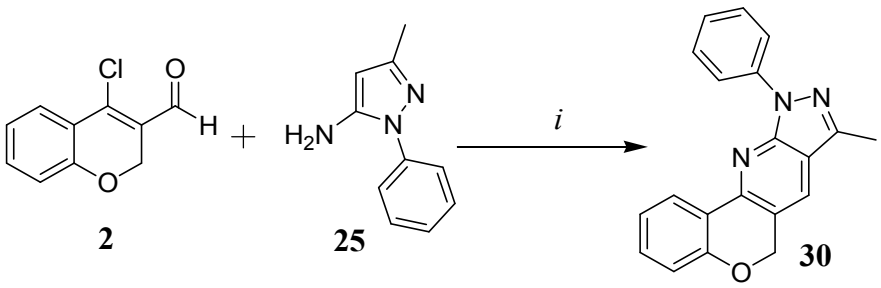


Figure21. Ortep Plot of compound **28a**

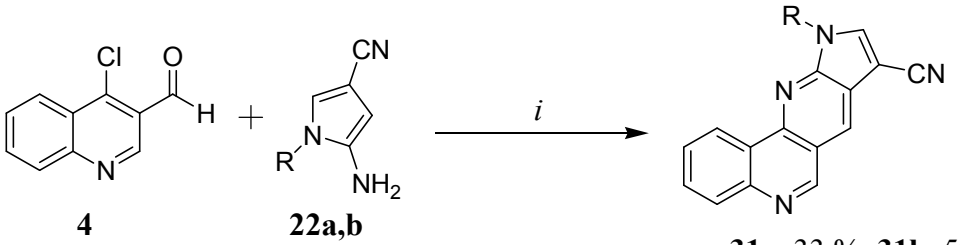
Fortunately, reaction of 4-chloro-*2H*-chromene-3-carbaldehyde **(2)** with 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **(25)** afforded linear heteroannulated compound **30** in 58% yield (Scheme 20).



Scheme 20. Syntheis of **30.** Reagents and conditions (i), **2** (1 mmol), **25** (1.2 mmol), $AlCl_3$ (3.0 equiv.), MeOH 10 ml, Reflux 8-10 hrs.

Inorder to extend the scope of synthesis, I chose to apply the strategy to 4-chloroquinoline-3-carbaldehyde **(4)** a heterocyclic chloroviny-aldehyde substrate analogous to substrate **2**. Unexpectedly, no reaction of substrate **4** with any heterocyclic enamine was observed in TMSCl and DMF, whereas very poor yields were obtained in case of $AlCl_3$ in MeOH reactions conditions. Iaroshenko and co-workers have successfully used glacial acetic acid as solvent and catalyst for the reaction between some selected aminoheterocylces and formylindoles.[89]Luckily, when

i used glacial CH_3COOH as solvent, I got the required annulated pyridines with desired regioselectivity (Scheme 21).



4 **22a,b**

R = *t* butyl, 4-methoxy benzyl

31a, 33 %; **31b,** 52 %

Scheme 21. Reagents and Conditions: (i) **4** (1mmol), **22a,b** (1.2 mmol) glacial CH_3COOH 10 ml, Reflux 8-10 hrs.

The structure of compound **30 and 31b** was confirmed by X-ray crystallographic analysis (Figure 22 and 23).

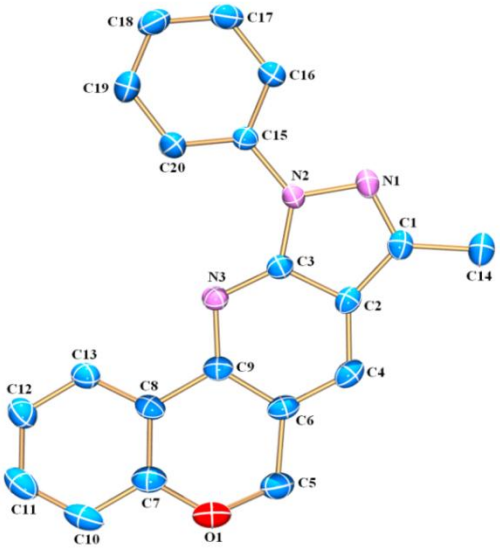


Figure22. The Ortep plot of **30**

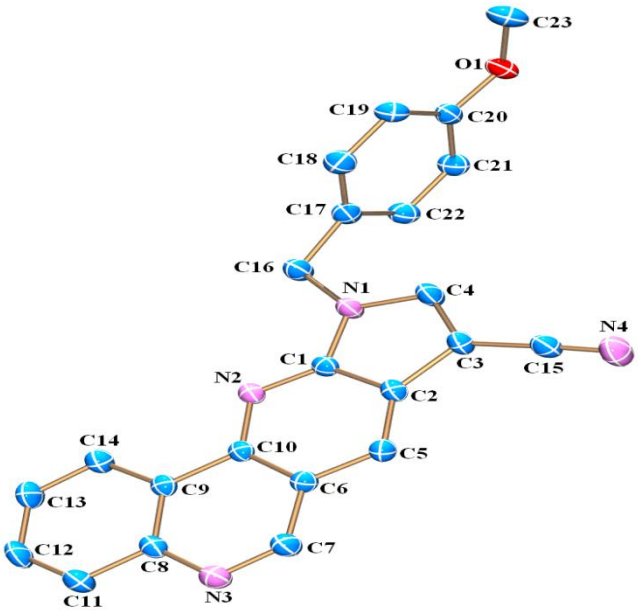
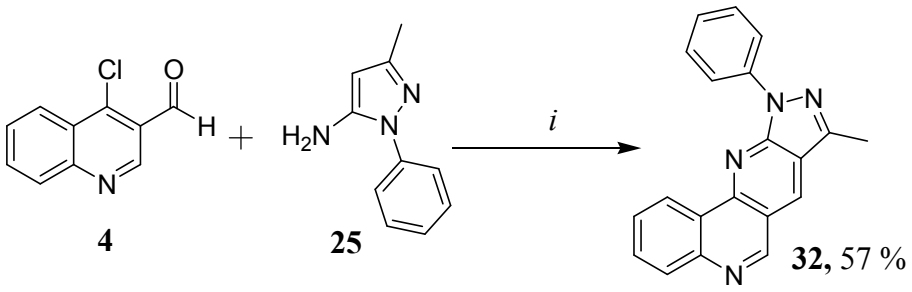


Figure.23 The Ortep plot of **31b**

Fruitfully, under similar reaction conditions, when i treated substrate **4** with 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **(25),** i got a tetracyclic heteroannulated pyridine **32** in 57% yield (Scheme 22).



Scheme 22. Reagents and Conditions: (i) **4** (1mmol), **25** (1.2 mmol) Glacial CH_3COOH 10 ml, Reflux 8-10 hrs.

5.2.1 Proposed Mechanism

Nevertheless, two different set of reaction conditions came up with successful condensation results. By taking into consideration acid surroundings in all the cases, a common mechanism could be postulated involving protonic specie used to activate the chloro-formyl substrate for nucleophilic attack, which is available directly, if acetic

acid is used as solvent or come through Lewis acid-solvent interaction in case of $AlCl_3$in MeOH.[91] However, depending on the binucleophilic nature of heterocyclic enamines, two cyclic modes A & B of the mechanism may be hypothesized for the synthesis of tetracyclic annulated pyridines **29-32 (**Figure 19).

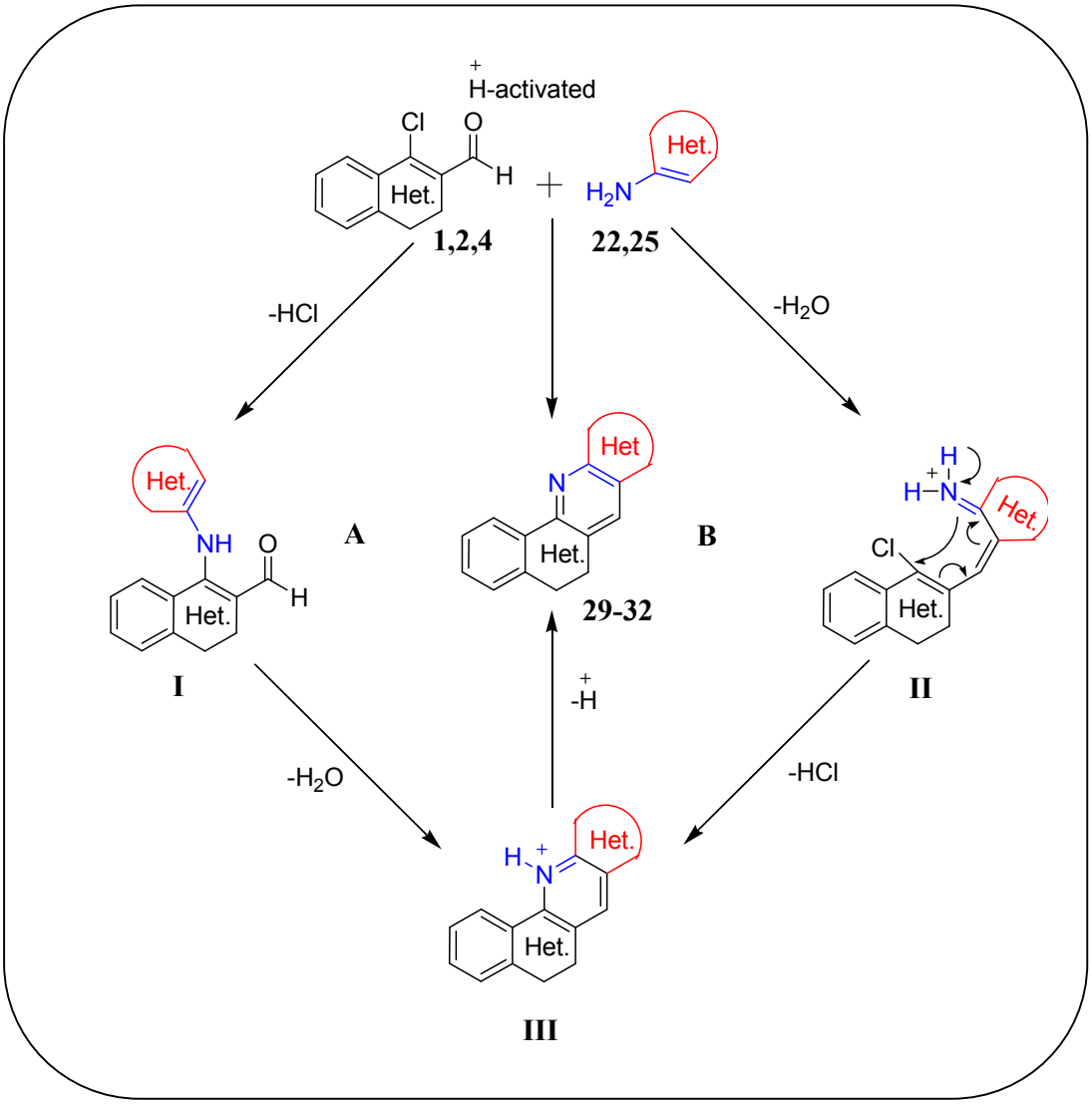


Figure 24. Plausible mechanism for the formation of heteroannulated pyridines.

Cycle A is assumed to proceed by nucleophilic attack of amino group of enamines **22** or **25** on the activated chloro group of substrates **1, 3, 4** leading to intermediate **I**, which underwent intramolecular cyclization via attack of C-4 nuculeophilic site on activated electrophilic carbonyl centre to afford annulated pyrdinium ion III, which on proton removal gave aromatized tetracyclic heteroannulated pyridine product. Cycle B started with the nucleophilic attack of C-4

of enamines **22** or **25** to carbonyl group of heterocyclic chloroviny-aldehydes substrates **1, 3, 4** leading to an iminium intermediate **II**, which is thought to undergo a pericyclic type rearrangement with concomitant removal of HCl to give pyridinium adduct **III**, which underwent aromatization after deprotonation affording desired linear heteroannulated pyridine compounds **29-32**.

Unfortunately I could not isolate the intermediate compounds I and II. However formation of schiff base **28a** as only product during the reaction of 4-chloro-2*H*-chromene-3-carbaldehyde **(2)** with5-amino-1-tert-butyl-1*H*-pyrrole-3-carbonitrile **22a** and the observation of schiff bases contaminations by TLC and GC-MS data for annulations reactions leading to cyclized products led me to conclusion that most probably, the linear tetracyclic annulated pyridines follows path A, whereas nonlinear or curved shape annulated pyridine compounds were formed by attack of amino group to carbonyl functionality leading to schiff base formation, which finally underwent cycloaromatization by the attack of C-4 of enamine to chloro group resulting non-linear heteroannulated pyridines. Based on these observations it is suggested that in literature the mechanistic postulation for the synthesis of non-linear heteroannulated pyridines via attack of C-4 site of enamine to chloro group first could be revised and reevaluated.

5.3 Conclusion

In conclusion, I have reported synthesis of novel heteroannulated pyridines of pharmacological interests. Different reaction conditions were used successfully for the reactions of heterocyclic enamines such as 2-aminopyrrole and 2-aminopyrazole with heterocyclic chlorovinyl-aldedhydes substrates to afford novel tetracyclic linear annulated pyridines. Anticancer evaluation of these heterocyclic compounds is under process. Moreover, we are in preparation to extend further the scope towards the reaction of variety of heterocyclic enamines with different bi-electrophilic substrates.

6 Experimental Section

6.1 Technique and Equipment

6.1.1 **^{1}H NMR Spectroscopy:** Bruker AM 250, Bruker ARX 300; δ = 0.00 ppm for Tetramethylsilane; δ = 7.26 ppm for ($CDCl_3$); Characterization of the signals: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quintet; sext = sextet, sept = septet, dt = doublets of triplet; td = triplets of doublet etc. All coupling constants are indicated as (*J*).

6.1.2 **^{13}C NMR Spectroscopy:** Bruker AM 250, (62.9 MHz); Bruker: ARX 300, (75 MHz); Ref: = 77.00 ppm for $CDCl_3$. The multiplicity of the carbon atoms was determined by the DEPT 135 and quoted as CH_3, CH_2, CH and C for primary, secondary, tertiary and quaternary carbon atoms, respectively.

6.1.3 **Mass Spectrometry:** AMD MS40, AMD 402 (AMD Intectra), Varian MAT CH 731. High Resolution mass spectroscopy: Finnigan MAT 95 or Varian MAT 311; Bruker FT CIR, AMD 402 (AMD Intecta).

6.1.4 **Infrared Spectrscopy (IR):** Bruker IFS 66 (FT IR), Nicolet FT IR; Nicolet Protégé 460, Nicolet 360 Smart rbit (ATR); KBr, KAP, Nujol, and ATR; Abbreviations for signal allocations: w = weak, m = medium, s = strong, br = broad.

6.1.5 **Elementary analysis:** LECO CHNS-932, Thermoquest Flash EA 1112.

6.1.6 **X-ray crystal structure analysis:** Bruker X8Apex Diffractometer with CCD-Kamera (Mo-Kα and graphite monochromator, λ = 0.71073 Å).

6.1.7 **Melting point:** Micro heating table HMK 67/1825 Kuestner (Buchi-app.). Melting points are uncorrected.

6.1.8 **Column chromatography:** Chromatography was performed over Merck silica gel 60 (0.063-0.200 mm, 70-230 mesh) as normal and/ or over silica

gel 60 (0.040-0.063 mm, 200-400 mesh) as flash chromatography. All solvents were distilled before use.

6.1.9 **Thin layer chromatography:** Merck DC finished aluminum foils silica gel 60 F254 and Macherey finished foils Alugram® Sil G/UV 254. Detection under UV light at 254 nm and/or 366 nm without dipping reagent, as well as with locating agent vanillin-sulfuric acid reagent (1 mL vanillin in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

6.2 Synthetic Procedures

6.2.1 General Procedure for the synthesis of compounds 9a-l

To a solution of 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde (**1**) (100 mg, 0.5 mmol) in THF (10 mL) was added K_2CO_3 (140 mg, 2.0 equiv.). To the stirred solution β-ketoester **8** (1mmol, 2.0 equiv.) was added dropwise. The reaction mixture was allowed to stir at 50 °C and monitored by TLC. After the complete consumption of the starting material **1**, the reaction mixture was acidified using few drops of HCl (1M) and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residues were purified by column chromatography (silica gel, *n*-heptane/EtOAc = 3:2).

6.2.2 General Procedure for the synthesis of compounds 11a and 11b

To a solution of 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde (**1**) (0.5 mmol) in THF (10 mL) was added K_2CO_3 (140 mg, 2.0 equiv.). To the stirred solutiondialkyl-3-oxopentanedioate **(10)** (1 mmol, 2.0 equiv.) was added dropwise. The reaction mixture was allowed to stir at 50 °C and was monitored by TLC. After the complete consumption of the starting material **1**, the reaction mixture was acidified using few drops of HCl (1M) and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residues were purified by column chromatography (silica gel, *n*-heptane/EtOAc=3:2).

6.2.3 General Procedure for the synthesis of compound14a-c, e, m

To a solution of 4-chloro-*2H*-chromene-3-carbaldehyde (**2**) (1 mmol) in DMF (10 mL) was added Cs_2CO_3 (650 mg, 2.0 equiv.). To the stirred solution was drop wise added the corresponding β-ketoester (2 mmol, 2.0 equiv.). The reaction mixture was allowed to stir at 50 °C and monitored by TLC. After the complete consumption of the starting material **2**, the reaction mixture was acidified using few drops of HCl (1M) and was extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residues were purified by column chromatography (silica gel, *n*-heptane/EtOAc = 4:1).

6.2.4 General Procedure for the synthesis of compound 16a-c

To a solution of 4-chloro-*2H*-chromene-3-carbaldehyde (**2**) (1 mmol) in THF (10 mL) was added K_2CO_3 (140 mg, 2.0 equiv.). To the stirred solutiondialkyl-3-oxopentanedioates (**10**) (2 mmol, 1.2 equiv.) was added dropwise. The reaction mixture was allowed to stir at 50 °C and was monitored by TLC. After the complete consumption of the starting material**2**, the reaction mixture was acidified using HCl (1M) and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residues were purified by column chromatography (silica gel, *n*-heptane/EtOAc = 3:2).

6.2.5 General Procedure for the synthesis of compound 17a-c

To a solution of 4-Chloro-2-phenyl-*2H*-chromene-3-carbaldehyde (**3**) (1 mmol) in DMF (10 mL) was added K_2CO_3 (140 mg, 2.0 equiv.). To the stirred solutiondialkyl-3-oxopentanedioate (**10**) (2 mmol, 1.0 equiv.) was added dropwise. The reaction mixture was allowed to stir at 50 °C and monitored by TLC. After the complete consumption of the starting material **3**, the reaction mixture was acidified using HCl (1M) and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, *n*-heptane/EtOAc = 3:2).

6.2.6 General Procedure for the synthesis of compound 21a-x

To a solution of **1** (1.0 mmol) in THF (7-8 mL) were added K_2CO_3 (180 mg, 1.5 equiv.). Under continuous supply of Argon was added $PdCl_2(PPh_3)_2$ (4 mol %) and CuI (7 mol %) followed by drop wise addition (after an interval of 2-5 min) of substituted terminal acetylene **18** (1.5 equiv.). The reaction mixture was allowed to stir at room temperature for 8 to 10 h and monitored by TLC. To the same reaction vessel was dropwise added the 1, 3-dicarbonyl compound **20** (1.5 equiv.). The reaction was then stirred at 50 °C for 5 to 6 h. After completion of reaction, the reaction mixture was acidified by addition of a few drops of hydrochloric acid (1 M). The mixture was then extracted with ethyl acetate. The solvent was removed under reduced pressure. The

residue was purified by column chromatography (silica gel, *n*-heptane/EtOAc = 3:2 and 4:1).

6.2.7 General Procedure for the synthesis of compound 29a-c and 30

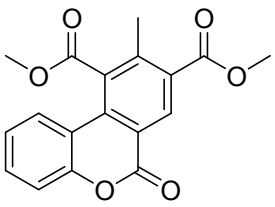
4-Chloro-2*H*-chromene-3-carbaldehyde (**2**) (1 mmol) was treated with each ofheterocyclic enamines **22** and **25** (1.2 mmol) in 10-15 mL of dry MeOH in separate reactions. To each reaction mixture anhydrous $AlCl_3$ (3 equiv.) was added. The reaction mixture was refluxed under moisture free environment for 8-10 hrs. The solid residue formed was filtered and washed with cold MeOH. The solid was again dissolved in hot MeOH and filtered. The two filtrates obtained were combined, adsorbed on silica gel and purified by chromatography using two solvent systems (silica gel, *n*-heptane/EtOAc = 3:2, chloroform/*n*-heptane = 9:1).

6.2.8 General Procedure for the synthesis of compound 31a, b and 32

4-Chloroquinoline-3-carbaldehyde (**4**) (1 mmol) was treated with each ofheterocyclic enamines **22** and **25** (1.2 mmol) in 10-15 mL glacial acetic acid in separate reactions. The reaction mixtures were allowed to reflux for 10 hrs under moisture free environment. The reaction mixtures were allowed to cool. Acetic acid was evaporated under vacuum. The dried residues were treated with 10 % Na_2CO_3solution and subjected to solvent extraction with ethyl acetate. The ethyl acetate extracts were dried with Na_2SO_4, adsorbed on silica gel and purified by chromatography (silica gel, *n*-heptane/EtOAc = 3:2) to give white crystalline solid.

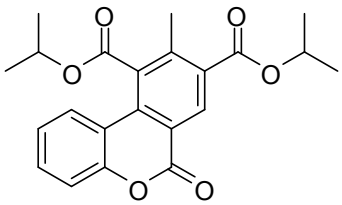
7. Spectroscopic data

Dimethyl 9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9a**): Starting



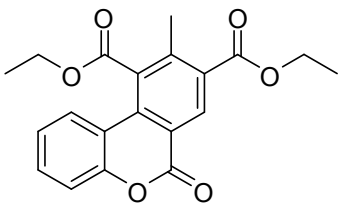
with **1** (100mg, 0.5 mmol) and **8a** (120 mg, 1.0 mmol), **9a** (120 mg, 75%) was isolated as white crystalline solid, m.p. 173-175 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.58 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 3.9 (s, 3H, OCH_3), 7.17-7.23 (m, 1H, ArH), 7.31(dd, J = 8.28 Hz, J = 1.29 Hz, 1H, ArH), 7.42-7.48 (m, 1H, ArH), 7.70 (dd, J = 8.31 Hz, J = 1.29 Hz, 1H, ArH), 8.89 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 18.1 (CH_3), 52.5, 53.1 (OCH_3), 116.1 (C), 118.4 (CH), 119.9 (C), 124.7, 124.7 (CH), 131.1 (C), 131.7 (CH), 131.7, 133.5 (C), 133.8 (CH), 144.0, 151.8 (C), 159.9, 166.0, 170.0 (CO). IR (ATR, cm^{-1}): ν = 2949 (w), 1716 (s), 1599(m), 1429 (m), 1115 (m), 1194 (s), 1292 (w) 1041 (m), 971 (m), 748 (s), 640 (m). GC-MS (EI, 70 eV): m/z (%) = 326 ($[M]^+$, 100), 295 (77), 266 (19), 237 (16), 208 (4). HRMS (EI): calcd. for $C_{18}H_{14}O_6$ ($[M]^+$): 326.07849.Found: 326.07846. Anal.calc. for $C_{18}H_{14}O_6$: C, 66.26; H, 4.32. Found: C, 66.48; H, 4.73.

Diisopropyl 9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9b**): Starting



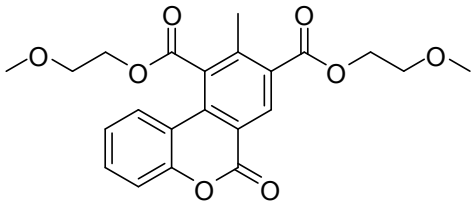
with **1** (100 mg, 0.5 mmol) and **8b** (140 mg, 1.0 mmol), **9b** (137 mg, 72%) was isolated as white crystalline solid,m.p. 122-124°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (d, J = 6.27 Hz, 6H, $2CH_3$), 1.34 (d, J = 6.27 Hz, 6H, $2CH_3$), 2.60 (s, 3H, CH_3), 5.22 (sp, J = 6.27 Hz, 1H, OCH), 5.40 (sp, J = 6.27 Hz, 1H, OCH), 7.17-7.23 (m, 1H, ArH), 7.32(dd, J = 8.31 Hz, J = 1.29 Hz, 1H, ArH), 7.43-7.49(m, 1H, ArH), 7.91 (dd, J = 8.31 Hz, J = 1.29 Hz, 1H, ArH), 8.82 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.9 (CH_3), 21.5, 21.7 ($2CH_3$), 69.5, 70.4 (OCH), 116.39(C), 118.3 (CH), 119.9 (C), 124,3, 125.3, 131.6 (CH), 132.4, 132.4, 132.9 (C), 133.1 (CH), 143.4, 151.7(C), 160.1, 166.6, 169.1 (CO). IR (ATR, cm^{-1}): ν = 2982 (w), 2932 (w), 1739 (s), 1718 (s), 1702 (s), 1603 (m), 1459 (m), 1293 (w), 1223 (s), 1194 (s), 1100 (s), 1039(m), 907 (m), 752 (s), 636 (m). GC-MS (EI, 70 eV): m/z (%) = 382 ($[M]^+$, 34), 323 (36), 298 (100), 297 (89), 281 (30), 252 (15). HRMS (EI): calcd. for $C_{22}H_{22}O_6$ ($[M]^+$): 382.14109.Found: 382.14092. Anal.calc. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 69.26; H, 5.99.

Diethyl 9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9c**): Starting with



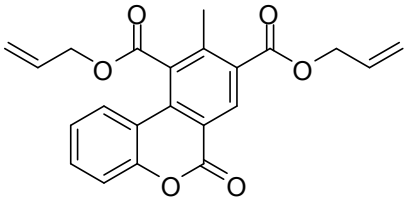
1 (100 mg, 0.5 mmol) and **8c** (130 mg, 1.0 mmol), **9c** (128 mg, 71%) was isolated as white crystalline solid, m.p. 121-123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32-1.38 (m, 6H, $2CH_3$), 2.60 (s, 3H, CH_3), 4.33 (q, J = 7.14 Hz, 2H, OCH_2), 4.46 (q, J = 7.14 Hz, 2H, OCH_2), 7.17-7.23 (m, 1H, ArH), 7.32 (dd, J = 8.10 Hz, J = 1.2 Hz, 1H, ArH), 7.43-7.48(m, 1H, ArH), 7.81 (dd, J = 8.4 Hz, J = 1.5 Hz, 1H, ArH), 8.87 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.8, 14.2, 18.1 (CH_3), 61.7, 62.5 (OCH_2), 116.3 (C), 118.4 (CH), 119.9 (C), 124.5, 125.0, 131.6 (CH), 131.7 (C), 132.1, 133.3 (C), 133.4 (CH), 143.8, 151.8 (C), 160.0, 165.8, 169.6 (CO). IR (ATR, cm^{-1}): ν = 2982 (w), 1712 (s), 1600(m), 1435 (m), 1293 (m), 1091 (s), 749 (s), 640 (m). GC-MS (EI, 70 eV): m/z (%) = 354 ($[M]^+$, 100), 309 (72), 297 (57), 281 (34), 252 (18), 152 (16). HRMS (EI): calcd. for $C_{20}H_{18}O_6$ ($[M]^+$): 354.10979. Found: 354.11034.

Bis(2-methoxyethyl)9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9d**):

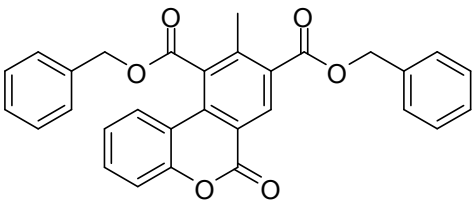


Starting with **1** (100 mg, 0.5 mmol) and **8d** (160 mg, 1.0 mmol), **9d** (120 mg, 60%) was isolated as off-white solid, m.p. 78-80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59 (s, 3H, CH_3), 3.27(s, 3H, OCH_3), 3.35 (s, 3H, OCH_3), 3.62-3.68 (m, 4H, $2OCH_2$), 4.41-4.44 (m, 2H, OCH_2), 4.54-4.57 (m, 2H, OCH_2), 7.15-7.21 (m, 1H, ArH), 7.29 (dd, J = 8.28 Hz, J = 1.29 Hz, 1H, ArH), 7.41-7.46 (m, 1H, ArH), 7.83 (dd, J = 8.28 Hz, J = 1.26 Hz, 1H, ArH), 8.87 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 18.0 (CH_3), 58.9, 59.0 (OCH_3), 64.6, 65.0, 69.8, 70.2 (OCH_2), 116.2 (C), 118.3 (CH), 119.9 (C), 124.6, 125.2 (CH), 131.4 (C), 131.7 (CH), 131.8, 133.5 (C), 133.6 (CH), 143.9, 151.8(C), 159.9, 165.8, 169.5 (CO). IR (ATR, cm^{-1}): ν = 2925 (w), 2880 (w), 2842 (w), 2820 (w), 1711 (s), 1602 (m), 1434 (m), 1213 (s), 1188 (s), 1120 (s), 1046 (m), 752 (s), 642 (m). GC-MS (EI, 70 eV): m/z (%) = 414 ($[M]^+$, 37), 339 (100), 298 (50), 252 (36), 152 (19). HRMS (EI): calcd. for $C_{22}H_{22}O_8$ ($[M]^+$): 414.13092. Found: 414.13143.

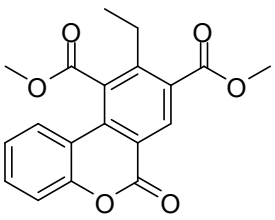
Diallyl 9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9e**): Starting with **1** (100 mg, 0.5 mmol) and **8e** (140 mg, 1.0 mmol), **9e** (145 mg, 60%) was isolated as white crystalline solid,m.p. 112-113 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.60 (s, 3H, CH_3), 4.78 (dt, J = 5.89 Hz, 1.26 Hz, 2H, CH_2), 4.89 (dt, J = 6.20 Hz, 1.12 Hz, 2H, CH_2), 5.24-5.43 (m, 4H, $2OCH_2$), 5.87-6.06 (m, 2H, 2CH), 7.15-7.22 (m, 1H, ArH), 7.32 (dd, J = 8.23, 1.46 Hz, 1H, ArH), 7.43-7.49 (m, 1H, ArH), 7.81 (dd, 8.32 Hz, 1.30 Hz, 1H, ArH), 8.91 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 18.1 (CH_3), 66.3, 67.0 (OCH_2), 116.1 (C), 118.3 (CH), 119.3 (CH_2), 119.9 (C), 120.8 (CH_2), 124.6, 125.2, 130.4 (CH), 131.3 (C), 131.5, 131.7 (CH), 131.8, 133.5 (C), 133.7 (CH), 144.0, 151.8(C), 159.9, 165.3, 169.2 (CO). IR (ATR, cm^{-1}): ν = 3086 (w), 2959 (w), 1721 (s), 1714 (s), 1598 (m), 1434 (m), 1290 (m), 1217 (s), 1185 (s), 1119 (m), 1037 (m), 939 (m), 753 (s).GC-MS (EI, 70 eV): m/z (%) = 378 ([M]$^+$, 94), 337 (28), 321 (100), 309 (64), 293 (47), 275 (18), 237 (23). HRMS (ESI-TOF/MS): calcd. for $C_{22}H_{19}O_6$ ([M+H]$^+$): 379.11761. Found: 379.11721.



Dibenzyl 9-methyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9f**): Starting with **1** (100 mg, 0.5 mmol) and **8f** (192 mg, 1.0 mmol), **9f** (148 mg, 62%) was isolated as white crystalline solid m.p. 142-144 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.53 (s, 3H, CH_3), 5.31 (s, 2H, OCH_2), 5.41 (s, 2H, OCH_2), 6.83-6.90 (m, 1H, ArH), 7.25-7.41(m, 12H, ArH), 7.60 (dd, J = 8.35 Hz, 1.32 Hz, 1H, ArH), 8.89 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 18.1 (CH_3), 67.4, 68.3 (OCH_2), 116.0 (C), 118.2 (CH), 119.9 (C), 124.4, 125.1 (CH), 128.4 (2CH), 128.5 (CH), 128.7 (2CH), 128.8 (2CH), 129.0 (CH), 129.5 (2CH), 131.3 (C), 131.6 (CH), 131.8, 133.5 (C), 133.6 (CH), 133.9, 135.3, 144.0 151.7(C),159.9, 165.5, 169.2 (CO). IR (ATR, cm^{-1}): ν = 3033 (w), 2966 (w), 1733 (s), 1712 (s), 1598(m), 1555 (w), 1454 (w), 1211 (s), 1189 (s), 1120 (m), 1031 (s), 1120 (m), 948 (m), 745 (s), 697 (s). GC-MS (EI, 70 eV): m/z (%) = 478 ([M] $^+$, 72), 387 (70), 371 (43), 369 (17), 344 (15), 281 (10), 91 (100), 65 (12). HRMS (EI): calcd. for $C_{30}H_{22}O_6$ ([M]$^+$): 478.14109. Found: 478.14154.

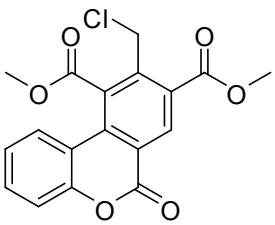


Dimethyl 9-ethyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9g**): Starting with



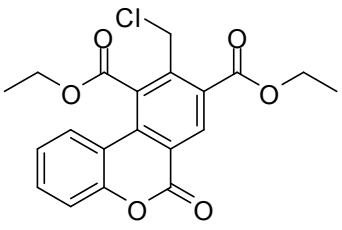
1 (100 mg, 0.5 mmol) and **8g** (130 mg, 1.0 mmol), **9g** (77 mg, 45%) was isolated as white crystalline solid, m.p. 174-176 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.48 Hz, 3H, CH_3), 2.98 (q, J = 7.41 Hz, 2H, CH_2), 3.89 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 7.19-7.21 (m, 1H, ArH), 7.32 (dd, J = 8.22 Hz, J = 1.17 Hz, 1H, ArH), 7.43-7.49(m, 1H, ArH), 7.74 (dd, J = 8.31 Hz, J = 1.23 Hz, 1H, ArH), 8.91 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.8 (CH_3), 24.1 (CH_2), 51.5, 51.9, (OCH_3), 115.3 (C), 117.4 (CH), 119.0 (C), 123.6, 123.8 (CH), 129.7 130.3 (C), 130.7 (CH), 132.8 (C), 133.3 (CH), 148.9 150.8(C),158.9, 164.9, 168.88(CO). IR (ATR, cm^{-1}): ν = 2954 (w), 1716 (s), 1598(m), 1431 (m), 1255 (m), 1216 (s), 987(m), 760 (s) 735 (s), 626 (m). GC-MS (EI, 70 eV): m/z (%) = 340 ([M]$^+$, 61), 325 (100),309 (36), 293 (31), 280 (16), 249 (13). HRMS (EI): calcd. for $C_{19}H_{16}O_6$ ([M]$^+$): 340.09414. Found: 340.09433.

Dimethyl 9-(chloromethyl)-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9h**):



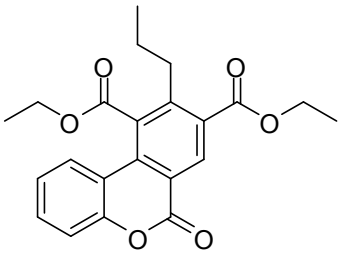
Starting with **1** (100 mg, 0.5 mmol) and **8h** (150 mg, 1.0 mmol), **9h** (130 mg, 72%) was isolated as light orange solid, m.p. 222-224 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89(s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 5.11 (s, 2H, CH_2Cl), 7.21-7.27 (m, 1H, ArH), 7.34 (dd, J = 8.10 Hz, J = 1.20 Hz, 1H, ArH), 7.47-7.528 (m, 1H, ArH), 7.70 (dd, J = 8.10 Hz, J = 1.20 Hz, 1H, ArH), 8.99 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 38.2 (CH_2), 53.0, 53.3 (OCH_3), 116.0 (C), 118.5 (CH), 122.1 (C), 124.8, 125.0 (CH), 130.3, 131.9 (C), 132.2, 134.7 (CH), 142.1, 151.9(C), 159.4, 165.3, 168.9 (CO). IR (ATR, cm^{-1}): ν = 2951 (w), 2922 (w), 1716 (s), 1598(m), 1438 (m), 1234 (s), 1120 (m), 1009 (m), 929 (m), 740 (s), 693 (m). GC-MS (EI, 70 eV): m/z (%) = 360 ([M]$^+$, 46), 309 (100), 324 (33), 293 (11), 266 (19). HRMS (EI): calcd. for $C_{18}H_{13}O_6Cl$ ([M]$^+$): 360.03952. Found: 360.03985.

Diethyl 9-(chloromethyl)-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**9i**):



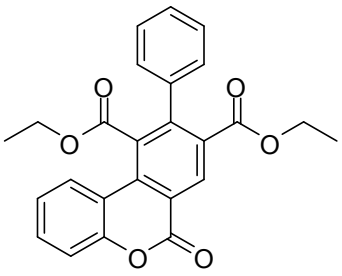
Starting with **1** (100 mg, 0.5 mmol) and **8i** (160 mg, 1.0 mmol), **9i** (139 mg, 73%) was isolated as light yellow flakes, m.p. 108-109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.17 Hz, 3H, CH_3), 1.39 (t, J = 7.17 Hz, 3H, CH_3), 4.37-4.51 (m, 4H, $2CH_2$), 5.11 (s, 2H, CH_2Cl), 7.20-7.25 (m, 1H, ArH), 7.34 (dd, 8.32 Hz, 1.32 Hz, 1H, ArH), 7.46-7.52 (m, 1H, ArH), 7.79 (dd, 8.27 Hz, 1.30 Hz, 1H, ArH), 8.96 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): 12.7, 13.1 (CH_3), 37.3 (CH_2), 61.3, 62.0 (OCH_2), 115.0 (C), 117.4 (CH), 121.1 (C), 123.6, 124.2, 129.8 (CH), 131, 131 (C), 133.4 (CH), 140.8, 150.8(C), 158.4, 163.9, 167.5 (CO). IR (ATR, cm^{-1}): ν = 2974 (w), 2934 (w), 1716 (s), 1600 (m), 1461 (m), 1439 (m), 1298 (m), 1230 (s), 1195 (m), 1013 (s), 743 (s). GC-MS (EI, 70 eV): m/z (%) = 295 ([M]$^+$, 100), 390 (22), 388 (62), 352 (19), 324 (22), 323 (25), 315 (36), 297 (29), 296 (61), 279 (36). HRMS (EI): calcd. for $C_{20}H_{17}O_6Cl$ ([M]$^+$): 388.07082. Found: 388.07071 and for $C_{20}H_{17}O_6{}^{37}Cl$ ([M]$^+$): 390.06787. Found: 390.06869.

Diethyl 6-oxo-9-propyl-6H-benzo[c]chromene-8,10-dicarboxylate (**9j**): Starting with



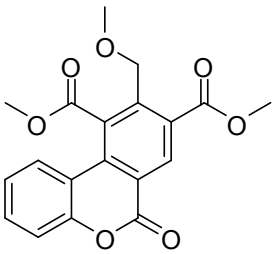
1 (100 mg, 0.5 mmol) and **8j** (158 mg, 1.0 mmol), **9j** (125 mg, 62%) was isolated as white solid, m.p. 104-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.32 Hz, 3H, CH_3), 1.31-1.38 (m, 6H, $2CH_3$), 1.53-1.66 (m, 2H, CH_2), 2.91-2.96 (m, 2H, CH_2), 4.35 (q, J = 7.12 Hz, 2H, OCH_2), 4.45 (q, 7.17 Hz, 2H, OCH_2), 7.17-7.23 (m, 1H, ArH), 7.32 (dd, J = 8.27 Hz, 1.25 Hz, 1H, ArH), 7.43-7.48 (m, 1H, ArH), 7.82 (dd, J = 8.33 Hz, 1.29 Hz, 1H, ArH), 8.87 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): 13.8, 14.2, 14.5 (CH_3), 25.1, 33.6 (CH_2), 61.7, 62.4 (OCH_2), 116.4 (C), 118.3 (CH), 120.0 (C), 124.5, 125.0 (CH), 131.5 (C), 131.6 (CH), 131.7, 133.5 (C), 133.9 (CH), 148.3 151.8(C), 160.0, 165.8, 169.5 (CO). IR (ATR, cm^{-1}): ν = 2965 (w), 2942 (w), 1722 (s), 1712 (s), 1596 (m), 1434 (w), 1320 (w), 1241 (s), 1213 (s), 1190 (s), 1016 (s), 748 (s), 735 (s). GC-MS (EI, 70 eV): m/z (%) = 382 ([M]$^+$, 65), 353 (84), 338 (22), 337 (100), 325 (58), 289 (40). HRMS (EI): calcd. for $C_{22}H_{22}O_6$ ([M]$^+$): 382.14109. Found: 382.14126.

Diethyl 6-oxo-9-phenyl-6H-benzo[c]chromene-8,10-dicarboxylate (**9k**): Starting with



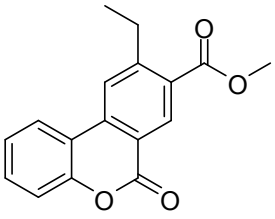
1 (100 mg, 0.5 mmol) and **8k** (200 mg, 1.0 mmol), **9k** (125 mg, 62%) was isolated as white solid, m.p. 95-97 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (q, J = 7.20 Hz, 6H, $2CH_3$), 3.93-4.03 (m, 4H, $2CH_2$), 7.14-7.21 (m, 3H, ArH), 7.31-7.33 (m, 4H, ArH), 7.42-7.47 (m, 1H, ArH), 7.80 (dd, J = 8.30, 1.24 Hz, 1H, ArH), 8.90 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 12.3, 12.6 (CH_3), 60.5, 61.1 (OCH_2), 115.2 (C), 117.3 (CH), 120.3 (C), 123.6, 124.1 (CH), 126.5 (2CH), 127.3 (CH), 127.4 (C), 127.9 (2CH), 129.1 (C), 130.7 (CH), 131.5 (C), 131.8 (CH), 135.6, 145.4, 150.8(C), 158.8, 164.6, 167.3 (CO). IR (ATR, cm^{-1}): ν = 3059 (w), 2980 (w), 1724 (s), 1598 (m), 1444 (m), 1315 (m), 1277 (m), 1213 (s), 1186 (s), 1112 (s), 1016 (s), 748 (s), 698 (s). GC-MS (EI, 70 eV): m/z (%) = 416 ($[M]^+$, 100), 371 (20), 343 (30), 325 (80), 213 (19). HRMS (EI): calcd. for $C_{25}H_{20}O_6$ ($[M]^+$): 416.12544. Found: 416.12603.

Dimethyl-(methoxymethyl)-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate **(9l)**:

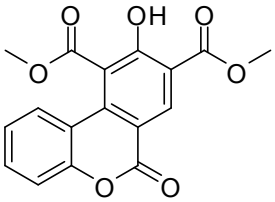


Starting with **1** (100 mg, 0.5 mmol) and **8l** (130 mg, 1.0 mmol), **9l** (139 mg, 77%) was isolated as white solid, m.p. 138-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.2 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.81 (s, 2H, CH_2), 7.18-7.23 (m, 1H, ArH), 7.31 (d, J = 8.36 Hz, 1H, ArH), 7.43-7.48 (m, 1H, ArH), 7.69 (d, 8.26 Hz, 1H, ArH), 8.80 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.7, 51.9, 57.7 (OCH_3), 67.7 (CH_2), 115.2 (C), 117.3 (CH), 120.6 (C), 123.6, 124.2 (CH), 129.9 (C), 130.7 (CH), 130.8 (C), 132.1 (CH), 133.0, 142.2 150.7(C), 158.6, 165.3, 168.4 (CO). IR (ATR, cm^{-1}): ν = 2991 (w), 2945 (w), 2892 (w), 1714 (s), 1597 (m), 1428 (m), 1299 (m), 1280 (m), 1226 (s), 1205 (s), 1083 (s), 1027 (m), 917 (m), 748 (s).GC-MS (EI, 70 eV): m/z (%) = 356 ($[M]^+$, 3), 325 (28), 324 (73), 310 (19), 309 (100), 251 (8), 139 (6). HRMS (EI): calcd. for $C_{19}H_{16}O_7$ ($[M]^+$): 356.08905. Found: 356.08889.

Methyl 9-ethyl-6-oxo-6H-benzo[c]chromene-8-carboxylate (**9g'**): Starting with **1** (100 mg, 0.5 mmol) and **8g** (130 mg, 1.0 mmol), **9g'** (42 mg, 30%) was isolated as white solid, m.p. 196-198 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.48 Hz, 3H, CH_3), 3.13 (q, J = 7.47 Hz, 2H, CH_2), 3.88 (s, 3H, OCH_3), 7.26-7.31 (m, 2H, ArH), 7.43-7.48 (m, 1H, ArH), 7.92 (s, 1H, ArH), 8.01-8.04 (m, 1H, ArH), 8.84 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.5 (CH_3), 28.1 (CH_2), 52.3 (OCH_3), 117.3 (C), 117.9 (CH), 118.9 (C), 123.2 (2CH), 124.7 (CH), 129.9 (C), 131.4, 133.7 (CH), 137.2, 152.0, 153.2 (C), 160.4, 166.3 (CO). IR (ATR, cm^{-1}): ν = 2950 (w), 2922 (w), 2851 (w), 1731 (s), 1714 (s), 1607 (s), 1552 (m), 1429 (m), 1296 (m), 1250 (m), 1227 (s), 1182 (s), 1108 (m), 1112 (m), 754 (s).GC-MS (EI, 70 eV): m/z (%) = 282 ($[M]^+$, 87), 251 (100), 178 (25), 139 (12). HRMS (ESI-TOF/MS): calcd. for $C_{17}H_{15}O_4$ ($[M^+H]^+$): 283.09649. Found: 283. 09663.



Dimethyl 9-hydroxy-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**11a**): Starting with **1** (100 mg, 0.5 mmol) and **10a** (174 mg, 1.0 mmol), **11a** (127 mg, 79%) was isolated as light yellow crystalline solid, m.p. 219-221 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.75 (s, 3H, OCH_3), 2.86 (s, 3H, OCH_3), 7.17-7.23 (m, 1H, ArH), 7.30 (dd, J = 8.37, 1.25 Hz, 1H, ArH), 7.44-7.50 (m, 1H, ArH), 7.70 (dd, J = 8.32 Hz, J = 1.32 Hz, 1H, ArH), 8.96 (s, 1H, ArH), 11.96 (s, 1H, ArOH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 53.23, 53.28 (OCH_3), 113.4, 113.8, 116 (C), 118.4 (CH), 118.6 (C), 124.7, 125.3, 132.3, 135.4 (CH), 137.2, 152.2 (C), 159.8(COH), 162.9, 167.5, 169.1 (CO). IR (ATR, cm^{-1}): ν = 3138 (w), 3095 (w), 2954(w), 1723 (s), 1687 (s), 1593 (m), 1430 (m), 1329 (w), 1290 (m), 1275 (m), 1197 (s), 1176 (s), 1109 (m), 992 (m), 739 (s). GC-MS (EI, 70 eV): m/z (%) = 328 ($[M]^+$, 94), 296, (62), 265 (100), 238 (98). 181 (20), 125 (23). HRMS (EI): calcd. for $C_{17}H_{12}O_7$ ($[M]^+$): 328.05775. Found: 328.05815.



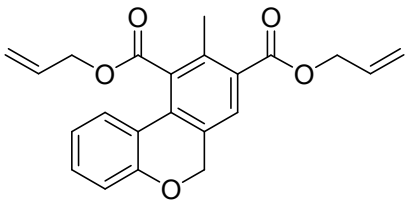
Diethyl 9-hydroxyl-6-oxo-6H-benzo[c]chromene-8,10-dicarboxylate (**11b**): Starting with **1** (100 mg, 0.5 mmol) and **10b** (202 mg, 1.0 mmol), **11b** (147 mg, 81%) was isolated as white crystalline solid, m.p. 172-174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33-1.42 (m, 6H, $2CH_3$), 4.39-4.52 (m, 4H, $2OCH_2$), 7.17-7.22 (m, 1H, ArH), 7.30 (d, J = 7.96 Hz, 1H, ArH), 7.44-7.50 (m, 1H, ArH), 7.80 (d, J = 8.33 Hz, 1H, ArH), 8.96 (s, 1H, ArH), 11.81 (s, 1H, ArOH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.9, 14.1 (CH_3), 62.5, 62.8 (OCH_2), 113.6, 113.7, 116.1 (C), 118.4 (CH), 119.0 (C), 124.6, 125.5, 132.2, 135.2 (CH), 136.9 152.1 (C), 159.9(COH), 163.1, 167.1, 168.8 (CO). IR (ATR, cm^{-1}): ν = 3066 (w), 2977 (w), 1713 (s), 1687 (s), 1592 (m), 1557 (m), 1446 (w), 1331 (m), 1275 (m), 1294 (s), 1191 (s), 1108 (m), 1015 (m), 759 (s), 741 (s). GC-MS (EI, 70 eV): m/z (%) = 356 ($[M]^+$, 52), 311 (18), 265 (46), 238 (100), 311(18), 210 (11), 181 (10). HRMS (EI): calcd. for $C_{19}H_{16}O_7$ ($[M]^+$): 356.08905. Found: 356.08960.

8-acetyl-9-methyl-6H-benzo[c]chromen-6-one (**13**): Starting with **1** (100 mg, 0.5 mmol), **12** (100 mg, 1.0 mmol) and K_2CO_3 (140 mg, 2.0 equiv.) dissolved in THF (10 mL). The reaction mixture was allowed to stir at 50 °C and monitored by TLC. After the complete consumption of the starting material (**1**), the reaction mixture was acidified using HCl (1M) and extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, heptanes/EtOAc = 3:2) to give **13** (65 mg, 54%) as white crystalline solid, m.p. 210-212 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3H, CH_3), 2.93 (s, 3H, CH_3), 7.27-7.32 (m, 2H, ArH), 7.44-7.50 (m, 1H, ArH), 7.89 (s, 1H, ArH), 8.01 (d, J = 8.40 Hz, 1H, ArH), 8.67 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 21.6, 28.3 (CH_3), 116.1 (C), 116.9 (CH), 117.8 (C), 122.2, 123.7, 124.1, 130.5, 131.2 (CH), 135.8, 136.5, 145.3,151.0(C), 159.5 198.6 (CO). IR (ATR, cm^{-1}): ν = 3062 (w), 2964 (w), 2922 (w), 1719 (s), 1681 (s), 1607 (s), 1443 (m), 1430 (m), 1354 (m), 1305 (m), 1175 (s), 1115 (m), 1108 (m), 1035 (m), 892 (s), 754 (s). GC-MS (EI, 70 eV): m/z (%) = 252 ($[M]^+$, 41), 238(15), 237 (100), 181 (23), 152 (21). HRMS (ESI-TOF/MS): calcd. for $C_{16}H_{13}O_3$ ($[M+H]^+$): 253.08592. Found: 253.0855.

Dimethyl 9-methyl-6H-benzo[c]chromene-8,10-dicarboxylate (**14a**): Starting with **2** (194 mg, 1.0 mmol) and **8a** (230 mg, 2.0mmol), **13** (5 mg, 2%) was isolated as white crystalline solid, m.p. 95-97 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.92 (s, 2H, CH_2), 6.92-6.99 (m, 2H, ArH), 7.19-7.25 (m, 1H, ArH), 7.48 (dd, *J* = 8.00 Hz, 0.7 Hz, 1H, ArH), 7.69 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 17.58 (CH_3), 52.1, 52.5 (OCH_3), 68.5 (CH_2), 117.9 (CH), 121.7 (C), 122.2, 125.4, 127.5, (CH), 129.3, 130.5(C), 130.7 (CH), 131.3, 131.3, 137.2, 156.4 (C), 167.2, 170.7 (CO). IR (ATR, cm^{-1}): ν = 2950 (w), 1720 (s), 1601 (m), 1433 (m), 1227 (s) 1095 (m), 754 (s). GC-MS (EI, 70 eV): m/z (%) = 312 ($[M]^+$, 100), 281 (29), 253 (23), 165 (23). HRMS (EI): calcd. for $C_{18}H_{16}O_5$ ($[M]^+$): 312.09923. Found: 312.09843.

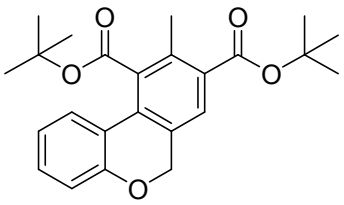
Diisopropyl 9-methyl-6H-benzo[c]chromene-8,10-dicarboxylate (**14b**): Starting with **2** (194 mg, 1.0 mmol) and **8b** (288 mg, 2.0 mmol), **14b** (115 mg, 31%) was isolated as white crystalline solid, m.p. 84-86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* = 1.21 (d, *J* = 6.34 Hz, 6H, CH_3), 1.30 (d, *J* = 6.24 Hz, 6H, CH_3), 2.48 (s, 3H, CH_3), 4.92 (s, 2H, CH_2), 5.14-5.28 (m, 2H, 2OCH) 6.90-6.98 (m, 2H, ArH), 7.18-7.24 (m, 1H, ArH), 7.61-7.64 (m, 2H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): *δ* = 16.3 (CH_3), 20.5, 20.9 ($2CH_3$), 67.6, 67.7 (OCH), 68.6 (CH_2) 116.7 (CH), 120.8 (C), 121.0, 124.9, 125.9 (CH), 128.9, 129.5 (C), 129.5 (CH), 130.2, 131.3, 135.4, 155.4 (C), 165.5, 168.8 (CO). IR (ATR, cm^{-1}): ν = 2981 (w), 1713 (s), 1703 (s), 1602 (w), 1454 (w), 1231 (s), 1216 (s), 1095 (s), 1037 (m), 754 (m). GC-MS (EI, 70 eV): m/z (%) = 368 ($[M]^+$, 100), 309 (40), 283 (89), 239 (30), 165 (31). HRMS (EI): calcd. for $C_{22}H_{24}O_5$ ($[M]^+$): 368.16183. Found: 368.16158.

Diethyl 9-methyl-6H-benzo[c]chromene-8,10-dicarboxylate **(14c)**: Starting with **2** (194 mg, 1.0 mmol) and **8c** (260 mg, 2.0 mmol), **14c** (75 mg, 22%) was isolated as white crystalline solid, m.p. 106-108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, J = 7.19 Hz, 3H, CH_3), 1.33 (t, J = 7.17 Hz, 3H, CH_3), 2.48 (s, 3H, CH_3), 4.26-4.34 (m, 4H, $2OCH_2$), 4.92 (s, 2H, CH_2), 6.91-6.99 (m, 2H, ArH), 7.18-7.24 (m, 1H, ArH), 7.55 (dd, J= 7.99 Hz; 1.45 Hz, 1H, ArH), 7.66 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.8, 14.2, 17.4, (CH_3), 61.1, 61.7 (OCH_2), 68.5 (CH_2), 117.8 (CH), 121.7 (C), 122.1, 125.6, 127.2 (CH), 129.7, 130.2 (C), 130.6 (CH), 131.2, 132.0, 136.8, 156.4 (C), 166.9, 170.3 (CO). IR (ATR, cm^{-1}): ν = 2974 (w), 1717 (s), 1706 (s), 1600(w), 1445 (w), 1235 (s), 1181 (m), 1150 (m), 1017 (m), 774 (s), 764 (s). GC–MS (EI, 70 eV): m/z (%) = 340 ([M] $^{+}$, 100), 295 (34), 267 (21), 165 (19). HRMS (EI): calcd. for $C_{20}H_{20}O_5$ ($[M]^{+}$): 340.13053. Found: 340.12994.



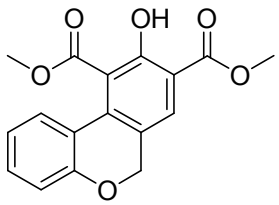
Diallyl 9-methyl-6H-benzo[c]chromene-8,10-dicarboxylate (**14e**):Starting with **2** (194 mg, 1.0 mmol) and **8e** (284 mg, 2.0 mmol), **14c** (140 mg, 38 %) was isolated as white crystalline solid, m.p. 70-72 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.49 (s, 3H, CH_3), 4.73-4.75 (m, 4H, $2OCH_2$), 4.92 (s, 2H, CH_2), 5.16-5.38 (m, 4H, $2CH_2$), 5.76-6.05 (m, 2H, 2CH), 6.89-6.99 (m, 2H, ArH), 7.18-7.25 (s, 1H, ArH), 7.53 (dd, J = 7.94 Hz; 0.70 Hz, 1H, ArH), 7.70 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.5 (CH_3), 65.8, 66.4, 68.5 (CH_2), 117.9 (CH), 118.7, 119.8 (CH_2), 121.6 (C), 122.2, 125.7, 127.4 (CH), 129.3, 130.6 (C), 130.7, 131.0 (CH), 131.3, 131.8 (C), 131.9 (CH), 137.2, 156.4 (C), 166.4, 169.9 (CO). IR (ATR, cm^{-1}): ν = 2918 (w), 1721 (s), 1711 (s), 1598(w), 1444 (w), 1225 (m), 1200 (s), 1173 (s), 1036 (m), 761 (s). GC-MS (EI, 70 eV): m/z (%) = 364 ([M] $^{+}$, 100), 307 (33), 281 (19), 237(15) 165 (21). HRMS (EI): calcd. for $C_{22}H_{20}O_5$ ($[M]^{+}$): 364.13053. Found: 364.12994.

Di-tert-butyl9-methyl-6H-benzo[c]chromene-8,10-dicarboxylate (**14m**): Starting with



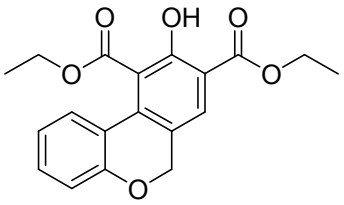
2 (194 mg, 1.0 mmol) and **8m** (316 mg, 2.0 mmol), **14m** (140 mg, 35 %) was isolated as white crystalline solid, m.p. 110-112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (s, 9H, $3CH_3$), 1.52 (s, 9H, $3CH_3$), 2.47 (s, 3H, CH_3), 4.91 (s, 2H, CH_2), 6.90-6.97 (m, 2H, ArH), 7.17-7.23 (m, 1H, ArH), 7.50 (s, 1H, ArH), 7.77 (dd, J = 7.78 Hz; 0.81Hz, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 17.2 (CH_3), 27.9, 28.2 ($3CH_3$) 68.7(CH_2) 81.7, 83.1 (C), 117.5, 121.8 (CH), 122.0 (C), 126.3, 126.6 (CH), 129.1 (C), 130.3 (CH), 131.2, 131.8, 133.3, 135.6, 156.3 (C), 166.7, 169.5 (CO). IR (ATR, cm^{-1}): ν = 2972 (w), 1715 (s), 1699 (s), 1602(w), 1465 (w), 1366 (m), 1240 (s), 1148 (s), 755 (s). GC-MS (EI, 70 eV): m/z (%) = 396 ($[M]^+$, 24), 284 (100), 283 (57), 239 (18), 165 (10). HRMS (EI): calcd. for $C_{24}H_{28}O_5$ ($[M]^+$): 396.19313. Found: 396.19291.

Dimethyl 9-hydroxyl-6H-benzo[c]chromene-8,10-dicarboxylate (**16a**):Starting with **2**

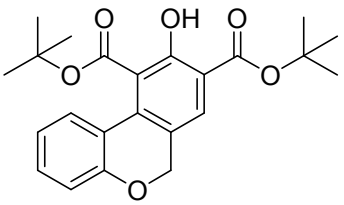


(194 mg, 1.0 mmol) and **10a** (348 mg, 2.0 mmol), **16a** (165 mg, 52%) was isolated as white crystalline solid, m.p. 239-230 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.84 (d, J = 0.39 Hz, 2H, CH_2), 6.90-6.96 (m, 2H, ArH), 7.20-7.25 (m, 1H, ArH), 7.44-7.47 (m, 1H, ArH), 7.62 (s, 1H, ArH), 11.08 (s, 1H, ArOH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.6, 52.7 (OCH_3), 68.3 (CH_2), 110.9 (C), 118.0 (CH), 119.1 (C), 121.2 (C), 122.2 (CH), 124.4 (C), 125.9, 126.7, 131.4 (CH), 134.2, 156.6 (C), 158.9 (COH), 168.2, 169.7 (CO). IR (ATR, cm^{-1}): ν = 3099(w), 2949 (w) 1723 (s), 1667 (s), 1621(m), 1605 (m), 1590 (m), 1438 (s), 1347 (m), 1236 (s), 1216 (s), 1172 (s), 1153 (s), 996 (s), 770(s), 750 (s), 738(s). GC–MS (EI, 70 eV): m/z (%) = 314 ($[M]^+$, 94), 282 (100), 281 (70), 251 (57), 224 (62), 223 (36)139 (76). HRMS (EI): calcd. for $C_{17}H_{14}O_6$ ($[M]^+$): 314.07849. Found: 314.07789.

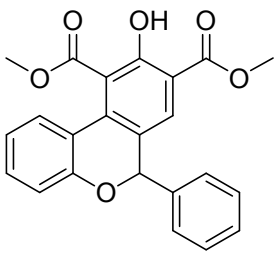
Diethyl 9-hydroxyl-6H-benzo[c]chromene-8,10-dicarboxylate (**16b**):Starting with **2** (194 mg, 1.0 mmol) and **10b** (404 mg, 2.0 mmol), **16b** (222 mg, 65%) was isolated as white crystalline solid, m.p. 145-147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.13 Hz, 3H, CH_3), 1.31 (t, J = 7.13 Hz, 3H, CH_3), 4.28-4.37 (m, 4H, $2OCH_2$), 4.83 (s, 2H, CH_2), 6.88-6.94 (m, 2H, ArH), 7.17-7.23 (m, 1H, ArH), 7.52 (dd, J = 7.86 Hz, 0.61 Hz, 1H, ArH), 7.61 (s, 1H, ArH), 11.15 (s, 1H, ArOH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 12.8, 13.1 (CH_3), 60.8, 60.9 (OCH_2), 67.3 (CH_2), 110.1 (C), 116.9 (CH), 118.5, 120.2 (C), 121.0 (CH), 123.3 (C), 125.3, 125.5 (CH), 130.2 (CH), 132.9, 155.6 (C), 157.9 (COH), 166.8, 168.3 (CO). IR (ATR, cm^{-1}): ν = 3085(w), 2970 (w) 1720 (s), 1666 (s), 1621(m), 1605 (m), 1594 (m), 1404 (m), 1330 (m), 1247 (s), 1216 (s), 1182 (s), 1019 (s), 770(s). GC-MS (EI, 70 eV): m/z (%) = 342 ($[M]^+$, 73), 296 (52), 251 (41), 224 (100), 139 (48). HRMS (EI): calcd. for $C_{19}H_{18}O_6$ ($[M]^+$): 342.10979. Found: 342.10955.



Di-tert-butyl 9-hydroxyl-6H-benzo[c]chromene-8,10-dicarboxylate (**16c**): Starting with **2** (194 mg, 1.0 mmol) and **10c** (516 mg, 2.0 mmol), **16c** (250 mg, 62%) was isolated as white crystalline solid, m.p. 138-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (s, 9H, $3CH_3$), 1.52 (s, 9H, $3CH_3$), 4.85 (d, J = 0.56 Hz, 2H, CH_2), 6.89-6.95 (m, 2H, ArH), 7.17-7.24 (m, 1H, ArH), 7.5 (s, 1H, ArH), 7.76 (dd, J = 7.8 Hz, 1.63 Hz, 1H, ArH), 11.26 (s,1H,ArOH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 26.9 ($3CH_3$), 27.1 ($3CH_3$), 67.5 (CH_2) 81.9, 82.4, 111.3 (C), 116.7 (CH), 120.2, 120.5 (C), 120.8 (CH), 122.8 (C), 125.1, 125.8, 130.0 (CH), 131.8, 155.5 (C), 158.1 (COH), 166.1, 168.0 (CO). IR (ATR, cm^{-1}): ν = 3006 (w), 2981 (w) 1718 (s), 1660 (s), 1618(m), 1605 (m), 1591 (m), 1449 (m), 1391 (m), 1365 (s), 1248(s), 1143 (s), 1038 (s), 796 (s), 773(s). GC–MS (EI, 70 eV): m/z (%) = 297 ($[M]^+$, 100), 298 (56), 139 (10), 253 (8). HRMS (ESI-TOF/MS): calcd. for $C_{23}H_{26}O_6$ ($[M+H]^+$): 399.18022. Found: 399.17966.

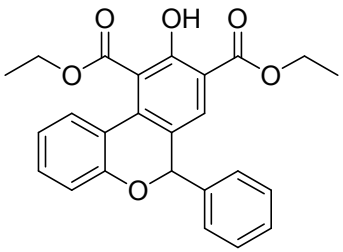


Dimethyl 9-hydroxyl-6-phenyl-6H-benzo[c]chromene-8,10-dicarboxylate (**17a**):



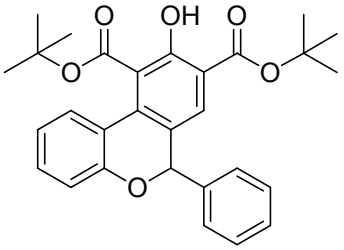
Starting with **3** (270 mg, 1.0 mmol) and **10a** (348 mg, 2.0 mmol), **17a** (210 mg, 54%) was isolated as white crystalline solid, m.p. 208-210 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 5.91 (s, 1H, CH-Ph), 6.88-6.97 (m, 2H, ArH), 7.18-7.29 (m, 7H, ArH), 7.48 (dd, J = 7.94 Hz, 1.4 Hz, 1H, ArH), 11.15 (s, 1H, ArOH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 52.6, 52.8 (OCH_3), 79.4 (CH), 111.0 (C), 118.7 (CH), 119.2, 121.2 (C), 122.3, 125.8 (CH), 127.3 (C), 128.1(2CH), 128.2 (CH), 128.6 (2CH), 128.7, 131.5 (CH), 134.4, 138.2, 155.3, 158.9(COH), 168.4, 169.8 (CO). IR (ATR, cm^{-1}): ν = 3003(w), 2953 (w) 1727 (s), 1674 (s), 1619(m), 1604 (m), 1589 (m), 1440 (s), 1349 (m), 1237 (s), 1155(s), 1143 (s), 994 (m), 989 (m) 796 (s), 773(s), 759 (s), 702 (s). GC-MS (EI, 70 eV): m/z (%) = 390 ([M] $^{+}$, 60), 313 (60), 282 (18), 281 (100), 213 (18). HRMS (EI): calcd. for $C_{23}H_{18}O_6$ ($[M]^{+}$): 390.10979. Found: 390.10943.

Diethyl 9-hydroxyl-6-phenyl-6H-benzo[c]chromene-8,10-dicarboxylate (**17b**):



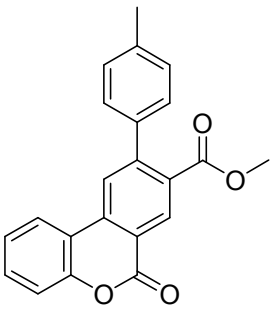
Starting with **3** (270 mg, 1.0 mmol) and **10b** (404 mg, 2.0 mmol), **17b** (258 mg, 60%) was isolated as white crystalline solid, m.p. 143-145 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (td 7.14 Hz, 0.92 Hz, 6H, $2CH_3$), 4.22-4.31 (m, 2H, CH_2), 4.36 (q, 7.14 Hz, 2H, CH_2), 5.95 (s, 1H, CH-Ph), 6.86-6.95 (m, 2H, ArH), 7.16-7.27 (m, 6H, ArH), 7.33 (d, 0.75 Hz, 1H, ArH), 7.54 (dd, 8.03 Hz, 0.69 Hz, 1H, ArH), 11.20 (s, 1H, ArOH). ^{13}CNMR (300 MHz, $CDCl_3$): δ = 13.9, 14.0 (CH_3), 61.88, 62.0 (OCH_2) 79.2 (CH),111.3 (C), 118.6 (CH), 119.6, 121.3 (C), 122.1, 126.0 (CH), 126.9 (C), 128.1 (2CH), 128.2, 128.5, (CH), 128.6 (2CH), 131.4 (CH), 134.0, 138.4 155.1(C), 159.0 (COH), 168.0, 169.4 (CO). IR (ATR, cm^{-1}): ν = 3032(w), 2979 (w) 1730 (s), 1666 (m), 1620(w), 1604 (w), 1461 (m), 1302(m), 1237 (s), 1155(s), 1148 (s), 1021(s), 762 (s) 702 (s). GC-MS (EI, 70 eV): m/z (%) = 418 ([M] $^{+}$, 83), 341 (90), 327 (23), 300 (40), 299 (27)295 (100), 271 (14), 242 (12). HRMS (EI): calcd. for $C_{25}H_{22}O_6$ ($[M]^{+}$): 418.14109. Found: 418.14049.

Di-tert-butyl 9-hydroxyl-6-phenyl-6H-benzo[c]chromene-8,10-dicarboxylate (**17c**):

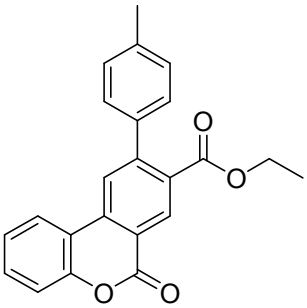


Starting with **3** (270 mg, 1.0 mmol) and **10c** (516 mg, 2.0 mmol), **17c** (304 mg, 66%) was isolated as white crystalline solid, m.p. 163-165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 9H, $3CH_3$), 1.52 (s, 9H, $3CH_3$), 5.93 (s, 1H, CH-Ph), 6.84-6.93 (m, 2H, ArH), 7.13-7.26 (m, 7H, ArH), 7.76 (dd, *J* = 7.95 Hz, 1.36 Hz, 1H, ArH), 11.24 (s, 1H,ArOH). ^{13}CNMR (300 MHz, $CDCl_3$): δ = 26.9, 26.9 ($3CH_3$), 78.2 (CH), 82.0, 82.3, 111.4 (C), 117.3 (CH), 120.2, 120.5 (C), 120.8 (CH), 125.3 (C), 125.6, 126.9 (CH), 127.0, 127.3 (2CH), 127.4, 130.14 (CH), 131.8, 137.5 153.9(C), 158.0 (COH), 166.1, 167.9 (CO). IR (ATR, cm^{-1}): ν = 3003(w), 2971 (w) 1716 (s), 1670 (s), 1605 (m), 1454 (m), 1355(s), 1243 (s), 1142(s), 764 (s), 703 (s). GC-MS (EI, 70 eV): m/z (%) = 297 ($[M]^+$, 100), 374 (30), 298 (22), 373 (18). HRMS (ESI-TOF/MS): calcd. for $C_{29}H_{30}O_6$ ($[M+Na]^+$): 497.19346. Found: 497.1940.

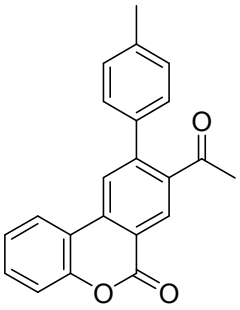
Methyl 6-oxo-9-p-tolyl-6H-benzo[c]chromene-8-carboxylate (**21a**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18a** (170 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21a** (165mg, 48%) was isolated as white crystalline solid, m.p. 139-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 7.21-7.32 (m, 6H, ArH), 7.42-7.48 (m, 1H, ArH), 7.97-8.00 (m, 2H, ArH), 8.77(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 20.2 (CH_3), 51.3 (OCH_3), 116.2 (C), 116.9 (CH), 118.6 (C), 122.2, 123.2, 123.7 (CH), 127.0, 128.1 (2CH), 130.2 (C), 130.4, 131.7 (CH), 135.6, 135.9, 137.3, 147.8, 150.9(C), 159.3, 166.1 (CO). IR (ATR, cm^{-1}): ν = 2954 (w), 2918 (w), 1731 (s), 1606(s), 1227 (m), 1183 (m) 1086 (m), 910(m), 815 (m), 746 (s). GC-MS (EI, 70 eV): m/z (%) = 344 ($[M]^+$, 100), 313 (91), 269 (17), 239 (14), 226 (15). HRMS (EI): calcd. for $C_{22}H_{16}O_4$ ($[M]^+$): 344.10431. Found: 344.10405.



Ethyl 6-oxo-9-p-tolyl-6H-benzo[c]chromene-8-carboxylate (**21b**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18a** (170 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21b** (170mg, 47%) was isolated as white crystalline solid, m.p. 156-157 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.14 Hz, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.13 (q, J = 7.14 Hz, 2H, OCH_2), 7.20-7.31 (m, 6H, ArH), 7.41-7.47 (m, 1H, ArH), 7.96-7.99 (m, 2H, ArH), 8.75(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.8, 21.2 (CH_3), 61.4 (OCH_2), 117.2 (C), 117.9 (CH), 119.6 (C), 123.2, 124.1, 124.7 (CH), 128.1, 129.0 (2CH), 131.4 (CH), 131.8 (C), 132.5 (CH), 136.5, 137.1, 138.2, 148.7 151.9 (C), 160.3, 166.8 (CO). IR (ATR, cm^{-1}): ν = 2947 (w), 2921 (w), 1731 (s), 1715 (s), 1613(s), 1292 (m), 1228 (s), 1184 (m) 1083 (m), 929 (m), 818 (m), 745 (s), 731 (m). GC-MS (EI, 70 eV): m/z (%) = 358 ($[M]^+$,88), 330 (15), 313 (100), 239 (18) 226 (20). HRMS (ESI-TOF): calcd. for $C_{23}H_{19}O_4$ ($[M+H]^+$): 359.12779. Found: 359.12757.



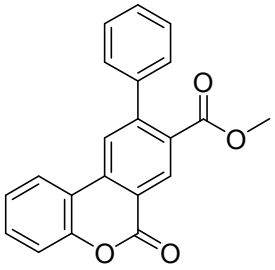
8-Acetyl-9-p-tolyl-6H-benzo[c]chromen-6-one (**21c**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18a** (170 mg, 1.5 mmol) and **20c** (150 mg, 1.5 mmol), **21c** (130mg, 43%) was isolated as white crystalline solid, m.p. 153-155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.09 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.23-7.32 (m, 6H, ArH), 7.42-7.48 (m, 1H, ArH), 7.98-8.01 (m, 2H, ArH), 8.49 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.2, 30.1 (CH_3), 117.3 (C), 117.9 (CH), 119.8 (C), 123.2, 123.7, 124.7, (CH), 128.5, 129.7 (2CH), 130.6, 131.3 (CH), 136.2, 136.5, 139.0, 141.0, 146.8 151.8(C), 160.4, 202.2 (CO). IR (ATR, cm^{-1}): ν = 2922 (w), 1730 (s), 1674 (s), 1602 (s), 1210 (m), 1113 (m), 822 (m), 743 (s). GC-MS (EI, 70 eV): m/z (%) = 328 ($[M]^+$, 58), 313 (100), 269 (22), 239 (18), 220 (20). HRMS (ESI-TOF): calcd. for $C_{22}H_{17}O_3$ ($[M+H]^+$): 329.11722. Found: 329.11748.



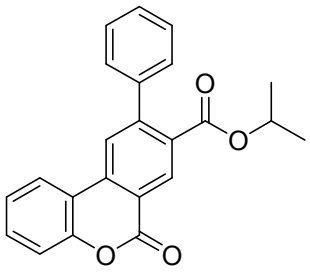
8-Acetyl-9-phenyl-6H-benzo[c]chromen-6-one (**21d**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18b** (150 mg, 1.5 mmol) and **20c** (150 mg, 1.5 mmol), **21d** (132 mg, 42%) was isolated as white crystalline solid, m.p. 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.09 (s, 3H, CH_3) 7.25-7.37 (m, 4H, ArH), 7.40-7.48 (m, 4H, ArH), 7.99-8.02 (m, 2H, ArH), 8.51 (s, 1H, ArH).^{13}C NMR (250 MHz, $CDCl_3$): δ = 30.1 (CH_3), 117.2 (C), 118.0 (CH), 120.0 (C), 123.2, 123.9, 124.7, (CH), 128.6 (2CH), 128.9 (2CH), 128.9, 130.7, 131.4 (CH), 136.2, 139.4, 140.9, 146.8, 151.9(C), 160.3, 201.9 (CO). IR (ATR, cm^{-1}): ν = 2922 (w), 1733 (s), 1684 (s), 1607(s), 1215 (m), 1184 (m), 1069 (w), 822 (m), 753 (s), 703 (s). GC-MS (EI, 70 eV): m/z (%) = 314 ([M]$^+$, 56), 299 (100), 255 (23), 226 (30), 213 (22). HRMS (EI): calcd. for $C_{21}H_{14}O_3$ ([M]$^+$): 314.09375. Found: 314.09378.

Ethyl 6-oxo-9-phenyl-6H-benzo[c]chromene-8-carboxylate (**21e**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18b** (150 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21d** (160 mg, 46%) was isolated as white crystalline solid, m.p. 119-121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.03 (t, J = 7.14 Hz, 3H, CH_3), 4.10 (q, J = 7.14 Hz, 2H, CH_2), 7.23-7.34 (m, 4H, ArH), 7.35-7.47 (m, 4H, ArH), 7.96-7.99 (m, 2H, ArH), 8.77(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.1 (CH_3), 61.4 (OCH_2), 116.2 (C), 116.9 (CH), 118.8 (C), 122.3, 123.1, 123.7 (CH), 127.1 (2CH), 127.2 (CH), 127.3 (2CH), 130.4 (CH), 130.8 (C), 131.6 (CH), 135.5, 139.1, 147.7, 150.9 (C), 159.2, 165.7 (CO). IR (ATR, cm^{-1}): ν = 2977 (w), 2927 (w), 1724 (s), 1709 (s), 1613(s), 1244 (m), 1226 (s), 1185 (m) 1087 (m), 923 (m), 748 (s), 701 (m). GC-MS (EI, 70 eV): m/z (%) = 344 ([M]$^+$, 79), 300 (22), 299 (100), 255 (17), 226 (24). HRMS (EI): calcd. for $C_{22}H_{16}O_4$ ([M]$^+$): 344.10431. Found: 344.10390.

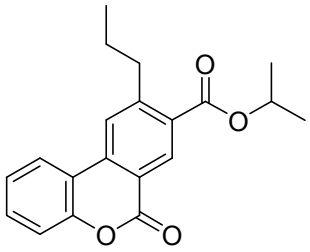
Methyl 6-oxo-9-phenyl-6H-benzo[c]chromene-8-carboxylate (**21f**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18b** (150 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21f** (155 mg, 47%) was isolated as white crystalline solid, m.p. 185-187 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.66 (s, 3H, OCH_3), 7.24-7.34 (m, 4H, ArH), 7.36-7.50 (m, 4H, ArH), 7.98-8.01 (m, 2H, ArH), 8.81(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.3 (OCH_3), 117.2 (C), 118.0 (CH), 119.8 (C), 123.3, 124.3, 124.8 (CH), 128.1 (2CH), 128.3 (3CH), 131.2 (C), 131.5, 132.8 (CH), 136.7, 139.9, 148.8, 152.01(C), 160.2, 167.0 (CO). IR (ATR, cm^{-1}): ν = 2947 (w), 1716 (s), 1608(m), 1228 (s), 1184 (m) 1083 (m), 977 (m), 751 (s), 703 (m). GC-MS (EI, 70 eV): m/z (%) = 330 ($[M]^+$, 97), 299 (100), 271 (8), 255 (20), 226 (25). HRMS (EI): calcd. for $C_{21}H_{14}O_3$ ($[M]^+$): 330.08866. Found: 330.08840.



Isopropyl 6-oxo-9-phenyl-6H-benzo[c]chromene-8-carboxylate (**21g**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18b** (150 mg, 1.5 mmol) and **20d** (200 mg, 1.5 mmol), **21f** (158 mg, 44%) was isolated as white crystalline solid, m.p. 124-126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.03 (d, J = 6.27 Hz, 6H, $2CH_3$), 4.97 (sept, J = 6.27 Hz, 1H, OCH), 7.24-7.34 (m, 4H, ArH), 7.35-7.48 (m, 4H, ArH), 7.97-8.01 (m, 2H, ArH), 8.75(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.4 ($2CH_3$), 69.3 (OCH), 117.2 (C), 117.9 (CH), 119.8 (C), 123.2, 124.0, 124.7 (CH), 128.2 (3CH),128.3 (2CH), 131.4, 132.4 (CH), 132.5, 136.4, 140.2, 148.5, 151.9 (C), 160.3, 166.4 (CO). IR (ATR, cm^{-1}): ν = 2983 (w), 2971 (w), 2933 (w), 1716 (s), 1700 (s), 1614(s), 1247 (m), 1229 (s), 1106 (m) 1088(m), 923(w), 751 (s), 701 (m). GC-MS (EI, 70 eV): m/z (%) = 358 ($[M]^+$, 82), 316 (100), 300 (29), 299 (97), 255(14), 226 (28). HRMS (EI): calcd. for $C_{23}H_{18}O_4$ ($[M]^+$): 358.11996. Found: 358.11963.

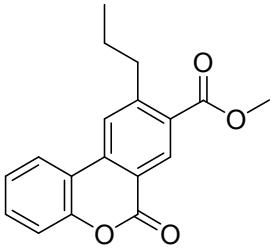


Isopropyl 6-oxo-9-propyl-6H-benzo[c]chromene-8-carboxylate (**21h**): Starting with **1**



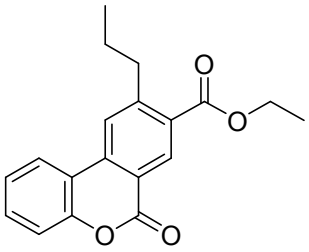
(200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18c** (100 mg, 1.5 mmol) and **20d** (200 mg, 1.5 mmol), **21h** (134 mg, 41%) was isolated as white crystalline solid, m.p. 93°C-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.35 Hz, 3H, CH_3), 1.33 (d, , J = 6.27 Hz, 6H, $2CH_3$), 1.58-1.70 (m, 2H, CH_2), 3.01-3.06 (m, 2H, CH_2), 5.20 (sept., J = 6.27 Hz,1H, OCH), 7.24-7.29 (m, 2H, ArH), 7.40-7.46 (m, 1H, ArH), 7.86 (s, 1H, ArH), 7.98-8.01 (m, 1H, ArH), 8.75(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.8 ($2CH_3$), 24.8, 39.9 (CH_2), 69.0 (OCH), 117.3 (C), 117.8 (CH), 118.8 (C), 123.2, 123.8, 124.6, 131.2, 133.2 (CH), 136.7 (C), 151.3 (2C), 151.9 (C), 160.5, 165.7 (CO). IR (ATR, cm^{-1}): ν = 2958 (w), 2931 (w), 2870 (w), 1722 (s), 1609 (s), 1242 (s), 1234 (s), 1189 (m), 1102 (m) 757 (s). GC-MS (EI, 70 eV): m/z (%) = 324 ([M] $^+$, 19), 282 (100), 267 (57), 265 (41), 249 (17), 152 (17), HRMS (EI): calcd. for $C_{20}H_{20}O_4$ ([M]$^+$): 324.13561. Found: 324.13556.

Methyl 6-oxo-9-propyl-6H-benzo[c]chromene-8-carboxylate (**21i**): Starting with **1**

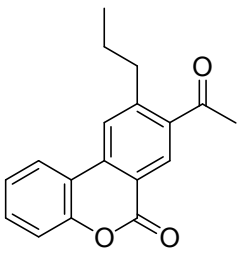


(200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18c** (100 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21i** (114 mg, 38%) was isolated as white crystalline solid, m.p. 100°C-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.38 Hz, 3H, CH_3), 1.57-1.70 (m, 2H, CH_2), 3.03-3.08 (m, 2H, CH_2), 3.86 (s, 3H, OCH_3), 7.25-7.29 (m, 2H, ArH), 7.40-7.46 (m, 1H, ArH), 7.87 (s, 1H, ArH), 7.99 (d, J = 6Hz, 1H, ArH), 8.81(s, 1H, ArH).^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.1 (CH_3), 24.7, 36.9 (CH_2), 52.2 (OCH_3), 117.2 (C), 117.9 (CH), 118.8 (C), 123.2, 123.9, 124.6, (CH), 130.0 (C), 131.3, 133.6 (CH), 136.9, 151.7, 151.9 (C), 160.4, 166.3 (CO). IR (ATR, cm^{-1}): ν = 2955 (w), 2929 (w), 2868 (w), 1714 (s), 1608 (s), 1229 (s), 1181 (s), 1072 (m), 907(w), 747 (s). GC-MS (EI, 70 eV): m/z (%) = 296 ([M] $^+$, 60), 265 100), 266 (20), 249 (34), 165 (11), 152 (16). HRMS (EI): calcd. for $C_{18}H_{16}O_4$ ([M]$^+$): 296.10431. Found: 296.10438.

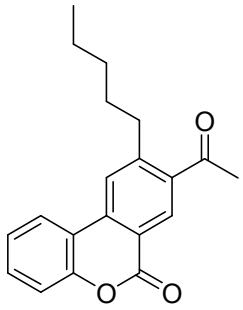
Ethyl 6-oxo-9-propyl-6H-benzo[c]chromene-8-carboxylate (**21j**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18c** (100 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21j** (130 mg, 43%) was isolated as white crystalline solid, m.p. 90 °C-92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.35 Hz, 3H, CH_3), 1.36 (t, J = 7.14 Hz, 3H, CH_3), 1.58-1.70 (m, 2H, CH_2), 3.03-3.08 (m, 2H, CH_2), 4.33 (q, J = 7.14 Hz, 2H,OCH_2), 7.25-7.29 (m, 2H, ArH), 7.41-7.46 (m, 1H, ArH), 7.87 (s, 1H, ArH), 8.00 (d, J = 7.8Hz, 1H,ArH), 8.80 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.1, 14.2 (CH_3), 24.7, 36.9(CH_2), 61.3 (OCH_2), 117.2 (C), 117.9 (CH), 118.8 (C), 123.2, 123.9, 124.6 (CH), 130.6 (C), 131.3, 133.5 (CH), 136.8,151.5, 151.9(C),160.4, 166.0 (CO). IR (ATR, cm^{-1}): ν = 2959 (w), 2930 (w), 2870 (w), 1731 (s), 1707 (s), 1608 (s), 1227 (s), 1179 (s), 1068 (m), 750 (s). GC-MS (EI, 70 eV): m/z (%) = 310 ([M] $^+$, 63), 267 (23), 265 (100), 249 (27), 165 (16), 152 (20). HRMS (EI): calcd. for $C_{19}H_{18}O_4$ ([M]$^+$): 310.11996. Found: 310.11984.



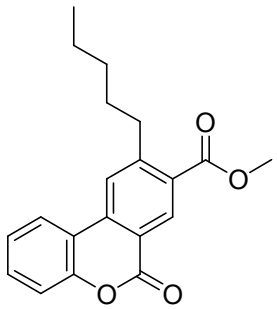
8-Acetyl-9-propyl-6H-benzo[c]chromen-6-one (**21k**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18c** (100 mg, 1.5 mmol) and **20c** (150 mg, 1.5 mmol), **21k** (115mg, 41%) was isolated as white crystalline solid, m.p. 113°C-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.38 Hz, 3H, CH_3), 1.54-1.66 (m, 2H, CH_2), 2.61 (s, 3H, CH_3), 2.93- 2.98 (m, 2H, CH_2), 7.25-7.30 (m, 2H, ArH), 7.42-7.47 (m, 1H, ArH), 7.87 (s, 1H, ArH), 7.99-8.02 (m, 1H, ArH), 8.5 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.1 (CH_3), 24.7 (CH_2), 29.8 (CH_3), 36.6 (CH_2), 117.2 (C), 117.9 (CH), 118.7 (C), 123.2, 124.2, 124.7, 131.4, 131.8 (CH), 136.6, 138.0, 150.5 151.9(C) 160.5, 200.1 (CO). IR (ATR, cm^{-1}): ν = 2964 (w), 2919 (w), 2871 (w), 1721 (s), 1682 (s), 1607 (s), 1229 (s), 1174 (s), 1082 (m), 751 (s). GC-MS (EI, 70 eV): m/z (%) = 280 ([M] $^+$, 13), 266 (19), 265 (100), 178 (11), 152 (9). HRMS (EI): calcd. for $C_{18}H_{16}O_3$ ([M]$^+$): 280.10940. Found: 280.10979.



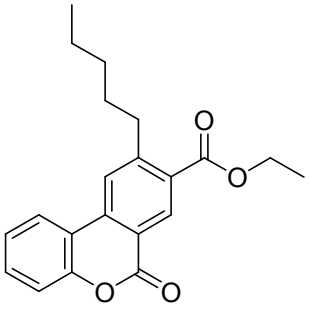
8-Acetyl-9-propyl-6H-benzo[c]chromen-6-one (**21l**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18d** (140 mg, 1.5 mmol) and **20c** (150 mg, 1.5 mmol), **21l** (130mg, 43%) was isolated as white crystalline solid, m.p. 60 °C-62 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81-0.86 (m, 3H, CH_3), 1.26-1.36 (m, 4H, $2CH_2$), 1.51- 1.62 (m, 2H, CH_2), 2.61 (s, 3H, CH_3), 2.94-3.00 (m, 2H, CH_2), 7.19-7.32 (m, 2H, ArH), 7.42-7.49 (m, 1H, ArH), 7.88 (s, 1H, ArH), 8.00-8.03 (m, 1H, ArH), 8.59 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.4 (CH_2), 29.7 (CH_3), 31.3, 31.9, 34.7 (CH_2), 117.2 (C), 117.9 (CH), 118.6 (C), 123.2, 124.2, 124.7, 131.4, 131.8 (CH), 136.7, 137.9, 150.8 151.9(C), 160.5, 200.1 (CO). IR (ATR, cm^{-1}): ν = 2952 (w), 2922 (w), 2854 (w), 1739 (s), 1683 (s), 1609 (s), 1229 (s), 1175 (s), 1077 (m), 749 (s). GC-MS (EI, 70 eV): m/z (%) = 308 ($[M]^+$, 11), 294 (20), 293 (100), 265 (15), 152 (10). HRMS (EI): calcd. for $C_{20}H_{20}O_3$ ($[M]^+$): 308.14070. Found: 308.14118.



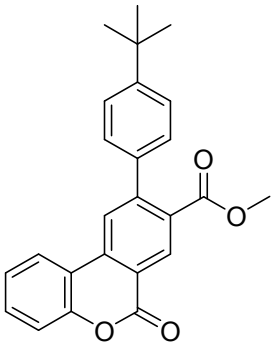
Methyl 6-oxo-9-pentyl-6H-benzo[c]chromene-8-carboxylate (**21m**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18d** (140 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21m** (146 mg, 45%) was isolated as white crystalline solid, m.p. 74°C-76 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, J = 7.05Hz, 3H, CH_3), 1.31-1.34 (m, 4H, $2CH_2$), 1.55- 1.62 (m, 2H, CH_2), 3.06 (t, J = 8.88 Hz, 2H, CH_2), 3.86 (s, 3H, OCH_3), 7.24-7.29 (m, 2H, ArH), 7.40-7.45 (m, 1H, ArH), 7.85 (s, 1H, ArH), 7.99 (d, J = 8.07 Hz, 1H, ArH), 8.79 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.5, 31.2, 31.9, 35.0 (CH_2), 52.2 (OCH_3), 117.2 (C), 117.9 (CH), 118.8 (C), 123.2, 123.8, 124.6 (CH), 130.0 (C), 131.3, 133.7 (CH), 137.0, 151.9, 152.0 (C), 160.4, 166.3 (CO). IR (ATR, cm^{-1}): ν = 2954 (w), 2929 (w), 2855 (w), 1727 (s), 1609 (s), 1227 (s), 1184 (s), 1071 (m), 750 (s). GC-MS (EI, 70 eV): m/z (%) = 324 ($[M]^+$, 77), 293 (100), 268 (52), 249 (47), 237 (25), 152 (16). HRMS (EI): calcd. for $C_{20}H_{20}O_4$ ($[M]^+$): 324.13561. Found: 324.13529.



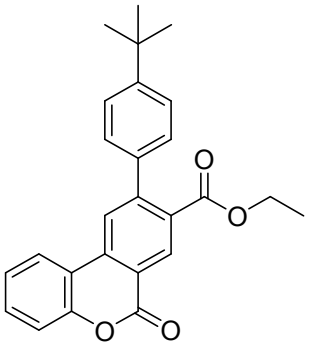
Methyl 6-oxo-9-pentyl-6H-benzo[c]chromene-8-carboxylate (**21n**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18d** (140 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21n** (150 mg, 44%) was isolated as brownish solid, m.p. 78°C-80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, J = 7.24Hz, 3H, CH_3), 1.32-1.38 (m, 6H, $3CH_2$), 1.56-1.66 (m, 2H, CH_2), 3.08 (t, J =7.95 Hz, 3H, CH_3), 4.34 (q, J = 7.24, 2H, OCH_2), 7.26-7.31 (m, 2H, ArH), 7.42-7.48 (m, 1H, ArH), 7.89 (s, 1H, ArH), 8.00 (d, J = 8.16, 1H, ArH), 8.81 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.0, 14.2 (CH_3), 22.5, 31.3, 31.9, 35.0, (CH_2), 61.3 (OCH_2), 117.3 (C), 117.9 (CH), 118.8 (C), 123.2, 123.8, 124.6 (CH), 130.6 (C), 131.3, 133.5 (CH), 136.8, 151.8 151.9 (C), 160.5, 166.1 (CO). IR (ATR, cm^{-1}): ν = 2957 (w), 2930 (w), 2856 (w), 1733 (s), 1614 (s), 1226 (s), 1181 (s), 1070 (m), 747 (s). GC-MS (EI, 70 eV): m/z (%) = 338 ([M] $^+$, 82), 293 (100), 282(40), 249 (44), 267 (37), 254 (29). HRMS (EI): calcd. for $C_{21}H_{22}O_4$ ($[M]^+$): 338.15126. Found: 338.15117.



Methyl 9-(4-tert-butylphenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21o**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18e** (158 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21o** (190mg, 50%) was isolated as white crystalline solid, m.p. 223°C - 225 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 9H, $3CH_3$), 3.66 (s, 3H, OCH_3), 7.22-7.30 (m, 4H, ArH), 7.39-7.46 (m, 3H, ArH), 7.95-7.99 (m, 2H, ArH), 8.75 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 30.3 ($3CH_3$), 33.6 (C), 51.3 (OCH_3), 116.2 (C), 116.9 (CH), 118.5 (C), 122.2, 123.3, 123.7 (CH), 124.3, 126.9 (2CH), 130.2 (C), 130.4, 131.7 (CH), 135.6, 135.8, 147.7, 150.4 150.9 (C), 159.2, 166.2 (CO). IR (ATR, cm^{-1}): ν = 2956 (w), 2904 (w), 1722(s), 1611 (s), 1255 (m), 1228 (m), 1183 (m) 1084(m), 977 (m), 836 (m), 754 (s). GC-MS (EI, 70 eV): m/z (%) = 386 ($[M]^+$, 26),371 (100), 299 (8),252 (10), 171 (7). HRMS (EI): calcd. for $C_{25}H_{22}O_4$ ($[M]^+$): 386.15126. Found: 386.15095.

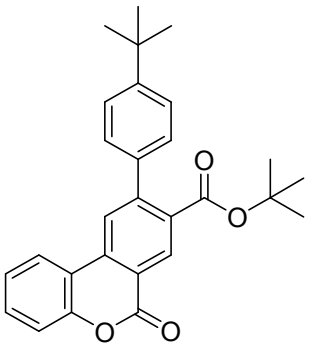


Ethyl 9-(4-tert-butylphenyl-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21p**):



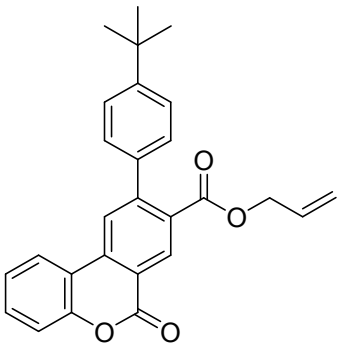
Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18e** (158 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21p** (190 mg, 47%) was isolated as white crystalline solid, m.p. 244 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00 (t, J = 7.50 Hz, 3H, CH_3), 1.31 (s, 9H, $3CH_3$), 4.10 (q, J = 7.50 Hz, 2H, OCH_2), 7.23-7.33 (m, 4H, ArH), 7.39-7.49 (m, 3H, ArH), 7.97-8.01 (m, 2H, ArH), 8.76 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.6 (CH_3), 31.3 ($3CH_3$), 34.6 (C), 61.4 (OCH_2), 117.3 (C), 117.9 (CH), 119.6 (C), 123.2, 124.1, 124.7 (CH), 124.7, 127.9 (2CH), 131.4 (CH), 132.0 (C), 132.6 (CH), 136.5, 137.1, 148.6, 151.4 151.9(C), 160.3, 167.0 (CO). IR (ATR, cm^{-1}): ν = 2957 (w), 2902 (w), 1709 (s), 1611(s), 1251 (m), 1229 (m), 1184 (m) 1015(m), 838 (m), 761 (s). GC-MS (EI, 70 eV): m/z (%) = 400 ($[M]^+$, 26), 385 (100), 299 (8), 252 (9), 14 (6),. HRMS (EI): calcd. for $C_{26}H_{24}O_4$ ($[M]^+$): 400.16691. Found: 400.16711.

Tert-butyl 9-(4-tert-butylphenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21q**):



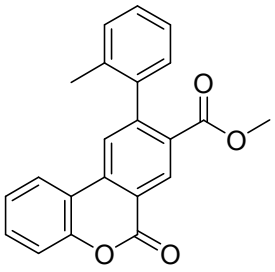
Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18e** (158 mg, 1.5 mmol) and **20e** (200 mg, 1.5 mmol), **21q** (198 mg, 45%) was isolated as white crystalline solid, m.p. 241-243 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.22 (s, 9H, $3CH_3$), 1.31 (s, 9H, $3CH_3$), 7.25-7.33 (m, 4H, ArH), 7.39-7.47 (m, 3H, ArH), 7.96-7.99 (m, 2H, ArH), 8.69 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 26.5, 30.3 ($3CH_3$), 33.6,81.1, 116.4 (C), 116.9 (CH), 18.6 (C), 122.2, 122.8, 123.6 (CH), 124.2, 127.1 (2CH), 130.2 (CH), 130.3 (C), 131.2 (CH), 135.0, 136.4, 147.1, 150.3, 150.8(C), 159.4, 165.4 (CO). IR (ATR, cm^{-1}): ν = 2962 (w), 2931 (w), 1729 (s), 1705 (s), 1611(s), 1251 (m), 1367 (m), 1257 (s), 1157 (s), 1184 (m), 1084(m), 840 (m), 759 (s). GC-MS (EI, 70 eV): m/z (%) = 428 ($[M]^+$, 13), 372 (79), 357 (100), 328 (35), 299 (27), 252 (18). HRMS (EI): calcd. for $C_{28}H_{28}O_4$ ($[M]^+$): 428.19821. Found: 428.19877.

Allyl 9-(4-tert-butylphenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21r**):



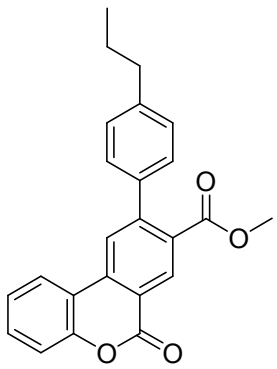
Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18e** (158 mg, 1.5 mmol) and **20f** (200 mg, 1.5 mmol), **21r** (182 mg, 44%) was isolated as white crystalline solid, m.p. 206-208 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 9H, $3CH_3$), 4.53 (d, J = 6.0 Hz, 2H, OCH_2), 5.03-5.09 (m, 2H, CH_2), 5.51-5.69 (m, 1H, CH), 7.25-7.32 (m, 4H, ArH), 7.39-7.44 (m, 3H, ArH), 7.96-8.00 (m, 2H, ArH), 8.77 (s, 1H, ArH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 31.3 ($3CH_3$), 34.7 (C), 66.1 (OCH_2), 117.3 (C), 118.0 (CH), 118.7 (CH_2), 119.6 (C), 123.3, 124.2, 124.7, (CH) 125.3, 128.0 (2CH), 131.3, 131.4, 132.8 (CH), 133.5, 136.6, 137.0, 148.6, 151.5, 152.0(C), 160.3, 166.7 (CO). IR (ATR, cm^{-1}): ν = 2953 (w), 2903, 2866 (w), 1731 (s), 1708 (s), 1610(s), 1249 (m), 1227 (s), 1190 (m) 1084(m), 925(m), 839 (m), 760 (s). GC-MS (EI, 70 eV): m/z (%) = 412 ($[M]^+$, 32), 397 (100), 299 (11), 252 (11), 156 (7),. HRMS (EI): calcd. for $C_{27}H_{24}O_4$ ($[M]^+$): 412.16691. Found: 412.16714.

Methyl 6-oxo-9-o-tolyl-6H-benzo[c]chromene-8-carboxylate (**21s**): Starting with **1**

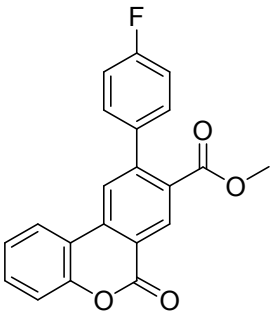


(200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18f** (174 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21s** (152mg, 44%) was isolated as white crystalline solid, m.p. 163-165 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 7.09-7.20 (m, 3H, ArH), 7.24-7.34 (m, 3H, ArH), 7.43-7.49 (m, 1H, ArH), 7.98-8.02 (m, 2H, ArH), 8.78(s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.47 (CH_3), 52.34 (OCH_3), 117.26 (C), 118.00 (CH), 119.76 (C), 123.34, 124.23, 124.78, 125.31, 128.22, 128.74, 129.11, (CH), 131.36 (C), 131.52, 132.74 (CH), 136.69, 138.11, 139.90, 148.94, 151.99(C), 160.32, 167.17 (CO). IR (ATR, cm^{-1}): ν = 2948 (w), 2918 (w), 1724 (s), 1605(s), 1229 (m), 1181 (m) 1082 (w), 972 (m), 757 (s). GC-MS (EI, 70 eV): m/z (%) = 344 ($[M]^+$, 95), 313 (100), 239 (22), 226 (22), 269 (19), 113(10). HRMS (EI): calcd. for $C_{22}H_{16}O_4$ ($[M]^+$): 344.10431. Found: 344.10410.

Methyl 6-oxo-9-(4-propylphenyl)-6H-benzo[c]chromene-8-carboxylate (**21t**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18g** (200 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21t** (174mg, 44%) was isolated as white crystalline solid m.p. 146 °C-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 0.91 (t, J = 7.41 Hz, 3H, CH_3), 1.63 (sext, J = 7.41 Hz 2H, CH_2), 2.59 (t, J = 7.41 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 7.17-7.31 (m, 4H, ArH), 7.41-7.47 (m, 3H, ArH), 7.96-7.99 (m, 2H, ArH) 8.75 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.8 (CH_3), 24.4 (CH_2), 37.7 (CH_2) 52.3 (OCH_3), 117.2 (C), 117.9 (CH), 119.6 (C), 123.3, 124.2, 124.7 (CH), 128.0, 128.4 (2CH), 131.3 (C), 131.4, 132.7 (CH), 136.6, 137.1, 139.9, 143.0 151.9(C), 160.3, 167.2 (CO). IR (ATR, cm^{-1}): ν = 2949 (w), 2929 (w), 2869 (w), 1715 (s), 1610(s), 1451 (m), 1430 (m), 1227 (s), 1187 (m) 1087 (m), 980 (m), 749(s). GC-MS (EI, 70 eV): m/z (%) = 372 ([M]$^+$, 64), 343 (100), 299 (10), 239 (15), 226 (14), 171 (4). HRMS (EI): calcd. for $C_{24}H_{20}O_4$ ([M]$^+$): 372.13561. Found: 372.13521.

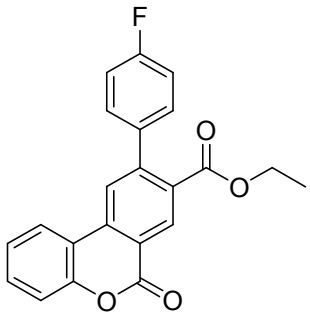


Methyl 9-(4-fluorophenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21u**): Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (28 mg, 4 mol%), CuI (13 mg, 7mol%), **18h** (180 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21u** (185 mg, 54%) was isolated as off-white crystalline solid, m.p. 187°C -189 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.68 (s, 3H, OCH_3), 7.05-7.13 (t, J = 8.64 Hz, 2H, ArH), 7.25-7.33 (m, 4H, ArH), 7.44-7.49 (m, 1H, ArH), 7.96-8.00 (m, 2H, ArH), 8.80 (s, 1H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -113.36 (s, ArF). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.4 (OCH_3), 115.4 (d, $J_{C,F}$ = 21.4 Hz, 2CH), 117.07 (C), 118.03 (CH), 119.98 (C), 123.32, 124.35, 124.83 (CH), 129.95 (d, $J_{C,F}$ = 8.2 Hz, 2CH), 131.02, 131.68 (CH), 136.40 (d, $J_{C,F}$ = 3.7 Hz, C), 136.85 (C), 147.86, 152.01, 159.32 (C), 160.17 (CO), 162.84 (d, $J_{C,F}$ = 248.4 Hz, CF), 166.79 (CO). IR (ATR, cm^{-1}): ν = 3077 (w), 2959 (w), 1727 (s), 1604 (s), 1514 (m), 1229 (s), 1185 (s) 1090 (m), 912 (m), 830 (m), 748 (s). GC-MS (EI, 70 eV): m/z (%) = 348 ([M]$^+$, 89), 317 (100), 289 (8), 273



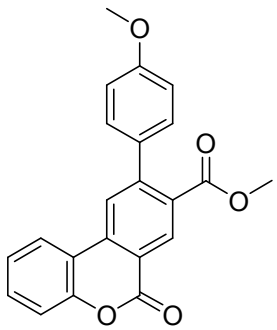
(20), 244 (30), 231 (18). HRMS (EI): calcd. for $C_{21}FH_{13}O_4$ ($[M]^+$): 348.07924. Found: 348.07917.

Ethyl 9-(4-fluorophenyl)-6- oxo-6H-benzo[c]chromene-8-carboxylate (**21v**): Starting



with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18h** (180 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21v** (188 mg, 54%) was isolated as off-white crystalline solid, m.p. 193°C. ^{1}H NMR (300 MHz, $CDCl_3$): 1.09 (t, J = 6.9 Hz, 3H, CH_3), 1.31, 4.13 (q, J = 6.9 Hz, 2H, OCH_2), 7.04-7.12 (m, 2H, ArH), 7.24-7.32 (m, 4H, ArH), 7.43-7.48 (m, 1H, ArH), 7.95-7.97 (m, 2H, ArH), 8.78 (s, 1H, ArH). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -113.50 (s, ArF). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.8 (CH_3), 52.4 (OCH_2), 115.3 (d, $J_{C,F}$ = 21.4 Hz, 2CH), 117.1 (C), 118.0 (CH), 119.9 (C), 123.3, 124.2 (CH), 124.5 (C), 124.8 (CH), 129.9 (d, $J_{C,F}$ = 8.2 Hz, 2CH), 131.6, 132.8 (CH), 136.1 (d, $J_{C,F}$ = 3.7 Hz, C), 136.7, 147.8 151.9 (C), 160.1 (CO), 162.8 (d, $J_{C,F}$ = 248.4 Hz, CF). 166.4 (CO). IR (ATR, cm^{-1}): ν = 2989 (w) 2910 (w), 1720 (s), 1604 (s), 1514 (m), 1216 (s), 1183 (s) 1088(m), 932(m), 839 (m), 743 (s). GC-MS (EI, 70 eV): m/z (%) = 362 ($[M]^+$, 75), 317 (100), 289 (11), 273 (19), 244 (31), 231 (19). HRMS (EI): calcd. for $C_{22}FH_{15}O_4$ ($[M]^+$): 362.09489. Found: 362.09481.

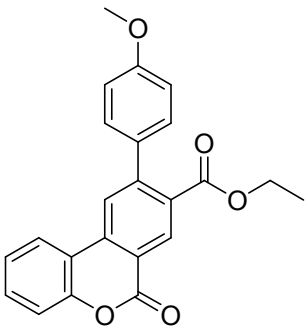
Methyl 9-(4-methoxyphenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21w**):



Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18i** (180 mg, 1.5 mmol) and **20a** (174 mg, 1.5 mmol), **21v** (198 mg, 55%) was isolated as white crystalline solid, m.p. 193 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.68 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.89-6.94 (m, 2H, ArH), 7.22-7.29 (m, 4H, ArH), 7.41-7.46 (m, 1H, ArH), 7.96-7.99 (m, 2H, ArH), 8.72 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.38, 55.33 (OCH_3), 113.88 (2CH), 117.24 (C), 117.95 (CH), 119.41 (C), 123.28, 124.11, 124.75 (CH), 129.51 (2CH), 131.26 (C), 131.46 (CH), 132.08 (C), 132.77 (CH), 136.63, 148.37, 151.94, 159.86(C), 160.31, 167.37 (CO). IR (ATR, cm^{-1}): ν = 2951 (w), 2835 (w), 1712 (s), 1607(s), 1226 (s),

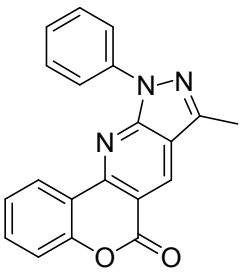
1178 (m) 1088(m), 832 (m), 748 (s). GC-MS (EI, 70 eV): m/z (%) = 360 ($[M]^+$, 100), 329 (65), 286 (8), 242 (11), 213 (9). HRMS (EI): calcd. for $C_{22}H_{16}O_5$ ($[M]^+$): 360.09923. Found: 360.09909.

Ethyl 9-(4-methoxyphenyl)-6-oxo-6H-benzo[c]chromene-8-carboxylate (**21x**):



Starting with **1** (200 mg, 1.0 mmol), K_2CO_3 (200 mg, 1.5 equiv.), $PdCl_2(PPh_3)_2$(28 mg, 4 mol%), CuI (13 mg, 7mol%), **18i** (180 mg, 1.5 mmol) and **20b** (200 mg, 1.5 mmol), **21x** (202 mg, 55%) was isolated as white crystalline solid, m.p. 152 °C-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, J = 7.14 Hz, 3H, CH_3), 3.79 (s, 3H, OCH_3),4.13 (q, J = 7.14 Hz, 2H, OCH_2), 7.06-7.12 (m, 2H, ArH), 7.24-7.32 (m, 4H, ArH), 7.43-7.48 (m, 1H, ArH), 7.95-8.00 (m, 2H, ArH), 8.78 (s, 1H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.93 (CH_3), 55.36 (OCH_3), 61.50 (OCH_2), 113.84 (2CH), 117.28 (C), 117.94 (CH), 119.41 (C), 123.27, 124.03, 124.74 (CH), 129.54 (2CH), 131.85 (C), 131.46 (CH), 132.26 (C), 132.59 (CH), 136.493, 148.30, 151.92 159.86 (C), 160.35, 167.04 (CO). IR (ATR, cm^{-1}): ν = 2976 (w), 2836 (w), 1715 (s), 1606(s), 1226 (s), 1177 (m) 1088 (m), 835 (m), 750 (s). GC-MS (EI, 70 eV): m/z (%) = 374 ($[M]^+$, 100), 329 (68), 286 (8), 242 (12), 202 (13),. HRMS (EI): calcd. for $C_{23}H_{18}O_5$ ($[M]^+$): 374.11488. Found: 374.11521.

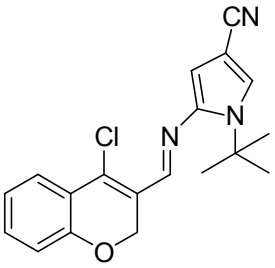
***8 - methyl-10-phenylchromeno[4,3- b]pyrazolo[4,3-e]pyridine*-6(10*H*)-one** (**27a**):



Starting with **1** (200 mg, 1.0 mmol), **25** (207 mg, 1.2 mmol), $AlCl_3$ (3equiv. 400 mg, 3.0 mmol) in 10-15 mL dry MeOH. The reaction mixture was refluxed under moisture free environment for 8-10 hrs. The precipitates formed were directly filtered washed with cold MeOH. The precipitate were re-dissolved in hot MeOH, and filtered again. Two filtrates obtained were combined, adsorbed on silica gel and purified by chromatography using two solvent systems (silica gel, *n*-heptane/EtOAc = 3:2 and chloroform/*n*-heptane = 9:1), **27a** (202 mg, 62%) was isolated as white crystalline solid, m.p. 240 °C - 241 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.5 (s, 3H, CH_3), 7.25 - 7.34 (m, 3H, ArH), 7.46 (m, 3H, ArH), 8.26 - 8.29

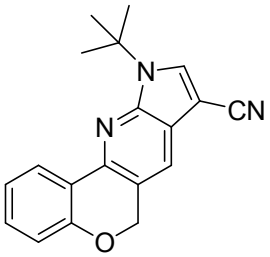
(m, 2H, ArH), 8.49 (dd, J = 7.91 Hz, 1.57 Hz, 1H, ArH), 8.89 (s, 1H, ArH).^{13}CNMR (300MHz, $CDCl_3$): δ = 12.5 (CH_3), 111.7 (C), 117.2 (CH), 117.9, 119.4 (C), 120.7 (2CH), 124.8, 125.1, 126.1 (CH), 129.1 (2CH), 132.5, 133.9 (CH), 138.9, 145.0, 150.9, 151.8, 152.7 (C), 161.5 (CO). IR (ATR, cm^{-1}): ν = 1719 (s), 1607 (m), 1590 (m), 1497 (s), 1487 (s), 1419 (m), 1384 (m), 1336 (w), 1251 (m), 1243 (m), 1187 (m), 1115 (m), 1089 (m), 908 (m), 752 (s). GC-MS (EI, 70 eV): m/z (%) = 327 ($[M]^+$, 100), 326 (25), 328 (21), 77 (12) 312 (11). HRMS (EI): calcd. for $C_{20}H_{13}N_3O_2$ ($[M+]^+$): 327.10023. Found:327.09982.

Tert-butyl-5-(4-chloro-2H-chromen-3-yl)methyleneamino)-1H-pyrrole-3-carbonitrile



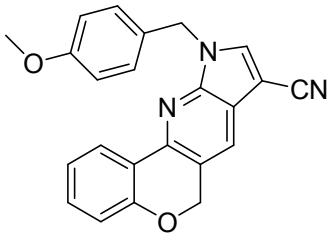
(**28a**): Starting with **2** (194 mg, 1.0 mmol) and **22a** (196 mg, 1.2 mmol) dissolved in 10 mL of dry DMF. After addition of 1 mL of TMSCL, the reaction mixture was stirred at 120 °C for 10 hrs. Workup procedure (**a**): The mixture was poured into ice water. The resulting yellow precipitates were filtered and dried. To remove minute inorganic impurities the precipitates were dissolved in ethyl acetate-water (2:1 by volume). The organic layer was dried and evaporated to get final product as yellow crystalline solid. Workup procedure (**b**): Half of the volume of DMF was evaporated and the reaction mixture was allowed to stand for several hrs. Precipitates formed were filtered, washed with cold MeOH and dried to give **28a** (260mg, 76%) as yellow crystalline solid, m.p. 232°C-233 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (s, 9H, $3CH_3$), 5.14 (s, 2H, CH_2), 6.42 (d, J = 1.8 Hz, 1H, ArH), 6.82 (dd, J = 8.1 Hz, J = 1.1 Hz, 1H, ArH), 6.95 (td, J = 7.6 Hz, J = 1.1 Hz, 1H, ArH), 7.18-7.23 (m, 2H, ArH), 7.54 (dd, J = 7.8 Hz, J = 1.4 Hz, 1H, ArH). 8.54 (s, 1H, ArH). ^{13}CNMR (62.8 MHz, $CDCl_3$): δ = 30.0 ($3CH_3$), 58.4 (C), 65.9 (OCH_2), 90.9 (C), 99.4, 116.1 (CH), 116.7, 121.3 (C), 122.0, 125.6 (CH), 125.7 (C), 125.8, 132.0 (CH), 134.2, 142.7 (C), 149.1 (CH), 155.5 (C). IR (ATR, cm^{-1}): ν = 3150 (w), 2977 (w), 2358 (w) 2217 (s) 1601 (m), 1562 (m), 1530 (w), 1473 (m), 1455 (w), 1361 (m), 1295 (m), 1203 (m), 1150 (m), 1085 (m), 1043 (m), 936 (w), 814 (s), 758 (s), 628 (s), 563 (m). GC-MS (EI, 70 eV): m/z (%) =339 ($[M]^+$, 28), 248 (100), 247 (36), 246 (57), 57 (33), 41(29). HRMS (EI): calcd. for $C_{19}H_{18}N_3OCl$ ($[M]^+$): 339.11329.Found: 339.11295 and for $C_{19}H_{18}N_3{}^{37}OCl$($[M]^+$): 341.11034. Found: 341.11043.

10-tert-butyl-6,10-dihydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile



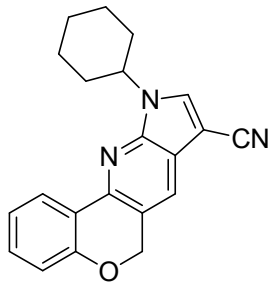
(**29a**): Starting with **2** (194 mg, 1.0 mmol) and **22a** (196 mg, 1.2 mmol), $AlCl_3$ (3equiv., 400mg, 3.0 mmol), **29a** (85mg, 28%) was isolated as white crystalline solid. m.p. 189°C - 191°C. ^{1}H NMR (300 MHz, $CDCl_3$):δ = 1.80 (s, 9H, $3CH_3$), 5.24 (d, 0.9 Hz, 2H, CH_2), 6.92 (dd, *J* = 8.14 Hz, 1.05 Hz, 1H, ArH), 7.04 (td, *J* = 7.54 Hz, 1.16 Hz, 1H, ArH), 7.21-7.27 (m, 1H, ArH), 7.68 (s, 1H, ArH), 7.75 (s, 1H, ArH), 8.18 (dd, *J* = 7.76 Hz, 1.68 Hz, 1H, ArH). ^{13}CNMR (250 MHz, $CDCl_3$): δ = 29.1 ($3CH_3$), 58.6 (C), 68.5 (OCH_2), 83.3, 115.4 (C), 117.1 (CH), 120.4, 121.1 (C), 122.2, 123.6 (CH), 123.7 (C), 124.7, 131.0, 133.2 (CH), 143.9, 147.1, 156.5 (C).IR (ATR, cm^{-1}): ν = 2972 (w), 2214 (s), 1615 (m), 1587 (m), 1526 (m), 1414 (s), 1315 (s), 1209 (s), 1170 (s), 1042 (m), 937 (w), 816 (w), 749 (s).GC-MS (EI, 70 eV): m/z (%) = 303($[M]^+$, 32), 247 (72), 246 (100),218 (11).HRMS (EI): calcd. for $C_{19}H_{17}N_3O$ ($[M]^+$): 303.13661. Found: 303.13642

10-(4-methoxybenzyl)-10H-benzo[h]pyrrolo[2,3-b][1,6]naphthyridine-8-carbonitrile



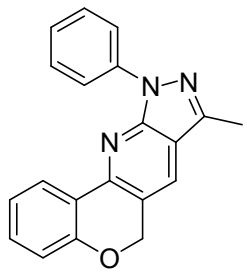
(**29b**):Starting with **2** (194 mg, 1.0 mmol), **22b**(272 mg, 1.2 mmol), $AlCl_3$ (3equiv., 400mg, 3.0 mmol), **29b** (170 mg, 46%) was isolated as white crystalline solid.m.p. 156°C-158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3), 5.25 (s, 2H, OCH_2), 5.53 (s, 2H, NCH_2), 6.80 (d, *J* = 8.63 Hz, 2H, ArH), 6.93 (dd, *J* = 8.15 Hz, 0.85 Hz, 1H, ArH), 7.06 (td, *J* = 7.60 Hz, 1.01 Hz, 1H, ArH), 7.20-7.29 (m, 3H, ArH), 7.54 (s, 1H, ArH), 7.70 (s, 1H, ArH), 8.27 (dd, *J* = 7.77 Hz, 1.60 Hz, 1H, ArH). ^{13}CNMR (75.4 MHz, $CDCl_3$): δ = 48.3 (NCH_2), 55.3 (OCH_3), 68.5 (OCH_2), 84.9 (C), 114.4 (2CH), 117.1 (CH), 118.9, 121.8 (C), 122.3 (CH), 123.4 (2C), 124.0, 124.7 (CH), 127.8 (C), 129.7 (2CH), 131.3, 134.6 (CH), 145.2, 146.8, 156.6, 159.7 (C). IR (ATR, cm^{-1}): ν = 2956 (w), 2913 (w), 2217 (m), 1513 (s), 1456 (m), 1440 (m), 1381 (s), 1245 (s), 1180 (s), 1171 (s), 1026 (s), 850 (m), 835 (m), 757 (s), 609 (m). GC-MS (EI, 70 eV): m/z (%) = 367 ($[M]^+$, 24), 364 (20), 121 (100), 122 (8), 91 (4). HRMS (EI): calcd. for $C_{23}H_{17}N_3O_2$ ($[M]^+$): 367.13153. Found: 367.13141.

10-cyclohexyl-6,10-dihydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile



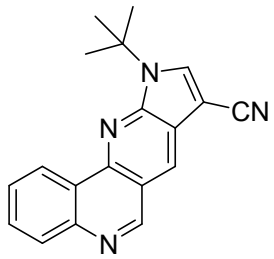
(**29c**): Starting with **2** (194 mg, 1.0 mmol), **22c** (227 mg, 1.2 mmol), $AlCl_3$ (3equiv.,400 mg, 3.0 mmol), **29c** (141mg, 43%) was isolated as white crystalline solid. m.p. 198°C-200°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16-1.77 (m, 6H, $3CH_2$), 1.88 (d, J = 13.04 Hz, 2H, CH_2), 2.09 (d, J = 10.58 Hz, 2H, CH_2), 4.77 (tt, J = 11.80 Hz, 3.77 Hz, 1H, NCH), 5.22 (d, J = 0.8 Hz, 2H, CH_2), 6.90 (dd, J = 8.20 Hz, 1.02 Hz, 1H, ArH), (td, J = 7.51 Hz, 1.10 Hz, 1H, ArH), 7.23 (ddd, J = 8.11 Hz, 7.32 Hz, 1.72 Hz, 1H, ArH), 7.66 (s, 1H, ArH), 7.68 (s, 1H, ArH), 8.22 (dd, J = 7.80 Hz, 1.66 Hz, 1H, ArH). ^{13}CNMR (300 MHz, $CDCl_3$): δ = 25.4 (CH_2), 25.7, 33.8 ($2CH_2$), 54.5 (NCH), 68.6 (CH_2), 84.2, 115.4 (C), 117.1 (CH), 119.2, 121.7 (C), 122.3 (CH), 123.5 (C), 123.8, 124.7, 131.1, 132.6 (CH), 144.6, 146.4, 156.6 (C). IR (ATR, cm^{-1}): ν = 2931 (w), 2848 (w), 2217 (s), 1584 (w), 1526 (m), 1459 (s), 1308 (m), 1257 (s), 1239 (s), 1173 (s), 1036 (s), 856 (m), 748 (s). GC-MS (EI, 70 eV): m/z (%) = 329 ($[M]^+$, 45), 247 (100), 246 (74), 248 (20), 245 (14). HRMS (EI): calcd. for $C_{21}H_{19}N_3O$ ($[M]^+$): 329.15226. Found: 329.15187.

8-methyl-10-phenyl-6,10-dihydrochromeno[4,3-b]pyrazolo[4,3-e]pyridine (**30**):



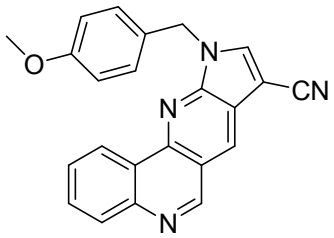
Starting with **2** (194 mg, 1.0 mmol), **25** (207 mg, 1.2 mmol), $AlCl_3$ (3equiv.,400mg, 3.0 mmol), **30** (180mg, 58%) was isolated as white crystalline solid, m.p. 179°C-180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 5.08 (d, J = 0.88Hz, 2H, CH_2), 6.84 (dd, J = 8.13, J = 1.05 Hz, 1H, ArH), 6.99 (td, J = 7.57Hz, J = 1.1 Hz, 1H, ArH), 7.12-7.24 (m, 2H, ArH), 7.37-7.43 (m, 3H, ArH), 8.17 (dd, 7.82 Hz, J = 1.66 Hz, 1H, ArH). 8.24-8.28 (m, 2H, ArH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 12.4 (CH_3), 68.5 (CH_2), 115.8 (C), 117.1 (2CH), 120.2 (CH), 120.2 (C), 122.3 (CH), 123.2 (C), 124.8, 125.1, 125.5 CH), 128.9 (2CH), 131.7 (CH), 139.7, 142.5, 148.3, 150.5, 157.1 (C). IR (ATR, cm^{-1}): ν = 2917 (w), 2852 (w), 1591 (m), 1562 (m), 1488 (m), 1473 (m), 1462 (w), 1388 (m), 1280 (w), 1249 (w), 1122 (m), 1033 (m), 886 (w), 936 (w), 779 (m), 754 (s), 746 (s), 691 (m). GC-MS (EI, 70 eV): m/z (%) = 313 ($[M]^+$, 77), 312 (100), 271 (5), 77 (9), 51 (4). HRMS (EI): calcd. for $C_{20}H_{16}N_3O$ ($[M+H]^+$): 314.12899. Found 314.12879.

10-tert-butyl-10H-benzo[h]pyrrole[2,3-b][1,6]naphthyridine-8-carbonitrile (**31a**):

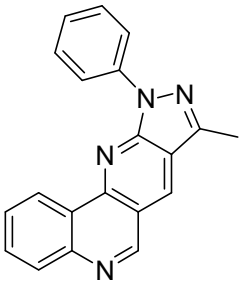


Starting with **4** (190 mg, 1.0 mmol) and **22a** (196 mg, 1.2 mmol), **31a** (101mg, 28%) was isolated as white crystalline solid. m.p. 239°C -241 °C.^{1}H NMR (300 MHz, $CDCl_3$):δ = 1.94 (s, 9H, $3CH_3$), 7.66-7.72 (m, 1H, ArH), 7.74-7.80 (m, 1H, ArH), 8.11 (s, 1H, ArH), 8.15 (d, J = 7.51 Hz, 1H, ArH), 8.63 (s, 1H, ArH), 9.07 (dd, J = 8.03 Hz, 1.41 Hz, 1H, ArH), 9.32 (s, 1H, ArH). ^{13}CNMR (300 MHz, $CDCl_3$): δ = 28.1 ($3CH_3$), 58.3, 83.3, 113.7, 116.3, 120.7 (C), 122.6 (CH), 124.5 (C), 126.3, 127.2, 128.2, 129.1, 136.2 (CH), 143.8, 144.6, 147.8 (C), 152.1 (CH).IR (ATR, cm^{-1}): ν = 3571 (m), 3564 (m), 2222 (s), 1596 (m), 1522 (m), 1485 (w), 1440 (w), 1399 (s), 1273 (m), 1187 (s), 934 (m), 785 (m), 766 (s). GC-MS (EI, 70 eV): m/z (%) = 300 ([M] $^{+}$, 21), 244 (100), 245 (18), 243 (11), 217 (6), 189 (7). HRMS (EI): calcd. for $C_{19}H_{16}N_4$ ([M]$^{+}$): 300.13695. Found: 300.13712.

10-(4-methoxybenzyl)-10H-benzo[h]pyrrolo[2,3-b][1,6]naphthyridine-8-carbonitrile (**31b**): Starting with **4** (190 mg, 1.0 mmol), **22b** (272 mg, 1.2 mmol), **29b** (190 mg, 52%) was isolated as white crystalline solid. m.p. 229°C -230 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 3H, OCH_3), 5.53 (s, 2H, NCH_2), 6.8 (d, J = 8.6 Hz, 2H, ArH), 7.29 (d, J = 8.6 Hz, 2H, ArH), 7.64-7.70 (m, 1H, ArH), 7.73-7.79 (m, 1H, ArH), 7.82 (s, 1H, ArH), 8.1 (dd, J = 8.16 Hz, J = 0.78 Hz, 1H, ArH), 8.5 (s, 1H, ArH), 9.09 (dd, J = 7.98 Hz, 1.39 Hz, 1H, ArH). 9.23 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 48.6 (CH_2), 55.3 (OCH_3), 85.7, 114.3 (C), 114.6 (2CH), 117.9, 120.3 (C), 123.6 (CH), 125.1 (C), 127.2 (CH), 127.3 (C), 128.5, 129.4 (CH), 129.9 (2 CH), 130.2, 138.5 (CH), 145.7 (C), 146.0 (C), 148.2 (C), 153.2 (CH), 159.9 (C). IR (ATR, cm^{-1}): ν = 2956 (w), 2913 (w), 2217 (m), 1513 (s), 1456 (m), 1440 (m), 1381 (s), 1245 (s), 1180 (s), 1171 (s), 1026 (s), 850 (m), 835 (m), 757 (s), 609 (m). GC-MS (EI, 70 eV): m/z (%) = 364 ([M] $^{+}$, 20), 122 (8),121 (100), 91 (4), 77 (7). HRMS (EI): calcd. for $C_{23}H_{16}N_4O$([M]$^{+}$): 364.13186. Found: 364.13187.



8-methyl-10-phenyl-10H-benzo[h]pyrozolo[3,4-b][1,6]naphthyridine (**32**): Starting with **4** (190 mg, 1.0 mmol), **25** (207 mg, 1.2 mmol), **32** (176mg, 57%) was isolated as white crystalline solid,. m.p. 163°C -165 °C. ^{1}H NMR (300 MHz, $CDCl_3$):δ = 2.5 (s, 3H, CH_3), 7.17-7.24 (m, 1H, ArH), 7.42-7.49 (m, 3H, ArH), 7.60-7.65 (m, 1H, ArH), 7.93 (dd, *J* = 8.07 Hz, 0.54 Hz, 1H, ArH), 8.14 (s, 1H, ArH), 8.28-8.32 (m, 2H, ArH), 8.69 (dd, *J* = 8.10 Hz, 1.27 Hz, 1H, ArH), 8.93 (s, 1H, ArH).^{13}C NMR (300 MHz, $CDCl_3$): δ = 12.5 (CH_3), 116.5, 117.7 (C), 120.0 (2CH), 124.0 (CH), 124.9 (C), 125.4, 127.0 (CH), 128.9 (2CH), 129.03, 130.1, 130.5 (CH), 139.4, 144.0, 146.2, 147.9, 150.5 (C), 153 (CH). IR (ATR, cm^{-1}): ν = 1621 (w), 1589 (m), 1495 (m), 1439 (w), 1421 (w), 1341 (w), 1223 (w), 798 (m), 757 (s), 750 (s), 659 (s). GC-MS (EI, 70 eV): m/z (%) = 310 ($[M]^+$, 100), 309 (37), 295 (12), 77 (11), 51 (7). HRMS (EI): calcd. for $C_{20}H_{14}N_4$ ($[M+]^+$): 310.12130. Found: 310.12062.



7 Crystallographic Data

7.1 Crystal data and Structure refinement of compound **9a**

Identification code	ch_ma18	
Empirical formula	$C_{18}H_{14}O_6$	
Formula weight	326.26	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic,	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.1722 (4) Å	α = 113.294 (2)°
	b = 9.0126 (4) Å	β = 94.407 (2)°
	c = 11.3331(5) Å	γ = 104.568 (2)°
Volume (Z)	2	
Density (calculated)	1.490 Mg m^{-3}	
F(000)	340	
Crystal size	0.47 x 0.15 x 0.08 mm	
Θrange for data collection	5.0-60.1°	
Measured reflections	14504	
Independent reflections	4111	
Absorption correction	multi-scan	
Max. and min. transmission	0.949 and 0.990	
Refinement method	Full Least-square matrix on F^2	
Goodness-of-fit on F^2	1.09	

7.2 Crystal data and Structure refinement of compound **9g'**

Identification code	ch_ma19a
Empirical formula	$C_{17}H_{14}O_4$
Formula weight	282.28
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2yn
Unit cell dimensions	a = 7.0981 (2) Å β = 97.262 (1)°
	b = 7.9858 (2) Å
	c = 11.8633 940 Å
Volume (Z)	4
Density (calculated)	1.405 Mg m^{-3}
F(000)	592
Crystal size	0.49 x 0.36 x 0.32
Θrange for data collection	5.8-60.0°
Measured reflections	14262
Independent reflections	3867
Absorption correction	multi-scan
Max. and min. transmission	0.953 and 0.969
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.06

7.3 Crystal data and Structure refinement of compound **13**

Identification code	av_ma24	
Empirical formula	$C_{16}H_{12}O_3$	
Formula weight	252.26	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.3113 (2) Å	α = 78.515 (1)°
	b = 7.8569 (2) Å	β = 83.383 (1)°
	c = 11.8633 (4) Å	γ = 64.034 (1)°
Volume (Z)	2	
Density (calculated)	1.396 Mg m^{-3}	
F(000)	264	
Crystal size	0.82 x 0.29 x 0.10	
Θrange for data collection	5.9-59.9°	
Measured reflections	12464	
Independent reflections	3457	
Max. and min. transmission	0.925 and 0.990	
Refinement method	Full Least-square matrix on F^2	
Goodness-of-fit on F^2	1.05	

7.4 Crystal data and Structure refinement of compound **9c**

Identification code	is_ma23	
Empirical formula	$C_{20}H_{18}O_6$	
Formula weight	354	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.5118 (2) Å	α = 68.412 (1)°
	b = 9.6807 (2) Å	β = 73.556 (1)°
	c = 10.2910 (3) Å	γ = 88.203 (1)°
Volume (Z)	2	
Density (calculated)	1.397 Mg m^{-3}	
F(000)	372	
Crystal size	0.48 x 0.28 x 0.08	
Θrange for data collection	4.5-64.9°	
Measured reflections	27837	
Independent reflections	6080	
Absorption correction	multi-scan	
Max. and min. transmission	0.952 and 0.992	
Refinement method	Full Least-square matrix on F^2	
Goodness-of-fit on F^2	1.04	

7.5 Crystal data and Structure refinement of compound **14c**

Identification code	is_ma4_2
Empirical formula	$C_{20}H_{20}O_5$
Formula weight	340.36
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/c$
Space group (Hall)	-P 2ybc
Unit cell dimensions	a = 11.9410 (3) Å β = 113.094 (1)°
	b = 12.7890 (4) Å
	c = 12.0032 (3) Å
Volume (Z)	4
Density (calculated)	1.341 Mg m^{-3}
F(000)	720
Crystal size	0.32 x 0.20 x 0.05
Θrange for data collection	4.5-57.9°
Measured reflections	24129
Independent reflections	4907
Absorption correction	multi-scan
Max. and min. transmission	0.970 and 0.995
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.02

7.6 Crystal data and Structure refinement of compound **17b**

Identification code	ah_ma_4_16_2
Empirical formula	$C_{25}H_{22}O_6$
Formula weight	418.43
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	$P\bar{1}$
Space group (Hall)	-P 1
Unit cell dimensions	a = 5.8372 (2) Å β = 90.372 (2)°
	b = 11.6055 (2) Å
	c = 15.6114 (4) Å
Volume (Z)	2
Density (calculated)	1.337 Mg m^{-3}
F(000)	440
Crystal size	0.44 x 0.24 x 0.19
Θrange for data collection	2.7-32.6°
Measured reflections	35203
Independent reflections	7505
Absorption correction	multi-scan
Max. and min. transmission	0.959 and 0.982
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.02

7.7 Crystal data and Structure refinement of compound **17f**

Identification code	Ch_ma35
Empirical formula	$C_{21}H_{14}O_4$
Formula weight	330.32
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/c$
Space group (Hall)	-P 2ybc
Unit cell dimensions	a = 12.1411 (11) Å β = 100.638 (6)°
	b = 14.7612 (15) Å
	c = 8.7159 (8) Å
Volume (Z)	4
Density (calculated)	1.429 Mg m^{-3}
F(000)	688
Crystal size	0.37 x 0.16 x 0.06
Θrange for data collection	5.5-63.4°
Measured reflections	15702
Independent reflections	4060
Absorption correction	multi-scan
Max. and min. transmission	0.964 and 0.994
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.09

7.8 Crystal data and Structure refinement of compound **28a**

Identification code	is_mafcr03
Empirical formula	$C_{19}H_{18}ClN_3O$
Formula weight	339.81
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group (H.-M.)	$P2_12_12_1$
Space group (Hall)	P 2ac 2ab
Unit cell dimensions	a = 6.4919 (5) Å
	b = 7.7941 (6) Å
	c = 33.820 (3) Å
Volume (Z)	4
Density (calculated)	1.319 Mg m^{-3}
F(000)	712
Crystal size	0.57 x 0.14 x 0.04
Θrange for data collection	4.8-50.2°
Measured reflections	18987
Independent reflections	5304
Absorption correction	multi-scan
Max. and min. transmission	0.878 and 0.991
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.03

7.9 Crystal data and Structure refinement of compound **30**

Identification code	is_fcr6b
Empirical formula	$C_{20}H_{15}N_3O$
Formula weight	313.35
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/c$
Space group (Hall)	-P 2ybc
Unit cell dimensions	a = 7.2639 (4) Å β = 95.886 (3)°
	b = 10.0858 (6) Å
	c = 20.6740 (11) Å
Volume (Z)	4
Density (calculated)	1.381 Mg m^{-3}
F(000)	656
Crystal size	0.49 x 0.10 x 0.07
Θrange for data collection	5.6-51.3°
Measured reflections	16019
Independent reflections	4374
Absorption correction	multi-scan
Max. and min. transmission	0.958 and 0.994
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.01

7.10 Crystal data and Structure refinement of compound **31b**

Identification code	is_fp01
Empirical formula	$C_{23}H_{16}N_4O$
Formula weight	364.40
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1/n$
Space group (Hall)	-P 2yn
Unit cell dimensions	a = 12.6335 (13) Å β = 95.092 (6)°
	b = 6.9137 (7) Å
	c = 20.278 (2) Å
Volume (Z)	4
Density (calculated)	1.372 Mg m^{-3}
F(000)	760
Crystal size	0.99 x 0.24 x 0.03
Θrange for data collection	6.5-60.8°
Measured reflections	17985
Independent reflections	4474
Absorption correction	multi-scan
Max. and min. transmission	0.919 and 0.997
Refinement method	Full Least-square matrix on F^2
Goodness-of-fit on F^2	1.02

8. References and notes

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AWARDS AND GRANTS

1. German Academic Exchange Service **(DAAD)** award, **2011-2014**, (Germany)
2. German Research Foundation **(DFG)** research grant, **2010-2011**, (Germany)

EXHIBITIONS/CONFERENCES/ WORKSHOPS

1. Participated in a German language course in June-Sept., 2011 held at DID institute Hamburg, Germany.
2. Participated in the training course on Atomic Absorption spectrometry “the basic theory and recent trends” in March 5-6, 2008 held at AIOU, Islamabad.
3. Participated in workshop for training of persons working in the laboratories of Industries and Government Institutes, held at AIOU, Islamabad in 2004.
4. Attended 5th International and 15th National Chemistry Conference organized by The Chemical Society of Pakistan, held at QAU, Islamabad in 2004.

SELECTED PUBLICATIONS

1. Iaroshenko, V. O.;* Ali, S.; Babar, T. A.; **Abbasi**, **M**. **S**. **A**.; Sosnovskikh, V. Y.; Villinger, A, Tolmachev, A.; Langer P. *Tetrahedron* **2013**, 69, 3167-3181. Efficient synthesis of novel thieno[3,2-b]-, [2,3-c]- and [3,2-c]pyridones by Sonogashira coupling of bromothiophenes with terminal alkynes and subsequent intramolecular C-N bond forming reaction.

http://www.sciencedirect.com/science/article/pii/S0040402013002950

2. Iaroshenko, V. O.* Herrera, V. M.; Gevorgyan, Ashot.; Mkrtchyan, S.; Arakelyan K.; Ostrovskyi, D.; **Abbasi**, **M**. **S**. **A**.; Supe, Linda.; Hakobyan Ani.; Villinger, A.; Volochnyuk, D. M.; Tolmachev, A *Tetrahedron* **2013**, 69, 1217-1228. Design, synthesis and transformation of some heteroanulated 3-Aminopyridines-purine isosteres with exocyclic nitrogen atom.

http://www.sciencedirect.com/science/article/pii/S004040201201719X

3. Iaroshenko, V. O.;* **Abbasi**, **M**. **S**. **A**.; Villinger, A.; Langer, P.* *Adv. Synth. Catal.* **2012**, 803-806. One pot synthesis of biaryl lactones by Sonogashira cross-coupling reactions of 4-chloro-3-formylcoumarine and subsequent domino [5+1] cyclization/deacetylation reactions with 1, 3-dicarbonyl compounds.

http://onlinelibrary.wiley.com/doi/10.1002/adsc.201100621/abstract

Highlighted in *Synafacts* **2012**, 8(6), 0603, as "Sonogashira-Mediated route to Benzo[c]chromen-6-ones".

https://www.thieme-connect.com/ejournals/html/10.1055/s-0031-1291071

4. Iaroshenko, V. O.;* **Abbasi**, **M**. **S**. **A**.; Villinger, A.; Langer, P.* *Tetrahedron Lett*., **2011**, 52, 5910-5912. Synthesis of 6*H*-Benzo[*c*]chromen-6-ones by cyclocondensation of 1, 3-dicarbonyl compounds with 4-chloro-3-formylcoumarin.

http://www.sciencedirect.com/science/article/pii/S0040403911012780

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