SYNTHESIS OF MULTIFUNCTIONAL HETEROCYCLIC SYSTEMS THROUGH DOMINO REACTIONS

Ph.D. THESIS

by

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ROORKEE – 247 667 (INDIA)
JUNE, 2018

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A THESIS

Submitted in partial fulfilment of the requirements for the award of the degree

of

DOCTOR OF PHILOSOPHY

in

CHEMISTRY

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ROORKEE

CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled **"SYNTHESIS OF MULTIFUNCTIONAL HETEROCYCLIC SYSTEMS THROUGH DOMINO REACTIONS"** in partial fulfilment of the requirements for the award of the degree of Doctor of Philosophy and submitted in the Department of Chemistry of the Indian Institute of Technology Roorkee, Roorkee is an authentic record of my own work carried out during a period from January 2013 to June 2018 under the supervision of Dr. Rama Krishna Peddinti, Associate Professor, Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee.

The matter presented in the thesis has not been submitted by me for the award of any other degree of this or any other Institution.

(SHWETA BISHT)

This is to certify that the above statement made by the candidate is correct to the best of my knowledge.

(R. K. Peddinti)
Supervisor

Date: ___ June, 2018

DEDICATION

To my beloved Parents

ACKNOWLEDGEMENTS

First and foremost, I would like to record my sincere gratitude to most respectable supervisor Dr. Rama Krishna Peddinti for his persistent support with splendid guidance, encouragement and excellent work ethics. I am privileged to work under his generous guidance in the lab. It was a very exciting, wonderful, and fulfilling 5 year journey! I am deeply thankful to my supervisor because of his patience, guidance, and constant support throughout my journey. My experiences in the group have really contributed to my growth as a chemist and have given me the skills to continue to grow long after the completion of my degree. I am especially thankful to my supervisor for giving me the independence to explore my own ideas, the opportunity to present my work at conferences, and the experience of writing papers. I can truly say that these 5 years of my Ph.D were some of the best years of my life.

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from their keen scientific insights, their knack for solving seemingly intractable practical difficulties, and their ability to put complex ideas into simple terms.

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CONTENTS

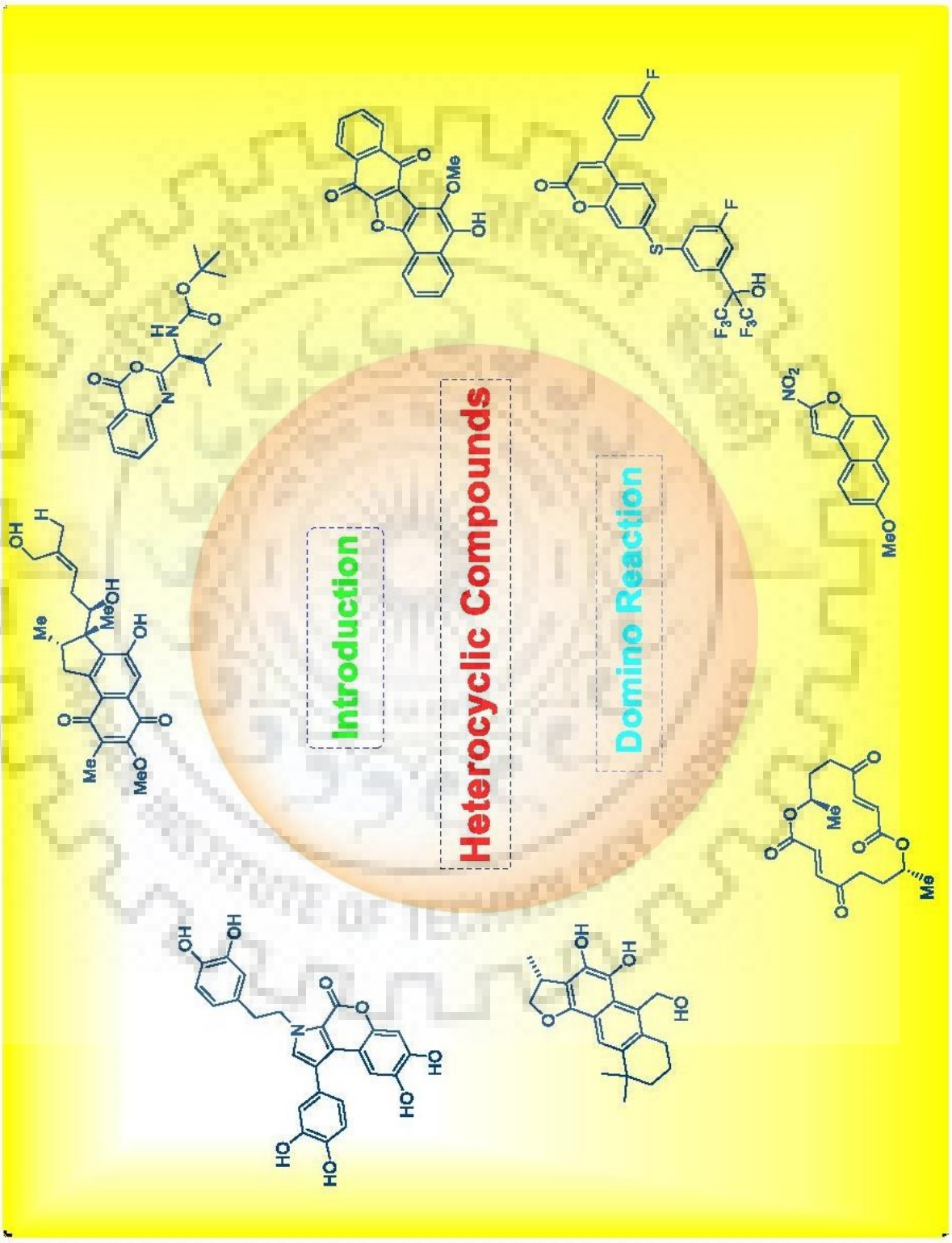
LIST OF ABBREVIATIONS

Ac	acetyl
B3LYP	Becke, 3-parameter, Lee–Yang–Parr
Boc	*tert*-butoxycarbonyl
Bn	Benzyl
n-Bu	*n*-butyl
t-Bu	*tert*-butyl
Bu	butyl
CAN	ceric ammonium nitrate
COSY	correlation spectroscopy
DA	Diels–Alder
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEPT	distortionless enhancement by polarization transfer
DHF	2,3-dihydrofuran
DHP	2,3-dihydropyran
DIB	diacetoxyiodobenzene
DIBAL-H	diisobutylaluminium hydride
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
Dr	diastereomeric ratio (s)
EDG	electron-donating group
Ee	enantiomeric excess (es)
EVE	ethyl vinyl ether
EWG	electron-withdrawing group
FT-IR	fourier transform infrared spectroscopy
GC	gas chromatography
HIV	human immunodeficiency virus

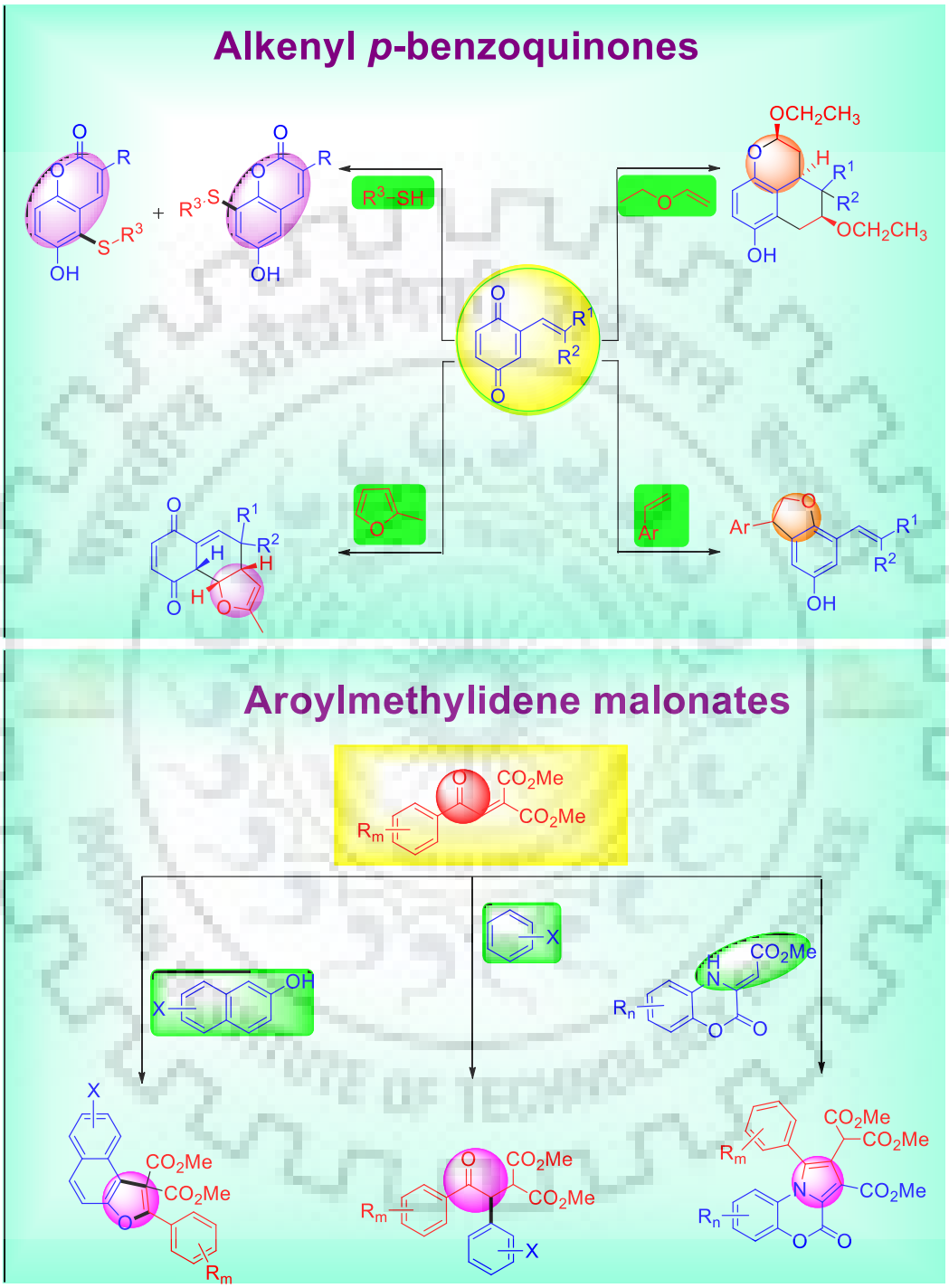
HMPA	hexamethylphosphoramide
HOMO	highest occupied molecular orbital
HRMS	high resolution mass spectroscopy
HSQC	heteronuclear single quantum coherence
HMQC	heteronuclear multiple quantum coherence
IED	inverse electron-demand
^{i}Pr	isopropyl
IR	infra red
LUMO	lowest unoccupied molecular orbital
m-CPBA	*meta*-chloroperbenzoic acid
Mob	masked *o*-benzoquinone
Mpb	masked *p*-benzoquinone
MS	mass spectroscopy
MW	microwave
N-Boc	*tert*-butyl carbamate
NBS	*N*-bromosuccinamide
NCS	*N*-chlorosuccinamide
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
ORTEP	oak ridge thermal ellipsoid plot program
Rt	room temperature
SET	single-electron-transfer
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	Tetrahydropyran
TLC	thin layer chromatography
TMS	tetramethylsilane
$TMSN_3$	trimethylsilyl azide
TsOH	*p*-toluenesulfonic acid
UV	ultraviolet

SUMMARY IN SCHEMES

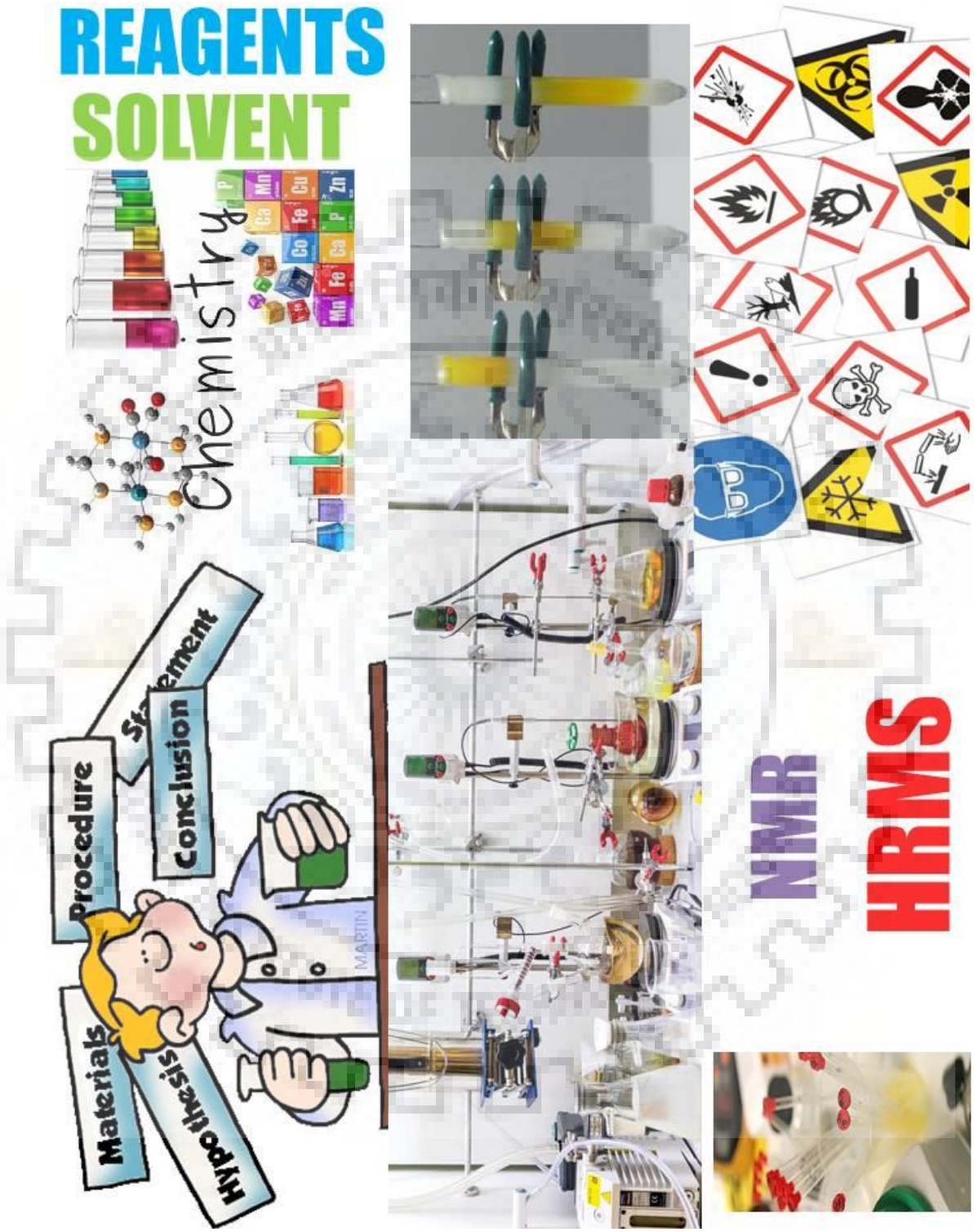
CHAPTER 1: INTRODUCTION



CHAPTER 2: OBJECTIVES, RESULTS AND DISCUSSION



CHAPTER 3: EXPERIMENTAL



ABSTRACT

The thesis entitled "**Synthesis of multifunctional heterocyclic systems through domino reactions**" is divided into three chapters, *viz*. (i) Introduction, (ii) Objectives, Results and Discussion, and (iii) Experimental.

This thesis describes rapid and efficient protocols for the synthesis of novel heterocycles such as alkyl/aryl sulfide derivatives of coumarin, and dihydrobenzofuran *via* domino reaction and [3 + 2] cycloaddition reaction of alkenyl *p*-benzoquinones which were generated by oxidative demethylation of alkenyl dimethoxy arenes by using cerium(IV) ammonium nitrate as an oxidizing agent. We have also calculated Fukui functions for alkenyl *p*-benzoquinone to support the observed regioselectivity obtained from the nucleophilic addition. Further, we have established conceptually novel approach to generate nitrogen and oxygen containing heterocycles, for example, fused-pyrroles and naphthofurans by the treatment of aroylmethylidene malonates with benzoxazinones and *β*-naphthols.

Chapter 1: Introduction

In the first chapter of the thesis, the synthetic aspects of heterocyclic compounds relevant to the research work are discussed. To conclude the chapter, literature describing investigations and development of heterocyclic compounds is presented. The field of organic chemistry has progressed intensely over the past decades, and present reaction methodologies deal with novel and effective strategies for the preparation of multifunctional heterocyclic compounds. Heterocycles play an important role in the design and discovery of new physiologically and pharmacologically active compounds. In recent years, synthesis of novel polyheterocyclic compounds has been at the forefront of today's research. The formation of C–C, C–S, C–N and C–O bond is very essential for the synthesis of heterocyclic compounds. Domino reactions exemplify green approaches for the production of polyfunctionalized complex molecules by endorsing multiple bond-formations in a one-pot process. Domino reactions are highly efficient and have environmental advantages as they generate molecular complexity in less number of steps. Various reactions of benzoquinones and aroylmethylidene malonates and synthesis of heterocycles such as

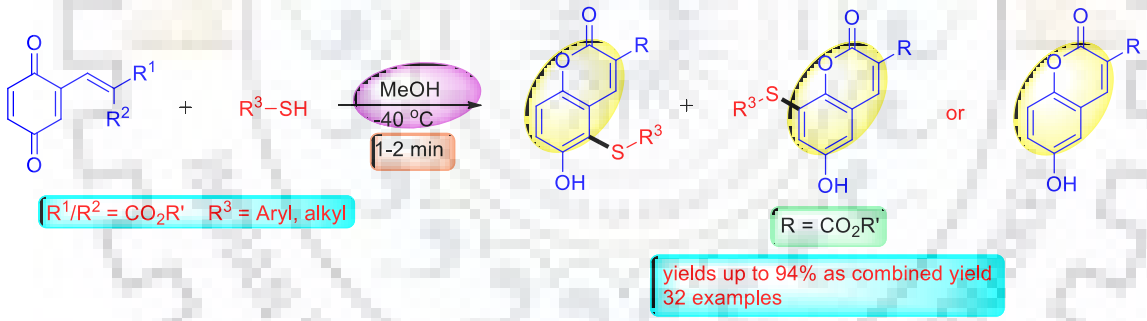
coumarins, biarylsulfides, dihydrobenzofurans, naphthofurans and multisubstituted pyrroles are depicted in this chapter.

Chapter 2: Objectives, Results and Discussion

This chapter deals with the objectives, results and discussion, which is divided into five sections.

2.1 Domino reaction of alkenyl *p*-benzoquinones with alkyl/aryl thiols

In this section, the synthetic aspects of novel alkyl/aryl sulfide derivatives of coumarin are presented. We have developed a novel, efficient and mild methodology towards the synthesis of alkyl/aryl sulfide derivative of coumarins *via* reaction between novel alkenyl *p*-benzoquinones and thiols. This protocol involved the formation of C–S and C–O bonds through domino reaction. This mild and catalyst-free approach delivered biarylsulfides in good to excellent yields. The reaction proceeded smoothly with good substrate scope.

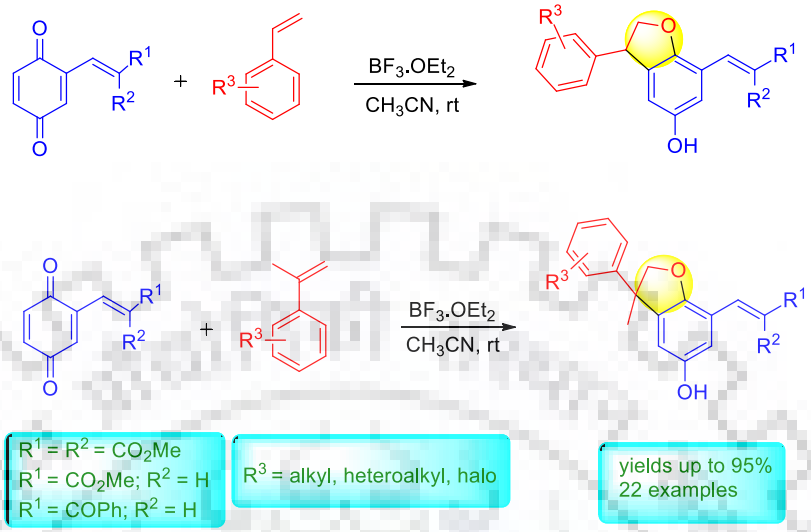


Scheme 1: Domino reaction between alkenyl *p*-benzoquinones and thiols.

2.2 [3 + 2] Cycloaddition of alkenyl *p*-benzoquinones with olefins

This section deals with harnessing the reactivity of alkenyl *p*-benzoquinones with styrenes. We have discussed an efficient and mild approach towards the synthesis of dihydrobenzofurans *via* [3 + 2] cycloaddition between alkenyl *p*-benzoquinones and olefins. Dihydrobenzofurans are very important motifs and are found in various natural products and biologically important compounds. This protocol works under Lewis acid conditions to

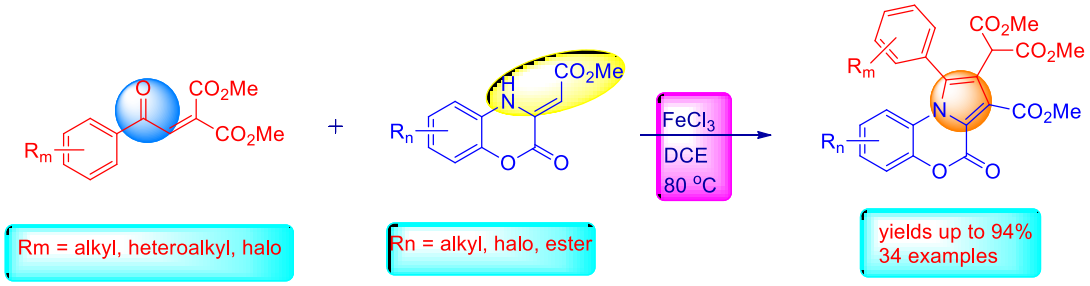
deliver bicyclic products with a plethora of functional groups regioselectively. The yields of these reactions are noteworthy.



Scheme 2: [3 + 2] Cycloaddition reaction between alkenyl *p*-benzoquinones and substituted styrenes.

2.3 Synthesis of functionalized pyrrolobenzoxazinones

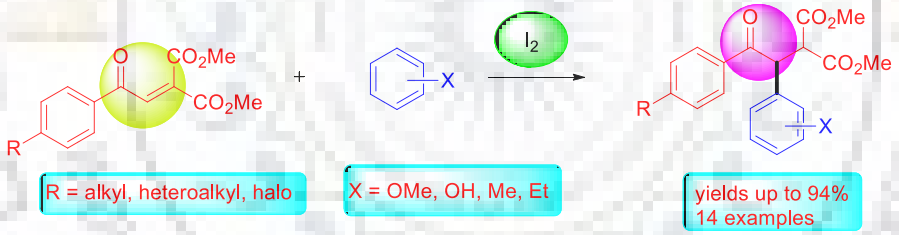
Aroylmethylidene malonates are useful precursors for the formation of various heterocyclic compounds. Several aroylmethylidene malonates have been synthesized and performed their reactions with benzoxazinone derivatives. Benzoxazinone compounds have wide chemistry and they have been found in biologically and pharmacologically important compounds. An efficient, novel and mild approach for the synthesis of pyrrolobenzoxazinones has been developed. This transition metal promoted domino protocol with aroylmethylidene malonates and benzoxazinones has been successfully established to afford the title compounds in good to excellent yield under mild reaction conditions. $FeCl_3$ is used as a promoter for this transformation to deliver pyrrolobenzoxazinones with high efficiency and excellent functional group tolerance. The synthesized pyrrolobenzoxazinone contain pyrrole as well as benzoxazine motiffs, which have an important role in biological field.



Scheme 3: Synthesis of fused pyrroles.

2.4 Synthesis of α-substituted aryl ketones

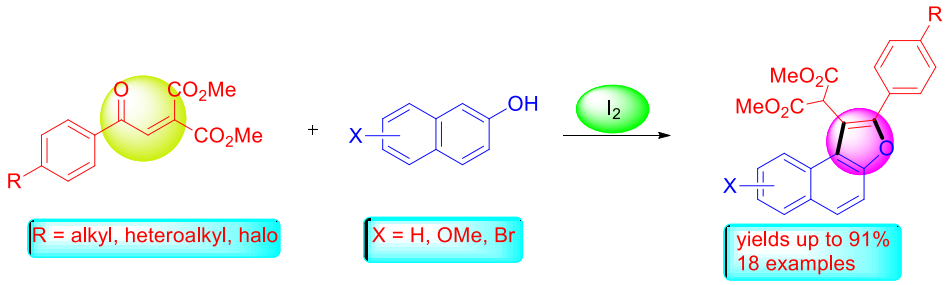
Encouraged by the results obtained from the reaction between aroylmethylidene malonates and benzoxazinones, the scope of aroylmethylidene malonates has been further extended. Consequently, a rapid, efficient metal-free and environmental-friendly approach has been established for the formation of α-substitited aryl ketones under mild reaction condition with electron-rich arenes. This iodine mediated reaction ensues under solvent-free and aerobic conditions to deliver products in good yields.



Scheme 4: Synthesis of α-substituted aryl ketones.

2.5 Synthesis of functionalized naphthofuran derivatives

In continuation of the above domino protocols a rapid and efficient method for the synthesis of naphthofuran derivatives has been developed. Aroylmethylidene malonates reacted with β-naphthol and its derivatives to afford tricyclic products in good to excellent yields. This protocol sustains a wide range of functional groups tolerance in providing the desired products with low catalyst loading.



Scheme 5: Domino reaction between aroylmethylidene malonates and naphthols.

Chapter 3: Experimental

The third chapter details the methods for preparation of compounds. Also the chapter includes all physical and spectroscopic data such as MP, IR ^{1}H NMR, ^{13}C NMR, 2D NMR and mass spectral data to characterize the synthesized compounds.

1. INTRODUCTION

Today the development of novel, efficient and useful multifunctional heterocyclic compounds has emerged as an important area of research. The science of today is the technology of tomorrow. Organic chemistry is the branch of chemistry which talks about compound containing mainly carbons. Around 200 years ago chemistry was undivided, later in 1900 it was divided into organic, inorganic and physical chemistry. Then further it was sub-divided into several parts in which heterocyclic chemistry is the subdivision of organic chemistry.

The cyclic compounds containing all carbon atoms are known as carbocyclic compounds whereas if any heteroatom is present in the cycle then they are referred to as heterocyclic compounds. Heterocyclic chemistry is an important division of organic chemistry and the compounds containing heterocyclic moiety have gained enormous attention, not only in biological and industrial field, but also in human system [1–7]. Heterocyclic compounds have very important role in biochemical processes like they are biosynthesized by plants, animals and are also linked with significant biological properties and have very essential role in living system. Nucleic acids for example DNA and RNA macromolecules present in human body contains nucleobases such as adenine, guanine, thymine, cytosine, and uracil in which pyrimidine and purine heterocyclic moieties are present [8]. The energy transfer molecules AMP, ADP and ATP also composed of nucleotide bases [9]. Heterocyclic compounds have very essential role in human life in various way like various organic compounds such as amino acids, vitamins, hemoglobin, hormones, alkaloids, antibiotics, pigments and many synthetic drugs contain heterocyclic ring system (Figure 1). In the recent decades, the synthesis of multifunctional heterocyclic systems is an important area of research [10–13]. Heterocyclic compounds display their large application in material science such as plastics, brightening agents, dyes, fluorescent sensors, and analytical reagents, therefore the main objective of today's research is the synthesis of heterocyclic compounds.

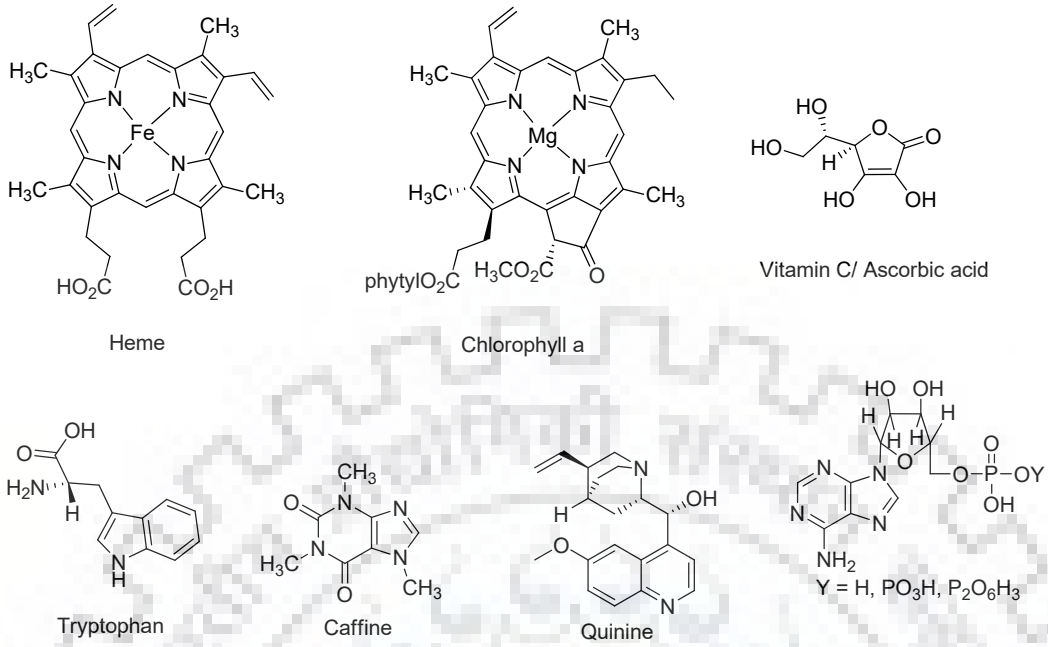


Figure 1: Structures of some naturally occurring heterocyclic compounds.

The heterocyclic compounds containing nitrogen, oxygen and sulfur are regarded as privileged key edifice for the production of biologically or medicinally significant molecules [14–18]. Among all the heterocyclic compounds, the compounds containing scaffolds such as coumarins [19–21], biarylsulfides [22–24], dihydrofurans [25–27], pyrroles [28–30] and benzoxazines [31,32] have remarkable attention due to their wide application in biological and pharmacological field (Figure 2). Besides having major structural attributes in many natural products, they show diverse medicinal properties such as antibiotic, antitumor, anti-HIV, antidepressant, antimalarial, antimicrobial, antifungal, antibacterial, anti-inflammatory, antiviral, antidiabetic, hypnotics, vasopressor modifier agent and cytotoxic effects [33–38]. Heterocyclic compounds have great ability to bind with metal ions and provide stable complexes having great biochemical significance [39].

One of the major concerns in the organic synthesis is the formation of complex polyheterocyclic scaffolds in a single step from simple starting materials in academia and industries. Normally the target products are synthesized *via* stepwise process which requires addition of extra reagents and isolation of intermediates.

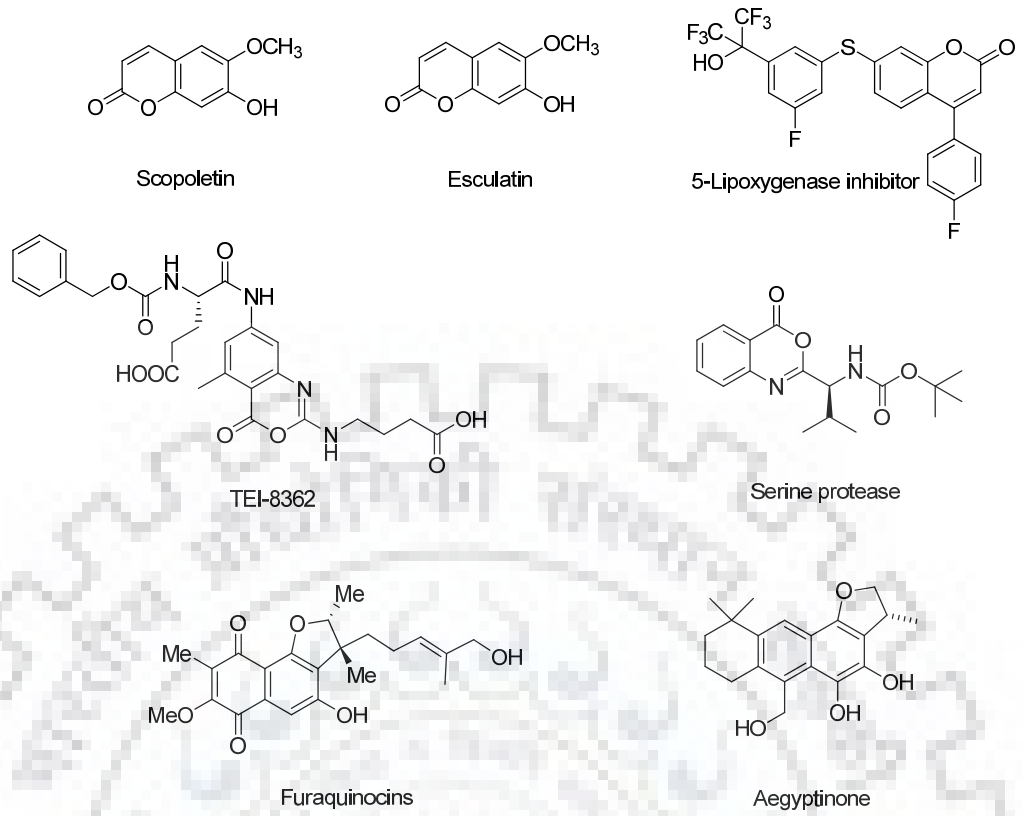


Figure 2: Some biologically active heterocyclic molecules containing coumarin, biarylsulfide, dihydrofuran, and benzoxazine moities.

Therefore, to circumvent the multistep procedures which are neither economically nor ecologically auspicious, the reactions forming multiple bonds, rings and chiral centres in the products are decisive for the construction of intricate molecules [40]. Domino reactions has unparalleled ability to generate complexity in the molecule *via* sequential bond formation and without isolating the starting materials [41]. Domino reactions have emerged as protocols that facilitate the efficient and rapid generation of polycyclic architecture bearing several stereogenic centres in operationally simple procedure by utilizing readily available precursors. The main features of domino reaction include rapid generation of molecular complexity with remarkable stereocontrol and low cost which enhances its use in organic synthesis. From the perspective of environmental friendly chemistry and atom economy, domino reactions have been used to synthesize innumerable natural products and biologically dynamic complex molecules in an ecologically and economically favourable way. Tietze defined the domino reaction as two or more bond forming reaction which

proceeded under identical reaction conditions without isolating the intermediates or adding reagents, and in which the consequent transformations take place at the functionalities achieved in the former transformations [42–44]. On the basis of the mechanism, domino reactions can be categorized as shown below [153] (Figure 3).

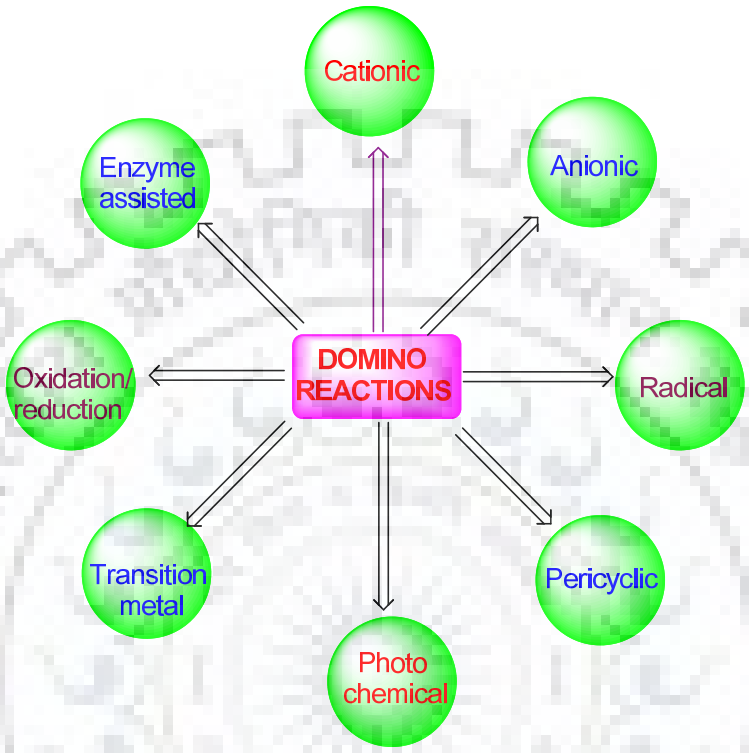


Figure 3: Classification of domino reactions.

The main advantages of domino reactions in organic synthesis are:

1) The reaction is often fast *i.e.* time resolved process and generates complexity in the target molecule
2) High atom economy
3) Domino reaction would enable the minimization of waste in contrast to stepwise reactions and avoids the purification of intermediates
4) The amount of solvents and reagents would be dramatically decreased
5) The reaction allows an ecologically and economically favorable construction of complex molecules [45,156].

A major area of our research group, and the main emphasis of this thesis, is the formation of multifunctional complex heterocyclic compounds *via* domino reaction of alkenyl *p*-benzoquinones and α,β-unsaturated esters/aroylmethylidene malonates with several nucleophiles.

1,4-Benzoquinone structural motif was found in a diversity of synthetic and isolated natural products and their structure was recognized as early as the 1830s [46] (Figure 4). *p*-Benzoquinone consists 6-membered ring, with two π-bonds in cross-conjugation and two carbonyl moieties at 1,4-position. Quinones are an important class of compounds furnished rich and enthralling chemistry and work as oxidizing as well as dehydrogenating agents [47,48]. 1,4-Benzoquinones have an interesting framework and undergoes a variety of reactions to form complex molecules [49–51]. Quinone molecules also work in an energy-harvesting and storage systems to enhance the efficiencies of the system [52].

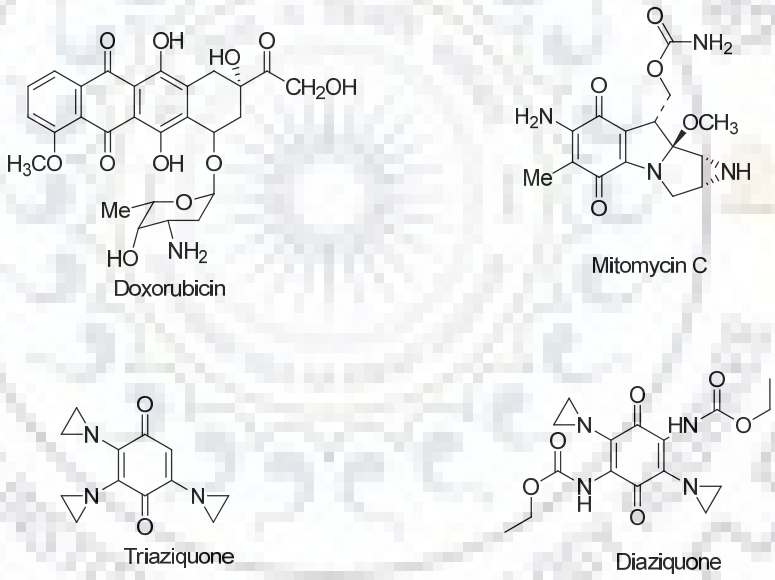


Figure 4: Some natural and synthetic products containing a quinone moiety.

The benzoquinones are important electrophilic precursors, and have been used in various reactions as a good Michael acceptors and reactive dienophiles in Diels–Alder reactions. Diels and Alder have reported the very first example of Diels−Alder cycloaddition of benzoquinone and cyclopentadiene to deliver a mixture of mono- and di-adducts. They have been used as an intermediate in several reactions for the building of complex heterocyclic molecules through C–C, C–N and C–S bonds in various fashions [53–55]. The

presence of two carbonyl groups and two alkenes in the system made them more electrophilic towards the reaction.

Similarly *α,β*-unsaturated esters are versatile acceptors in organic synthesis; they are an essential portion of numerous natural products and bioactive molecules such as (-)-pyrenophorin, (-)-A26771B, and (+)-patulolide A [56–58] (Figure 5). They have been utilized for the synthesis of several heterocyclic molecules such as 2,4,5-trisubstituted oxazole, quinoxalines, furans, and imidazole products with numerous starting partners.

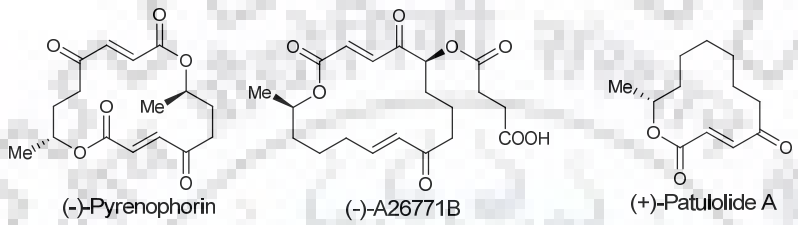
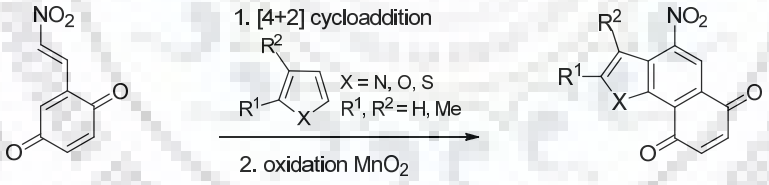


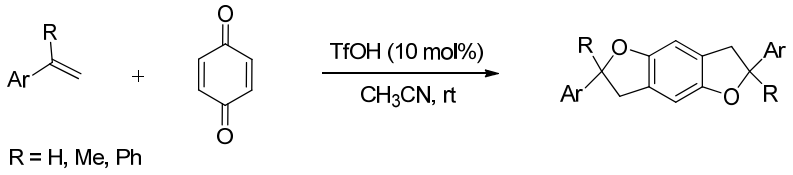
Figure 5: Biologically active compounds containing *α,β*-unsaturated systems.

Noland and co-workers reported a strategy towards the synthesis of fused quinoid heterocyclic ring arrangements *via* the reaction of nitrovinyl-benzoquinone with furans, indoles, and enol ethers. This protocol involved formal inverse electron-demand [4 + 2] cycloaddition reaction with good regioselectivity [59] (Scheme 1).



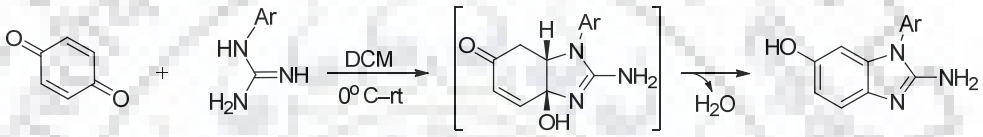
Scheme 1: Synthesis of quinoid heterocycles from nitrovinyl-quinones.

Lei *et al.* introduced a mild and transition metal-free production of tetrahydrobenzodifurans through oxidative C–H transformation of quinones. This protocol intricated the reaction of benzoquinone with substituted styrenes with catalytic amount of TFA at rt. The role of TfOH was to assist the reaction by activating benzoquinone. This reaction involved firstly [3 + 2] cycloaddition to generate 2,3-dihydrobenzofuran-5-ol and subsequent second addition of styrene *via* cationic/radical pathway to produce tetrahydrobenzodifurans [60] (Scheme 2).



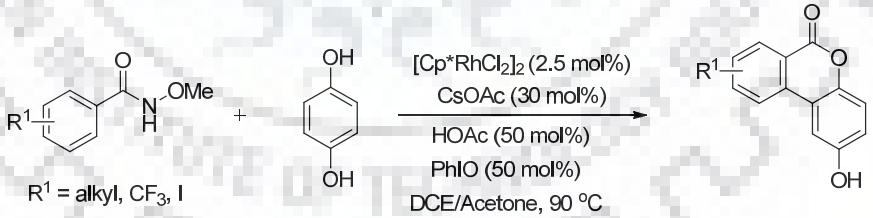
Scheme 2: Synthesis of tetrahydrobenzodifuran from benzoquinone and alkenes.

Al-Mourabit and co-workers efficiently used benzoquinone to produce 2-aminobenzimidazol-6-ol under metal-free conditions. They reported a simple and efficient reaction between quinone and guanidine derivatives for the generation of diverse range of aminobenzimidazols *via* addition, cyclization reactions and described their utility for the synthesis of several benzimidazole systems [61] (Scheme 3).



Scheme 3: Synthesis of 2-aminobenzimidazoles from quinone and arylguanidines.

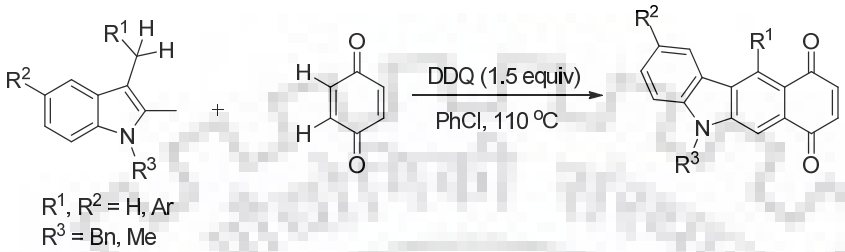
Xu *et al.* reported a novel synthesis of dibenzopyranones and benzonaphthopyranones *via* rhodium-catalyzed C–H arylation of hydroquinones. Benzoquinone was *in situ* generated by oxidation of hydroquinone to form carbon–carbon and carbon–oxygen bonds in a cascade fashion. Oxidizing agent and acetic acid played very important role for this reaction [62] (Scheme 4).



Scheme 4: Synthesis of dibenzo-pyran-6-ones from hydroquinone and *N*-ethoxybenzamide derivatives.

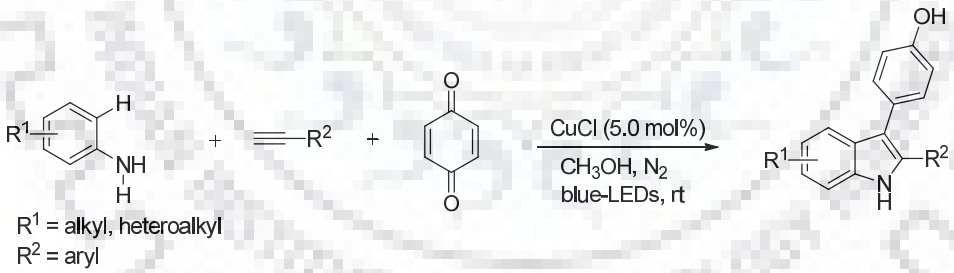
Zhang and co-workers established Diels–Alder reaction to synthesize tetrahydrocarbazoles, carbazoles, and heteroacenes *via* reaction of alkylindoles with electron deficient species. They developed a metal-free reaction in which *ortho*-quinodimethanes (*o*-

QDMs) were *in situ* generated from alkylmethylindoles by DDQ or BQ-mediated dehydrogenative route. The *in situ* generated *o*-QDMs were surrounded by benzoquinone to afford synthetically important benzocarbazole-diones. This metal-free and highly efficient methodology involved the direct C–H bond functionalization by a facile [4 + 2] cycloaddition [63] (Scheme 5).



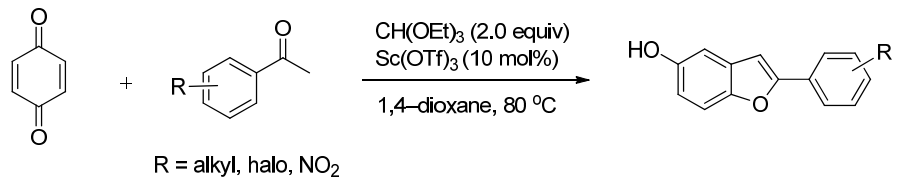
Scheme 5: DDQ-mediated synthesis of carbazoles.

Hwang *et al.* established first examples of regioselective synthesis of functionalized indoles *via* visible light induced copper-catalyzed process. This reaction proceeded through C–H functionalization of arylamine, terminal alkyne and benzoquinone in one-pot. This three-component reaction featured an atom-economical method towards the construction of polysubstituted indoles under light irradiation at rt and water was the only by-product in the reaction [64] (Scheme 6).



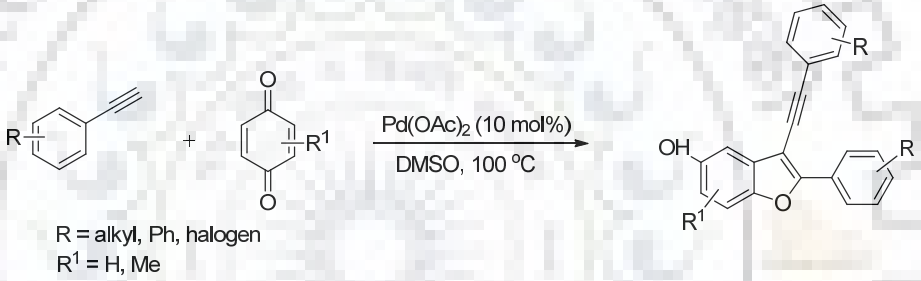
Scheme 6: Transition metal-catalyzed indole synthesis.

Gu and co-workers developed the synthesis of 5-hydroxybenzofuran. This protocol proceeded through Michael addition and intramolecular cyclization of ketones and 1,4-benzoquinones in the presence of catalytic amount of $Sc(OTf)_3$ and triethyl orthoformate. The additive orthoformate enhanced the nucleophilicity of enolizable ketone by converting it into ethyl vinyl ether [65] (Scheme 7).



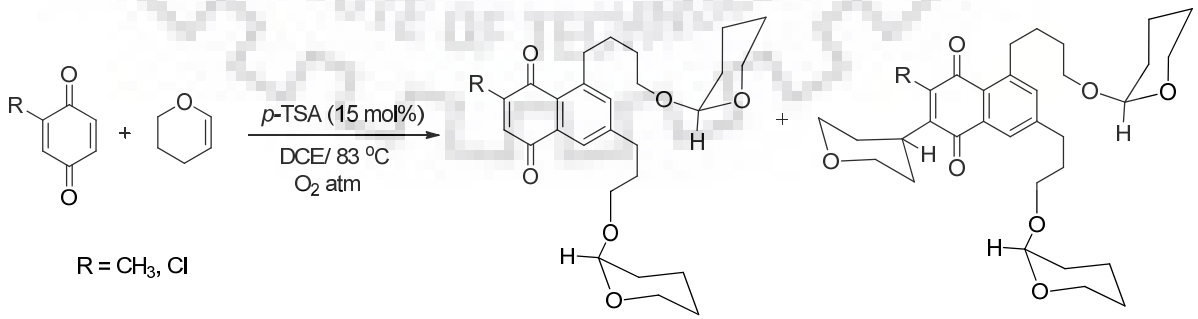
Scheme 7: Synthesis of substituted benzofurans from arylketones and quinone.

Yao and co-workers described a new methodology to develop biologically active disubstituted hydroxybenzofuran derivatives through palladium catalysis *via* C–H functionalization and cyclization strategy of benzoquinone and terminal alkynes. Benzoquinone played double role in this reaction as a reactant and oxidant. The process was free from base, ligand and extra oxidant. The self-coupling of alkynes was not observed in this protocol [66] (Scheme 8).



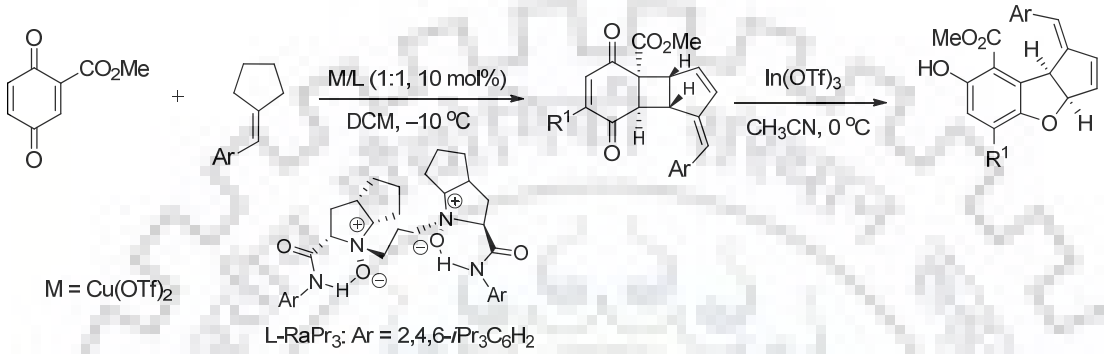
Scheme 8: Synthesis of 5-hydroxybenzofuran derivatives.

Easwaramoorthy *et al.* developed original and effective protocol for the construction of Diels–Alder cycloadduct between *p*-quinones and *in situ* generated diene from dihydropyran in the presence of *p*-TSA. The novelty of this reaction was generation of diene intermediate [67] (Scheme 9).



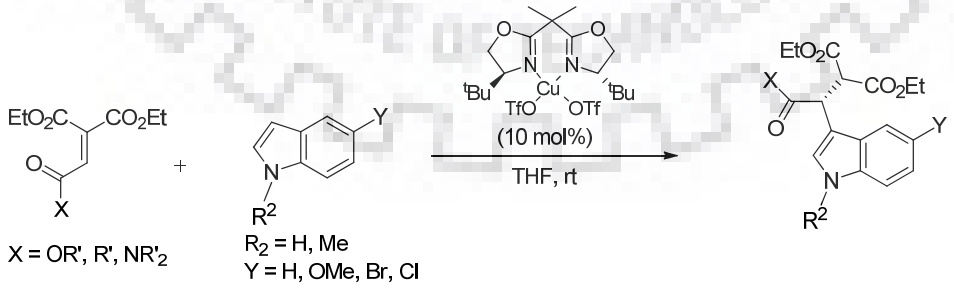
Scheme 9: Reaction of *p*-quinones with dihydropyran.

Feng *et al*. developed for the first time a catalytic enantioselective [2 + 2] cycloaddition reaction between fulvenes and quinone using a chiral copper based catalyst to access regio- and enantiomerically enriched tricyclic cyclobutane derivatives with good yields. These tricyclic systems could be easily converted into dihydro-cyclopentabenzofuran scaffolds stereoselectively by $In(OTf)_3$. Thus they synthesized 4- and 5-membered cyclic systems regio- and stereoselectively under mild reaction conditions [68] (Scheme 10).



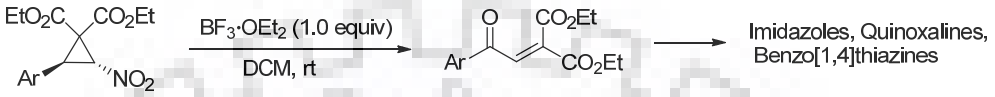
Scheme 10: [2 + 2] Cycloaddition reaction between fulvenes and quinones.

Yamazaki and co-workers reported Friedel–Crafts reaction to construct C–C bonds. The reaction was performed between α,β-unsaturated esters and indoles with catalytic amount of chiral copper(II) complex at rt. The synthesized compounds were achieved in high yields and up to 95% ee. For understanding the stereochemical model and chiral ligand complex structure, they performed calculations using UB3LYP/LANL2MB model and by this they explained the enantioselectivity *via* secondary orbital interaction approach of indoles which proceeded towards the less hindered position of the Cu(II)-ligand [69] (Scheme 11).



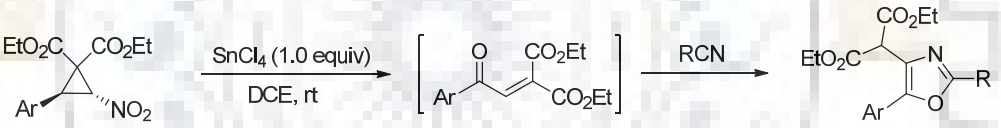
Scheme 11: Reaction of α,β-unsaturated esters and indoles.

Srinivasan and his group depicted the synthesis of aroylmethylidene malonates *via* cyclopropane ring opening. The reaction proceeded through $BF_3{\cdot}OEt_2$-mediated cyclopropane ring opening and rearrangements, further Nef reaction delivered the aroylmethylidene malonates. These aroylmethylidene malonates further used in the construction of medicinally essential compounds, such as quinoxaline, imidazole, and benzo[1,4]thiazine [70] (Scheme 12).



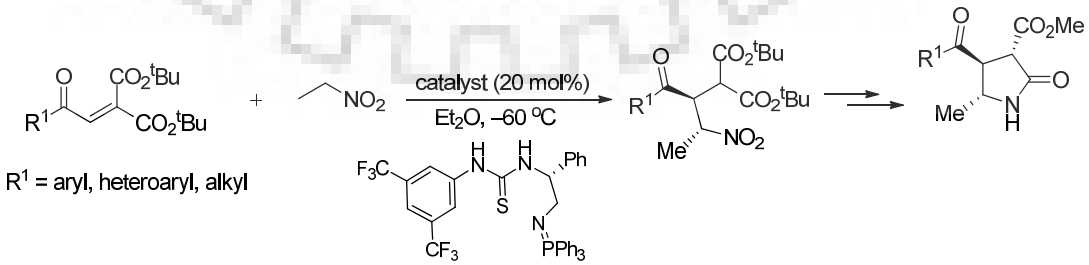
Scheme 12: Synthesis of aroylmethylidene malonates *via* ring opening of cyclopropanes.

Srinivasan and Selvi achieved a direct method for the synthesis of trisubstituted oxazoles by treating nitro-cyclopropane-dicarboxylates with alkyl nitriles in the presence of $SnCl_4$. They developed an entirely new approach in which conjugate addition of nitrile took place on *in situ* generated aroylmethylidene malonates, and provided nitrilium ion intermediate which on cyclization delivered oxazoles [71] (Scheme 13).



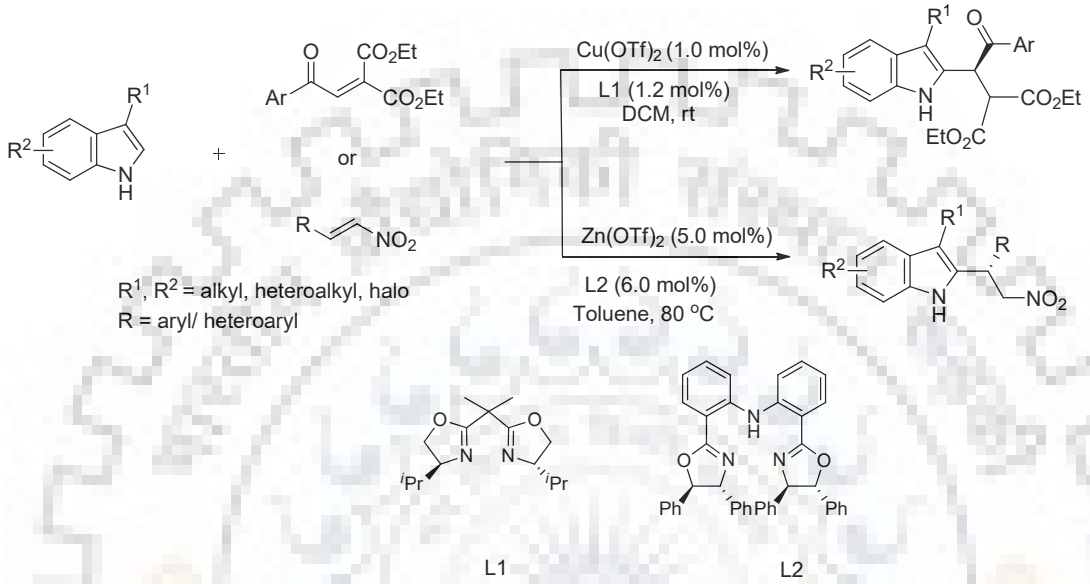
Scheme 13: Synthesis of trisubstituted oxazoles through $SnCl_4$-promoted reaction.

Johnson and co-workers depicted an enantioselective and diastereoselective addition methodology between enone diesters and nitroethane or nitropropane to generate molecules containing two chiral centres. For this reaction they used a bifunctional organocatalyst triaryliminophosphorane to deliver products with excellent stereoselectivities and good yields. The reaction showed good substrate scope [72] (Scheme 14).



Scheme 14: Enantioselective conjugate addition of nitroalkanes to enone diesters.

Jia *et al.* constructed an enormously enantioselective Friedel–Crafts alkylation protocol to access chiral indoles. The Lewis acid catalyzed reaction proceeded between C–3 substituted indoles and unsaturated esters or nitroalkenes. The reaction had good substrate scope and afforded the products in excellent yields and enantioselectivities [73] (Scheme 15).



Scheme 15: Friedel–Crafts alkylation reaction of indoles with aroylmethylidene malonates.

1.1 Synthesis of heterocyclic compounds containing heteroatoms N, O and S

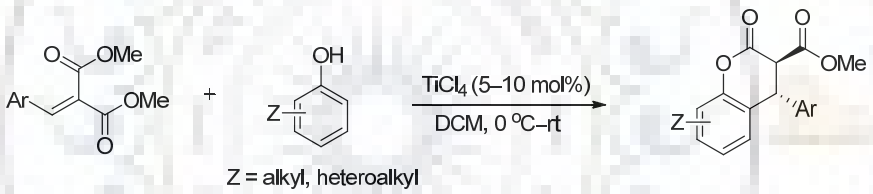
1.1.1. Synthesis of coumarins

Coumarins are bicyclic heterocyclic compounds containing benzene and pyrone ring and it was isolated in 1820 as natural product. Coumarins have wide applications in several fields such as drugs, pesticides, cosmetics and fluorescent dyes [74–76]. Due to their extensive pharmacological activities and low toxicity, they have been used as medicinal agents and food preservatives. Coumarin can be synthesized by various well known methods such as Knoevenagel condensation, Pechmann condensation, Claisen, Reformatsky, and Wittig reactions [77–80].

Generally, these methods have some drawbacks such as

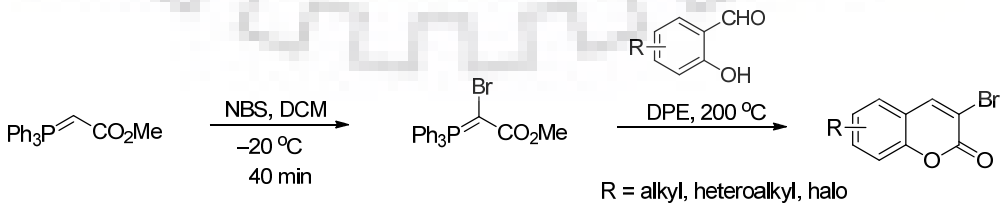
1. the requirement of a large amount of catalysts
2. rigid reaction conditions
3. requirement of high temperatures
4. use of toxic or expensive reagents
5. low yield of products and purification problem
6. poor selectivity
7. co-production of acidic waste leading to environmental pollution

Tunge *et al.* studied a simple and mild synthesis of 3,4-disubstituted dihydrocoumarins in the presence of various Lewis–acids and they observed that $TiCl_4$ worked well in the reaction. The reaction proceeded *via* hydroarylation of benzylidene malonic esters with phenols and subsequent transesterification produced *trans*-substituted dihydrocoumarins diastereoselectively [81] (Scheme 16).



Scheme 16: Diastereoselective synthesis of *trans*-substituted dihydrocoumarins.

Alami *et al.* depicted a highly efficient synthesis of 3-bromocoumarins at 200 °C in sealed schlenk tube with good yields. The one-pot reaction of methyl (triphenyl-phosphoranylidene)acetate, NBS and salicylaldehyde derivatives in DPE (diphenyl ether) delivered functionalized 3-bromocoumarins *via* bromination of methyl (triphenylphosphoranylidene)-acetate then Wittig olefination and cyclization in a tandem process [82] (Scheme 17).

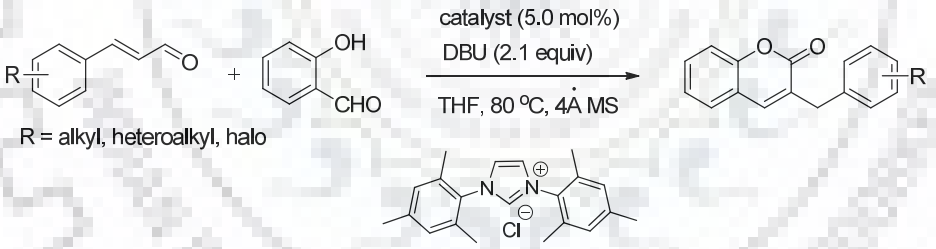


Scheme 17: Synthesis of 3-bromocoumarins from salicylaldehyde derivatives.

Karimi *et al*. introduced periodic mesoporous silica chloride (PMSCl) as an effective and biodegradable catalyst for the synthesis of coumarin under Pechmann reaction. Thus they developed a mild and effective protocol for the synthesis of coumarin derivatives in the presence of PMSCl with 2D P6mm hexagonal structures. The reaction was well tolerable with different substituents and provided coumarins with good to excellent yields [83] (Scheme 18).

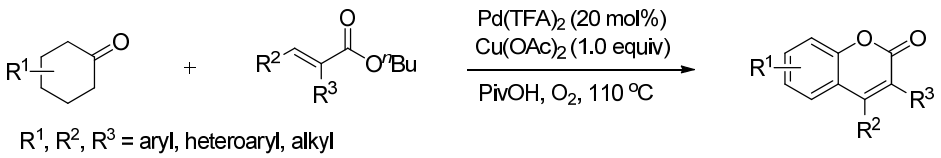
Scheme 18: PMSCl-mediated reaction towards the synthesis of 4-substituted coumarins.

Lu and co-workers described highly efficient NHC-catalyzed condensation reaction for the formation of benzylchromenones. Homoenolate intermediates were generated through the reaction between cinnamaldehydes and salicylaldehydes. The main features of the reaction were good efficiency, low catalyst loading and excellent functional group tolerance. When aliphatic α,β-unsaturated aldehydes were used then catalyst supplying improved to 10 mol% [84] (Scheme 19).



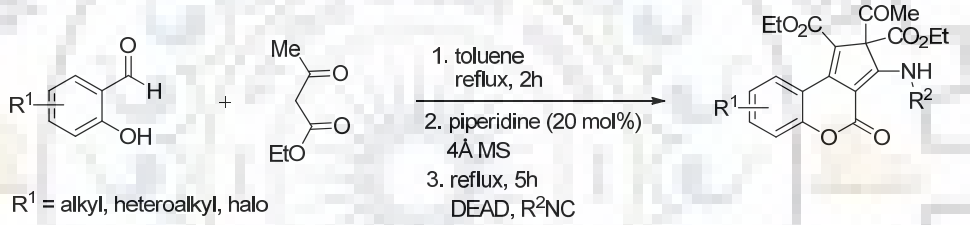
Scheme 19: The condensation reaction of substituted cinnamaldehydes with salicylaldehyde.

Hong *et al*. introduced an effective and straightforward procedure for the synthesis of coumarin through C–H functionalization *via* Pd(II)-catalyzed dehydrogenation–oxidative Heck–cyclization process. This protocol involved cyclohexanones and alkenes, providing a variety of coumarins. This Pd(II) catalyzed dehydrogenation reaction, proceeded through *in situ* generation of phenols and further oxidative cross-coupling with same catalyst took place, which after cyclization furnished diversely substituted coumarins [85] (Scheme 20).



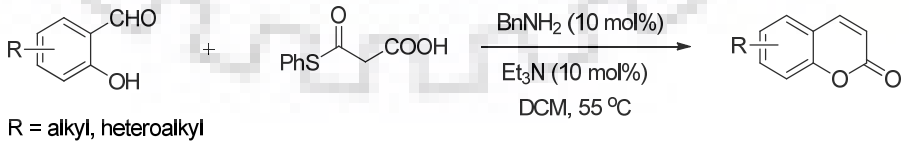
Scheme 20: Synthesis of coumarins *via* dehydrogenation reaction of cyclohexanones.

Kubicki and co-workers established an effective, mild one-pot methodology to synthesize novel functionalized cyclopentadiene-fused chromanone scaffolds. This one-pot multi-component reaction proceeded *via* ethyl acetoacetate and hydroxybenzaldehydes in toluene with 1:1 acetylenecarboxylate/ isocyanides and catalytic amount of piperidine under reflux condition. This method involved the *in-situ* generation of acetyl-2*H*-chromenones which underwent Michael addition with acetylenecarboxylate-isocyanide zwitterionic intermediates, and subsequent intramolecular cyclization, double acyl shift rearrangement produced cyclopentadiene-fused chromanones [86] (Scheme 21).



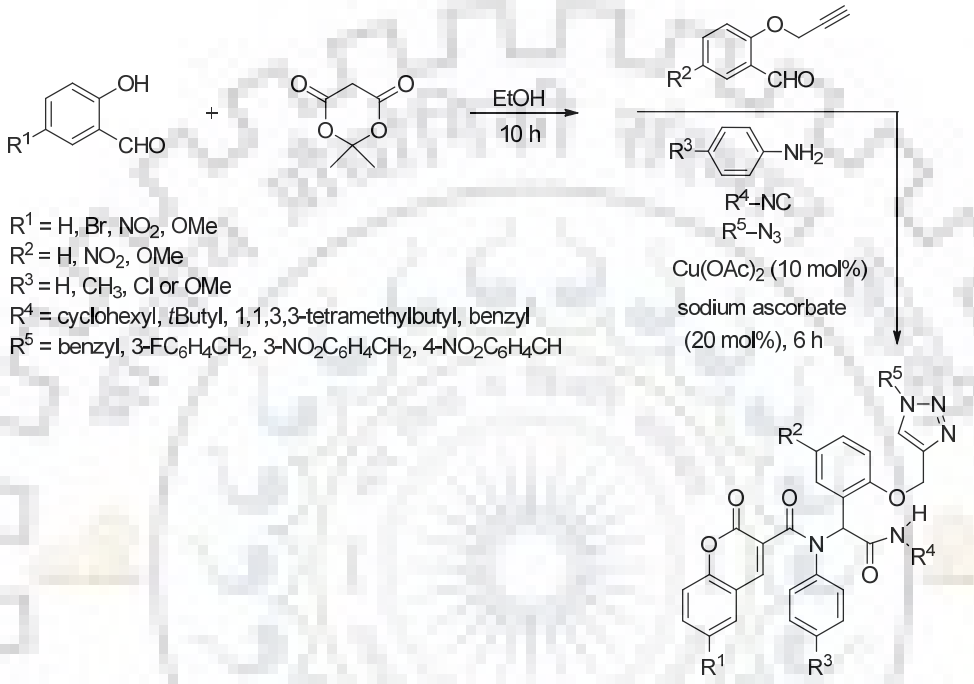
Scheme 21: Multi-component one-pot reaction for the synthesis of chromanones fused with cyclopentadiene.

Wang *et al*. reported a candid approach for the production of coumarins through a cascade organocatalytic reaction between malonic acid half-thioester and salicylaldehydes with catalytic amount of benzylamine and triethylamine. This metal-free approach delivered 3,4-diunsubstituted coumarins in good yields [87] (Scheme 22).



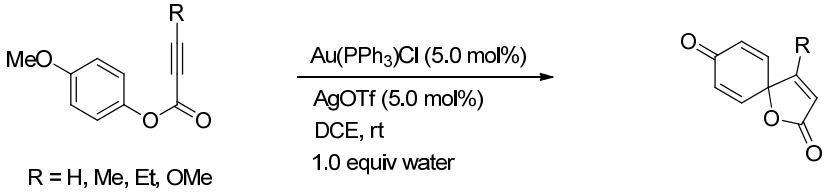
Scheme 22: Synthesis of diunsubstituted coumarins *via* tandem reaction of salicylaldehydes and malonic acid half-thioester.

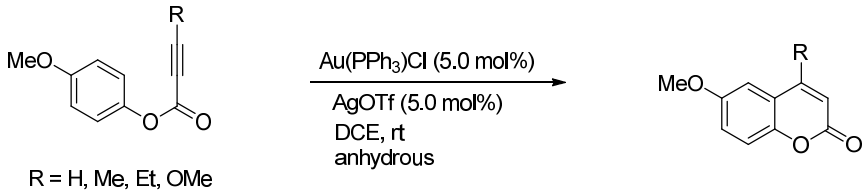
Ng e*t al.* developed an efficient, simple, and environmental friendly method to develop trifunctional coumarin-amide-triazole encompassing compounds. In this one-pot reaction 5-bromosalicylaldehyde, maldrum acid, aniline, propargyloxy aldehyde, and cyclohexyl isocyanide were mixed in EtOH at room temperature. Later treatment with aryl azides by using catalytic amount of sodium ascorbate and $Cu(OAc)_2$ delivered the target compounds [88] (Scheme 23).



Scheme 23: Synthesis of coumarin-3-carboxamides *via* multicomponent reaction.

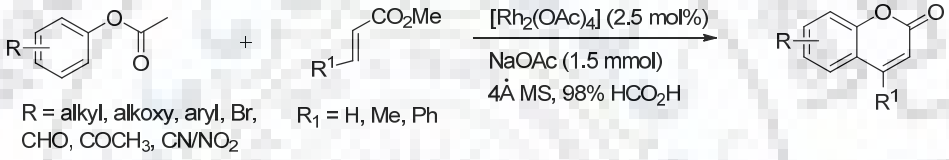
Vadola and co-workers established a practical and highly novel synthesis of spirolactone and coumarin products selectively in high yields. Water played an important role in the reaction for the selectivity of the products. Aryl alkynoate esters underwent gold-catalyzed cyclization in water and delivered spirolactones, while in anhydrous conditions, coumarin derivatives were produced. This reaction required halogenating agent for the activation of alkyne [89] (Scheme 24).





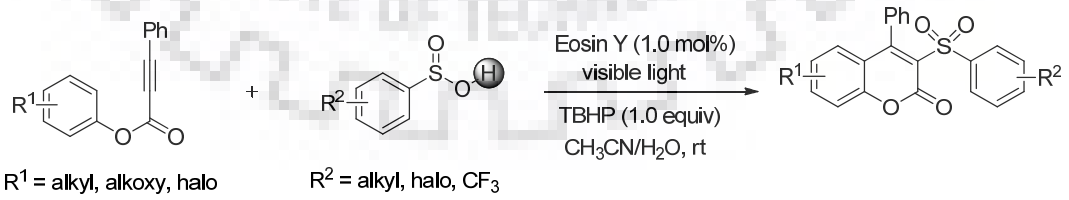
Scheme 24: Synthesis of spirocyclic lactones and coumarins.

Sudalai and co-workers introduced an efficient and regioselective C–H functionalization of phenolic acetates with acrylates catalyzed by $[Rh_2(OAc)_4]$ and formic acid as reducing agent for the synthesis of coumarin derivatives. This was a simple annulation strategy towards the formation of coumarins with good yields. The reaction proceeded through C–H bond activation, which was confirmed by deuterium incorporation studies [90] (Scheme 25).



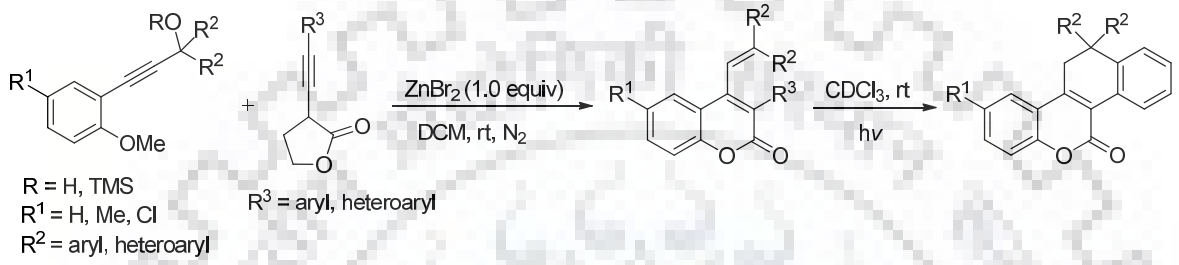
Scheme 25: Synthesis of coumarin derivatives *via* Rh-catalyzed reaction between phenolic acetates and acrylates.

The metal-free synthesis of coumarins through visible-light originated oxidative cyclization of phenyl propiolates and sulfinic acids in the presence of TBHP at rt was introduced by Wang and co-workers. The reaction involved formation of C–C and C–S bonds to synthesize 3-sulfonated coumarins and proceeded *via* radical pathway. The reaction ensued *via* tandem process and delivered regioselective products in good yields [91] (Scheme 26).



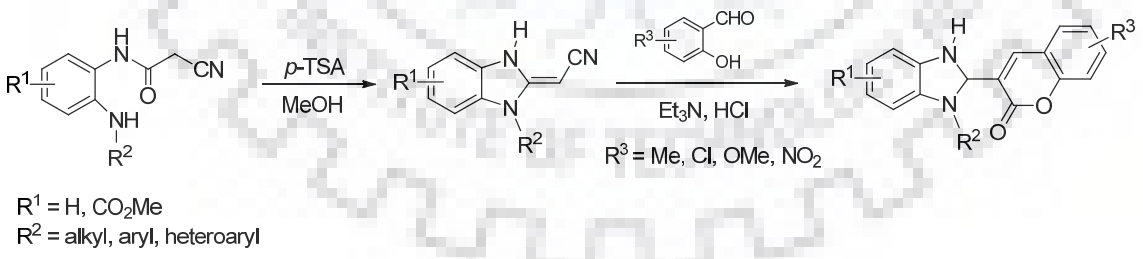
Scheme 26: Synthesis of coumarin derivatives under metal-free conditions.

An efficient and facile [4 + 2] cycloaddition approach for the formation of 4-vinyl coumarins introduced *via* reaction of substituted propargyl silyl ethers and ynamides by Xu *et al.* The reaction proceeded through formation of carbocation intermediate from propargyl silyl ether which reacted with ynamide to deliver 4-vinyl coumarins. This 4-vinyl coumarin after 6π-electrocyclization followed by 1,5-H shift delivered polycyclic coumarin derivatives. For this purpose, they performed fluorescence analysis strategy for screening the reaction conditions [92] (Scheme 27).



Scheme 27: Synthesis of polycyclic coumarin derivatives *via* [4 + 2] cycloaddition reaction.

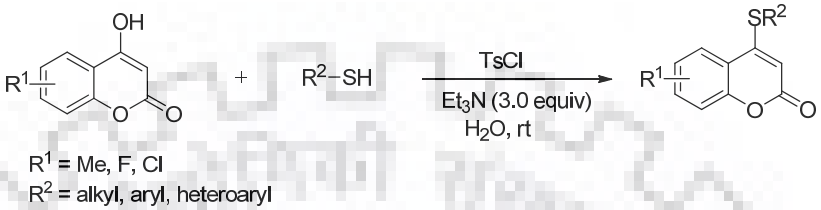
One-pot, multi-component, intramolecular Knoevenagel cyclization was carried out by Sun and co-workers towards an efficient synthesis of coumarin benzimidazoles. Coumarin attached benzimidazoles were obtained from aminophenyl substituted cyanoacetamide and salicylaldehydes in excellent yields. Benzimidazole intermediate formed by intramolecular cyclization of *N*-(2-aminophenyl)-2-cyanoacetamide. The main features of the reaction were short reaction time, reduction in purification steps, less expensive catalyst and high yields of the products [93] (Scheme 28).



Scheme 28: Synthesis of coumarin-linked benzimidazole derivatives.

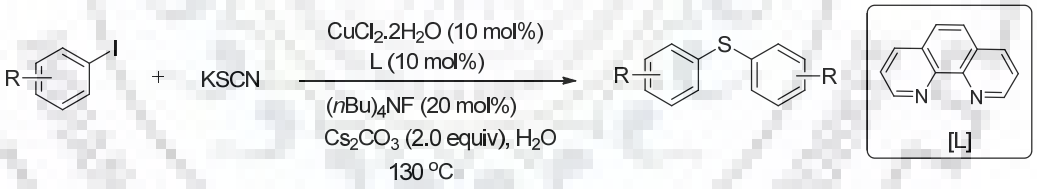
1.1.2. Synthesis of biaryl sulfides

Peng and co-workers reported highly efficient, green, novel and mild approach towards the synthesis of 4-sulphanyl coumarin *via* C–OH bond activation of 4-hydroxy-coumarins through direct sulfanylation with thiols. The reaction was performed in water at rt in air [94] (Scheme 29).



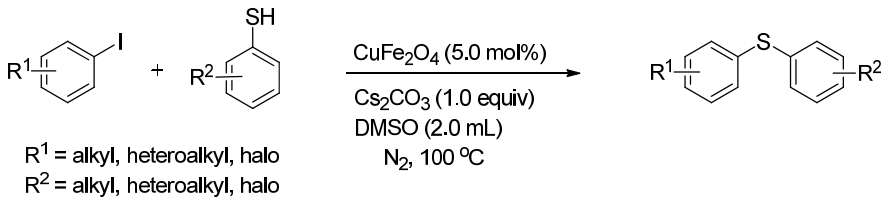
Scheme 29: Synthesis of coumarin-aryl/alkyl-sulfides.

Zhou *et al*. accounted an efficient C–S bond formation protocol *via* copper-catalyzed reaction between aryl halides and KSCN in water. In this protocol, aromatic halide was activated through Cu catalyst and generated arylthiocyanate with potassium thiocyanate. In the presence of water arylthiocyanate hydrolyzed and formed thiolate anion which again reacted with aryl halide and delivered biaryl sulfides in good yields. The base was used to hydrolyze cyanide anion in the reaction [95] (Scheme 30).



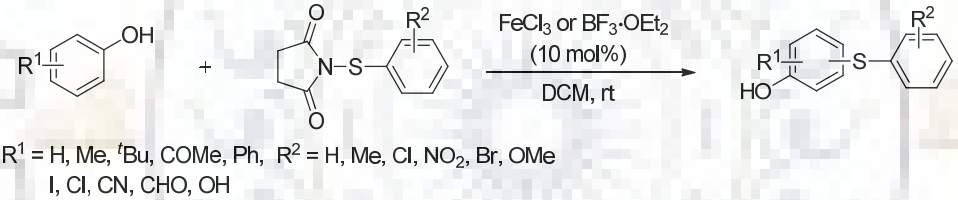
Scheme 30: C–S bond formation in the presence of water.

Nageswar *et al.* described $CuFe_2O_4$ nanopowder magnetically distinguishable and ecofriendly catalyst for the creation of C–S bond *via* coupling reaction. The coupling reaction proceeded *via* oxidative addition followed by reductive elimination. A wide-ranging of thiophenols was used in the reaction to provide a convenient way to synthesize aryl/alkyl sulfides [96] (Scheme 31).



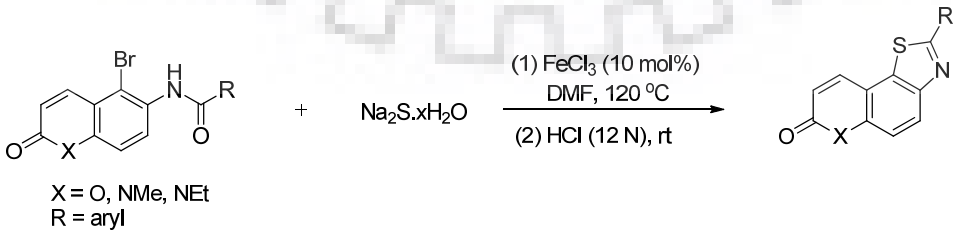
Scheme 31: Synthesis of biarylsulfides in the presence of Cu catalyst.

Fu *et al.* introduced a novel, effectual and environmental friendly methodology to synthesize C–S bond *via* C–H arylthiation of substituted phenols through iron or boron-catalyzed reaction at room temperature. This protocol was well tolerated with both aryl as well as alkyl disulfides and utilized substituted *N*-(phenylthio)succinimides as arylthiation reagents. The reaction proceeded *via* N–S bond cleavage activated by acid catalyst and generated cationic and anionic intermediates, this cationic intermediate reacted with phenol and produced products in good yields. The main features of this reaction were obviating additives and ligands [97] (Scheme 32).



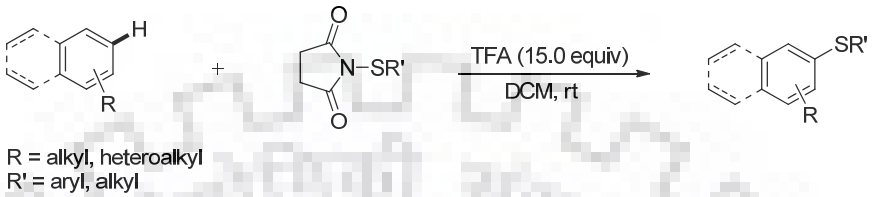
Scheme 32: Arylthiation of substituted phenols *via* $FeCl_3$ or $BF_3{\cdot}OEt_2$.

Ghosh and Majumdar described an efficient and mild protocol for the formation of coumarins, and quinolone-fused thiazoles. The synthetic route involved iron-catalyzed ligand-free coupling reaction followed by condensation. Sodium sulfide was used as sulfur source and $FeCl_3$ as a catalyst for the first time to deliver fused thiazoles with good yields in a one-pot reaction [98] (Scheme 33).



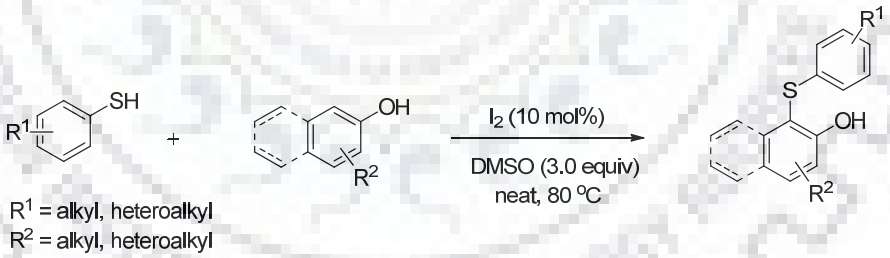
Scheme 33: Synthesis of coumarin and quinolone-fused thiazole derivatives catalyzed by $FeCl_3$.

A successful and simple approach to access biaryl sulfides in metal-free conditions was represented by Cossy *et al.* In this protocol *N*–alkyl/aryl-thio-succinimides were used as sulfur source for C–H sulfenylation of various arenes at room temperature. This TFA-mediated metal-free approach was highly regioselective and afforded products in excellent yields [99] (Scheme 34).



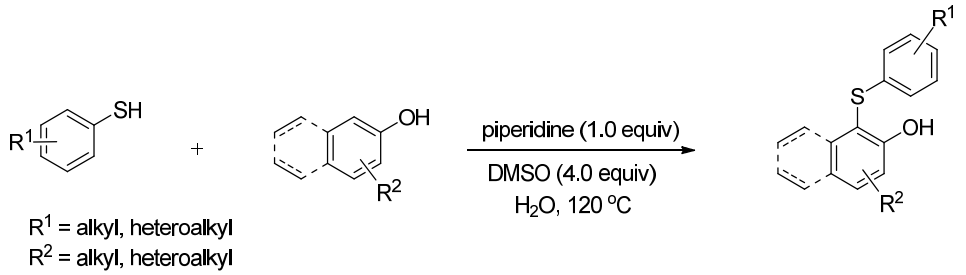
Scheme 34: Metal-free synthesis of aryl sulfides.

Our group reported iodine-catalyzed novel and green protocol for cross-dehydrogenative C–S coupling. The reaction proceeded between aryl thiols and electron-rich arenes to access aryl sulfides under neat conditions. We extended this protocol with 4-hydroxycoumarin and dithioacetal to deliver the analogous products in good yields. This protocol proceeded through the construction of electrophilic intermediate Ar–SI which reacted with electron-rich species to deliver aryl sulfides in excellent yields [100] (Scheme 35).



Scheme 35: Synthesis of alkyl/aryl sulfides from aryl thiols.

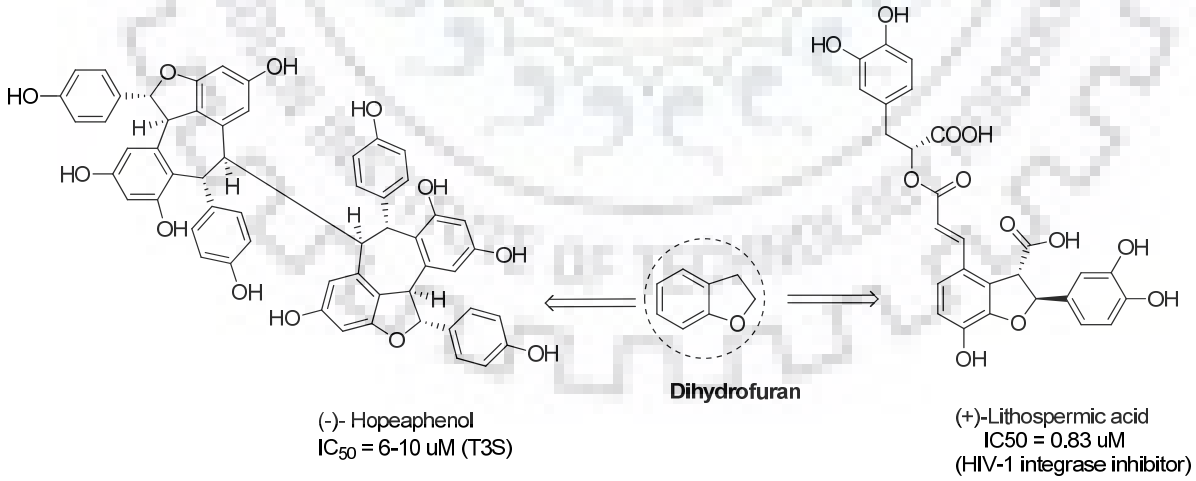
Xiao group accounted the alkyl/aryl sulfide synthesis in presence of piperidine under aqueous conditions. Various thiophenols were well endured under this reaction conditions and efficiently provided the products in good yields [101] (Scheme 36).



Scheme 36: Synthesis of aryl sulfides from aryl thiols in the presence of piperidine.

1.1.3. Synthesis of dihydrobenzofurans and naphthofurans

Benzofurans are bicyclic heterocyclic compounds containing benzene and furan rings and are isoelectronic with indole. Benzofuran skeletons are the common motifs in agrochemicals, pharmaceuticals and natural products [102] and their hydrogenated form known as 2,3-dihydrobenzofurans which was previously termed as coumarane, was firstly reported in 1892 by Alexander [103]. Later various methods have been reported for the synthesis of these heterocycles. The 2,3-dihydrobenzofuran motif founds in various natural products (Figure 6) [104,105] and possesses interesting biological activities [25–27]. They are found in plant metabolites such as neolignans and also present in morphine alkaloid. Similarly naphthofuran motifs, consist benzene ring fused with benzofuran, they are also a part of various natural products (Figure 6) [106] and are found in pharmaceutical compounds [37,38].



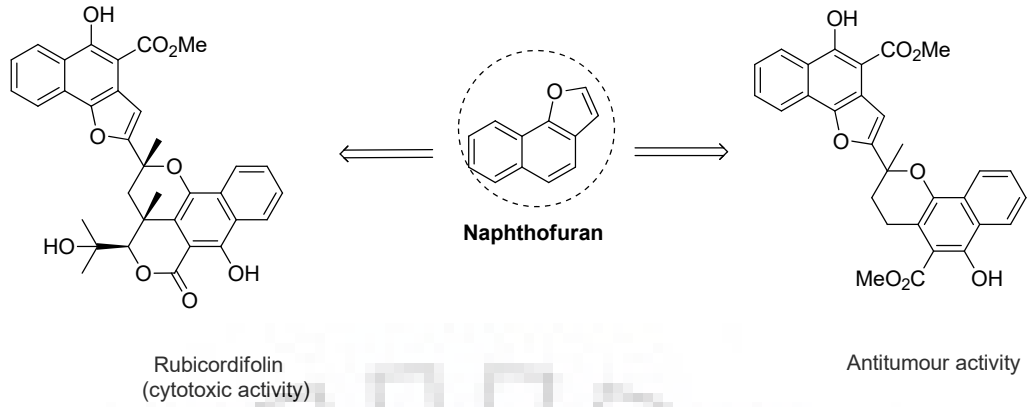
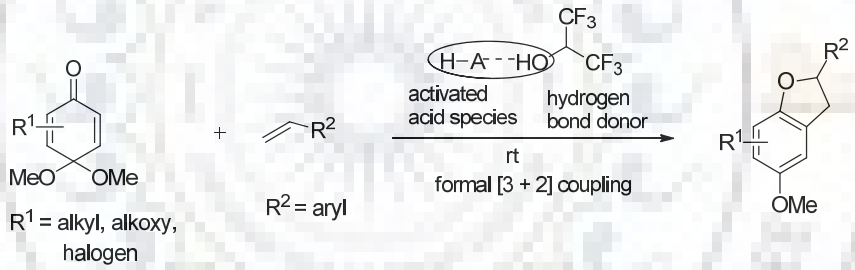


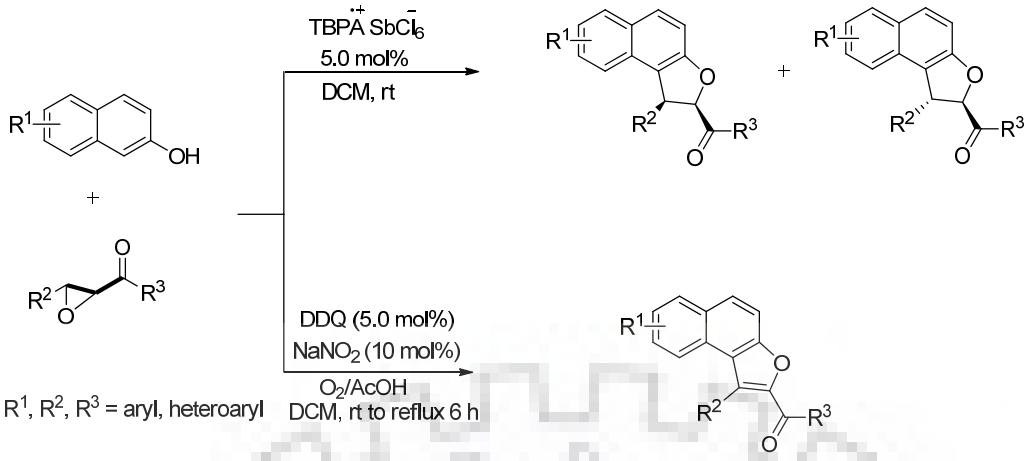
Figure 6: Naturally occurring molecules bearing dihydrofuran and naphthofuran moiety.

Kita *et al.* introduced the synthesis of 2,3-dihydrobenzofurans *via* [3 + 2] cyclo-addition of quinone monoacetals and olefins. This protocol progressed in the presence of Brønsted acid and perfluorinated alcohol. The main role of perfluorinated alcohol is to activate Brønsted acid. Various substituted dihydrobenzofurans and naphthalene dihydro-furans were synthesized by this methodology [107] (Scheme 37).



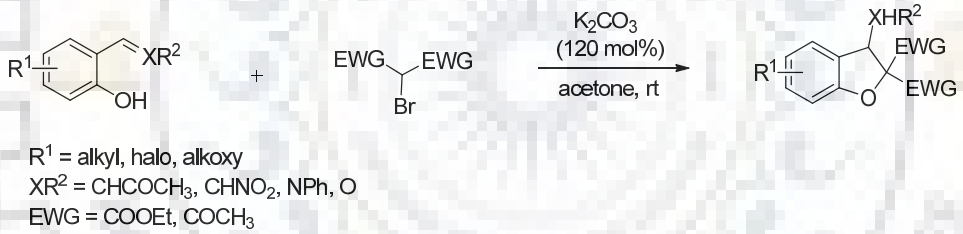
Scheme 37: Synthesis of dihydrobenzo-furans *via* [3 + 2] coupling between quinone mono-acetals and substituted styrenes.

Wang and co-workers developed a novel Friedel–Crafts alkylation/annulation domino reaction to access polysubstituted dihydronaphthofurans by using chalcone epoxides and *β*-naphthols in catalytic amount of $TBPA^{+}\cdot SbCl_6^{-}$. Dihydronaphthofurans were further oxidized by DDQ to generate substituted naphthofurans in one-pot. In this protocol, triaryl-aminium salt worked as a highly effective initiator and the combination of DDQ/$NaNO_2$/ $AcOH/O_2$ were used for the oxidative aromatization [108] (Scheme 39).



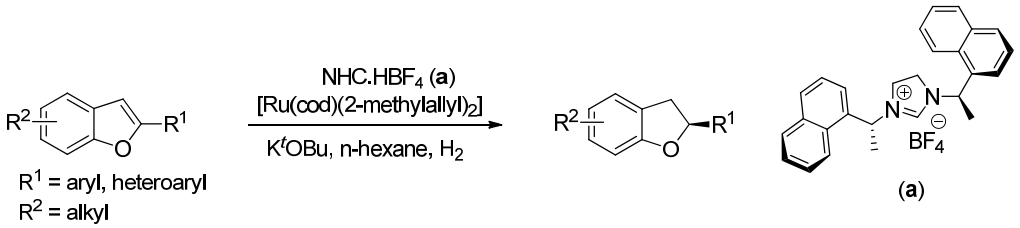
Scheme 38: Synthesis of substituted dihydronaphthofurans and their oxidative aromatization.

Xie *et al.* developed a novel domino reaction of salicylaldehyde derivatives and halodicarbonyl compounds in presence of K_2CO_3 to deliver functionalized 2,3-dihydrobenzofurans in excellent yields under mild conditions. The reaction exhibited good substrate scope [109] (Scheme 39).



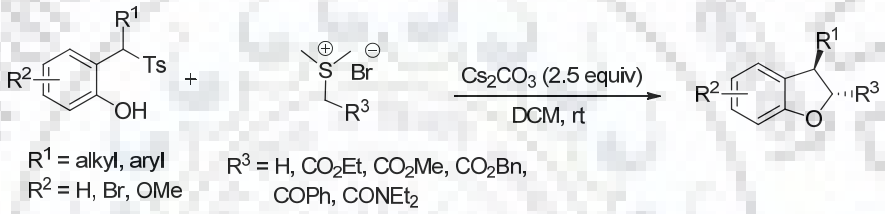
Scheme 39: K_2CO_3-mediated domino reaction to access functionalized 2,3-dihydrobenzofurans.

Glorius *et al.* reported asymmetric hydrogenation of benzofurans by using chiral ruthenium NHC complex. This protocol provided highly regioselective and highly enantioselective straightforward approach towards the synthesis of dihydrobenzofurans in good yields. The reactions were well tolerable with aliphatic and aromatic substituted benzofurans. In this reaction non-polar aprotic solvent delivered the products in excellent enantiomeric ratio [110] (Scheme 40).



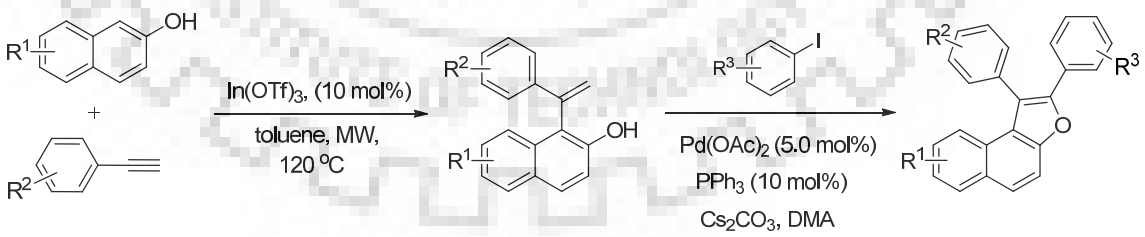
Scheme 40: Asymmetric hydrogenation of benzofurans to dihydrobenzofurans *via* ruthenium NHC catalysis.

Zhou and co-workers developed a method to deliver *trans*-2,3-dihydrobenzofurans *via in situ* generation of *o*-quinone methides under basic conditions. They developed a novel and effective method by utilizing tosylalkylphenols and sulfur ylides to produce stereoselective dihydrobenzofurans [111] (Scheme 41).



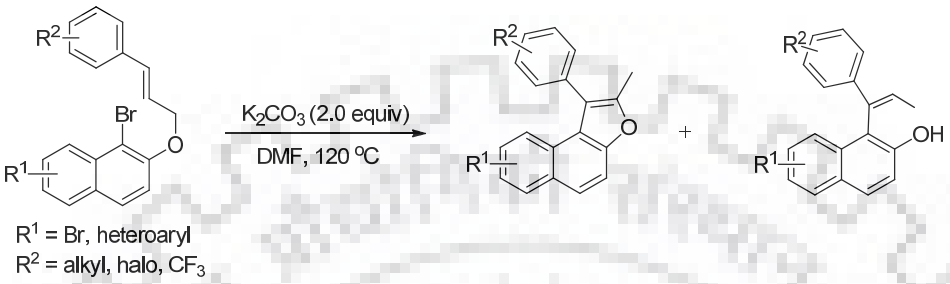
Scheme 41: Reaction of tosylalkylphenols with sulfonium salts.

Kumar *et al.* established a simple, efficient, and mild protocol to access 2,3-diaryl naphthofurans by using *β*-naphthols and substituted alkynes *via* Lewis acid-mediated reaction under microwave irradiation. The reaction proceeded *via* one-pot Heck-oxyarylation of derivatized-hydroxy styrenes to deliver substituted naphthofurans [112] (Scheme 42).



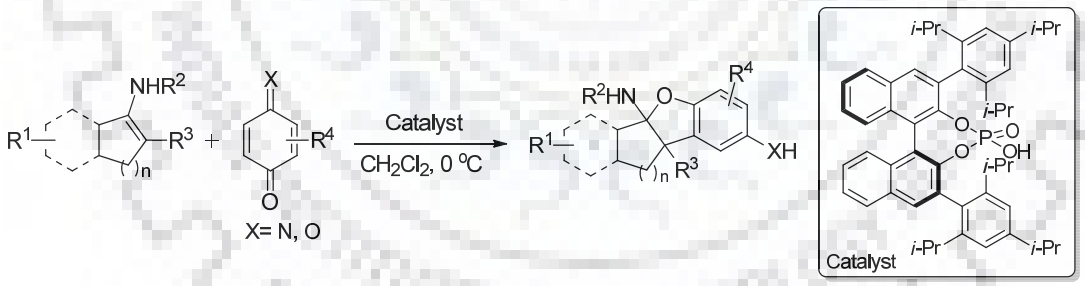
Scheme 42: Hydroarylation/Heck oxyarylation reaction towards synthesis of naphthofurans.

Li and co-workers introduced Claisen rearrangement or cyclization of bromonaphthyl 3-phenylallyl ether to construct naphthofurans. This transition metal-free reaction proceeded under basic conditions and K_2CO_3 played a very important role to determine the ratio of naphthofurans and naphthols produced in the reaction [113] (Scheme 43).



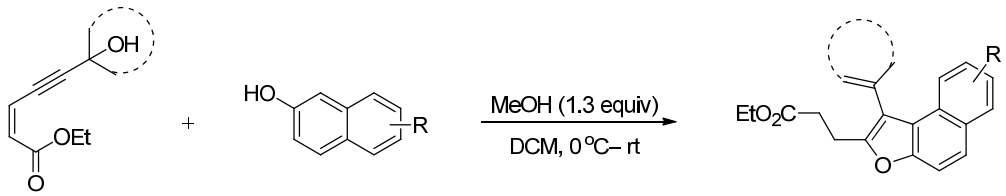
Scheme 43: Claisen rearrangement or cyclization of bromonaphthyl-phenylallyl ethers for synthesis of substituted naphthofurans.

Zhang and co-workers devised a chiral phosphoric acid promoted reaction for the formation of highly enantioenriched polycyclic dihydrobenzofurans. The target products were synthesized from cyclic enamides and quinone monoimines *via* enantioselective [3 + 2] coupling. The polycyclic 2,3-dihydrobenzofurans were achieved in good to excellent yields with upto 99.9% ee [114] (Scheme 44).



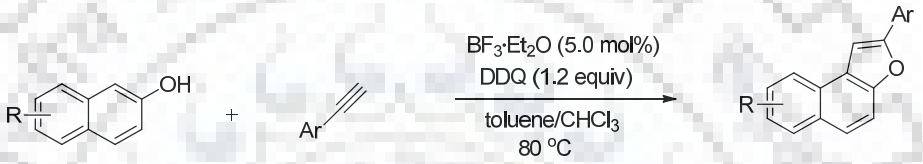
Scheme 44: [3 + 2] coupling of cyclic enamides with quinone monoimines and quinones.

Baire and co-workers presented an innovative route for the synthesis of complex naphthofurans from acid-promoted, cascade [3 + 2] approach. In this protocol *β*-naphthols were used as nucleophiles and *in situ* generated alkoxyfuranylallene was engaged as 1,2-bis-electrophile. The formed naphthofurans can be transformed into the skeleton of amycofuran and frondosin B natural products [115] (Scheme 45).



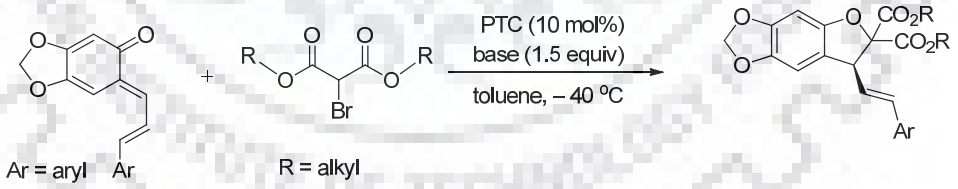
Scheme 45: Synthesis of complex naphtho(benzo)furans.

Zhou *et al.* established an efficient and novel oxidative annulation route to afford 2-arylnaphthofurans in good yields under metal-free conditions from 2-naphthols and terminal alkynes. The present strategy involved radical pathway, C–H bond activation, C–C coupling, and C–O cyclization [116] (Scheme 46).



Scheme 46: $BF_3 \cdot OEt_2$-mediated reaction for the synthesis of naphthofurans.

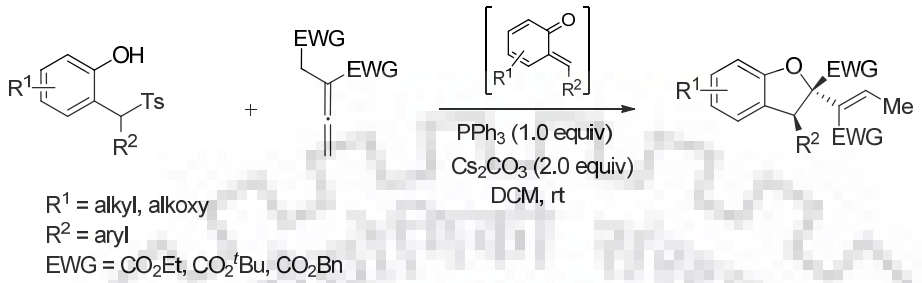
Han *et al.* accounted an enantioselective [4 + 1] cycloaddition reaction to prepare optically active dihydrobenzofurans from *in situ* generated *ortho*-quinone methides and bromomalonates with quinine in presence of BINOL derived phase-transfer catalyst. The reaction proceeded very well, accounted good substrate scope and delivered dihydrofurans with good yields and high ee [117] (Scheme 47).



Scheme 47: Synthesis of dihydrobenzofurans *via* [4 + 1] cycloaddition between *ortho*-quinone methides and bromomalonates *via* phase-transfer catalysis.

In 2018, Waser and co-workers applied PPh_3 promoted [4 + 1] annulation of *in situ* generated *o*-quinone methides with allenoates to access highly functionalized dihydrobenzofurans with excellent diastereoselectivities and high yields. They observed that

reaction was successful with PPh_3 and not with trialkyl phosphines. For understanding the mechanistic route they carried out the reaction with γ-dideuterated allenoate or deuterated solvent CD_2Cl_2 which showed that intra- and intermolecular proton transfers were possible on the intermediate synthesized during reaction [118] (Scheme 48).



Scheme 48: Diastereoselective synthesis of dihydrobenzofurans *via* [4 + 1] cycloaddition reaction of *o*-quinone methides.

1.1.4. Synthesis of pyrroles

Pyrrole was deduced for the first time in 1834 by Runge, in coal tar where he noticed a substance that dyes pine splinters red and he named it pyrrole (meaning, fiery oil). The actual structure of pyrrole was established in 1870 [119]. Pyrroles are a class of heterocyclic compounds containing 5-membered ring with four carbon and one nitrogen heteroatom. Pyrrole moiety presents in a variety of natural products and medicinally important compounds (Figure 7) [28–30]. Pyrrole containing compounds show various pharmacological and biological activities such as anti-inflammatory, antibacterial, antitumor, antifungal, antioxidative, and ionotropic. Pyrrole ring contains a part of non-steroidal anti-inflammatory drugs (NSAIDs), therefore it is recognised as a crucial core to access new anti-inflammatory agents [35,120–122]. Several methods have been reported for the synthesis of pyrrole core.

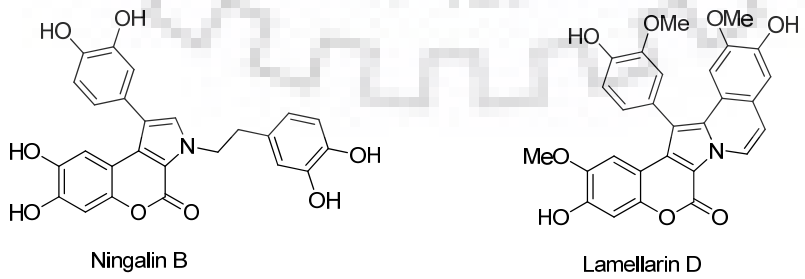
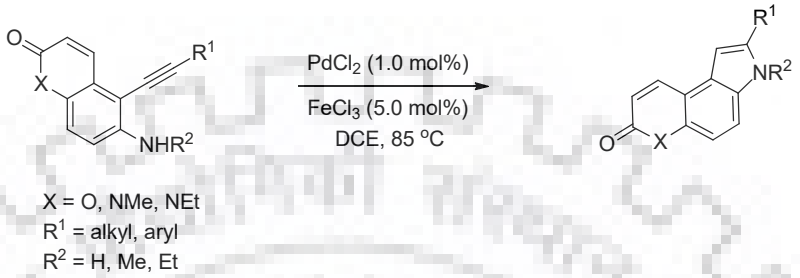


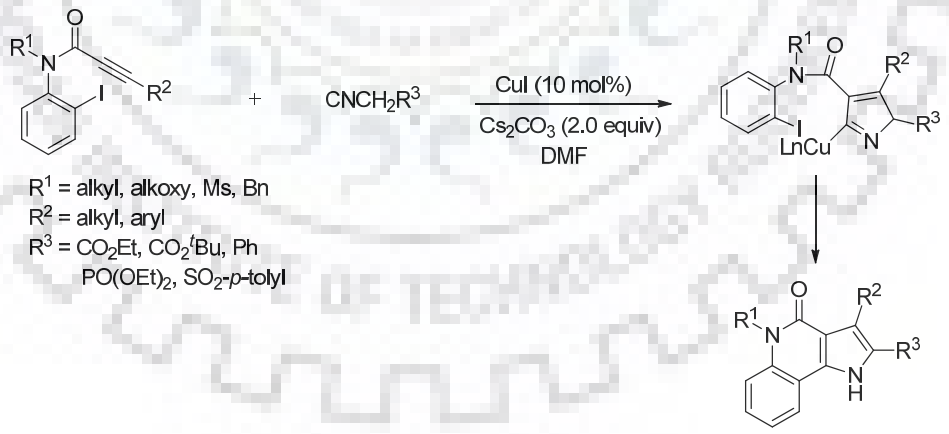
Figure 7: Natural products containing pyrrole subunit.

Majumdar *et al.* reported the synthesis of pyrrole-fused with coumarin and quinolone derivatives. The reaction proceeded *via* intramolecular hydroamination reaction of aminoalkynes to access the pyrrolocoumarin and pyrroloquinolone catalyzed by $PdCl_2/FeCl_3$. Aliphatic and aromatic substituted alkynes were amenable to the current protocol and produced the analogous products in good yields [123] (Scheme 49).



Scheme 49: Synthesis of pyrrole-fused coumarin and quinolones.

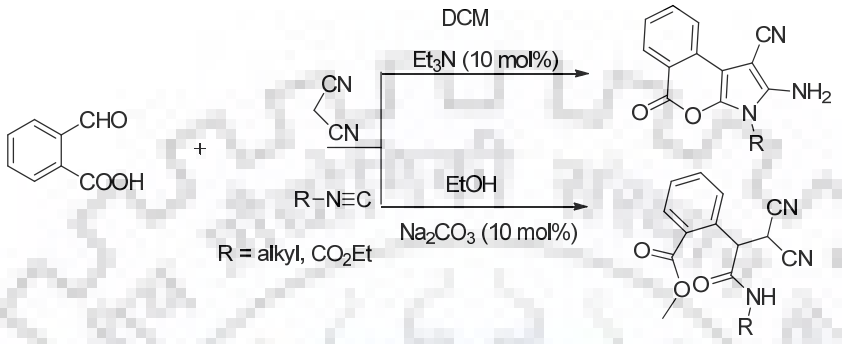
Cai *et al.* established copper-catalyzed synthesis of pyrroloquinolin-4-ones *via* tandem reaction of isocyanides with *N*-(2-haloaryl)propiolamides. The reaction proceeded between isocyanides and triple bonds, in which generation of reactive organocopper intermediates followed by [3 + 2] cycloaddition with alkyne and then the formation of C–C bond leading to pyrroles. They extended this methodology to synthesize pyrrolo-fused quinoline by copper-catalyzed Ugi 4-component reaction [124] (Scheme 50).



Scheme 50: Synthesis of quinolinones fused pyrroles.

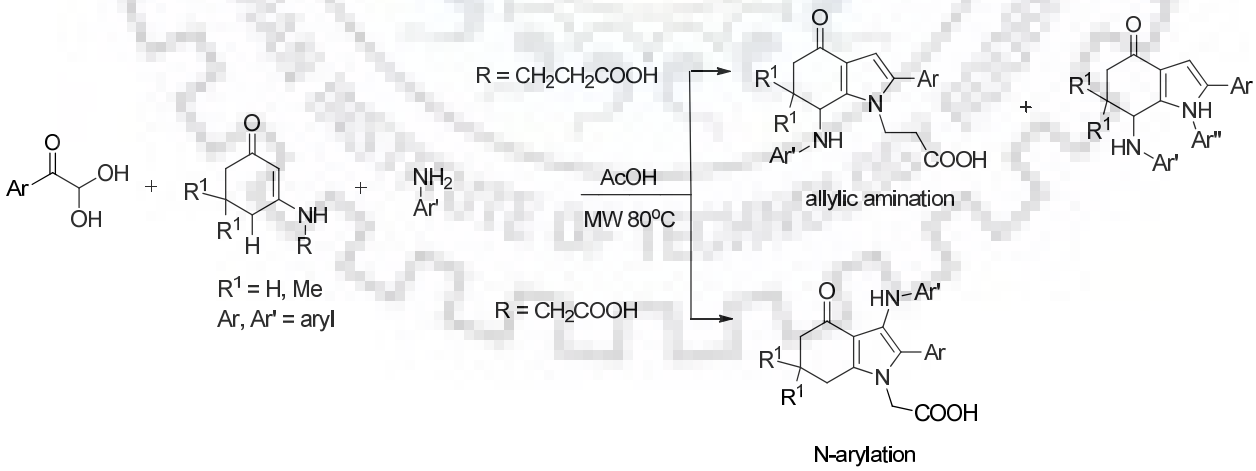
A novel and efficient multi-component protocol was introduced to deliver arylpropanamide and isochromenopyrrole derivatives by Zainali and Soleimani. They

synthesized arylpropanamide derivatives through reaction between malononitrile, 2-formylbenzoic acids, isocyanides in EtOH. This protocol involved the formation of carbon–carbon bonds, one ester and one amide bond in one-pot. Later they developed the synthesis of pyrroles *via* reaction of formylbenzoic acids, malonic dinitrile, and isocyanides in DCM [125] (Scheme 51).



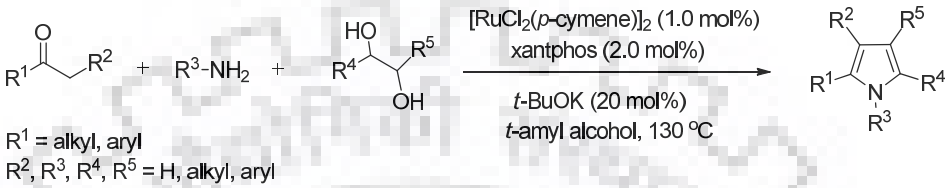
Scheme 51: Synthesis of benzoate and fused pyrroles *via* multicomponent reactions.

A three-component domino reaction was developed for the synthesis of fused pyrroles by Li *et al*. The protocol involved condensation, isomerization, intramolecular cyclization, double bonds nucleophilic substitution and protonation steps to lead the final products. The reaction proceeded *via* chemoselectively and regioselectively under microwave conditions while mixing all the reactants in acetic acid delivered the products in good yields and in less time [126] (Scheme 52).



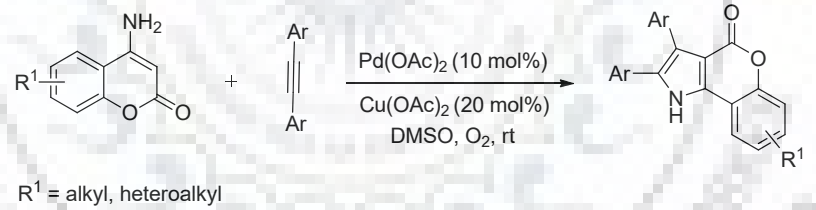
Scheme 52: Three-component domino reactions for rapid synthesis of fused pyrroles.

Beller *et al.* reported highly effective and versatile method for the regioselective synthesis of pyrrole *via* three-component reaction using ruthenium catalyst. The protocol involved enamine formation from ketone and amine which further converted into iminium ion *via* reaction with vicinal diol, followed by hydrogen transfer, C–H alkylation and dehydrogenation steps pyrroles generated. They reported several ways for the synthesis of pyrroles [127] (Scheme 53).



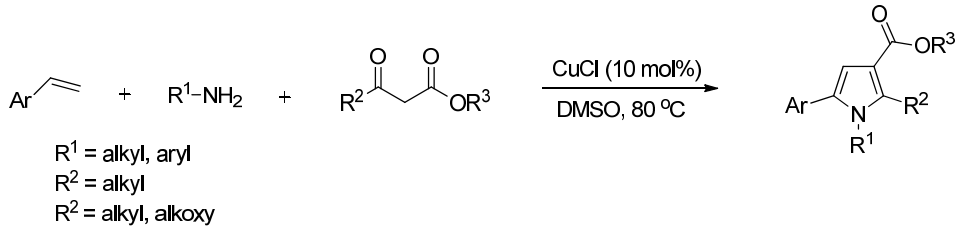
Scheme 53: Regioselective synthesis of pyrroles *via* multicomponent reactions catalyzed by ruthenium catalyst.

Wang *et al.* studied the formation of pyrroles *via* palladium-catalyzed oxidative annulation of cyclic *trans*-enamines with several internal alkynes. Copper acetate was used as an oxidant and DMSO as a solvent in the reaction. After C–H/ N–H functionalization, the reaction delivered pyrroles at rt [128] (Scheme 54).



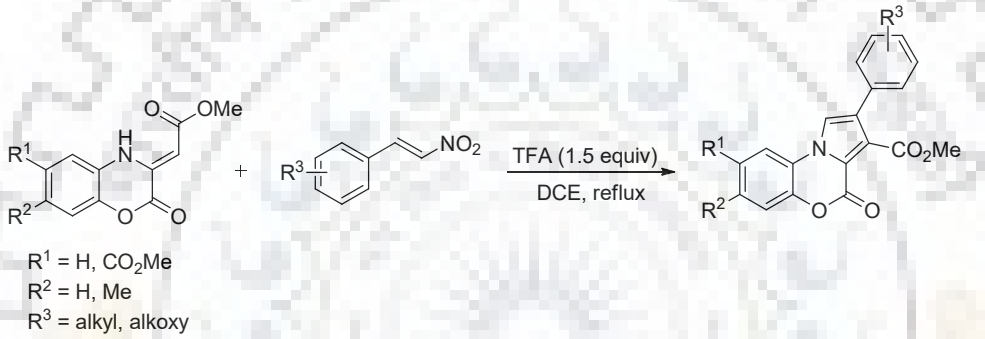
Scheme 54: Synthesis of substituted fused pyrroles *via* palladium-catalyzed oxidative annulation.

An efficient and novel method to access polysubstituted pyrroles was established by Chen and co-workers. Cuprous chloride catalyzed one-pot reaction between terminal olefins, alkyl/aryl amines and ketoesters proceeded through cross-coupling, cyclization-oxidation and delivered polysubstituted pyrroles in good yields [129] (Scheme 55).



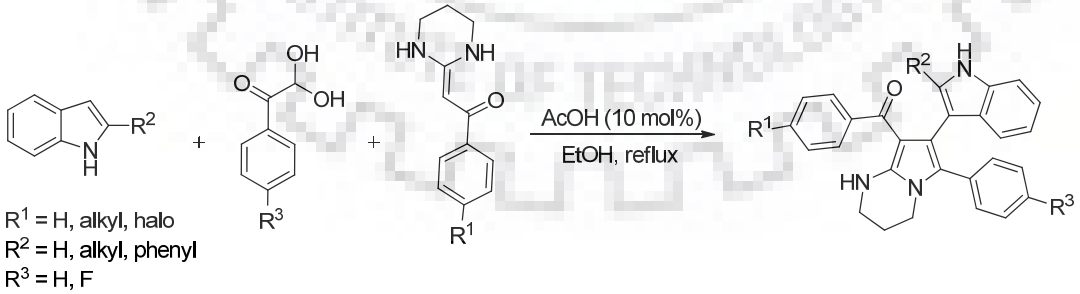
Scheme 55: One-pot reaction to synthesize substituted pyrroles.

In 2014, our group reported a mild and efficient methodology for the synthesis of fused pyrroles *via* Michael addition–cyclization reaction of vinylogous carbamates with nitrostyrenes in the presence of TFA. Further we extended this protocol to access amino coumarin derivatives from vinylogous carbamates and benzoquinones [130] (Scheme 56).



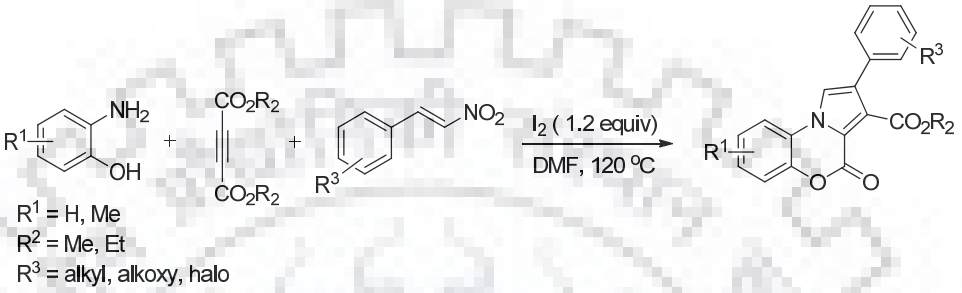
Scheme 56: Michael addition–cyclization reaction of benzoxazinones with electron-deficient alkenes.

Lin *et al.* developed a protocol to synthesize functionalized pyrroles *via* three-component domino reaction of ketene aminals, aryl glyoxals, and indoles in the presence of catalytic amount of acetic acid. This one-pot reaction presented broad substrate scope [131] (Scheme 57).



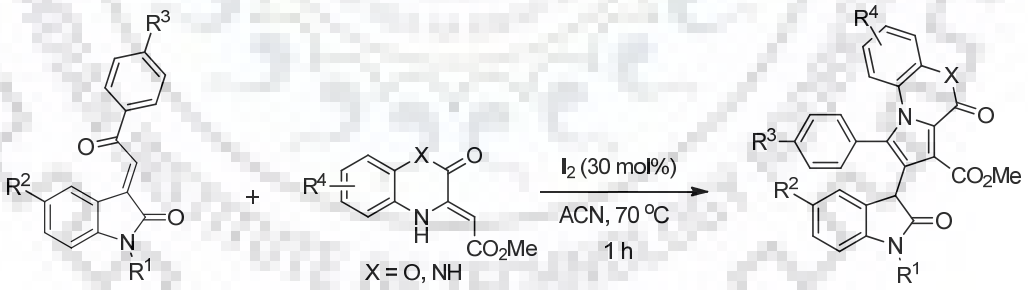
Scheme 57: Synthesis of highly functionalized pyrrole derivatives *via* three-component domino reaction.

In 2015, Sharda and co-workers reported a simple and efficient protocol to synthesize fused pyrroles catalyzed by iodine. The protocol involved metal-free and one-pot synthesis through reaction between amino phenols, acetylene dicarboxylates and benzoxazines in DMF as solvent at 120 °C. This iodine-promoted denitrative one-pot reaction showed good substrate scope and provided products in good yields [132] (Scheme 58).



Scheme 58: Synthesis of pyrrolobenzoxazinones.

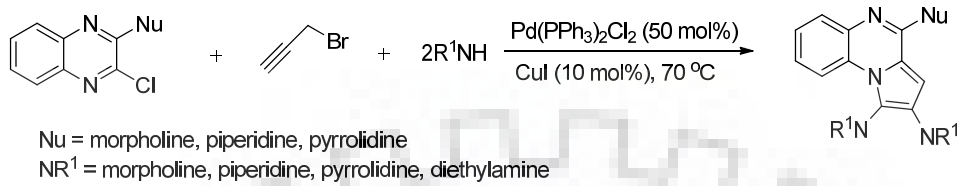
Recently our group reported an environmental benign and atom economical, synthesis of multisubstiuted pyrrole polyheterocycles *via* highly regioselective iodine-mediated cascade reaction between oxindoles and 1,4-benzoxazinones. The reaction was successful and showed good substrate scope and proceeded through C–C and C–N bond formation to deliver polysubstituted pyrroles in good yields [133] (Scheme 59).



Scheme 59: Synthesis of pyrrole-fused polyheterocyclic compounds.

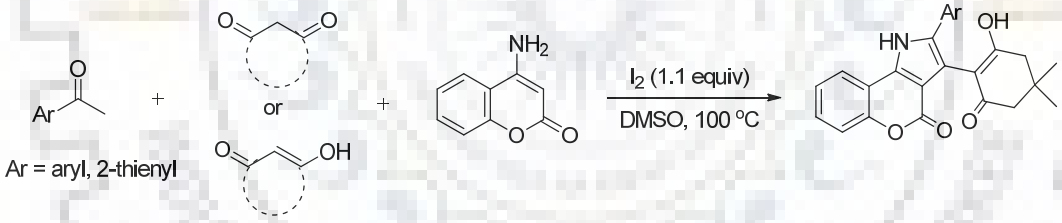
Keivanloo and co-workers established the synthesis of trisubstituted pyrroloquinoxalines through one-pot reaction of quinoxalines, secondary amines and propargyl bromide, *via* palladium-catalyzed cascade reaction. The reaction proceeded *via* Sonogashira coupling through the formation of various intermediates such as alkyne, allene,

and amino dyne intermediate in which after isomerization and intramolecular cyclization followed by aerial oxidation and aromatization final products were formed. Some synthesized compounds were screened against the bacterial strains such as *Micrococcus luteus*, *Pseudomonas aeruginos*, and *Bacillus subtilis* [134] (Scheme 60).



Scheme 60: Palladium-catalyzed cascade reaction for the synthesis of fused pyrroles.

Foroumadi *et al.* developed a one-pot oxidative coupling reaction for the synthesis of coumarin-fused pyrroles. Iodine was used as a promoter for the subsequent transformation in which first of all Kornblum oxidation took place to form phenylglyoxal from acetophenone. Then Knoevenagel reaction proceeded between phenylglyoxal and active methylene compounds followed by Michael addition of 4-amino coumarin, cyclization and 1,3-H shift to generate disubstituted chromenopyrrole-4(1*H*)-one derivatives [135] (Scheme 61).

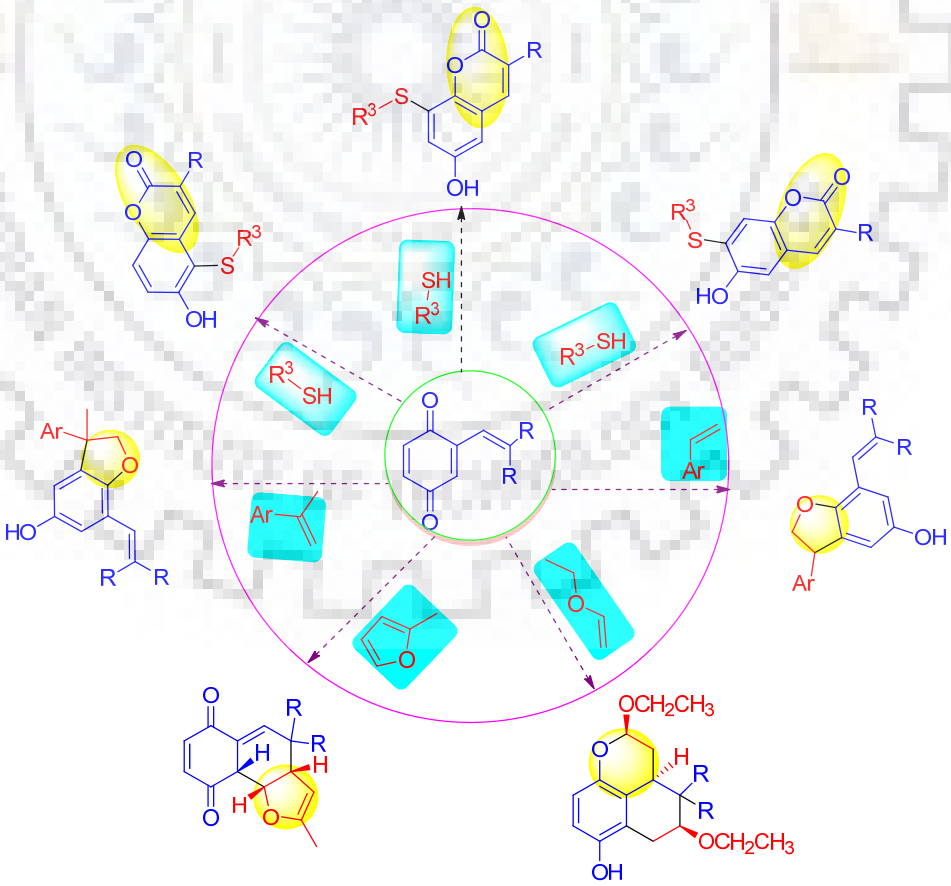


Scheme 61: Tandem oxidative coupling reaction for the synthesis of pyrrole fused coumarin.

2.1. OBJECTIVES

- The main aim of this thesis was to delineate various influential reacting partners and intrigue their reactivity towards the synthesis of innumerable novel complex multifunctional heterocyclic compounds. Therefore our efforts are engrossed on the incorporation of chemical diversity in the molecular frame work in order to synthesize interesting compounds of widely applications.

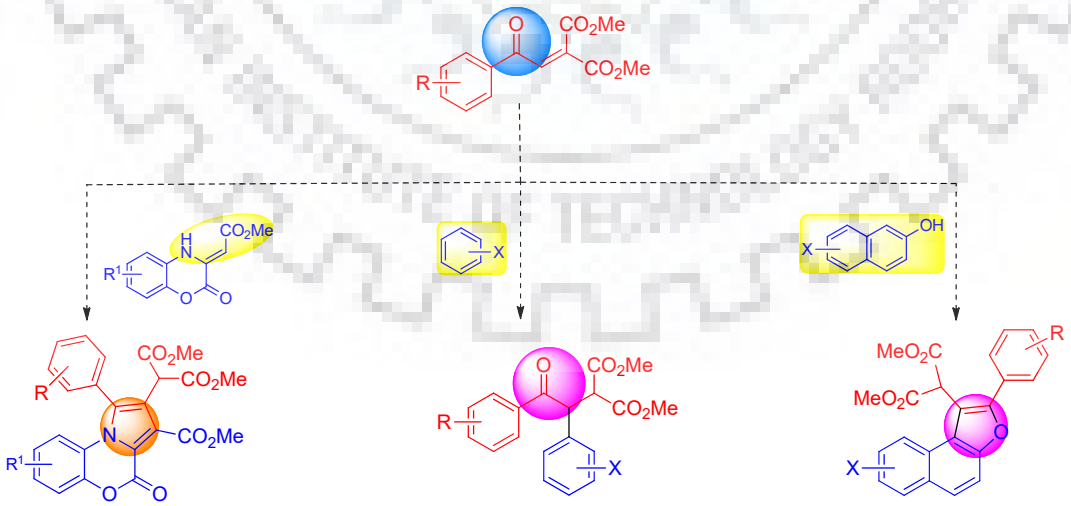
- Inspired by the benzoquinone chemistry and their role in natural product synthesis, biologically and pharmacologically influential compounds therefore for the first we selected benzoquinone moiety and envisaged to incorporate substituents on benzoquinones. This motif embraced an external olefinic bond with esters/ketone moiety and we intended their reaction with different reacting partners to synthesize complex compounds through various positions of benzoquinones. We executed their reaction with several nucleophiles such as alkyl/aryl thiols and various olefins.



- We have envisioned the synthesis of various novel coumarin alkyl/aryl-sulfides or biarylsulfides *via* reaction of alkenyl *p*-benzoquinones with alkyl/aryl thiols. Coumarin and biarylsufide motifs have various applications in biological field. Inspired by the synthesis of various coumarin alkyl/aryl sulfides, and motivating by the chemistry of alkenyl *p*-benzoquinones further we utilized alkenyl *p*-benzoquinones to synthesize numerous polyheterocyclic compounds with 2-methylfuran, ethyl vinyl ether and various substituted styrenes. Heterocyclic compounds containing dihydrofuran, dihydropyran and dihydrobenzofuran skeleton plays a very important role in nature.

- The assembly of highly valuable functionalized compounds represents a highly desirable aim and challenge in green chemistry. Motivating from the electrophilic nature of benzoquinones and their chemistry further we were interested to synthesize particular electrophilic precursor, we have synthesized aroylmethylidene malonates and carried out their reaction with benzoxazinones which lead to the formation of *N*-heterocyclic moieties such as fused pyrroles.

- Today, in synthetic organic chemistry, sustainability is the main concern; therefore it is necessary to develop facile, efficient and green protocols which reduce the use of organic solvents, hazardous reagents and formation of waste products. Keeping these things in mind, we implemented α-substituted aryl ketones and naphthofurans in environmental sustainable route.



2.2. RESULTS AND DISCUSSION

In our previous chapter we conferred about various synthetic methods towards the synthesis of heterocyclic moieties such as coumarin, biaryl sulfide, pyrrole and naphthofuran. This chapter deals with the results and discussion, which is further divided into five sections as shown below.

2.2.1. Synthesis of alkyl/aryl sulfide derivatives of coumarin *via* domino reaction of alkenyl *p*-benzoquinones

2.2.2. Regioselective synthesis of polyheterocycles by cycloaddition reaction of alkenyl *p*-benzoquinones

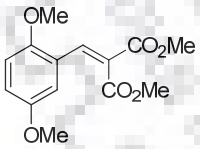
2.2.3. Synthesis of functionalized pyrrolobenzoxazinones *via* transition metal-catalyzed reaction

2.2.4. Synthesis of α-substituted aryl ketones

2.2.5. Synthesis of functionalized naphthofuran derivatives

The precursors used in this work were either obtained from commercial sources or synthesized in the laboratory. For the smooth discussion in the thesis, the following numbering is assigned to these reaction partners.

1. 1,4-Dimethoxy-alkenylarene derivatives



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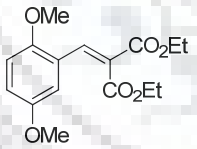

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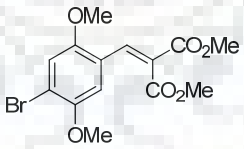

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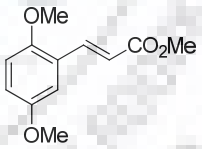

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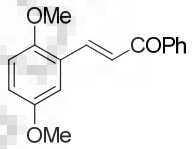
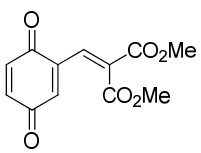


1e

2. Alkenyl *p*-benzoquinone derivatives



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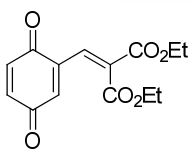

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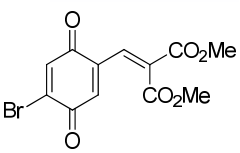

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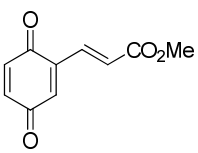

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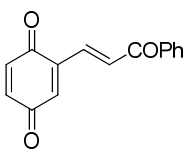
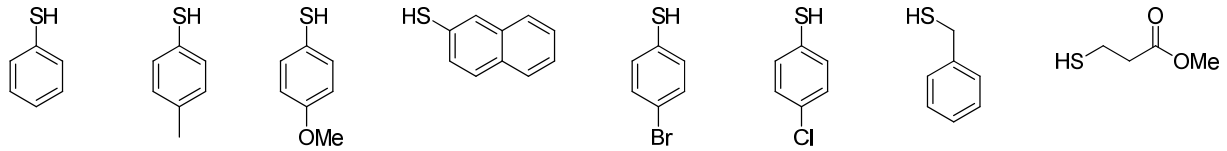


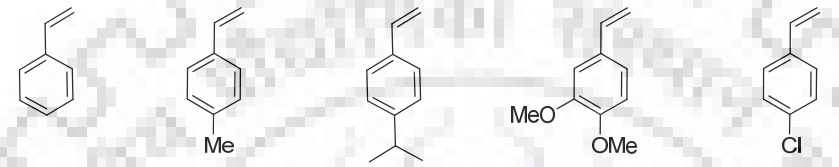
2e

3. Alkyl/Aryl thiols

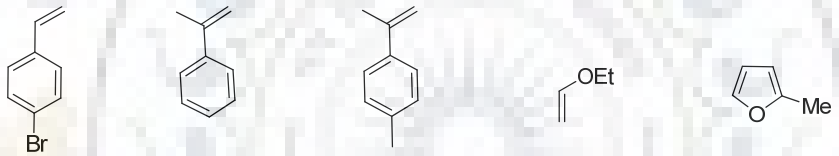


3a **3b** **3c** **3d** **3e** **3f** **3g** **3h**

4. Styrene derivatives

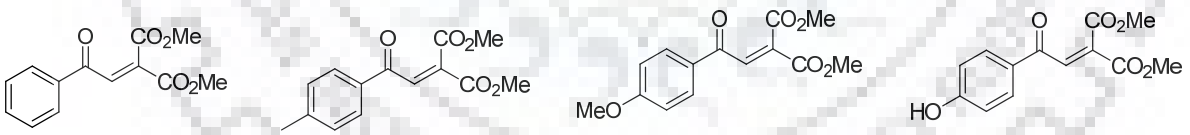


4a **4b** **4c** **4d** **4e**

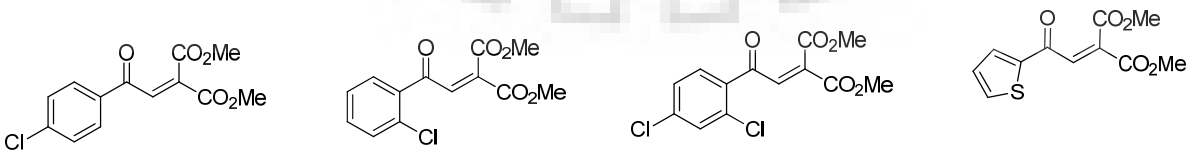


4f **4g** **4h** **4i** **4j**

5. Aroylmethylidene malonates

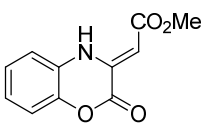


5a **5b** **5c** **5d**



5e **5f** **5g** **5h**

6. Benzoxazinones



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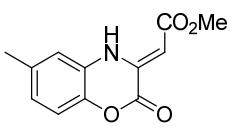

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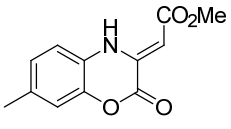

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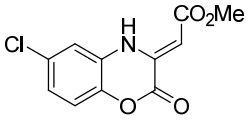

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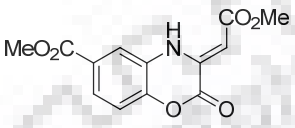

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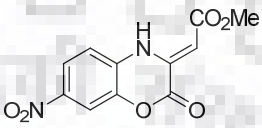

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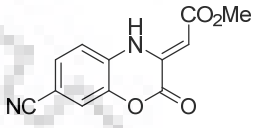
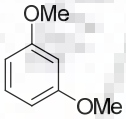


6g

7. Electron-rich arenes



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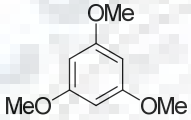

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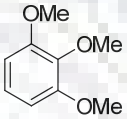

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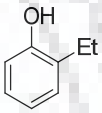

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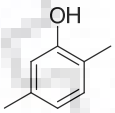
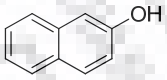


7e

8. *β*-Naphthol derivatives



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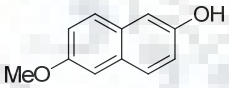
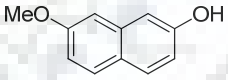
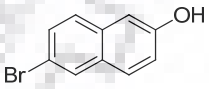


8b



8c



8d

2.2.1. Synthesis of alkyl/aryl sulfide derivatives of coumarin *via* domino reaction of alkenyl *p*-benzoquinones

p-Quinones [136–139] are one of the persuasive starting materials for the generation of compounds having biological profiles and they have been served as precursors for the synthesis of several natural products and pharmacological active compounds [140–143] (Figure 1). The benzoquinones [144–147] belong to an important class of electrophilic precursors and they serve as Michael acceptors, reactive dienophiles in Diels–Alder reactions and work as oxidizing as well as dehydrogenating agents in organic synthesis [148–152]. Various methods have been reported for the synthesis of *p*-benzoquinones and because of their occurrence in biological field, the synthesis of *p*-quinones has been attracted by synthetic chemists.

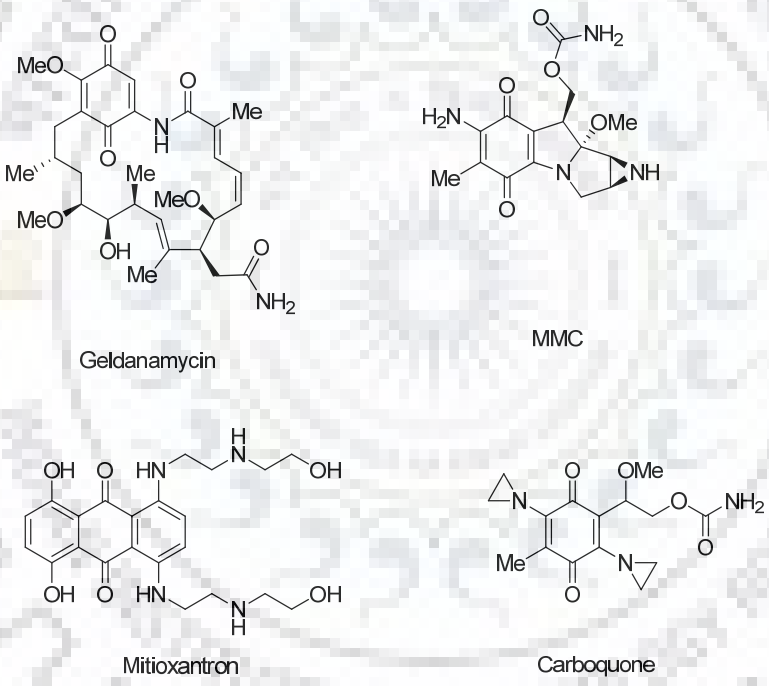


Figure 1: Some biologically active compounds containing quinone core.

In the immensely progressing area of synthetic chemistry, the edifice of carbon–carbon and carbon–heteroatom bond formation is an important strategy for the construction of complex organic molecules [153–155]. Domino approach is one of the major tools to construct biologically important complex molecules from simple substrates in one-pot

fashion which is ecologically and economically benign [156,157]. *p*-Quinones react with thiols to generate hydroquinones bearing arylthio moiety [158]. In recent years, *p*-quinones have been derivatized in more useful forms like nitrovinyl *p*-quinones [159] and alkenyl *p*-benzoquinones [160]. The alkenyl *p*-benzoquinones are fascinating precursors for the cascade protocol due to their inherent multiple functionalities. The alkenyl *p*-benzoquinones have potential to react with alkyl and aryl thiols to generate alkyl or aryl sulfide derivatives of coumarin which seem to be promising bioactive compounds since coumarins [161] and biaryl sulfides [162–163] have enriched literature of bioactivity such as anti-inflammatory, anti-malarial, anti-cancer and anti-HIV activities [164–167] (Figure 2).

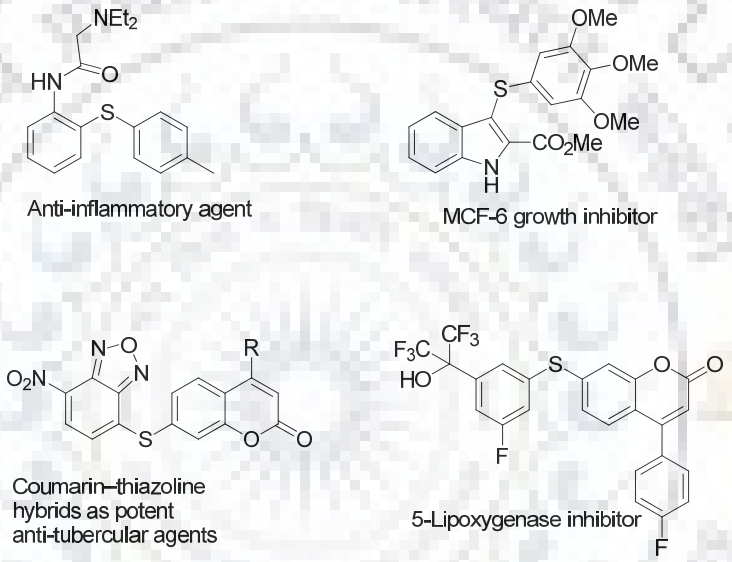
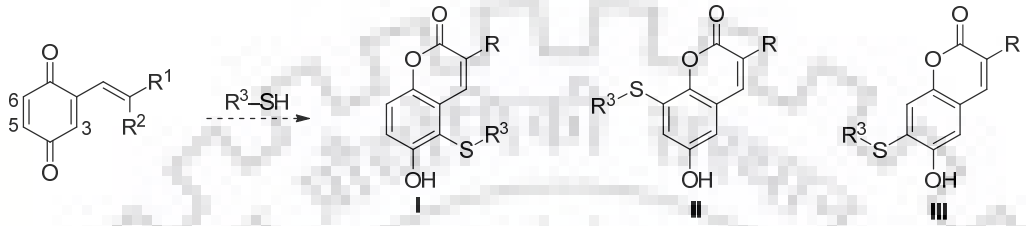


Figure 2: Some of the biaryl sulfide and coumarin containing biologically active compounds.

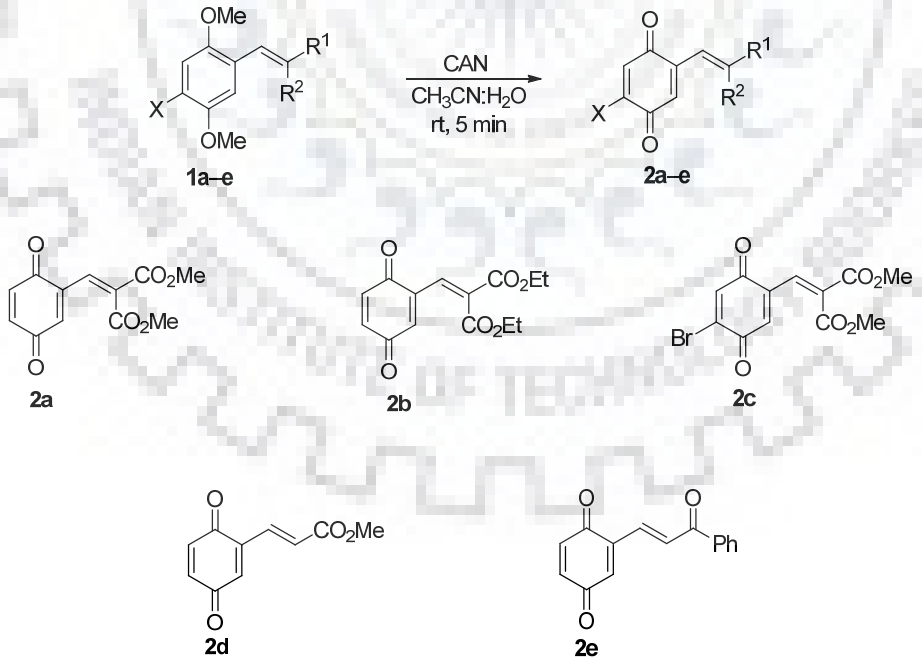
In addition, coumarin derivatives derived from alkenyl *p*-benzoquinones have also found application in fluorescence probe [168]. However, the reports on the synthesis of coumarin-coupled aryl sulfides are scarce [169–171]. Keeping the above in mind, we hypothesized that alkenyl *p*-benzoquinones having multiple sites for nucleophilic attack, can undergo Michael addition with thiols followed by cyclization in domino fashion, resulting in the formation of novel alkyl/aryl sulfide derivatives of coumarin of types I, II and III (Scheme 1). These compounds are interesting due to the presence of both coumarin and alkyl/aryl sulfide moieties.

In continuation of our work on harnessing the reactivity of benzoquinone derivatives [172–175] (*i.e.*, masked *o*- and *p*-benzoquinones) and synthesis of diaryl sulfides [176,177], herein, we developed a rapid, novel and efficient method for the synthesis of alkyl/aryl sulfide derivatives of coumarin through sequential construction of C–S and C–O bonds in a domino fashion. The current strategy involves one-pot domino Michael addition cyclization protocol to produce coumarin-based aryl sulfides.



Scheme 1: Working hypothesis for Michael addition of thiols to alkenyl *p*-benzoquinones.

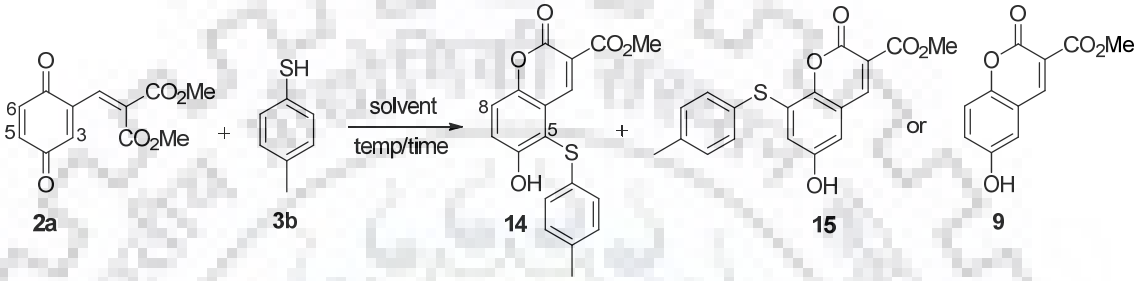
Accordingly, the alkenyl *p*-benzoquinones **2a**–**e**, were synthesized [178] by the oxidative demethylation of the corresponding alkenylarenes **1a**–**e** (Scheme 2). Since the oxidized products **2a**–**e** were pure, as checked by ^{1}H NMR, they are used as such after work-up without purification for further transformation.



Scheme 2: Oxidation of 1,4-dimethoxy-alkenyl arenes to *p*-quinones **2a**–**e**.

As a prelude to our objective, we performed the reaction of alkenyl *p*-benzoquinone **2a** and 4-methylthiophenol (**3b**) in acetonitrile at room temperature. To our delight, aryl sulfide derivative of coumarin **14** was obtained in 55% yield along with a mixture of coumarin derivatives **15** and **9** in a combined yield of 18% (Table 1, entry 1) where the regioisomers **14** and **15** resulted *via* the addition of **3b** on alkenyl *p*-benzoquinone **2a** at position 3 and position 6, respectively.

Table 1: Optimization of reaction conditions.[a]

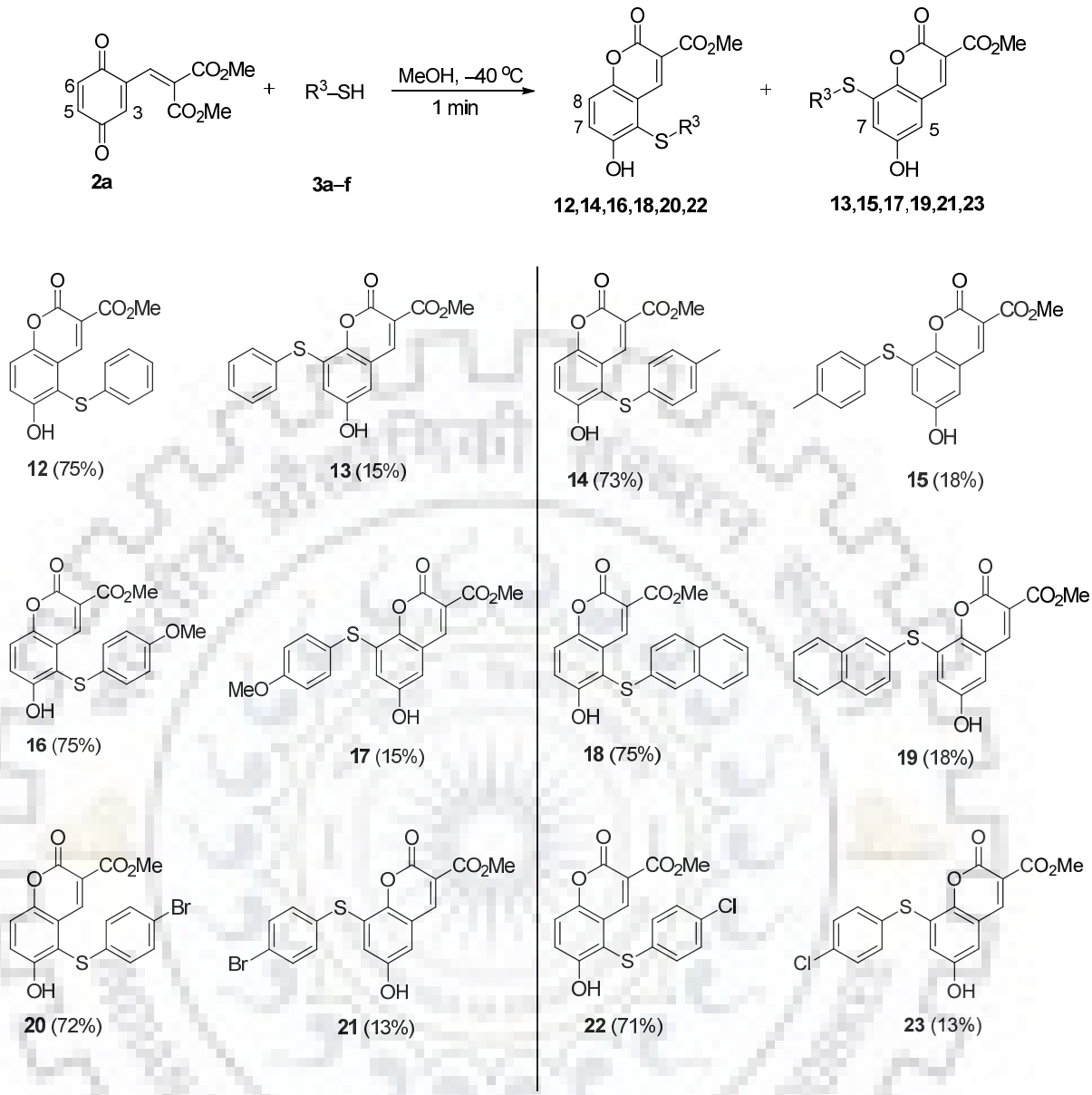


Entry	Solvent	Temp/ Time (min)	Yield (%)[b]	
			14	**15/9**
1	CH_3CN	rt/5	55	18[c]
2	THF	rt/5	47	35[c]
3	Ethyl lactate	rt/5	50	22[c]
4	Toluene	rt/5	57	20[c]
5	CH_2Cl_2	rt/5	60	23[c]
6	$CHCl_3$	rt/5	55	22[c]
7	H_2O	rt/10	41	**9**/22
8	Ethanol	rt/5	55	**15**/19)
9	MeOH	rt/1	63	**15**/21
10[d]	MeOH+H_2O	rt/10	42	**9**/27
11	MeOH	0 °C /1	65	**15**/18
12	MeOH	–20 °C /1	68	**15**/17
13	MeOH	–40 °C /1	70	**15**/18
14[e]	**MeOH**	**–40 °C /1**	**73**	**15/18**

[a]All reactions were performed with **2a** (0.5 mmol), **3b** (0.5 mmol) in 1.0 mL of solvent.
[b]Yield of isolated products after column chromatography, unless otherwise noted.
[c]Combined yields of **15** and **9** as determined by ^{1}H NMR analysis.
[d]MeOH and H_2O (1:1).
[e]**2a** (1.0 mmol) and **3b** (0.6 mmol) were used.

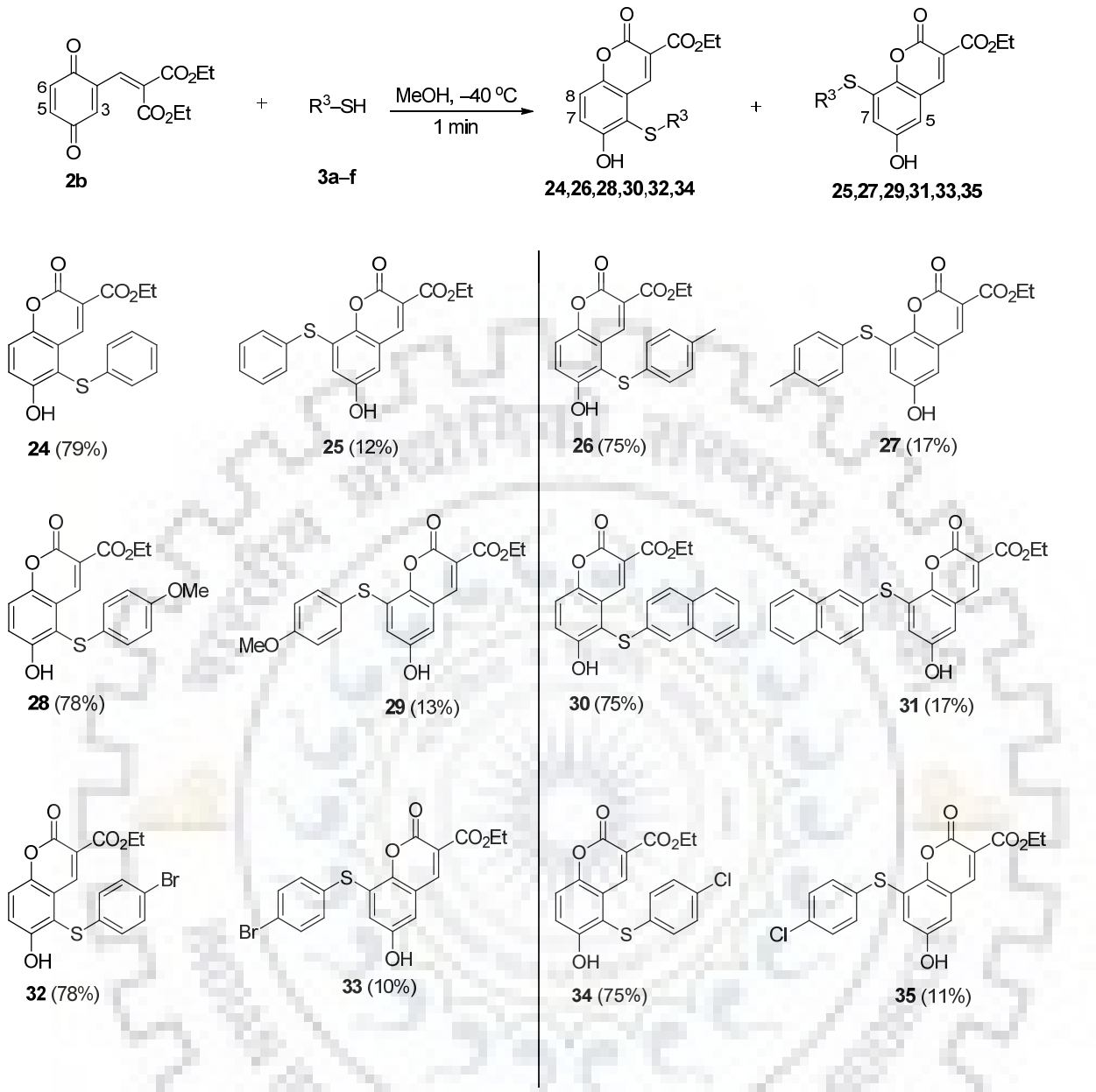
Encouraged by this result, we sought to optimize the reaction conditions in various solvents such as THF, ethyl lactate, toluene, CH_2Cl_2, $CHCl_3$, EtOH, MeOH, H_2O and found that the nature of solvent has great impact on the reaction outcome. In polar/non-polar aprotic solvents, **14** was obtained in comparatively lower yield along with varying amounts of **15** and **9** (entries 2–6). On switching towards the polar protic solvents, as in case of water, **14** was obtained selectively in 41% yield along with **9** in 22% (entry 7). The reaction performed in EtOH and MeOH, both regioisomers **14** and **15** were formed in good yields (entries 8 and 9). Further, the reaction in a 1:1 mixture of MeOH and H_2O proved to be less reactive (entry 10). Though the reaction proceeded in all solvents, it worked more efficiently in MeOH where **14** was obtained as major isomer and **15** in minor quantity. After identifying the suitable solvent, we performed the reaction at lower temperature and found that the reaction temperature had a good effect on the reaction outcome. The decrease in temperature led to an increase in the yield of the products (entries 11–13). When the amount of **2a** was increased from 1.0 to 1.3 equiv, the reaction worked efficiently to afford a separable mixture of two regioisomers **14** and **15** in 73 and 18% yields, respectively (Table 1, entry 14). Thus, the screening of various parameters identified the above as the optimal condition for this transformation.

In view of the success of the above reaction, the scope of the reaction of **2a** was exemplified with various substituted thiophenols under the optimized reaction conditions. The nature of substituent on aryl ring of thiophenols **3a**–**f** affected the reaction yield of diaryl sulfides **12**–**23** slightly. The reaction of **2a** with thiophenol (**3a)** delivered **12** and **13** in 75 and 15% yields, respectively. Electron-donating groups on aryl ring of thiophenol showed more reactivity than those with electron-withdrawing groups (Scheme 3). For example, 4-methoxythiophenol (**3c**) produced the products **16** and **17** in 75 and 15% yields, respectively. Use of 2-naphthalenethiol (**3d**), delivered **18** and **19** in 75 and 18% yields, respectively. Notably, the reactions of **3e** and **3f** bearing electron-withdrawing halo groups furnished the sulfides **20** and **21** in 72 and 13%, and **22** and **23** in 71 and 13% yields, respectively. The slight reduction in the yield may be attributed to the moderate electron-withdrawing nature of the halo substituents.



Scheme 3: Reaction of alkenyl *p*-benzoquinone **2a** with aromatic thiols.

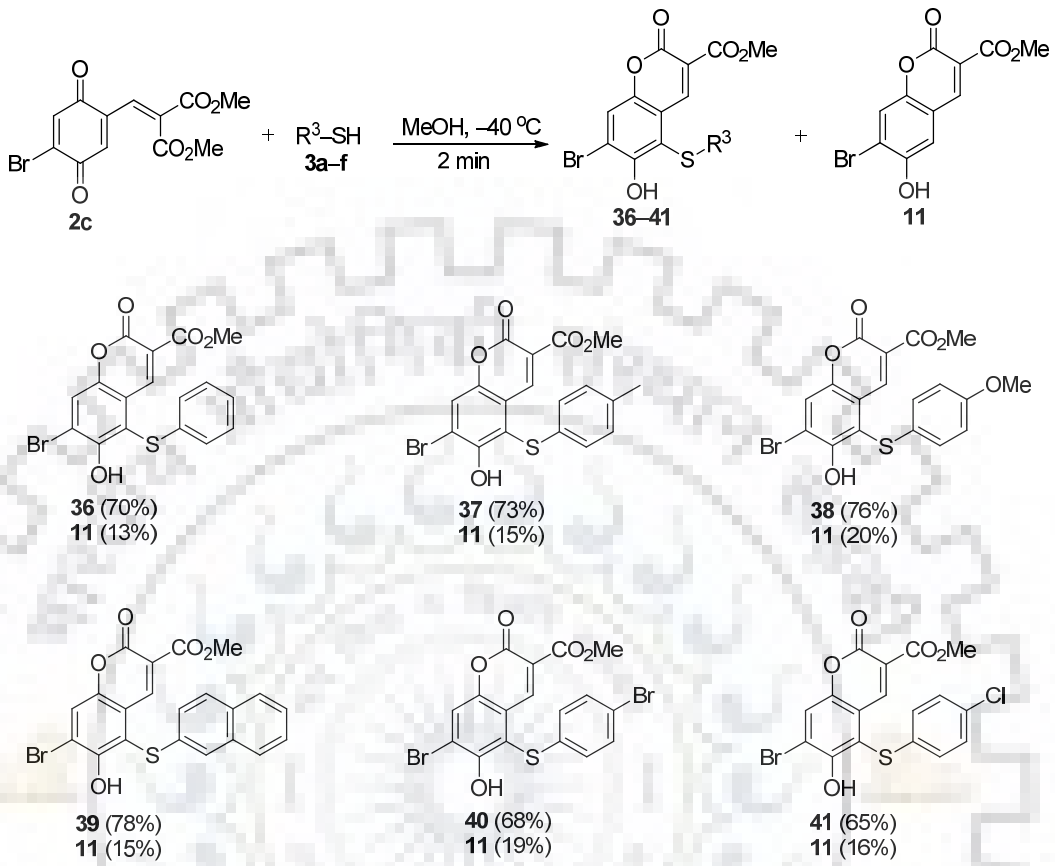
Inspired by the above results, we further extended the scope of the reaction of alkenyl *p*-benzoquinone **2b** bearing ethyl ester with various thiophenols and here again the reaction proceeded smoothly under the optimized conditions. Moreover, electron-donating and -withdrawing groups on the aryl ring of thiophenol were well tolerated, leading to the desired major and minor products **24**–**35** in good yields (Scheme 4).



Scheme 4: Reaction of alkenyl *p*-benzoquinone **2b** with aryl thiols.

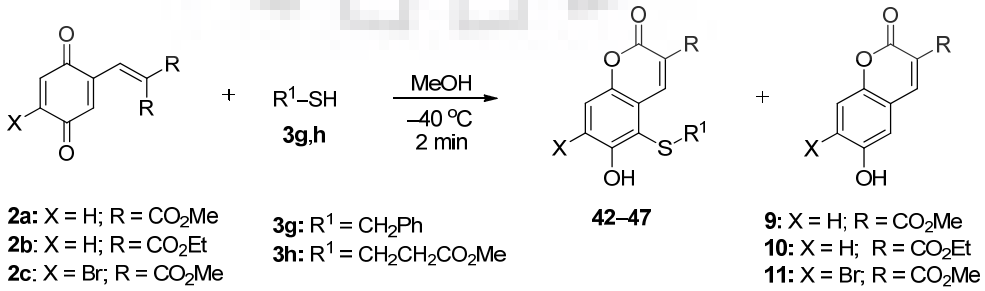
To further extend the scope of the current domino protocol, bromo derivative **2c** of alkenyl *p*-benzoquinone was treated with various thiophenols under the same conditions. Astonishingly, regioselective addition of the nucleophile at position 3 of **2c** was observed resulting in the formation of the diaryl sulfides **36**–**41** (Scheme 5). This may be attributed due to the stereoelectronic effect of bromo group situated at 5th position of **2c**. Thus a series of thiophenols bearing methyl, methoxy, chloro, bromo substituted at *para* position of phenyl ring and 2-naphthalenethiol were well tolerated under the optimized conditions and

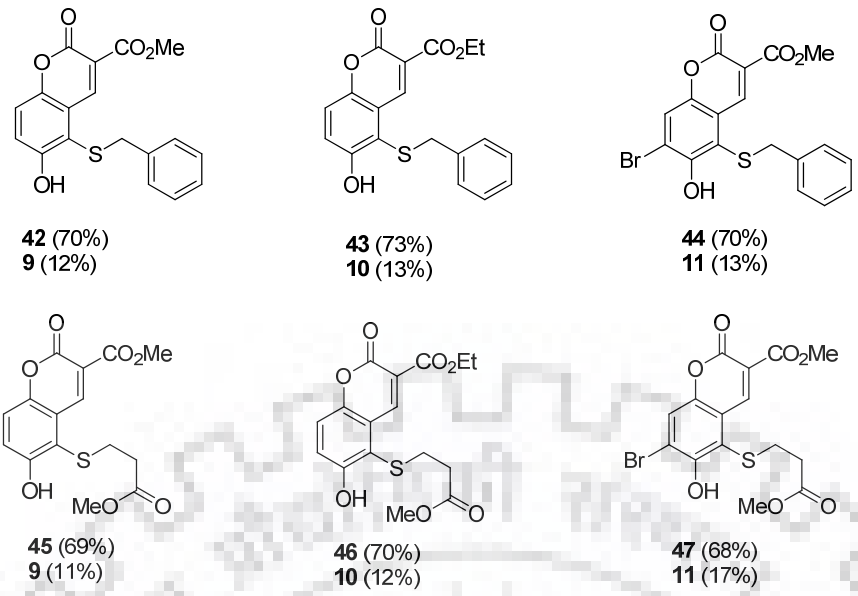
afforded the anticipated products **36**–**41** in good yields of 65–78% (Scheme 5). In addition, coumarin **11** was obtained as minor product in each case.



Scheme 5: Domino reaction of alkenyl *p*-benzoquinone **2c** with aryl thiols.

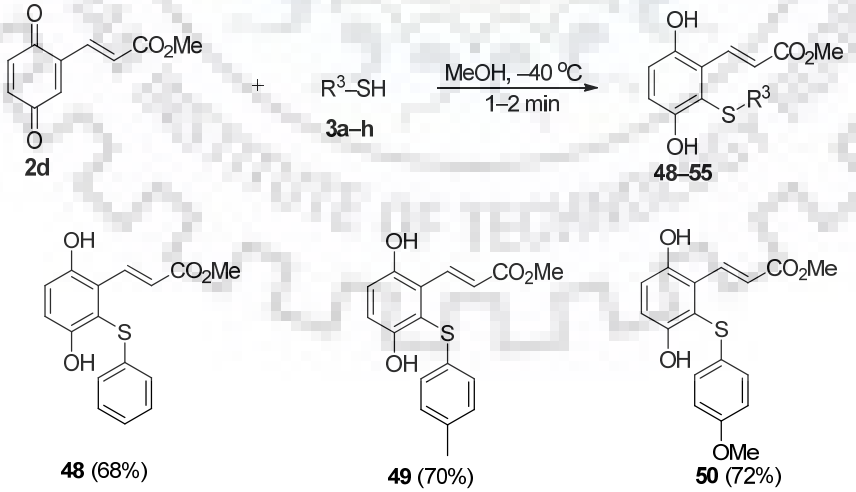
The feasibility and scope of the above reaction was also evaluated with aliphatic thiols **3g**,**h**. To our delight, it was found that when aliphatic thiols reacted with alkenyl *p*-benzoquinones **2a**–**c**, a single regioisomer was produced exclusively in each case with good yields along with **9**–**11** in 2 min (Scheme 6). The aliphatic thiols are relatively harder than aromatic thiols [179,180] so complete regioselectivity can be explained on this basis.

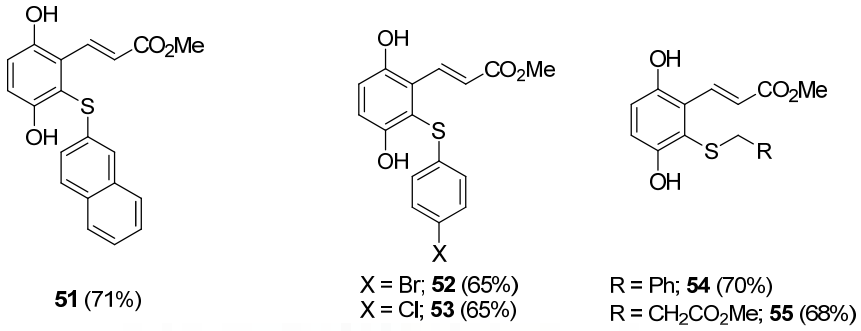




Scheme 6: Reaction of alkenyl *p*-benzoquinones **2a**–**c** with aliphatic thiols **3g**,**h**.

Encouraged by these results, we further employed this protocol to the addition of various thiophenols bearing either electron-donating groups **3b**–**d** and electron-withdrawing groups **3e**,**f** with alkenyl *p*-benzoquinone **2d**. The reaction underwent smoothly and afforded the sole Michael addition products **48**–**53** in 1 min with good yields as shown in Scheme 7. This may be due to the less electrophilicity of **2d** in comparison with **2a** and **2b**. The reaction of **2d** with aliphatic thiols **3g** and **3h** worked well to afford the products **54** and **55** regioselectively in 2 min with 70 and 68% yields, respectively (Scheme 7).





Scheme 7: Reaction of alkenyl *p*-benzoquinone **2d** with thiols.

The regiochemistry of the obtained products were confirmed by the analysis of data obtained from ^{1}H and ^{13}C NMR, DEPT and HRMS spectra. For instance in regioisomers **16** and **17**, the structures of the both regioisomers were unambiguously confirmed by ^{1}H NMR analysis by the inspection of coupling constants. Further, in regioisomer **16**, *ortho* coupling (J = 9.0 Hz) is observed between H–7 and H–8 protons which indicates that thiophenol is attached at 3rd position of alkenyl *p*-benzoquinone **2a**. The methoxy group (*–OMe*) of ester moiety resonates at δ 3.80 ppm and methoxy group (*-OMe*) of thiophenol moiety resonates at 3.68 ppm as singlets. Olefinic proton of the lactone ring resonates at δ 8.99 ppm as singlet. The ester and lactone carbonyl carbons appear at δ 163 and 156 ppm, respectively, in ^{13}C NMR. HRMS spectrum of compound **16** shown a peak at *m/z* 381.0399 which is in well agreement with the calculated value *m/z* 381.0403 for $[M + Na]^{+}$ (Figure 3).

In case of regioisomer **17**, H–5 and H–7 protons shows *meta* coupling (J = 2.5 Hz) confirming the addition of thiophenol at 6th position of **2a**. Similarly the methoxy group (*–OMe*) of ester moiety resonates at 3.83 ppm and methoxy group of thiophenol moiety resonates at δ 3.82 ppm as singlets. In ^{1}H NMR, the olefinic proton of the lactone ring resonates at δ 8.69 ppm as singlet. In ^{13}C NMR, the ester and lactone carbonyl carbons resonates at δ 163 and 158 ppm, respectively, (Figure 3). A peak observed at *m/z* 381.0391 in HRMS spectrum of compound **17** is in well agreement with the calculated value *m/z* 381.0403 for $[M + Na]^{+}$. Moreover, the structures of **20** (Figure 4, Table 2) and **21** (Figure 5, Table 3) were confirmed by their single crystal X-ray analysis. The crystals **20** and **21** were grown on the mixture of EtOH/ethylacetate/hexane *via* slow evaporation.

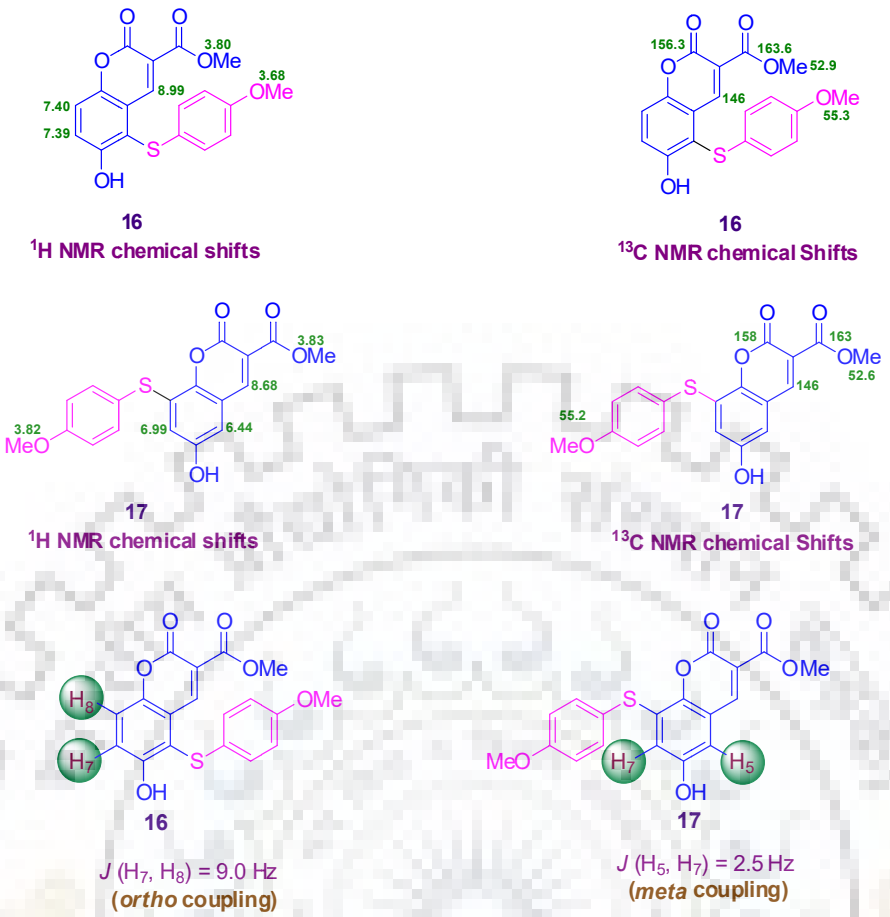


Figure 3: ^{1}H and ^{13}C NMR chemical shifts and coupling constant values of coumarin aryl sulfides **16** and **17**.

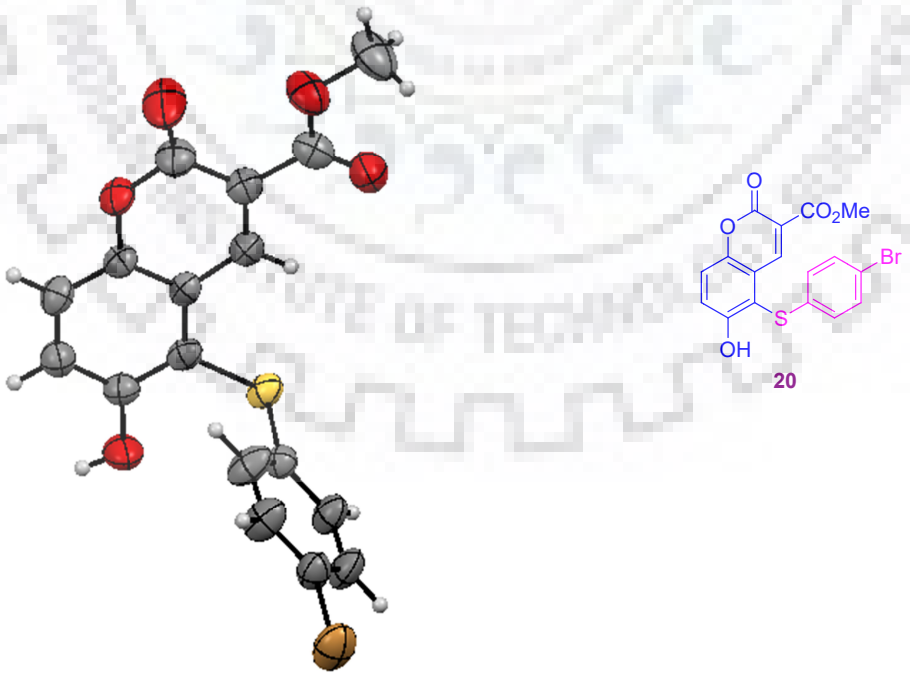
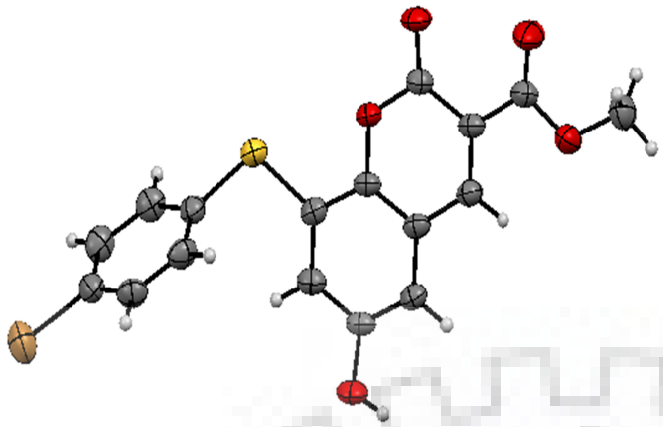
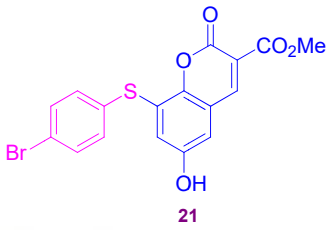


Figure 4: ORTEP representation of crystal structure of **20**.

Table 2: Crystallographic data for **20**.

Empirical formula	$C_{17}H_{11}BrO_5S$
Formula weight	407.22
Temperature	296 (2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P b n^{-1}
Unit cell dimensions	a = 7.657 (5) Å
	b = 10.828 (7) Å
	c = 11.642 (8) Å
	α = 99.27 (3)°
	β = 101.07 (3)°
	γ = 98.10 (2)°
Volume	920.1(10) $Å^3$
Z	2
Density (calculated)	1.636 Mg/m^3
Absorption coefficient	2.382 mm^{-1}
F(*000*)	460.0
Crystal size	0.36 x 0.24 x 0.18 mm^3
Theta range for data collection	1.82 to 29.29°
Index ranges	$-10 \leq h \geq 10$
	$-14 \leq k \geq 13$
	$-15 \leq l \geq 15$
Reflections collected	11494
Independent reflections	4808 [R(int) = 0.0371]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4808 / 0 / 251
Goodness-of-fit on F^2	1.005
Final R indices [I>2sigma(I)]	*R1* = 0.0409, *wR2* = 0.1049
R indices (all data)	*R1* = 0.0856, *wR2* = 0.1212





21

Figure 5: ORTEP representation of crystal structure of **21**.

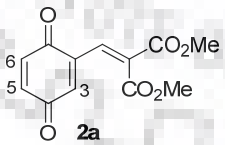
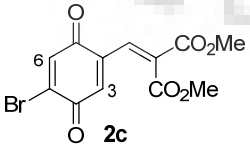
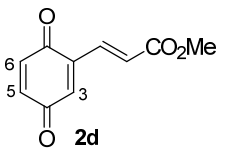
Table 3: Crystallographic data for **21**.

Empirical formula	$C_{17}H_{11}BrO_5S$
Formula weight	407.22
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P 21/c
Unit cell dimensions	a = 8.3811 (12) Å
	b = 22.700 (3) Å
	c = 16.633 (2) Å
	α = 90.00 (3)°
	β = 90.00 (3)°
	γ = 90.00 (2)°
Volume	3164.4 (7) $Å^3$
Z	8
Density (calculated)	1.709 Mg/m^3
Absorption coefficient	2.755 mm^{-1}
F(*000*)	1632.0
Crystal size	0.23 x 0.23 x 0.23 mm^3
Theta range for data collection	1.52 to 31.13°
Index ranges	$-12 \leq h \geq 12$,

	$-33 \leq k \geq 33$
	$-24 \leq l \geq 24$
Reflections collected	37948
Independent reflections	10209 [R(int) = 0.0845]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7538 / 0 / 433
Goodness-of-fit on F^2	1.121
Final R indices [I>2sigma(I)]	*R1* = 0.0492, *wR2* = 0.1206
R indices (all data)	*R1* = 0.1107, *wR2* = 0.1635

To support the observed regioselectivity of the reaction, we calculated Fukui functions [181–183] for carbon atoms of alkenyl *p*-benzoquinones. These calculations were performed with GAUSSIAN 09 program at B3LYP/6-31** level of theory. The Fukui function for nucleophilic attack was associated with the lowest unoccupied molecular orbital (LUMO) density (Figure 6). Higher the electrophilic activation (f_k^+) value, greater the probability for nucleophilic attack of thiols. There are three electrophilic sites (C–3, C–5, C–6) available in alkenyl *p*-benzoquinones **2a**–**d** for the attack of thiols. The calculated f_k^+ values indicates that the C–3 is more electrophilic (f_k^+ = 0.09) site than C–6 (f_k^+ = 0.06), and C–5 (f_k^+ = 0.05) (**2a**, Table 4). Similar electrophilic trend is observed in quinones **2c** and **2d**. These calculated values supported our experimental results where thiols are attached at 3rd (major) and 6th (minor) positions of alkenyl *p*-benzoquinones.

Table 4: Fukui functions (f_k^+) for carbons of alkenyl *p*-benzoquinones for attack of thiol.

***p*-Quinone**	**C–3**	**C–5**	**C–6**
 **2a**	0.09	0.05	0.06
 **2c**	0.06	–	0.03
 **2d**	0.09	0.05	0.06

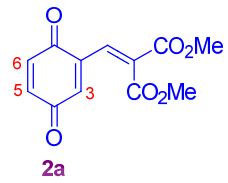
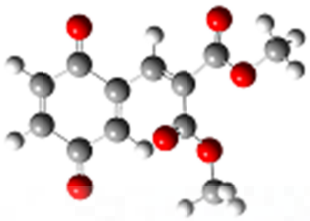
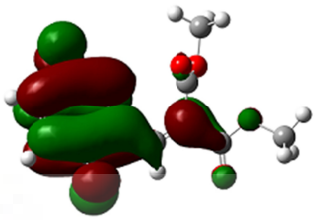
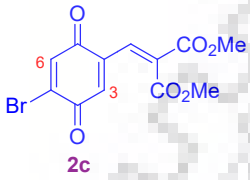
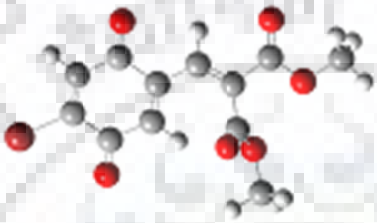
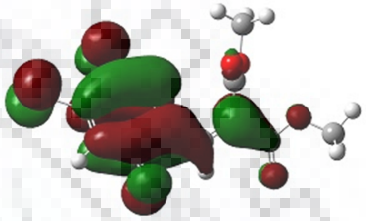
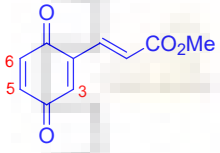
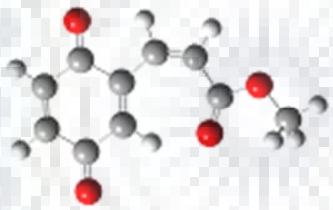
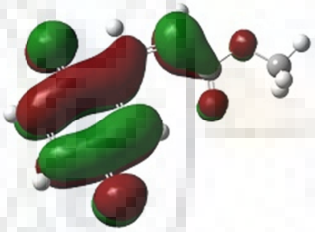
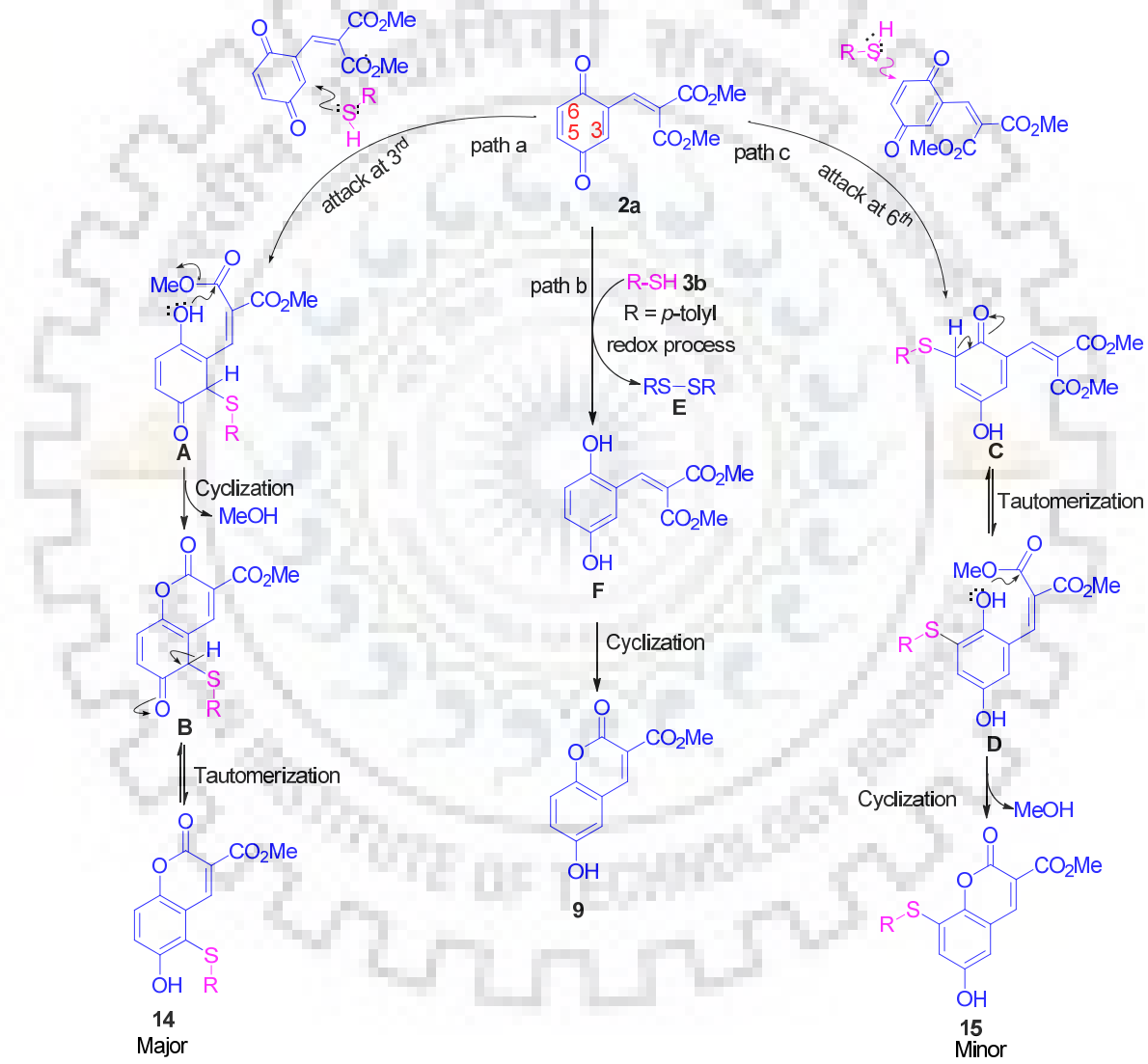
p-Quinone	Optimized geometry	LUMO Structure
 2a		
 2c		
 2d		

Figure 6: Optimized geometries and LUMO structures of alkenyl *p*-benzoquinones **2a**, **2c**, and **2d**.

Based on the above experimental results, a reasonable mechanism for the formation of coumarin aryl sulfide derivatives **14**, **15** and cyclized product **9** is depicted in Scheme 8. Since the C_2–C_3 double bond is in conjugation with C–1 carbonyl and two ester groups of vinylic moiety at 2nd position and as supported by theoretical observations (Table 4), 3rd position of **2a** is more electrophilic than 6th position. More electrophilicity of 3rd position facilitates the quick Michael attack of 4-methylthiophenol (**3b**) to form species **A** (*path a*). Then the nucleophilic oxygen of hydroxy function of **A** attacks on the electrophilic carbon of ester moiety to give the cyclized species **B** spontaneously with the concomitant release of

methanol. Tautomerization of **B** produces **14** as major product. In addition to affording **14** and **15**, the alkenyl *p*-benzoquinone **2a** may also undergo self-cyclization to produce **9** (*path b*). This cyclization is triggered by the oxidation of thiophenol **3b** by quinone **2a** to disulfide **E** with simultaneous reduction of **2a** to hydroquinone **F**, which undergoes cyclization to form coumarin **9** (*path b*). Michael attack of **3b** on the less electrophilic 6th position of **2a** leads to the formation of minor product **15** from *path c*. Initial attack of thiol resultes in generation of intermediate **C** which immediately tautomerizes to hydroquinone **D**. Cyclization of **D** gives the minor product **15** with the release of MeOH



Scheme 8: Proposed mechanism for the formation of coumarin derivatives **14**, **15** and cyclized product **9**.

2.2.2. Regioselective synthesis of polyheterocycles by cycloaddition reaction of alkenyl *p*-benzoquinones

Today in organic synthesis, the edifice of carbon–carbon and carbon–heteroatom bonds through cycloaddition reactions is one of the most important approaches for the formation of heterocyclic compounds in which [3 + 2] cycloaddition reactions are recognised as a powerful weapon to construct carbocyclic and heterocyclic compounds with diverse biological activities [184–189]. The construction of tricyclic and tetracyclic heterocyclic systems through one-pot strategy has engrossed continuous attention in recent years since their presence in various natural products [190,191]. Dihydrobenzofuran derivatives are versatile building blocks in organic synthesis and are widely distributed in nature [192,193] (Figure 7). These compounds are reported to have various biological activities such as antiviral, antibacterial, anti-inflammatory, antiangiogenic, and antimitotic.

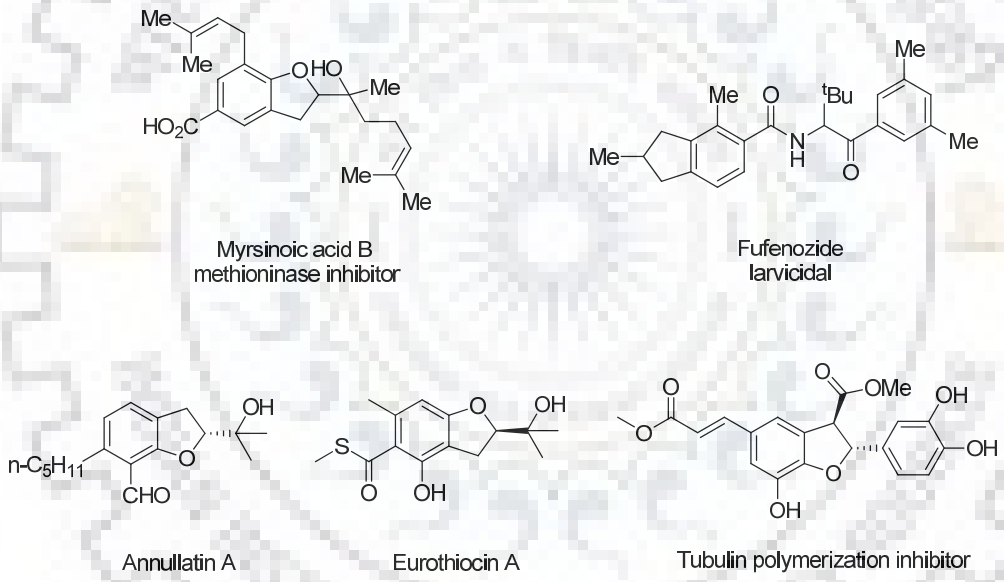
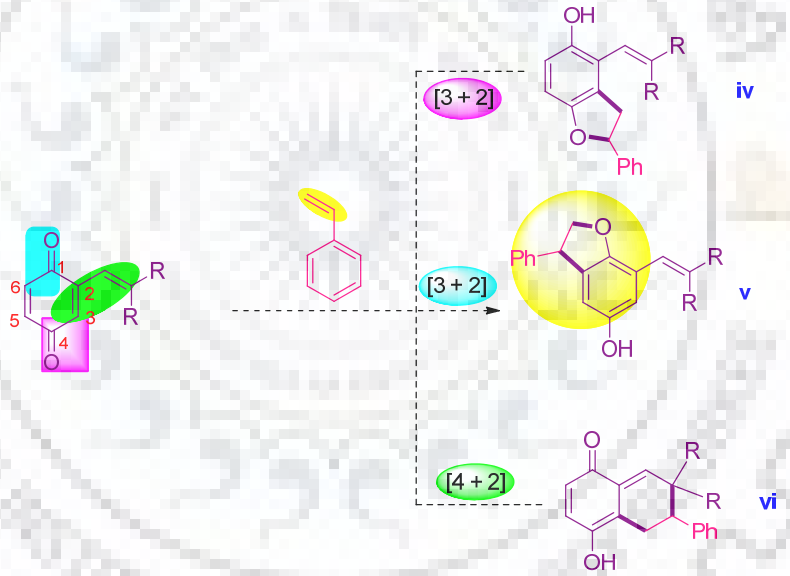


Figure 7: Some biologically active compounds containing dihydrobenzofuran.

The unique structures and highly pronounced biological and pharmacological activities displayed by these systems have attracted attention for their synthesis [194–198]. Recently, dihydrobenzofuran derivatives have been prepared *via* several reactions [199–205]. In general, benzoquinone [206,207] motif has been found in numerous natural products and exhibits important biological activities such as antimalarial, antitumor,

antibacterial and antifungal actions [208]. Importance of these scaffolds coupled with our on-going efforts in the exploration of the reactivity of benzoquinones [172–177,209–211] encouraged us to examine the mode of cycloaddition of alkenyl *p*-benzoquinones, with various olefinic partners.

In continuation of our efforts on harnessing the reactivity of alkenyl *p*-benzoquinones, we next sought to examine whether alkenyl *p*-benzoquinones could react with styrenes in the same manner. Therefore we hypothesized the reactivity of alkenyl *p*-benzoquinones with styrene and it was imagined that either the styrene would add at position-3 or position-6 of the alkenyl *p*-benzoquinone to provide dihydrobenzofurans of type **iv** and/or **v**, respectively, *via* [3 + 2] cycloaddition reaction or in another way alkenyl *p*-benzoquinones would act as electron-deficient diene and styrene as electron-rich dienophile to deliver bicyclic product **vi** *via* inverse-electron-demand Diels-Alder reaction (Scheme 9).

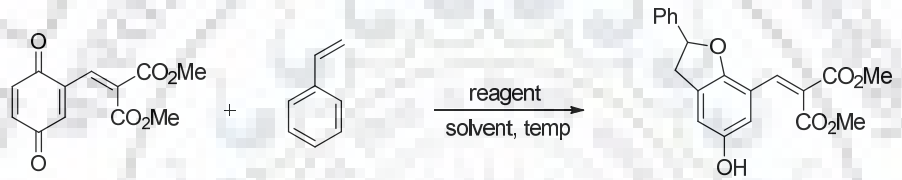


Scheme 9: Hypothesis for the reaction between styrene and alkenyl *p*-benzoquinone.

To test our hypothesis, in a preliminary step, we carried out the cycloaddition of alkenyl *p*-benzoquinone **2a** with styrene (**4a**). However no reaction was observed (Table 5, entry 1). We reasoned that **2a** is not reactive enough to drive the cycloaddition process with relatively less nucleophilic styrene. This prompted us to use an acid promoter. Consequently, we performed the reaction of **2a** with styrene in DCM in the presence of

Brønsted acids such as TFA, 2,4-dintrobenzoic acid (2,4-DNB) and *p*-TSA.H_2O; however, the reaction did not take place and starting materials were recovered as such (Table 5, entries 2–4). The reaction using iodine as catalyst could not afford the product (entry 5). The reaction of using silica-sulfuric acid (SSA) as a catalyst afforded 2,3-dihydrobenzofuran **56** in 50% yield (entry 6). The formation of dihydrobenzofuran **56** took place by the attack of *β*-carbon of styrene regioselectively at 6th position of alkenyl *p*-benzoquinone followed by ring closure, in a overall [3 + 2] cycloaddition. Delightedly, when the reaction was carried out by employing Lewis acids as reagents, dihydrobenzofuran derivative **56** was procured in good yields. Interestingly, when the reaction of alkenyl *p*-benzoquinone **2a** and **4a** was performed with 1.0 equiv of $BF_3{\cdot}OEt_2$ in DCM, **56** was obtained in 65% yield (entry 7).

Table 5: Optimization conditions for the synthesis of dihydrobenzofuran **56**.[a]



2a **4a** **56**

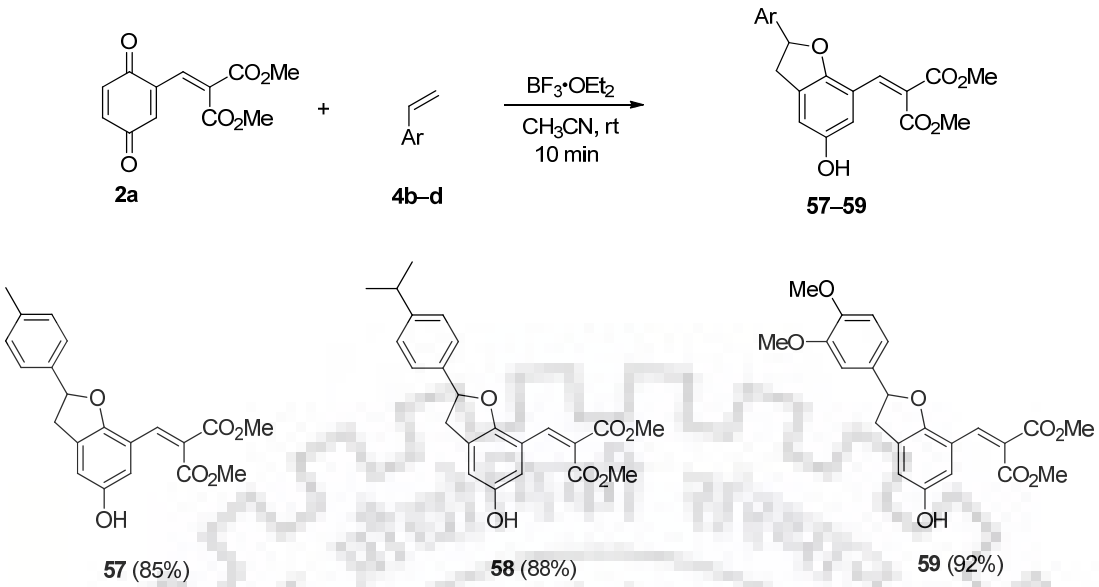
Entry	Reagent	Solvent	Time	Yield (%)[b]
1	–	DCM	24 h	NR
2	TFA (1.0 equiv)	DCM	24 h	NR
3	*p*-TSA.H_2O (1.0 equiv)	DCM	24 h	NR
4	2,4-DNB (1.0 equiv)	DCM	24 h	NR
5	Iodine (1.0 equiv)	DCM	24 h	NR
6	SSA (1.0 equiv)	DCM	1 h	50
7	$BF_3{\cdot}OEt_2$ (1.0 equiv)	DCM	30 min	65
8	$ZrCl_4$ (1.0 equiv)	DCM	30 min	55
9	$FeCl_3$ (1.0 equiv)	DCM	30 min	45
10	$SnCl_4$ (1.0 equiv)	DCM	30 min	58
11	$BF_3{\cdot}OEt_2$ (2.0 equiv)	DCM	15 min	80
12	$BF_3{\cdot}OEt_2$ (2.0 equiv)	DCE	30 min	60
13	**$BF_3{\cdot}OEt_2$ (2.0 equiv)**	**CH_3CN**	**10 min**	**86**

14	$BF_3{\cdot}OEt_2$ (0.5 equiv)	CH_3CN	1 h	44
15	$BF_3{\cdot}OEt_2$ (0.7 equiv)	CH_3CN	1 h	49
16[c]	$BF_3{\cdot}OEt_2$ (2.0 equiv)	CH_3CN	10 min	70
17[d]	$BF_3{\cdot}OEt_2$ (2.0 equiv)	CH_3CN	40 min	83

[a]The reaction was carried out with **2a** (0.5 mmol) and **4a** (1.0 mmol) and 1 equiv of reagent in 2 mL solvent at rt.
[b]Yield of pure and column chromatographically isolated product. NR: no reaction.
[c]Temp: 50 °C.
[d]Temp: 0 °C

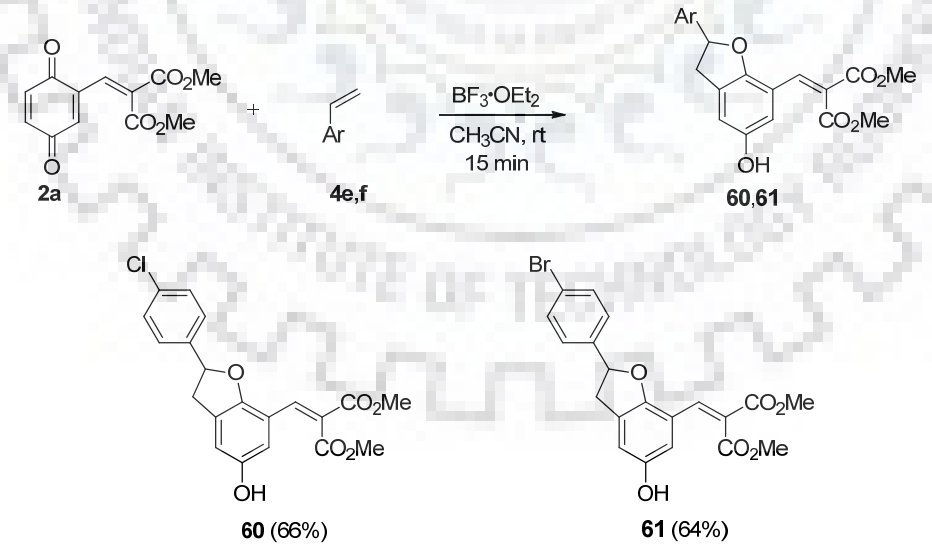
In this respect we optimized the following reaction with Lewis acids such as $ZrCl_4$, $FeCl_3$ and $SnCl_4$ (entries 8–10). In all the tested Lewis acids, optimum results were obtained with $BF_3{\cdot}OEt_2$. Further, we evaluated the reaction with varying amount of $BF_3{\cdot}OEt_2$. On increasing the amount of $BF_3{\cdot}OEt_2$ in DCM, the product was obtained in an increased yield of 80% (entry 11) and on changing the solvent from DCM to DCE and CH_3CN, **56** was obtained at room temperature in 60 and 86% yields, respectively (entries 12 and 13). The reaction with lower amounts of $BF_3{\cdot}OEt_2$ in CH_3CN did not improve the yield of **56** (entries 14 and 15). Additionally, the effect of temperature was also investigated which suggested that the reaction at rt was the best condition for this transformation. A significant decrease in yield was observed when the reaction was performed at 50 °C (entry 16). The reaction of **2a** and **4a** at 0 °C furnished the cycloadduct **56** in good yield with slightly longer reaction time (entry 17). Then the optimized conditions (entry 13) were used to explore the generality of the reaction. At first, styrenes **4a**–**h** were investigated in reactions with alkenyl *p*-benzoquinone **2a** in CH_3CN at room temperature.

Styrenes **4b**–**d** with electron-donating groups underwent this cycloaddition process successfully and produced the corresponding dihydrobenzofuran derivatives **57**–**59** in good yields as shown in Scheme 10. For example, when 4-methyl, 4-isopropyl, and 3,4-dimethoxy substituted styrenes were employed, the corresponding products **57**–**59** were obtained in 10 min with 85, 88, and 92% yields, respectively (Scheme 10). Thus the reaction proceeded very well with electron-rich species.



Scheme 10: Reaction of alkenyl *p*-benzoquinone **2a** with electron-rich styrenes **4b**–**d**.

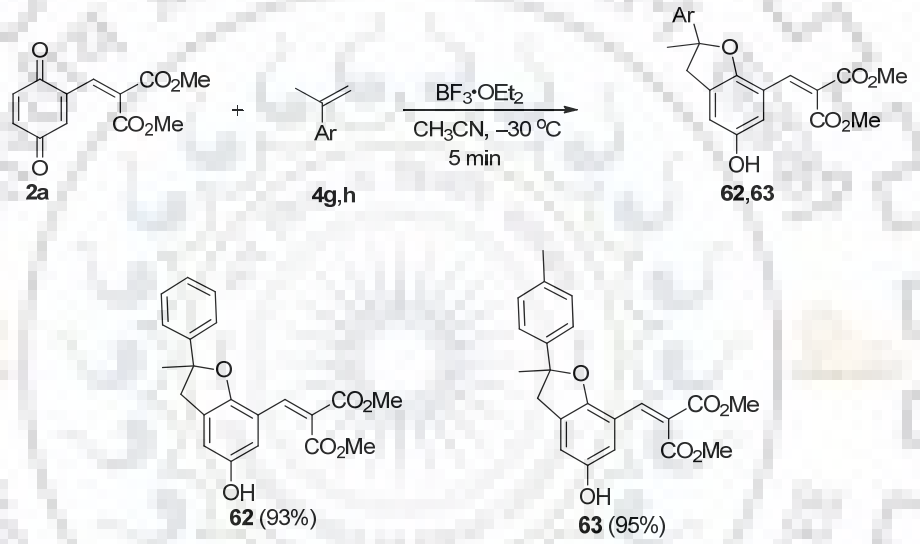
Delighted by the above results, we synthesized styrenes containing electron-withdrawing groups at *para*-position **4e**,**f** and performed their reaction with benzoquinone **2a** under the optimized reaction condition. When styrenes **4e** and **4f** having electron-withdrawing groups were used, the reaction progressed persuasively and the analogous adducts **60** and **61** were obtained in relatively low yields as a outcome of the electron-withdrawing nature of halo group of the nucleophile as can be seen in Scheme 11.



Scheme 11: Reaction of alkenyl *p*-benzoquinone **2a** with electron-deficient styrenes **4e**,**f**.

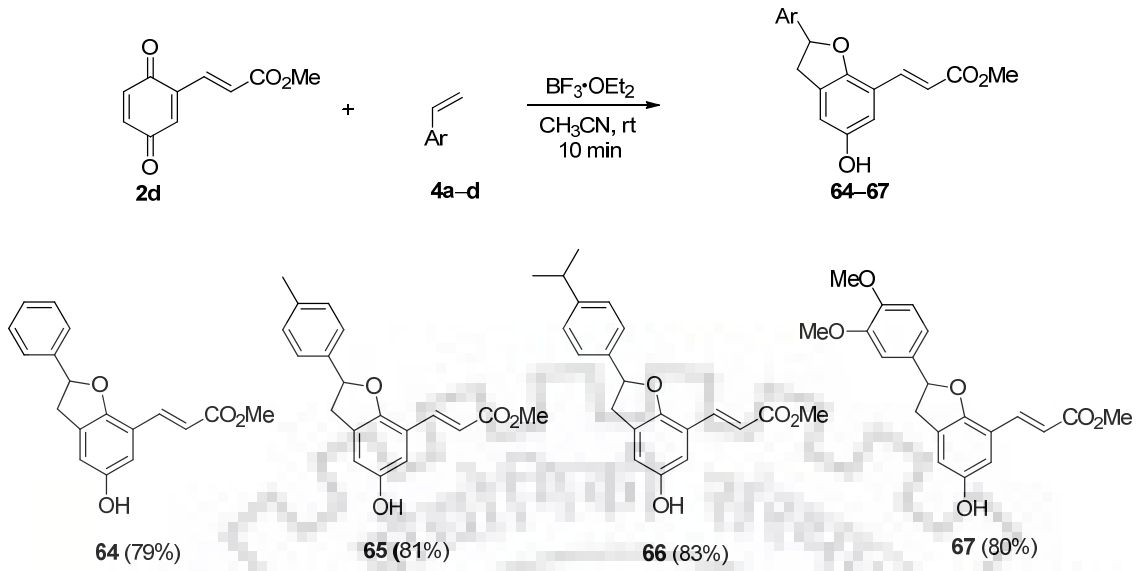
Further we synthesized styrenes containing electron-withdrawing groups such as chlorine, bromine at *ortho* and *meta* position and carried out their reaction with **2a**, unfortunately we could not get any product.

To show the generality of the present protocol, we synthesized α-substituted styrenes and performed the reaction of alkenyl *p*-benzoquinone **2a** under optimized reaction conditions which did not proceed well at room temperature. Consequently, we performed the reaction at low temperature. Amazingly, the reaction at –30 ^{o}C resulted in the formation of dihydrobenzofuran derivatives **62** and **63** in excellent yields (Scheme 12). Recations were more clean and rapid as in case of previous reactions.



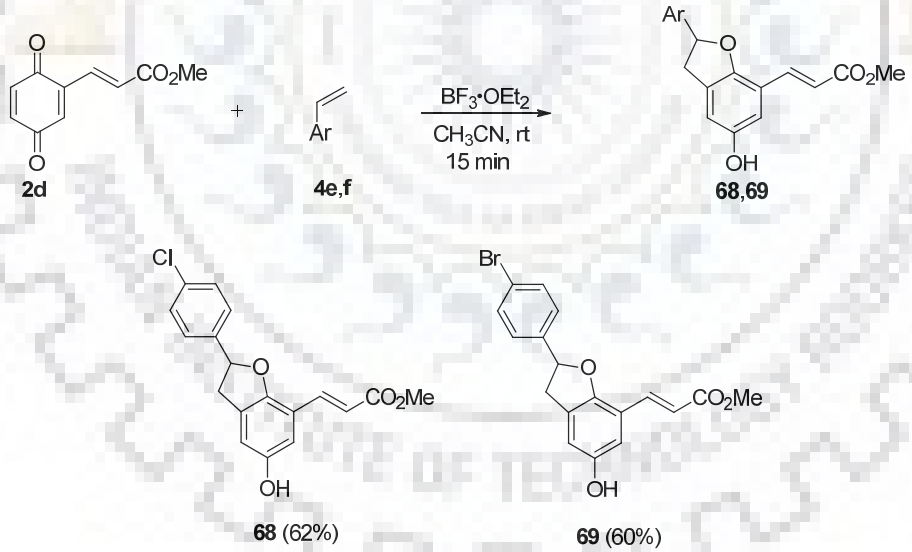
Scheme 12: Reaction of alkenyl *p*-benzoquinone **2a** with α-substituted styrenes **4g**,**h**.

Subsequently, we examined the substrate scope and limitations of this [3 + 2] cycloaddition reaction. The reactions of **2d** with electron-rich styrenes **4a**–**d** were proved to be synthetically compatible and the corresponding dihydrobenzofuran derivatives **64**–**67** were produced in moderate to good yields (Scheme 13). Styrene reacted with **2d** to deliver **64** in 79% yield. 4-methylstyrene reacted well to afford dihydrobenzofuran derivative **65** in 81% yield. Similar results were obtained when reactions were carried out with 4-isopropyl and 3,4-dimethoxy styrenes (**66** and **67**, Scheme 13).



Scheme 13: Reaction of electron-rich styrenes **4a**–**d** with alkenyl *p*-benzoquinone **2d**.

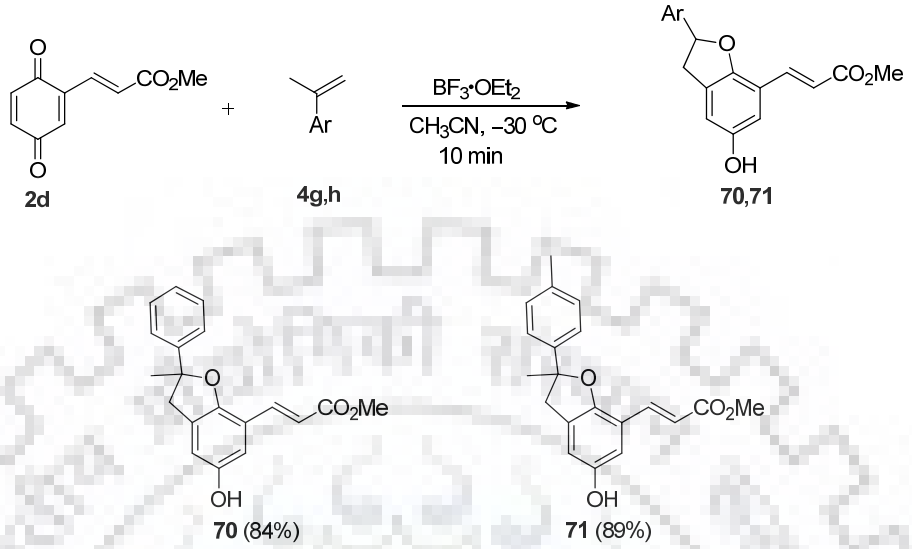
Likewise, the reaction with electron-deficient styrenes such as 4-chloro and 4-bromo styrenes under optimized conditions were also compatible and desired dihydrobenzofuran derivatives **68** and **69** were obtained in good yields (Scheme 14).



Scheme 14: Reaction of alkenyl *p*-benzoquinone **2d** with styrenes containing electron-withdrawing groups **4e**,**f**.

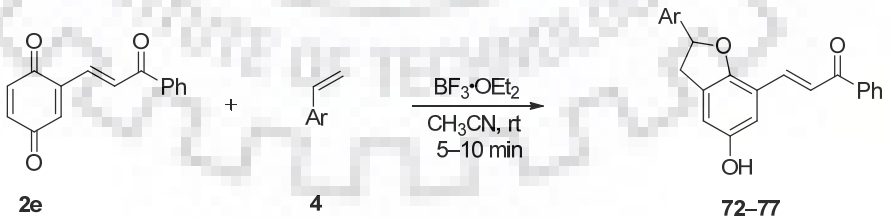
Delighted by our previous efforts and to see the effect of substitution on α-position of styrenes on reaction, we carried out the reaction of **2d** with styrenes **4g** and **4h** under

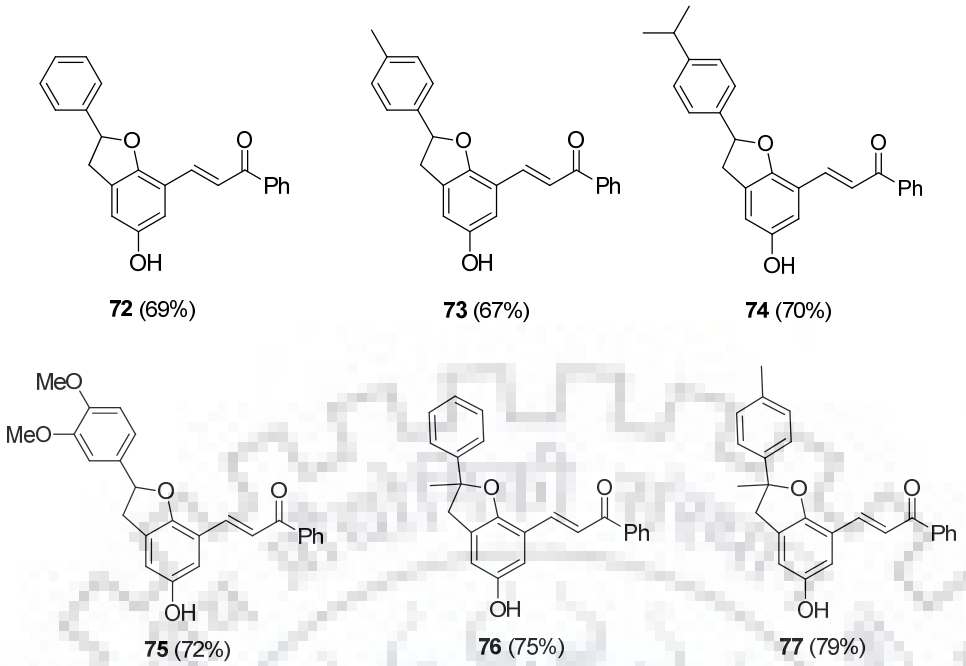
optimized conditions. It was found that all these styrenes were also successful and furnished **70** and **71** in excellent yields (Scheme 15).



Scheme 15: Reaction of alkenyl *p*-benzoquinone **2d** with α-substituted styrenes **4g**,**h**.

The compatibility and generality of the present method were further explored by employing alkenyl *p*-benzoquinone **2e** and styrenes **4** (Scheme 16). The yields of the products **72**–**77** obtained from **2e** were lower as comparison to those obtained in previous case, apparently due to the less reactivity of **2e**. Although the reactions of **2e** worked well with electron-rich styrenes **4b**–**d**, while styrenes **4e**,**f** equipped with electron-withdrawing groups failed to undergo [3 + 2] cycloaddition with **2e**. Furthermore, α-methylstyrenes **4g**,**h** also worked well and furnished the products **76**,**77** in 75 and 79% yields, respectively (Scheme 16).



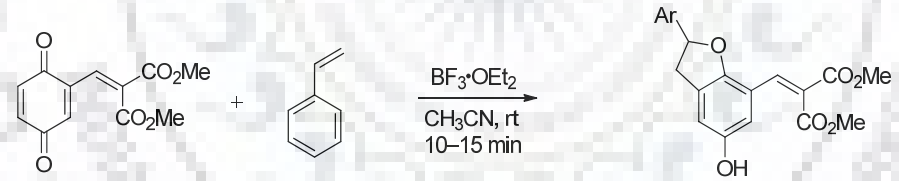


72 (69%) **73** (67%) **74** (70%)

75 (72%) **76** (75%) **77** (79%)

Scheme 16: [3 + 2] cycloaddition of various styrenes with alkenyl *p*-benzoquinone **2e**.

To see the utility of the reaction, we performed gram-scale reaction of alkenyl *p*-benzoquinone **2a** (4 mmol), and styrene (8 mmol). The reaction worked well and afforded the dihydrobenzofuran **56** in high yield (Scheme 17).



1a
4 mmol

4
8 mmol

56
1.17 g, (83 %)

Scheme 17: Gram-scale synthesis of **56**.

Structural elucidation of dihydrobenzofurans 56–77

The structure of products **56–77** were confirmed by detailed spectral analysis of the data obtained from ^{1}H and ^{13}C NMR, DEPT, and HRMS experiments of pure and isolated products. The connectivity of the protons that are coupled with each other and between protons and carbons of **56**–**77** were identified by two-dimensional ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments, respectively.

Homonuclear correlation

It is used to identify the correlation between same type of nucleus which are coupled to each other.

- Through bond correlation:

COSY	COrrelation SpectroscopY
TOCSY	TOtal Correlated SpectroscopY
2D-INADEQUATE	Incredible Natural Abundance DoublE QUAntum Transfer Experiment
2D-ADEQUATE	Adequate DoubleE QUAntum Transfer Experiment

- Through space correlation:

NOESY	Nuclear Overhauser Effect SpectroscopY
ROESY	Rotating -frame nuclear Overhauser Effect correlation SpectroscopY

Heteronuclear correlation

It is used to identify the correlation between different types of nucleus and called as $^{13}C-^{1}H$ COSY. It shows the connection between carbon atoms and proton directly bonded to them.

- One bond correlation:

HSQC	Heteronuclear Single Quantum Correlation
HMQC	Heteronuclear Mutiple Quantum Correlation

- Long range correlation:

HMBC	Heteronuclear Mutiple Bond Correlation

As we hypothesized in Scheme 9, three products are possible in the cycloaddition reaction of alkenyl *p*-benzoquinones and styrenes. The final authentication of the [3 + 2] cycloadducts **56**–**77**, *viz* the regiochemistry of the given structures was confirmed based on the analysis of data obtained from ^{1}H NMR. As in case of dihydrobenzofuran **56**, the H–2 proton appears as triplet, downfield at δ 5.72 ppm because of the adjacent oxygen. The olefinic proton H–8 resonates at δ 7.89 ppm. The *meta* coupling (J = 2.8 Hz) of two aromatic protons H-4 and H-6, resonates at δ 6.76 and 6.64 ppm indicates the addition of styrene is being taking place on *p*-benzoquinone at 6th position (Figure 8). In ^{13}C NMR, one methylene carbon *i.e.*, C–3 resonates at δ 38.2 ppm which was confirmed by analyzing

DEPT-135 NMR spectrum. The ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments carried out to identify the protons that are coupled with each other and the connectivity between protons and carbons, respectively (Figure 9,10). The HMBC study provides proton–carbon correlations over two and three bonds which were found to be particularly supportive in the regiochemistry of the structure of the product **56** which reveales the correlation of H–4 with C–3 methylene carbon, indicating that the attack of styrene *β*-carbon takes place at position 6 on alkenyl *p*-benzoquinone to produce **56** (Figure 11).

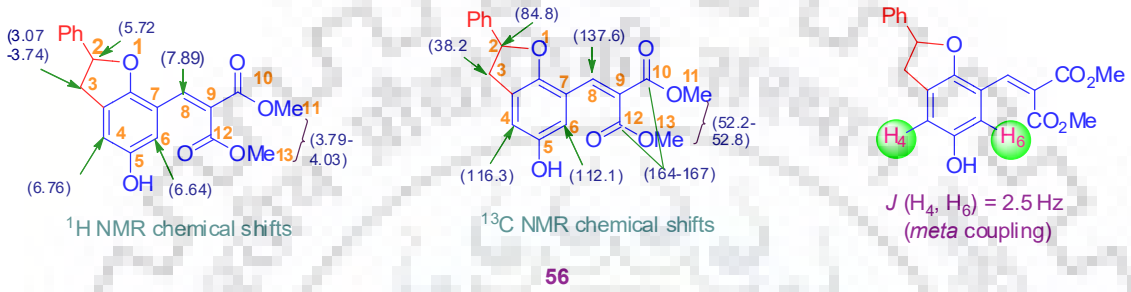


Figure 8: ^{1}H and ^{13}C NMR Chemical shifts and coupling constant values of dihydrobenzofuran **56**.

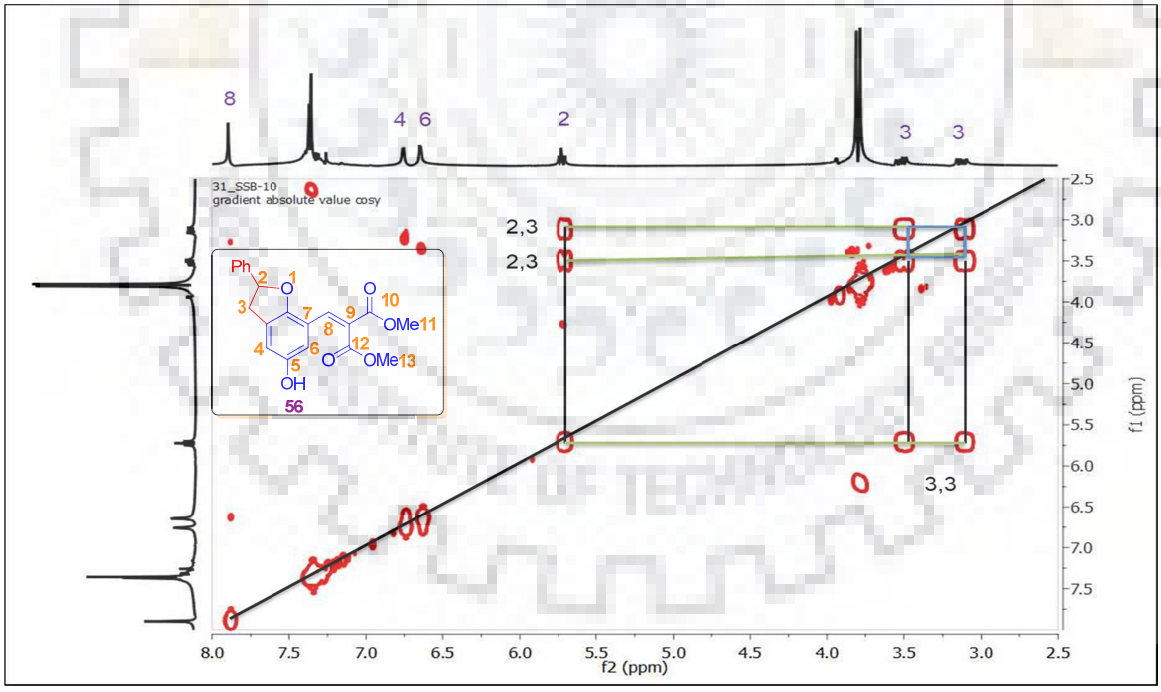


Figure 9: ^{1}H–^{1}H COSY spectrum of **56**.

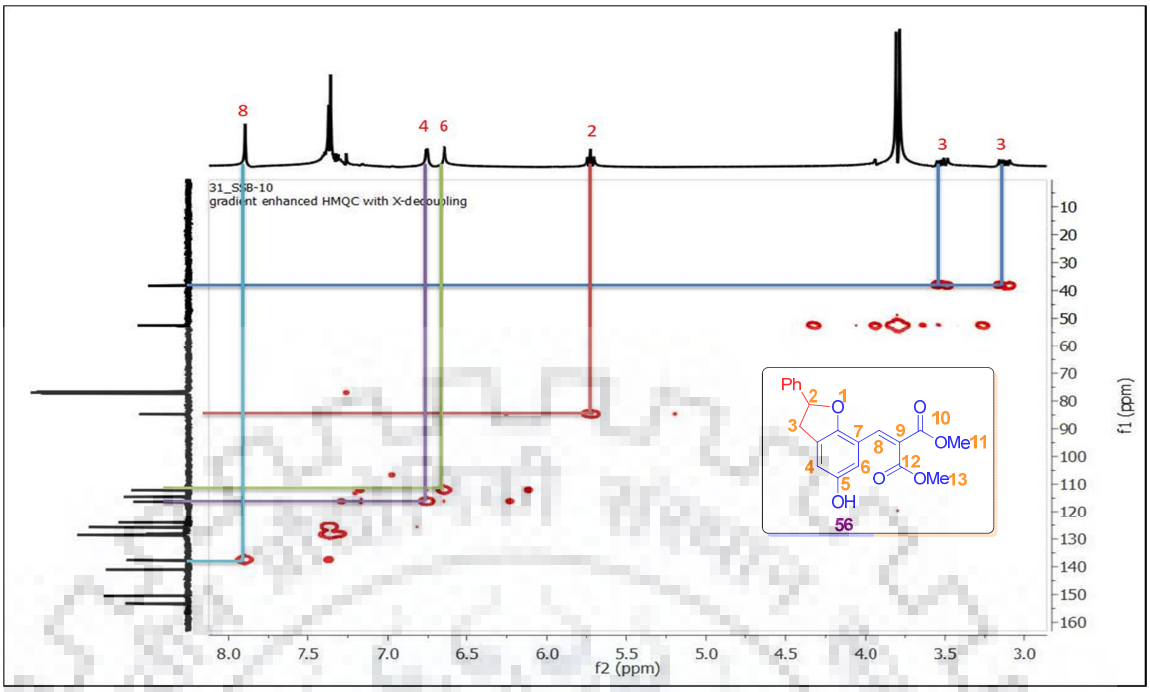


Figure 10: ^{1}H–^{13}C (HMQC) COSY spectrum of **56**.

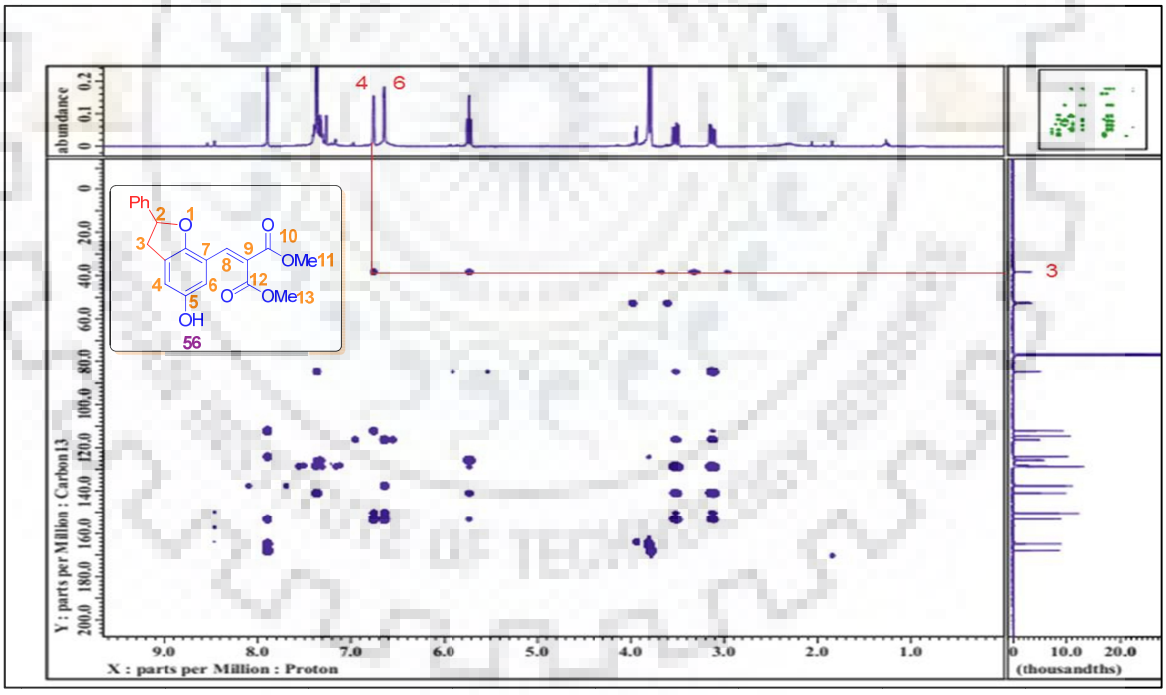
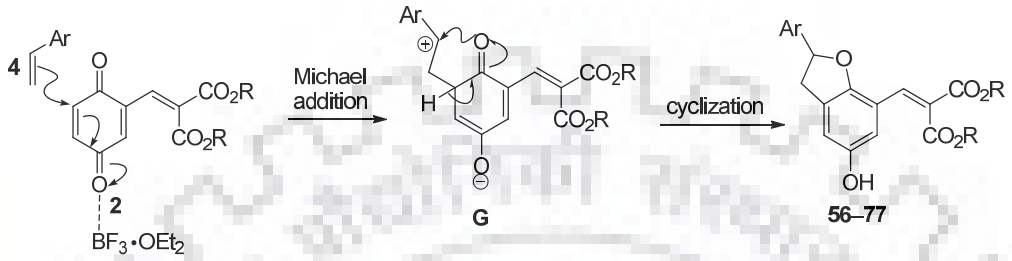


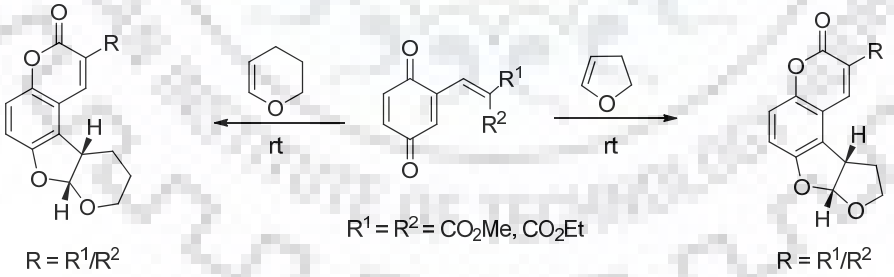
Figure 11: ^{1}H–^{13}C (HMBC) COSY spectrum of **56**.

The possible mechanism for the formation of dihydrobenzofuran derivatives **56**–**77** is depicted in Scheme 18. Firstly, $BF_3 \cdot OEt_2$ coordinates with the carbonyl group of alkenyl *p*-benzoquinone **2** to enhance the electrophilicity at 6th position, where the Michael attack of *β*–carbon of styrene **4** takes place to produce intermediate **G**. The subsequent cyclization delivers the target [3 + 2] cycloadduct (Scheme 18).



Scheme 18: Plausible reaction mechanism for the formation of dihydrobenzofuran derivatives.

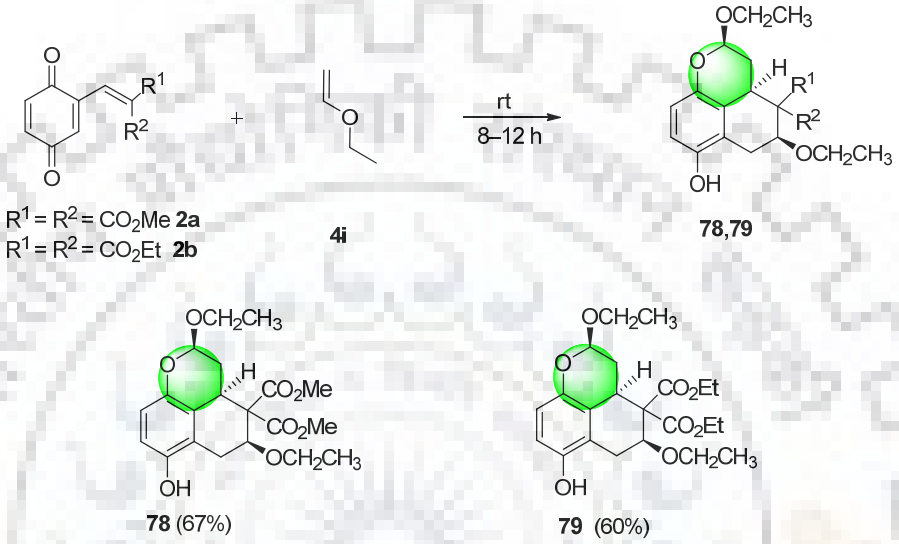
From our laboratory we have reported [212] an efficient synthesis of derivatives of dihydrofurocoumarin, dihydrofuropyranocoumarin, dihydrobenzopyran, and fused dihydrofuran using alkenyl *p*-benzoquinones with cyclic enol ethers such as dihydrofuran and dihydropyran. The reaction proceeded *via* [3 + 2] cyclocaddition followed by domino reaction sequence. The obtained tetracyclic products (Scheme 19) were characterized by 2D experiments. The stereochemistry of the products was determined by coupling constant values obtained from ^{1}H NMR as well as by its single crystal X-ray analysis.



Scheme 19: Synthesis of tetracyclic compounds *via* domino reaction.

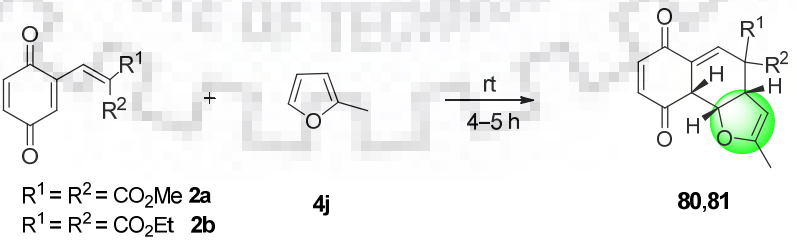
Motivating by the reactivity of alkenyl *p*-benzoquinones with styrenes and cyclic enol ethers which proceeded *via* [3 + 2] cycloaddition and domino sequence. Next we turned

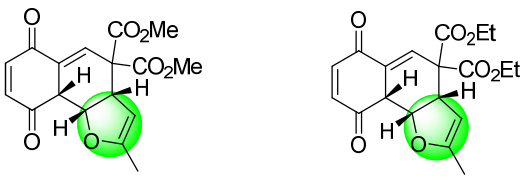
our attention towards the reaction of ethyl vinyl ether with alkenyl *p*-benzoquinones. The reaction of **2a** and **2b** with 10.0 equiv of ethyl vinyl ether at rt furnished tricyclic products **78** and **79** regioselectively with good yields in 8–12 h (Scheme 20). These tetrahydrobenzochromene products were obtained through tandem double inverse electron-demand [4 + 2] cycloaddition. However in this reaction alkenyl *p*-benzoquinones acted as electron deficient diene and ethyl vinyl ether as electron rich dienophile.



Scheme 20: Synthesis of tricyclic compounds *via* reaction with ethyl vinyl ether.

Next we turned our attention towards the use of oxygen containing aromatic heterocycle, 2-methylfuran. Interestingly, the reaction of **2a** and **2b** with 2-methylfuran, under the standard conditions, produced the tricyclic systems **80** and **81** in 78 and 75% yields, respectively, *via* inverse electron-demand [4 + 2] cycloaddition reaction in 4–5 h (Scheme 21).





80 (78%) **81** (75%)

Scheme 21: Reaction of benzoquinones **2a**,**b** with 2-methylfuran (**4j**).

Structural elucidation of tricyclic products 78 and 79

The structures of tricyclic products were confirmed by detailed spectral analysis obtained from ^{1}H and ^{13}C NMR, DEPT, and HRMS experiments of pure and isolated products. In the ^{1}H NMR of **78** and **79**, H–2 proton appears at δ 5.08–5.09 as doublet of doublet, H–3a appears as multiplate around δ 3.59–3.48 and H–5 appears as doublet of doublet at δ 4.15 ppm (Figure 12). The connectivity of the protons that are coupled with each other and between protons and carbons of **78** was identified by two-dimensional ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments, respectively (Figure 13–15). For more insight into the stereochemistry of the tricyclic products we performed NOESY experiment to understand the spatial correlation between H-2, H-3a and H-5 protons. The NOESY experiment of **78** (Figure 16) showed a significant correlation between H-2 and H-3a indicating the *cis*-geometry of these two protons. Similarly, NOESY correlations between H-5 and H-3a, established spatial proximity of these protons in the molecule which was further confirmed by its single crystal X-ray analysis (Figure 17, Table 6). The crystal was obtained from $CDCl_3$ solution through slow evaporation.

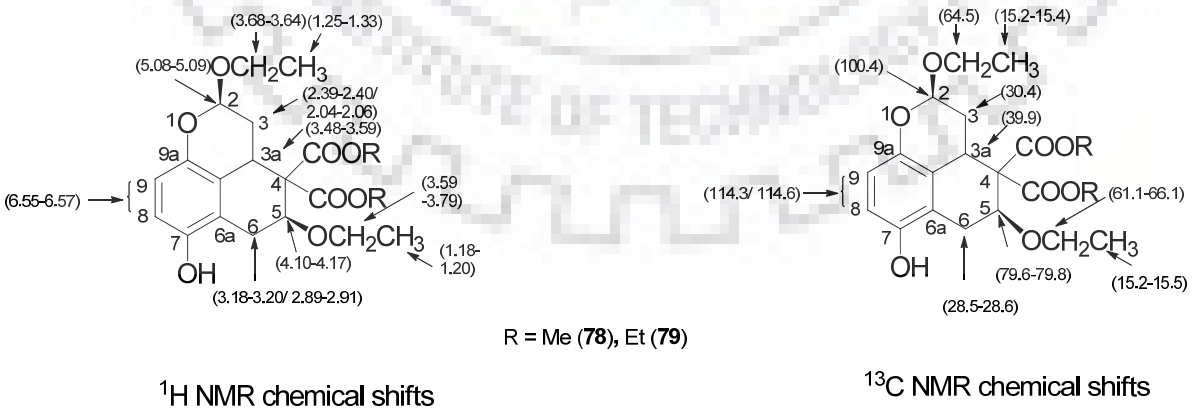


Figure 12: Selected ^{1}H and ^{13}C NMR chemical shifts (δ in ppm) of **78** and **79**.

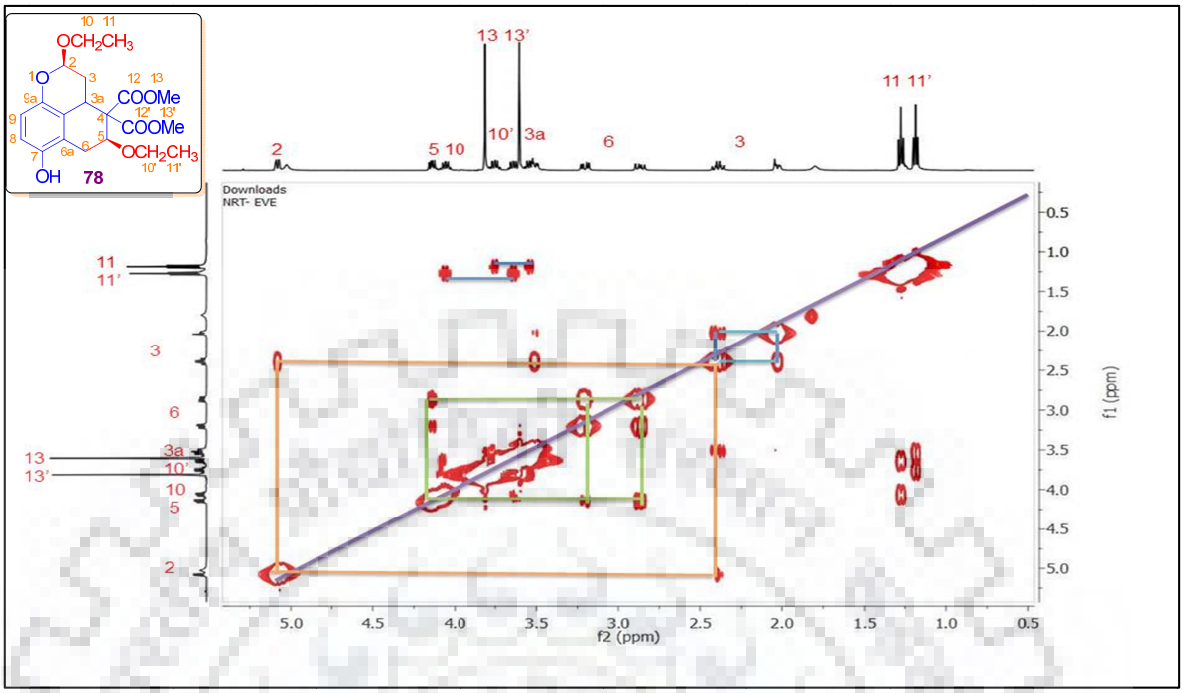


Figure 13: ^{1}H–^{1}H COSY spectrum of **78**.

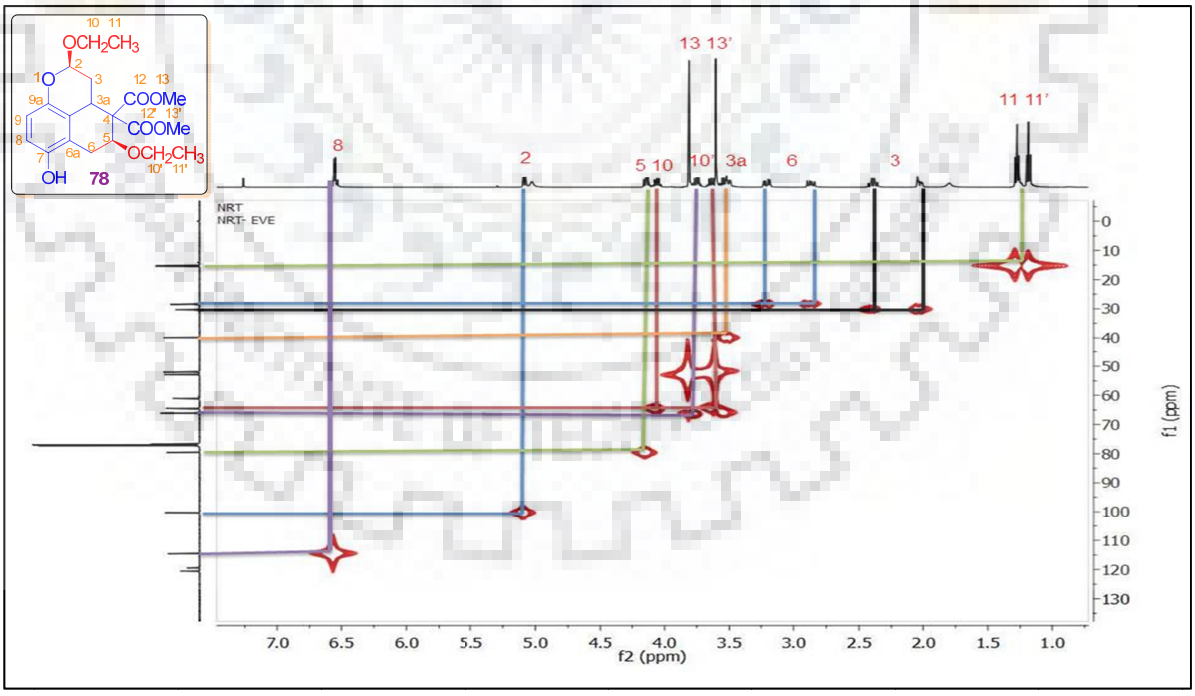


Figure 14: ^{1}H–^{1}H HMQC spectrum of **78**.

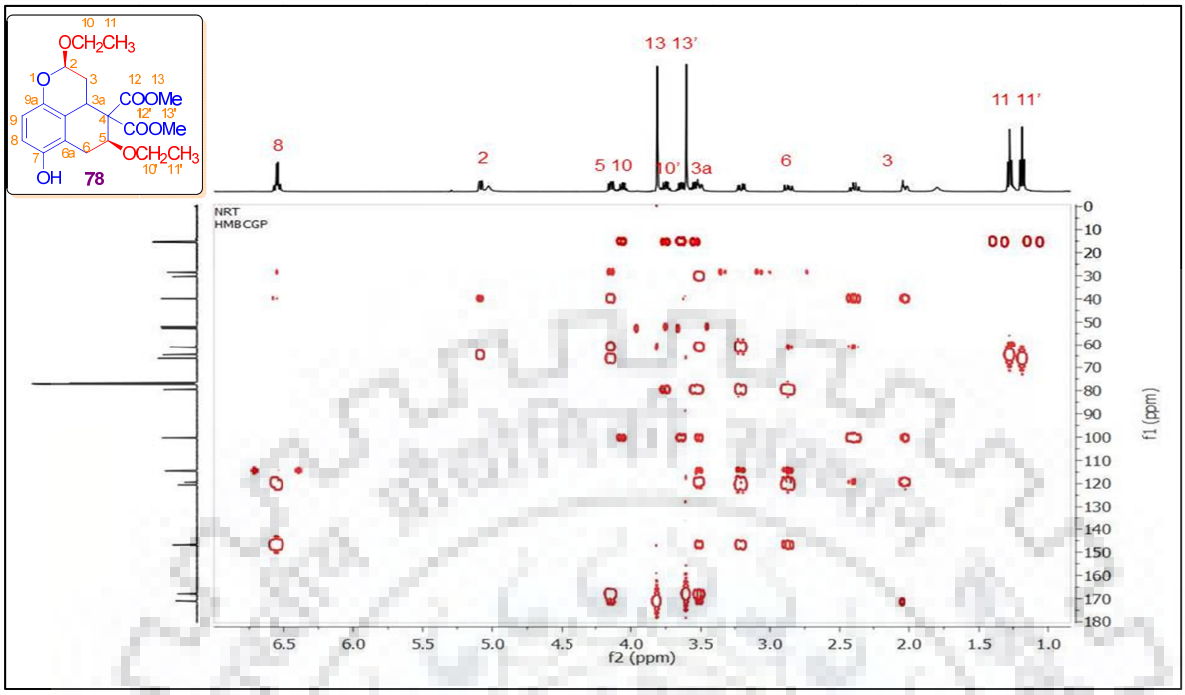


Figure 15: ^{1}H–^{1}H HMBC spectrum of **78**.

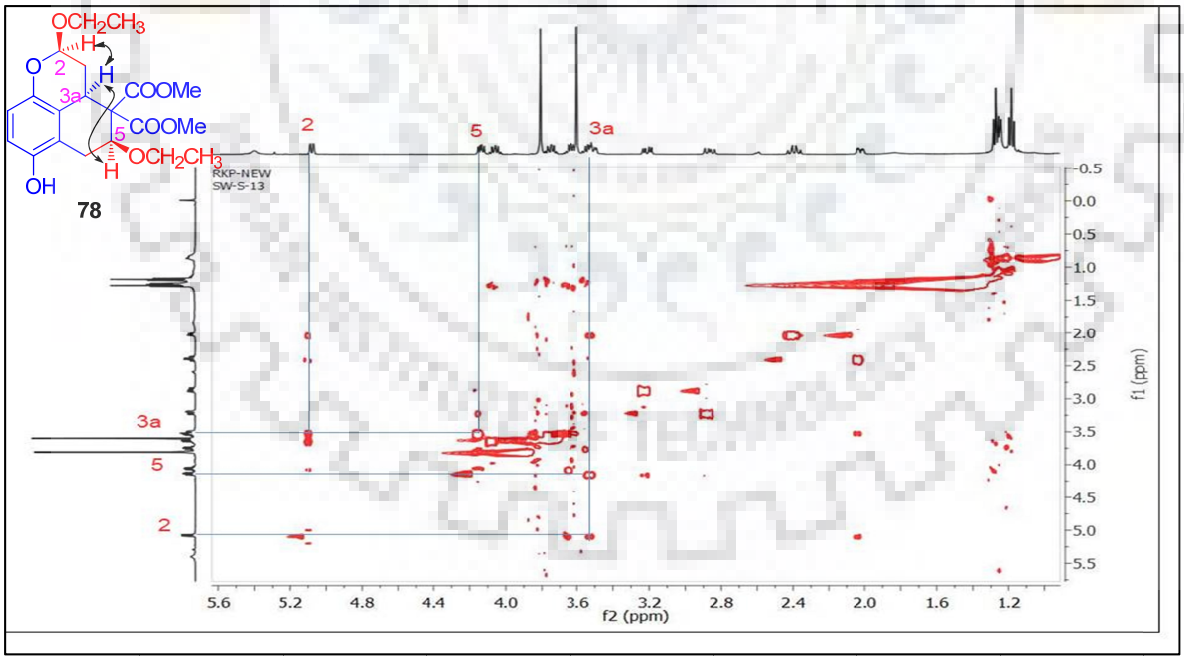
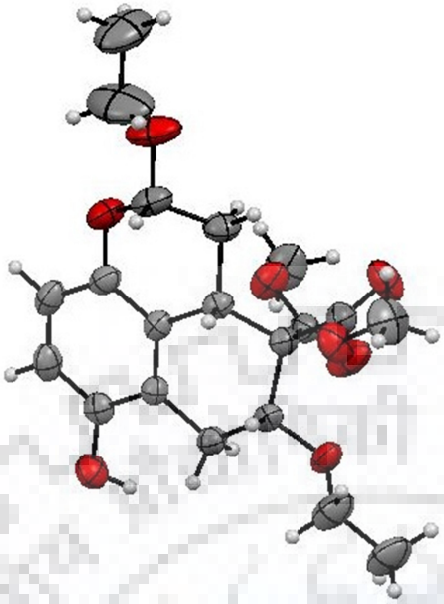
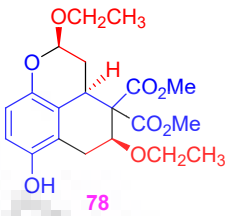


Figure 16: ^{1}H–^{1}H NOESY spectrum of **78**.





78

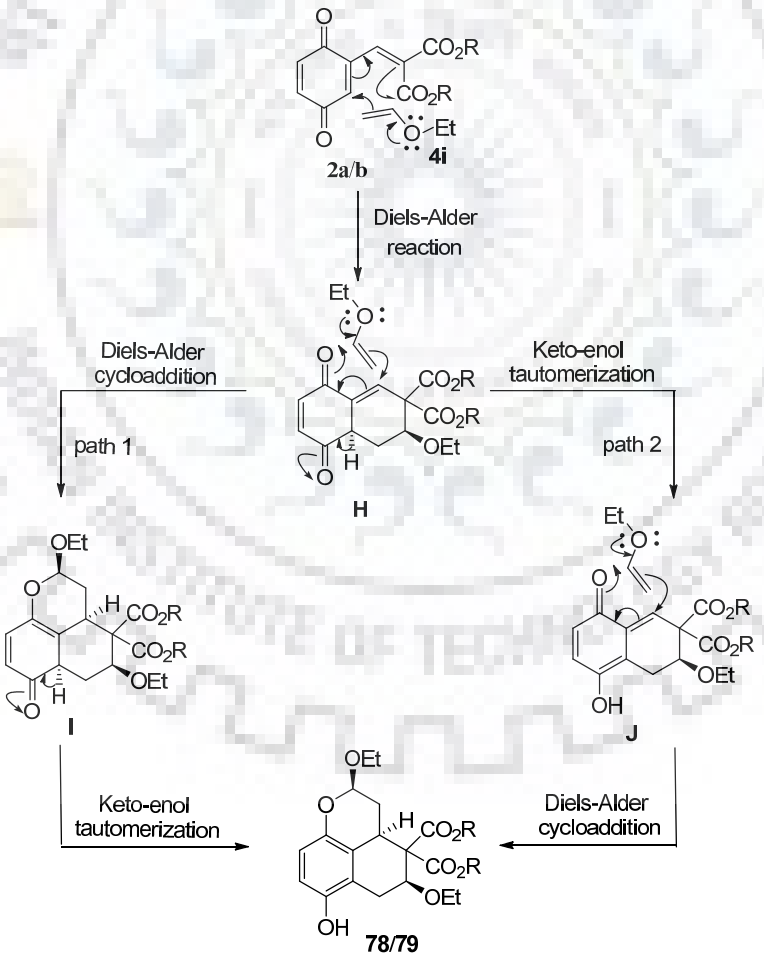
Figure 17: ORTEP representation of crystal structure of **78**.

Table 6: Crystallographic data for **78**.

Empirical formula	$C_{20}\ H_{26}\ O_8$
Formula weight	394.41
Temperature	296 (2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 10.377 (5) Å
	b = 22.737 (5) Å
	c = 8.394 (5) Å
	$\alpha = 90^{\circ}$
	$\beta = 103.551\ (5)^{\circ}$
	$\gamma = 90^{\circ}$
Volume	1925.4 (15) $Å^3$
Z	4
Density (calculated)	1.361 mg/m^3
Absorption coefficient	0.105 mm^{-1}
F(*000*)	840
Crystal size	0.22 x 0.20 x 0.18 mm^3

Theta range for data collection	0.977 to 0.981°
Index ranges	-12 ≤ h ≥ 12
	-27 ≤ k ≥ 27
	-10 ≤ l ≥ 9
Reflections collected	24989
Independent reflections	3580
Max. and min. transmission	0.977 and 0.981
Goodness-of-fit on F^2	1.263
Final R indices [I>2sigma(I)]	*R1* = 0.0588, *wR2* = 0.1660
R indices (all data)	*R1* = 0.1162, *wR2* = 0.2172
Largest diff. peak and hole	0.561 and - 0.467e.Å^{-3}

The formation of tetrahydro-benzochromene derivatives **78** and **79** could be explained based on the probable mechanism (Scheme 22).

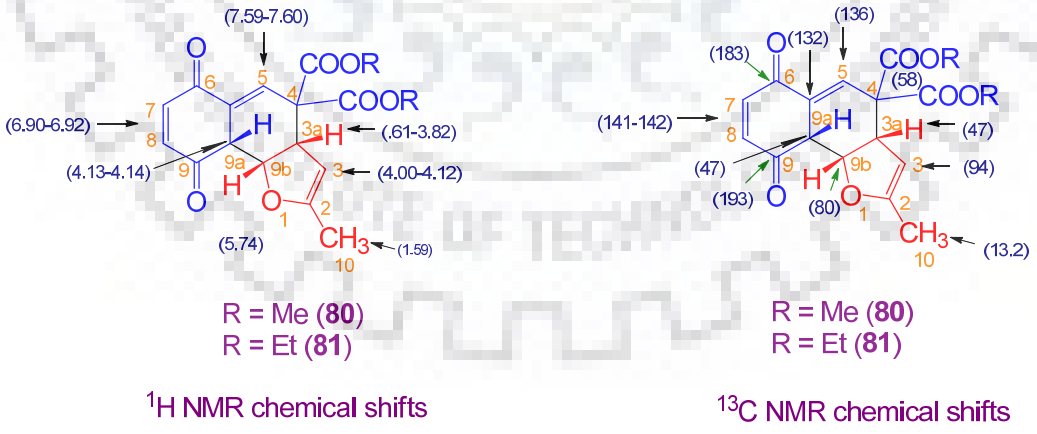


Scheme 22. Plausible reaction mechanism for the formation of **78** and **79**.

The highly electron-deficient diene **2a**/**b** undergoes inverse electron-demand Diels–Alder cycloaddition with electron-rich dienophilic ethyl vinyl ether (**4i**) to produce Diels–Alder adduct **H**, which further reacts (path 1) with the second molecule of ethyl vinyl ether to generate the target tricyclic system **78**/**79** *via* the keto-enol tautomerization of the adduct **I**. In another pathway, the adduct **H** tautomerizes to form intermediate **J** where the second molecule of ethyl vinyl ether reacts to deliver the desired product **78** and **79**.

Structure elucidation of tricyclic compounds 80 and 81

In case of **80** and **81**, the structure was confirmed by the analysis of collective information obtained from ^{1}H and ^{13}C NMR, DEPT, and 2D spectra. In ^{1}H NMR, AB quartet for two protons appear at δ 6.90–6.92 ppm, and in ^{13}C NMR, two peaks appear at δ 193 and 183 ppm, respectively, which indicate the presence of enone carbonyls (Figure 18). The connectivity of the protons that are coupled with each other and between protons and carbons in **80** was identified by two-dimensional ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments, respectively (Figure 19–21). The NOESY experiment of **80** (Figure 22) displayed correlations between H-3a and H-9b and H-9a and H-9b, indicating *cis*-geometry of these protons which was further confirmed by its single crystal X-ray analysis (Figure 23, Table 7). The crystal of tricyclic compound **80** was grown in $CDCl_3$ solvent *via* slow evaporation.



^{1}H NMR chemical shifts ^{13}C NMR chemical shifts

Figure 18: Selected ^{1}H and ^{13}C NMR chemical shifts (δ in ppm) of **80** and **81**.

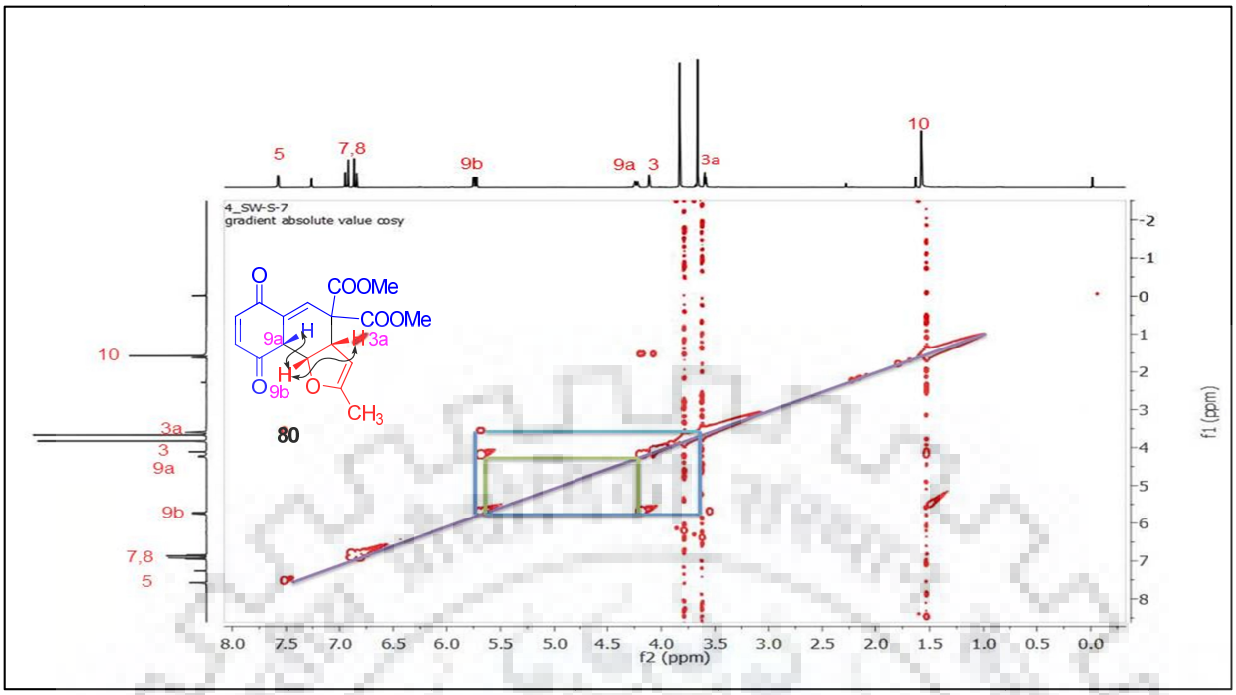


Figure 19: ^{1}H–^{1}H COSY spectrum of **80**.

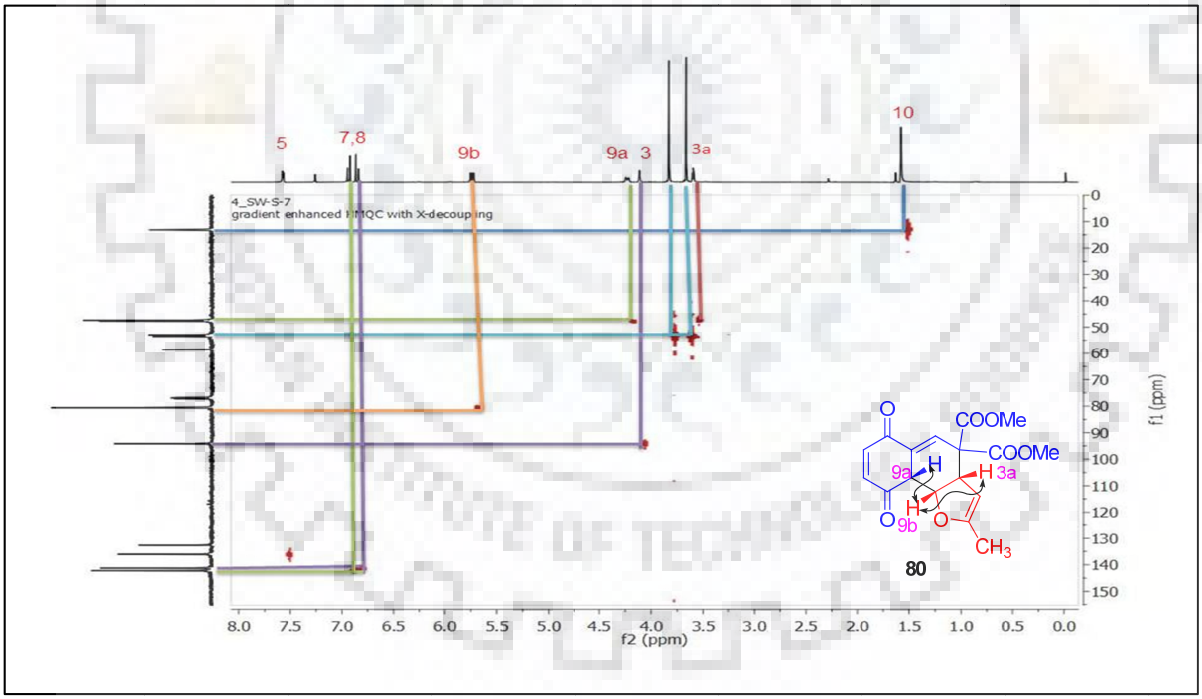


Figure 20: ^{1}H–^{13}C (HMQC) COSY spectrum of **80**.

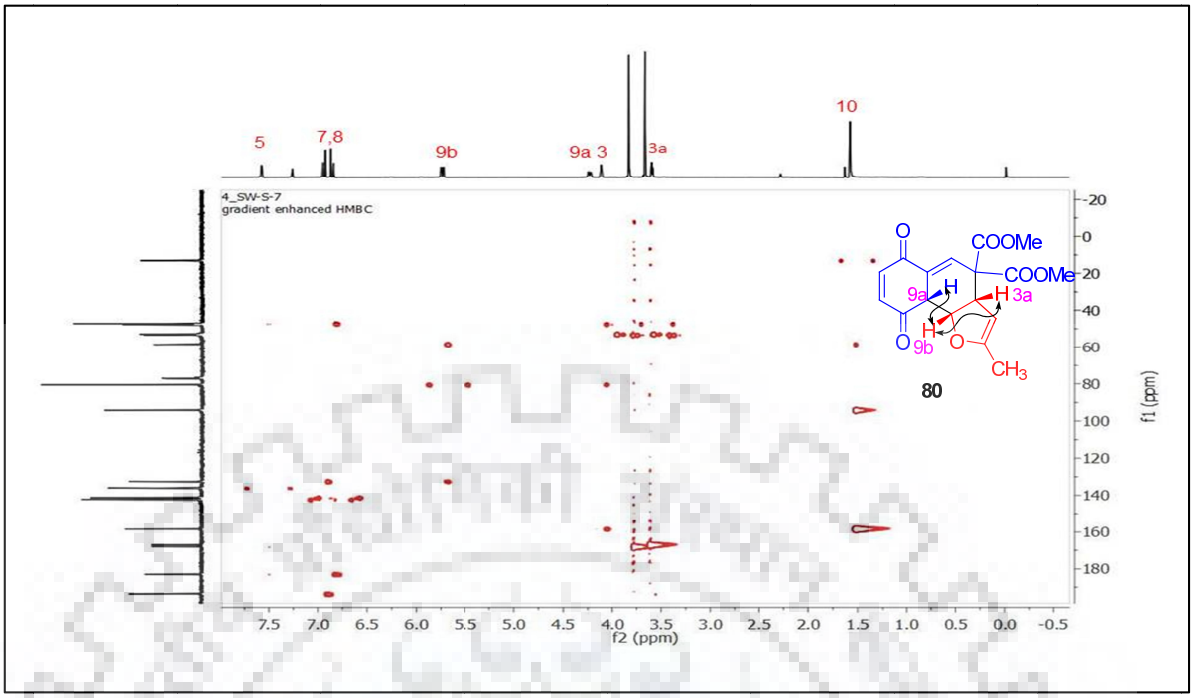


Figure 21: $^{1}H–^{13}C$ (HMBC) COSY spectrum of **80**.

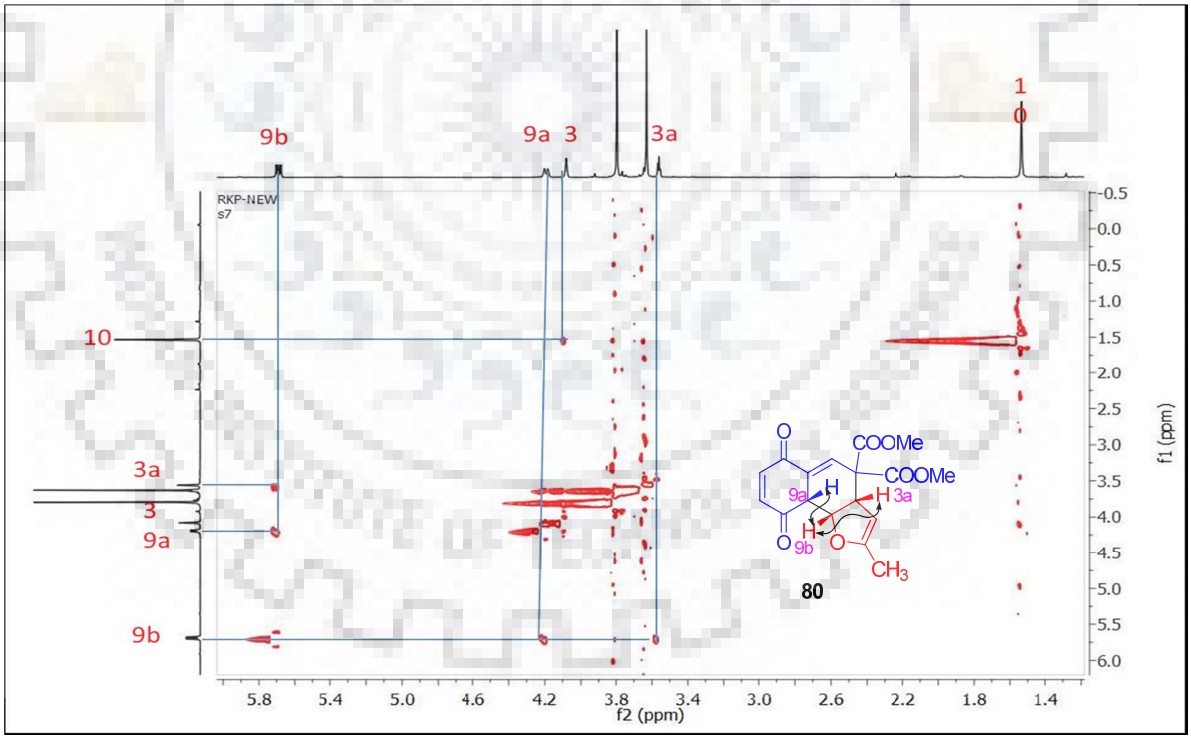


Figure 22: $^{1}H–^{1}H$ NOESY spectrum of **80**.

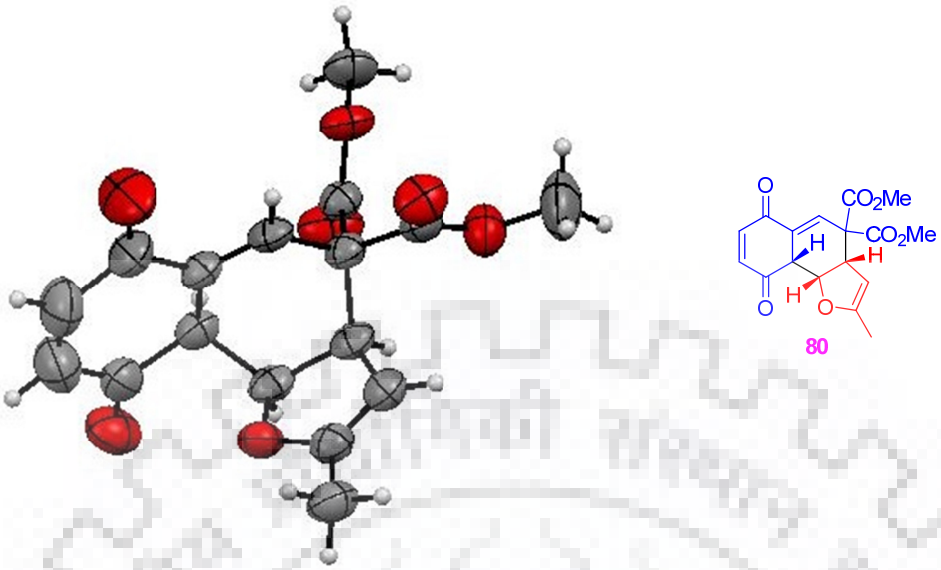


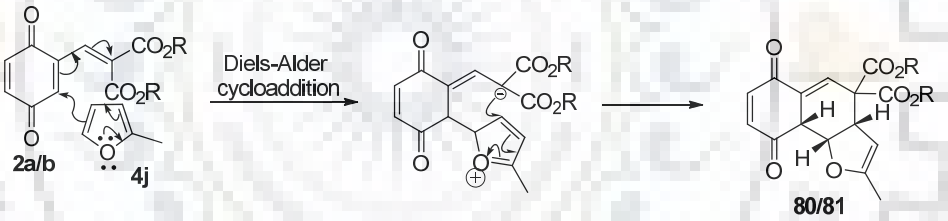
Figure 23: ORTEP representation of crystal structure of **80**.

Table 7: Crystallographic data for **80**.

Empirical formula	$C_{17}H_{16}O_7$
Formula weight	332.30
Temperature	296 (2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 7.7348 (17) Å
	b = 11.031 (2) Å
	c = 18.970 (4) Å
	$\alpha = 90^{\circ}$
	$\beta = 99.071\ (2)^{\circ}$
	$\gamma = 90^{\circ}$
Volume	1598.3 (6) $Å^3$
Z	4
Density (calculated)	1.381 mg/m^3
Absorption coefficient	0.108 mm^{-1}
F(*000*)	696

Crystal size	0.42 x 0.38 x 0.32 mm^3
Theta range for data collection	0.980 to 0.970°
Index ranges	$-10 \leq h \geq 10$
	$-14 \leq k \geq 14$
	$-21 \leq l \geq 25$
Reflections collected	20107
Independent reflections	3933
Max. and min. transmission	0.980 to 0.970°
Goodness-of-fit on F2	1.316
Final R indices [I>2sigma(I)]	*R1* = 0.1334, *wR2* = 0.3750
R indices (all data)	*R1* = 0.2126, *wR2* = 0.4194
Largest diff. peak and hole	0.567and - 0.561e.$Å^{-3}$

The formation of tricyclic systems **80** and **81** can be explained on the basis of probable mechanism (Scheme 23) in which the highly electron-deficient diene **2a**/**b** undergoes inverse electron-demand Diels–Alder cycloaddition with electron-rich dienophilic 2-methylfuran (**4j**) to produce Diels–Alder adduct **80** and **81**.



Scheme 23: Plausible reaction mechanism for the formation of **80** and **81**.

2.2.3. Synthesis of functionalized pyrrolobenzoxazinones *via* transition metal-catalyzed reaction

The compounds containing nitrogen heterocycles play preponderant role in drug discovery and this heterocycle edifies the main structure in various natural products [28, 213–216,237]. Among them, pyrroles are a class of compounds endowed with broad and decisive biological and pharmacological activities such as antimicrobial, analgesic, antibacterial, antitubercular, anticancer, antidiabetic, fungicidal, anti-inflammatory, antiviral, antibiotic, cholesterol reduction, antioxidant and antihypoxic activities [217–222]. Moreover pyrroles can serve as intermediates in natural product synthesis and are building blocks for the synthesis of porphyrins [223]. Owing to their wide spectrum of biological activity, the synthesis of pyrrole derivatives attracted tremendous attention in the field of organic synthesis. Consequently, myriad methods have been developed for the synthesis of diversely structured pyrroles (Figure 24) [224–228].

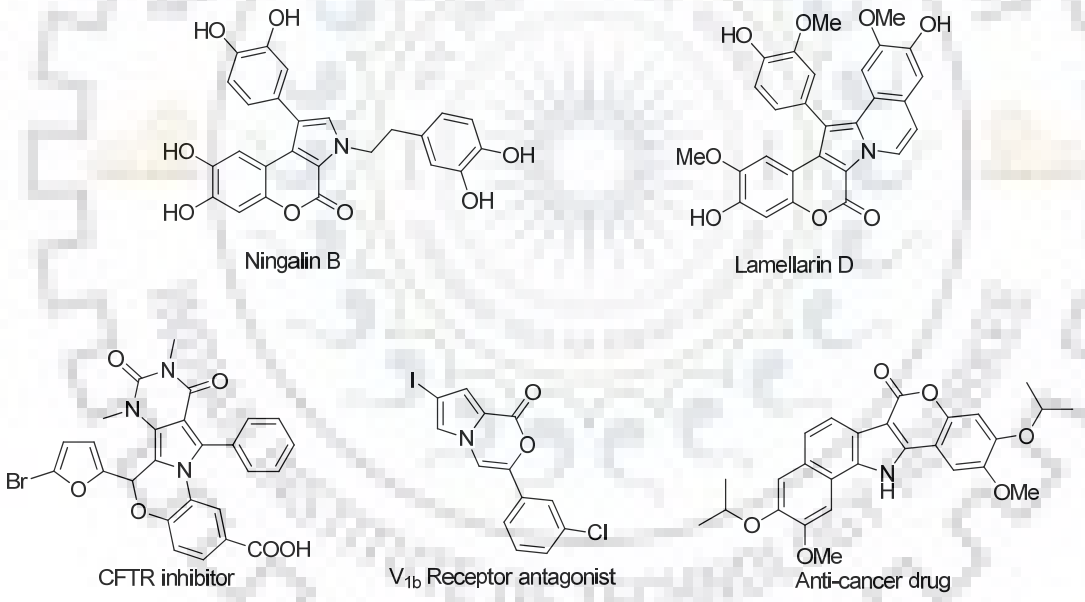


Figure 24: Some biologically active compounds containing fused pyrroles.

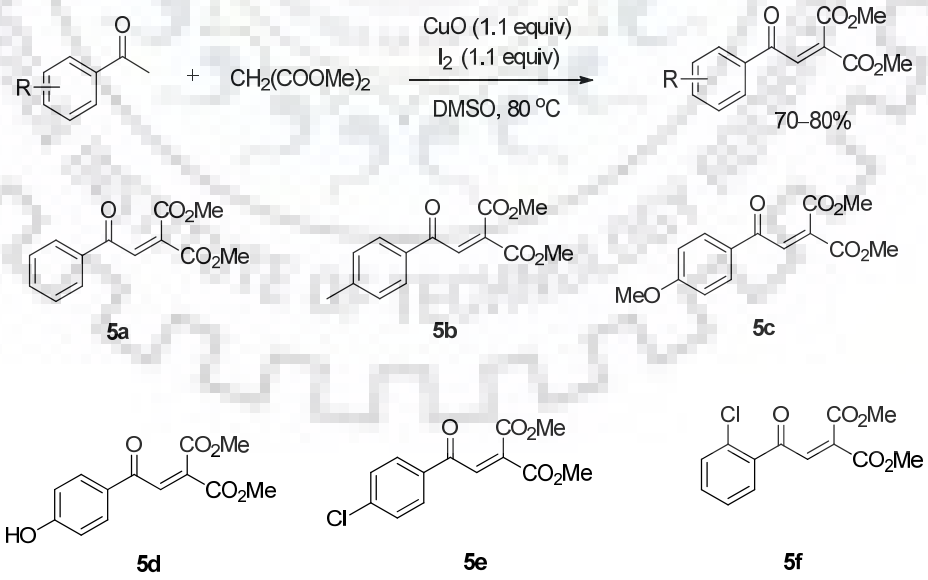
Among the pyrrole-fused derivatives, pyrrole-fused benzoxazinones, benzothiazines, and benzoxazepines attracted considerable attention because they exhibit a wide range of pharmacological activities [132,229–235]. The incorporation of two or more different heterocyclic moieties in a single molecule may amplify the biological activity appreciably

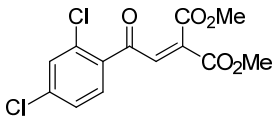
[236]. The development of more convenient and efficient protocols for these useful polyheterocyclic compounds from simple substrates [237] is a great challenge and is still an active research area in current synthetic and medicinal chemistry. All these engrossing eccentricity of this moiety embolden us to develop routes to these polyheterocycles.

Aroylmethylidene malonates are ubiquous motifs found in various natural products. They have been amply deployed for the synthesis of furans, quinoxalines, imidazoles, benzo[1,4]thiazines, and 2,4,5-trisubstituted oxazole derivatives with various reacting partners. Aroylmethylidene malonates are attractive substrates having prodigious prominence in organic chemistry, which not only play a prominent role in the synthesis of heterocyclic moieties but also serve as resourceful synthetic building blocks. They are usually used as intermediates for the preparation of oxazoles and isoxazoles and other oxygen and nitrogen containing molecules [69–73,238].

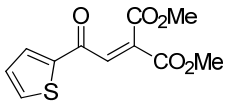
Synthesis of aroylmethylidene malonates

Aroylmethylidene malonates can be synthesized by the cross coupling of aryl ketones with dimethylmalonates in the presence of iodine as a promoter and CuO as an oxidant [239]. We have synthesized a series of aroylmethylidene malonates by this methodology (Scheme 24).





5g

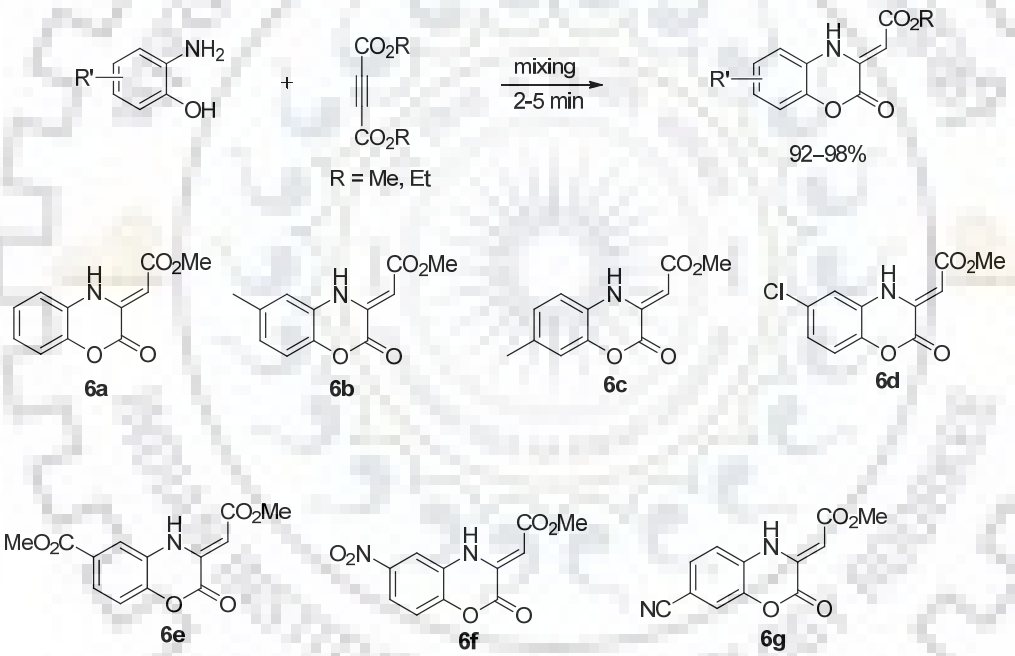


5h

Scheme 24: Synthesis of aroylmethylidene malonate derivatives **5a**–**h**.

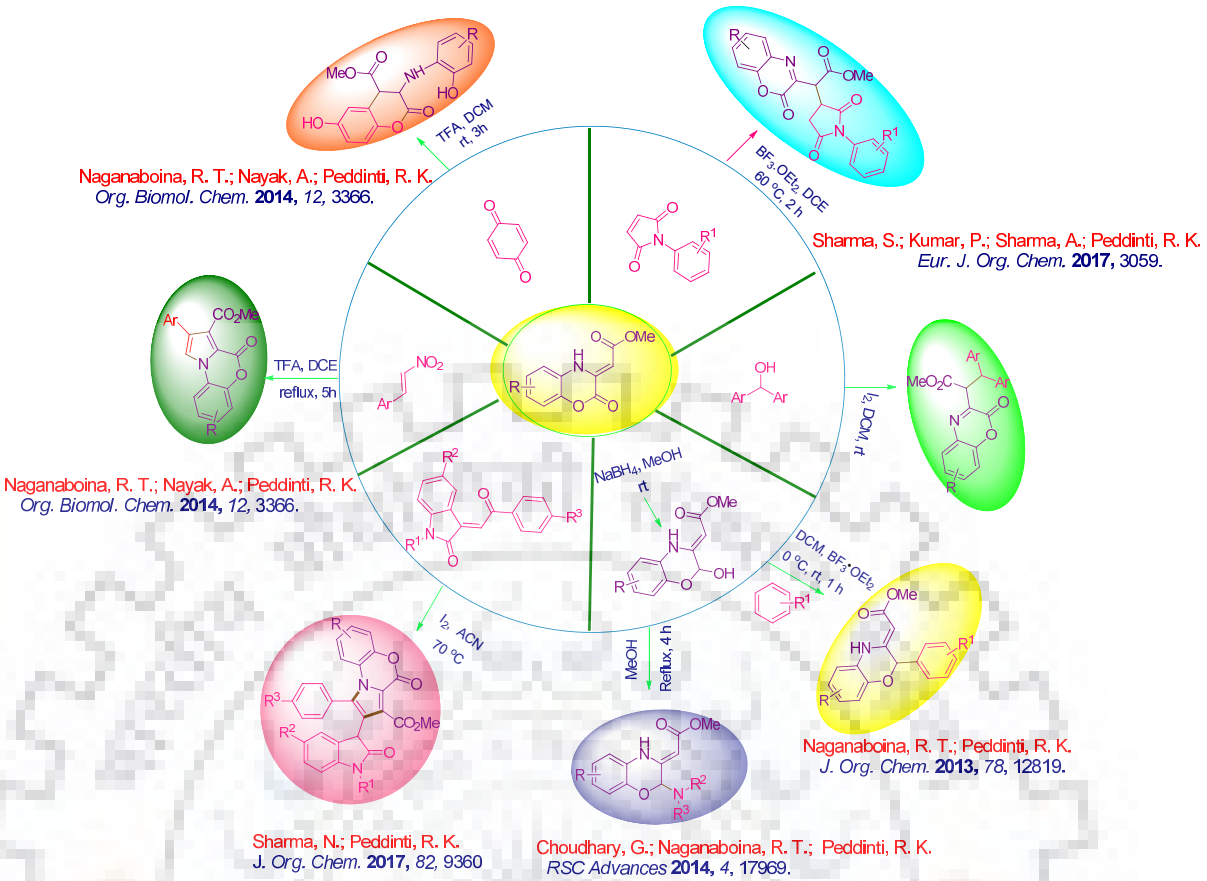
Synthesis of benzoxazines

Benzoxazines were synthesized by following a method reported from our laboratory [240]. In a petri-dish, *o*-aminophenol and dimethyl acetylenedicarboxylate were mixed for 2–5 min to obtain the corresponding vinylogous carbamate **6a** as a yellow coloured solid in quantitative yield. Similarly, the other 1,4-benzoxazinone derivatives **6b**–**g** were also prepared (Scheme 25).



Scheme 25: Synthesis of benzoxazinone derivatives **6a**–**g**.

Intrigued by their unique structural features in our laboratory, we synthesized alkenyl 1,4-benzoxazinones, a type of vinylogous carbamates and performed their reactions with several nucleophiles and studied their reactivity (Scheme 26) [130,133,241–243].

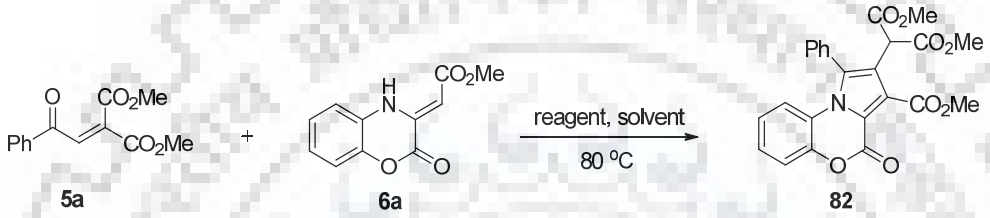


Scheme 26: Schematic representation of the diversity of 1,4-benzoxazinone derivatives shown in our group.

In the field of organic synthesis, the development of simple and efficient methods for the formation of polyheterocyclic compounds is a great challenge. A domino reaction is a transformation that forms two or more bonds under identical conditions and converts simple starting materials to diversified molecules [153]. Transition metal mediated functionalization/activation of carbon–carbon bonds in both the electrophilic and nucleophilic species can also be considered as domino reaction. Iron(III) chloride is the simplest iron compound, which is an effective, low-cost and ecologically benign Lewis acid and has high functional group tolerance ability for a variety of domino reactions [244–249]. Inspired by the advantages of domino protocols [250–252] and in continuation to our own efforts on the domino reaction of benzoxazinones [130,133], we carried out $FeCl_3$-promoted domino reaction of benzoxazinones with aroylmethylidene malonates to furnish benzoxazine fused pyrroles.

To establish the optimum reaction conditions, we commenced our research by investigating the reaction using benzoylmethylidene malonate **5a** and benzoxazinone **6a** as model substrates. When the reaction was performed with TFA in DCE for 12 h at 80 °C, pyrrolobenzoxazine **82** was obtained in 50% yield (Table 8, entry 1). The heterocycle **82** was formed *via* Michael addition of benzoxazinone **6a** to benzoylmethylidene malonate **5a** followed by intramolecular cyclization in a domino process. Encouraged by this initial finding several acids were examined to evaluate their effect in the reaction (entries 2–9).

Table 8: Optimization of the reaction conditions.[a]



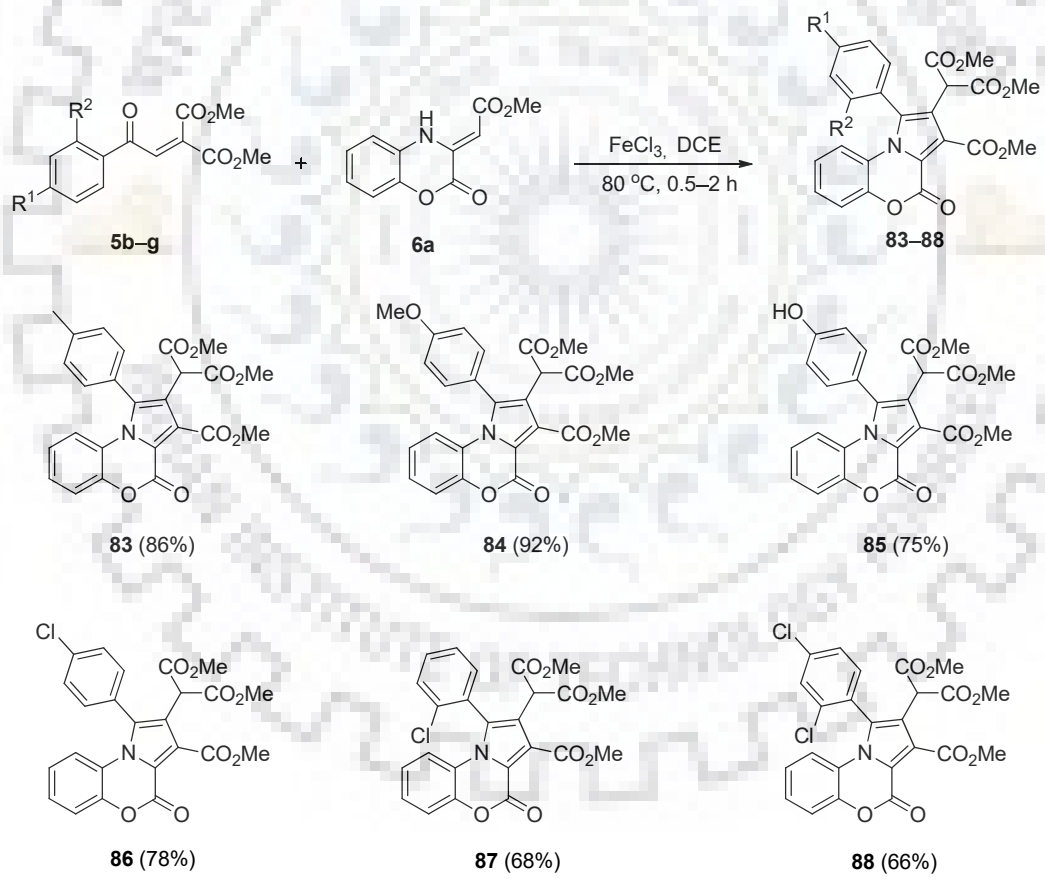
Entry	Reagent (equiv)	Solvent	Time (h)	Yield (%)[b]
1	TFA (1.0)	DCE	12	50
2	$MeSO_3H$ (1.0)	DCE	8	55
3	*p*-TSA·H_2O (1.0)	DCE	12	45
4	$BF_3 \cdot OEt_2$ (1.0)	DCE	4	60
5	$BF_3 \cdot OEt_2$ (2.0)	DCE	4	55
6	$ZrCl_4$ (1.0)	DCE	24	30
7	$ZnCl_2$ (1.0)	DCE	24	25
8	**$FeCl_3$ (1.0)**	**DCE**	**3**	**85**
9	$SnCl_4$ (1.0)	DCE	3	53
10	Iodine (1.0)	DCE	24	Nr
11	$FeCl_3$ (1.0)	CH_3CN	3	70
12	$FeCl_3$ (1.0)	THF	4	57
13	$FeCl_3$ (1.0)	Toluene	4	40
14	$FeCl_3$ (1.0)	EtOH	12	Nr
15	$FeCl_3$ (1.0)	MeOH	12	Nr
16	$FeCl_3$ (1.0)	DMF	6	Nr

17	$FeCl_3$ (0.5)	DCE	8	50
18	$FeCl_3$ (1.5)	DCE	3	79
19[c]	$FeCl_3$ (1.0)	DCE	3	77
20[d]	$FeCl_3$ (1.0)	DCE	7	80

[a]Unless otherwise specified, all reactions were carried out using **5a** (0.25 mmol), **6a** (0.3 mmol) and reagent in 2 mL solvent.
[b]Isolated yield. Nr: No reaction was observed.
[c]temp: 100 °C.
[d]temp: 60 °C

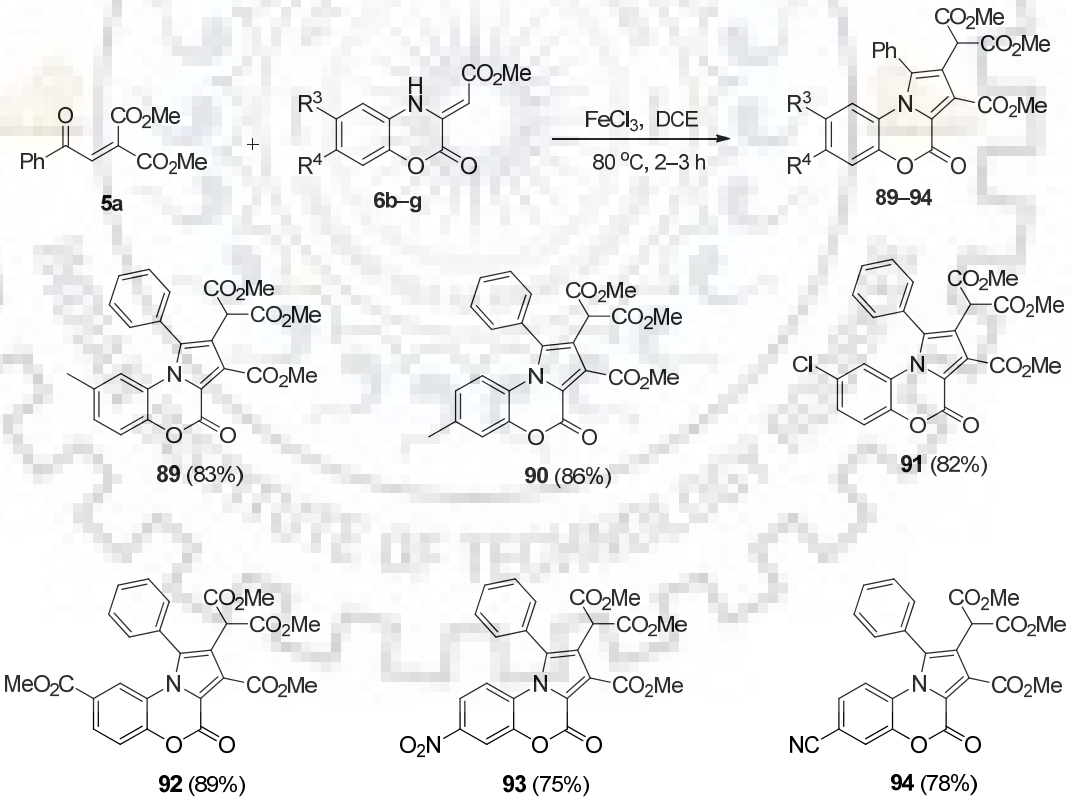
Like in case of $MeSO_3H$, **82** was obtained in 8 h in 55% yield (entry 2). *p*-toluenesulfonic acid monohydrate (*p*-TSA.H_2O), produced **82** after 12 h in 45% yield (entry 3). When we moved towards the Lewis acid like in case of $BF_3{\cdot}OEt_2$ **82** was obtained in 4 h in 60% yield (entry 4). Further increase the amount of $BF_3{\cdot}OEt_2$ could not improve the yield of the product (entry 5). Further a sequence of Lewis acids such as $ZrCl_4$, $ZnCl_2$, $FeCl_3$, and $SnCl_4$ were examined to evaluate their effect in the reaction (entries 6–9). In case of $ZrCl_4$ and $ZnCl_2$, reaction was very slow and the polyheterocycle **82** was obtained in 30 and 25% yields, respectively (entries 6 and 7). After screening of the acids, $FeCl_3$ was found to be superior in furnishing the cyclized product **82** in 85% yield (entry 8). The use of iodine did not drive the reaction (entry 10). Subsequently, to evaluate the solvent effect, the reaction was studied by performing the reaction in different solvents such as CH_3CN, THF, toluene, EtOH, MeOH and DMF (entries 11–16). In case of polar solvents such as MeOH, EtOH, and DMF, the reaction failed to proceed, this may be due to the insolubility of reactants in polar protic solvents (entries 14–16). Hence DCE was identified as the ideal solvent, producing the heterocycle **82** after 3 h in excellent yield (entry 8). Encouraged by the favorable results, we further varied the amount of $FeCl_3$ and found that no appreciable variation in the yield of the product ensued by increasing or decreasing the amount of reagent in the reaction. When 0.5 equiv of $FeCl_3$ was used, the pyrrolobenzoxazine **82** was obtained in a diminished yield of 50% (entry 17), and further increase in the reagent loading to 1.5 equiv resulted in the formation of **82** in 79% yield (entry 18). Thus, 1 equiv of $FeCl_3$ found to be optimal loading to provide the desired product in very high yield. Further, screening of the reaction at higher or lower temperature led to no improvement (entries 19 and 20).

With the optimal conditions established for this domino reaction, the substrate scope was explored by using various aroylmethylidene malonates **5a**–**g** with benzoxazinone **6a**. As shown in Scheme 27, a variety of aroylmethylidene malonates bearing electron-rich groups, such as methyl, methoxy, hydroxy **5b**–**d**, and electron-deficient group **5e** at the *para*-position of benzene ring, were amenable to the reaction. The reaction of aroylmethylidene malonate **5b** with benzoxazinone **6a** afforded the tricyclic pyrrolobenzoxazinone **83** in 2 h with 86% yield. Delighted with the results obtained, we performed the reaction of various substituted aroylmethylidene malonates with benzoxazinone **6a** to produce the products **84**–**86** in 30 min to 1 h with yields in the range of 75–92%. Notably, the acceptors **5f** and **5g** with 2-chloro substituent and 2,4-dichloro substituents in aromatic ring could also be well tolerated, and the corresponding products **87** and **88** were obtained in 2 h in 68 and 66% yields, respectively (Scheme 27).



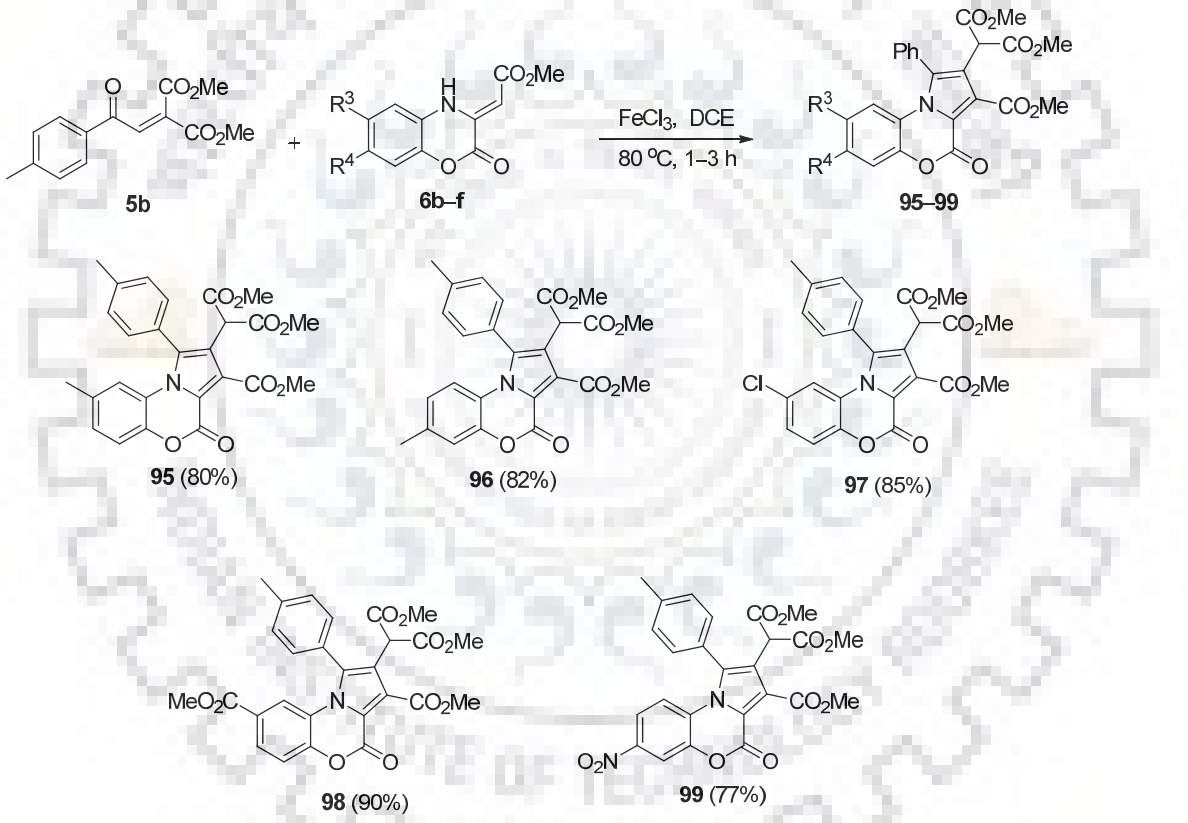
Scheme 27: Reaction of aroylmethylidene malonates **5b**–**g** with benzoxazinone **6a**.

Then we explored the scope of benzoxazinone derivatives **6b**–**g** with benzoylmethylidene malonate **5a**. As expected, the reaction proceeded smoothly under the optimized reaction conditions to afford the corresponding products **89**–**94** in good to excellent yields. We examined the reactivity of methyl substituted benzoxazinone derivatives **6b** and **6c** where slight differences were observed in the yield of the corresponding products **89** and **90**. These results encouraged us to continue to study the electronic environment on benzoxazinone moiety. The reaction of benzoxazinones **6d** and **6e** bearing Cl and CO_2Me substituents with **5a** worked well and afforded the products **91** and **92** in 82 and 89% yields, respectively. However, when nitro substituted benzoxazinone **6f** was employed as a substrate; the reaction, under similar reaction conditions, furnished pyrrolobenzoxazine **93** in 3 h with 75% yield. The marginal reduction in the chemical yield may be ascribed to the less solubility of nitro derivative **6f**. The benzoxazinone **6g**, bearing 7-cyano group delivered pyrrolobenzoxazinone derivative **94** in 2 h with 78% yield (Scheme 28).



Scheme 28: Reaction of aroylmethylidene malonate **5a** with benzoxazinones **6b**–**g**.

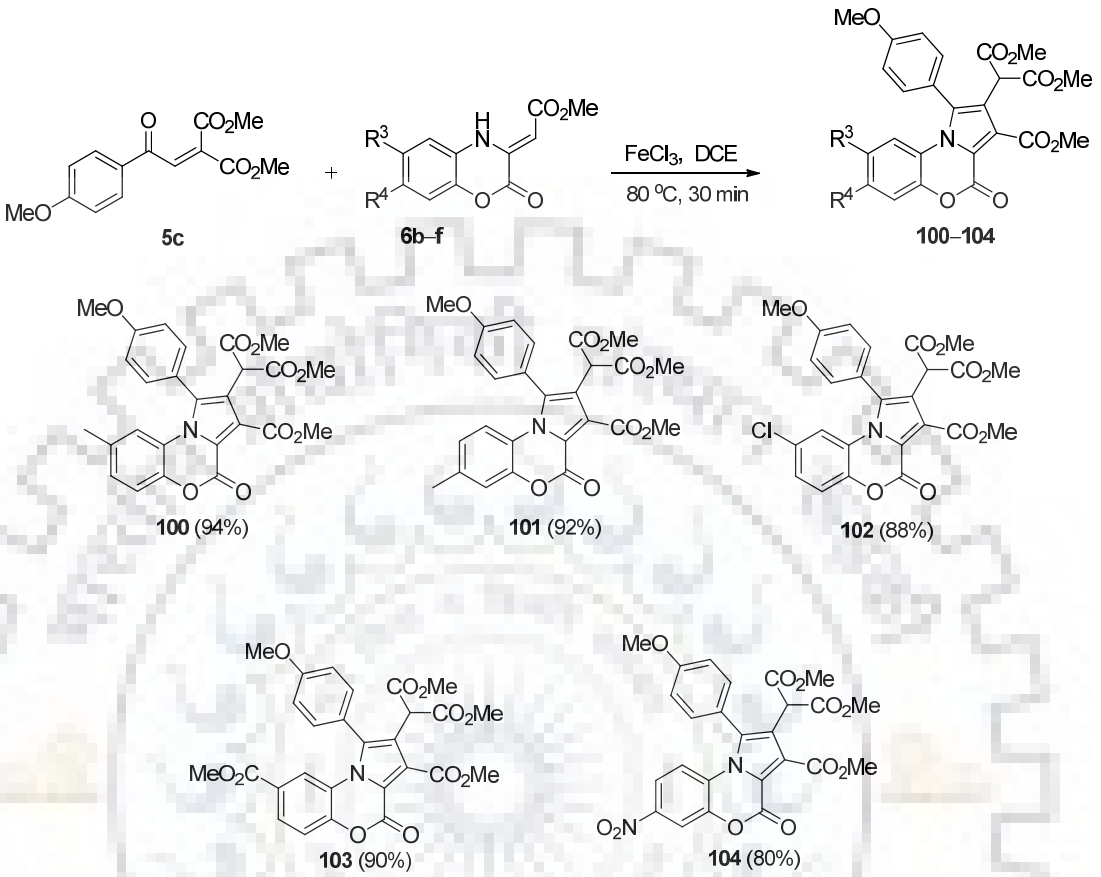
The reaction represented a broad substrate scope and worked well with various aroylmethylidene malonates **5a**–**g** possessing electron-donating as well as electron-withdrawing groups, and benzoxazinones **6a**–**f**. Methyl substituted benzoylmethylidene malonate **5b**, reacted with various benzoxazinones and produced **95**–**99** in 2–3 h with good yields. The reaction of benzoylmethylidene malonate **5b** with benzoxazinone **6b** (methyl substitution at 6th position) produced pyrrolobenzoxazinone **95** in 1.5 h with 80% yield while with benzoxazinone **6c** (methyl substitution at 7th position) delivered **96** in 1.5 h in 82% yield. Subsequently, various benzoxazinone derivatives bearing electron-withdrawing groups such as Cl, CO_2Me and NO_2 **6d–f** were well tolerated and produced tricyclic pyrrolobenzoxazinones **97–99** in 77–90 % yields, respectively (Scheme 29).



Scheme 29: Reaction of aroylmethylidene malonate **5b** with benzoxazinones **6b**–**f**.

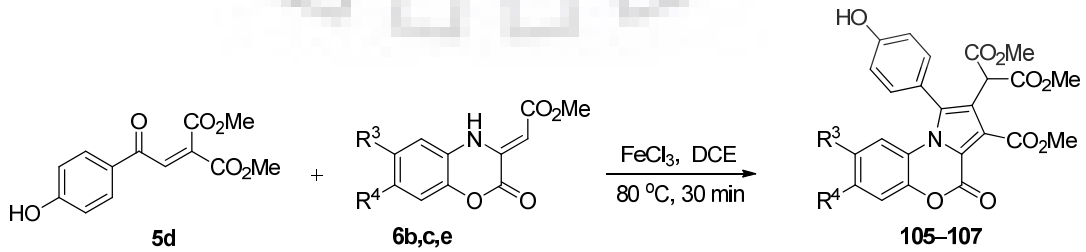
The reaction was very efficient in case of 4-methoxy substituted benzoylmethylidene malonate **5c,** and afforded products **100**–**104** in 30 min in excellent yields. The reaction of **5c** with electron-rich benzoxazinones **6b**,**c** afforded desired products in 30 min with

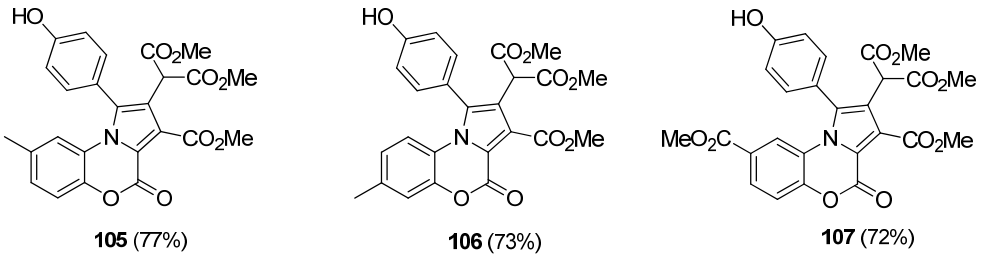
excellent yields. Similarly, benzoxazinones **6d**–**f** bearing electron-withdrawing groups gave tricyclic products in good yields (Scheme 30).



Scheme 30. Reaction of aroylmethylidene malonate **5c** with benzoxazinones **6b**–**f**.

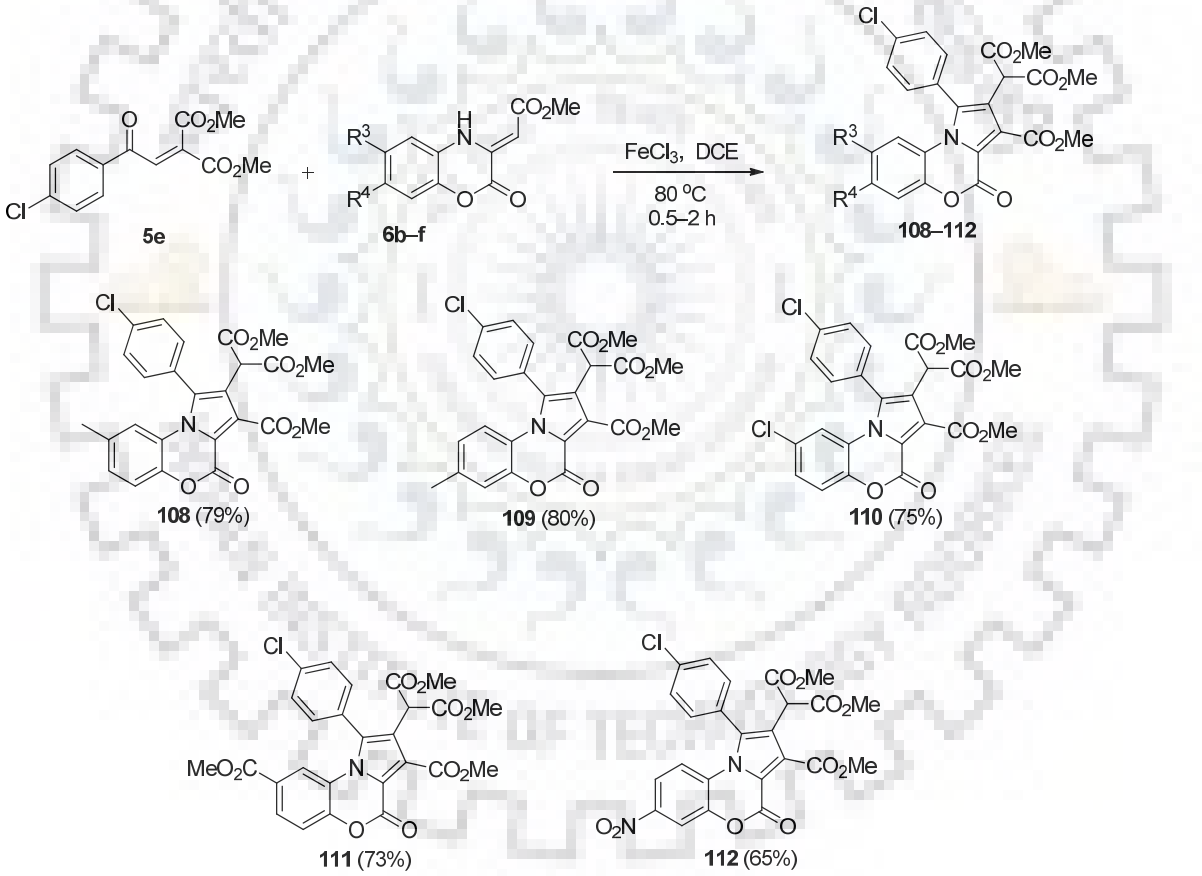
We further extended this strategy for the reaction of 4-hydroxy substituted benzoylmethylidine malonate **5d** with benzoxazinone derivatives. It is noteworthy to mention that the reactions of **5d** with benzoxazinones **6b,c,e** furnished products **105**–**107** slightly in lower yields in comparison to other substituted aroylmethylidene malonates (Scheme 31).





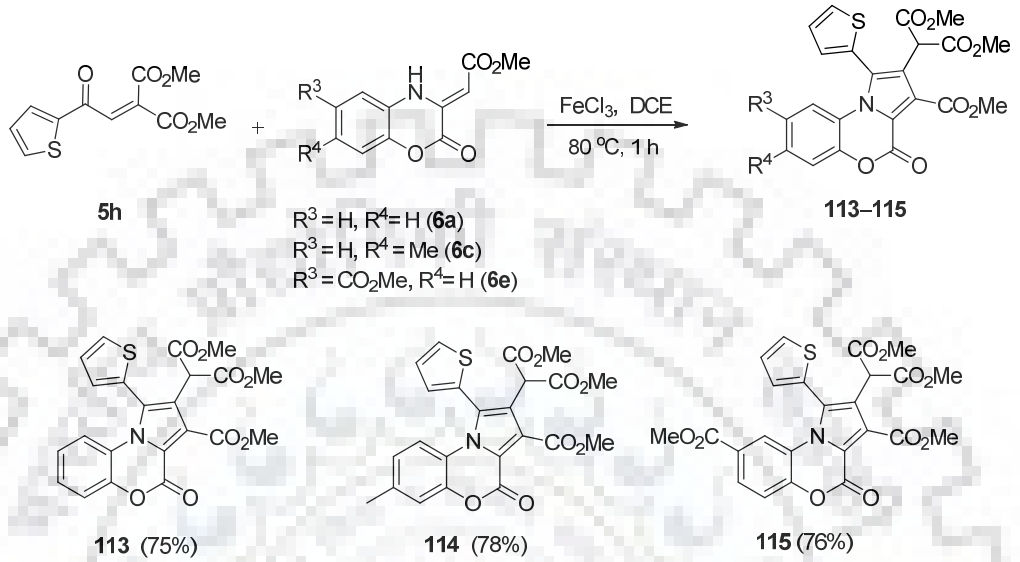
Sceme 31: Reaction of aroylmethylidene malonate **5d** with benzoxazinones **6b**,**c**,**e**.

We were delighted with the results described above and proceeded further to examine the scope of the reaction with respect to the electron-withdrawing group substituted aroylmethylidene malonate such as chlorine **5e**. The reaction underwent successfully and delivered cyclized products **108**–**112** in good to moderate yields (Scheme 32).



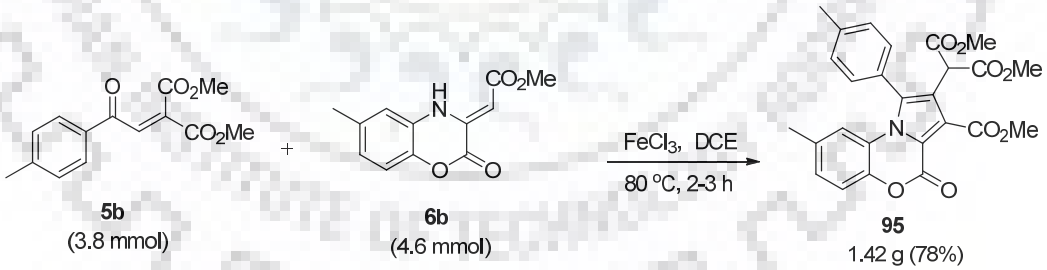
Scheme 32: Reaction of aroylmethylidene malonate **5e** with benzoxazinones **6b**–**f**.

To ensure that the current protocol was compatible with heteroaromatic systems, we performed the reaction of thenoylmethylidene malonate **5h**, with benzoxazinones **6a**,**c**,**e**. To our delight, the reaction showed excellent compatibility and produced pyrrolo-benzoxazinones **113**–**115** in 1 h with good yields (Scheme 33).



Scheme 33: Reaction of benzoxazinones with thenoylmethylidene malonate **5h**.

For more insight into the utility of this reaction, we carried out the gram-scale reaction of **5b** and **6b** under the similar optimal reaction conditions and the reaction progressed smoothly to furnish **95** in 78% yield (Scheme 34).



Scheme 34: Gram-scale synthesis of **95**.

The structures of pyrrolobenzoxazinone **82**–**115** were confirmed by the analysis of the data obtained from ^{1}H and ^{13}C NMR, DEPT and HRMS spectra. For instance, in compound **82**, the methoxy group (*–OMe*) of ester moiety in benzoxazinone motif resonates

at δ 3.93 ppm and two methoxy groups of ester moiety of benzoylmethylidene malonate resonate together at δ 3.69 ppm as singlet of six protons. The –C*H* proton near to two ester moiety resonates at δ 4.54 ppm as singlet which indicates that there is no proton available adjacent to carbon. This concluded the formation of unsaturated pyrrole ring. HRMS spectrum of compound **82** showed a peak at *m/z* 472.0980 which is in well agreement with the calculated value *m/z* 472.1003 for $[M + Na]^+$. Further the structure of compound **82** was also confirmed by single crystal X-ray analysis (Figure 25, Table 9). The crystal was grown in the mixture of ethylacetate/hexane solvent systems through slow evaporation technique.

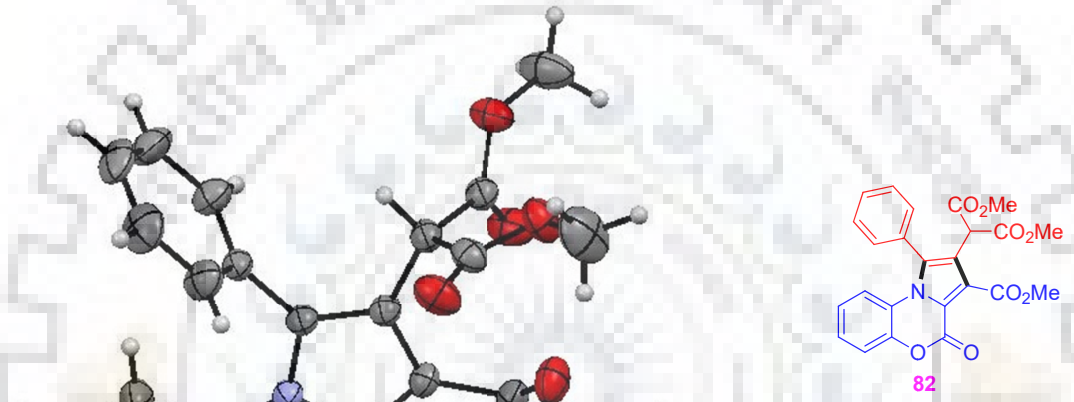


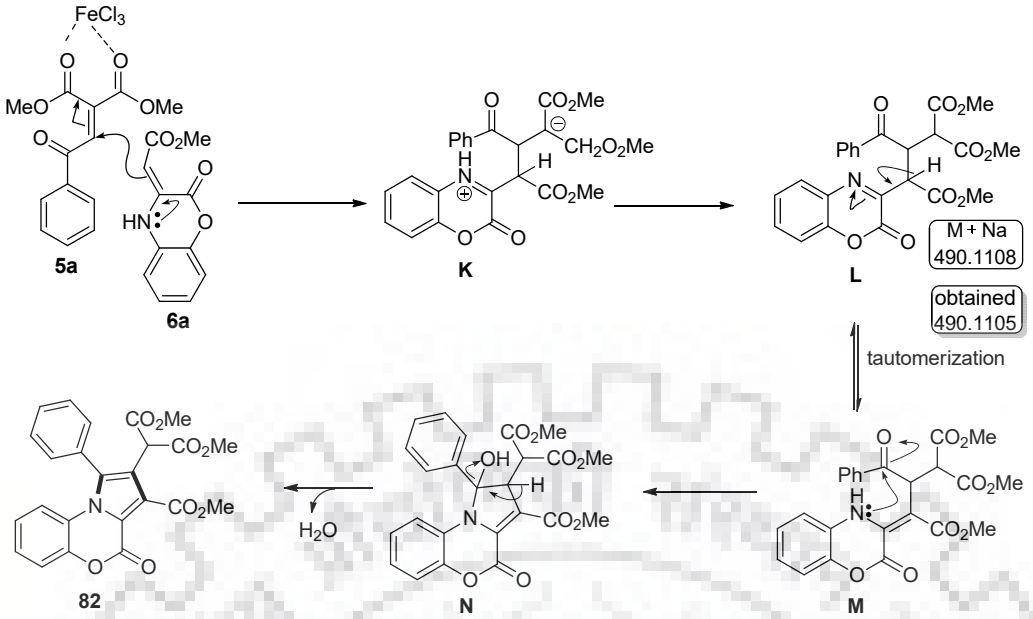
Figure 25: ORTEP representation of crystal structure of **82**.

Table 9. Crystallographic data for pyrrolobenzoxazine derivative **82**.

Empirical formula	$C_{24}H_{19}NO_8$
Formula weight	449.40
Temperature	295 (2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1

Unit cell dimensions	a = 8.1655 (13) Å
	b = 10.6003 (18) Å
	c = 12.896 (2) Å
	α = 76.273 (6)°
	β = 87.655 (7)°
	γ = 78.310 (6)°
Volume	1061.8 (3) $Å^3$
Z	2
Density (calculated)	1.406 mg/m^3
Absorption coefficient	0.107 mm^{-1}
F(*000*)	468
Crystal size	0.27 x 0.19 x 0.12 mm^3
Theta range for data collection	2.547 to 26.420°
Index ranges	$-10 \leq h \geq 10$
	$-13 \leq k \geq 13$
	$-16 \leq l \geq 16$
Reflections collected	38115
Independent reflections	4302 [R(int) = 0.0303]
Completeness to theta = 25.242°	99.1 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4302 / 0 / 305
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	*R1* = 0.0428, *wR2* = 0.1187
R indices (all data)	*R1* = 0.0490, *wR2* = 0.1240
Largest diff. peak and hole	0.228 and -0.253 $e.Å^{-3}$

A plausible mechanism for this transformation is illustrated in Scheme 35. Initially the $FeCl_3$ coordinates with ester moiety of benzoylmethylidene malonate **5a**, and enhances the electrophilicity at α-carbon of benzoylmethylidene malonate and facilitates benzoxazinone **6a** to attack at this position to generate the intermediate **K**. Proton shift occurs in this species to generate adduct **L** whose formation was confirmed by HRMS as well as ^{1}H NMR spectral analysis. This species **L** undergoes tautomerization to form intermediate **M**. The subsequent intramolecular cyclization of **M** generates aminol intermediate **N**, which upon dehydration liberates the product **82**.



Scheme 35: Proposed reaction mechanism for the formation of **82**.

2.2.4. An efficient access to *α*-substituted aryl ketones

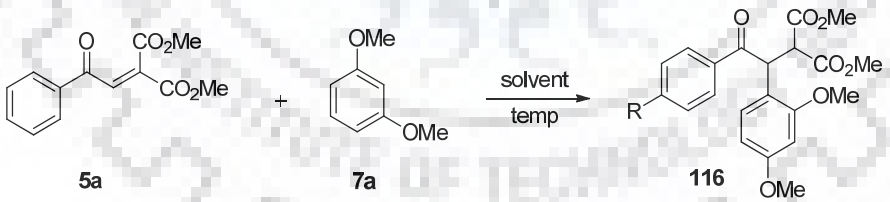
Nowadays efforts have been made towards the development of green and synthetic methods to reduce the waste and to develop the greener approach for the synthesis of heterocyclic molecules [253–255]. Friedel–Crafts/Michael addition reaction is one of the most fundamental and important reactions for the formation of carbon–carbon bonds in organic synthesis [256–261]. Indeed, a number of Lewis acid catalysts have been reported for the Friedel–Crafts alkylation reaction [262–265]. Aroylmethylidene malonates are attractive substrates having great importance in organic chemistry, which not only play a prominent role in the synthesis of heterocyclic moieties but also serve as versatile synthetic building blocks. They are usually used as intermediates for the preparation of oxazoles and isoxazoles and other oxygen and nitrogen containing molecules [69–73]. To date, a number of synthetic methodologies have been established for the synthesis of *β*-substituted carbonyl compounds through Michael addition [266–271]. On the other hand, Friedel–Crafts alkylation of electron-rich arenes with aroylmethylidene malonates, offers an easy access to *α*-substituted aryl ketones.

A novel synthesis of polysubstituted pyrroles *via* $FeCl_3$ promoted domino Michael addition of benzoxazinones with aroylmethylidene malonates is depicted in the previous section. As part of our continuous efforts in the synthesis of heterocycles [100,130,133,210–212,241,243], we thought to explore the feasibility of aroylmethylidene malonates with other nucleophiles such as electron-rich arenes.

Molecular iodine considered as an environmental benign Lewis acid catalyst in organic synthesis. Therefore, it is not surprising that I_2 is frequently employed both as a stoichiometric reagent and as a catalyst in many different organic reactions [272–277]. The attractiveness of molecular iodine as a catalyst is due to its high tolerance ability towards moisture and air, readily accessibility, low cost and low toxicity. Thus, the development of an efficient and environmental benign iodine-mediated protocol could be highly appropriate for the synthesis of *α*-substituted carbonyl compounds. Thus, an efficient and eco-friendly vinylogous Friedel–Crafts alkylation reaction of electron-rich arenes with reactive aroylmethylidene malonates, has been developed successfully using iodine as a mild Lewis acid.

Initially, we carried out the reaction of dimethoxybenzene with benzoylmethylidene malonate **5a** in DCE in presence of $MeSO_3H$ at 80 ^oC. The α-substituted aryl ketone **116** was obtained in 12 h with 58% yield (Table 10, entry 1). TFA-mediated reaction of **5a** with **7a** provided the product in 12 h with 55% yield (entry 2). Further we performed this reaction with various Lewis acids such as $ZrCl_4$, $ZnCl_2$, $BF_3{\cdot}OEt_2$, $SnCl_4$, $SnCl_2$, and $FeCl_3$ to provide **116** in good to moderate yields (entries 3–8). When we performed the reaction in presence of iodine, the α-substituted aryl ketone **116** was obtained in an improved yield of 77% (entry 9). To study the effect of solvents on the reaction, we performed the model reaction in different solvents such as DMF, toluene, THF and CH_3CN in presence of stoichiometric amount of iodine. However there was no much effect of the solvent on the reaction (entries 10–13). In order to find the best reaction conditions, next we carried out the Friedel–Crafts/Michael addition reaction of dimethoxybenzene with benzoylmethylidene malonate under neat condition at 80 ^oC with 1.0 equiv of iodine to afford **116** in good yield (entry 14). Accordingly, the neat condition was chosen for the further investigation. Reducing the iodine loading from 1.0 to 0.5 equiv resulted in the formation of **116** in an improved yield of 90% (entry 15). On increasing/decreasing the temperature there was no improvement in the yield of the product **116** (entries 16 and 17) and further reducing the amount of iodine from 50 mol% to 30 mol% led to a significant decrease in the yield of **116** (entry 18).

Table 10: Optimization of the reaction conditions.[a]



5a 7a 116

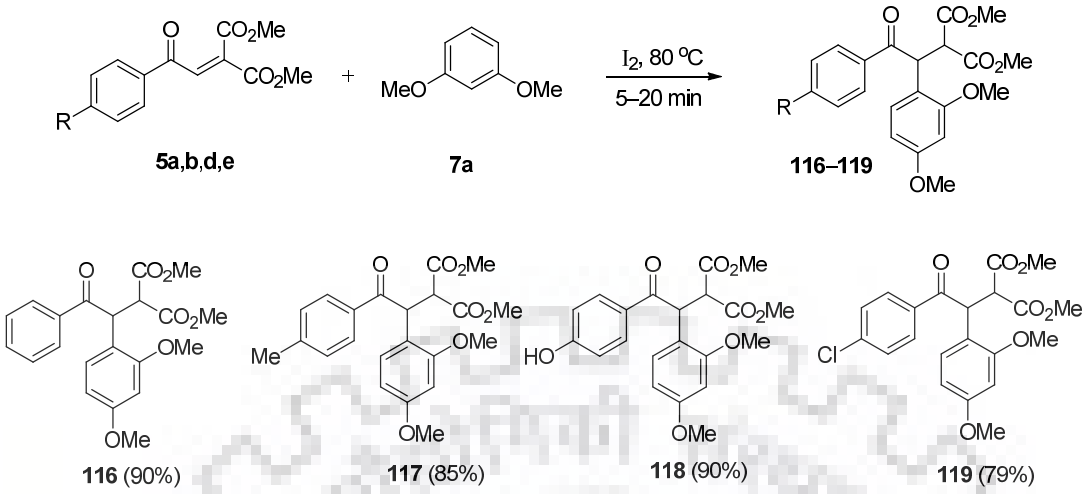
Entry	Solvent	Reagent	Temp (^oC)	Time	Yield[b](%)
1	DCE	$MeSO_3H$	80	12 h	58
2	DCE	TFA	80	12 h	55
3	DCE	$ZrCl_4$	80	30 min	67
4	DCE	$ZnCl_2$	80	30 min	65
5	DCE	$BF_3.OEt_2$	80	30 min	67

6	DCE	$SnCl_4$	80	20 min	63
7	DCE	$SnCl_2$	80	30 min	62
8	DCE	$FeCl_3$	80	20 min	69
9	DCE	I_2	80	30 min	77
10	DMF	I_2	80	15 min	67
11	Toluene	I_2	80	15 min	65
12	THF	I_2	80	15 min	62
13	CH_3CN	I_2	80	15 min	67
14	Neat	I_2	80	10 min	86
15[c]	**Neat**	**I_2**	**80**	**5 min**	**90**
16[c]	Neat	I_2	60	30 min	79
17[c]	Neat	I_2	100	5 min	82
18[d]	Neat	I_2	80	30 min	70

[a]Unless otherwise specified, all reactions were carried out using **5a** (0.2 mmol), **7a** (0.4 mmol) and reagent (1 equiv).
[b]Isolated yields.
[c]I_2 = 50 mol% was used.
[d]I_2 = 30 mol% was used.

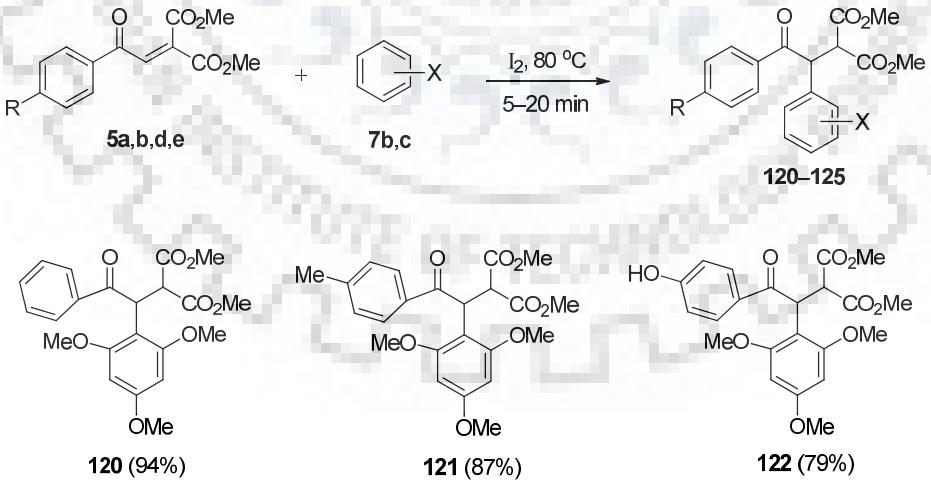
Invigorated by these results, the versatility of F–C alkylation reactions/Michael addition reactions were examined by varying the electronic and steric properties of both aroylmethylidene malonates **5** and electron-rich arenes **7** under the optimized conditions. Aroylmethylidene malonates with both electron-donating **5a**,**b**,**d** and electron-withdrawing groups **5e** on the aryl group were well tolerated and delivered the corresponding Michael adducts **116**–**129** with good to excellent yields.

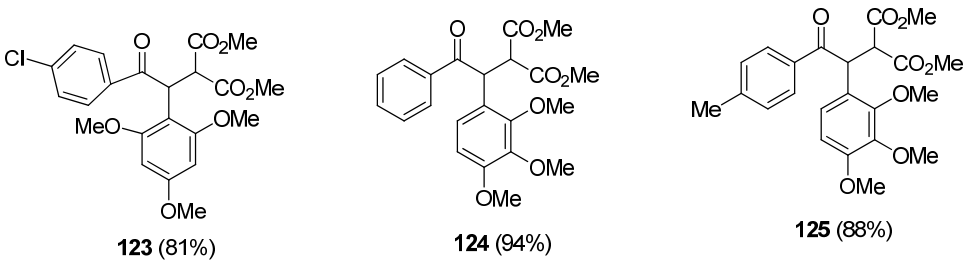
The reaction of 1,3 dimethoxybenzene, with aroylmethylidene malonates containing electron-donating groups **5b**,**d** delivered products **117** and **118** in good to excellent yields. Similarly the reaction of chlorine substituted aroylmethylidene malonate **5e** with dimethoxybenzene **7a** afforded product **119** in 79% yield and the results are summarized in Scheme 36.



Scheme 36: Reaction of aroylmethylidene malonates **5** with 1,3-dimethoxybenzene **7a**.

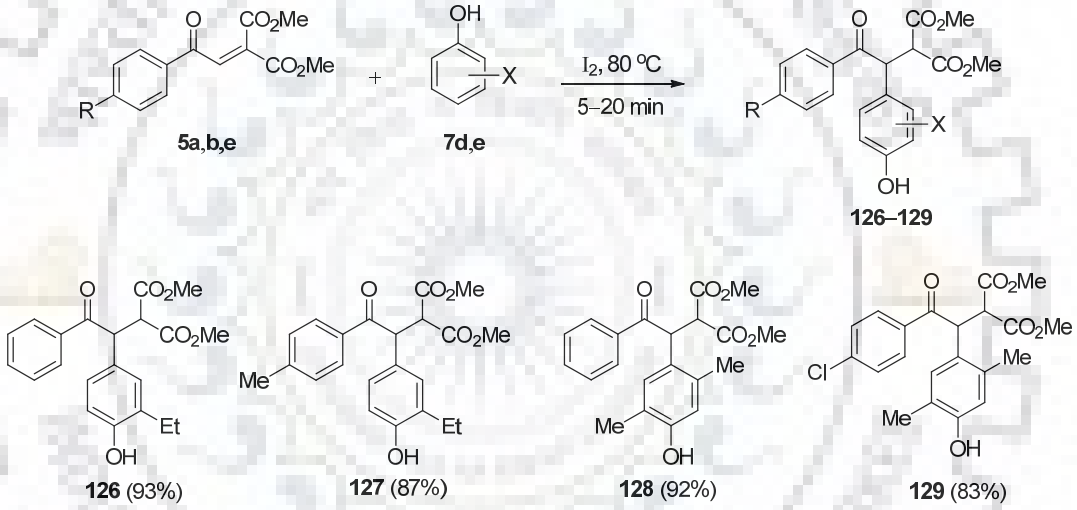
We further extended the scope of this protocol with more electron-rich arenes such as 1,3,5-trimethoxybenzene (**7b**), with different aroylmethylidene malonates **5a**,**b**,**d**,**e** under optimized reaction conditions to yield the corresponding products **120**–**123** in 79–94% yields. Similarly, we also examined the reactivity of 1,2,3-trimethoxybenzene (**7c**) with aroylmethylidene malonates **5a**,**b** under optimized conditions, the corresponding *α*-substituted aryl ketones **124** and **125** were obtained in 94–88% yields respectively (Scheme 37).





Scheme 37: Reaction of aroylmethylidene malonates **5a**,**b**,**d**,**e** with trimethoxybenzenes.

To show the scope of the reaction and inspired by the above results we further demonstrated the efficacy of the present methodology by performing the reaction of hydroxy substituted arenes such as 2-ethylphenol and 2,5-dimethylphenol. These reactions were successful and delivered the products **126**–**129** in good yields (Scheme 38).



Scheme 38: Reaction of aroylmethylidene malonates with electron-rich arenes.

The structures of the above products were unambiguously analyzed by the data obtained from ^{1}H and ^{13}C NMR, DEPT and HRMS spectra. For instance, in compound **116**, two aliphatic protons resonate at δ 5.66 and 4.39 ppm as doublets. The coupling constant of these protons (J = 11.2 Hz) indicates that these protons are vicinal to each other. The aliphatic –*C*H appears at δ 45 and 99 ppm in ^{13}C NMR. The carbonyl peak of ketone appears at δ 197 ppm. HRMS spectrum of compound **116** showed a peak at *m/z* 409.1250 which was in well agreement with the calculated value *m/z* 409.1258 for $[M + Na]^{+}$.

2.2.5. Synthesis of functionalized naphthofurans

Naphthofurans are the class of heterocyclic compounds containing fused furan moiety with naphthalene and possess wide range of biological and pharmacological activity [37,38,278–281]. These heterocycles are reported to be part of various natural products such as furomollugin and rubicordifolin which possess significant anticancer properties [282,283] (Figure 26). Naphthofurans are normally synthesized by transition metal-catalyzed annulation reactions of substituted phenols with alkenes, tandem reaction of *o*-halophenols with terminal alkynes through cross-coupling and subsequent annulation, oxidative functionalization of phenols with alkynes, alkylation of 1/2-acyl naphthols with α-halo ketones or esters followed by dehydrative cyclization and direct annulation-aromatization of naphthols with alkenes [284–296]. The wide application of these heteroaromatic compounds made them popular synthetic targets. Hence with the significance of this skeleton we scrutinized the feasibility and efficacy of our methodology to synthesis naphthofuran derivatives.

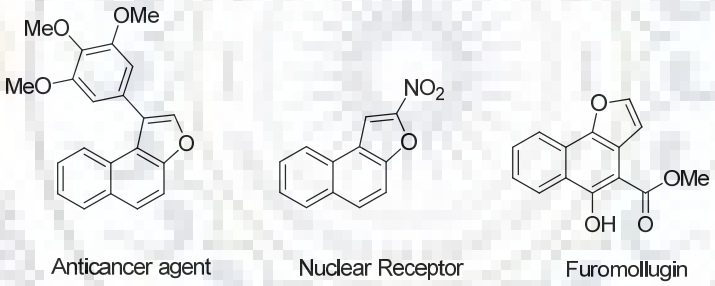
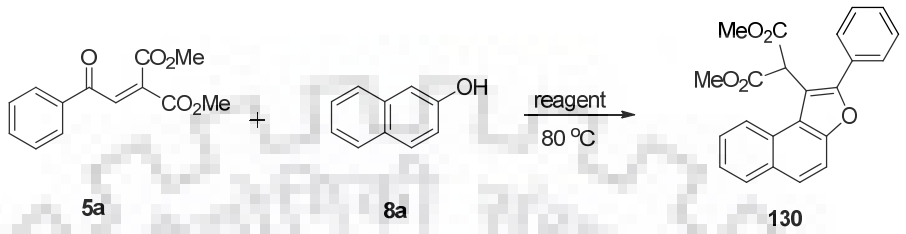


Figure 26: Some biologically active compounds containing naphthofuran motif.

We initiated our studies by inspecting the reaction conditions using benzoylmethylidene malonate **5a** and β-naphthol as the starting precursors. To our delight naphthofuran **130** was obtained in 30 min in 61% yield in the presence of catalytic amount of TFA at 80 ^{o}C (Table 11, entry 1). The reaction in the presence of methanesulphonic acid delivered the product **130** in 1 h with 72% yield (entry 2). Encouraged by these promising results, we further performed the reaction with various Lewis acids such as $BF_3{\cdot}OEt_2$, $ZrCl_4$, $FeCl_3$ and $SnCl_4$ to deliver naphthofuran **130** in 74, 50, 60 and 52% yields, respectively

(entries 3–6). We were delighted to find that in the presence of iodine, the reaction proceeded very well and provided **130** with 92% yield (entry 7). With the lower amount of iodine, reaction proceeded to deliver **130** in a slightly lower yield of 81% yield (entry 8).

Table 11: Optimization of the reaction condition.[a]

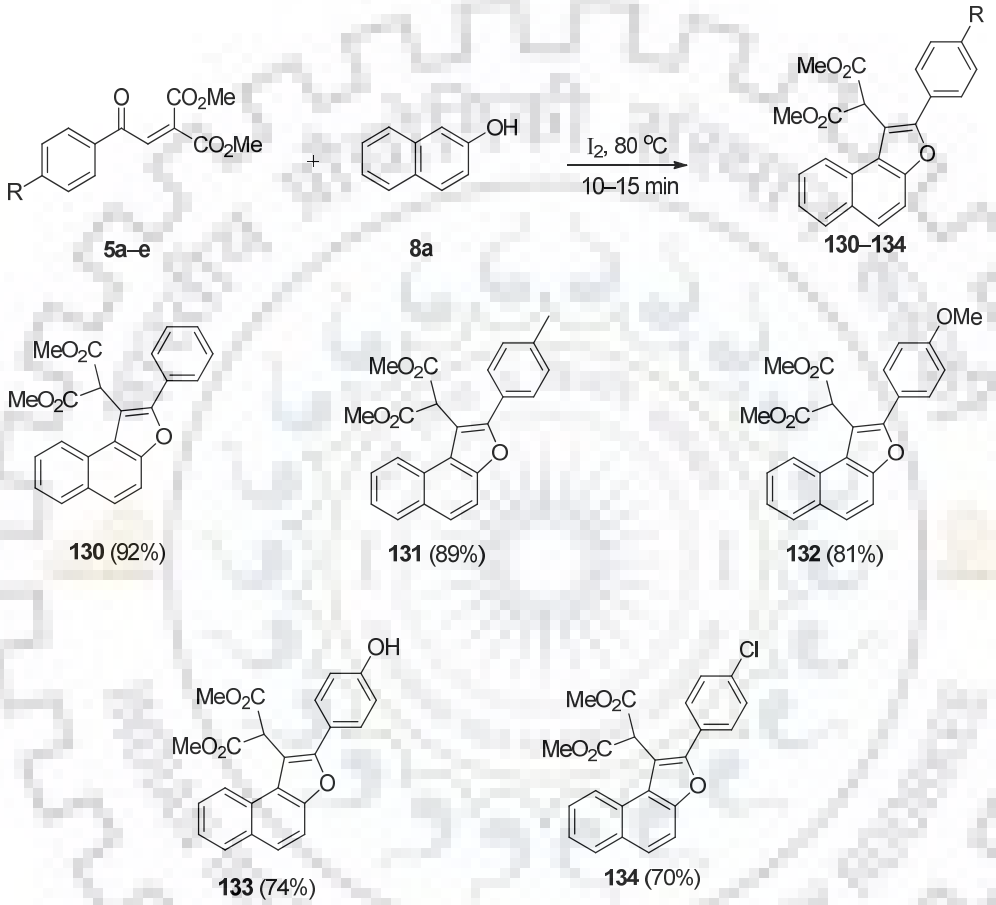


Entry	Reagent	Solvent	Time (h)	Yield[b](%)
1	TFA	Neat	30 min	61
2	$MeSO_3H$	Neat	1 h	72
3	$BF_3{\cdot}OEt_2$	Neat	1 h	74
4	$ZrCl_4$	Neat	1 h	50
5	$FeCl_3$	Neat	1 h	60
6	$SnCl_4$	Neat	1 h	52
7	**Iodine**	**Neat**	**10 min**	**92**
8[c]	Iodine	Neat	20 min	81

[a]Unless otherwise specified, all reactions were carried out using **5a** (0.2 mmol), **8a** (0.2 mmol) and reagent (50 mol%).
[b]Isolated yield.
[c]I_2 (25 mol%) was used.

With the successful results and the optimal conditions at hand, we moved on towards the application of the optimized reaction conditions to *β*-naphthol derivatives. This protocol delivered the substituted naphthofuran in high yields. Thus the reaction of **5a** with *β*-naphthol (**8a**), under the optimized reaction conditions provided naphthofuran **130** in 10 min with 92% yield. Reaction of *β*-naphthol with various substituted aroylmethylidene malonates **5b**–**f** smoothly delivered naphthofuran derivatives **131**–**134** in good yields as

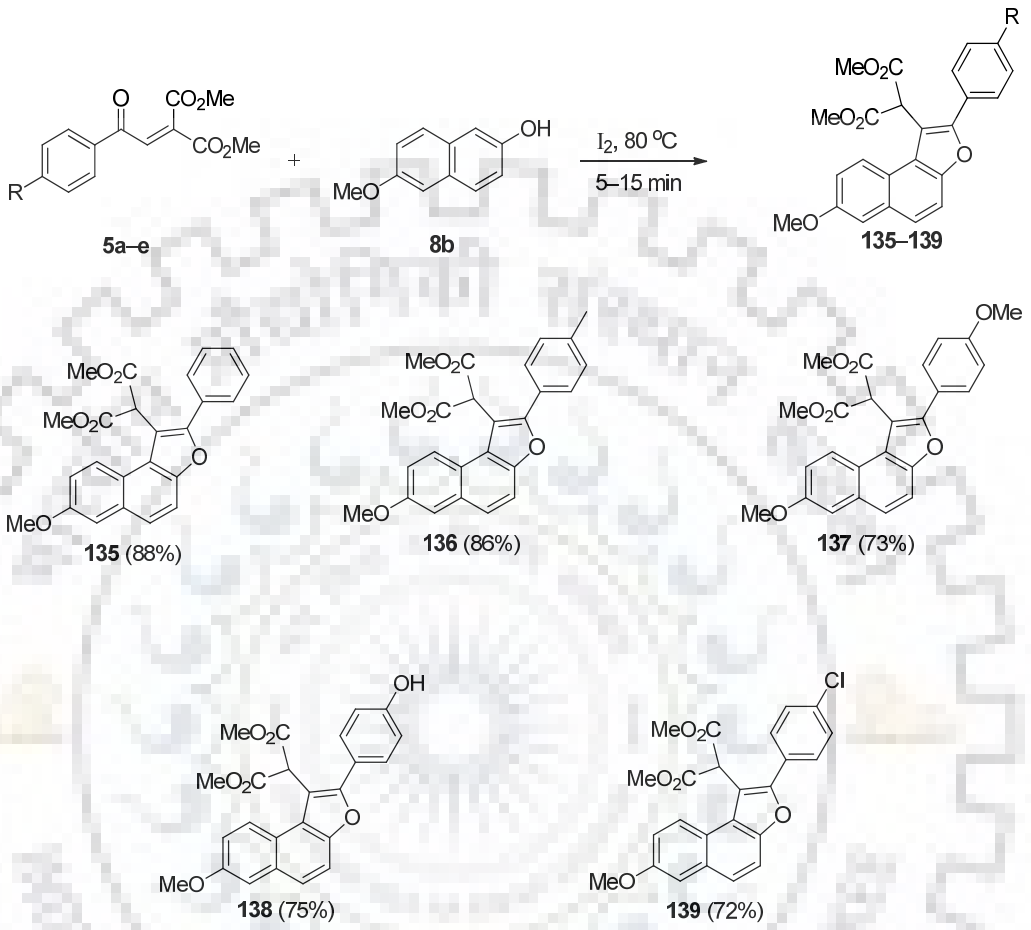
shown in Scheme 39. The reaction of *β*-naphthol with **5b** delivered naphthofuran derivative **131** in 10 min with 89% yield. Aroylmethylidene malonates bearing methoxy **5c** and hydroxy substituents **5d** at *para*-position reacted smoothly and resulted **132** and **133** in 81, and 74% yields, respectively. Aroylmethylidene malonate **5e** containing electron-withdrawing group such as chlorine substituted at *para*-position **5e** worked well and delivered tricyclic product **134** in 15 min with 70% yield (Scheme 39).



Scheme 39: Reaction of *β*-naphthol (**8a**) with aroylmethylidene malonates **5a**–**e**.

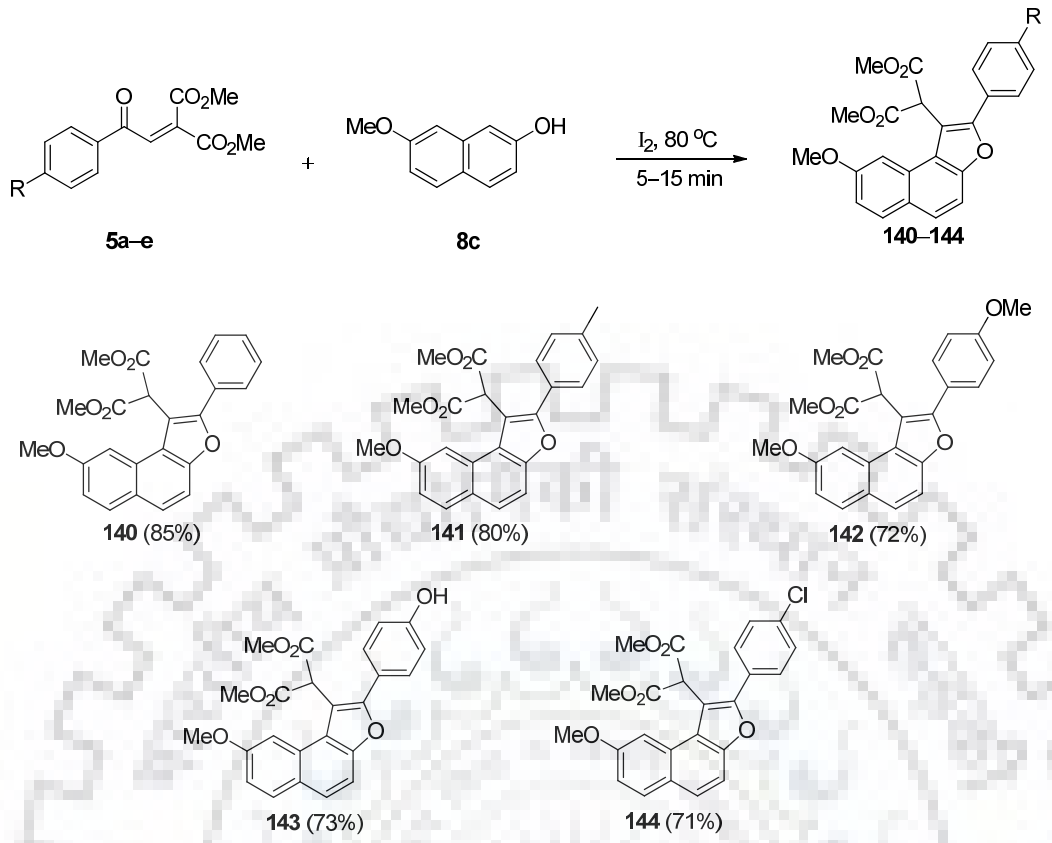
Encouraged by above results, we examined the influence of the substituent on naphthol in the reaction. We noticed that electronic effects slightly influenced the formation of products. For this, we performed the reaction of 6-methoxy-2-naphthol with **5a** and it was observed that *β*-naphthol **8b** bearing the methoxy group at 6^{th} position with aroylmethylidene malonate **5a** delivered tricyclic product **135** in 88% yield. In the same

way, other aroylmethylidene malonates **5b**–**e** were also examined under optimized conditions with 6-methoxy-2-naphthol to furnish adducts **136**–**139** in good to moderate yields (Scheme 40).



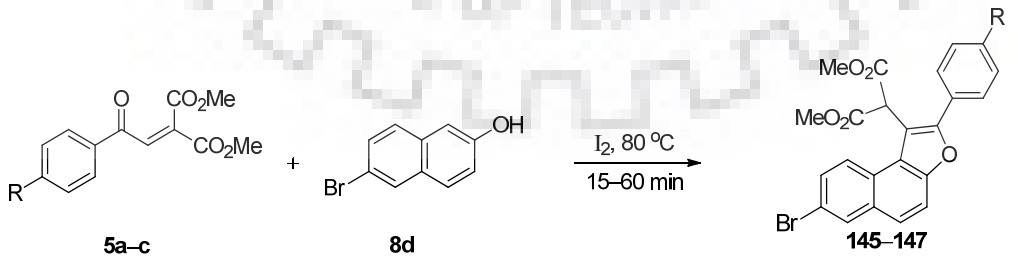
Scheme 40. Synthesis of naphthofuran derivatives from aroylmethylidene malonates **5a**–**e** and 6-methoxy-2-naphthol (**8b**).

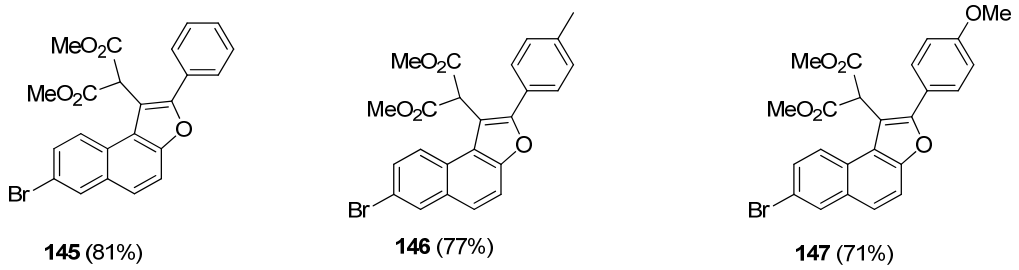
The reaction proceeded very well in case of 7-methoxy substituted *β*-naphthol and gave the corresponding products **140**–**144** rapidly in good yields. The yields of the naphthofurans **140**–**144** obtained in case of *β*-naphthol bearing methoxy at 7th position were comparatively less than those obtained from *β*-naphthol bearing methoxy at 6th position (Scheme 41).



Scheme 41. Synthesis of naphthofuran derivatives with aroylmethylidene malonates **5a**–**e** and 7-methoxy-2-naphthol (**8c**).

Similarly we examined the reactivity of 6-bromo-2-naphthol (**8d**) with various aroylmethylidene malonate derivatives **5a**–**c**. For this, we carried out the reaction between *β*-naphthol bearing bromine at 6th position and aroylmethylidene malonates **5a**–**c** to produce the desired compounds **145**–**147** slightly in low yields with longer reaction time which may be attributed to the electronic effect. In case of methoxy substituted aroylmethylidene malonate **5c**, the reaction proceeded to produce tricyclic compound **147** in 1h (Scheme 42).



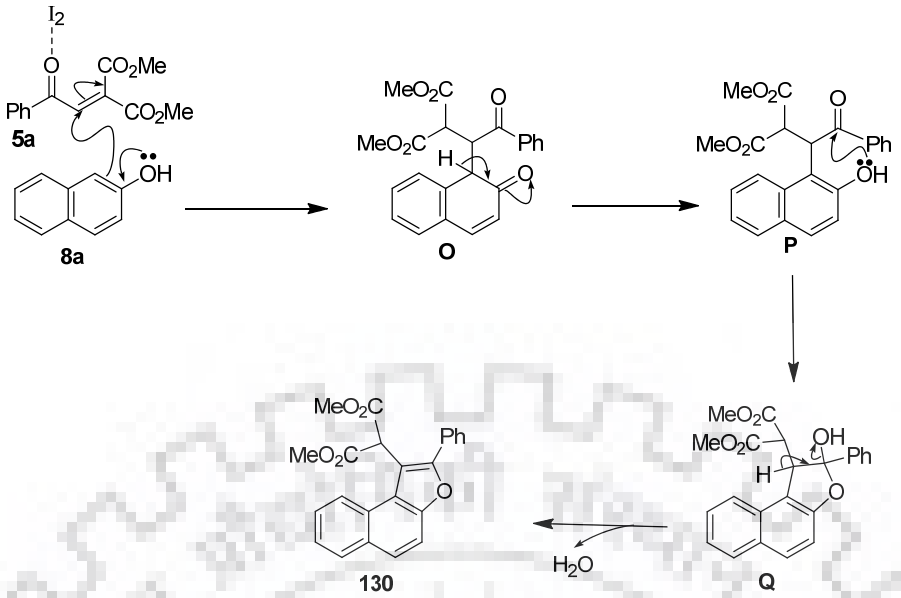


145 (81%) **146** (77%) **147** (71%)

Scheme 42: Synthesis of naphthofuran derivatives **5a**–**c** with aroylmethylidene malonates and 6-bromo-2-naphthol (**8d**).

The structures of the above products **130**–**147** were assigned on the basis of data obtained from their ^{1}H and ^{13}C NMR, DEPT and HRMS spectra. For instance, in compound **130**, the aliphatic proton resonates at δ 5.42 ppm as singlet. The aliphatic –*C*H appears at δ 50 ppm in ^{13}C NMR. The carbonyl peak of esters appears at δ 168 ppm. In ^{13}C NMR spectrum of compound **130**, the absence of ketonic peak indicates cyclization in the molecule which was further confirmed by HRMS analysis. HRMS spectrum of compound **130** displayed a peak at *m/z* 397.1046 which is in well agreement with the calculated value *m/z* 397.1032 for $[M + Na]^{+}$.

Based on these observations, a tentative mechanism is depicted in Scheme 43 for the iodine-catalyzed Michael addition followed by cyclization for the formation of naphthofuran derivatives. Initially, aroylmethylidene malonate **5a** gets activated with iodine, while *β*-naphthol (**8a**), from its *α*-position attacks on *α*-position, of activated aroylmethylidene malonate to generate intermediate **O**, which upon proton shifts, delivers species **P**. Subsequently, **P** undergoes an intramolecular cyclization *via* attack of more nucleophilic hydroxy group to carbonyl moiety to generate species **Q**, which on dehydration produces naphthofuran derivative **130** (Scheme 43).



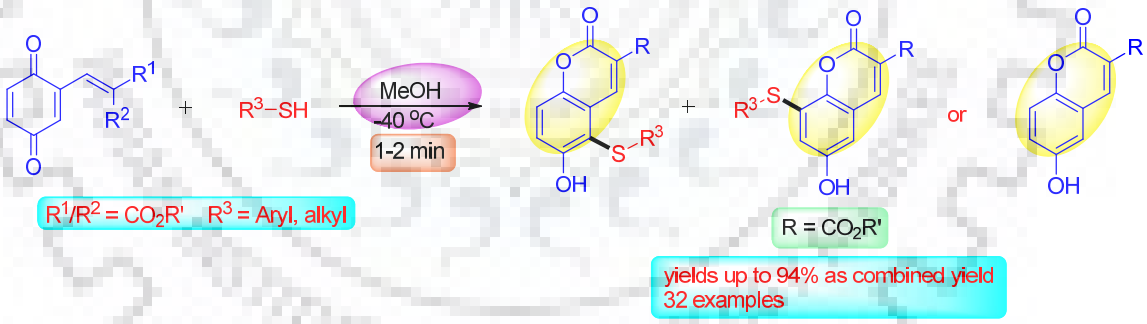
Scheme 43: Proposed mechanism for the formation of naphthofuran.

2.3. CONCLUSIONS

We have synthesized alkenyl *p*-benzoquinones and studied their reactivity with several nucleophiles to form C–C, C–S, and C–O bonds *via* Michael type addition and cycloaddition reactions. Similarly we have synthesized aroylmethylidine malonates and vinylogous carbamates and performed their reaction to access polyheterocyclic compounds.

Synthesis of alkyl/aryl sulfide derivatives of coumarins *via* domino reaction of alkenyl *p*-benzoquinones

We have demonstrated a concise simple, efficient and novel approach for the generation of coumarin alkyl/aryl sulfide derivatives *via* regioselective Michael addition of thiols on alkenyl *p*-benzoquinones in domino fashion (Scheme 44). The reaction proceeded regioselectively under mild conditions within short reaction time to afford the title products in good to excellent yields. This catalyst-free reaction showed good substrate scope. Thus this protocol constituted a straight forward route to aryl sulfide derivatives of coumarin. As the products contain coumarin as well as aryl sulfide moieties, these are potential structural motifs in medicinal chemistry. The calculation of Fukui indices on the benzoquinone derivatives supported the obtained regioselectivity of the reaction.

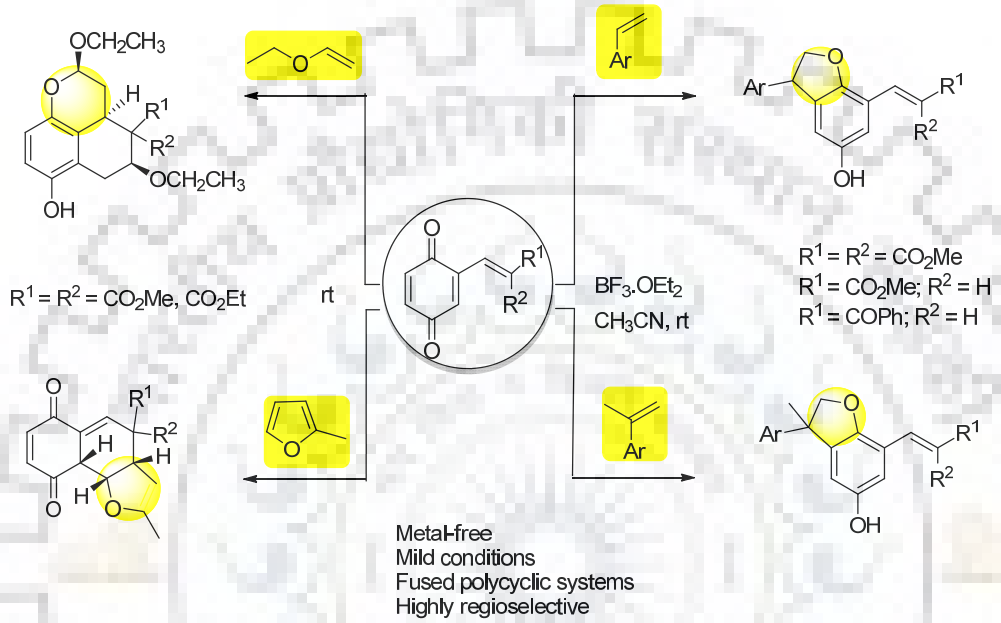


Scheme 44: Domino reaction of alkenyl *p*-benzoquinones with alkyl/aryl thiols.

Regioselective synthesis of bicyclic and polycyclic systems by cycloaddition reactions of alkenyl *p*-benzoquinones

We have introduced alkenyl *p*-bezoquinone derivatives and explored their reactivity with several electron-rich cyclic, acyclic enol ethers and styrene derivatives (Scheme 45). Based on the nature of the nucleophile or reaction conditions it provided the products in diversified

pathways. In each case the reaction was very regioselective and provided single diastereomer which indicated the high selectivity of the current high atom economy domino protocol. The yields of these one-pot reactions were noteworthy and generated polycyclic products with a plethora of functional groups. This one-pot transformation constructed C–C and C–O bonds and generated molecular complexity by domino process to produce the heterocyclic systems in good yields.

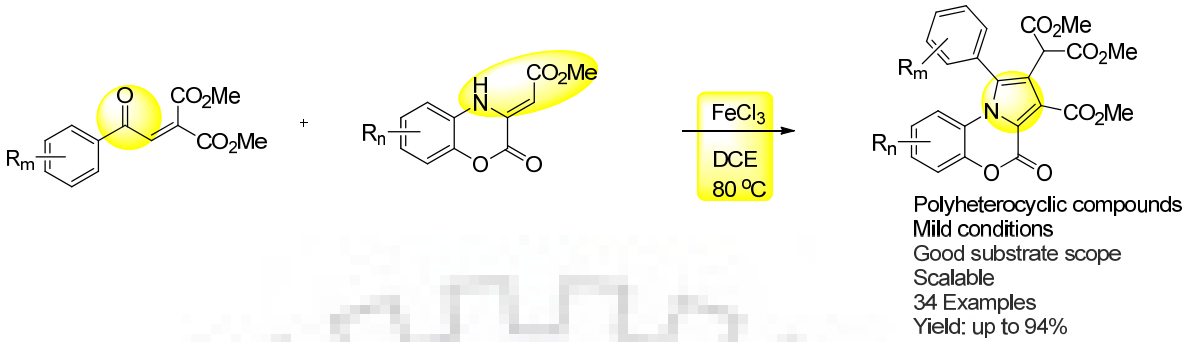


Scheme 45: Regioselective synthesis of polyheterocyclic systems.

$FeCl_3$-mediated domino reaction of benzoxazinones with aroylmethylidene malonates: Synthesis to functionalized pyrrolobenzoxazines

We have developed an efficient domino approach for the synthesis of pyrrolobenzoxazine derivatives by using aroylmethylidene malonates and benzoxazinones (Scheme 46). The $FeCl_3$-promoted domino reaction between aroylmethylidene malonates and benzoxazinones was successfully established to afford the title compounds in good to excellent yields. This reaction proceeded under mild conditions and it showed wide substrate scope. In this domino reaction water was the only by-product. The domino protocol provided a concise and straightforward access to highly substituted pyrrolobenzoxazines with high efficiency and excellent functional group tolerance.This present methodology has the prospective to pave the way for the endowment

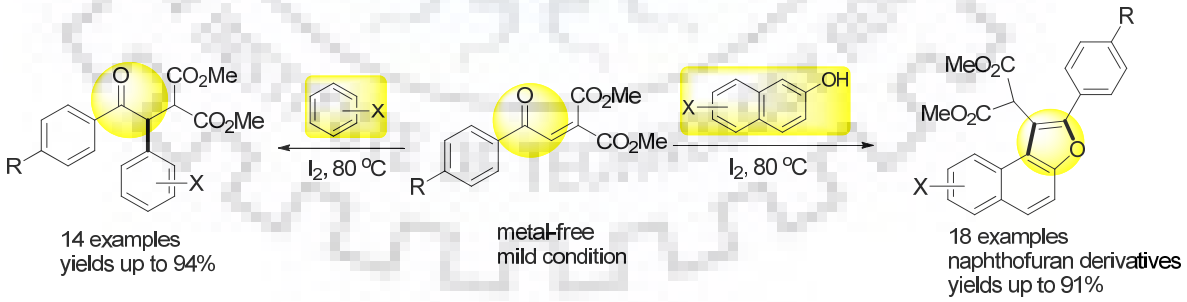
of biologically-important scaffolds.



Scheme 46: Synthesis of pyrrolobenzoxazinones.

Iodine catalyzed Friedel-Crafts/Michael addition reaction of electron-rich arenes, *β*-naphthol derivatives with aroylmethylidene malonates

We have developed a rapid and an efficient iodine catalyzed approach for the formation of *α*-substituted aryl ketones and valuable substituted naphthofuran derivatives under mild reaction conditions (Scheme 47). This metal-free and environmental friendly reaction proceeded very well under solvent-free and aerobic conditions and delivered the products in good to excellent yields. This work highlighted the formation of naphthofuran derivatives under low-cost, non-toxic and eco-friendly catalyst amount of iodine. This methodology endured a wide range of functional groups tolerance to provide the desired products in good to excellent yields at low catalyst loading. The construction of the tricyclic products proceeded well.



Scheme 47: Sythesis of *α*-substituted aryl ketones and naphthofurans.

3.1. GENERAL REMARKS

The reactions associated with the formation of gasses and applications of heat were performed in a well–ventilated hood for safety reasons. Moisture sensitive reactions were carried out by using guard tube filled with either blue silica gel or calcium chloride. Reagents and solvents were transferred under nitrogen using syringes or cannulae.

3.1.1. Solvents

The solvents for anhydrous reactions were dried and purified by using solvent purification system according to standard techniques.

Acetonitrile	Distilled over P_2O_5
CH_2Cl_2	Distilled over P_2O_5
DMSO	Purchased from S. D. Fine chemicals and used as such
EtOH	Distilled from magnesium cake
MeOH	Distilled from magnesium cake
THF	Distilled from Na/benzophenone ketyl radical
Toluene	Distilled over CaH_2

3.1.2. Chemicals

Reagents and solvents were purchased from commercial sources Aldrich, Acros, Merck, Fluka, TCI, Alfa-Aesar, Avra, Hi-media and S. D. Fine at the highest purity grade available. More sensitive compounds were stored in a desiccator if required. Reagents were used without further purification, unless otherwise noted.

3.1.3. Determination of the physical properties of the synthesized compounds

Melting Point

Melting points were measured in open glass capillaries with Perfit and Opti Melt automated melting point apparatus and are uncorrected.

IR Spectroscopy

IR Spectra were measured on a Perkin-Elmer spectrometer as KBr pellets or neat (in case of liquid compounds). Only characteristic absorption bands were reported. The spectra are reported in cm^{-1}.

^{1}H NMR Spectroscopy

^{1}H NMR spectra were recorded on Brüker AMX-500 instrument (500 MHz) or on JEOL (400 MHz) instrument. Chemical shifts (δ) are quoted in parts per million (ppm) downfield of tetramethylsilane (TMS, δ 0.00 ppm), using residual protonated solvent as internal standard $CDCl_3$ (δ 7.26 ppm), DMSO (δ 2.50 ppm). Coupling patterns are described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), dt (doublet of triplet), td (triplet of doublet), dd (doublet of doublet), m (multiplet), br (broad). Coupling constants (*J*) are reported in Hz.

^{13}C NMR Spectroscopy

^{13}C NMR Spectra were recorded on Brüker AMX-500 spectrometer (125 MHz) or on JEOL (100 MHz) instruments. Chemical shifts are given in ppm and referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak) and DMSO (δ 39.5 ppm, the middle peak).

Mass Spectrometry

The accurate masses were measured by the mass spectrometry such as High resolution mass spectrometer (HRMS) on Brüker micrOTOF™-Q II mass spectrometer (ESI–MS) using electron spray ionization.

3.1.4. Chromatographic Methods

Thin Layer Chromatography

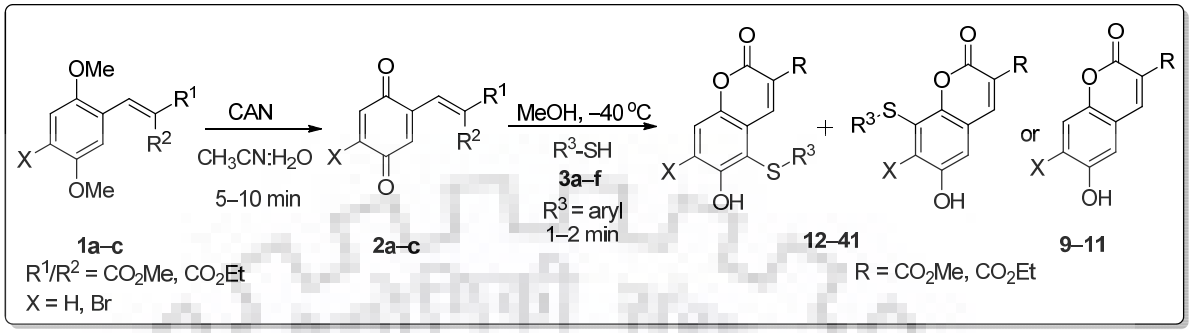
Thin layer chromatography was performed on Merck pre-coated 0.25 mm silica gel plates (60F-254) using UV light as visualizing agent and/or iodine as developing agent.

Preparative Column Chromatography

Purification by gravity column chromatography was carried out on glass column (10–50 mm diameter) using silica gel with 100–200 mesh.

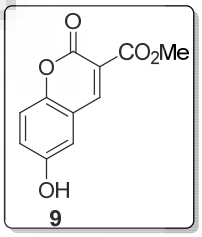
3.2. SYNTHETIC PROCEDURES

3.2.1. General procedure for the synthesis of alkyl/aryl sulfide derivatives of coumarins 12-41:



A solution of cerium(IV) ammonium nitrate (1.37g, 2.5 mmol) in H_2O (3 mL) was added to a solution of alkenyl arene **1** (1.0 mmol) in CH_3CN (1.0 mL) with rapid stirring. The color changed rapidly from orange to red. After 5 min, the contents were diluted with dichloromethane (10 mL) and brine solution was added. The aqueous layer was extracted with DCM. The combined organic layer was dried over anhyd. Na_2SO_4, concentrated under reduced pressure and the residue was used as such without further purification. Thus obtained benzoquinone **2** was dissolved in MeOH (0.5 mL) at –40 °C was added thiol derivative **3** (0.6 mmol) in MeOH (0.5 mL) and stirred the reaction mixture for 1 min. After completion of the reaction, as checked by TLC, the solvent was removed under *vacuo* and the residue was purified by silica gel column chromatography (100–200 mesh) using 30% ethyl acetate in hexanes to furnish the pure aryl sulfide derivative of coumarin **12–47**.

Methyl 6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (9):



MP: 195–196 °C.

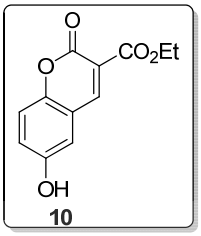
IR (KBr): ν_{max} 3437, 2928, 2369, 1731, 1569, 1486, 1378, 1026, 800 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.95 (s, 1H), 8.69 (s, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.21 (d, *J* = 3.0 Hz, 1H), 7.16 (dd, *J* = 3.0, 9.0 Hz, 1H), 3.82 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$+DMSO-d_6): δ 163.2 (*C*O), 156.8 (*C*O), 153.8 (C), 148.8 (C), 148.8 (*C*H), 148.2 (C), 122.9 (*C*H), 117.7 (C), 116.9 (*C*H), 113.0 (*C*H), 52.2 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{11}H_8O_5Na$ $[M + Na]^+$: 243.0263, found: 243.0133.

Ethyl 6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (10):



MP: 174–175 °C.

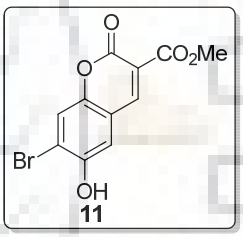
IR (KBr): ν_{max} 3333, 2922, 1744, 1572, 1256, 1386, 1184, 1038, 797, 670 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 8.65 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.20–7.14 (m, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 6.4 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8 (*C*O), 156.3 (*C*O), 154.0 (C), 148.4 (*C*H), 147.9 (C), 122.7 (*C*H), 118.3 (C), 117.8 (*C*H), 117.1 (C), 113.8 (*C*H), 61.2 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{12}H_{10}O_5Na[M + Na]^+$: 257.0420, found: 257.0430.

Methyl 7-bromo-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (11):



MP: 214–215 °C.

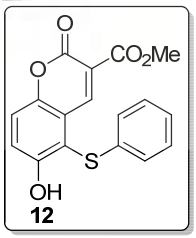
IR (KBr): ν_{max} 3343, 2920, 1746, 1572, 1348, 1180, 1038, 760, 670 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.80 (s, 1H), 8.71 (s, 1H), 7.71 (s, 1H), 7.34 (s, 1H), 3.82 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 163.2 (*C*O), 155.8 (*C*O), 151.0 (C), 148.4 (*C*H), 147.6 (C), 120.4 (*C*H), 117.8 (C), 117.6 (C), 117.5 (C), 114.0 (*C*H), 52.4 (OCH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{11}H_7BrO_5Na$ $[M + Na]^+$: 320.9370, found: 320.9370.

Methyl 6-hydroxy-2-oxo-5-(phenylthio)-2*H*-chromene-3-carboxylate (12):



Reaction time: 1 min.

Yield: 0.147 g (75%) as yellow solid.

MP: 167–168 °C.

IR (KBr): ν_{max} 3467, 2945, 2728, 1743, 1701, 1566, 1363, 1263, 1226, 1039, 691 cm^{-1}.

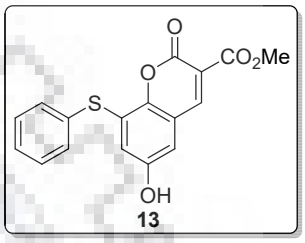
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (s, 1H), 7.41, 7.38 (ABq, 2H, J_{AB} = 9.2 Hz), 7.25–7.20 (m, 2H), 7.19–7.14 (m, 1H), 7.03 (d, *J* = 7.5 Hz, 2H), 6.89 (s, 1H), 3.88 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (*C*O), 156.2 (*C*O), 155.2 (C), 150.2 (C), 146.6 (*C*H), 133.7 (C), 129.6 (*C*H), 126.9 (*C*H), 122.3 (*C*H), 120.6 (*C*H), 120.3 (*C*H), 118.9 (C), 113.9 (C), 52.9 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{12}O_5SNa$ $[M + Na]^+$: 351.0298, found: 351.0302.

Methyl 6-hydroxy-2-oxo-8-(phenylthio)-2*H*-chromene-3-carboxylate (13):

Reaction time: 1 min.



13

Yield: 0.029 g (15%) as yellow solid.

MP: 219–220 °C.

IR (KBr): ν_{max} 3433, 2949, 1750, 1566, 1385, 1260, 1039, 688 cm^{-1}.

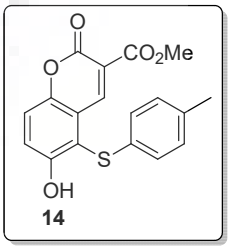
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.96 (s, 1H), 8.71 (s, 1H), 7.49–7.46 (m, 5H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.68 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 163.1 (*C*O), 155.5 (*C*O), 153.9 (C), 148.9 (*C*H), 144.8 (C), 133.1 (*C*H), 130.8 (C), 130.0 (*C*H), 128.8 (*C*H), 124.9 (C), 121.5 (*C*H), 118.7 (C), 117.8 (C), 112.8 (*C*H), 52.4 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{12}O_5SNa$ $[M + Na]^+$: 351.0298, found: 351.0299.

Methyl 6-hydroxy-2-oxo-5-(4-methylphenylthio)-2*H*-chromene-3-carboxylate (14):

Reaction time: 1 min.



14

Yield: 0.150 g (73%) as yellow solid.

MP: 151–152 °C.

IR (KBr): ν_{max} 3383, 2954, 2907, 1753, 1707, 1567, 1261, 1228, 1026, 800, 673 cm^{-1}.

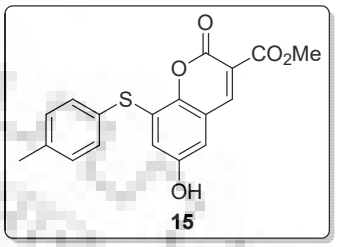
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.97 (s, 1H), 7.39, 7.36 (ABq, 2H, J_{AB} = 9.2 Hz), 7.05 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.88 (s, 1H), 3.90 (s, 3H), 2.26 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (*C*O), 156.3 (*C*O), 155.0 (C), 150.2 (C), 146.8 (*C*H), 137.3 (C), 130.4 (*C*H), 130.0 (C), 127.5 (*C*H), 122.2 (*C*H), 120.5 (C), 120.1 (*C*H), 118.8 (C), 114.7 (C), 52.9 (O*C*H_3), 20.9 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0447.

Methyl 6-hydroxy-2-oxo-8-(4-methylphenylthio)-2*H*-chromene-3-carboxylate (15):

Reaction time: 1 min.



15

Yield: 0.036 g (18%) as yellow solid.

MP: 196–197 °C.

IR (KBr): ν_{max} 3430, 2916, 2849, 2366, 1747, 1566, 1403, 1268, 1026, 803, 641 cm^{-1}.

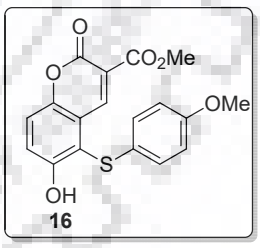
^{1}H NMR (500 MHz, DMSO-d_6): δ 9.90 (s, 1H), 8.69 (s, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.05 (s, 1H), 6.58 (s, 1H), 3.83 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.6 (*C*O), 156.1 (*C*O), 154.4 (C), 149.5 (*C*H), 144.8 (C), 139.7 (C), 134.6 (*C*H), 131.3 (*C*H), 126.9 (C), 126.8 (C), 120.8 (*C*H), 119.0 (C), 118.3 (C), 112.6 (*C*H), 53.0 (O*C*H_3), 21.3 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0446.

Methyl 6-hydroxy-5-(4-methoxyphenylthio)-2-oxo-2*H*-chromene-3-carboxylate (16):

Reaction time: 1 min.



16

Yield: 0.161 g (75%) as yellow solid.

MP: 105–106 °C.

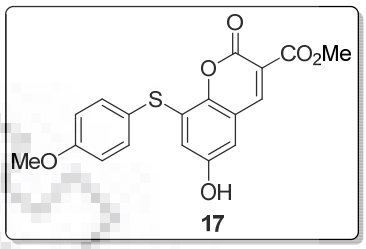
IR (KBr): ν_{max} 3415, 2928, 2848, 1749, 1624, 1562, 1436, 1241, 1032, 815, 623 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.40 (s, 1H), 9.00 (s, 1H), 7.40 (d, *J* = 9.5 Hz, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.09 (d, *J* = 9.0 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (*C*O), 156.3 (*C*O), 154.9 (C), 150.0 (C), 146.9 (*C*H), 130.0 (*C*H), 124.3 (C), 122.3 (*C*H), 120.3 (C), 119.7 (C), 119.6 (*C*H), 118.6 (C), 116.0 (C), 115.2 (*C*H), 55.3 (O*C*H_3), 52.8 (O*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_6SNa$ $[M + Na]^+$: 381.0403, found: 381.0399.

Methyl 6-hydroxy-8-(4-methoxyphenylthio)-2-oxo-2*H*-chromene-3-carboxylate (17):



17

Reaction time: 1 min.

Yield: 0.032 g (15%) as yellow solid.

MP: 199–200 °C.

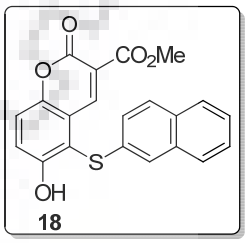
IR (KBr): ν_{max} 3420, 2937, 2848, 1750, 1629, 1570, 1433, 1260, 1032, 820, 620 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.85 (s, 1H), 8.69 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 9.0 Hz, 2H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.43 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2 (*C*O), 158.2 (*C*O), 156.1 (C), 155.7 (C), 148.9 (C), 146.5 (*C*H), 129.9 (*C*H), 126.4 (C), 123.0 (*C*H), 120.6 (C), 118.8 (C), 118.0 (*C*H), 116.2 (C), 114.9 (*C*H), 55.2 (O*C*H_3), 52.6 (O*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_6SNa$ $[M + Na]^+$: 381.0403, found: 381.0391.

Methyl 6-hydroxy-5-(naphthalen-2-ylthio)-2-oxo-2*H*-chromene-3-carboxylate (18):



18

Reaction time: 1 min.

Yield: 0.170 g (75%) as yellow solid.

MP: 123–124 °C.

IR (KBr): ν_{max} 3346, 2919, 2852, 2375, 1757, 1566, 1373, 1262, 1030, 829, 606 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.99 (s, 1H), 7.78–7.72 (m, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.48–7.38 (m, 5H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.85 (s, 1H), 3.88 (s, 3H) ppm.

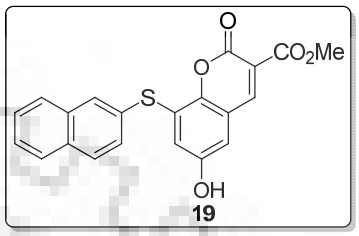
^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (*C*O), 156.2 (*C*O), 155.3 (C), 150.2 (C), 146.6 (*C*H), 133.6 (C), 131.9 (C), 131.1 (C), 129.5 (*C*H), 127.7 (*C*H), 127.1 (*C*H), 126.4 (*C*H), 125.4

(*C*H), 124.6 (*C*H), 122.4 (*C*H), 120.6 (C), 120.4 (*C*H), 119.0 (C), 113.8 (C), 52.9 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{14}O_5SNa$ $[M + Na]^+$: 401.0454, found: 401.0451.

Methyl 6-hydroxy-8-(naphthalen-2-ylthio)-2-oxo-2*H*-chromene-3-carboxylate (19):

Reaction time: 1 min.



19

Yield: 0.041 g (18%) as yellow solid.

MP: 238–239 °C.

IR (KBr): ν_{max} 3429, 2928, 2852, 2360, 1754, 1575, 1397, 1265, 1038, 806, 591 cm^{-1}.

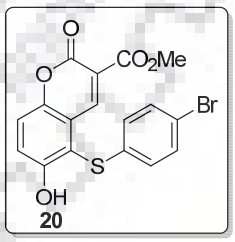
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.89 (s, 1H), 8.72 (s, 1H), 8.15 (s, 1H), 8.02–7.96 (m, 3H), 7.60–7.59 (m, 2H), 7.51–7.50 (m, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 163.0 (*C*O), 155.6 (*C*O), 154.0 (C), 149.0 (*C*H), 144.7 (C), 133.5 (C), 132.8 (*C*H), 132.6 (C), 130.0 (*C*H), 129.7 (*C*H), 128.0 (*C*H), 127.8 (*C*H), 127.7 (C), 127.2 (*C*H), 127.0 (*C*H), 125.2 (C), 121.2 (*C*H), 118.7 (C), 117.8 (C), 112.7 (*C*H), 52.5 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{14}O_5SNa$ $[M + Na]^+$: 401.0454, found: 401.0454.

Methyl 5-(4-bromophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (20):

Reaction time: 1 min.



20

Yield: 0.175 g (72%) as yellow solid.

MP: 182–183 °C.

IR (KBr): ν_{max} 3421, 2946, 2849, 1757, 1566, 1315, 1247, 1079, 803, 670 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.90 (s, 1H), 7.43 (s, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.76 (s, 1H), 3.92 (s, 3H) ppm.

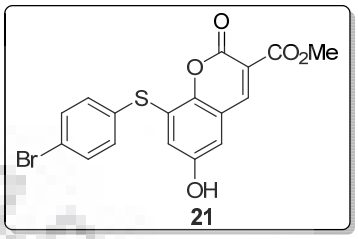
^{13}C NMR (125 MHz, CDCl$_3$): δ 163.5 (*C*O), 156.1 (*C*O), 155.2 (C), 150.3 (C), 146.3 (*C*H),

132.9 (*C*H), 132.7 (C), 128.4 (*C*H), 122.5 (*C*H), 121.0 (C), 120.8 (*C*H), 120.5 (C), 119.3 (C), 113.2 (C), 53.0 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9404.

Methyl 8-(4-bromophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (21):

Reaction time: 1 min.



21

Yield: 0.032 g (13%) as yellow solid.

MP: 221–222 °C.

IR (KBr): ν_{max} 3422, 2854, 2372, 1751, 1569, 1391, 1264, 1032, 841, 659 cm^{-1}.

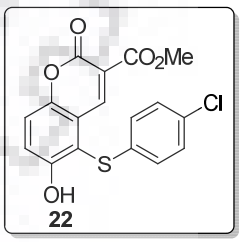
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.00 (s, 1H), 8.71 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 2.8 Hz, 1H), 6.81 (d, *J* = 2.8 Hz, 1H), 3.83 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 163.0 (*C*O), 155.5 (*C*O), 153.9 (C), 148.8 (*C*H), 145.2 (C), 134.1 (*C*H), 132.8 (*C*H), 131.1 (C), 123.4 (C), 122.4 (*C*H), 121.8 (C), 118.9 (C), 117.9 (C), 113.6 (*C*H), 52.4 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9402.

Methyl 5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (22):

Reaction time: 1 min.



22

Yield: 0.154 g (71%) as yellow solid.

MP: 177–178 °C.

IR (KBr): ν_{max} 3355, 2937, 2840, 1748, 1558, 1364, 1036, 800, 610 cm^{-1}.

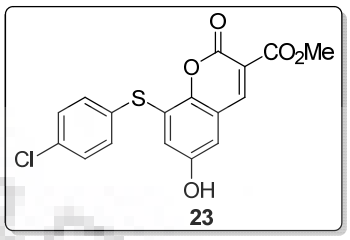
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.90 (s, 1H), 7.41 (s, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.85 (s, 1H), 3.91 (s, 3H) ppm.

^{13}C NMR (125 MHz, CDCl$_3$): δ 163.6 (*C*O), 156.2 (*C*O), 155.2 (C), 150.4 (C), 146.4 (*C*H), 133.2 (C), 132.4 (C), 129.8 (*C*H), 128.3 (*C*H), 122.6 (*C*H), 120.7 (*C*H), 120.6 (C), 119.3

(C), 113.5 (C), 53.1 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}ClO_5SNa$ $[M + Na]^+$: 384.9908, found: 384.9907.

Methyl 8-(4-chlorophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (23):



23

Reaction time: 1 min.

Yield: 0.028 g (13%) as yellow solid.

MP: 210–211 °C.

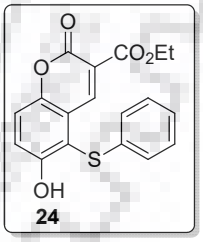
IR (KBr): ν_{max} 3418, 2923, 2852, 2345, 1747, 1632, 1574, 1390, 1270, 1032, 832, 606 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 10.00 (s, 1H), 8.71 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 2.0 Hz, 1H), 6.77 (d, *J* = 1.5 Hz, 1H), 3.82 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 163.1 (*C*O), 155.5 (*C*O), 153.9 (C), 148.9 (*C*H), 145.2 (C), 134.1 (*C*H), 133.5 (C), 130.5 (C), 129.9 (*C*H), 123.8 (*C*H), 122.2 (C), 118.9 (C), 118.0 (C), 113.4 (*C*H), 52.5 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}ClO_5SNa$ $[M + Na]^+$: 384.9908, found: 384.9906.

Ethyl 6-hydroxy-2-oxo-5-(phenylthio)-2*H*-chromene-3-carboxylate (24):



24

Reaction time: 1 min.

Yield: 0.162 g (79%) as yellow solid.

MP: 132–133 °C.

IR (KBr): ν_{max} 3165, 1740, 1676, 1561, 1453, 1306, 1229, 1135, 1045, 797, 726 cm^{-1}.

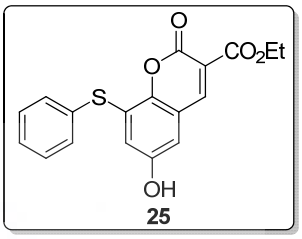
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.92 (s, 1H), 7.42 (s, 2H), 7.28–7.24 (m, 2H), 7.22–7.20 (m, 1H), 7.06 (d, *J* = 7.5 Hz, 2H), 7.05 (s, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, CDCl$_3$): δ 163.0 (*C*O), 156.3 (*C*O), 155.1 (C), 150.2 (C), 146.1 (*C*H), 133.8 (C), 129.6 (*C*H), 127.1 (*C*H), 127.0 (*C*H), 122.1 (*C*H), 120.6 (C), 120.3 (*C*H), 119.4

(C), 113.9 (C), 62.0 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0460.

Ethyl 6-hydroxy-2-oxo-8-(phenylthio)-2*H*-chromene-3-carboxylate (25):



25

Reaction time: 1 min.

Yield: 0.024 g (12%) as yellow solid.

MP: 147–148 °C.

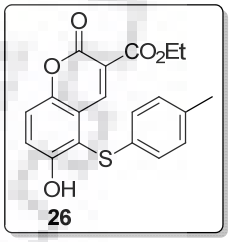
IR (KBr): ν_{max} 3400, 3058, 2925, 1748, 1571, 1444, 1385, 1268, 1034, 800, 735 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.96 (s, 1H), 8.67 (s, 1H), 7.47–7.46 (m, 5H), 7.10 (s, 1H), 6.69 (s, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 162.6 (*C*O), 155.7 (*C*O), 154.0 (C), 148.6 (*C*H), 144.8 (C), 133.1 (*C*H), 130.8 (*C*H), 130.1 (C), 128.9 (*C*H), 124.9 (C), 121.5 (*C*H), 118.8 (C), 118.2 (C), 112.8 (*C*H), 61.3 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0454.

Ethyl 6-hydroxy-2-oxo-5-(4-methylphenylthio)-2*H*-chromene-3-carboxylate (26):



26

Reaction time: 1 min.

Yield: 0.160 g (75%) as yellow solid.

MP: 108–109 °C.

IR (KBr): ν_{max} 3469, 2922, 1742, 1698, 1565, 1465, 1377, 1256, 1224, 1035, 676 cm^{-1}.

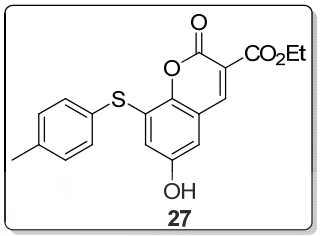
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.38, 7.35 (ABq, 2H, J_{AB} = 9.5 Hz), 7.05 (d, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.86 (s, 1H), 4.36 (q, *J* = 7.0 Hz, 2H), 2.26 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 156.3 (*C*O), 154.9 (C), 150.1 (C), 146.2 (*C*H), 137.3 (C), 130.4 (*C*H), 130.2 (C), 127.7 (*C*H), 122.0 (*C*H), 120.5 (C), 120.0 (*C*H), 119.3 (C), 114.8 (C), 62.0 (CH_2), 20.9 (CH_3), 14.0 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found: 379.0606.

Ethyl 6-hydroxy-2-oxo-8-(4-methylphenylthio)-2*H*-chromene-3-carboxylate (27):

Reaction time: 1 min.



27

Yield: 0.036 g (17%) as yellow solid.

MP: 207–208 °C.

IR (KBr): ν_{max} 3469, 2920, 1745, 1569, 1460, 1390, 1250, 1229, 1130, 679 cm^{-1}.

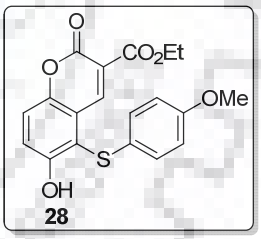
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.93 (s, 1H), 8.66 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 2.5 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 4.28 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 162.9 (*C*O), 156.1 (*C*O), 154.2 (C), 148.9 (*C*H), 144.6 (C), 139.5 (C), 134.2 (*C*H), 131.1 (*C*H), 126.7 (C), 126.4 (C), 120.8 (*C*H), 118.8 (C), 118.4 (C), 112.4 (*C*H), 61.7 (CH_2), 21.0 (CH_3), 14.3 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found: 379.0606.

Ethyl 6-hydroxy-7-(4-methoxyphenylthio)-2-oxo-2*H*-chromene-3-carboxylate (28):

Reaction time: 1 min.



28

Yield: 0.174 g (78%) as yellow solid.

MP: 153–154 °C.

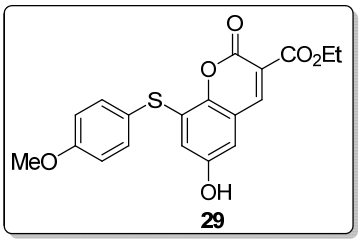
IR (KBr): ν_{max} 3419, 2923, 1754, 1683, 1565, 1492, 1380, 1267, 1033, 797, 608 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.98 (s, 1H), 7.35, 7.32 (ABq, 2H, J_{AB} = 9.0 Hz), 7.08 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 4.37 (q, *J* = 7.0 Hz, 2H), 3.72 (s, 3H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 159.2 (*C*O), 156.2 (C), 154.7 (C), 150.1 (C), 146.3 (*C*H), 130.2 (*C*H), 124.2 (C), 122.0 (*C*H), 120.3 (C), 119.8 (*C*H), 119.1 (C), 116.0 (C), 115.3 (*C*H), 62.0 (O*C*H$_3$), 55.3 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_6SNa$ $[M + Na]^+$: 395.0560, found: 395.0565.

Ethyl 6-hydroxy-8-(4-methoxyphenylthio)-2-oxo-2*H*-chromene-3-carboxylate (29):



29

Reaction time: 1 min.

Yield: 0.028 g (13%) as yellow solid.

MP: 191–192 °C.

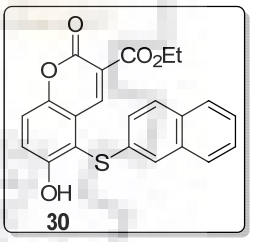
IR (KBr): ν_{max} 3424, 2924, 1701, 1573, 1438, 1383, 1266, 1098 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.88 (s, 1H), 8.65 (s, 1H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.44 (d, *J* = 3.0 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): 163.5 (*C*O), 161.2 (*C*O), 156.8 (C), 154.5 (C), 149.6 (*C*H), 144.5 (C), 137.6 (*C*H), 128.5 (C), 120.1 (C), 119.9 (*C*H), 119.0 (C), 118.6 (C), 116.6 (*C*H), 112.0 (*C*H), 62.4 (*C*H$_2$), 56.1 (O*C*H$_3$), 14.7 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{17}O_6S$ $[M + H]^+$: 373.0740, found: 373.0741.

Ethyl 6-hydroxy-5-(naphthalen-2-ylthio)-2-oxo-2*H*-chromene-3-carboxylate (30):



30

Reaction time: 1 min.

Yield: 0.176 g (75%) as yellow solid.

MP: 179 °C.

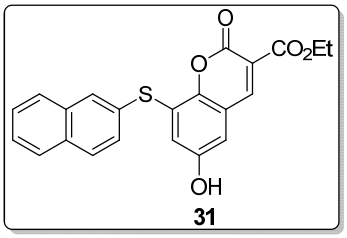
IR (KBr): ν_{max} 3414, 2920, 1749, 1570, 1459, 1382, 1252, 1038, 800, 672 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.93 (s, 1H), 7.74–7.69 (m, 2H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.45–7.36 (m, 5H), 7.15 (d, *J* = 8.5 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, CDCl$_3$): δ 162.9 (*C*O), 156.3 (*C*O), 155.2 (C), 150.2 (C), 146.1 (*C*H), 133.6 (C), 131.9 (C), 131.2 (C), 129.5 (*C*H), 127.7 (*C*H), 127.1 (*C*H), 126.4 (*C*H), 125.6 (*C*H), 125.6 (*C*H), 124.8 (*C*H), 122.2 (*C*H), 120.6 (C), 120.3 (*C*H), 119.4 (C), 113.9 (C), 62.0 (*C*H$_2$), 14.0 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{16}O_5SNa$ $[M + Na]^+$: 415.0611, found: 415.0612.

Ethyl 6-hydroxy-8-(naphthalen-2-ylthio)-2-oxo-2*H*-chromene-3-carboxylate (31):



31

Reaction time: 1 min.

Yield: 0.040 g (17%) as yellow solid.

MP: 230–231 °C.

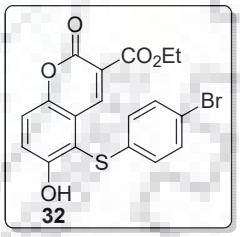
IR (KBr): ν_{max} 3414, 2918, 1749, 1570, 1462, 1382, 1250, 1038, 800, 658 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.92 (s, 1H), 8.68 (s, 1H), 8.14 (s, 1H), 8.03–7.95 (m, 3H), 7.60–7.57 (m, 2H), 7.50 (dd, *J* = 1.0, 8.5 Hz, 1H), 7.10 (d, *J* = 2.5 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 4.29 (q, *J* = 6.5 Hz, 2H), 1.30 (t, *J* = 7.5 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-*d*$_6$): 162.6 (*C*O), 156.4 (*C*O), 155.7 (C), 149.1 (C), 146.0 (*C*H), 134.0 (C), 133.3 (C), 131.2 (C), 128.8 (*C*H), 127.7 (*C*H), 127.0 (*C*H), 126.9 (*C*H), 125.8 (*C*H), 125.2 (*C*H), 124.5 (*C*H), 123.1 (*C*H), 120.9 (C), 119.4 (C), 118.4 (*C*H), 114.1 (C), 61.4 (CH_2), 14.0 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{16}O_5SNa$ $[M + Na]^+$: 415.0611, found: 415.0610.

Ethyl 5-(4-bromophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (32):



32

Reaction time: 1 min.

Yield: 0.197 g (78%) as yellow solid.

MP: 160–161 °C.

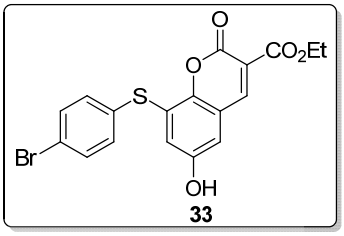
IR (KBr): ν_{max} 3423, 2921, 1750, 1566, 1381, 1229, 1035, 802, 659 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (s, 1H), 7.41 (s, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.73 (s, 1H), 4.38 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9 (*C*O), 156.1 (*C*O), 155.1 (C), 150.2 (C), 145.8 (*C*H), 133.1 (C), 132.6 (*C*H), 128.5 (*C*H), 122.3 (*C*H), 120.9 (C), 120.6 (*C*H), 120.5 (C), 119.6 (C), 113.3 (C), 62.1 (CH_2), 14.0 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}BrO_5S$ $[M + H]^+$: 420.9739, found: 420.9753.

Ethyl 8-(4-bromophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (33):



33

Reaction time: 1 min.

Yield: 0.025 g (10%) as yellow solid.

MP: 221–222 °C.

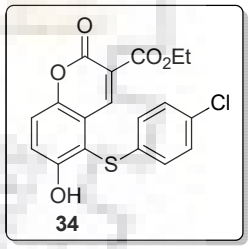
IR (KBr): ν_{max} 3421, 2946, 2849, 1757, 1566, 1315, 1247, 1079, 803, 670 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.69 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.16 (s, 1H), 6.80 (s, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6 (*C*O), 155.6 (*C*O), 154.0 (C), 148.6 (*C*H), 145.3 (C), 134.2 (*C*H), 132.9 (*C*H), 131.2 (C), 123.5 (C), 122.4 (*C*H), 121.9 (C), 119.0 (C), 118.3 (C), 113.6 (*C*H), 61.4 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}BrO_5S$ $[M + H]^+$: 420.9739, found: 420.9740.

Ethyl 5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (34):



34

Reaction time: 1 min.

Yield: 0.169 g (75%) as yellow solid.

MP: 156–157 °C.

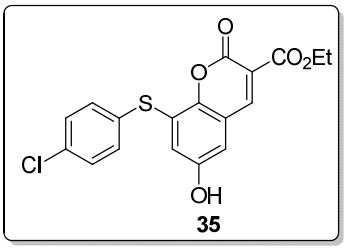
IR (KBr): ν_{max} 3432, 2931, 1749, 1632, 1570, 1470, 1370, 1229, 1035, 805 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (s, 1H), 7.41 (s, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.79 (s, 1H), 4.37 (q, *J* = 7.5 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 156.1 (*C*O), 155.1 (C), 150.2 (C), 145.9 (*C*H), 133.1 (C), 132.3 (C), 129.8 (*C*H), 128.3 (*C*H), 122.3 (*C*H), 120.6 (*C*H), 120.4 (C), 119.6 (C), 113.4 (C), 62.2 (CH_2), 14.1 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}ClO_5SNa$ $[M + Na]^+$: 399.0064, found: 399.0060.

Ethyl 8-(4-chlorophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (35):



35

Reaction time: 1 min.

Yield: 0.025 g (11%) as yellow solid.

MP: 233–234 °C.

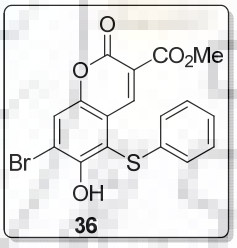
IR (KBr): ν_{max} 3366, 2934, 2857, 1748, 1573, 1477, 1444, 1388, 1270, 1035, 812, 644 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.68 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 9.0 Hz, 2H), 7.14 (d, *J* = 2.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 162.7 (*C*O), 155.9 (*C*O), 153.9 (C), 148.3 (*C*H), 145.4 (C), 134.8 (*C*H), 134.5 (C), 129.9 (*C*H), 129.7 (C), 129.5 (C), 125.9 (C), 122.3 (*C*H), 118.1 (C), 111.9 (*C*H), 61.6 (CH_2), 13.9 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}ClO_5SNa$ $[M + Na]^+$: 399.0064, found: 399.0064.

Methyl 7-bromo-6-hydroxy-2-oxo-5-(phenylthio)-2*H*-chromene-3-carboxylate (36):



36

Reaction time: 2 min.

Yield: 0.170 g (70%) as yellow solid.

MP: 179–180 °C.

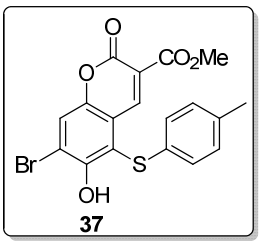
IR (KBr): ν_{max} 3414, 2922, 1771, 1622, 1550, 1415, 1318, 1203, 1041, 806, 617 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.91 (s, 1H), 7.70 (s, 1H), 7.30–7.22 (m, 3H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.04 (s, 1H), 3.92 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 155.6 (*C*O), 152.3 (C), 149.5 (C), 146.4 (*C*H), 133.0 (C), 129.8 (*C*H), 127.6 (*C*H), 127.5 (*C*H), 123.5 (*C*H), 120.1 (C), 119.4 (C), 117.0 (C), 115.4 (C), 53.0 (OCH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9402.

Methyl 7-bromo-6-hydroxy-2-oxo-5-(4-methylphenylthio)-2*H*-chromene-3-carboxylate (37):



37

Reaction time: 2 min.

Yield: 0.184 g (73%) as yellow solid.

MP: 167–168 °C.

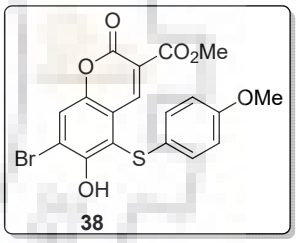
IR (KBr): ν_{max} 3414, 2922, 1771, 1622, 1550, 1415, 1318, 1203, 1041, 806, 617 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.95 (s, 1H), 7.67 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.08 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.92 (s, 3H), 2.29 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 155.7 (*C*O), 152.2 (C), 149.4 (C), 146.5 (*C*H), 138.0 (C), 130.6 (*C*H), 129.4 (C), 128.2 (*C*H), 123.2 (*C*H), 120.0 (C), 119.2 (C), 117.0 (C), 116.3 (C), 53.0 (O*C*H_3), 21.0 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_5SNa$ $[M + Na]^+$: 442.9559, found: 442.9559.

Methyl 7-bromo-6-hydroxy-5-(4-methoxy-phenylthio)-2-oxo-2*H*-chromene-3-carboxylate (38):



38

Reaction time: 2 min.

Yield: 0.199 g (76%) as yellow solid.

MP: 187–188 °C.

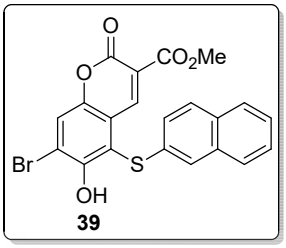
IR (KBr): ν_{max} 3417, 2924, 1702, 1571, 1498, 1374, 1266, 1028, 803 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): 9.01 (s, 1H), 7.63 (s, 1H), 7.17–7.13 (m, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 3.94 (s, 3H), 3.76 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 159.7 (*C*O), 155.7 (C), 151.9 (C), 149.4 (C), 146.6 (*C*H), 130.9 (*C*H), 123.3 (C), 123.0 (*C*H), 119.8 (C), 119.0 (C), 117.5 (C), 117.0 (C), 115.5 (*C*H), 55.4 (O*C*H_3), 53.0 (O*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_6SNa$ $[M + Na]^+$: 458.9508, found: 458.9509.

Methyl 7-bromo-6-hydroxy-5-(naphthalen-2-ylthio)-2-oxo-2*H*-chromene-3-carboxylate (39):



39

Reaction time: 2 min.

Yield: 0.214 (78%) as yellow solid.

MP: 193–194 °C.

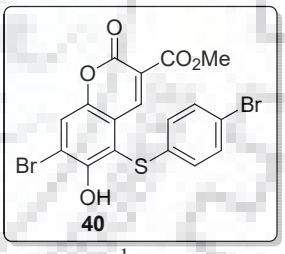
IR (KBr): ν_{max} 3437, 2928, 1731, 1569, 1486, 1378, 1178, 1026, 800, 635 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.96 (s, 1H), 7.78–7.74 (m, 2H), 7.70–7.65 (m, 2H), 7.52–7.45 (m, 3H), 7.16 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.12 (s, 1H), 3.89 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.6 (*C*O), 152.4 (C), 149.5 (C), 146.3 (*C*H), 133.6 (C), 132.2 (C), 130.3 (C), 129.8 (*C*H), 127.8 (*C*H), 127.3 (*C*H), 127.2 (*C*H), 126.7 (*C*H), 126.4 (*C*H), 125.0 (*C*H), 123.5 (*C*H), 120.2 (C), 119.3 (C), 117.2 (C), 115.5 (C), 53.0 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{13}BrO_5SNa$ $[M + Na]^+$: 478.9559, found: 478.9559.

Methyl 7-bromo-5-(4-bromophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (40):



40

Reaction time: 2 min.

Yield: 0.198 g (68%) as yellow solid.

MP: 204–205 °C.

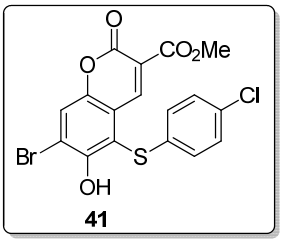
IR (KBr): ν_{max} 3414, 2945, 1762, 1622, 1542, 1453, 1244, 1032, 812, 620 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H), 7.70 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 3.93 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.5 (*C*O), 152.3 (C), 149.6 (C), 146.0 (*C*H), 132.9 (*C*H), 132.3 (C), 129.0 (*C*H), 123.7 (*C*H), 121.6 (C), 120.0 (C), 119.6 (C), 117.2 (C), 114.9 (C), 53.0 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{10}Br_2O_5SNa$ $[M + Na]^+$: 506.8508, found: 506.8507.

Methyl 7-bromo-5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (41):



Reaction time: 2 min.

Yield: 0.172 g (65%) as yellow solid.

MP: 206–207 °C.

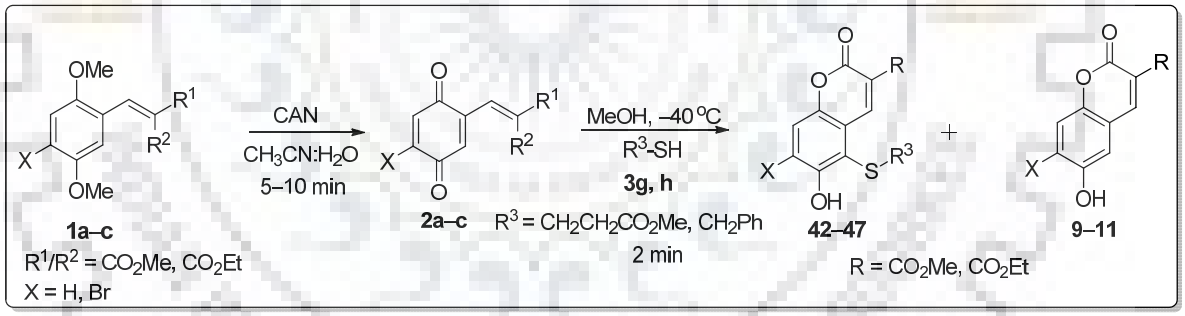
IR (KBr): ν_{max} 3411, 2925, 1770, 1700, 1622, 1550, 1182, 1035, 797, 617 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (s, 1H), 7.63 (s, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.89 (s, 1H), 3.86 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.5 (*C*O), 152.2 (C), 149.5 (C), 146.1 (*C*H), 133.6 (C), 131.6 (C), 129.9 (*C*H), 128.8 (*C*H), 123.6 (*C*H), 120.0 (C), 119.4 (C), 117.3 (C), 115.0 (C), 53.1 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{10}BrClO_5SNa$ $[M + Na]^+$: 462.9013, found: 462.9012.

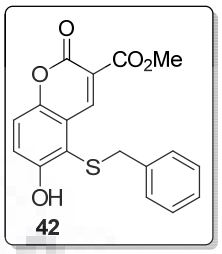
3.2.2. General procedure for the synthesis of alkyl sulfide derivative of coumarins 42-47.



A solution of cerium(IV) ammonium nitrate (1.37 g, 2.5 mmol) in H_2O (3.0 mL) was added to a solution of alkenyl arene **1** (1.0 mmol) in CH_3CN (1.0 mL) with rapid stirring. The color changed rapidly from orange to red. After 5 min, reaction mixture was diluted with dichloromethane (10 mL). Then brine solution was added and organic layer was separated. Combined organic layer was dried over anhyd. Na_2SO_4, concentrated under reduced pressure and the residue was used as such without further purification. Thus obtained benzoquinone **2** was dissolved in MeOH (0.5 mL) at –40 °C was added alkyl thiol derivative **3** (0.6 mmol) in MeOH (0.5 mL) and stirred the reaction mixture for 2 min. After

completion of the reaction, as checked by TLC, the solvent was removed under *vacuo* and the residue was purified by silica gel column chromatography (100–200 mesh) using 30% ethyl acetate in hexanes to furnish pure alkyl sulfide derivatives of coumarin **42**–**47**.

Methyl 5-(benzylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (42):



42

Reaction time: 2 min.

Yield: 0.144 g (70 %) as yellow solid.

MP: 121–122 °C.

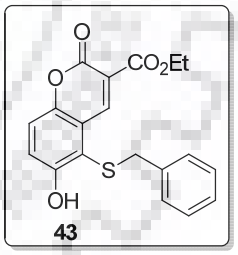
IR (KBr): ν_{max} 3403, 2919, 1748, 1633, 1559, 1312, 1224, 1044, 709, 600 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.30, 7.28 (ABq, 2H, J_{AB} = 9.2 Hz), 7.18–7.13 (m, 3H), 6.90 (d, J = 7.0 Hz, 2H), 6.84 (s, 1H), 3.92 (s, 3H), 3.82 (s, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 156.3 (*C*O), 155.0 (C), 149.6 (C), 146.6 (*C*H), 136.0 (C), 128.8 (*C*H), 128.7 (*C*H), 127.8 (*C*H), 121.2 (*C*H), 119.5 (*C*H), 117.8 (C), 115.4 (C), 52.7 (O*C*H_3), 40.9 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0453.

Ethyl 7-(benzylthio)-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (43):



43

Reaction time: 2 min.

Yield: 0.156 g (73 %) as yellow solid.

MP: 110–111 °C.

IR (KBr): ν_{max} 3369, 2925, 1752, 1563, 1468, 1383, 1248, 1041, 803, 703 cm^{-1}.

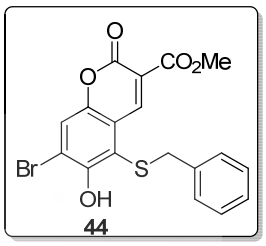
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.29, 7.27 (ABq, 2H, J_{AB} = 9.5 Hz), 7.17–7.10 (m, 3H), 6.90–6.85 (m, 3H), 4.37 (q, J = 7.0 Hz, 2H), 3.82 (s, 2H), 1.41 (t, J = 7.5 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 162.8 (*C*O), 156.3 (*C*O), 154.9 (C), 149.4 (C), 146.1 (*C*H), 136.0 (C), 128.8 (*C*H), 128.6 (*C*H), 127.8 (*C*H), 121.3 (*C*H), 121.1 (C), 119.4 (*C*H),

118.1(C), 115.4 (C), 61.7 (CH_2), 40.7 (CH_2), 14.2 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found: 379.0611.

Methyl 5-(benzylthio)-7-bromo-6-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (44):



44

Reaction time: 2 min.

Yield: 0.176 g (70%) as yellow solid.

MP: 167–168 °C.

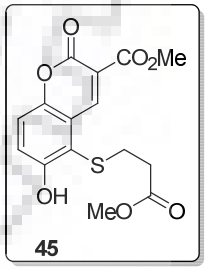
IR (KBr): ν_{max} 3455, 2925, 1758, 1633, 1553, 1399, 1240, 1140, 1039, 879, 656 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.54 (s, 1H), 7.20 (s, 1H), 7.14–7.12 (m, 3H), 6.89 (d, *J* = 7.0 Hz, 2H), 3.89 (s, 3H), 3.86 (s, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.1 (*C*O), 155.7 (*C*O), 152.2 (C), 148.7 (C), 146.3 (*C*H), 135.6 (C), 128.8 (*C*H), 128.7 (*C*H), 127.9 (*C*H), 122.6 (*C*H), 120.7 (C), 117.8 (C), 116.6 (C), 116.0 (C), 52.7 (O*C*H_3), 40.8 (CH_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_5SNa$ $[M + Na]^+$: 442.9559, found: 442.9561.

Methyl 6-hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2*H*-chromene-3-carboxylate (45):



45

Reaction time: 2 min.

Yield: 0.139 g (69%) as yellow solid.

MP: 108–109 °C.

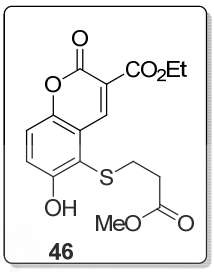
IR (KBr): ν_{max} 3469, 2922, 1742, 1698, 1565, 1465, 1377, 1256, 1224, 1035, 676 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.00 (s, 1H), 7.40 (s, 1H), 7.29, 7.25 (ABq, 2H, J_{AB} = 11.2 Hz), 3.90 (s, 3H), 3.66 (s, 3H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.51 (t, *J* = 6.8 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8 (*C*O), 163.4 (*C*O), 156.4 (*C*O), 155.6 (C), 149.3 (C), 147.1 (*C*H), 122.3 (*C*H), 120.5 (C), 118.4 (*C*H), 117.6 (C), 116.2 (C), 52.6 (O*C*H_3), 51.7 (O*C*H_3), 33.5 (CH_2), 30.1 (CH_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{15}H_{14}O_7SNa$ $[M + Na]^+$: 361.0352, found: 361.0355.

Ethyl 6–hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2*H*-chromene-3-carboxylate (46):



46

Reaction time: 2 min.

Yield: 0.148 g (70%) as yellow solid.

MP: 114–115 °C.

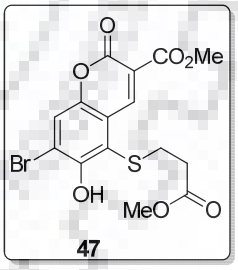
IR (KBr): ν_{max} 3246, 2946, 1742, 1697, 1561, 1366, 1251, 1161, 1041, 835, 667 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 7.42 (s, 1H), 7.34, 7.31 (ABq, 2H, J_{AB} = 9.2 Hz), 4.43 (q, *J* = 7.5 Hz, 2H), 3.73 (s, 3H), 2.98 (t, *J* = 6.5 Hz, 2H), 2.57 (t, *J* = 6.5 Hz, 2H), 1.42 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.9 (*C*O), 163.0 (*C*O), 156.4 (*C*O), 155.4 (C), 149.7 (*C*H), 146.3 (C), 122.0 (*C*H), 120.5 (C), 119.3 (*C*H), 118.8 (C), 115.7 (C), 61.9 (CH_2), 52.0 (OCH_3), 33.2 (CH_2), 31.1 (CH_2), 14.0 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{16}H_{16}O_7SNa$ $[M + Na]^+$: 375.0509, found: 375.0507.

Methyl 7-bromo-6-hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2*H*-chromene-3-carboxylate (47):



47

Reaction time: 2 min.

Yield: 0.170 g (68%) as yellow solid.

MP: 170–171 °C.

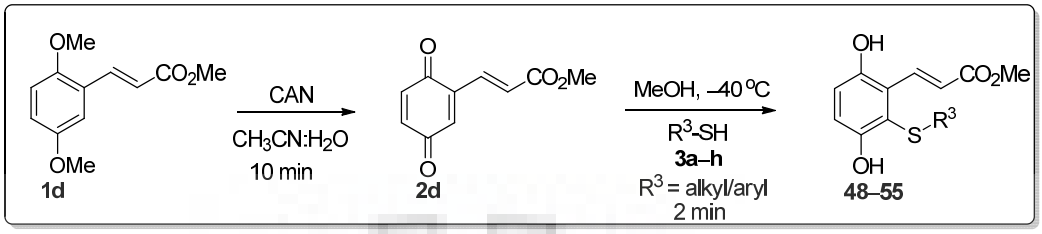
IR (KBr): ν_{max} 3248, 2946, 1740, 1697, 1561, 1366, 1161, 1044, 820, 667 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): 9.00 (s, 1H), 7.88 (s, 1H), 7.60 (s, 1H), 3.95 (s, 3H), 3.74 (s, 3H), 3.02 (t, *J* = 6.5 Hz, 2H), 2.60 (t, *J* = 7.0 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 172.1 (*C*O), 163.5 (*C*O), 155.8 (*C*O), 152.7 (C), 149.1 (*C*), 146.6 (*C*H), 122.7 (*C*H), 120.0 (C), 118.9 (C), 117.3 (C), 116.9 (C), 52.0 (OCH_3), 52.3 (OCH_3), 33.0 (CH_2), 31.3 (CH_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{15}H_{13}BrO_7SNa$ $[M + Na]^+$: 438.9458, found: 438.9456.

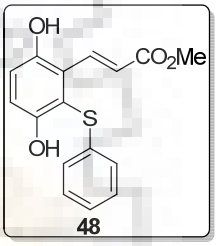
3.2.3. General procedure for the synthesis of alkyl/aryl sulfide derivatives 48–55.



Compounds **48–55** were synthesized using alkenyl *p*-benzoquinone **2d** (0.192 g, 1.0 mmol), and thiophenol **3** (0.6 mmol), by following general procedure described for the synthesis of coumarin alkyl/aryl sulfides **12**–**47**.

Methyl (*E*)-3-(3,6-dihydroxy-2-(phenylthio)phenyl)acrylate (48):

Reaction time: 1 min.



Yield: 0.123 g (68%) as brown solid.

MP: 205–206 °C

IR (KBr): ν_{max} 3344, 1685, 1626, 1438, 1338, 1265, 1170, 824, 646 cm^{-1}.

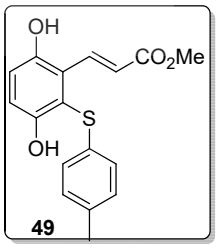
^{1}H NMR (400 MHz, DMSO-d_6): δ 10.12 (s, 1H), 9.35 (s, 1H), 8.22 (d, *J* = 16.0 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.00–6.91 (m, 5H), 3.64 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6 (*C*O), 152.2 (C), 151.5 (C), 140.3 (*C*H), 137.6 (C), 129.0 (*C*H), 125.9 (*C*H), 125.0 (C), 123.6, (*C*H), 121.7 (*C*H), 119.2 (*C*H), 118.7 (*C*H), 117.2 (C), 51.3 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{16}H_{14}O_4SNa$ $[M + Na]^+$: 325.0505, found: 325.0519.

Methyl (*E*)-3-(3,6-dihydroxy-2-(4-methylthio)phenyl)acrylate (49):

Reaction time: 1 min.



Yield: 0.132 g (70%) as brown solid.

MP: 205–206 °C.

IR (KBr): ν_{max} 3326, 2919, 1686, 1628, 1433, 1338, 1264, 1195, 808, 643 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.10 (s, 1H), 9.30 (s, 1H), 8.23 (d, *J* = 16.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.98–6.91 (m, 3H), 6.90–6.86 (m, 2H), 3.65 (s, 3H), 2.20 (s, 3H) ppm.

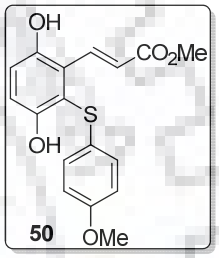
^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 167.6 (*C*O), 152.0 (C), 151.4 (C), 140.4 (*C*H), 134.5 (C), 133.9 (C), 129.6 (*C*H), 126.3 (C), 123.5 (*C*H), 121.5 (*C*H), 119.0 (*C*H), 118.6 (*C*H), 118.0 (C), 51.3 (O*C*H$_3$), 20.4 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{17}O_4S$ $[M + H]^+$: 317.0842, found: 317.0853.

Methyl (*E*)-3-(3,6-dihydroxy-2-(4-methoxyphenylthio)phenyl)acrylate (50):

Reaction time: 1 min.

Yield: 0.143 g (72%) as light brown solid.



MP: 182–183 °C.

IR (KBr): ν_{max} 3394, 1679, 1629, 1497, 1436, 1339, 1271, 820, 518 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.00 (s, 1H), 9.24 (s, 1H), 8.31 (d, *J* = 16.0 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.94–6.88 (m, 3H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H) ppm.

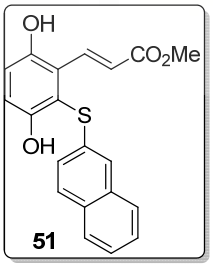
^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 167.7 (*C*O), 157.7 (C), 151.9 (C), 151.4 (C), 140.7 (*C*H), 129.0 (*C*H), 127.8 (C), 123.4 (*C*H), 121.4 (C), 119.4 (C), 118.8 (*C*H), 118.6 (*C*H), 114.8 (*C*H), 55.2 (O*C*H$_3$), 51.4 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{17}O_5S$ $[M + H]^+$: 333.0791, found: 333.0811.

Methyl (*E*)-3-(3,6-dihydroxy-2-(naphthalen-2-ylthio)phenyl)acrylate (51):

Reaction time: 1 min.

Yield: 0.150 g (71%) as light brown solid.



MP: 194–195 °C.

IR (KBr): ν_{max} 3387, 2916, 1681, 1625, 1384, 1265, 1179, 1124, 815, 614 cm^{-1}.

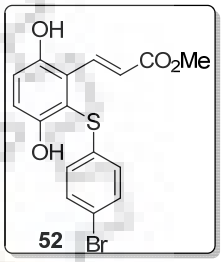
^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 9.27 (s, 1H), 8.20 (d, *J* = 16.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.36–7.27 (m, 3H), 7.13 (d, *J* = 6.0 Hz, 1H), 7.03 (s, 1H), 7.00–6.97 (m, 1H), 6.91 (t, *J* = 8.8 Hz, 1H), 3.62 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 168.1 (*C*O), 151.6 (C), 151.0 (C), 139.9 (*C*H), 138.9 (C), 133.3 (C), 131.3 (C), 128.4 (*C*H), 127.3 (*C*H), 126.7 (*C*H), 126.2 (*C*H), 125.3 (*C*H), 124.8 (*C*H), 124.5 (*C*H), 123.9 (C), 122.4 (*C*H), 119.6 (*C*H), 117.1 (*C*H), 51.1 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{17}O_4S$ $[M + H]^+$: 353.0842, found: 353.0861.

Methyl (*E*)-3-(2-(4-bromophenylthio)-3,6-dihydroxyphenyl)acrylate (52):

Reaction time: 1 min.



Yield: 0.149 g (65%) as light brown solid.

MP: 218–219 °C.

IR (KBr): ν_{max} 3328, 2919, 1690, 1628, 1433, 1338, 1264, 1190, 806, 642 cm^{-1}.

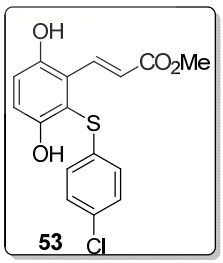
^{1}H NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.47 (s, 1H), 8.16 (d, *J* = 16.0 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.01–6.88 (m, 5H), 3.65 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): 167.6 (*C*O), 152.1 (C), 151.5 (C), 140.0 (*C*H), 137.3 (C), 131.8 (*C*H), 127.8 (*C*H), 123.5 (C), 121.8 (*C*H), 119.5 (*C*H), 118.7 (*C*H), 117.8 (C), 116.6 (C), 51.4 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{16}H_{13}BrO_4SNa$ $[M + Na]^+$: 402.9610, found: 402.9533.

Methyl (*E*)-3-(2-(4-chlorophenylthio)-3,6-dihydroxyphenyl)acrylate (53):

Reaction time: 1 min.



Yield: 0.131 g (65%) as light brown solid.

MP: 216–217 °C

IR (KBr): ν_{max} 3412, 2950, 1690, 1624, 1432, 1358, 1193, 1080, 815, 620 cm^{-1}.

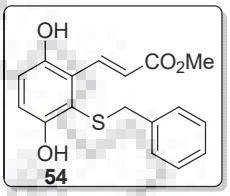
^{1}H NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.48 (s, 1H), 8.22 (d, *J* = 16.0 Hz, 1H), 7.27 (d, *J* =8.4 Hz, 2H), 7.03–6.93 (m, 5H), 3.65 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 167.7 (*C*O), 152.2 (C), 151.6 (C), 140.2 (*C*H), 136.8 (C), 129.8 (C), 129.0 (*C*H), 127.6 (*C*H), 123.7 (C), 122.0 (*C*H), 119.6 (*C*H), 118.8 (*C*H), 117.0 (C), 51.4 (O*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{16}H_{14}ClO_4S$ $[M + H]^+$: 337.0295, found: 337.0290.

Methyl (*E*)-3-(2-(benzylthio)-3,6-dihydroxyphenyl)acrylate (54):

Reaction time: 2 min.



54

Yield: 0.129 g (70%) as light brown solid.

MP: 169–170 °C.

IR (KBr): ν_{max} 3328, 2930, 1689, 1628, 1436 1338, 1264, 1190, 800, 647 cm^{-1}.

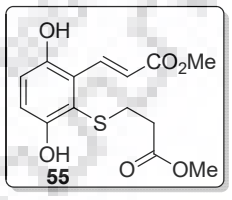
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.82 (s, 1H), 9.25 (s, 1H), 8.15 (d, *J* = 16.0 Hz, 1H), 7.21–7.12 (m, 5H), 6.84–6.72 (m, 3H), 3.97 (s, 2H), 3.69 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6): δ 167.8 (*C*O), 151.6 (C), 150.9 (C), 140.8 (*C*H), 138.0 (C), 128.8 (*C*H), 128.2 (*C*H), 126.9 (*C*H), 123.5 (C), 120.9 (*C*H), 120.7 (C), 117.7 (*C*H), 117.5 (*C*H), 51.3 (O*C*H$_3$), 38.4 (*C*H$_2$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{17}H_{16}O_4S$ $[M + Na]^+$: 339.0661, found: 339.0657.

Methyl (*E*)-3-(3,6-dihydroxy-2-((3-methoxy-3-oxopropyl)thio)phenyl)acrylate (55):

Reaction time: 2 min.



55

Yield: 0.131 g (68%) as brown solid.

MP: 130–131 °C.

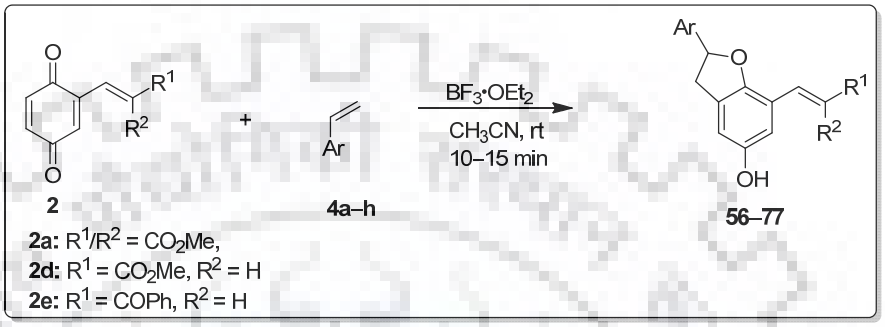
IR (KBr): ν_{max} 3389, 2919, 1684, 1585, 1384, 1269, 1171, 988, 829, 614 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 9.04 (s, 1H), 8.23 (d, *J* = 16.0 Hz, 1H), 7.02 (d, *J* = 16.0 Hz, 1H), 6.89 (s, 1H), 6.82 (dd, *J* = 8.8, 21.6 Hz, 2H), 3.73 (s, 3H), 3.59 (s, 3H), 2.82 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 6.8 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 171.9 (*C*O), 168.5 (*C*O), 151.6 (C), 150.9 (C), 140.1 (*C*H), 123.5 (C), 122.5 (*C*H), 119.0 (*C*H), 118.7 (C), 116.5 (*C*H), 51.75 (O*C*H_3), 51.40 (O*C*H_3), 33.4 (*C*H_2), 30.8 (*C*H_2) ppm.

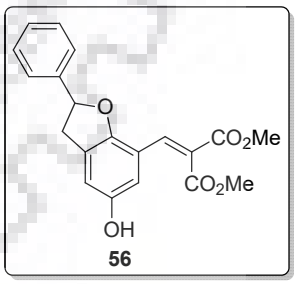
HRMS (ESI+): *m/z* calcd for $C_{14}H_{17}O_6S$ $[M+H]^+$: 313.0740, found: 313.0737.

3.2.4. General procedure for the synthesis of dihydrobenzofuran derivatives 56–77:



To a solution of alkenyl *p*-benzoquinone 2**a/2d/2e** (0.5 mmol) and styrene derivative **4a–h** (1.0 mmol) in CH_3CN (2.0 ml) at rt, was added $BF_3.OEt_2$ (0.1 mL, 1.0 mmol) and stirred the reaction mixture. After completion of the reaction, as checked by TLC, the solvent was removed under *vacuo* and the residue was purified by silica gel column chromatography (100–200 mesh) using 30% ethyl acetate in hexanes to furnish pure dihydrofuran derivative.

Dimethyl 2-((5-hydroxy-2-phenyl-2,3-dihydrobenzofuran-7-yl)methylene)malonate (56):



Reaction time: 10 min.

Yield: 0.152 g (86%) as yellow viscous liquid.

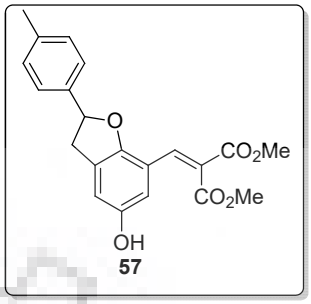
IR (KBr) ν_{max}: 3463, 2984, 2822, 2360, 1635, 1556, 1468, 1303, 1174, 1024, 629 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.40–7.35 (m, 5H), 6.76 (d, *J* = 2.8 Hz, 1H), 6.64 (d, *J* = 2.8 Hz, 1H), 5.72 (t, *J* = 9.2 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.51 (dd, *J* = 9.2, 16.4 Hz, 1H), 3.12 (dd, *J* = 9.2, 16.8 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8 (*C*O), 164.8 (*C*O), 153.2 (C), 150.4 (C), 141.0 (C), 137.6 (*C*H), 128.7 (*C*H), 128.5 (*C*H), 128.1 (*C*H), 125.7 (C), 124.0 (C), 116.3 (*C*H), 114.5 (C), 112.1 (*C*H), 84.8 (*C*H), 52.8 (O*C*H_3), 52.55 (O*C*H_3), 38.25 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{18}O_6Na$ $[M + Na]^+$: 377.0996, found: 377.0992.

Dimethyl 2-((5-hydroxy-2-(4-methylphenyl)-2,3-dihydrobenzofuran-7-yl)methylene)-malonate (57):



57

Reaction time: 10 min.

Yield: 0.156 g (85%) as yellow viscous liquid.

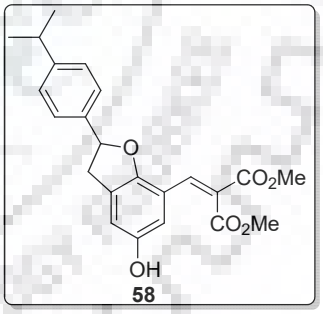
IR (KBr): ν_{max} 3852, 2851, 1639, 1550, 1459, 1417, 1261, 1170, 1079, 1011, 617 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 5.69 (t, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.48 (dd, *J* = 9.0, 16.0 Hz, 1H), 3.13 (dd, *J* = 8.5, 16.0 Hz, 1H), 2.34 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0 (*C*O), 164.8 (*C*O), 153.4 (C), 150.2 (C), 138.0 (C), 138.0 (C), 137.7 (*C*H), 129.2 (*C*H), 129.0 (C), 125.9 (*C*H), 124.0 (C), 116.3 (*C*H), 114.5 (C), 112.1 (*C*H), 84.9 (*C*H), 52.9 (O*C*H_3), 52.6 (O*C*H_3), 38.3 (*C*H_2), 21.1 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{20}O_6Na$ $[M + Na]^+$: 391.1152, found: 391.1148.

Dimethyl 2-((5-hydroxy-2-(4-isopropylphenyl)-2,3-dihydrobenzofuran-7-yl)methylene)malonate (58):



58

Reaction time: 10 min.

Yield: 0.174 g (88%) as yellow viscous liquid.

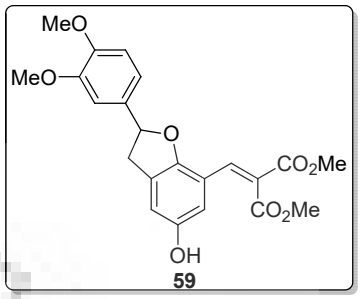
IR (KBr): ν_{max} 3442, 2969, 1635, 1558, 1464, 1376, 1303, 1244, 1173, 1070, 611 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.76 (s, 1H), 6.64 (d, *J* = 2.5 Hz, 1H), 6.62 (s, 1H), 5.70 (t, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.50 (dd, *J* = 9.0, 16.0 Hz, 1H), 3.16 (dd, *J* = 8.5, 16.0 Hz, 1H), 2.91 (quin, *J* = 7.0 Hz, 1H), 1.25 (d, *J* = 7.0 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0 (*C*O), 164.8 (*C*O), 153.4 (C), 150.2 (C), 149.0 (C), 138.3 (C), 137.6 (*C*H), 129.0 (C), 126.6 (*C*H), 126.0 (*C*H), 124.0 (C), 116.3 (*C*H), 114.5 (C), 112.0 (*C*H), 84.9 (*C*H), 52.8 (O*C*H_3), 52.6 (O*C*H_3), 38.2 (*C*H_2), 33.8 (*C*H), 23.9 (2**C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{24}O_6Na$ $[M + Na]^+$: 419.1465, found: 419.1458.

Dimethyl 2-((2-(3,4-dimethoxyphenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)methylene)malonate (59):



59

Reaction time: 10 min.

Yield: 0.190 g (92%) as yellow solid.

MP: 115–117 °C.

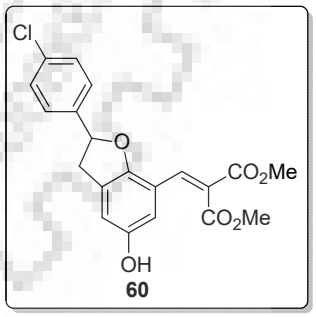
IR (KBr): ν_{max} 3448, 2998, 1746, 1636, 1561, 1417, 1370, 1244, 1126, 1035, 711, 619 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 1H), 6.91 (d, *J* = 7.6 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.76 (s, 1H), 6.63 (s, 1H), 5.65 (t, *J* = 8.8 Hz, 1H), 3.86 (s, 6H), 3.78 (s, 3H), 3.73 (s, 3H), 3.45 (dd, *J* = 9.6, 16.0 Hz, 1H), 3.14 (dd, *J* = 9.2, 16.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (*C*O), 164.9 (*C*O), 153.2 (C), 150.3 (C), 149.1 (C), 149.0 (C), 137.7 (*C*H), 133.3 (C), 129.0 (C), 124.3 (C), 118.6 (*C*H), 116.2 (*C*H), 114.7 (C), 112.4 (*C*H), 111.0 (*C*H), 109.3 (*C*H), 85.2 (*C*H), 55.9 (O*C*H$_3$), 55.9 (O*C*H$_3$), 52.7 (O*C*H$_3$), 52.5 (O*C*H$_3$), 38.2 (*C*H$_2$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{22}O_8Na$ $[M + Na]^+$: 437.1207, found: 437.1201.

Dimethyl 2-((2-(4-chlorophenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)methylene)malonate (60):



60

Reaction time: 15 min.

Yield: 0.128 g (66%) as yellow viscous liquid.

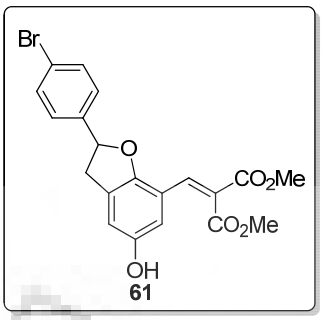
IR (KBr): ν_{max} 3428, 2954, 2854, 1632, 1559, 1461, 1373, 1244, 1179, 1070, 920, 614 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.75 (s, 1H), 6.64 (s, 1H), 6.06 (s, 1H), 5.71 (t, *J* = 9.0 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.54 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.09 (dd, *J* = 8.0, 16.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9 (*C*O), 164.8 (*C*O), 153.1 (C), 150.4 (C), 139.6 (C), 137.4 (*C*H), 133.9 (C), 128.8 (*C*H), 128.5 (C), 127.2 (*C*H), 124.4 (C), 116.2 (*C*H), 114.8 (C), 112.2 (*C*H), 84.0 (*C*H), 52.9 (O*C*H$_3$), 52.7 (O*C*H$_3$), 38.4 (*C*H$_2$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{17}O_6ClNa$ $[M + Na]^+$: 411.0606, found: 411.0609.

Dimethyl 2-((2-(4-bromophenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)methylene)-malonate (61):



61

Reaction time: 15 min.

Yield: 0.138 g (64%) as light yellow solid.

MP: 115–117 °C.

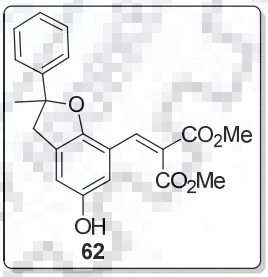
IR (KBr): ν_{max} 3447, 2933, 2848, 1637, 1556, 1453, 1417, 1373, 1250, 1170, 1064, 936, 620 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 2.5 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 6.31 (s, 1H), 5.69 (t, *J* = 8.5 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.53 (dd, *J* = 9.0, 16.0 Hz, 1H), 3.07 (dd, *J* = 8.5, 15.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0 (*C*O), 164.8 (*C*O), 153.0 (C), 150.5 (C), 140.1 (C), 137.4 (*C*H), 131.7 (*C*H), 128.4 (C), 127.4 (*C*H), 124.3 (C), 122.0 (C), 116.3 (*C*H), 114.7 (C), 112.2 (*C*H), 84.0 (*C*H), 52.9 (O*C*H_3), 52.7 (O*C*H_3), 38.3 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{17}O_6BrNa$ $[M + Na]^+$: 455.0101, found: 455.0123.

Dimethyl 2-((5-hydroxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran-7-yl)methylene)-malonate (62):



62

Reaction time: 5 min.

Yield: 0.171 g (93%) as yellow viscous liquid.

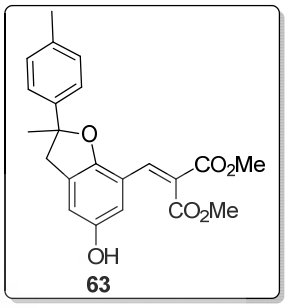
IR (KBr): ν_{max} 3437, 2975, 2830, 1632, 1547, 1476, 1417, 1297, 1173, 1073 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.29–7.26 (m, 1H), 6.71 (d, *J* = 1.0 Hz, 1H), 6.65 (d, *J* = 1.0 Hz, 1H)), 3.88 (s, 3H), 3.87 (s, 3H), 3.29 (q, *J* = 16.0 Hz, 2H), 1.74 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2 (*C*O), 164.9 (*C*O), 152.8 (C), 150.1 (C), 146.0 (C), 137.5 (*C*H), 128.8 (C), 128.3 (*C*H), 127.2 (*C*H), 124.4 (*C*H), 123.8 (C), 116.6 (*C*H), 114.7 (C), 111.7 (*C*H), 90.3 (C), 52.9 (O*C*H_3), 52.6 (O*C*H_3), 44.5 (*C*H_2), 29.3 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{20}O_6Na$ $[M + Na]^+$: 391.1152, found: 391.1179.

Dimethyl 2-((5-hydroxy-2-methyl-2-(4-methylphenyl)-2,3-dihydrobenzofuran-7-yl)methylene)malonate (63):



63

Reaction time: 5 min.

Yield: 0.181 g (95%) as yellow viscous liquid.

IR (KBr): ν_{max} 3456, 2851, 1638, 1541, 1464, 1373, 1308, 1252, 1082, 1023, 808, 620 cm^{-1}.

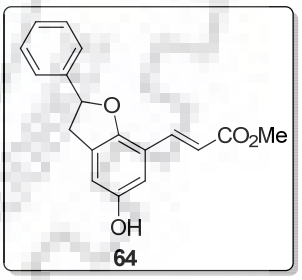
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.78 (s, 1H), 6.70 (d, *J* = 1.0 Hz, 1H), 6.63 (d, *J* = 1.0 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.25 (q, *J* = 15.5 Hz, 2H), 2.33 (s, 3H), 1.70 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2 (*C*O), 164.9 (*C*O), 152.9 (C), 150.1 (C), 143.0 (C), 137.6 (C), 136.8 (*C*H), 128.9 (*C*H), 128.9 (C), 124.4 (*C*H), 123.7 (C), 116.6 (*C*H), 114.6 (C), 111.6 (*C*H), 90.3 (C), 52.9 (O*C*H_3), 52.6 (O*C*H_3), 44.5 (*C*H_2), 29.2 (*C*H_3), 20.9 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{22}O_6Na$ $[M + Na]^+$: 405.1309, found: 405.1308.

Methyl (*E*)-3-(5-hydroxy-2-phenyl-2,3-dihydrobenzofuran-7-yl)acrylate (64):

Reaction time: 10 min.



64

Yield: 0.117 g (79%) as light yellow solid.

MP: 166–168 °C.

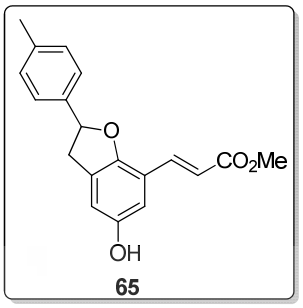
IR (KBr): ν_{max} 3448, 2978, 2919, 1639, 1552, 1464, 1414, 1305, 1085, 1020, 611, 976 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.0 Hz, 1H), 7.39–7.37 (m, 4H), 7.34–7.32 (m, 1H), 6.76–6.70 (m, 3H), 5.83 (t, *J* = 8.5 Hz, 1H), 3.78 (s, 3H), 3.60 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.16 (dd, *J* = 8.0, 16.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5 (*C*O), 153.2 (C), 150.1 (C), 141.6 (C), 140.6 (*C*H), 128.8 (C), 128.6 (*C*H), 128.1 (*C*H), 125.6 (*C*H), 119.4 (*C*H), 116.9 (C), 114.7 (*C*H), 114.2 (*C*H), 84.7 (*C*H), 51.7 (O*C*H_3), 38.3 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{16}O_4Na$ $[M + Na]^+$: 319.0941, found: 319.0932.

Methyl (*E*)-3-(5-hydroxy-2-(4-methylphenyl)-2,3-dihydrobenzofuran-7-yl)acrylate (65):



65

Reaction time: 10 min.

Yield: 0.125 g (81%) as light yellow solid.

MP: 143–145 °C.

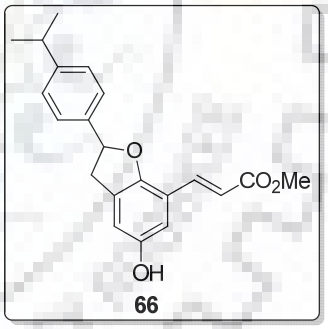
IR (KBr): ν_{max} 2981, 1639, 1553, 1471, 1415, 1306, 1121, 1077, 1018, 611 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 16.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 5.85 (s, 1H), 5.77 (t, *J* = 8.5 Hz, 1H), 3.77 (s, 3H), 3.54 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.13 (dd, *J* = 8.0, 16.0 Hz, 1H), 2.35 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6 (*C*O), 153.2 (C), 150.1 (C), 140.8 (*C*H), 138.5 (C), 137.9 (C), 129.3 (*C*H), 129.0 (C), 125.7 (*C*H), 119.2 (*C*H), 116.9 (C), 114.7 (*C*H), 114.1 (*C*H), 84.82 (*C*H), 51.72 (O*C*H_3), 38.22 (*C*H_2), 21.13 (*C*H_3) ppm.

HRMS (ESI+): m/z calcd for $C_{19}H_{18}O_4Na$ $[M + Na]^+$: 333.1097, found: 333.1126.

Methyl (*E*)-3-(5-hydroxy-2-(4-isopropylphenyl)-2,3-dihydrobenzofuran-7-yl)acrylate (66):



66

Reaction time: 10 min.

Yield: 0.140 g (83%) as light yellow solid.

MP: 147–149 °C.

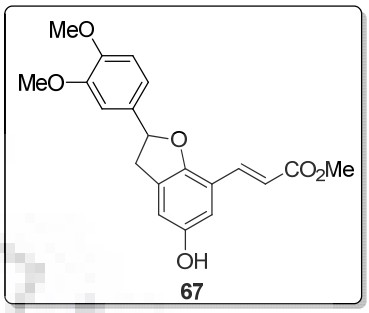
IR (KBr): ν_{max} 2963, 2869, 1680, 1554, 1420, 1371, 1350, 1280, 1209, 1168, 979, 620 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 4.5 Hz, 2H), 6.71 (d, *J* = 16.0 Hz, 1H), 5.79 (t, *J* = 9.0 Hz, 1H), 5.66 (s, 1H), 3.78 (s, 3H), 3.56 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.17 (dd, *J* = 8.0, 16.0 Hz, 1H), 2.91 (quin, *J* = 7.0 Hz, 1H), 1.25 (d, *J* = 7.0 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5 (*C*O), 153.3 (C), 150.0 (C), 148.9 (C), 140.7 (*C*H), 138.9 (C), 129.0 (C), 126.7 (*C*H), 125.8 (*C*H), 119.3 (*C*H), 116.9 (C), 114.7 (*C*H), 114.1 (*C*H), 84.9 (*C*H), 51.7 (O*C*H_3), 38.22 (*C*H_2), 33.8 (*C*H), 23.9 (2*CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{22}O_4Na$ $[M + Na]^+$: 361.1410, found: 361.1417.

Methyl (*E*)-3-(2-(3,4-dimethoxy-phenyl)-5-hydroxy-2,3-dihydro-benzofuran-7-yl)acrylate (67):



67

Reaction time: 10 min.

Yield: 0.142 g (80%) as light yellow solid.

MP: 151–153 °C.

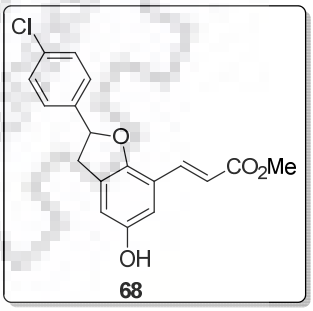
IR (KBr): ν_{max} 2963, 2843, 1639, 1559, 1421, 1330, 1283, 1250, 1177, 1024, 856, 765, 620 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 7.67 (d, *J* = 16.0 Hz, 1H), 6.95–6.91 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.76 (s, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 5.76 (t, *J* = 8.4 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.77 (s, 3H), 3.54 (dd, *J* = 9.2, 15.6 Hz, 1H), 3.17 (dd, *J* = 9.6, 17.2 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (*C*O), 153.2 (C), 150.0 (C), 149.2 (C), 149.0 (C), 140.5 (*C*H), 133.9 (C), 129.1 (C), 119.4 (*C*H), 118.3 (*C*H), 117.0 (C), 114.7 (*C*H), 114.0 (*C*H), 111.2 (*C*H), 109.0 (*C*H), 85.0 (*C*H), 55.96 (O*C*H$_3$), 55.92 (O*C*H$_3$), 51.68 (O*C*H$_3$), 38.2 (*C*H$_2$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{20}O_6Na$ $[M + Na]^+$: 379.1152, found: 379.1164.

Methyl (*E*)-3-(2-(4-chlorophenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)acrylate (68):



68

Reaction time: 15 min.

Yield: 0.102 g (62%) as light yellow solid.

MP: 178–181 °C.

IR (KBr): ν_{max} 3451, 2984, 1634, 1555, 1412, 1303, 1247, 1177, 1071, 1018, 912, 608 cm^{-1}.

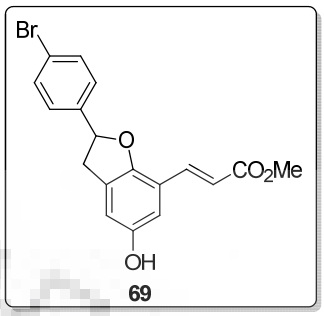
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.36–7.28 (m, 4H), 6.75 (d, *J* = 7.5 Hz, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 5.80 (t, *J* = 8.5 Hz, 1H), 5.21 (s, 1H), 3.79 (s, 3H), 3.60 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.11 (dd, *J* = 8.0, 16.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1 (*C*O), 153.0 (C), 150.1 (C), 140.1 (C), 140.1 (*C*H), 133.9 (C), 128.8 (*C*H), 128.5 (C), 127.0 (*C*H), 119.8 (C), 117.2 (*C*H), 114.6 (*C*H), 114.2 (*C*H), 84.0 (*C*H), 51.7 (O*C*H$_3$), 38.3 (*C*H$_2$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{15}O_4ClNa$ $[M + Na]^+$: 353.0551, found: 353.0550.

Methyl (*E*)-3-(2-(4-bromophenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)acrylate (69):

Reaction time: 15 min.



Yield: 0.112 g (60%) as light yellow solid.

MP: 200–202 °C.

IR (KBr): ν_{max} 3446, 2928, 1638, 1550, 1417, 1338, 1244, 1176, 1079, 979, 622 cm^{-1}.

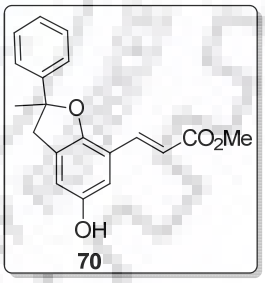
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.58 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 2.4 Hz, 2H), 6.58 (d, *J* = 16.0 Hz, 1H), 5.69 (t, *J* = 8.8 Hz, 1H), 3.70 (s, 3H), 3.51 (dd, *J* = 9.6, 16.0 Hz, 1H), 3.01 (dd, *J* = 8.0, 16.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9 (*C*O), 152.0 (C), 151.4 (C), 140.8 (*C*H), 140.4 (C), 131.5 (*C*H), 127.9 (C), 127.2 (*C*H), 121.6 (C), 119.0 (*C*H), 116.9 (C), 114.6 (*C*H), 113.9 (*C*H), 83.57 (*C*H), 51.38 (O*C*H_3), 38.16 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{18}H_{15}O_4BrNa$ $[M + Na]^+$: 397.0046, found: 397.0046.

Methyl (*E*)-3-(5-hydroxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran-7-yl)acrylate (70):

Reaction time: 10 min.



Yield: 0.130 g (84%) as light yellow solid.

MP: 119–121 °C.

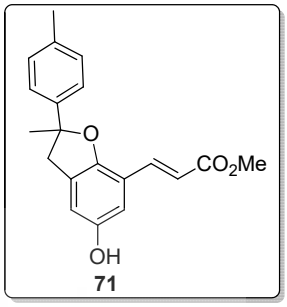
IR (KBr): ν_{max} 3441, 2987, 2852, 1686, 1555, 1445, 1377, 1298, 1203, 1097, 988, 695, 621 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 16.0 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.0 Hz, 1H), 6.81–6.76 (m, 2H), 6.70 (s, 1H), 6.31 (s, 1H), 3.81 (s, 3H), 3.32 (q, *J* = 15.5 Hz, 2H), 1.75 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7 (*C*O), 152.4 (C), 150.0 (C), 146.3 (C), 141.1 (*C*H), 128.8 (C), 128.4 (*C*H), 127.1 (*C*H), 124.3 (*C*H), 119.0 (*C*H), 117.0 (C), 115.0 (*C*H), 114.2 (*C*H), 90.5 (C), 51.8 (O*C*H_3), 44.4 (*C*H_2), 29.4 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{19}H_{19}O_5$ $[M + H]^+$: 311.1277, found: 311.1301.

Methyl (*E*)-3-(5-hydroxy-2-methyl-2-*p*-tolyl-2,3-dihydrobenzofuran-7-yl)acrylate (71):



71

Reaction time: 10 min.

Yield: 0.144 g (89%) as light yellow solid.

MP: 159–161 °C.

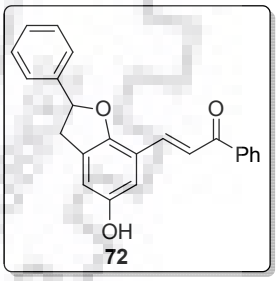
IR (KBr): ν_{max} 3442, 2984, 2854, 1631, 1556, 1297, 1206, 1172, 1028, 865, 695, 622 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 16.0 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 16.0 Hz, 1H), 6.77 (d, *J* = 2.0 Hz, 1H), 6.71 (d, *J* = 2.0 Hz, 1H), 3.82 (s, 3H), 3.32 (q, *J* = 15.5 Hz, 2H), 2.33 (s, 3H), 1.76 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8 (*C*O), 152.5 (C), 150.0 (C), 143.3 (C), 141.1(*C*H), 136.8 (C), 129.0 (*C*H), 128.9 (C), 124.3 (*C*H), 119.0 (*C*H), 117.0 (C), 115.0 (*C*H), 114.1 (*C*H), 90.5 (C), 51.7 (O*C*H_3), 44.4 (*C*H_2), 29.4 (*C*H_3), 20.9 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{20}H_{20}O_4Na$ $[M + Na]^+$: 347.1254, found: 347.1254.

(*E*)-3-(5-Hydroxy-2-phenyl-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (72):



72

Reaction time: 10 min.

Yield: 0.118 g (69%) as light yellow solid.

MP: 174–177 °C.

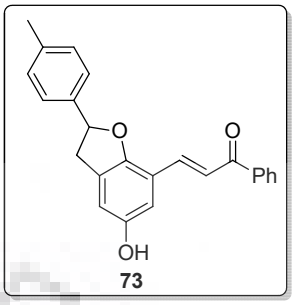
IR (KBr):ν_{max} 3431, 2975, 2845, 1647, 1563, 1420, 1370, 1270, 1338, 1173, 1088, 976, 694, 610 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 8.60 (d, *J* = 13.6 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 2H), 7.88–7.74 (m, 2H), 7.57–7.54 (m, 1H), 7.50–7.33 (m, 6H), 7.32 (d, *J* = 7.2 Hz, 1H), 6.85 (s, 1H), 6.80 (s, 1H), 5.90 (t, *J* = 8.0 Hz, 1H), 3.64 (dd, *J* = 10.4, 15.6 Hz, 1H), 3.16 (dd, *J* = 7.6, 15.6 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 191.0 (*C*O), 152.7 (C), 151.6 (C), 141.9 (C), 140.7 (*C*H), 138.3 (C), 132.6 (*C*H), 128.6 (*C*H), 128.5 (*C*H), 128.4 (*C*H), 127.9 (*C*H), 125.4 (*C*H), 123.5 (*C*H), 117.5 (C), 115.2 (*C*H), 114.4 (*C*H), 84.4 (*C*H), 38.3 (*C*H_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{18}O_3Na$ $[M + Na]^+$: 365.1148, found: 365.1165.

(*E*)-3-(5-Hydroxy-2-(4-methylphenyl)-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (73):



73

Reaction time: 10 min.

Yield: 0.119 g (67%) as light yellow solid.

MP: 159–161 °C.

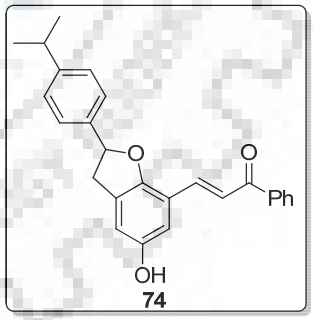
IR (KBr): ν_{max} 3453, 2993, 2837, 1642, 1560, 1424, 1350, 1244, 1024, 968, 782, 616 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.92 (d, *J* = 15.5 Hz, 1H), 7.82 (d, *J* = 16.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 6.80 (s, 1H), 6.08 (s, 1H), 5.88 (t, *J* = 8.5 Hz, 1H), 3.60 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.16 (dd, *J* = 8.0, 16.0 Hz, 1H), 2.36 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6 (*C*O), 153.6 (C), 150.3 (C), 141.1 (C), 138.8 (*C*H), 138.2 (C), 137.8 (C), 132.8 (*C*H), 129.3 (*C*H), 129.0 (*C*H), 128.6 (*C*H), 125.4 (*C*H), 123.9 (*C*H), 117.6 (C), 115.3 (*C*H), 115.1 (*C*H), 84.80 (*C*H), 38.19 (CH_2), 21.14 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{20}O_3Na$ $[M + Na]^+$: 379.1305, found: 379.1302.

(*E*)-3-(5-Hydroxy-2-(4-isopropylphenyl)-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (74):



74

Reaction time: 10 min.

Yield: 0.134 g (70%) as yellow viscous liquid.

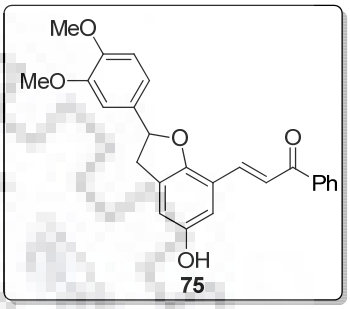
IR (KBr): ν_{max} 3444, 2978, 1645, 1559, 1464, 1417, 1370, 1308, 1167, 1079, 1017, 778, 605 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.93 (d, *J* = 15.5 Hz, 1H), 7.83 (d, *J* = 15.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 2.0 Hz, 1H), 6.81 (s, 1H), 6.64 (s, 1H), 5.87 (t, *J* = 8.5 Hz, 1H), 3.58 (dd, *J* = 9.5, 15.5 Hz, 1H), 3.16 (dd, *J* = 8.0, 16.0 Hz, 1H), 2.90 (quin, *J* = 7.0 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7 (*C*O), 153.5 (C), 150.4 (C), 148.8 (C), 141.3 (*C*H), 139.1 (C), 138.1 (C), 132.8 (*C*H), 129.0 (*C*H), 128.6 (*C*H), 128.6 (C), 126.7 (*C*H), 125.4 (*C*H), 123.8 (*C*H), 117.6 (C), 115.3 (*C*H), 115.1 (*C*H), 84.74 (*C*H), 38.12 (CH_2), 33.82 (*C*H), 23.94 (2**C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{24}O_3Na$ $[M + Na]^+$: 407.1618, found: 407.1615.

(*E*)-3-(2-(3,4-Dimethoxyphenyl)-5-hydroxy-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (75):



75

Reaction time: 10 min.

Yield: 0.144 g (72%) as yellow solid.

MP: 168–170 °C.

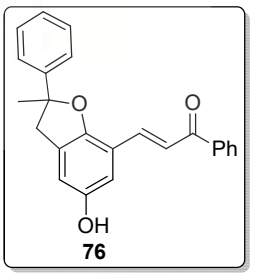
IR (KBr): ν_{max} 3447, 2987, 2834, 1641, 1559, 1415, 1359, 1288, 1135, 1026, 770, 626 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.88 (d, *J* = 15.5 Hz, 1H), 7.78 (d, *J* = 15.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 6.0 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 6.79 (s, 1H), 5.84 (t, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.58 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.19 (dd, *J* = 8.5, 16.5 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7 (*C*O), 153.4 (C), 150.4 (C), 149.1 (C), 148.9 (C), 141.2 (*C*H), 138.1 (C), 134.0 (C), 132.9 (*C*H), 129.1 (*C*H), 128.6 (*C*H), 128.6 (*C*H), 123.7 (*C*H), 118.0 (C), 117.6 (C), 115.2 (*C*H), 115.1 (*C*H), 111.2 (*C*H), 108.8 (*C*H), 84.91 (*C*H), 55.94 (O*C*H_3), 55.89 (O*C*H_3), 38.08 (CH_2) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{22}O_5Na$ $[M + Na]^+$: 425.1359, found: 425.1379.

(*E*)-3-(5-Hydroxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (76):



76

Reaction time: 5 min.

Yield: 0.133 g (75%) as yellow solid.

MP: 168–170 °C.

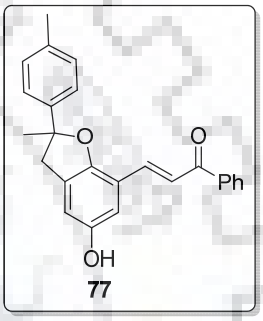
IR (KBr): ν_{max}:3450, 2959, 2830, 1641, 1552, 1451, 1333, 1140, 1028, 774, 620 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.5 Hz, 2H), 8.00 (d, *J* = 15.0 Hz, 1H), 7.87 (d, *J* = 15.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.50–7.47 (m, 4H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.94 (s, 1H), 6.76 (s, 1H), 3.38 (q, *J* = 16.0 Hz, 2H), 1.83 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8 (*C*O), 152.7 (C), 150.3 (C), 146.4 (C), 141.5 (*C*H), 138.2 (C), 132.9 (C), 130.1 (*C*H), 128.9 (*C*H), 128.6 (*C*H), 128.4 (*C*H), 127.2 (*C*H), 124.3 (*C*H), 123.5 (*C*H), 117.7 (C), 115.4 (*C*H), 115.1 (*C*H), 90.63 (C), 44.29 (CH_2), 29.69 (CH_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{20}O_3Na$ $[M + Na]^+$: 379.1305, found: 379.1317.

(*E*)-3-(5-Hydroxy-2-methyl-2-*p*-tolyl-2,3-dihydrobenzofuran-7-yl)-1-phenylprop-2-en-1-one (77):



77

Reaction time: 5 min.

Yield: 0.146 g (79%) as yellow viscous solid.

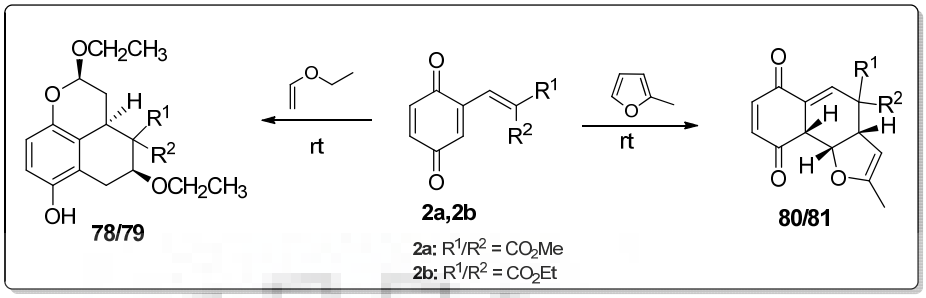
IR (KBr): ν_{max} 3451, 2978, 1643, 1553, 1461, 1373, 1297, 1170, 1073, 1011, 773, 612 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06–8.03 (m, 2H), 8.01 (s, 1H), 7.89 (d, *J* = 17.0 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 6.76 (s, 1H), 6.46 (s, 1H), 3.36 (q, *J* = 16.0 Hz, 2H), 2.34 (s, 3H), 1.81 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6 (*C*O), 152.8 (C), 150.2 (C), 143.5 (C), 141.4 (*C*H), 138.3 (C), 136.8 (C), 132.8 (*C*H), 129.1 (*C*H), 129.0 (C), 128.9 (*C*H), 128.6 (*C*H), 124.3 (*C*H), 123.6 (*C*H), 117.7 (C), 115.4 (*C*H), 115.2 (*C*H), 90.67 (C), 44.32 (CH_2), 29.69 (CH_3), 20.96 (CH_3) ppm.

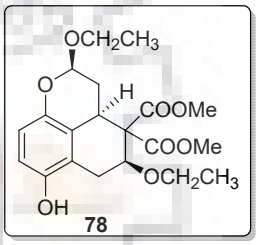
HRMS (ESI+): *m/z* calcd for $C_{25}H_{22}O_3H$ $[M + H]^+$: 371.1641, found: 371.1637.

3.2.5. General procedure for the synthesis of tricyclic compounds 78–81:



A mixture of **4i/4j** (10.0 mmol) and alkenyl *p*-benzoquinone **2a**/**2b** (1.0 mmol) was stirred at room temperature. Then about 5 mL of hexane was added to the reaction mixture and the flask was kept at 0 °C for 30 min. During this period a solid was formed and it was filtered to afford pure tricyclic products **78**–**81** [212].

Dimethyl 2,5-diethoxy-7-hydroxy-3,3*a*,5,6-tetrahydrobenzo[*de*]chromene-4,4(2*H*) dicarboxylate (78):



Reaction time: 12 h.

Yield: 263 mg (67%) as cream white solid.

MP: 216–218 °C.

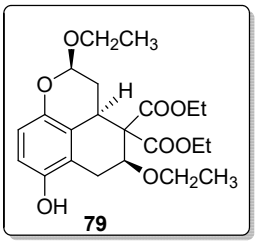
IR (KBr) ν_{max}: 3464, 1610, 1339, 1250, 1148, 1073, 810 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.58, 6.55 (ABq, 2H, J_{AB} = 8.75), 5.09 (dd, *J* = 2.5, 9.5 Hz, 1H), 4.50 (s, 1H), 4.15 (dd, *J* = 6.5, 10.0 Hz, 1H), 4.10–4.03 (m, 1H), 3.82 (s, 3H), 3.79–3.73 (m, 1H), 3.68–3.64 (m, 1H), 3.62 (s, 3H), 3.59–3.50 (m, 2H), 3.20 (dd, *J* = 6.5, 17.0 Hz, 1H), 2.89 (dd, *J* = 10.5, 17.5 Hz, 1H), 2.39 (dt, *J* = 9.5, 13.0 Hz, 1H), 2.04 (qd, *J* = 2.5, 13.0 Hz, 1H), 1.28 (t, *J* =7.0 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.0 (*C*O), 168.0 (*C*O), 146.9, (C), 146.7 (C), 120.5 (C), 119.5 (C), 114.6 (*C*H), 114.4 (*C*H), 100.4 (*C*H), 79.6 (*C*H), 66.2 (CH_2), 64.5 (CH_2), 61.1 (C), 52.9 (OCH_3), 52.1 (OCH_3), 39.9 (*C*H), 30.4 (CH_2), 28.5 (CH_2), 15.5 (CH_3), 15.2 (CH_3) ppm.

HRMS (ESI-TOF): *m/z* $[M + Na]^+$calcd for $C_{20}H_{26}O_8Na$ 417.1519; found 417.1524.

Diethyl 2,5-diethoxy-7-hydroxy-3,3*a*,5,6-tetrahydrobenzo[*de*]chromene-4,4(2*H*)dicarboxylate (79):



Reaction time: 8 h.

Yield: 253 mg (60%) as cream white solid.

MP: 136–138 °C.

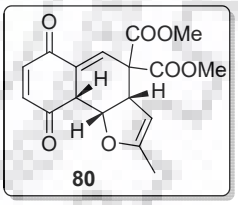
IR (KBr) ν_{max}: 3446, 1613, 1461, 1376, 1253, 1150, 1075, 811 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.56, 6.54 (ABq, 2H, J_{AB} = 8.7 Hz), 5.08 (dd, *J* = 2.5, 9.5 Hz, 1H), 4.98 (s, 1H), 4.34–4.22 (m, 2H), 4.17–4.10 (m, 2H), 4.09–4.02 (m, 2H), 3.79–3.71 (m, 1H), 3.68–3.61 (m, 1H), 3.57–3.48 (m, 2H), 3.18 (dd, *J* = 6.5, 17.0 Hz, 1H), 2.91 (dd, *J* = 10.0, 17.0 Hz, 1H), 2.40 (dt, *J* = 9.5, 12.5 Hz, 1H), 2.06 (qd, *J* = 2.5, 12.5 Hz, 1H), 1.33–1.25 (m, 6H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.7 (*C*O), 167.5 (*C*O), 147.3, (C), 146.4 (C), 120.7 (C), 119.6 (C), 114.4 (*C*H), 114.3 (*C*H), 100.4 (*C*H), 79.8 (*CH*), 66.1 (CH_2), 64.6 (CH_2), 62.0 (CH_2), 60.9 (CH_2), 39.8 (*C*H), 30.4 (CH_2), 28.6 (CH_2), 15.4 (CH_3), 15.2 (CH_3), 14.1 (CH_3), 13.8 (CH_3) ppm.

HRMS (ESI-TOF): *m/z* $[M + Na]^+$calcd for $C_{22}H_{30}O_8Na$ 445.1832; found 445.1828.

Dimethyl 2-methyl-6,9-dioxo-6,9,9*a*,9*b*-tetrahydronaphtho[1,2-*b*]furan-4,4(3a*H*)dicarboxylate (80):



Reaction time: 5 h.

Yield: 258 mg (78%) as yellow solid.

MP: 134–136 °C.

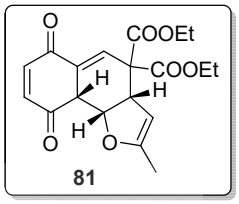
IR (KBr) ν_{max}: 2956, 2852, 1731, 1684, 1219, 1121, 1073, 1018, 725 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.59 (q, *J* = 1.0 Hz, 1H), 6.95, 6.87 (ABq, 2H, J_{AB} = 10.5 Hz), 5.75 (dd, *J* = 4.0, 10.0 Hz, 1H), 4.24 (d, *J* = 10.0 Hz, 1H), 4.12 (q, *J* = 1.0 Hz, 1H), 3.84 (s, 3H), 3.68 (s, 3H), 3.61 (t, *J* = 3.5 Hz, 1H), 1.59 (t, *J* = 1.5 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.7 (*C*O), 183.0 (*C*O), 168.1 (*C*O), 167.1 (*C*O), 158.5 (C), 142.3 (*C*H), 141.4 (*C*H), 136.2 (*C*H), 132.6 (*C*), 94.2 (*C*H), 80.6 (*C*H), 58.6 (*C*), 53.5 (CH_3), 53.1 (CH_3), 47.8 (*C*H), 47.4 (*C*H), 13.2 (CH_3) ppm

HRMS (ESI-TOF): *m/z* $[M + Na]^+$calcd for $C_{17}H_{16}O_7Na$ 355.0788; found 355.0790.

Diethyl 2-methyl-6,9-dioxo-6,9,9*a*,9*b*-tetrahydronaphtho[1,2-*b*]furan-4,4(3a*H*)dicarcarboxylate (81):



81

Reaction Time: 4 h.

Yield: 270 mg (75%) as yellow solid.

MP: 202–204 °C.

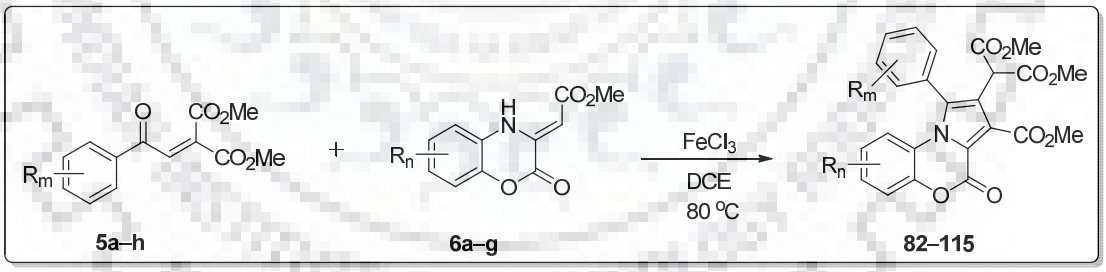
IR (KBr) ν_{max}: 2978, 2930, 1727, 1681, 1251, 1203, 1085, 1013, 730 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.60 (d, *J* = 3.0 Hz, 1H), 6.95, 6.86 (ABq, 2H, J_{AB} = 10.5 Hz), 5.75 (dd, *J* = 4.0, 10.0 Hz, 1H), 4.37–4.26 (m, 2H), 4.25–4.17 (m, 2H), 4.16–4.14 (m, 1H), 4.04 (qd, *J* = 7.0, 18.5 Hz, 1H), 3.63 (t, *J* = 3.0 Hz, 1H), 1.59 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.8 (*C*O), 183.1 (*C*O), 167.6 (*C*O), 166.6 (*C*O), 158.3 (C), 142.4 (*C*H), 141.3 (*C*H), 136.6 (*C*H), 132.4 (*C*), 94.3 (*C*H), 80.7 (*C*H), 62.5 (CH_2), 62.0 (CH_2), 58.8 (*C*), 47.6 (*C*H), 47.5 (*C*H), 14.0 (CH_3), 13.8 (CH_3), 13.2 (CH_3) ppm.

HRMS (ESI-TOF): *m/z* $[M + Na]^+$calcd for $C_{19}H_{20}O_7Na$ 383.1101; found 383.1110.

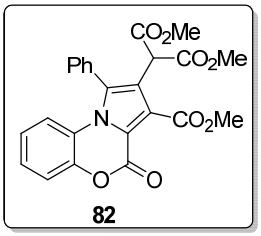
3.2.6. General experimental procedure for the synthesis of pyrrolobenzoxazine derivatives 82–115.



5a–h **6a–g** **82–115**

To a mixture of benzoylmethylidene malonate **5** (0.25 mmol) and benzoxazinone **6** (0.3 mmol) in 2 mL of DCE, was added $FeCl_3$ (0.25 mmol) and the contents were stirred at 80 °C for appropriate time. The reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated under reduced pressure, the crude product was purified by column chromatography on silica gel (100–200 mesh) using 10–40% ethyl acetate in hexanes to afford pyrrolobenzoxazine **3** as a light yellow solid.

Dimethyl 2-(3-(methoxycarbonyl)-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]-oxazin-2-yl)-malonate (82):



82

Reaction time: 3 h.

Yield: 0.095 g (85%) as light yellow solid.

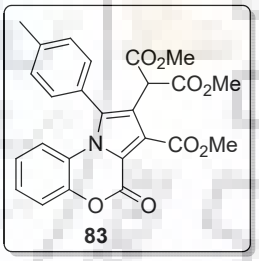
MP: 197–199 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64–7.56 (m, 3H), 7.45 (d, *J* = 6.8 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 4.54 (s, 1H), 3.93 (s, 3H), 3.69 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 163.9 (*C*O), 151.7 (*C*O), 143.2 (C), 134.4 (C), 130.7 (*C*H), 130.6 (*C*H), 129.6 (*C*H), 129.4 (C), 126.8 (*C*H), 124.1 (*C*H), 122.7 (C), 122.5 (C), 120.0 (C), 118.2 (*C*H), 116.9 (*C*H), 116.3 (C), 52.8 (2*O*C*H$_3$), 52.3 (O*C*H$_3$), 48.4 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{19}NO_8Na$ $[M + Na]^+$: 472.1003, found: 472.0980.

Dimethyl 2-(3-(methoxycarbonyl)-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)-malonate (83):



83

Reaction time: 2 h.

Yield: 0.099 g (86%) as light yellow solid.

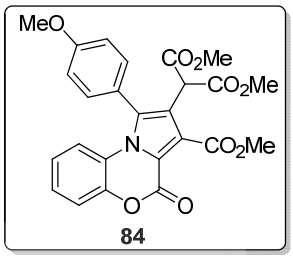
MP: 180–182 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.30 (m, 5H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.85 (t, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.53 (s, 1H), 3.92 (s, 3H), 3.69 (s, 6H), 2.50 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7 (2**C*O), 164.0 (*C*O), 151.8 (*C*O), 143.3 (C), 140.8 (C), 134.7 (C), 130.5 (*C*H), 130.3 (*C*H), 126.7 (C), 126.4 (*C*H), 124.1 (*C*H), 122.7 (C), 122.7 (C), 120.0 (C), 118.2 (*C*H), 117.0 (C), 116.2 (*C*H), 52.8 (2*O*C*H$_3$), 52.3 (O*C*H$_3$), 48.5 (*C*H), 21.5 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_8Na$ $[M + Na]^+$: 486.1159, found: 486.1135.

Dimethyl 2-(3-(methoxycarbonyl)-1-(4-methoxyphenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (84):



84

Reaction time: 30 min.

Yield: 0.110 g (92%) as light yellow solid.

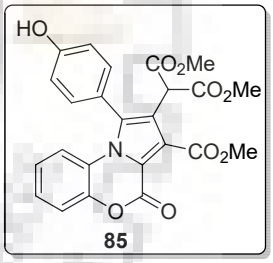
MP: 153–155 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.31 (m, 3H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.87 (t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 4.57 (s, 1H), 3.93 (s, 6H), 3.71 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 163.9 (*C*O), 161.0 (C), 151.7 (*C*O), 143.2 (C), 134.4 (C), 132.0 (*C*H), 126.7 (*C*H), 124.1 (*C*H), 122.6 (C), 122.5 (C), 121.0 (C), 120.1 (*C*H), 118.1 (*C*H), 116.9 (C), 114.9 (*C*H), 55.3 (O*C*H$_3$), 52.8 (2*O*C*H$_3$), 52.2 (O*C*H$_3$), 48.4 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_9Na$ $[M + Na]^+$: 502.1108, found: 502.1106.

Dimethyl 2-(1-(4-hydroxyphenyl)-3-(methoxycarbonyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (85):



85

Reaction time: 30 min.

Yield: 0.087 g (75%) as light yellow solid.

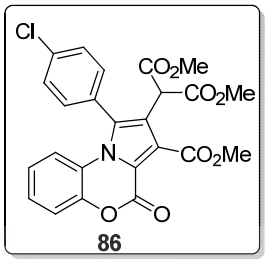
MP: 207–209 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.45 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.06–7.04 (m, 3H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.72–6.65 (m, 2H), 4.39 (s, 1H), 3.72 (s, 3H), 3.52 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$ + DMSO-d_6, 100 MHz): δ 167.8 (2**C*O), 164.0 (*C*O), 159.5 (C), 152.0 (*C*O), 143.2 (C), 135.3 (C), 131.9 (*C*H), 126.8 (*C*H), 124.3 (*C*H), 122.7 (C), 122.5 (C), 120.1 (C), 119.4 (C), 118.1 (*C*H), 117.2 (*C*H), 116.8 (*C*H), 115.9 (C), 52.9 (2*O*C*H$_3$), 52.3 (O*C*H$_3$), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{19}NO_9Na$ $[M + Na]^+$: 488.0952, found: 488.0940.

Dimethyl 2-(1-(4-chlorophenyl)-3-(methoxycarbonyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (86):



86

Reaction time: 1 h.

Yield: 0.094 g (78%) as light yellow solid.

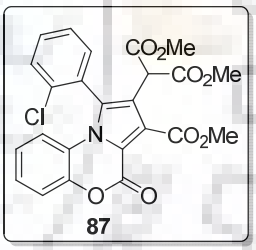
MP: 125–127 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.25–7.19 (m, 1H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.51 (s, 1H), 3.92 (s, 3H), 3.68 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.8 (*C*O), 151.6 (*C*O), 143.3 (C), 137.0 (C), 132.9 (C), 132.2 (*C*H), 129.9 (*C*H), 127.9 (C), 127.0 (*C*H), 124.3 (*C*H), 122.8 (C), 122.5 (C), 120.3 (C), 118.5 (*C*H), 116.8 (*C*H), 116.6 (C), 52.9 (2*O*CH_3), 52.5 (O*CH_3), 48.4 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{18}O_8NClNa$ $[M + Na]^+$: 506.0613, found: 506.0619.

Dimethyl 2-(1-(2-chlorophenyl)-3-(methoxycarbonyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (87):



87

Reaction time: 2 h.

Yield: 0.082 g (68%) as light yellow solid.

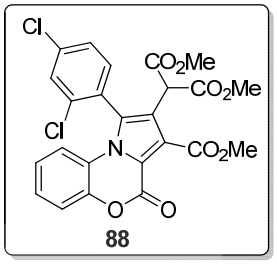
MP: 148–150 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61–7.49 (m, 3H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.26–7.20 (m, 2H), 6.88 (t, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 9.2 Hz, 1H), 4.43 (s, 1H), 3.94 (s, 3H), 3.73 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (*C*O), 167.3 (*C*O), 163.9 (*C*O), 151.7 (*C*O), 143.1 (C), 136.1 (C), 132.9 (*C*H), 132.3 (*C*H), 131.1 (C), 130.4 (*C*H), 128.9 (C), 127.9 (*C*H), 127.0 (*C*H), 124.6 (*C*H), 122.7 (C), 122.7 (C), 120.6 (C), 118.5 (*C*H), 116.9 (C), 115.6 (*C*H), 52.9 (2*O*CH_3), 52.4 (O*CH_3), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{18}ClNO_8Na$ $[M + Na]^+$: 506.0613, found: 506.0607.

Dimethyl 2-(1-(2,4-dichlorophenyl)-3-(methoxycarbonyl)-4-oxo-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (88):



88

Reaction time: 2 h.

Yield: 0.085 g (66%) as light yellow solid.

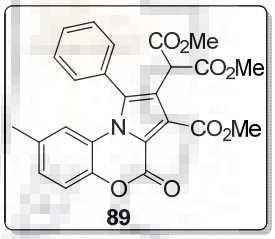
MP: 125–126 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63 (s, 1H), 7.54–7.48 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.27–7.23 (m, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.42 (s, 1H), 3.93 (s, 3H), 3.73 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.4 (*C*O), 167.3 (*C*O), 163.8 (*C*O), 151.6 (*C*O), 143.1 (C), 138.0 (C), 137.0 (C), 133.8 (*C*H), 130.5 (*C*H), 129.7 (C), 128.5 (*C*H), 127.4 (*C*H), 124.7 (*C*H), 122.8 (C), 122.6 (C), 120.8 (C), 118.7 (*C*H), 117.1 (C), 115.4 (*C*H), 52.9 (2*O*C*H$_3$), 52.5 (O*C*H$_3$), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{17}Cl_2NO_8Na$ $[M + Na]^+$: 540.0223, found: 540.0236.

Dimethyl 2-(3-(methoxycarbonyl)-8-methyl-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (89):



89

Reaction time: 2 h.

Yield: 0.096 g (83%) as light yellow solid.

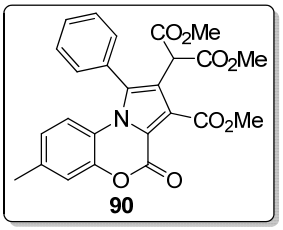
MP: 186–188 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65–7.56 (m, 3H), 7.44 (d, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.35 (s, 1H), 4.56 (s, 1H), 3.92 (s, 3H), 3.69 (s, 6H), 1.97 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 164.0 (*C*O), 151.9 (*C*O), 141.1 (C), 134.2 (C), 133.9 (C), 130.8 (*C*H), 130.4 (*C*H), 129.5 (*C*H), 129.4 (C), 127.4 (*C*H), 122.5 (C), 122.0 (C), 119.6 (C), 117.7 (*C*H), 117.4 (*C*H), 116.3 (C), 52.8 (2*O*C*H$_3$), 52.3 (O*C*H$_3$), 48.5 (*C*H), 20.9 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_8Na$ $[M + Na]^+$: 486.1159, found: 486.1136.

Dimethyl 2-(3-(methoxycarbonyl)-7-methyl-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-d][1,4]oxazin-2-yl)malonate (90):



90

Reaction time: 2 h.

Yield: 0.099 g (86%) as light yellow solid.

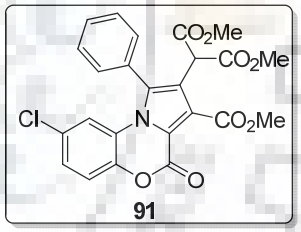
MP: 179–181 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63–7.54 (m, 3H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.12 (s, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 4.54 (s, 1H), 3.92 (s, 3H), 3.68 (s, 6H), 2.29 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 164.0 (*C*O), 151.9 (*C*O), 143.1 (C), 137.3 (C), 134.1 (C), 130.8 (*C*H), 130.5 (*C*H), 129.5 (*C*H), 124.9 (*C*H), 122.4 (C), 120.2 (C), 119.7 (C), 118.3 (*C*H), 116.6 (*C*H), 116.1 (C), 52.8 (2*O*CH_3), 52.3 (O*C*H_3), 48.5 (*C*H), 20.64 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_8Na$ $[M + Na]^+$: 486.1159, found: 486.1151.

Dimethyl 2-(8-chloro-3-(methoxycarbonyl)-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (91):



91

Reaction time: 2 h.

Yield: 0.099 g (82%) as light yellow solid.

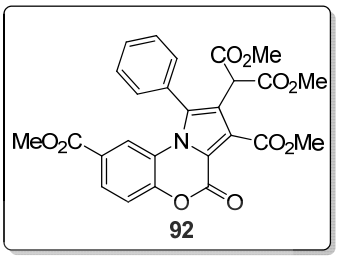
MP: 179–180 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69–7.60 (m, 3H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.28–7.26 (m, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 6.56 (s, 1H), 4.57 (s, 1H), 3.94 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.7 (*C*O), 151.2 (*C*O), 141.9 (C), 134.7 (C), 130.9 (*C*H), 130.7 (*C*H), 129.8 (*C*H), 129.3 (C), 128.8 (C), 126.8 (*C*H), 123.3 (C), 123.1 (C), 120.3 (C), 119.3 (*C*H), 117.3 (*C*H), 116.1 (C), 52.9 (2*O*CH_3), 52.5 (O*C*H_3), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{18}NO_8ClNa$ $[M + Na]^+$: 506.0613, found: 506.0611.

Dimethyl 2-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazine-3,8-dicarboxylate (92):



92

Reaction time: 2 h.

Yield: 0.112 g (89%) as light yellow solid.

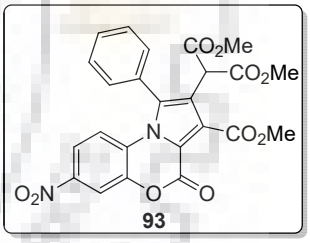
MP: 175–176 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.72–7.61 (m, 3H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 9.2 Hz, 2H), 4.59 (s, 1H), 3.94 (s, 3H), 3.72 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 164.8 (*C*O), 163.7 (*C*O), 151.0 (*C*O), 146.3 (C), 135.0 (C), 130.6 (*C*H), 129.8 (*C*H), 128.9 (C), 127.9 (*C*H), 126.0 (C), 123.2 (C), 122.3 (C), 120.3 (C), 118.9 (*C*H), 118.2 (*C*H), 115.9 (C), 52.9 (2*O*CH_3), 52.4 (O*C*H_3), 52.1 (O*C*H_3), 48.4 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{21}NO_{10}Na$ $[M + Na]^+$: 530.1057, found: 530.1055.

Dimethyl 2-(3-(methoxycarbonyl)-7-nitro-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (93):



93

Reaction time: 3 h.

Yield: 0.092 g (75%) as light yellow solid.

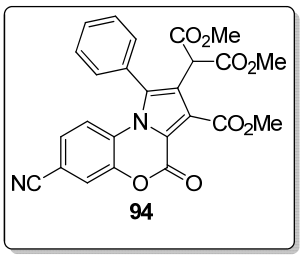
MP: 161–163 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.20 (s, 1H), 7.75–7.60 (m, 4H), 7.45 (d, *J* = 7.2 Hz, 2H), 6.80 (d, *J* = 9.2 Hz, 1H), 4.54 (s, 1H), 3.95 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3 (2**C*O), 163.4 (*C*O), 150.4 (*C*O), 144.8 (C), 143.2 (C), 135.4 (C), 131.2 (*C*H), 130.6 (*C*H), 130.0 (*C*H), 128.5 (C), 127.2 (C), 124.4 (C), 121.4 (C), 119.3 (*C*H), 117.4 (*C*H), 116.0 (C), 114.1 (*C*H), 53.0 (2*O*CH_3), 52.6 (O*C*H_3), 48.3 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{18}N_2O_{10}Na$ $[M + Na]^+$: 517.0853, found: 517.0835.

Dimethyl 2-(7-cyano-3-(methoxycarbonyl)-4-oxo-1-phenyl-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (94):



94

Reaction time: 2 h.

Yield: 0.092 g (78%) as light yellow solid.

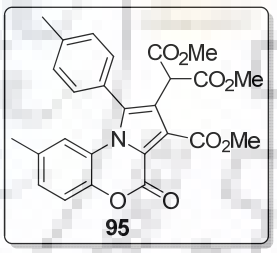
MP: 201–203 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67–7.60 (m, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 1H), 7.02–6.97 (m, 1H), 6.74 (d, *J* = 9.2 Hz, 1H), 6.61 (d, *J* = 8.0 Hz, 1H), 4.53 (s, 1H), 3.94 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 167.4 (2**C*O), 163.5 (*C*O), 150.4 (*C*O), 143.3 (C), 135.2 (C), 131.1 (*C*H), 130.6 (*C*H), 129.9 (*C*H), 128.7 (C), 128.0 (C), 127.8 (*C*H), 126.1 (C), 124.2 (C), 122.1 (*C*H), 117.8 (*C*H), 116.8 (C), 116.1 (C), 110.2 (*C*N), 53.0 (O*C*H_3), 52.9 (O*C*H_3), 52.6 (O*C*H_3), 48.4 (*C*H).

HRMS (ESI+): *m/z* calcd for $C_{25}H_{18}N_2O_8Na$ $[M + Na]^+$: 497.0955 , found: 497.0977.

Dimethyl 2-(3-(methoxycarbonyl)-8-methyl-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (95):



95

Reaction time: 1.5 h.

Yield: 0.095 g (80%) as light yellow solid.

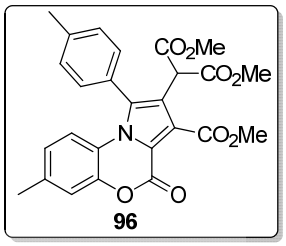
MP: 202–204 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.44 (s, 1H), 4.55 (s, 1H), 3.92 (s, 3H), 3.69 (s, 6H), 2.50 (s, 3H), 1.99 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 164.0 (*C*O), 151.9 (*C*O), 141.1 (C), 140.7 (C), 134.5 (C), 133.8 (C), 130.6 (*C*H), 130.0 (*C*H), 127.3 (*C*H), 126.4 (C), 122.4 (C), 122.1 (C), 119.7 (C), 117.6 (*C*H), 117.4 (*C*H), 116.2 (C), 52.7 (2*O*CH_3), 52.2 (O*C*H_3), 48.5 (*C*H), 21.4 (*C*H_3), 20.9 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{23}NO_8Na$ $[M + Na]^+$: 500.1315, found: 500.1327.

Dimethyl 2-(3-(methoxycarbonyl)-7-methyl-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (96):



96

Reaction time: 1.5 h.

Yield: 0.098 g (82%) as light yellow solid.

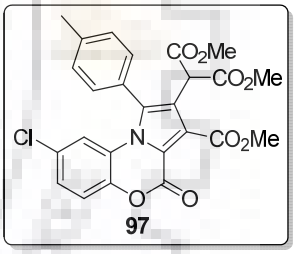
MP: 176–177 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35 (d, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.12 (s, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 4.53 (s, 1H), 3.92 (s, 3H), 3.69 (s, 6H), 2.49 (s, 3H), 2.29 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7 (2**C*O), 164.0 (*C*O), 152.0 (*C*O), 143.2 (C), 140.6 (C), 137.2 (C), 134.4 (C), 130.5 (*C*H), 130.2 (*C*H), 126.4 (C), 124.9 (*C*H), 122.4 (C), 120.3 (C), 119.7 (C), 118.3 (*C*H), 116.7 (*C*H), 116.0 (C), 52.7 (2*O*C*H_3), 52.2 (O*C*H_3), 48.5 (*C*H), 21.5 (*C*H_3), 20.7 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{23}NO_8Na$ $[M + Na]^+$: 500.1315, found: 500.1323.

Dimethyl 2-(8-chloro-3-(methoxycarbonyl)-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (97):



97

Reaction time: 40 min.

Yield: 0.105 g (85%) as light yellow solid.

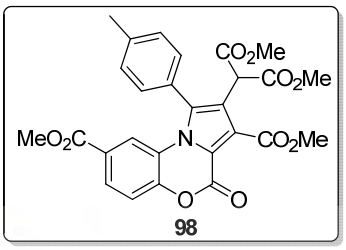
MP: 186–187 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 6.63 (s, 1H), 4.54 (s, 1H), 3.91 (s, 3H), 3.68 (s, 6H), 2.50 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.8 (*C*O), 151.2 (*C*O), 141.8 (C), 141.2 (C), 134.9 (C), 130.4 (*C*H), 130.4 (*C*H), 129.2 (C), 126.7 (*C*H), 125.6 (C), 123.2 (C), 123.2 (C), 120.3 (C), 119.2 (*C*H), 117.3 (*C*H), 116.0 (C), 52.8 (2*O*C*H_3), 52.4 (O*C*H_3), 48.5 (*C*H), 21.5 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}NO_8ClNa$ $[M + Na]^+$: 520.0769, found: 520.0777.

Dimethyl 2-(1,3-dimethoxy-1,3-di-oxopropan-2-yl)-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrr-olo[1,2-*d*][1,4]-oxazine-3,8-dicarboxylate (98):



98

Reaction time: 1.5 h.

Yield: 0.117 g (90%) as light yellow solid.

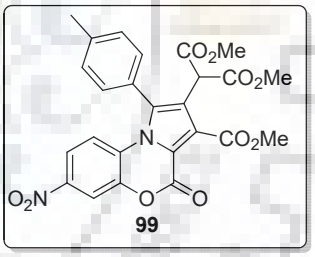
MP: 176–177 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.87 (d, *J* = 8.4 Hz, 1H), 7.45–7.43 (m, 3H), 7.38–7.27 (m, 3H), 4.60 (s, 1H), 3.94 (s, 3H), 3.73 (s, 3H), 3.71 (s, 6H), 2.55 (s, 3H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 167.5 (2**C*O), 164.8 (*C*O), 163.7 (*C*O), 150.9 (*C*O), 146.3 (C), 140.9 (C), 135.2 (C), 130.4 (*C*H), 130.4 (*C*H), 127.9 (*C*H), 126.0 (C), 125.8 (C), 123.2 (C), 122.3 (C), 120.2 (C), 118.8 (*C*H), 118.2 (*C*H), 115.7 (C), 52.8 (2*O*C*H$_3$), 52.3 (O*C*H$_3$), 52.0 (O*C*H$_3$), 48.4 (*C*H), 21.4 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{27}H_{23}NO_{10}Na$ $[M + Na]^+$: 544.1214, found: 544.1215.

Dimethyl 2-(3-(methoxycarbonyl)-7-nitro-4-oxo-1-(*p*-tolyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (99):



99

Reaction time: 3 h.

Yield: 0.098 g (77%) as light yellow solid.

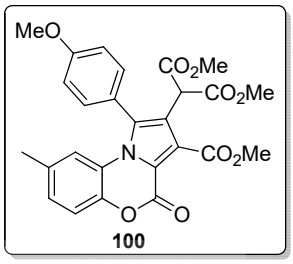
MP: 193–195 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.19 (d, *J* = 2.0 Hz, 1H), 7.75 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 1H), 4.54 (s, 1H), 3.94 (s, 3H), 3.70 (s, 6H), 2.52 (s, 3H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 167.5 (2**C*O), 163.6 (*C*O), 150.6 (*C*O), 145.0 (C), 143.4 (C), 141.7 (C), 135.8 (C), 130.8 (*C*H), 130.6 (*C*H), 127.5 (C), 125.6 (C), 124.5 (C), 121.5 (C), 119.4 (*C*H), 117.6 (*C*H), 116.0 (C), 114.2 (*C*H), 53.1 (2*O*C*H$_3$), 52.7 (O*C*H$_3$), 48.5 (*C*H), 21.7 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}N_2O_{10}Na$ $[M + Na]^+$: 531.1010, found: 531.0982.

Dimethyl 2-(3-(methoxycarbonyl)-1-(4-methoxy-phenyl)-8-methyl-4-oxo-4*H*-benzo-[*b*]-pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (100):



100

Reaction time: 30 min.

Yield: 0.116 g (94%) as light yellow solid.

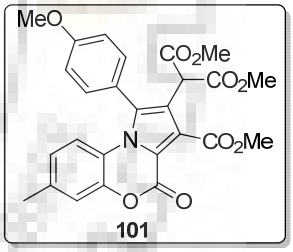
MP: 147–148 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.48 (s, 1H), 4.57 (s, 1H), 3.92 (s, 6H), 3.69 (s, 6H), 2.02 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7 (2**C*O), 164.0 (*C*O), 161.1 (C), 151.9 (*C*O), 141.1 (C), 134.3 (C), 133.8 (C), 132.1 (*C*H), 127.3 (*C*H), 122.4 (C), 122.1 (C), 121.2 (C), 119.9 (C), 117.7 (*C*H), 117.4 (*C*H), 116.1 (C), 114.8 (*C*H), 55.4 (O*C*H_3), 53.0 (2*O*C*H_3), 52.2 (O*C*H_3), 48.5 (*C*H), 21.1 (CH_3), ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{23}NO_9Na$ $[M + Na]^+$: 516.1265, found: 516.1262.

Dimethyl 2-(3-(methoxycarbonyl)-1-(4-methoxyphenyl)-7-methyl-4-oxo-4*H*-benzo[*b*]-pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (101):



101

Reaction time: 30 min.

Yield: 0.113 (92%) as light yellow solid.

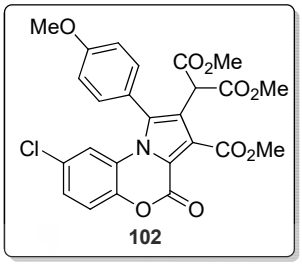
MP: 173–175 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (d, *J* = 8.8 Hz, 2H), 7.12 (s, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 1H), 6.60 (d, *J* = 8.8 Hz, 1H), 4.56 (s, 1H), 3.92 (s, 6H), 3.69 (s, 6H), 2.30 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.8 (2**C*O), 164.1 (*C*O), 161.0 (C), 152.1 (*C*O), 143.2 (C), 137.3 (C), 134.2 (C), 132.0 (*C*H), 125.0 (*C*H), 122.3 (C), 121.2 (C), 120.4 (C), 119.9 (C), 118.4 (*C*H), 116.6 (*C*H), 116.0 (C), 114.9 (*C*H), 55.4 (2*O*C*H_3), 52.9 (O*C*H_3), 52.4 (O*C*H_3), 48.5 (*C*H), 20.8 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{23}NO_9Na$ $[M + Na]^+$: 516.1265, found: 516.1262.

Dimethyl 2-(8-chloro-3-(methoxycarbonyl)-1-(4-methoxyphenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (102):



Reaction time: 30 min.

Yield: 0.112 (88%) as light yellow solid.

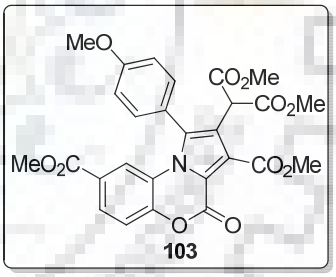
MP: 133–135 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (d, *J* = 8.8 Hz, 2H), 7.27–7.26 (m, 2H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 4.58 (s, 1H), 3.93 (s, 6H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 (2**C*O), 163.8 (*C*O), 161.4 (C), 151.3 (*C*O), 141.9 (C), 134.8 (C), 132.1 (*C*H), 129.3 (C), 126.7 (*C*H), 123.3 (C), 123.2 (C), 120.6 (C), 120.4 (C), 119.3 (*C*H), 117.3 (*C*H), 115.9 (C), 115.2 (*C*H), 55.5 (2*O*C*H$_3$), 53.0 (O*C*H$_3$), 52.5 (O*C*H$_3$), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}NO_9ClNa$ $[M + Na]^+$: 536.0718, found: 536.0703.

Dimethyl 2-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-1-(4-methoxy-phenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]-oxazine-3,8-dicarboxylate (103):



Reaction time: 30 min.

Yield: 0.120 g (90%) as light yellow solid.

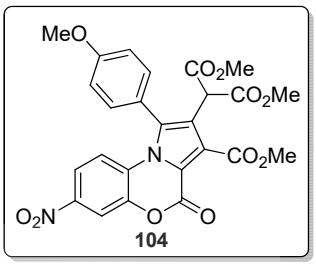
MP: 152–154 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 1H), 7.37–7.35 (m, 3H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.62 (s, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.72 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7 (2**C*O), 164.9 (*C*O), 163.8 (*C*O), 161.5 (C), 151.1 (*C*O), 146.4 (C), 135.1 (C), 132.1 (*C*H), 128.0 (*C*H), 126.1 (C), 123.2 (C), 122.4 (C), 120.6 (C), 120.5 (C), 118.9 (*C*H), 118.3 (*C*H), 115.8 (C), 115.2 (*C*H), 55.5 (2*O*C*H$_3$), 52.9 (O*C*H$_3$), 52.5 (O*C*H$_3$), 52.1 (O*C*H$_3$), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{27}H_{23}NO_{11}Na$ $[M + Na]^+$: 560.1163, found: 560.1160.

Dimethyl 2-(3-(methoxycarbonyl)-1-(4-methoxyphenyl)-7-nitro-4-oxo-4*H*-benzo[*b*]-pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (104):



Reaction time: 30 min.

Yield: 0.104 g (80%) as light yellow solid.

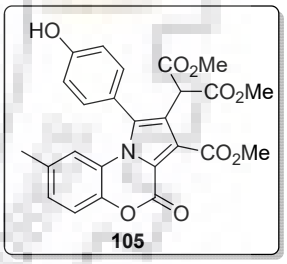
MP: 151–153 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (s, 1H), 7.63 (d, *J* = 9.2 Hz, 1H); 7.21 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 9.6 Hz, 1H), 4.40 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.55 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): 167.5 (2**C*O), 163.6 (*C*O), 161.6 (C), 150.5 (*C*O), 144.9 (C), 143.4 (C), 135.6 (C), 132.1 (*C*H), 127.5 (C), 124.4 (C), 121.6 (C), 120.2(C), 119.4 (*C*H), 117.5 (*C*H), 115.9 (*C*H), 115.5 (C), 114.1 (*C*H), 55.5 (2*O*CH_3), 53.0 (O*C*H_3), 52.7 (O*C*H_3), 48.5(*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}N_2O_{11}Na$ $[M + Na]^+$: 547.0959, found: 547.0988.

Dimethyl 2-(1-(4-hydroxyphenyl)-3-(methoxycarbonyl)-8-methyl-4-oxo-4*H*-benzo[*b*]-pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (105):



Reaction time: 30 min.

Yield: 0.092 g (77%) as light yellow solid.

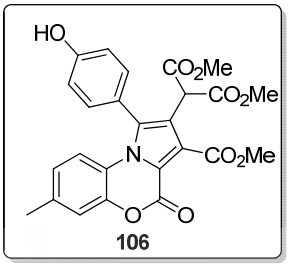
MP: 204–206 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28–7.26 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.03 (d, J = 15.6 Hz, 2H), 6.98 (d, J = 8.4 Hz, 1H), 6.52 (s, 1H), 4.60 (s, 1H), 3.92 (s, 3H), 3.70 (s, 6H), 2.02 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$ + DMSO-d_6, 100 MHz): δ 167.3 (2**C*O), 163.6 (*C*O), 159.0 (C), 151.6 (*C*O), 140.5 (C), 134.7 (C), 133.5 (C), 131.5 (*C*H), 126.9 (*C*H), 121.8 (C), 121.7 (C), 119.3 (C), 118.9 (C), 117.1 (*C*H), 116.1 (*C*H), 115.4 (C), 52.3 (2*O*CH_3), 51.7 (O*C*H_3), 48.0 (*C*H), 20.6 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_9Na$ $[M + Na]^+$: 502.1108, found: 502.1107.

Dimethyl 2-(1-(4-hydroxyphenyl)-3-(methoxycarbonyl)-7-methyl-4-oxo-4*H*-benzo[*b*]-pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (106):



Reaction time: 30 min.

Yield: 0.087 g (73%) as light yellow solid.

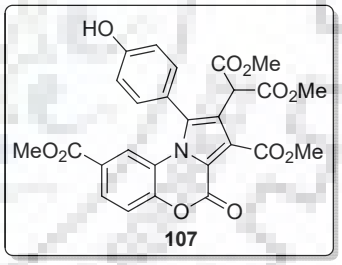
MP: 193–195 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.27 (s, 1H), 7.15 (d, *J* = 7.6 Hz, 2H), 7.04 (s, 1H), 6.97 (d, J =8.0 Hz, 2H), 6.61 (s, 2H), 4.51 (s, 1H), 3.84 (s, 3H), 3.63 (s, 6H), 2.24 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$ + DMSO-d_6, 100 MHz): δ 167.8 (2**C*O), 164.1 (*C*O), 159.4 (C), 152.1 (*C*O), 143.1 (C), 137.2 (C), 135.0 (C), 132.0 (*C*H), 125.1 (*C*H), 122.2 (C), 120.4 (C), 119.8 (C), 119.4 (C), 118.2 (*C*H), 116.9 (*C*H), 116.7 (*C*H), 115.7 (C), 52.8 (2*O*C*H_3), 52.2 (O*C*H_3), 48.5 (*C*H), 20.8 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{21}NO_9Na$ $[M + Na]^+$: 502.1108, found: 502.1080.

Dimethyl 2-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-1-(4-hydroxy-phenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]-oxazine-3,8-dicarboxylate (107):



Reaction time: 30 min.

Yield: 0.088 g (72%) as light yellow solid.

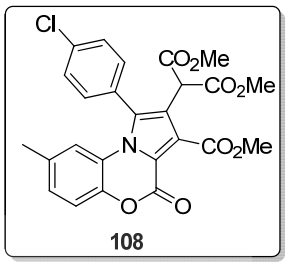
MP: 214–216 °C.

^{1}H NMR ($CDCl_3$ + DMSO-d_6, 400 MHz): δ 9.44 (s, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.39 (s, 1H), 7.26–7.22 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 4.52 (s, 1H), 3.83 (s, 3H), 3.64 (s, 3H), 3.59 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$ + DMSO-d_6, 100 MHz): δ 167.5 (2**C*O), 164.7 (*C*O), 163.5 (*C*O), 159.6 (C), 151.0 (*C*O), 146.1 (C), 135.6 (C), 131.6 (*C*H), 127.6 (*C*H), 125.9 (C), 122.8 (C), 122.2 (C), 120.0 (C), 118.9 (*C*H), 118.6 (C), 117.9 (*C*H), 116.7 (*C*H), 115.3 (C), 52.6 (2*O*C*H_3), 52.1 (O*C*H_3), 51.9 (O*C*H_3), 48.2 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{21}NO_{11}Na$ $[M + Na]^+$: 546.1001, found: 546.0974.

Dimethyl 2-(1-(4-chlorophenyl)-3-(methoxycarbonyl)-8-methyl-4-oxo-4*H*-benzo-[*b*]pyrrolo[1,2-*d*][1,4]-oxazin-2-yl)malonate (108):



108

Reaction time: 40 min.

Yield: 0.098 g (79%) as light yellow solid.

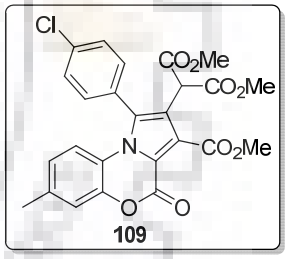
MP: 183–185 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 2H), 7.60–7.53 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 4.88 (s, 1H), 4.26 (s, 3H), 4.03 (s, 6H), 2.38 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.8 (*C*O), 151.7 (*C*O), 141.0 (C), 136.8 (C), 134.1 (C), 132.7 (C), 132.2 (*C*H), 129.7 (*C*H), 127.9 (C), 127.6 (*C*H), 122.5 (C), 121.8 (C), 119.9 (C), 117.9 (*C*H), 117.1 (*C*H), 116.6 (C), 52.8 (2*O*C*H_3), 52.3 (O*C*H_3), 48.4 (*C*H), 21.0 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}NO_8ClNa$ $[M + Na]^+$: 520.0769, found: 520.0778.

Dimethyl 2-(1-(4-chlorophenyl)-3-(methoxycarbonyl)-7-methyl-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (109):



109

Reaction time: 40 min.

Yield: 0.099 g (80%) as light yellow solid.

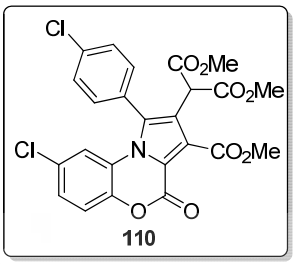
MP: 147–149 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.13 (s, 1H), 6.69 (d, *J* = 8.8 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 4.51 (s, 1H), 3.92 (s, 3H), 3.68 (s, 6H), 2.30 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.9 (*C*O), 151.9 (*C*O), 143.2 (C), 137.6 (C), 136.9 (C), 132.7 (C), 132.3 (*C*H), 129.9 (*C*H), 128.0 (C), 125.1 (*C*H), 122.6 (C), 120.1 (C), 120.0 (C), 118.6 (*C*H), 116.5 (*C*H), 52.9 (2*O*C*H_3), 52.4 (O*C*H_3), 48.5 (*C*H), 20.7 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{25}H_{20}NO_8ClNa$ $[M + Na]^+$: 520.0769, found: 520.0772.

Dimethyl 2-(8-chloro-1-(4-chlorophenyl)-3-(methoxycarbonyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (110):



110

Reaction time: 30 min.

Yield: 0.097 g (75%) as light yellow solid.

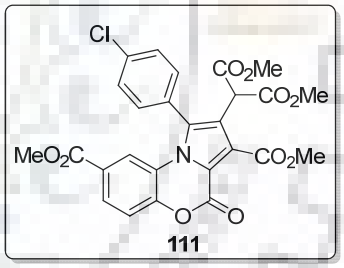
MP: 166–168 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 4.8 Hz, 1H), 7.15 (d, *J* = 10.0 Hz, 1H), 6.60 (s, 1H), 4.49 (s, 1H), 3.90 (s, 3H), 3.66 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3 (2**C*O), 163.6 (*C*O), 151.1 (*C*O), 141.8 (C), 137.4 (C), 133.2 (C), 132.1 (*C*H), 130.1 (*C*H), 129.4 (C), 127.2 (*C*H), 127.0 (C), 123.3 (C), 122.9 (C), 120.6 (C), 119.5 (*C*H), 117.0 (*C*H), 116.4 (C), 53.0 (2*O*CH_3), 52.5 (O*C*H_3), 48.4 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{17}NO_8Cl_2Na$ $[M + Na]^+$: 540.0223, found: 540.0228.

Dimethyl 1-(4-chlorophenyl)-2-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-4-oxo-4*H*-benzo-[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3,8-dicarboxylate (111):



111

Reaction time: 40 min.

Yield: 0.098 g (73%) as light yellow solid.

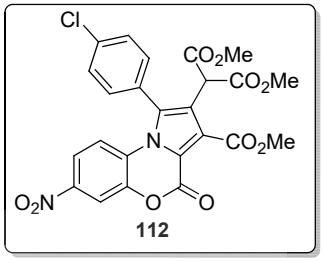
MP: 185–187 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.34 (s, 1H), 4.60 (s, 1H), 3.94 (s, 3H), 3.77 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.4 (2**CO*), 164.8 (*CO*), 163.6 (*C*O), 150.9 (*C*O), 146.4 (C), 137.2 (C), 133.5 (C), 132.3 (*C*H), 130.1 (*C*H), 128.2 (*C*H), 127.5 (C), 126.2 (C), 123.4 (C), 122.2 (C), 120.5 (C), 118.6 (*C*H), 118.5 (*C*H), 116.2 (C), 52.9 (2*O*CH_3), 52.6 (O*C*H_3), 52.4 (O*C*H_3), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{26}H_{20}NO_{10}ClNa$ $[M + Na]^+$: 564.0667, found: 564.0687.

Dimethyl 2-(1-(4-chlorophenyl)-3-(methoxycarbonyl)-7-nitro-4-oxo-4*H*-benzo-[*b*]-pyrr-olo-[1,2-*d*][1,4]oxazin-2-yl)malonate (112):



112

Reaction time: 2 h.

Yield: 0.086 g (65%) as light yellow solid.

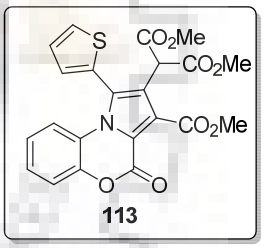
MP: 198–200 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (s, 1H), 7.80 (d, *J* = 9.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 9.2 Hz, 1H), 4.53 (s, 1H), 3.95 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3 (2**C*O), 163.4 (*C*O), 150.3 (*C*O), 145.2 (C), 143.5 (C), 137.8 (C), 134.1 (C), 132.2 (*C*H), 130.5 (*C*H), 127.3 (C), 127.2 (C), 124.6 (C), 121.8 (C), 119.5 (*C*H), 117.4 (*C*H), 116.4 (C), 114.4 (*C*H), 53.2 (2*O*CH_3), 52.8 (O*C*H_3), 48.5 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{17}ClN_2O_{10}Na$ $[M + Na]^+$: 551.0463, found: 551.0479.

Dimethyl 2-(3-(methoxycarbonyl)-4-oxo-1-(thiophen-2-yl)-4*H*-benzo[*b*]pyrrolo-[1,2-*d*][1,4]oxazin-2-yl)malonate (113):



113

Reaction time: 1 h.

Yield: 0.085 g (75%) as light white solid.

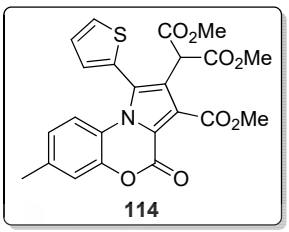
MP: 166–168 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70 (d, *J* = 5.2 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.28–7.27 (m, 2H), 7.23–7.21 (m, 1H), 6.94 (t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 4.65 (s, 1H), 3.93 (s, 3H), 3.72 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.5 (2**C*O), 163.7 (*C*O), 151.6 (*C*O), 143.3 (C), 132.4 (*C*H), 130.8 (*C*H), 128.8 (C), 128.3 (*C*H), 127.1 (*C*H), 126.6 (C), 124.4 (*C*H), 122.6 (C), 122.5 (C), 122.4 (C), 118.3 (*C*H), 117.3 (C), 116.7 (*C*H), 53.0 (2*O*CH_3), 52.5 (O*C*H_3), 48.6 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{17}NO_8SNa$ $[M + Na]^+$: 478.0567, found: 478.0572.

Dimethyl 2-(3-(methoxycarbonyl)-7-methyl-4-oxo-1-(thiophen-2-yl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-2-yl)malonate (114):



114

Reaction time: 1 h.

Yield: 0.091 g (78%) as light white solid.

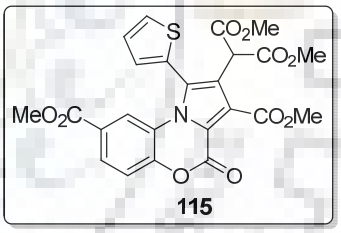
MP: 160–162 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.68 (dd, *J* = 1.6, 4.8 Hz, 1H), 7.27–7.25 (m, 2H), 7.14 (d, *J* = 1.2 Hz, 1H), 6.74 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.61 (d, *J* =8.8 Hz, 1H), 4.65 (s, 1H), 3.92 (s, 3H), 3.72 (s, 6H), 2.32 (s, 3H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 167.5 (2**C*O), 163.8 (*C*O), 151.8 (*C*O), 143.2 (C), 137.6 (C), 132.3 (*C*H), 130.8 (*C*H), 128.9 (C), 128.2 (*C*H), 126.2 (C), 125.2 (*C*H), 122.3 (C), 122.2 (C), 120.1 (C), 118.4 (*C*H), 117.2 (C), 116.4 (*C*H), 52.9 (2*O*C*H$_3$), 52.4 (O*C*H$_3$), 48.6 (*C*H) 20.8 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{19}NO_8SNa$ $[M + Na]^+$: 492.0723, found: 492.0728.

Dimethyl 2-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-4-oxo-1-(thiophen-2-yl)-4*H*-benzo-[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3,8-dicarboxylate (115):



115

Reaction time: 1 h.

Yield: 0.097 g (76%) as light white solid.

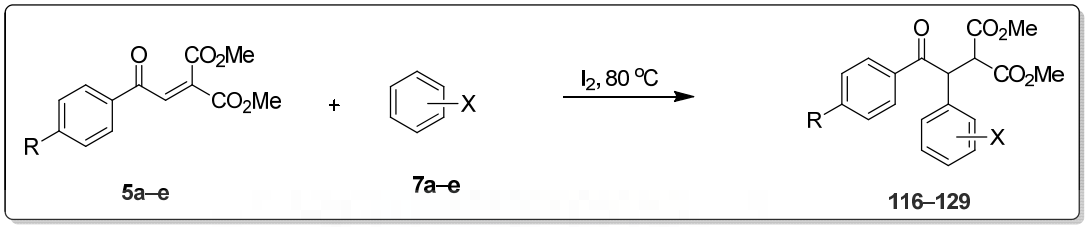
MP: 170–172 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.91 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 12.4 Hz, 1H), 7.49 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.35–7.32 (m, 2H), 4.70 (s, 1H), 3.94 (s, 3H), 3.80 (s, 3H), 3.73 (s, 6H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 167.4 (2**C*O), 165.1 (*C*O), 163.5 (*C*O), 150.8 (*C*O), 146.4 (C), 132.5 (*C*H), 131.0 (*C*H), 128.4 (*C*H), 128.3 (*C*H), 128.2 (C), 127.2 (C), 126.4 (C), 123.1 (C), 123.0 (C), 122.2 (C), 118.9 (*C*H), 118.3 (*C*H), 116.9 (C), 53.0 (2*O*C*H$_3$), 52.5 (O*C*H$_3$), 52.3 (O*C*H$_3$), 48.6 (*C*H) ppm.

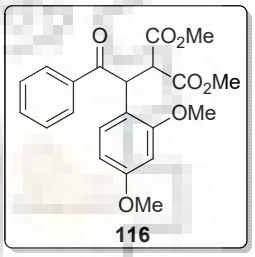
HRMS (ESI+): *m/z* calcd for $C_{24}H_{19}NO_{10}SNa$ $[M + Na]^+$: 536.0621, found: 536.0629.

3.2.7. General experimental procedure for the synthesis of α-substituted aryl ketones 116–129:



To a mixture of aroylmethylidene malonates **5** (0.2 mmol) and electron-rich arenes **7** (0.4 mmol) was added iodine (25 mg, 0.1 mmol) and the contents were stirred at 80 °C for an appropriate period of time. The reaction was monitored by TLC. After completion of the reaction, the mixture was purified by column chromatography on silica gel (100–200 mesh) using 10–40% ethyl acetate in hexanes to afford addition products **116**–**129**.

Dimethyl 2-(1-(2,4-dimethoxyphenyl)-2-oxo-2-phenylethyl)malonate (116):



Reaction time: 5 min.

Yield: 0.069 g (90%) as light brown solid.

MP: 115–117°C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.39 (s, 1H), 6.38 (s, 1H), 5.66 (d, *J* = 11.2 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 6H), 3.48 (s, 3H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 197.7 (*C*O), 168.9 (*C*O), 168.5 (*C*O), 160.6 (C), 157.6 (C), 135.7 (C), 132.8 (*C*H), 130.1 (*C*H), 128.6 (*C*H), 128.2 (*C*H), 115.3 (C), 105.0 (*C*H), 98.9 (*C*H), 55.6 (O*C*H$_3$), 55.1 (O*C*H$_3$), 54.5 (*C*H), 52.7 (O*C*H$_3$), 52.2(O*C*H$_3$), 45.6 (*C*H) ppm.

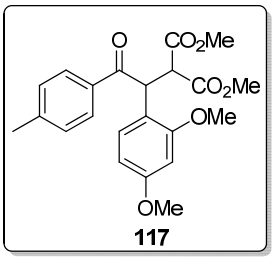
HRMS (ESI+): *m/z* calcd for $C_{21}H_{22}O_7Na$ $[M + Na]^+$: 409.1257, found: 409.1250.

Dimethyl 2-(1-(2,4-dimethoxyphenyl)-2-oxo-2-(*p*-tolyl)ethyl)malonate (117):

Reaction time: 5 min.

Yield: 0.068 g (85%) as yellow solid.

MP: 106–108 °C.



117

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 9.2 Hz, 1H), 6.38 (d, *J* = 6.4 Hz, 2H), 5.64 (d, *J* = 11.2 Hz, 1H), 4.38 (d, *J* = 11.2 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 6H), 3.48 (s, 3H), 2.32 (s, 3H) ppm.

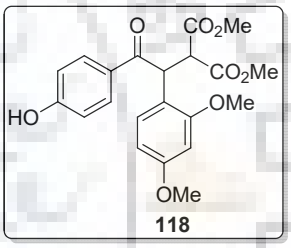
^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.3 (*C*O), 168.9 (*C*O), 168.6 (*C*O), 160.5 (C), 157.6 (C), 143.6 (C), 133.1 (C), 130.0 (*C*H), 129.0 (*C*H), 128.8 (*C*H), 115.6 (C), 105.0 (*C*H), 98.1 (*C*H), 55.6 (O*C*H$_3$), 55.2 (O*C*H$_3$), 54.5 (*C*H), 52.6 (O*C*H$_3$), 52.2 (O*C*H$_3$), 45.4 (*C*H), 21.5 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{24}O_7Na$ $[M + Na]^+$: 423.1414, found: 423.1409.

Dimethyl 2-(1-(2,4-dimethoxyphenyl)-2-(4-hydroxyphenyl)-2-oxoethyl)malonate (118):

Reaction time: 5 min.

Yield: 0.072 g (90%) as yellow solid.



118

MP: 133–135 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 9.2 Hz, 1H), 6.78 (s, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 5.6 Hz, 2H), 5.62 (d, *J* = 11.2 Hz, 1H), 4.38 (d, *J* = 11.2 Hz, 1H), 3.80 (s, 3H), 3.71 (s, 6H), 3.48 (s, 3H) ppm.

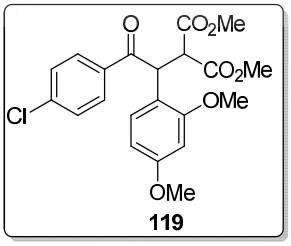
^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.5 (*C*O), 169.5 (*C*O), 168.9 (*C*O), 160.6 (C), 160.5 (C), 157.5 (C), 131.3 (*C*H), 129.8 (*C*H), 128.2 (C), 115.6 (C), 115.2 (*C*H), 105.1 (*C*H), 99.0 (*C*H), 55.6 (O*C*H$_3$), 55.2 (O*C*H$_3$), 54.6 (*C*H), 52.8 (O*C*H$_3$), 52.4 (O*C*H$_3$), 45.1 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{22}O_8Na$ $[M + Na]^+$: 425.1207, found: 425.1215.

Dimethyl 2-(2-(4-chlorophenyl)-1-(2,4-dimethoxyphenyl)-2-oxoethyl)malonate (119):

Reaction time: 20 min.

Yield: 0.066 g (79%) as yellow solid.



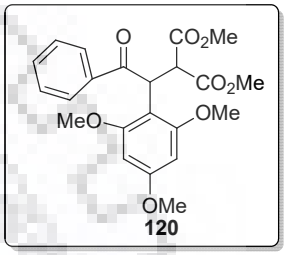
119

MP: 124–126 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90 (d, *J* = 8.8 Hz, 2H), 7.31–7.22 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.40–6.36 (m, 2H), 5.58 (d, *J* = 11.2 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 3.82 (s, 3H), 3.71 (s, 6H), 3.47 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.5 (*C*O), 168.8 (*C*O), 168.3 (*C*O), 160.7 (C), 157.5 (C), 139.3 (C), 134.0 (C), 130.1 (*C*H), 130.0 (*C*H), 128.6 (*C*H), 114.9 (C), 105.1 (*C*H), 99.0 (*C*H), 55.6 (O*C*H$_3$), 55.2 (O*C*H$_3$), 54.4 (*C*H), 52.8 (O*C*H$_3$), 52.3 (O*C*H$_3$), 45.5 (*C*H) ppm.

Dimethyl 2-(2-oxo-2-phenyl-1-(2,4,6-trimethoxyphenyl)ethyl)malonate (120):



120

Reaction time: 5 min.

Yield: 0.078 g (94%) as light brown solid.

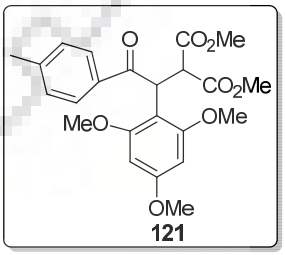
MP: 121–123 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.25–7.21 (m, 2H), 5.97 (s, 2H), 5.61 (d, *J* = 10.8 Hz, 1H), 4.47 (d, *J* = 10.8 Hz, 1H), 3.76 (s, 9H), 3.70 (s, 3H), 3.41 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.7 (*C*O), 169.3 (*C*O), 168.9 (*C*O), 161.2 (C), 158.8 (C), 136.3 (C), 132.2 (*C*H), 128.0 (*C*H), 105.5 (C), 90.7 (*C*H), 55.7 (O*C*H$_3$), 55.1 (O*C*H$_3$), 52.6 (O*C*H$_3$), 52.1 (2*O*C*H$_3$), 51.5 (*C*H), 44.2 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{24}O_8Na$ $[M + Na]^+$: 439.1363, found: 439.1373.

Dimethyl 2-(2-oxo-2-(*p*-tolyl)-1-(2,4,6-trimethoxyphenyl)ethyl)malonate (121):



121

Reaction time: 10 min.

Yield: 0.075 g (87%) as yellow solid.

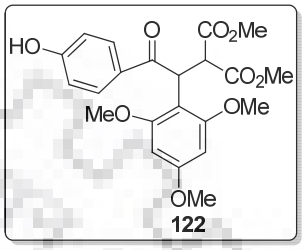
MP: 123–125 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 5.98 (s, 2H), 5.58 (d, *J* = 10.8 Hz, 1H), 4.47 (d, *J* = 10.8 Hz, 1H), 3.76 (s, 9H), 3.70 (s, 3H), 3.40 (s, 3H), 2.26 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.2 (*C*O), 169.3 (*C*O), 168.9 (*C*O), 161.1 (C), 158.7 (C), 142.7 (C), 133.6 (C), 128.6 (*C*H), 128.1 (*C*H), 105.7 (C), 90.7 (*C*H), 55.6 (O*C*H_3), 55.0 (O*C*H_3), 52.5 (O*C*H_3), 52.0 (2*O*C*H_3), 51.4 (*C*H), 44.2 (*C*H), 21.4 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{26}O_8Na$ $[M + Na]^+$: 453.1520, found: 453.1526.

Dimethyl 2-(2-(4-hydroxyphenyl)-2-oxo-1-(2,4,6-trimethoxyphenyl)ethyl)malonate (122):



122

Reaction time: 5 min.

Yield: 0.068 g (79%) as brown solid.

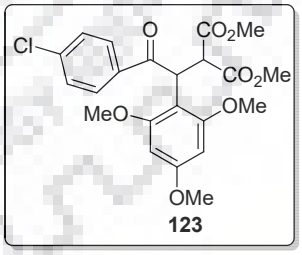
MP: 184–186 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 6.43 (s, 1H), 5.99 (s, 2H), 5.53 (d, *J* = 10.8 Hz, 1H), 4.48 (d, *J* = 10.8 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 9H), 3.41 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.4 (*C*O), 170.0 (*C*O), 169.1 (*C*O), 161.1 (C), 159.9 (C), 130.7 (*C*H), 128.6 (C), 114.8 (*C*H), 105.8 (C), 90.7 (*C*H), 55.7 (O*C*H_3), 55.2 (O*C*H_3), 52.7 (O*C*H_3), 52.2 (2*O*C*H_3), 51.5 (*C*H), 44.1 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{24}O_9Na$ $[M + Na]^+$: 455.1313, found: 455.1310.

Dimethyl 2-(2-(4-chlorophenyl)-2-oxo-1-(2,4,6-trimethoxyphenyl)ethyl)malonate (123):



123

Reaction time: 20 min.

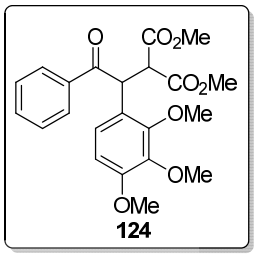
Yield: 0.073 g (81%) as brown solid.

MP: 144–146 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73 (d, *J* = 8.8 Hz, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 5.99 (s, 2H), 5.56 (d, *J* = 10.8 Hz, 1H), 4.46 (d, *J* = 10.8 Hz, 1H), 3.77 (s, 6H), 3.72 (s, 6H), 3.41 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.4 (*C*O), 169.2 (*C*O), 168.7 (*C*O), 161.3 (C), 158.7 (C), 138.4 (C), 134.6 (C), 129.4 (*C*H), 128.3 (*C*H), 105.1 (C), 90.8 (*C*H), 55.7 (O*C*H_3), 55.1 (O*C*H_3), 52.6 (O*C*H_3), 52.1 (2*O*C*H_3), 51.3 (*C*H), 44.2 (*C*H) ppm.

Dimethyl 2-(2-oxo-2-phenyl-1-(2,3,4-trimethoxyphenyl)ethyl)malonate (124):



124

Reaction time: 5 min.

Yield: 0.078 g (94%) as light brown solid.

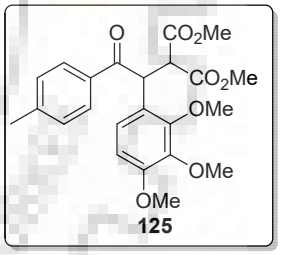
MP: 134–136 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.54 (d, *J* = 8.8 Hz, 1H), 5.64 (d, *J* = 11.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 3.94 (s, 3H), 3.76 (s, 3H), 3.74 (s, 3H), 3.71 (s, 3H), 3.49 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.5 (*C*O), 168.7 (*C*O), 168.6 (*C*O), 153.5 (C), 151.5 (C), 141.9 (C), 135.6 (C), 132.9 (*C*H), 128.8 (*C*H), 128.2 (*C*H), 123.7 (*C*H), 119.9 (C), 107.1 (*C*H), 61.0 (O*C*H$_3$), 60.4 (O*C*H$_3$), 55.7 (O*C*H$_3$), 54.6 (*C*H), 52.6 (O*C*H$_3$), 52.3 (O*C*H$_3$), 46.1 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{22}H_{24}O_8Na$ $[M + Na]^+$: 439.1363, found: 439.1368.

Dimethyl 2-(2-oxo-2-(*p*-tolyl)-1-(2,3,4-trimethoxyphenyl)ethyl)malonate (125):



125

Reaction time: 5 min.

Yield: 0.076 g (88%) as yellow solid.

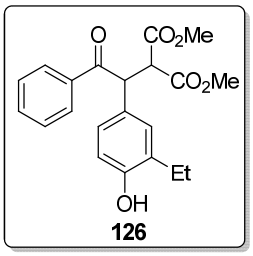
MP: 145–147 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 1H), 6.53 (d, *J* = 8.8 Hz, 1H), 5.62 (d, *J* = 11.2 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 3.95 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.71 (s, 3H), 3.48 (s, 3H), 2.31 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.1 (*C*O), 168.8 (*C*O), 168.7 (*C*O), 153.4 (C), 151.5 (C), 143.8 (C), 141.9 (C), 133.0 (C), 128.9 (*C*H), 123.7 (*C*H), 120.2 (C), 107.1 (*C*H), 61.0 (O*C*H$_3$), 60.4 (O*C*H$_3$), 55.7 (O*C*H$_3$), 54.7 (*C*H), 52.6 (O*C*H$_3$), 52.3 (O*C*H$_3$), 45.9 (*C*H), 21.5 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{26}O_8Na$ $[M + Na]^+$: 453.1520, found: 453.1519.

Dimethyl 2-(1-(3-ethyl-4-hydroxyphenyl)-2-oxo-2-phenylethyl)malonate (126):



126

Reaction time: 15 min.

Yield: 0.069 g (93%) as brown solid.

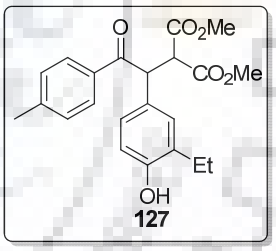
MP: 100–102 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.01 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 5.24 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 3.67 (s, 3H), 3.48 (s, 3H), 2.52 (q, *J* = 7.2 Hz, 2H), 1.12 (t, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.7 (*C*O), 168.7 (2**C*O), 153.6 (C), 135.7 (C), 133.1 (*C*H), 131.0 (C), 129.5 (*C*H), 128.8 (*C*H), 128.4 (*C*H), 127.1 (*C*H), 125.7 (C), 115.7 (*C*H), 55.7 (*C*H), 52.8 (O*C*H$_3$), 52.5 (O*C*H$_3$), 52.3 (*C*H), 22.9 (*C*H$_2$), 13.9 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{22}O_6Na$ $[M + Na]^+$: 393.1309, found: 393.1266.

Dimethyl 2-(1-(3-ethyl-4-hydroxyphenyl)-2-oxo-2-(*p*-tolyl)ethyl)malonate (127):



127

Reaction time: 20 min.

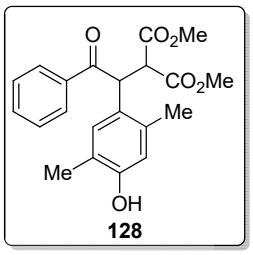
Yield: 0.068 g (87%) as brown solid.

MP: 122–124 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.94 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 5.27 (s, 1H), 5.22 (d, *J* = 11.2 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 3.69 (s, 3H), 3.50 (s, 3H), 2.53 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.14 (t, *J* = 7.6 Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.1 (*C*O), 168.7 (2**C*O), 153.3 (C), 144.0 (C), 133.3 (C), 130.8 (C), 129.5 (*C*H), 129.2 (*C*H), 129.1 (*C*H), 127.2 (*C*H), 126.3 (C), 115.7 (*C*H), 55.7 (*C*H), 52.8 (O*C*H$_3$), 52.5 (O*C*H$_3$), 52.2 (*C*H), 22.9 (*C*H$_2$), 21.6 (*C*H$_3$), 13.9 (*C*H$_3$) ppm.

Dimethyl 2-(1-(4-hydroxy-2,5-dimethylphenyl)-2-oxo-2-phenylethyl)malonate (128):



128

Reaction time: 15 min.

Yield: 0.068 (92%) as yellow solid.

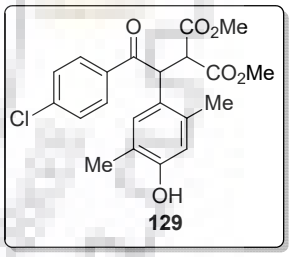
MP: 153–155°C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 6.89 (s, 1H), 6.49 (s, 1H), 5.49 (s, 1H), 5.40 (d, *J* = 11.2 Hz, 1H), 4.44 (d, *J* = 11.2 Hz, 1H), 3.70 (s, 3H), 3.46 (s, 3H), 2.37 (s, 3H), 2.05 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.0 (*C*O), 169.2 (*C*O), 168.9 (*C*O), 153.7 (C), 136.6 (C), 135.3 (C), 133.1 (*C*H), 130.6 (*C*H), 128.6 (*C*H), 123.8 (C), 122.5 (C), 117.6 (*C*H), 55.6 (*C*H), 52.9 (O*C*H$_3$), 53.0 (O*C*H$_3$), 48.0 (*C*H), 19.3 (*C*H$_3$), 15.4 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{21}H_{22}O_6Na$ $[M + Na]^+$: 393.1309, found: 393.1270.

Dimethyl 2-(2-(4-chlorophenyl)-1-(4-hydroxy-2,5-dimethylphenyl)-2-oxoethyl)malonate (129):



129

Reaction time: 20 min.

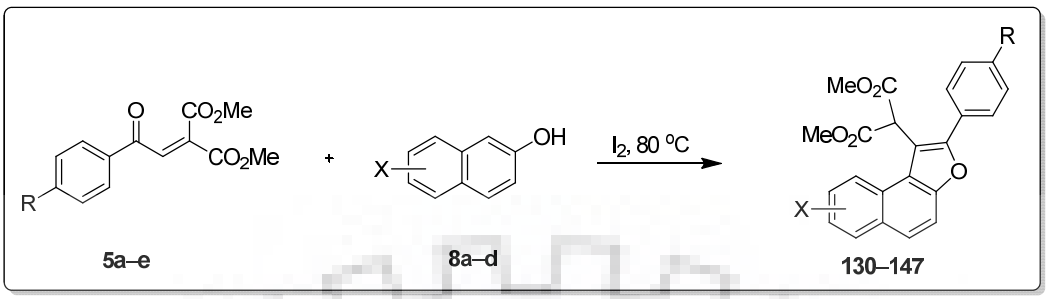
Yield: 0.067 g (83%) as yellow solid.

MP: 189–191 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 6.87 (s, 1H), 6.50 (s, 1H), 5.33 (d, *J* = 11.2 Hz, 1H), 5.19 (s, 1H), 4.42 (d, *J* = 11.2 Hz, 1H), 3.72 (s, 3H), 3.47 (s, 3H), 2.37 (s, 3H), 2.07 (s, 3H) ppm.

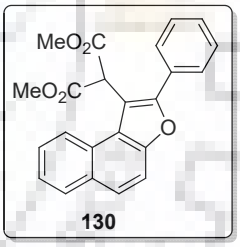
^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.5 (*C*O), 168.9 (*C*O), 168.5 (*C*O), 153.5 (C), 139.3 (C), 135.2 (C), 134.8 (C), 130.3 (*C*H), 129.9 (*C*H), 128.8 (*C*H), 123.6 (C), 122.3 (C), 117.5 (*C*H), 55.3 (*C*H), 52.9 (O*C*H$_3$), 52.4 (O*C*H$_3$), 47.8 (*C*H), 19.2 (*C*H$_3$), 15.3 (*C*H$_3$) ppm.

3.2.8. General experimental procedure for the synthesis of naphthofuran derivatives 130–147:



To a mixture of benzoylmethylidene malonate **5** (0.2 mmol) and *β*-naphthols **7** (0.2 mmol) was added iodine (0.025 g, 0.1 mmol) and the contents were stirred at 80 °C for appropriate time. In some cases DCM (2–3 drops) was added for better miscibility of the reactants. The reaction was monitored by TLC. After completion of the reaction, the mixture was purified by column chromatography on silica gel (100–200 mesh) using 10–40% ethyl acetate in hexanes to afford naphthofuran **130–147.**

Dimethyl 2-(2-phenylnaphtho[2,1-*b*]furan-1-yl)malonate (130):



Reaction time: 10 min.

Yield: 0.068 (91%) as white solid.

MP: 140–142°C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.82–7.78 (m, 3H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.60–7.47 (m, 5H), 5.46 (s, 1H), 3.69 (s, 6H) ppm.

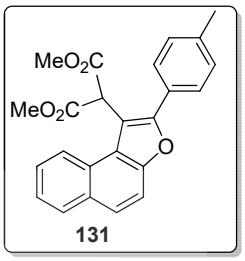
^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5 (2**C*O), 154.2 (C), 152.3 (C), 131.1 (C), 130.0 (C), 129.2 (*C*H), 128.7 (*C*H), 128.6 (*C*H), 127.9 (C), 126.6 (*C*H), 126.2 (*C*H), 124.3 (*C*H), 123.9 (*C*H), 122.2 (C), 112.3 (*C*H), 110.1 (C), 53.0 (2*OCH_3), 50.1 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{18}O_5Na$ $[M + Na]^+$: 397.1046, found: 397.1032.

Dimethyl 2-(2-(*p*-tolyl)naphtho[2,1-*b*]furan-1-yl)malonate (131):

Reaction time: 10 min.

Yield: 0.069 (89%) as brown solid.



MP: 144–146 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.26 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.70–7.66 (m, 3H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.42 (s, 1H), 3.69 (s, 6H), 2.44 (s, 3H) ppm.

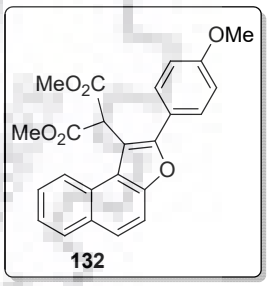
^{13}C NMR (CDCl$_3$, 100 MHz): δ 168.5 (2**C*O), 154.5 (C), 152.2 (C), 139.3 (C), 131.0 (C), 129.4 (C), 129.1 (*C*H), 128.5 (*C*H), 127.9 (*C*H), 127.1 (C), 126.3 (*C*H), 126.1 (*C*H), 124.2 (*C*H), 124.0 (*C*H), 122.2 (C), 112.3 (*C*H), 109.6 (C), 52.1 (2*O*C*H$_3$), 50.1 (*C*H), 21.4 (*C*H$_3$) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{20}O_5Na$ $[M + Na]^+$: 411.1203, found: 411.1219.

Dimethyl 2-(2-(4-methoxyphenyl)naphtho[2,1-*b*]furan-1-yl)malonate (132):

Reaction time: 10 min.

Yield: 0.065 g (81%) as light brown solid.



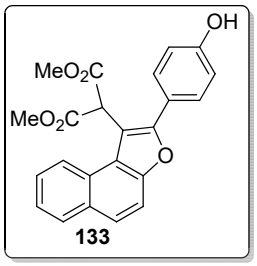
MP: 174–176 °C.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.78–7.67 (m, 4H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 5.40 (s, 1H), 3.89 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR (CDCl$_3$, 100 MHz): δ 168.6 (2**C*O), 160.3 (C), 154.4 (C), 152.0 (C), 131.0 (C), 130.1 (*C*H), 129.1 (*C*H), 127.8 (C), 126.2 (*C*H), 126.1 (*C*H), 124.2 (*C*H), 123.9 (*C*H), 122.4 (C), 122.2 (C), 114.2 (*C*H), 112.3 (*C*H), 109.1 (C), 55.3 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.1 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{20}O_6Na$ $[M + Na]^+$: 427.1152, found: 427.1130.

Dimethyl 2-(2-(4-hydroxyphenyl)naphtho[2,1-*b*]furan-1-yl)malonate (133):



Reaction time: 15 min.

Yield: 0.058 g (74%) as light yellow solid.

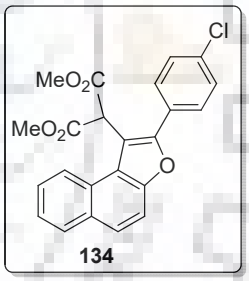
MP: 186–188 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.69–7.65 (m, 3H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 5.67 (s, 1H), 5.41 (s, 1H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.7 (2**C*O), 156.7 (C), 154.4 (C), 152.0 (C), 131.0 (C), 130.4 (*C*H), 129.2 (*C*H), 127.8 (C), 126.2 (*C*H), 124.2 (*C*H), 123.8 (*C*H), 122.5 (C), 122.2 (C), 115.7 (*C*H), 112.3 (*C*H), 109.1 (C), 53.1 (2*OCH_3), 50.2 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{18}O_6Na$ $[M + Na]^+$: 413.0995, found: 413.0994.

Dimethyl 2-(2-(4-chlorophenyl)naphtho[2,1-*b*]furan-1-yl)malonate (134):



Reaction time: 15 min.

Yield: 0.057 g (70%) as light yellow solid.

MP: 170–172 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.80–7.74 (m, 3H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.51–7.47 (m, 3H), 5.40 (s, 1H), 3.70 (s, 6H) ppm.

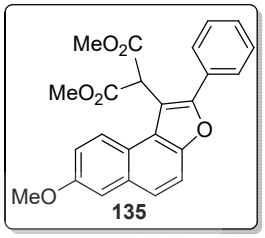
^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.3 (2**C*O), 153.0 (C), 152.4 (C), 135.3 (C), 131.1 (C), 129.8 (*C*H), 129.3 (*C*H), 129.0 (*C*H), 128.4 (C), 127.9 (C), 126.9 (*C*H), 126.4 (*C*H), 124.4 (*C*H), 123.8 (*C*H), 122.1 (C), 112.2 (*C*H), 110.5 (C), 53.1 (2*O*C*H_3), 50.0 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{23}H_{17}ClO_5Na$ $[M + Na]^+$: 431.0657, found: 431.0640.

Dimethyl 2-(7-methoxy-2-phenylnaphtho[2,1-*b*]furan-1-yl)malonate (135):

Reaction time: 10 min.

Yield: 0.071 g (88%) as light brown solid.



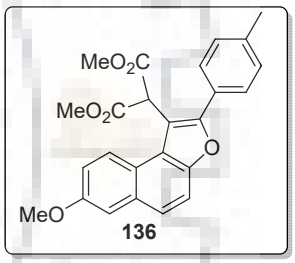
MP: 191–193 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, *J* = 9.2 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.69–7.63 (m, 2H), 7.52–7.45 (m, 3H), 7.29 (d, *J* = 2.8 Hz, 1H), 7.26–7.23 (m, 1H), 5.39 (s, 1H), 3.94 (s, 3H), 3.68 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5 (2**C*O), 156.2 (C), 154.2 (C), 151.3 (C), 132.4 (C), 130.0 (C), 129.2 (*C*H), 128.7 (*C*H), 128.6 (*C*H), 125.4 (*C*H), 122.7 (C), 122.3 (C), 117.8 (*C*H), 112.6 (*C*H) 109.7 (C), 108.2 (*C*H), 55.2 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.0 (*C*H) ppm.

Dimethyl 2-(7-methoxy-2-(*p*-tolyl)naphtho[2,1-*b*]furan-1-yl)malonate (136):

Reaction time: 5 min.



Yield: 0.072 g (86%) white solid.

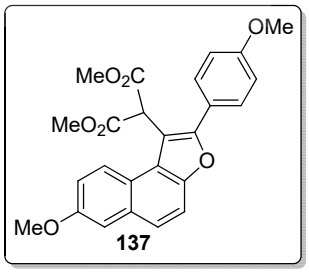
MP: 176–178 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, *J* = 9.2 HZ, 1H), 7.67–7.64 (m, 4H), 7.33–7.28 (m, 3H), 7.25–7.22 (m, 1H), 5.37 (s, 1H), 3.94 (s, 3H), 3.69 (s, 6H), 2.43 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.7 (2**C*O), 156.2 (C), 154.5 (C), 151.2 (C), 139.3 (C), 132.4 (C), 129.5 (*C*H), 128.5 (*C*H), 127.1 (C), 125.5 (*C*H), 125.2 (*C*H), 122.8 (C), 122.4 (C), 117.8 (*C*H), 112.7 (*C*H), 109.3 (C), 108.1 (*C*H), 55.3 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.0 (*C*H), 21.4 (*C*H$_3$) ppm.

Dimethyl 2-(7-methoxy-2-(4-methoxyphenyl)naphtho[2,1-*b*]furan-1-yl)malonate (137):

Reaction time: 10 min.



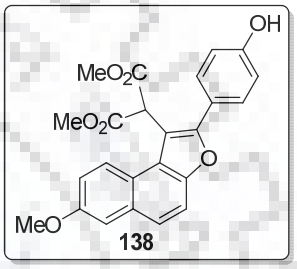
Yield: 0.063 g (73%) as brown solid.

MP: 163–165 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, *J* = 9.2 Hz, 1H), 7.71 (d, *J* = 9.2 Hz, 2H), 7.64 (s, 2H), 7.28 (d, *J* = 3.2 Hz, 1H), 7.23 (dd, *J* = 2.4, 9.6 Hz, 1H), 7.04 (d, *J* = 9.2 Hz, 2H), 5.36 (s, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.69 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.6 (2**C*O), 160.3 (C), 156.2 (C), 154.4 (C), 151.1 (C), 132.4 (C), 130.1 (*C*H), 125.4 (*C*H), 125.0 (*C*H), 122.7 (C), 122.4 (C), 117.7 (*C*H), 114.2 (*C*H), 112.6 (*C*H), 108.8 (C), 108.1 (*C*H), 55.4 (O*C*H$_3$), 55.3 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.1 (*C*H) ppm.

Dimethyl 2-(2-(4-hydroxyphenyl)-7-methoxynaphtho[2,1-*b*]furan-1-yl)malonate (138):



138

Reaction time: 10 min.

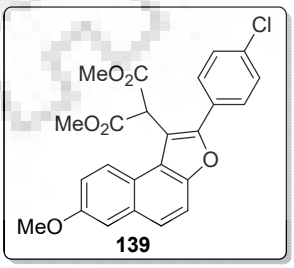
Yield: 0.063 g (75%) as light brown solid.

MP: 194–196 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 (d, *J* = 9.2 Hz, 1H), 7.60–7.54 (m, 4H), 7.24 (d, *J* = 2.8 Hz, 1H), 7.16 (dd, *J* = 2.4, 9.2 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 5.30 (s, 1H), 3.90 (s, 3H), 3.65 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$ + DMSO-d_6 100 MHz): δ 168.6 (2**C*O), 158.2 (C), 156.0 (C), 154.9 (C), 150.8 (C), 132.2 (C), 130.0 (*C*H), 125.4 (*C*H), 124.7 (*C*H), 122.6 (C), 122.4 (C), 121.0 (C), 117.5 (*C*H), 115.8 (*C*H), 112.5 (*C*H), 108.3 (C), 108.0 (*C*H), 55.2 (O*C*H$_3$), 52.9 (2*O*C*H$_3$), 49.9 (*C*H) ppm.

Dimethyl 2-(2-(4-chlorophenyl)-7-methoxynaphtho[2,1-*b*]furan-1-yl)malonate (139):



139

Reaction time: 10 min

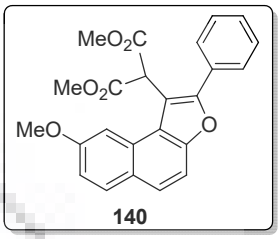
Yield: 0.063 g (72%) as light brown solid.

MP: 144–146 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, *J* = 9.2 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.65 (q, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 2.8 Hz, 1H), 7.25 (dd, *J* = 2.4, 8.0 Hz, 1H), 5.35 (s, 1H), 3.93 (s, 3H), 3.69 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.3 (2**C*O), 156.3 (C), 153.0 (C), 151.3 (C), 135.3 (C), 132.5 (C), 129.8 (*C*H), 129.0 (*C*H), 128.5 (C), 125.7 (*C*H), 125.3 (*C*H), 122.7 (C), 122.3 (C), 118.0 (*C*H), 112.6 (*C*H), 110.2 (C), 108.3 (*C*H), 55.3 (O*C*H$_3$), 53.1 (2*O*C*H$_3$), 50.0 (*C*H) ppm.

Dimethyl 2-(8-methoxy-2-phenylnaphtho[2,1-*b*]furan-1-yl)malonate (140):



140

Reaction time: 10 min

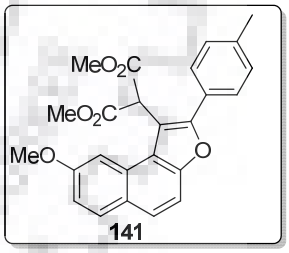
Yield: 0.068 g (85%) as white solid.

MP: 133–135°C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85–7.79 (m, 3H), 7.72–7.69 (m, 2H), 7.56–7.51 (m, 3H), 7.49–7.45 (m, 1H), 7.13 (dd, *J* = 2.0, 8.8 Hz, 1H), 5.42 (s, 1H), 3.97 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.7 (2**C*O), 158.2 (C), 154.0 (C), 152.9 (C), 130.4 (*C*H), 130.0 (C), 129.2 (*C*H), 128.8 (*C*H), 128.6 (*C*H), 126.4 (*C*H), 125.9 (C), 121.6 (C), 116.5 (*C*H), 109.8 (*C*H), 103.8 (*C*H), 55.5 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 49.9 (*C*H) ppm.

Dimethyl 2-(8-methoxy-2-(*p*-tolyl)naphtho[2,1-*b*]furan-1-yl)malonate (141):



141

Reaction time: 5 min.

Yield: 0.067 (80%) as white solid.

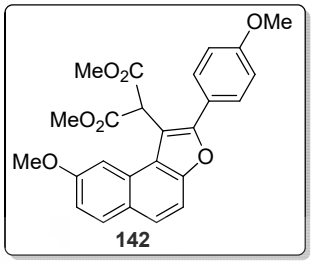
MP: 168–170 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, *J* = 8.8 Hz, 1H), 7.72–7.68 (m, 4H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.12 (dd, *J* = 2.4, 8.8 Hz, 1H), 5.40 (s, 1H), 3.96 (s, 3H), 3.70 (s, 6H), 2.44 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.8 (2**C*O), 158.1 (C), 154.3 (C), 152.8 (C), 139.3 (C), 130.3 (*C*H), 129.5 (*C*H), 129.1 (C), 128.5 (*C*H), 127.1 (C), 126.1 (*C*H), 125.9 (C), 121.6 (C), 116.5 (*C*H), 109.8 (*C*H), 109.3 (C), 103.9 (*C*H), 55.5 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.0 (*C*H), 21.4 (CH$_3$) ppm.

Dimethyl 2-(8-methoxy-2-(4-methoxyphenyl)naphtho[2,1-*b*]furan-1-yl)malonate (142):

Reaction time: 15 min.



142

Yield: 0.062 g (72%) as brown solid.

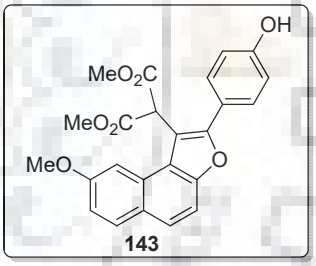
MP: 199–201 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, *J* = 9.2 Hz, 1H), 7.76–7.72 (m, 2H), 7.70–7.63 (m, 2H), 7.54 (d, *J* = 9.2 Hz, 1H), 7.13 (dd, *J* = 3.2, 9.2 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 5.40 (s, 1H), 3.98 (s, 3H), 3.88 (s, 3H), 3.70 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.8 (2**C*O), 160.3 (C), 158.1 (C), 154.2 (C), 152.6 (C), 130.3 (*C*H), 130.1 (*C*H), 129.1 (C), 126.0 (*C*H), 122.4 (C), 121.6 (C), 116.5 (*C*H), 114.2 (*C*H), 109.7 (*C*H), 108.8 (C), 103.8 (*C*H), 55.4 (O*C*H$_3$), 55.3 (O*C*H$_3$), 53.0 (2*O*C*H$_3$), 50.0 (*C*H) ppm.

Dimethyl 2-(2-(4-hydroxyphenyl)-8-methoxynaphtho[2,1-*b*]furan-1-yl)malonate (143):

Reaction time: 10 min.



143

Yield: 0.061g (73%) as brown solid.

MP: 171–173 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, *J* = 9.2 Hz, 1H), 7.70–7.66 (m, 4H), 7.53 (d, *J* = 8.8 Hz, 1H), 7.13 (dd, *J* = 1.6, 8.8 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 5.84 (s, 1H), 5.40 (s, 1H), 3.97 (s, 3H), 3.71 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.1 (2**C*O), 158.1 (C), 156.8 (C), 154.2 (C), 152.6 (C), 130.5 (*C*H), 129.0 (C), 125.9 (*C*H), 122.3 (C), 121.6 (C), 116.4 (*C*H), 115.7 (*C*H), 109.8 (*C*H), 108.7 (C), 103.7 (*C*H), 55.4 (O*C*H$_3$), 53.2 (2*O*C*H$_3$), 50.1 (*C*H) ppm.

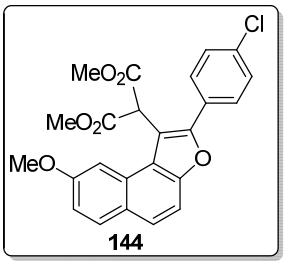
Dimethyl 2-(2-(4-chlorophenyl)-8-methoxynaphtho[2,1-*b*]furan-1-yl)malonate (144):

Reaction time: 10 min.

Yield: 0.062 g (71%) as yellow solid.

MP: 186–188 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.55–7.49 (m, 3H), 7.14 (dd, *J* = 2.4, 9.2 Hz, 1H), 5.37 (s, 1H), 3.97 (s, 3H), 3.70 (s, 6H) ppm.



144

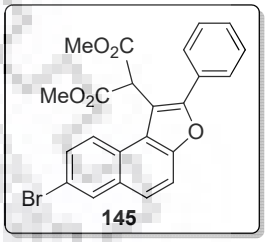
^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5 (2**C*O), 158.3 (C), 153.0 (C), 152.7 (C), 135.3 (C), 130.5 (*C*H), 129.8 (*C*H), 129.1 (*C*H), 128.5 (C), 126.7 (*C*H), 126.0 (C), 121.5 (C), 116.7 (*C*H), 110.2 (C), 109.7 (*C*H), 103.8 (*C*H), 55.5 (O*C*H$_3$), 53.1 (2*O*C*H$_3$), 49.9 (*C*H) ppm.

Dimethyl 2-(7-bromo-2-phenylnaphtho[2,1-*b*]furan-1-yl)malonate (145):

Reaction time: 15 min.

Yield: 0.073 g (81%) as white solid.

MP: 181–183 °C.



145

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, *J* = 9.2 Hz, 1H), 8.10 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.73–7.68 (m, 2H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.56–7.46 (m, 3H), 5.40 (s, 1H), 3.72 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.4 (2**C*O), 154.8 (C), 152.4 (C), 132.4 (C), 131.1 (*C*H), 129.6 (*C*H), 129.4 (*C*H), 129.3 (*C*H), 128.8 (*C*H), 128.6 (C), 126.4 (C), 125.9 (*C*H), 125.6 (*C*H), 122.3 (C), 118.1 (C), 113.4 (*C*H), 109.9 (C), 53.1 (2*O*C*H$_3$), 49.9 (*C*H) ppm.

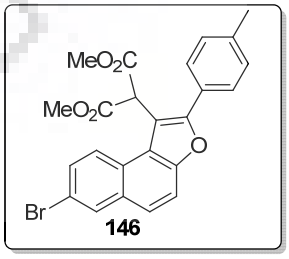
HRMS (ESI+): *m/z* calcd for $C_{23}H_{17}BrO_5Na$ $[M + Na]^+$: 475.0152, found: 475.0152.

Dimethyl 2-(7-bromo-2-(*p*-tolyl)naphtho[2,1-*b*]furan-1-yl)malonate (146):

Reaction time: 15 min.

Yield: 0.072 g (77%) as brown solid.

MP: 140–142 °C.



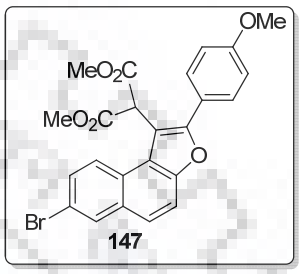
146

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, *J* = 9.2 Hz, 1H), 8.10 (d, *J* = 2.8 Hz, 1H), 7.72–7.64 (m, 5H), 7.35 (d, *J* = 8.4 Hz, 2H), 5.39 (s, 1H), 3.72 (s, 6H), 2.45 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.4 (2**C*O), 155.1 (C), 152.3 (C), 139.6 (C), 132.4 (C), 131.0 (*C*H), 129.5 (*C*H), 129.2 (*C*H), 128.5 (*C*H), 126.7 (C), 126.3 (C), 126.0 (*C*H), 125.3 (*C*H), 122.4 (C), 118.0 (C), 113.4 (*C*H), 109.4 (C), 53.1 (2*O*C*H_3), 49.9 (*C*H), 21.4 (*C*H_3) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{19}BrO_5Na$ $[M + Na]^+$: 489.0308, found: 489.0290.

Dimethyl 2-(7-bromo-2-(4-methoxyphenyl)naphtho[2,1-*b*]furan-1-yl)malonate (147):



147

Reaction time: 60 min.

Yield: 0.068 g (71%) as brown solid.

MP: 156–158 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, *J* = 9.2 Hz, 1H), 8.09 (s, 1H), 7.70 (t, *J* = 8.4 Hz, 3H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 5.36 (s, 1H), 3.88 (s, 3H), 3.72 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5 (2**C*O), 160.5 (C), 155.0 (C), 152.1 (C), 132.4 (C), 130.8 (*C*H), 130.1 (*C*H), 129.2 (*C*H), 126.3 (C), 125.9 (*C*H), 125.1 (*C*H), 122.4 (C), 122.1 (C), 118.0 (C), 114.4 (*C*H), 113.4 (*C*H), 109.0 (C), 55.3 (O*C*H_3), 53.1 (2*O*C*H_3)), 49.9 (*C*H) ppm.

HRMS (ESI+): *m/z* calcd for $C_{24}H_{19}BrO_6Na$ $[M + Na]^+$: 505.0257, found: 505.0274.

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NMR Spectra for Selected Compounds

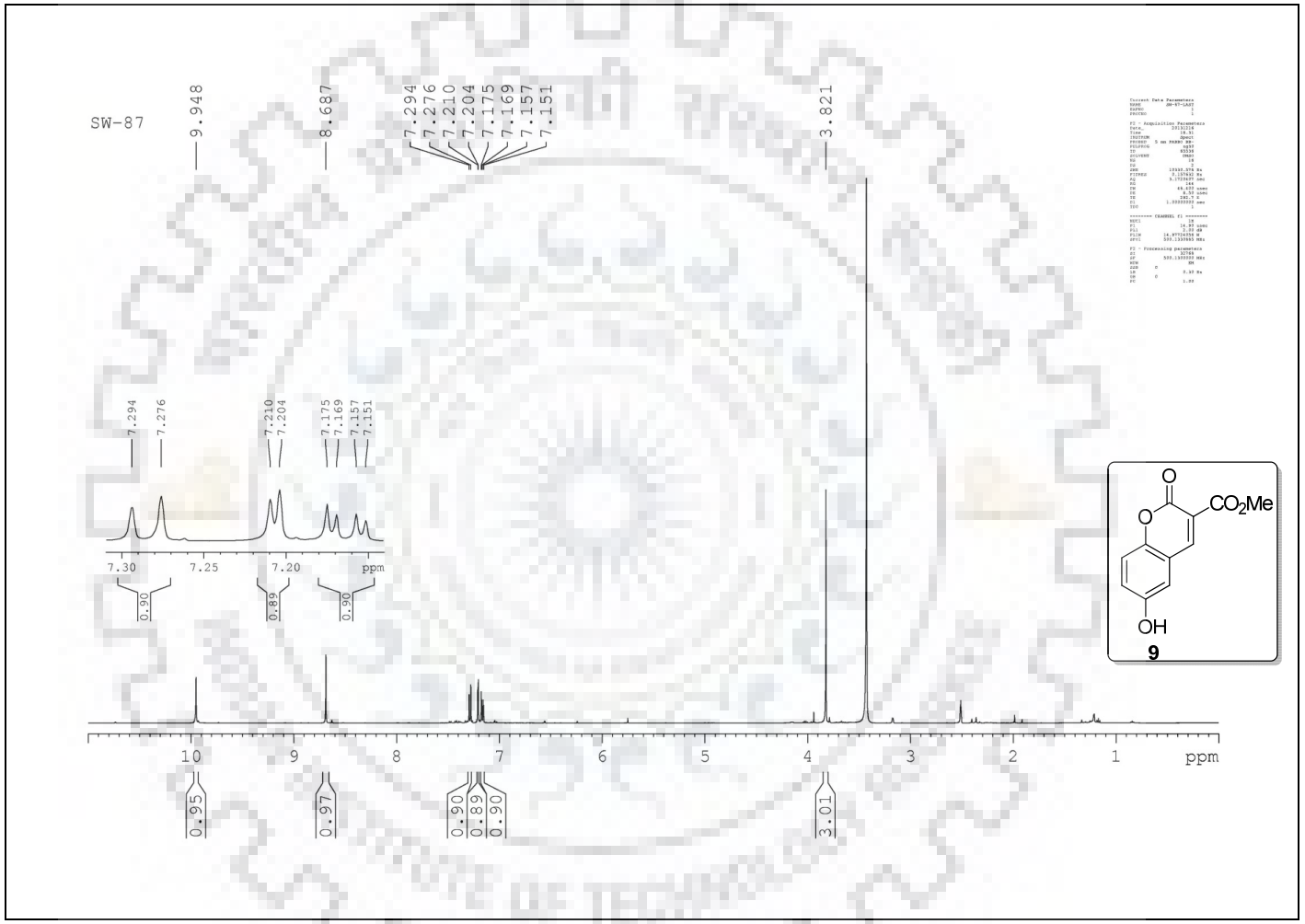


Figure S-1: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **9**.

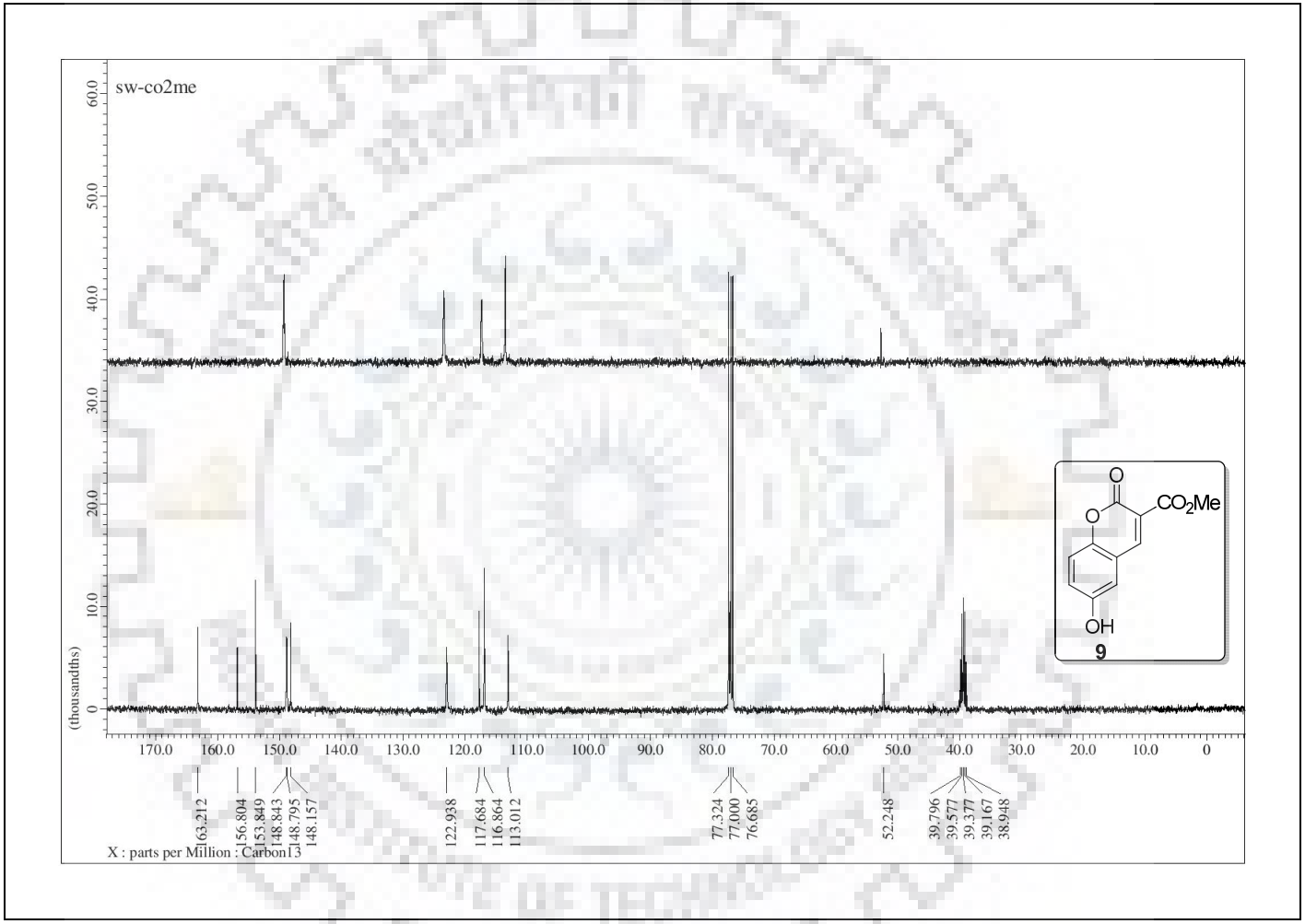


Figure S-2: ^{13}C and DEPT NMR (100 MHz, DMSO-d_6) Spectra of **9**.

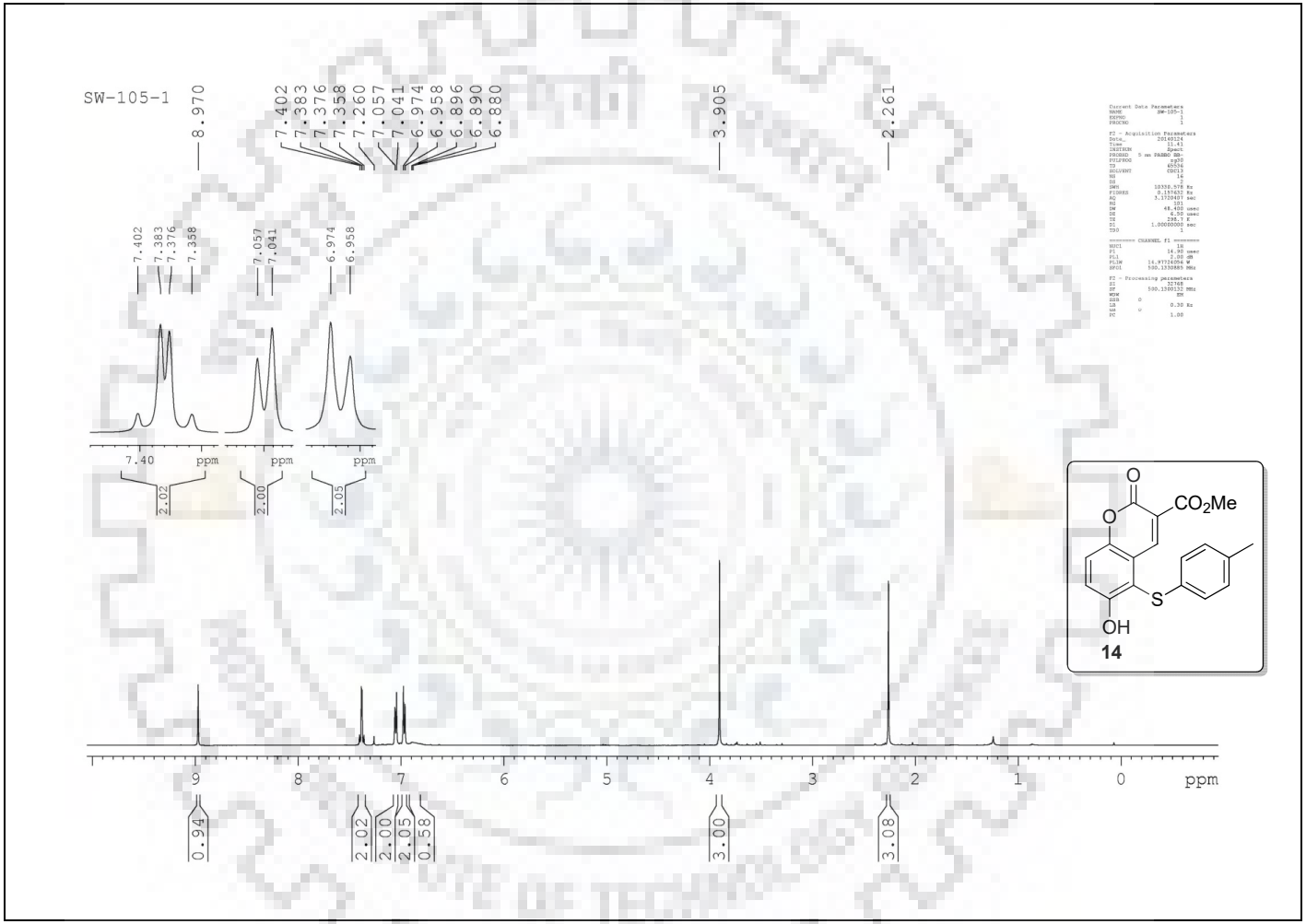


Figure S-3: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **14**.

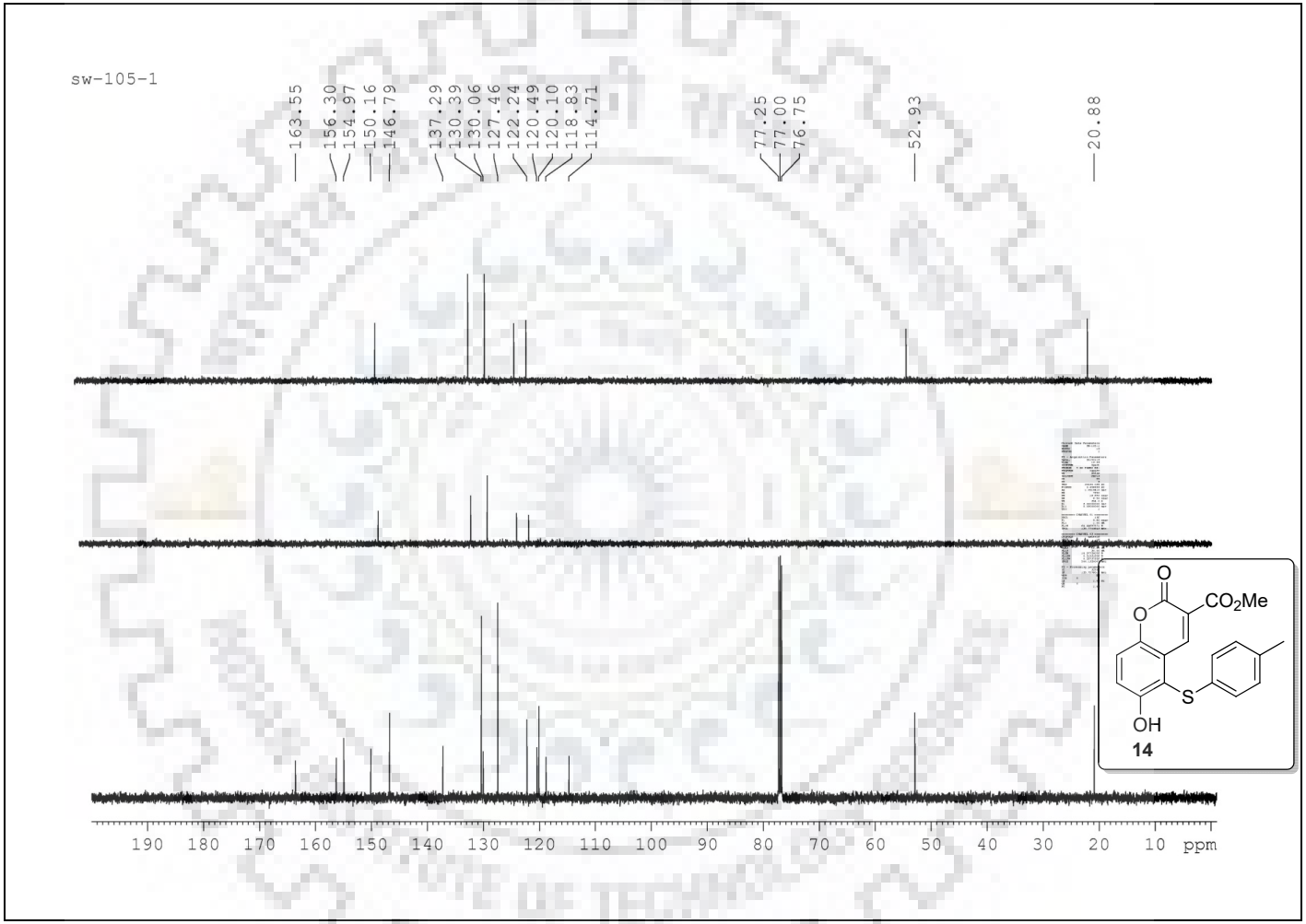


Figure S-4: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **14**.

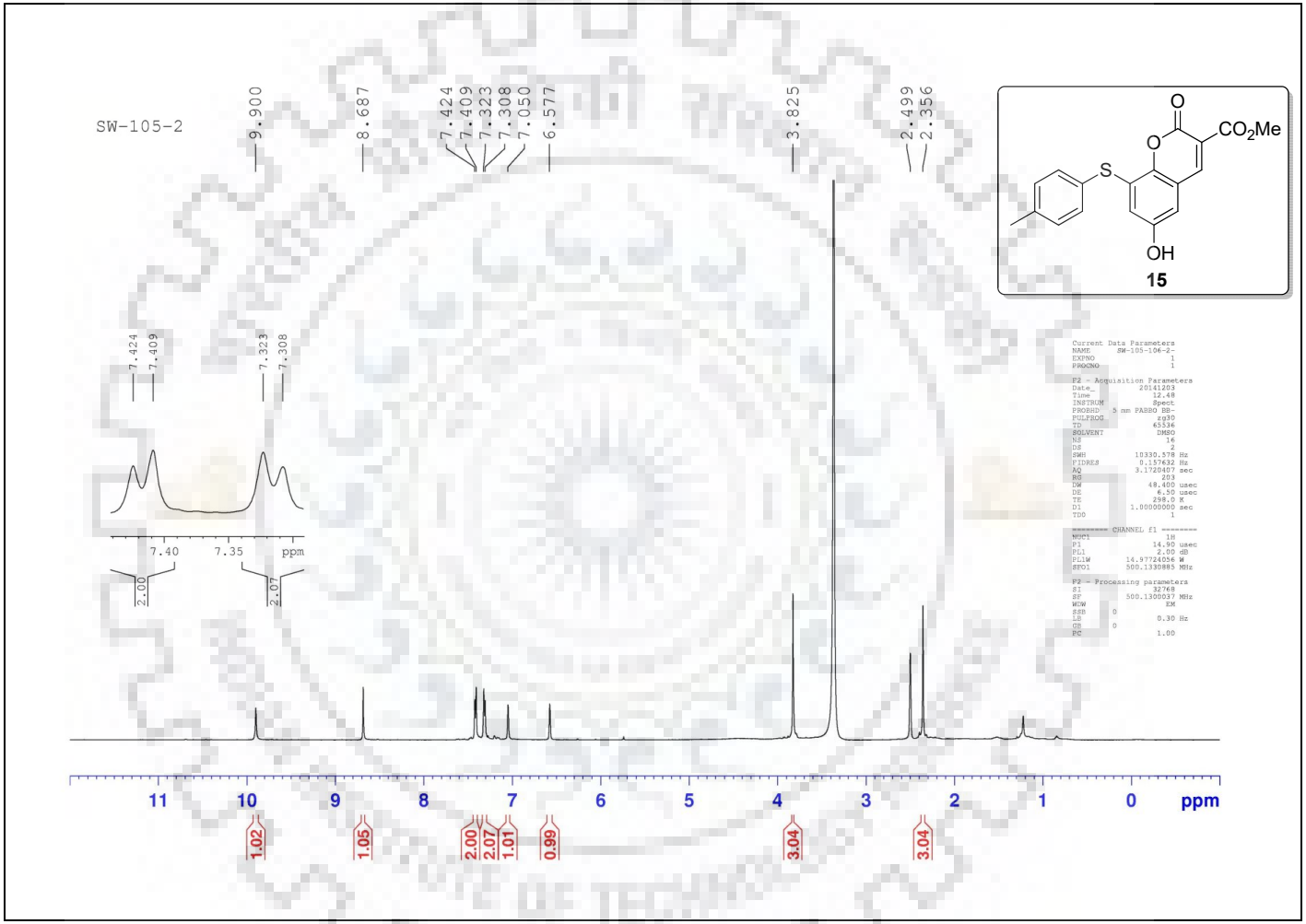


Figure S-5: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **15**.

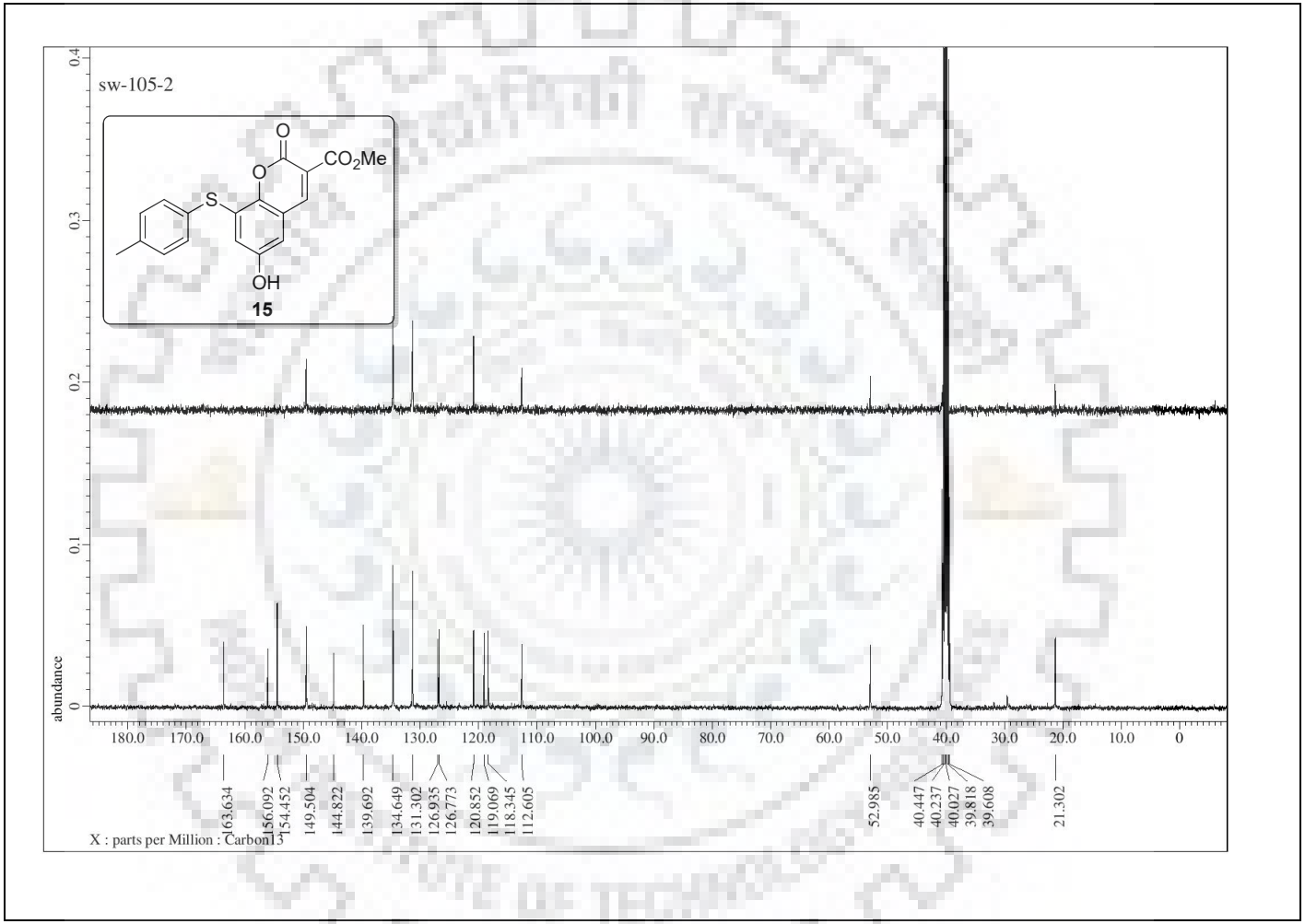


Figure S-6: ^{13}C and DEPT NMR (100 MHz, DMSO-d_6) Spectra of **15**.

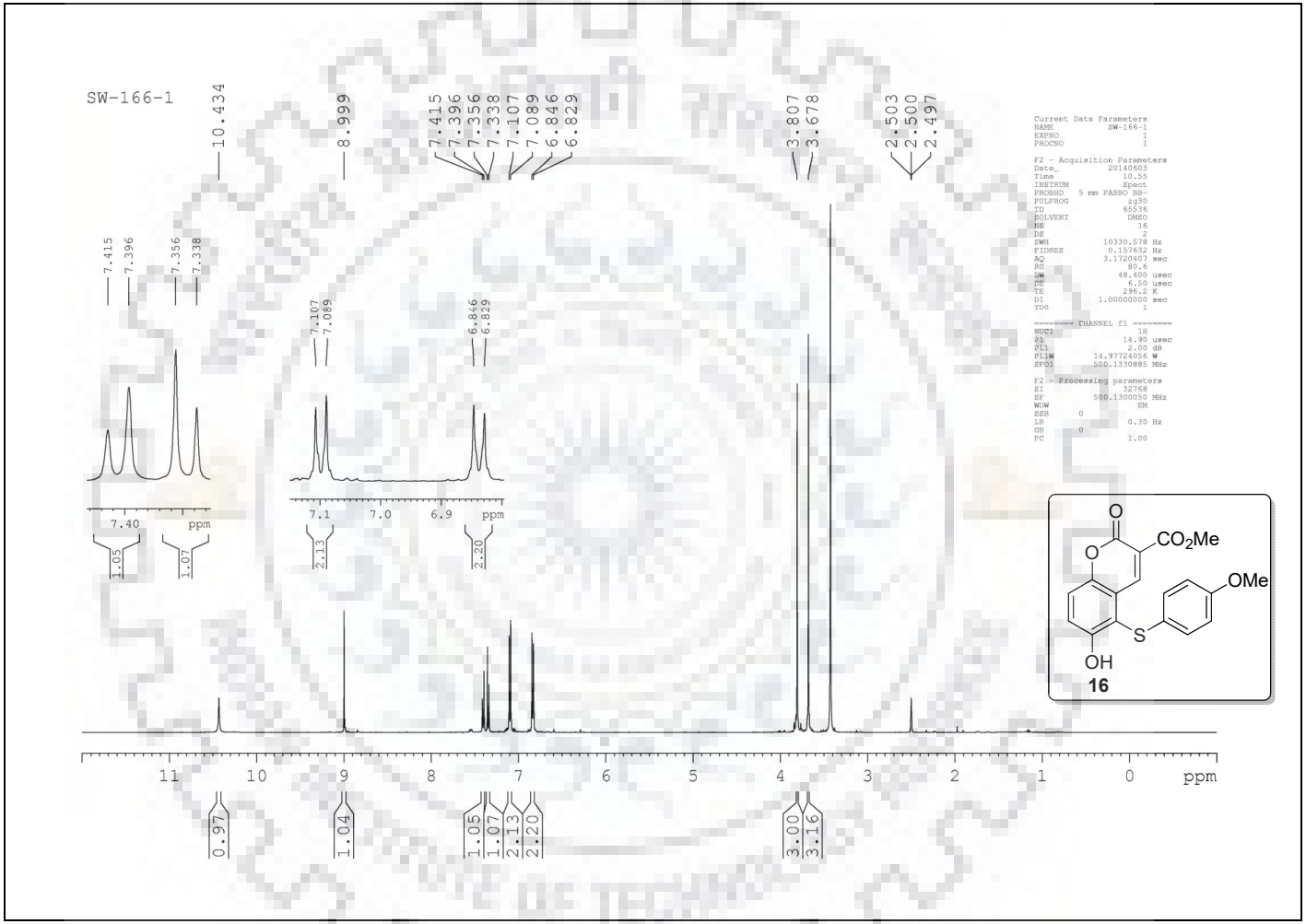


Figure S-7: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **16**.

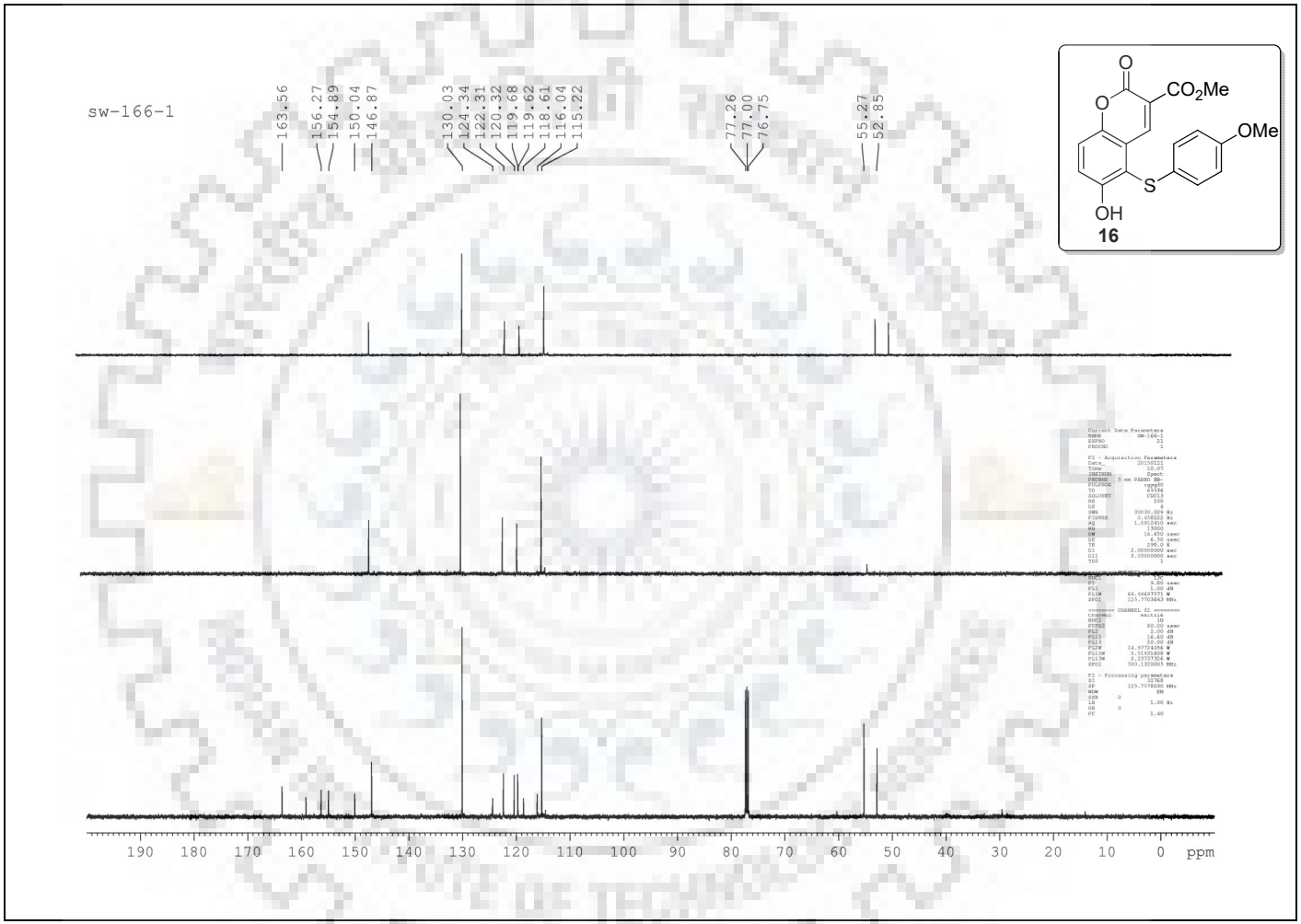


Figure S-8: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **16**.

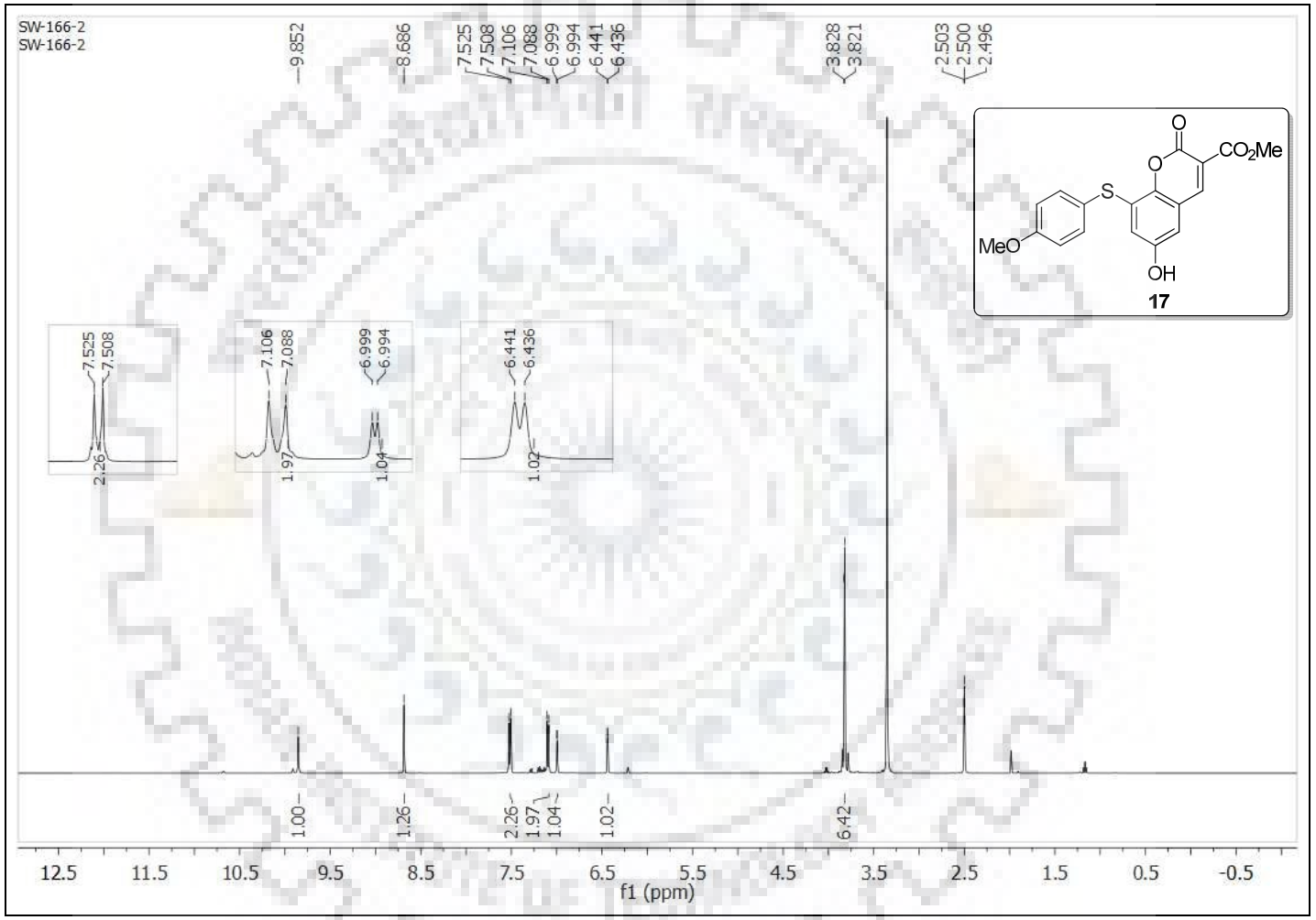


Figure S-9: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **17**.

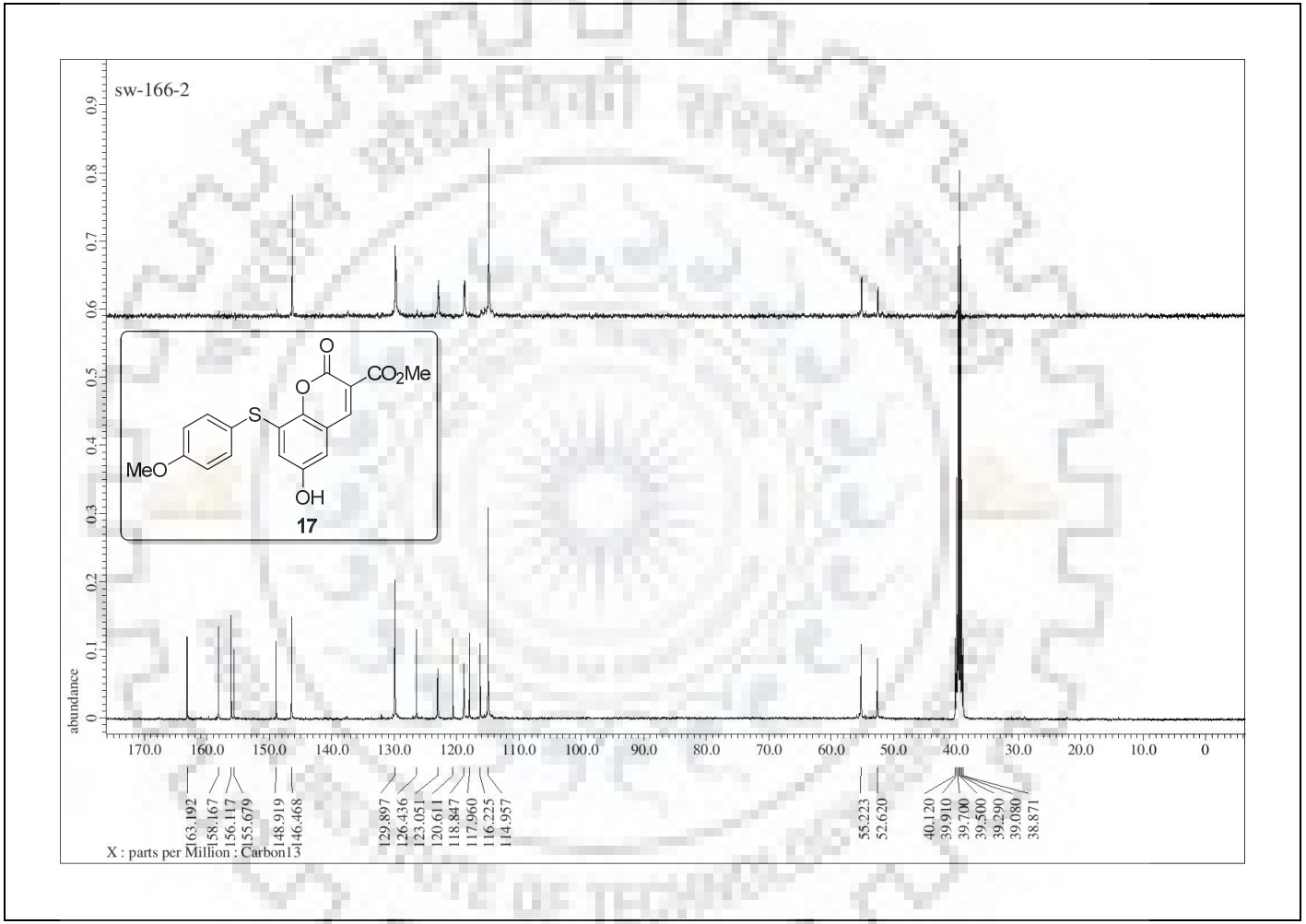


Figure S-10: ^{13}C and DEPT NMR (100 MHz, DMSO) Spectra of **17**.

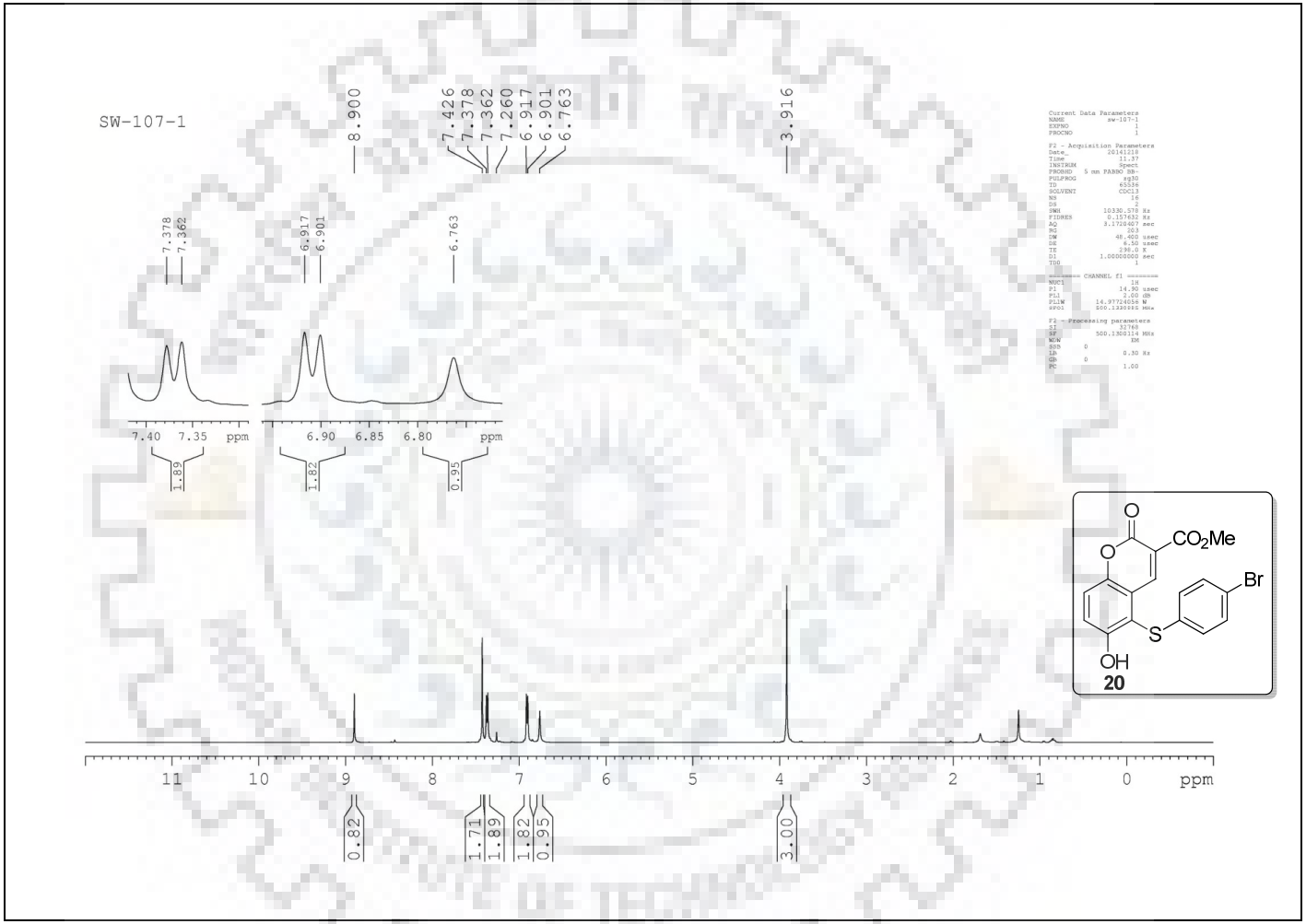


Figure S-11: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **20**.

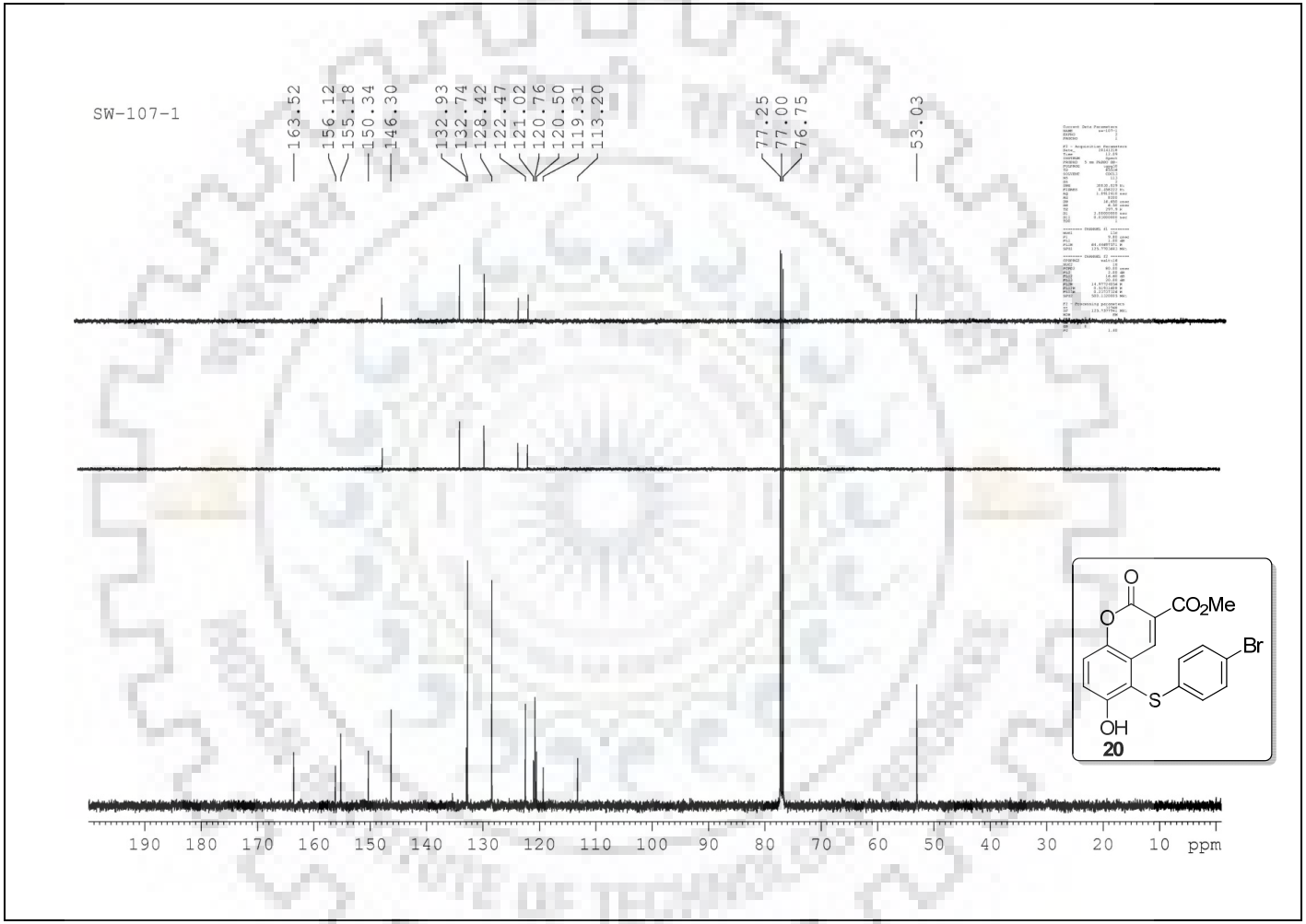


Figure S-12: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **20**.

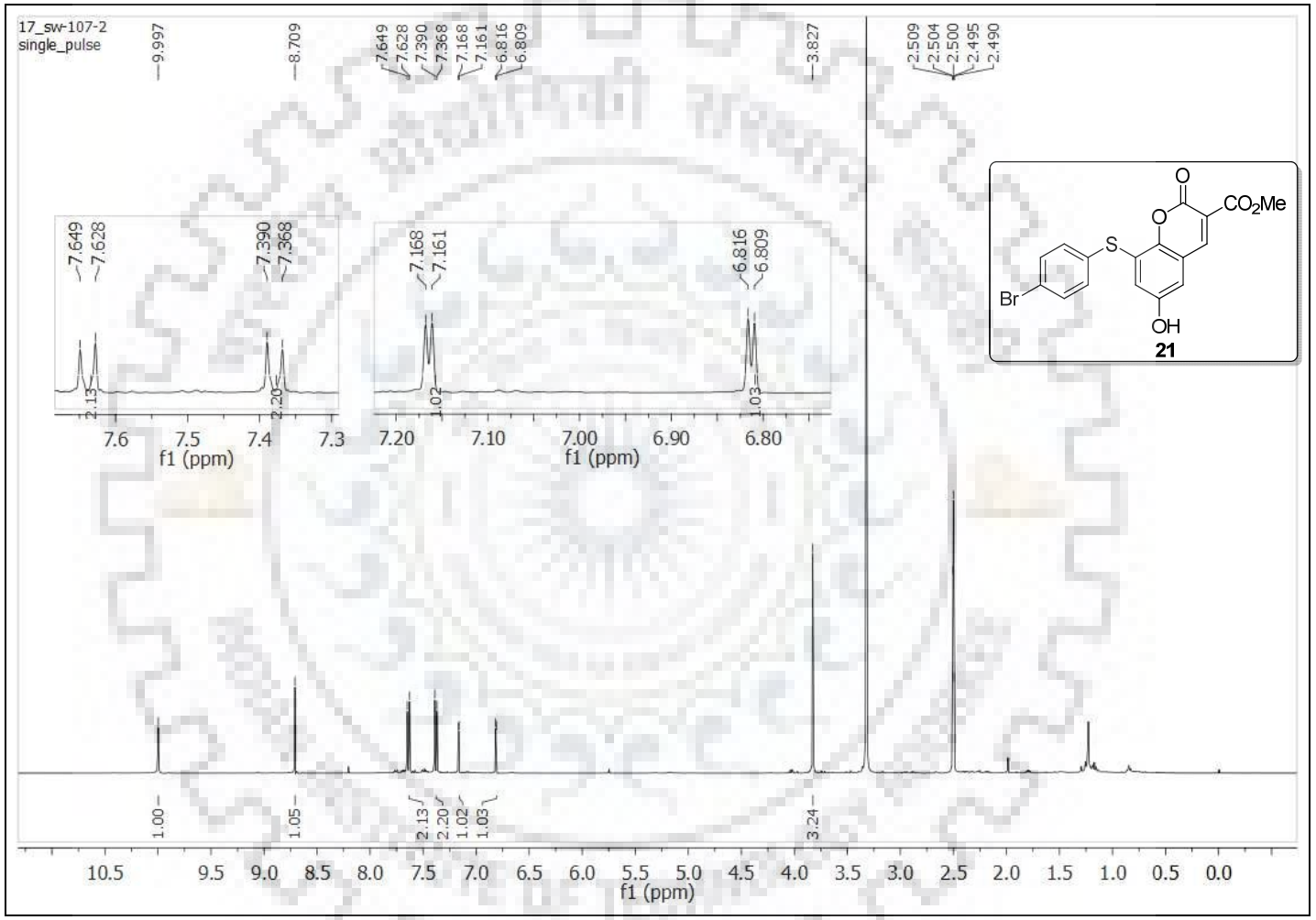


Figure S-13: ^{1}H NMR (400 MHz, DMSO-d_6) Spectrum of **21**.

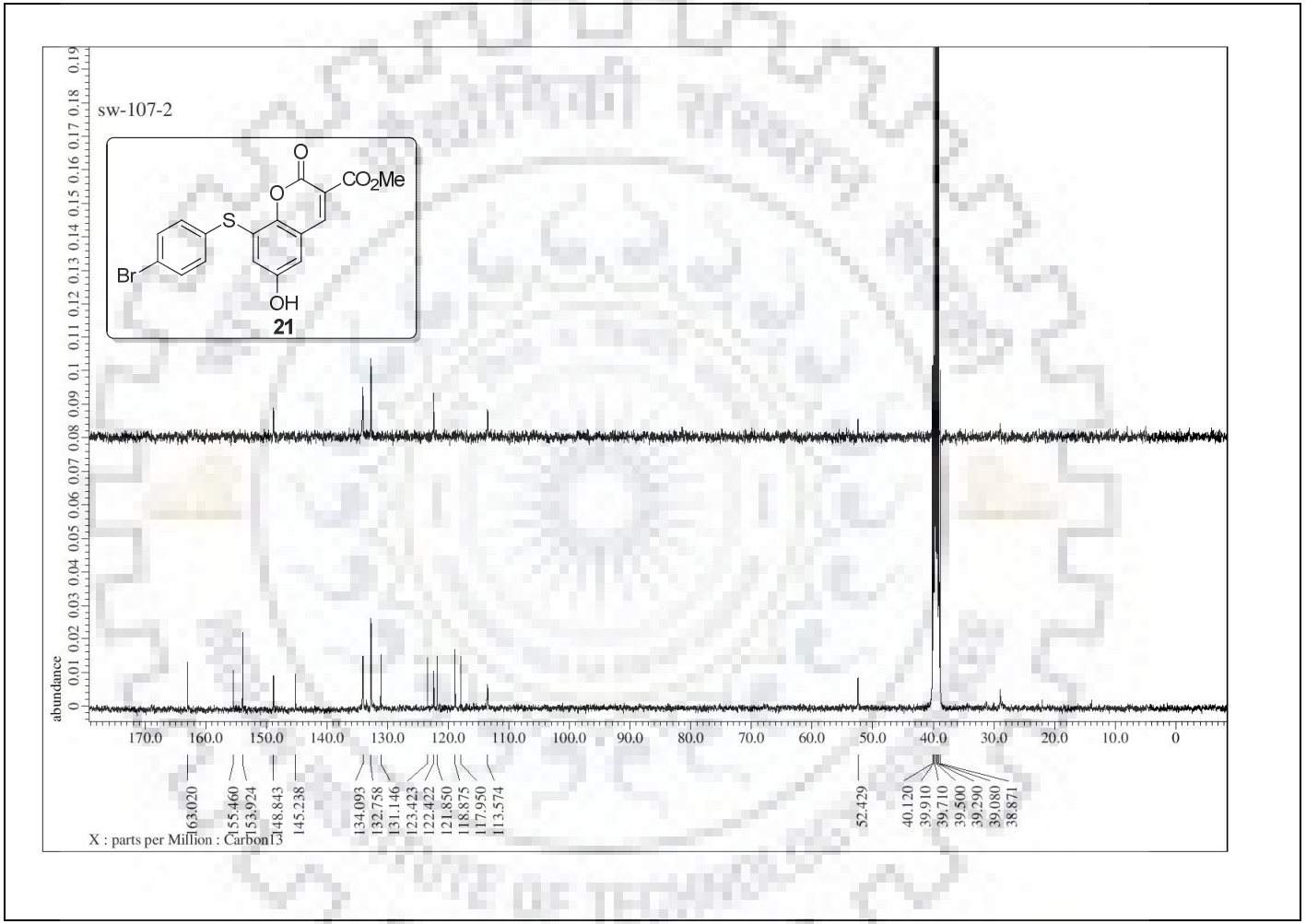


Figure S-14: ^{13}C and DEPT NMR (100 MHz, DMSO-d_6) Spectra of **21**.

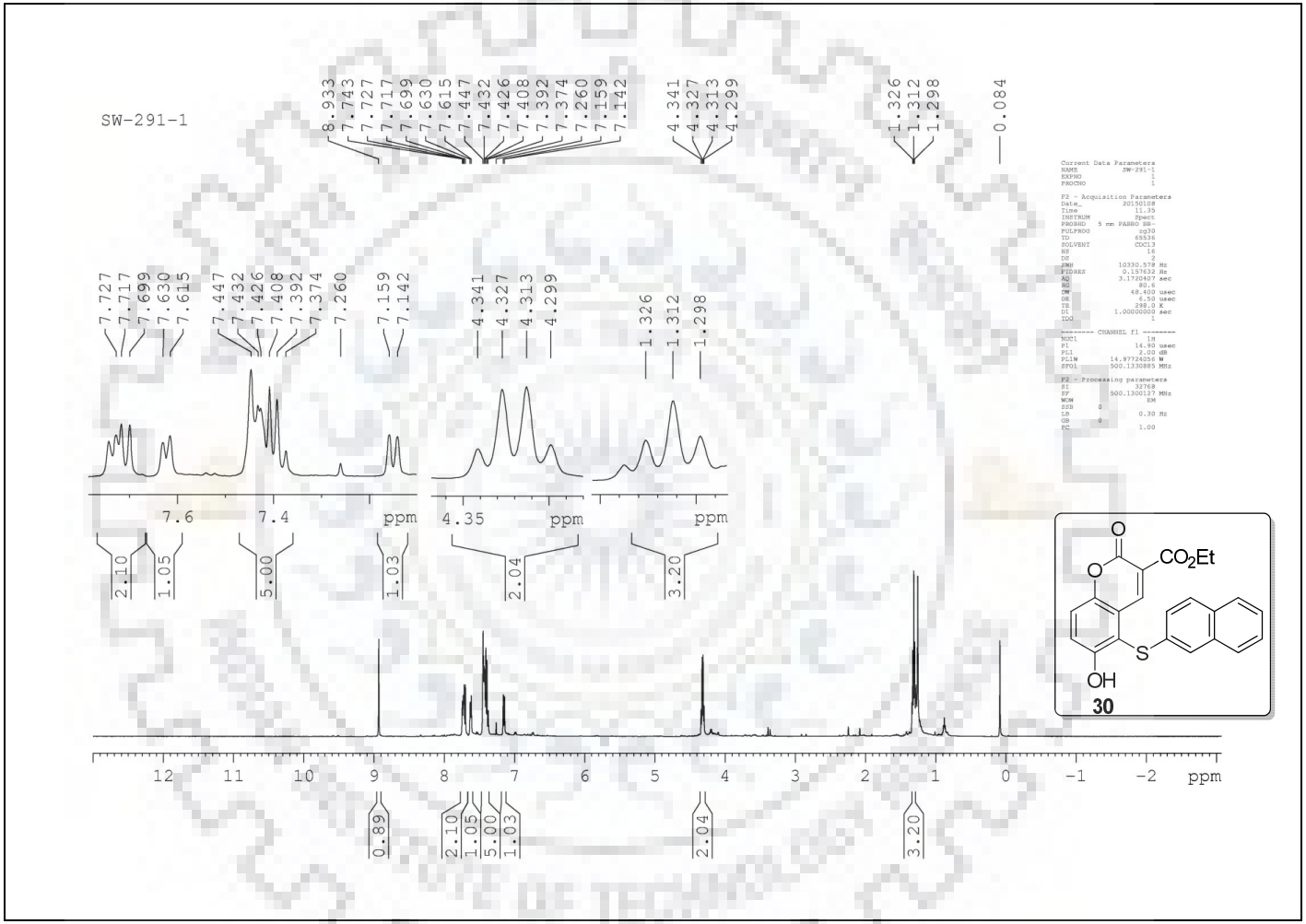


Figure S-15: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **30**.

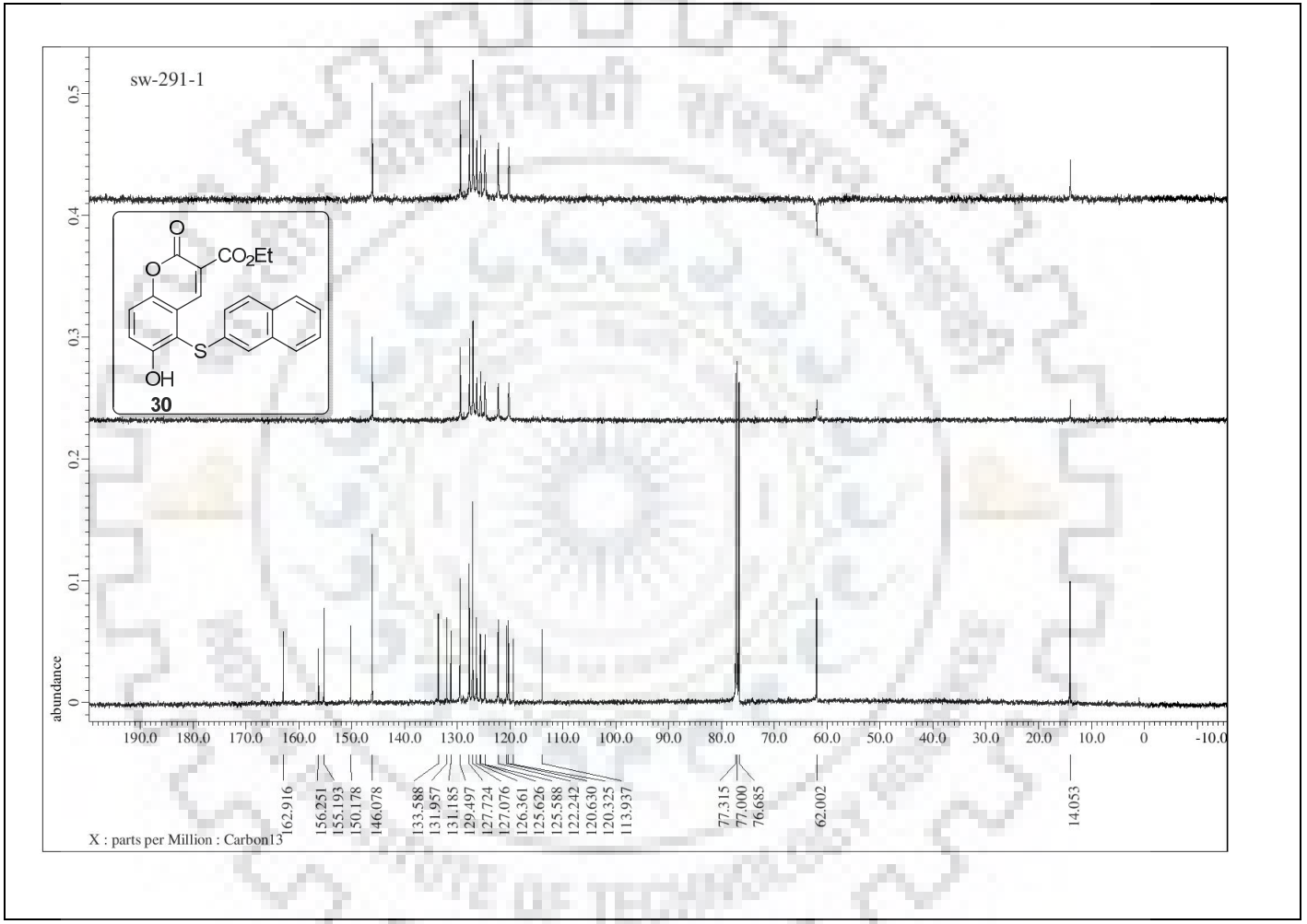


Figure S-16: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **30**.

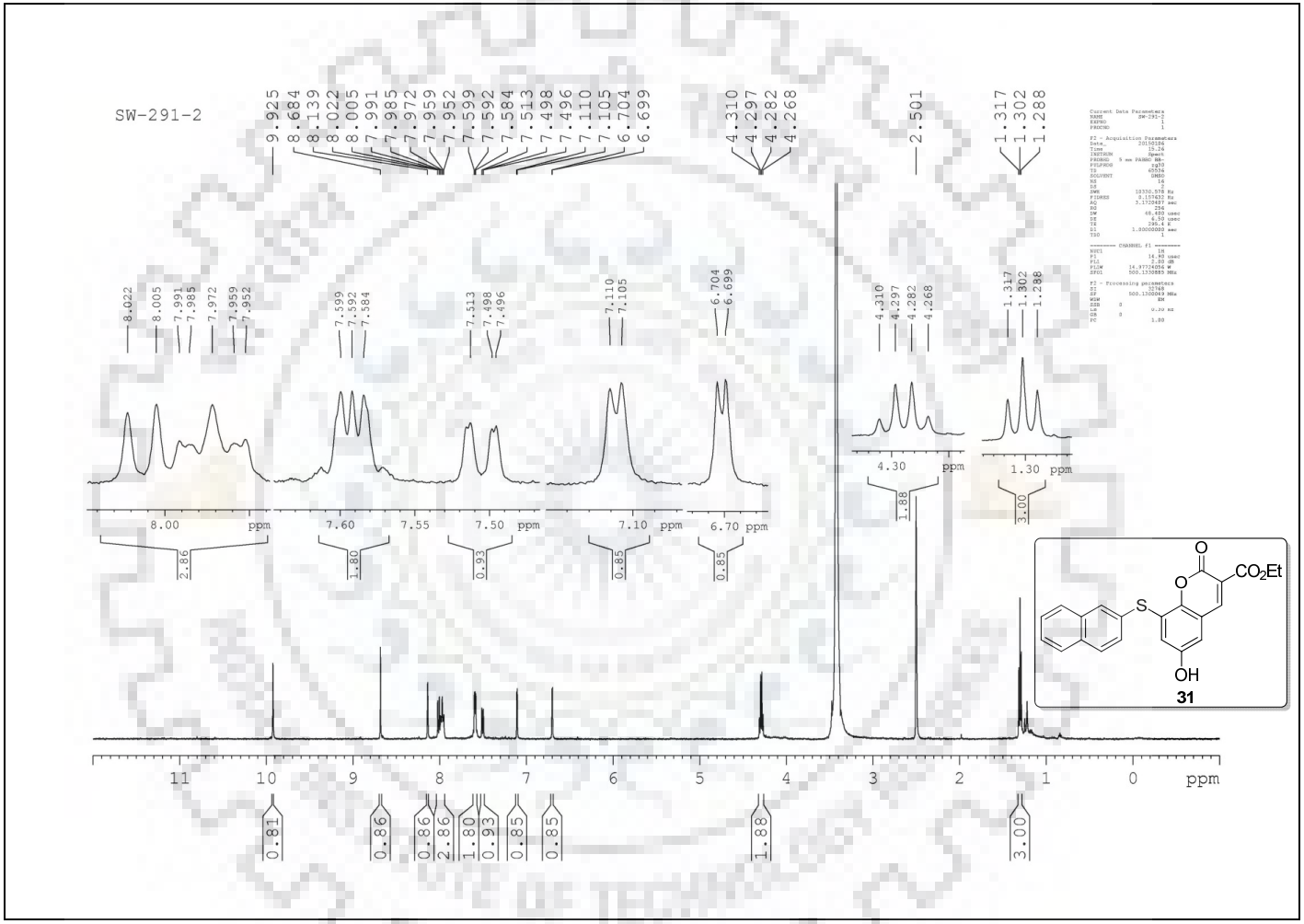


Figure S-17: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **31**.

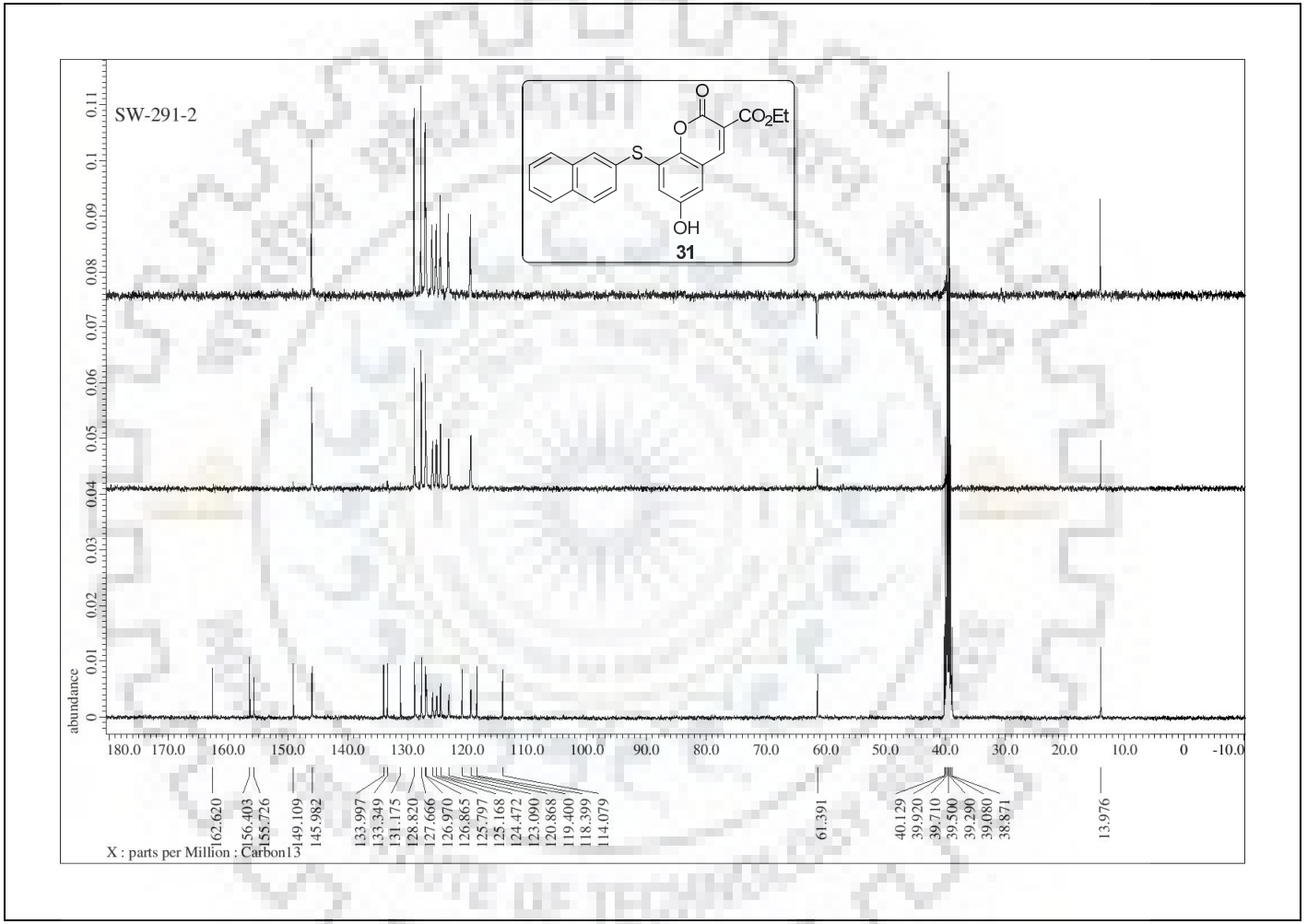


Figure S-18: ^{13}C and DEPT NMR (100 MHz, DMSO-d_6) Spectra of **31**.

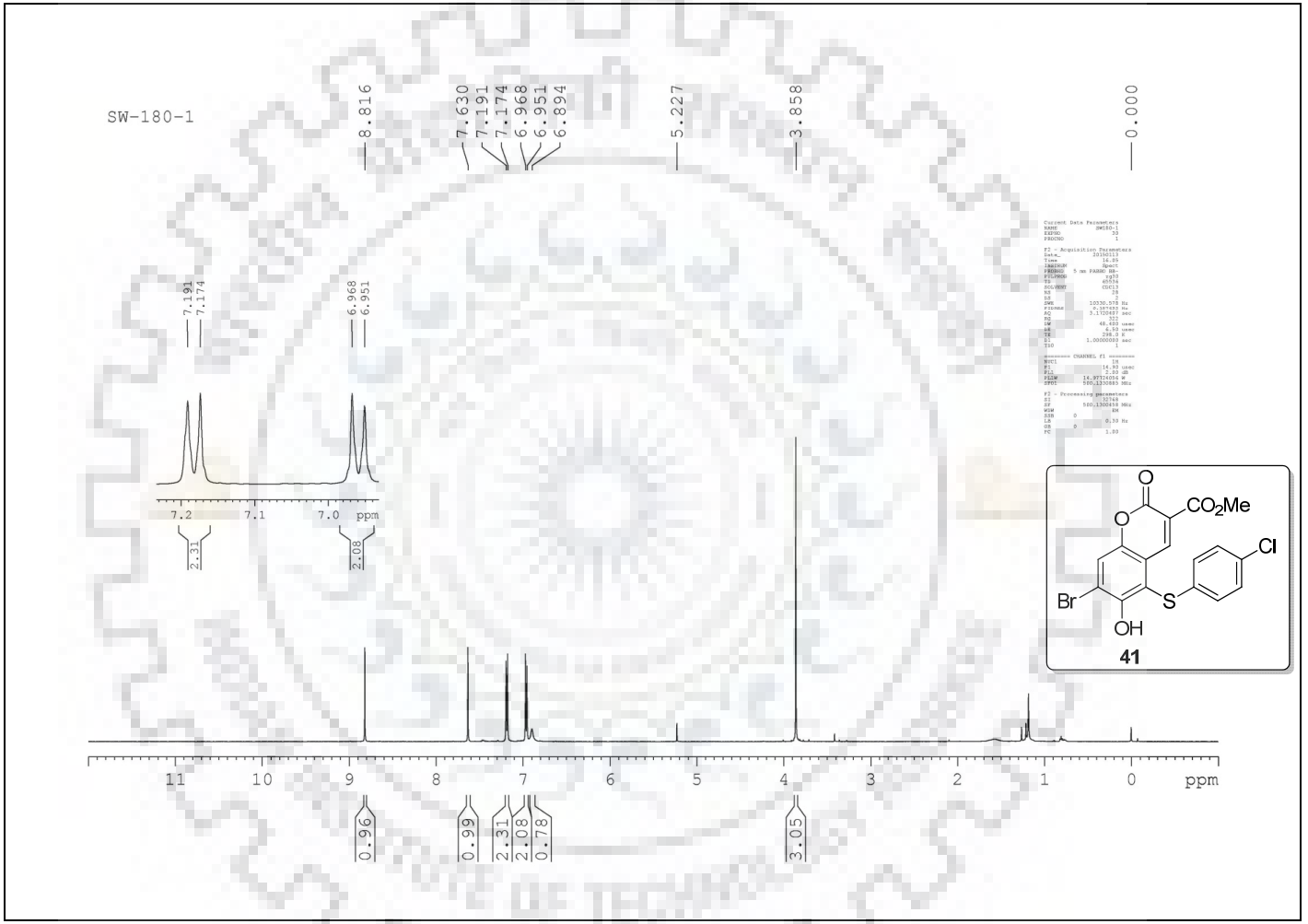


Figure S-19: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **41**.

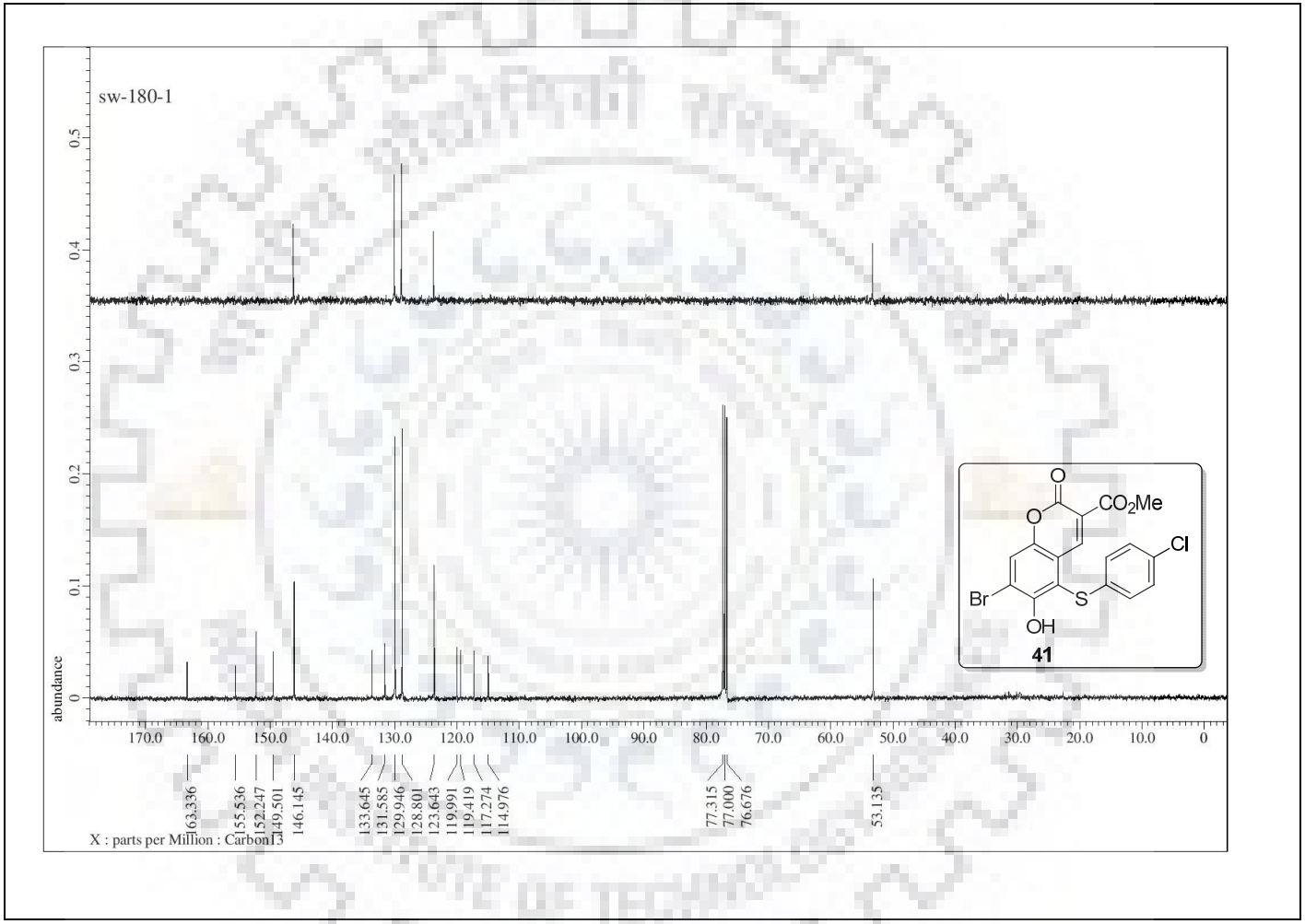


Figure S-20: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **41**.

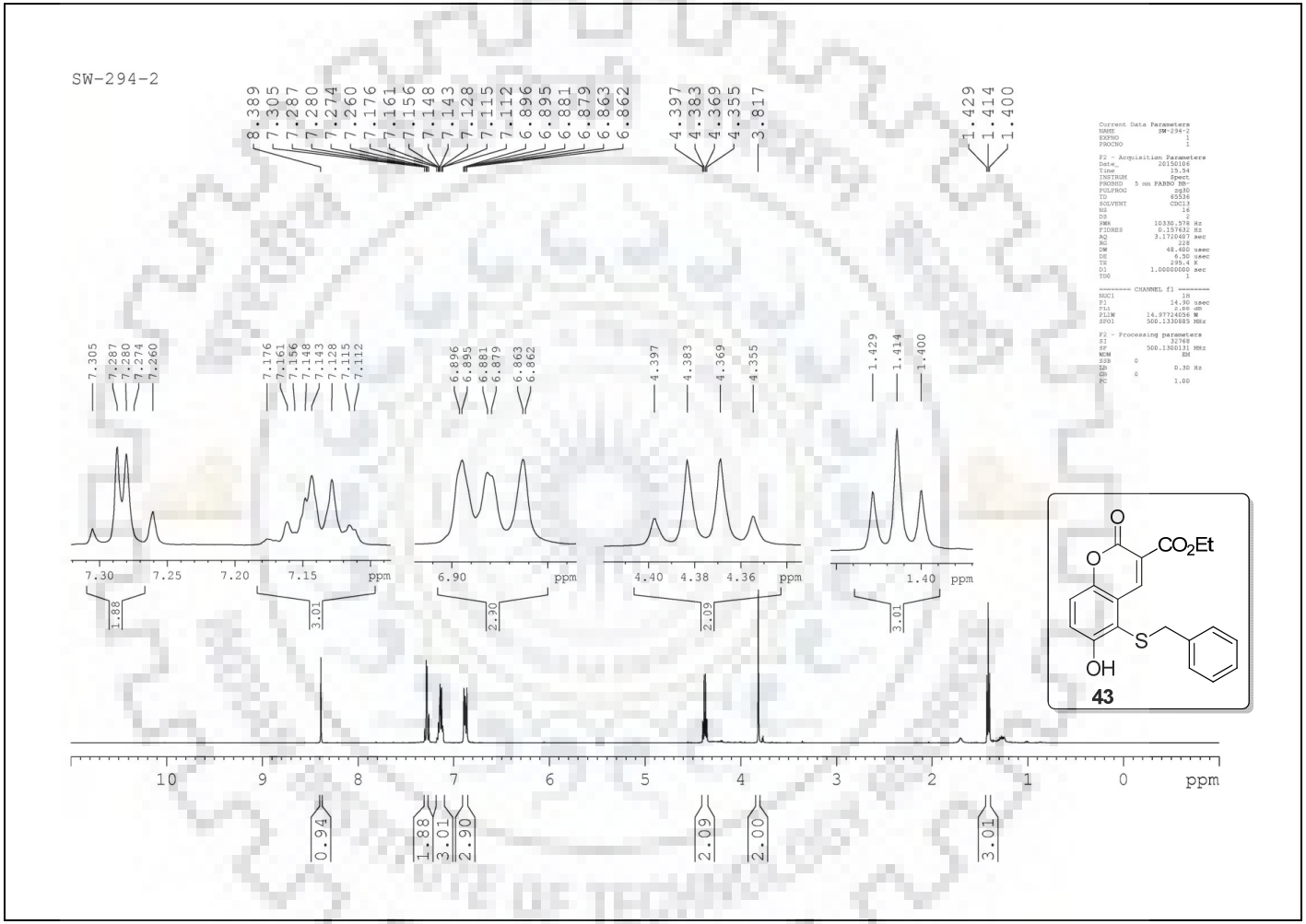


Figure S-21: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **43**.

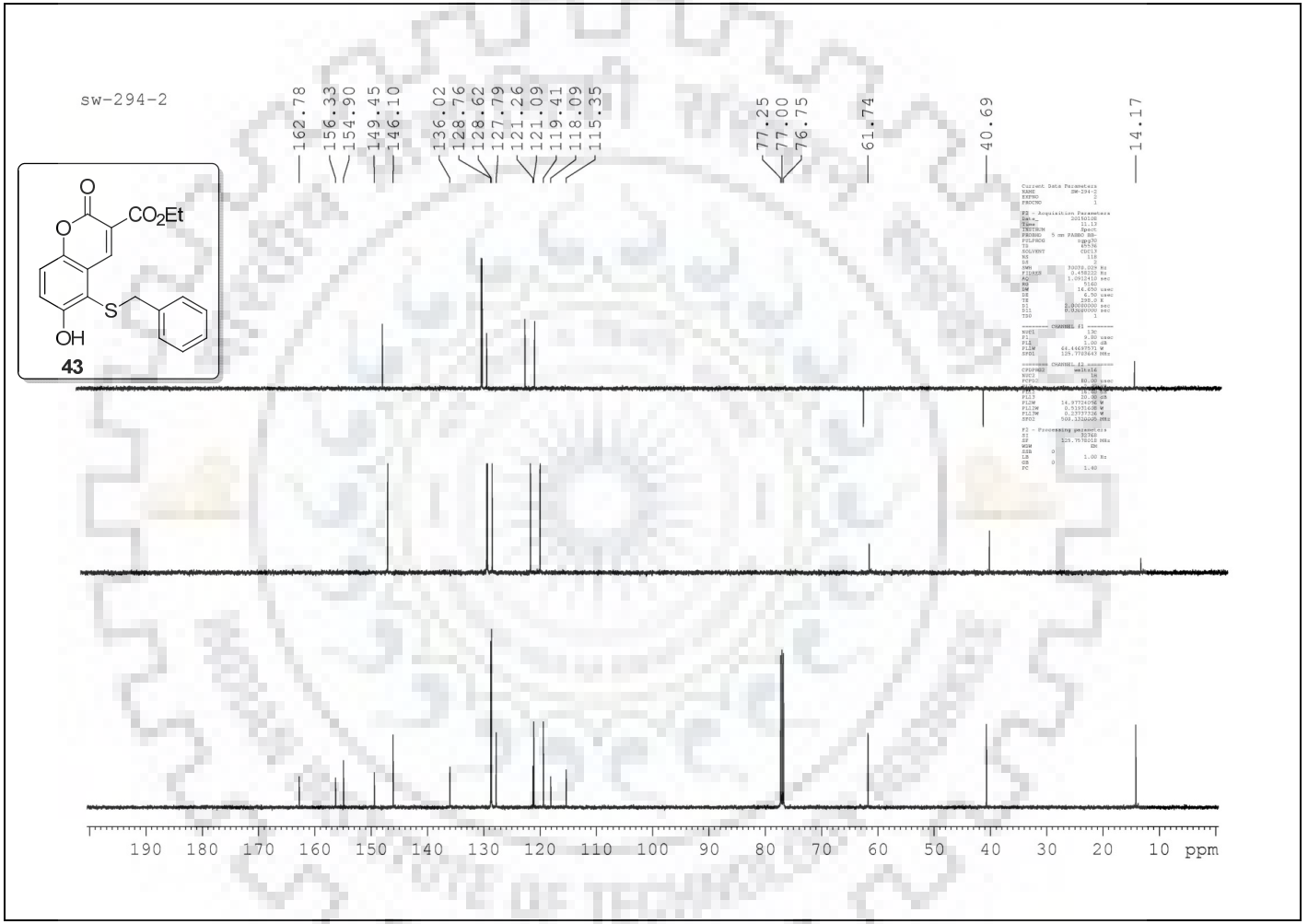


Figure S-22: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **43**.

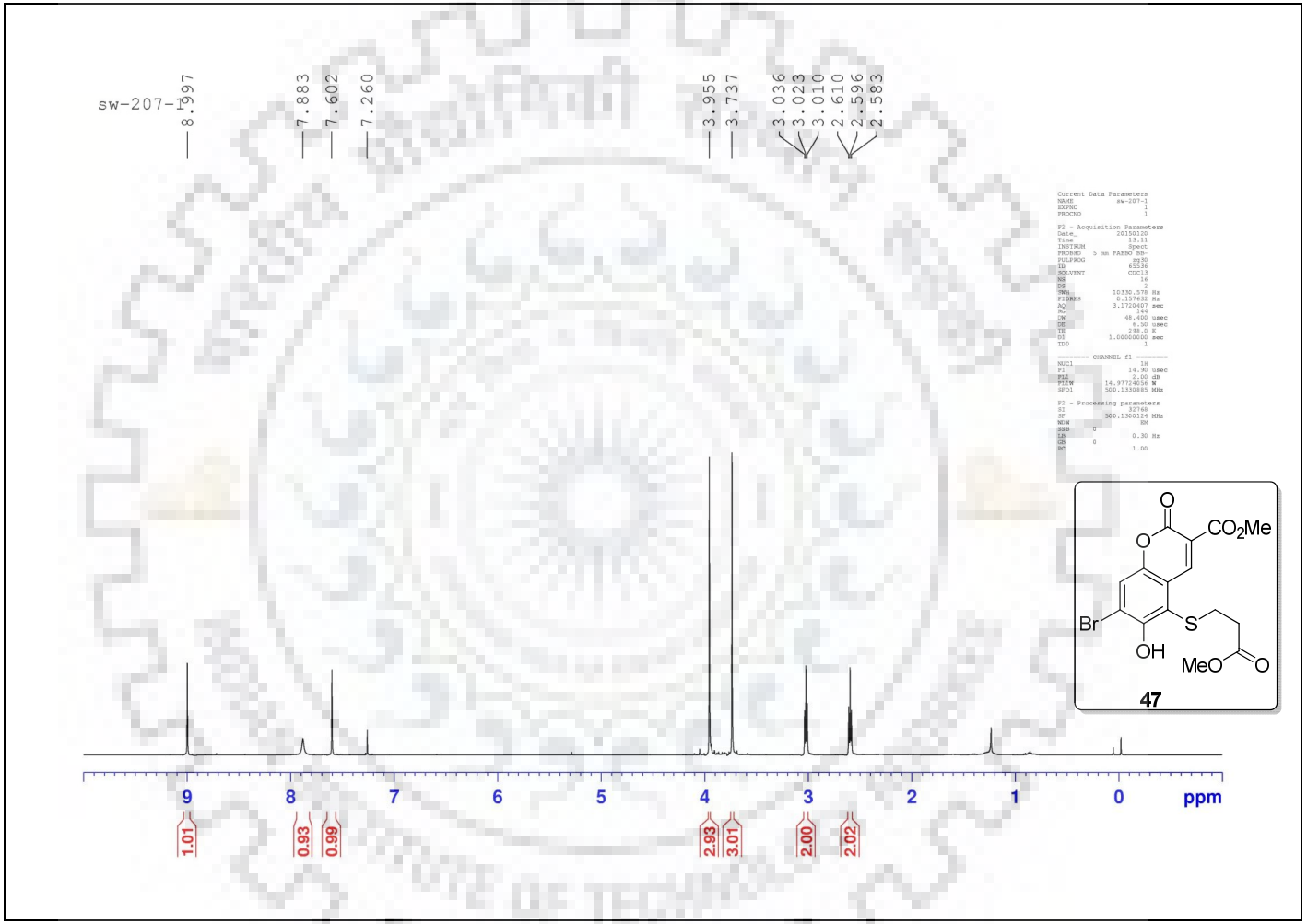


Figure S-23: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **47**.

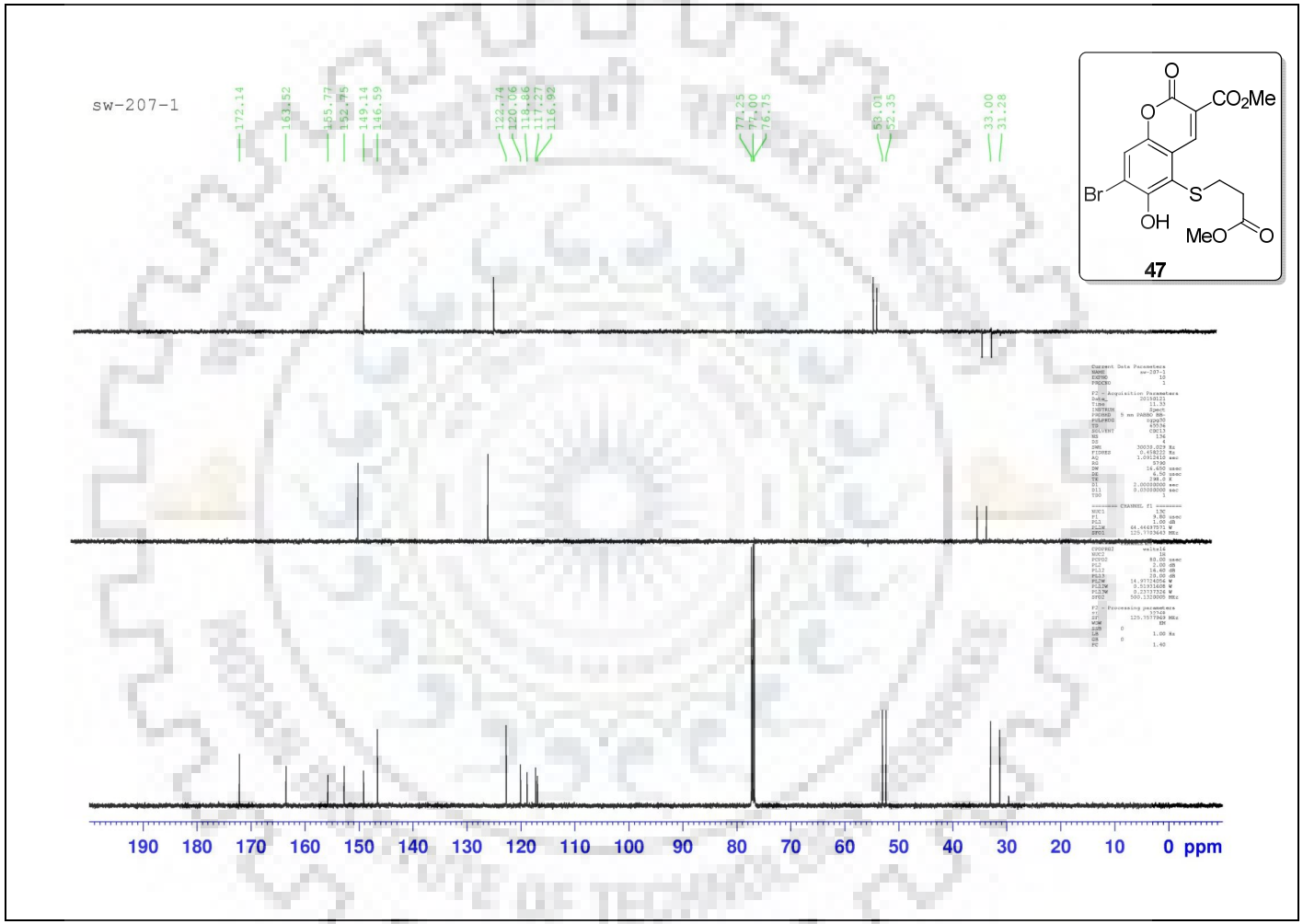


Figure S-24: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **47**.

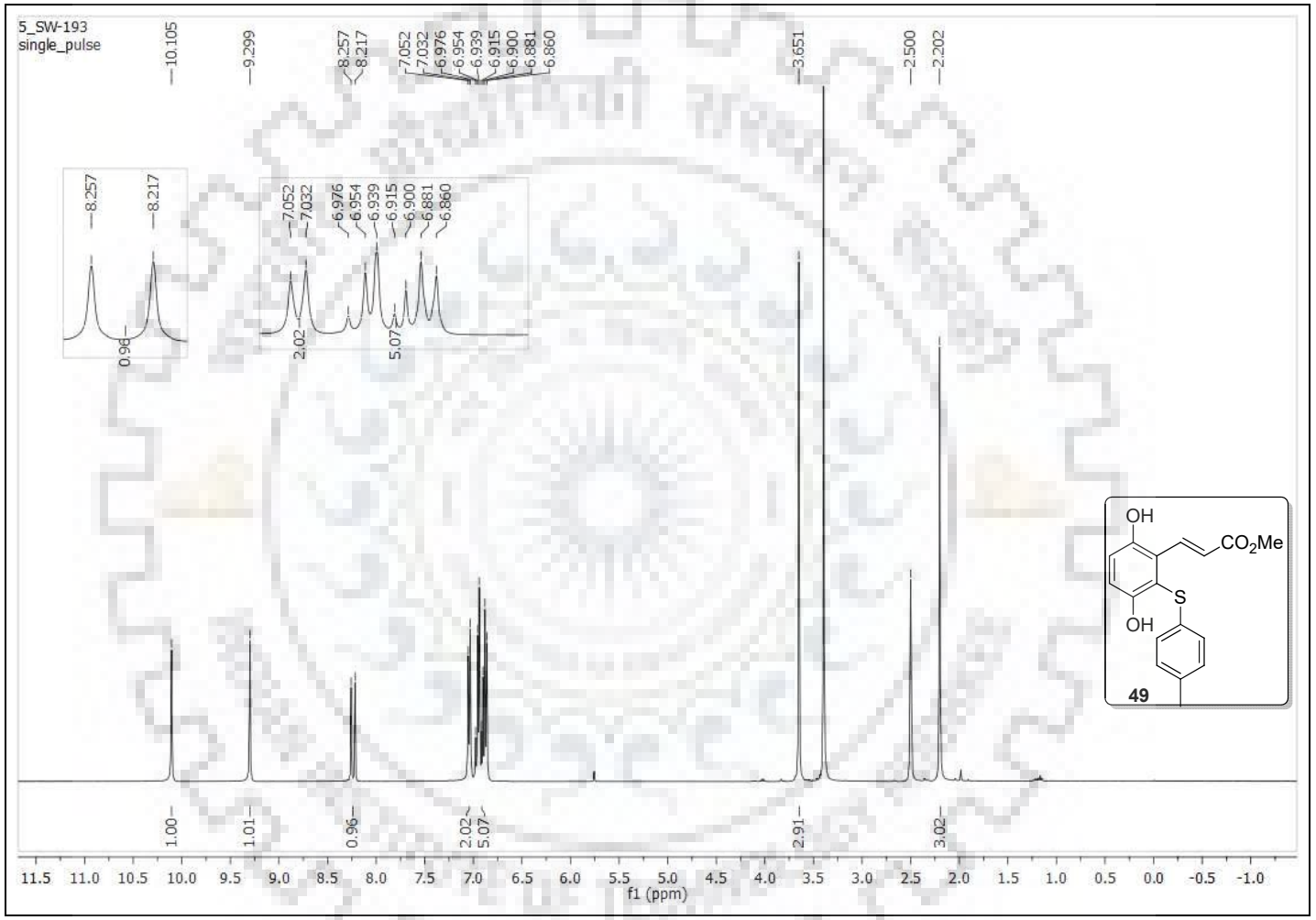


Figure S-25: ^{1}H NMR (400 MHz, DMSO-d_6) Spectrum of **49**.

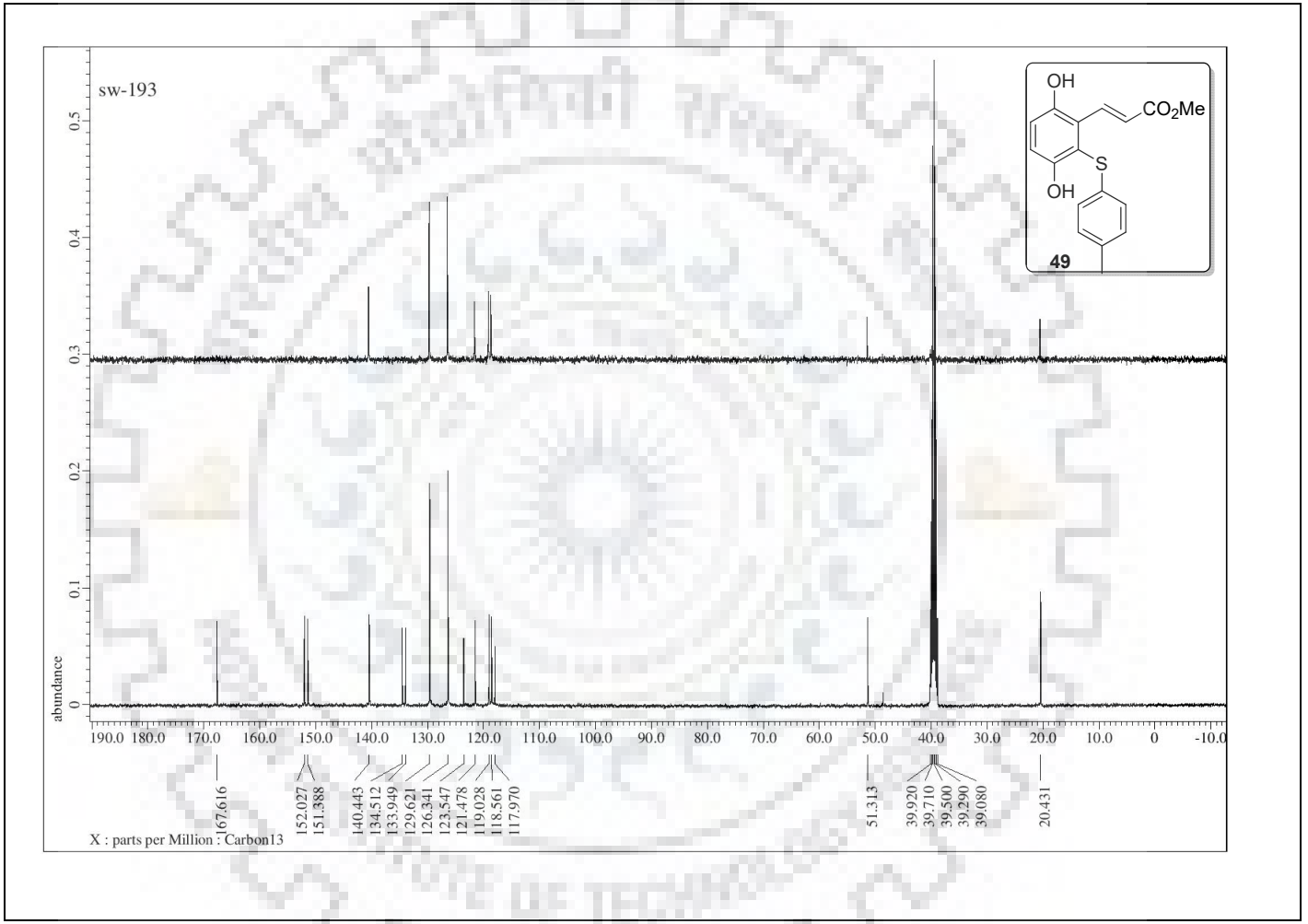


Figure S-26: ^{13}C and DEPT NMR (100 MHz, DMSO-d_6) Spectra of **49**.

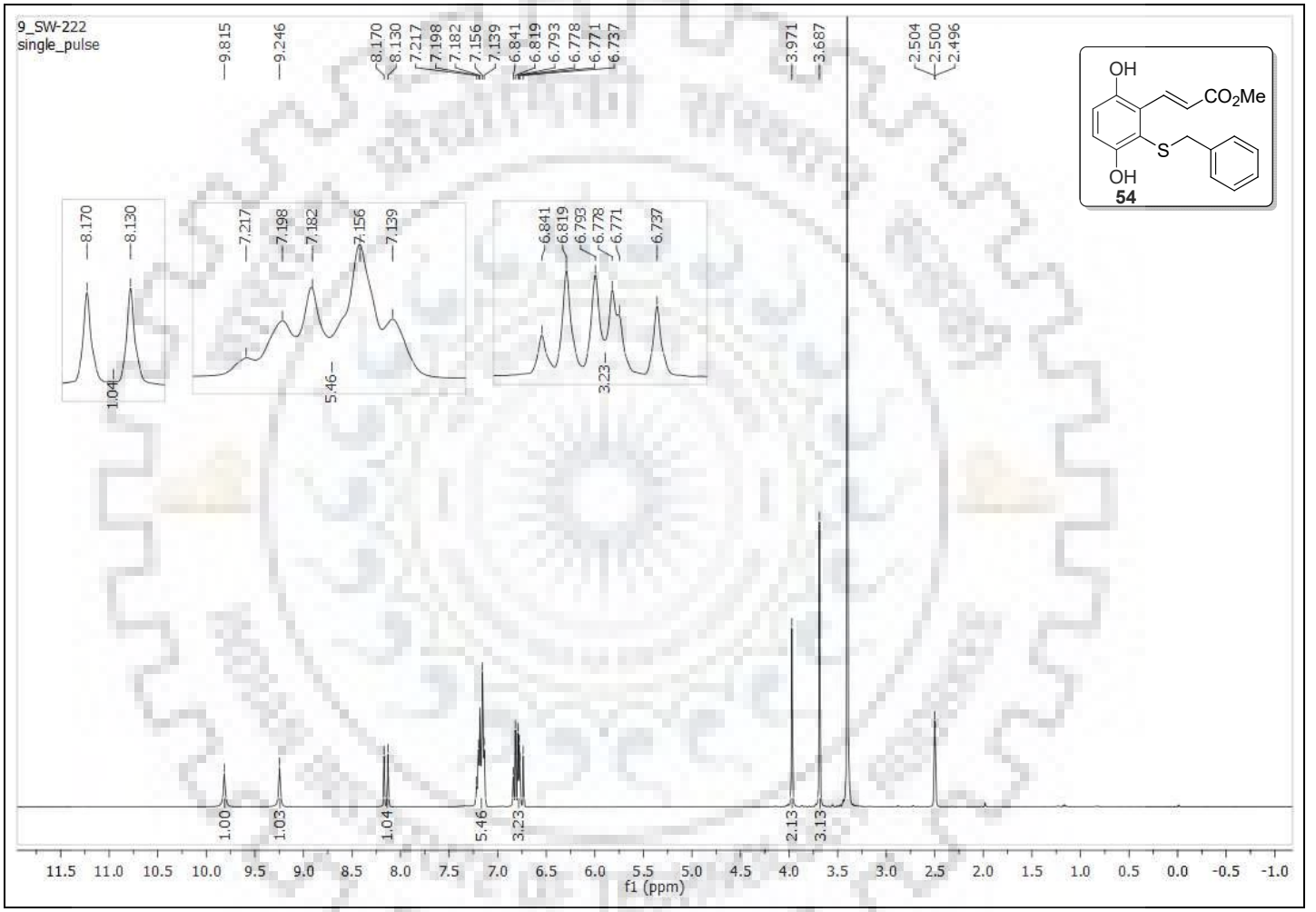


Figure S-27: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **54**.

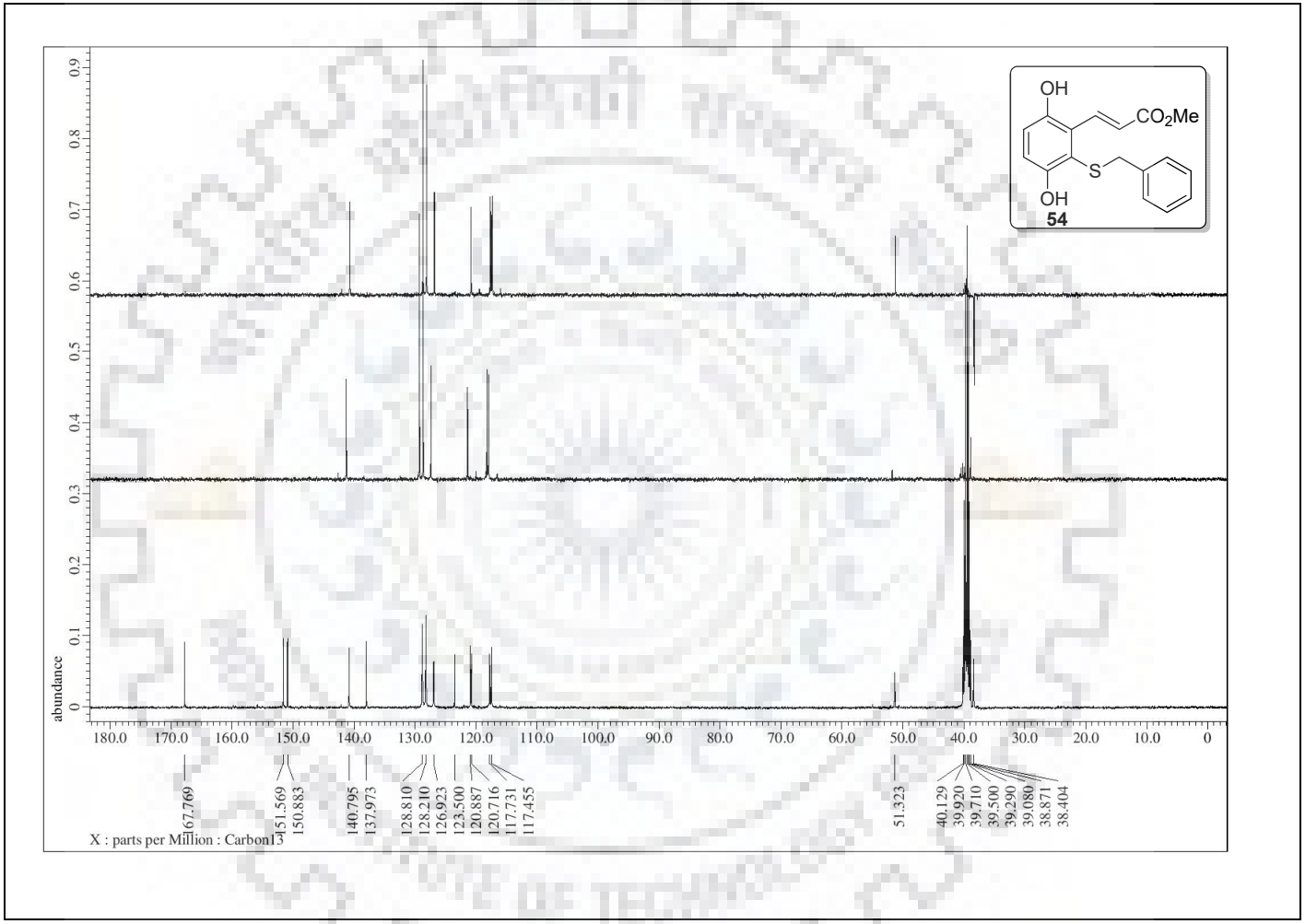


Figure S-28: ^{13}C and DEPT NMR (125 MHz, DMSO-d_6) Spectra of **54**.

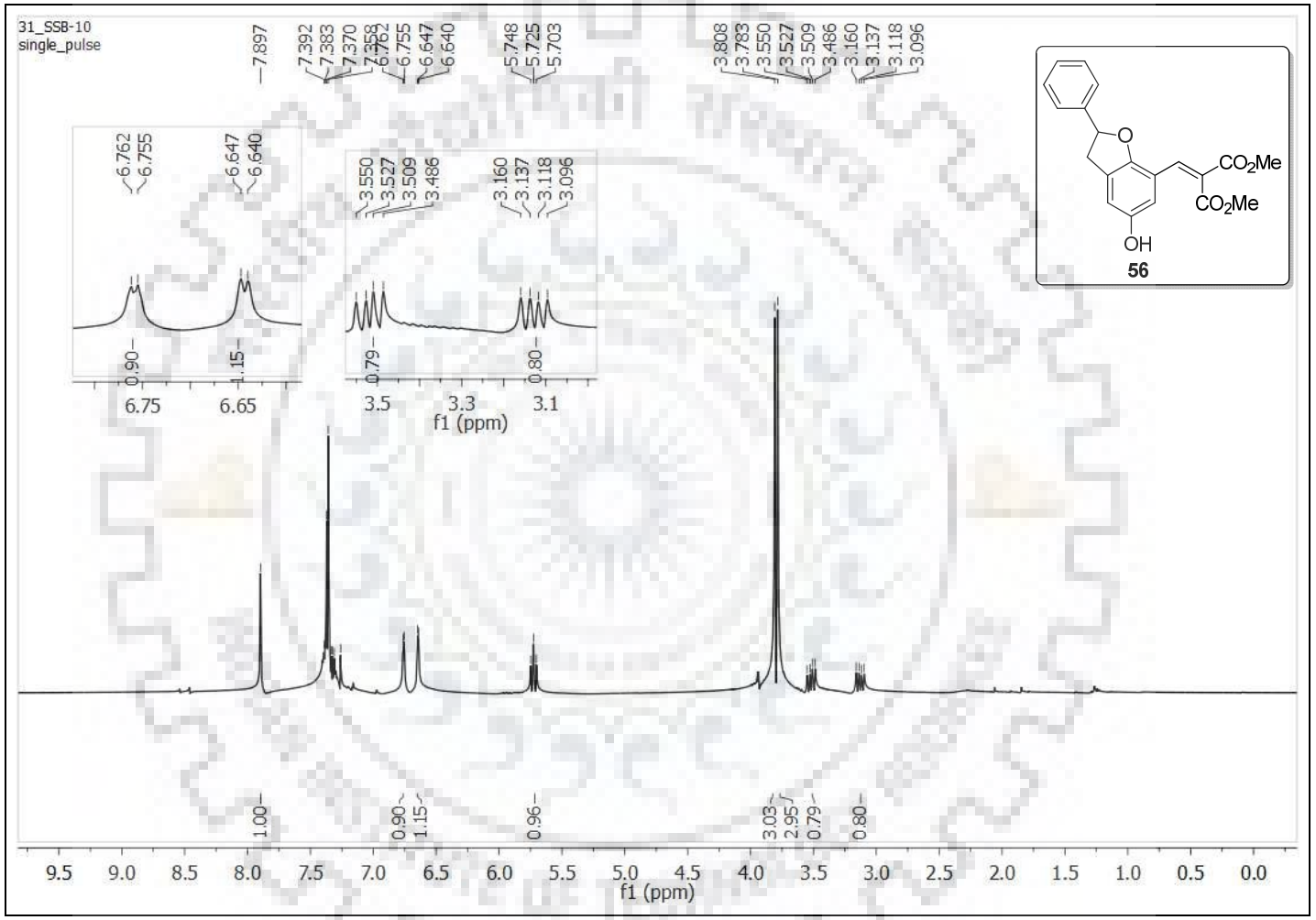


Figure S-29: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **56**.

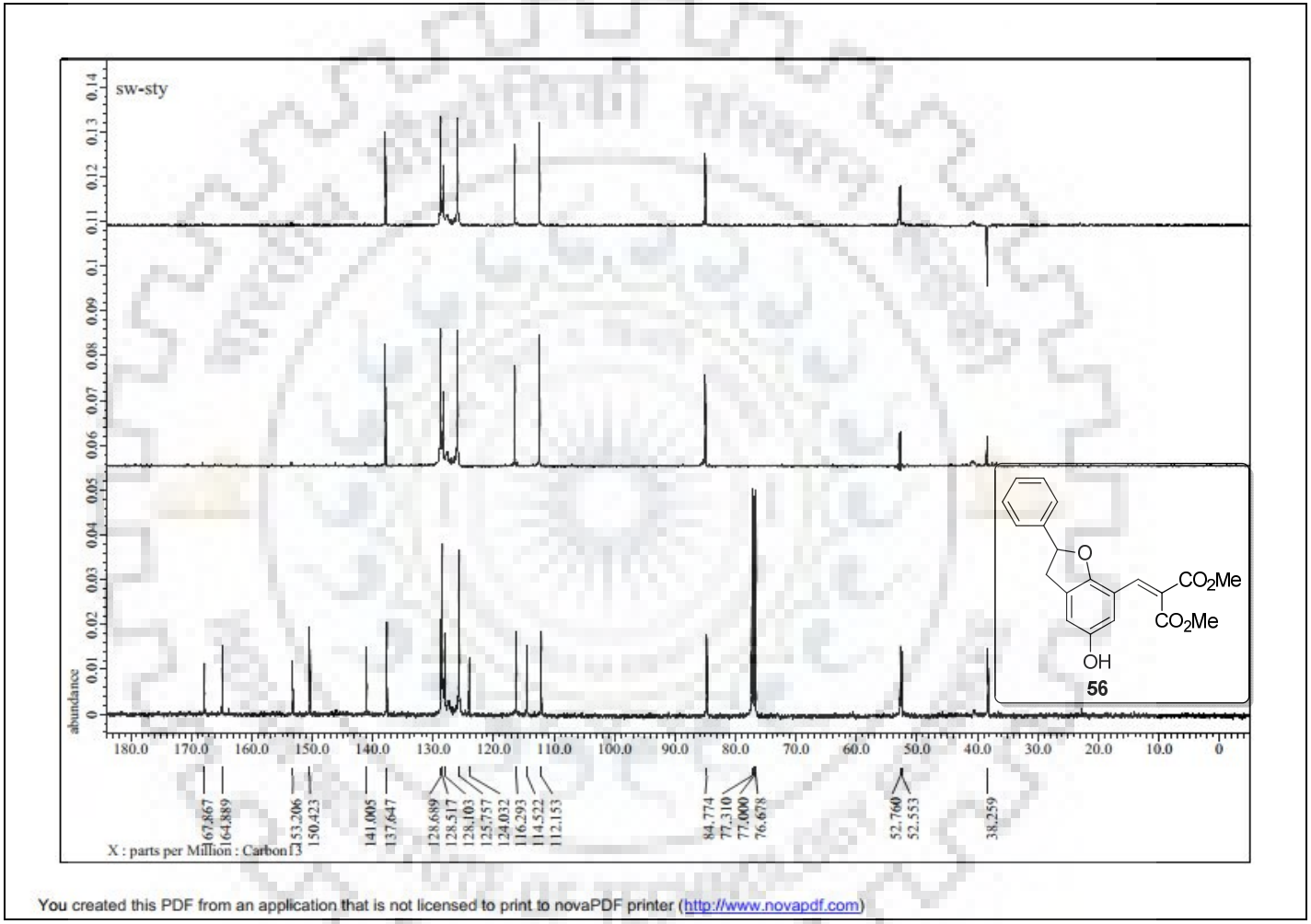


Figure S-30: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **56**.

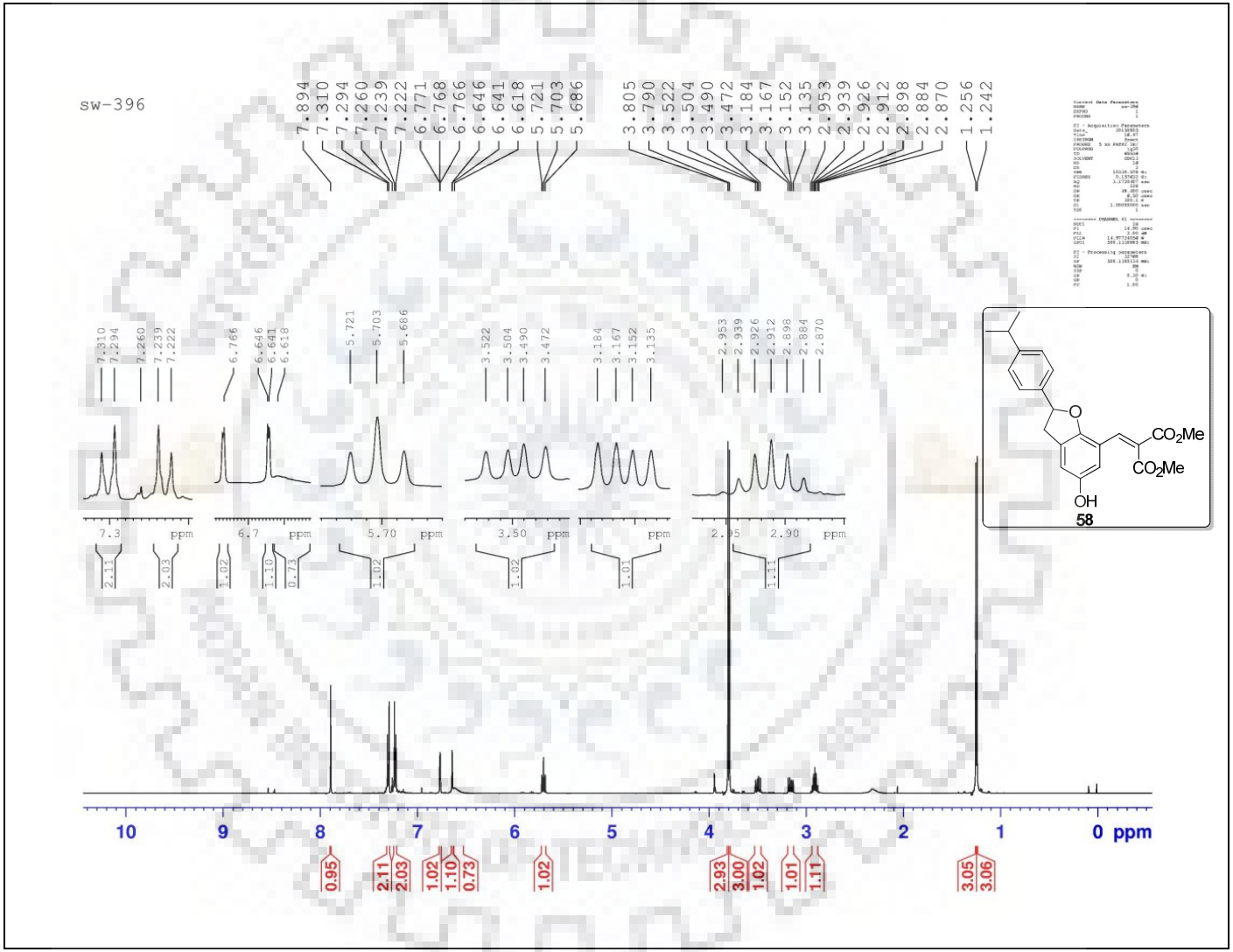


Figure S-31: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **58**.

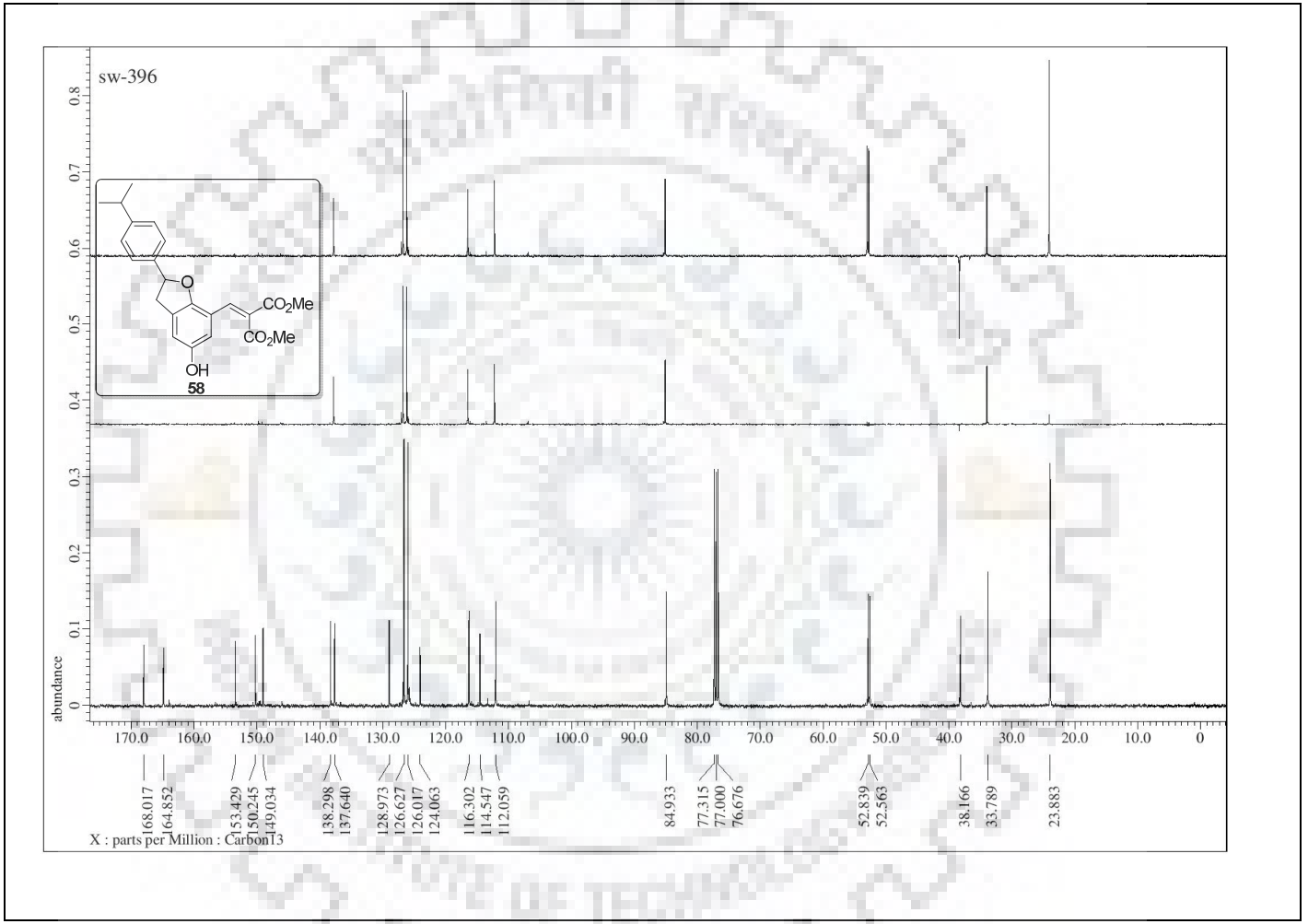


Figure S-32: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **58**.

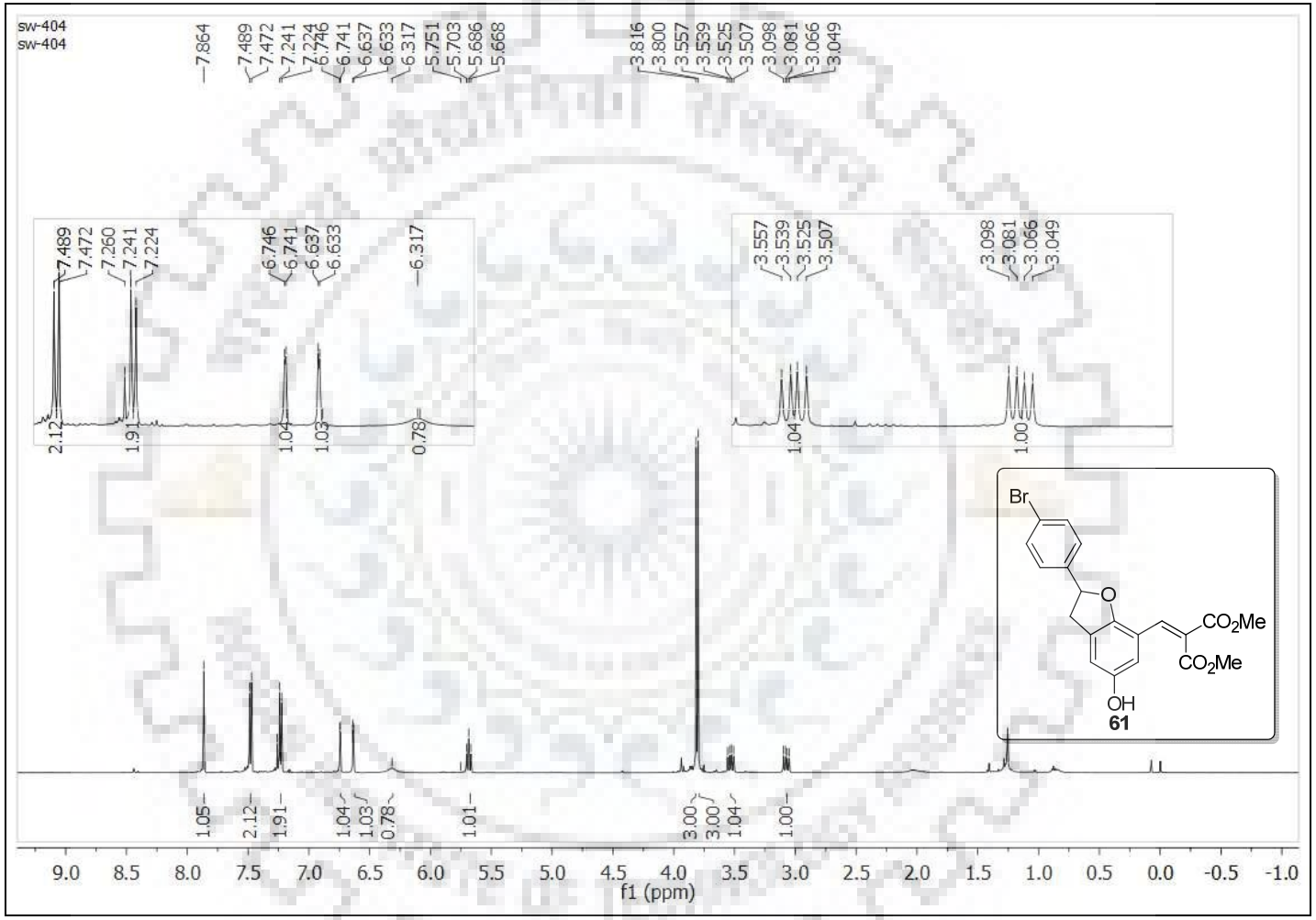


Figure S-33: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **61**.

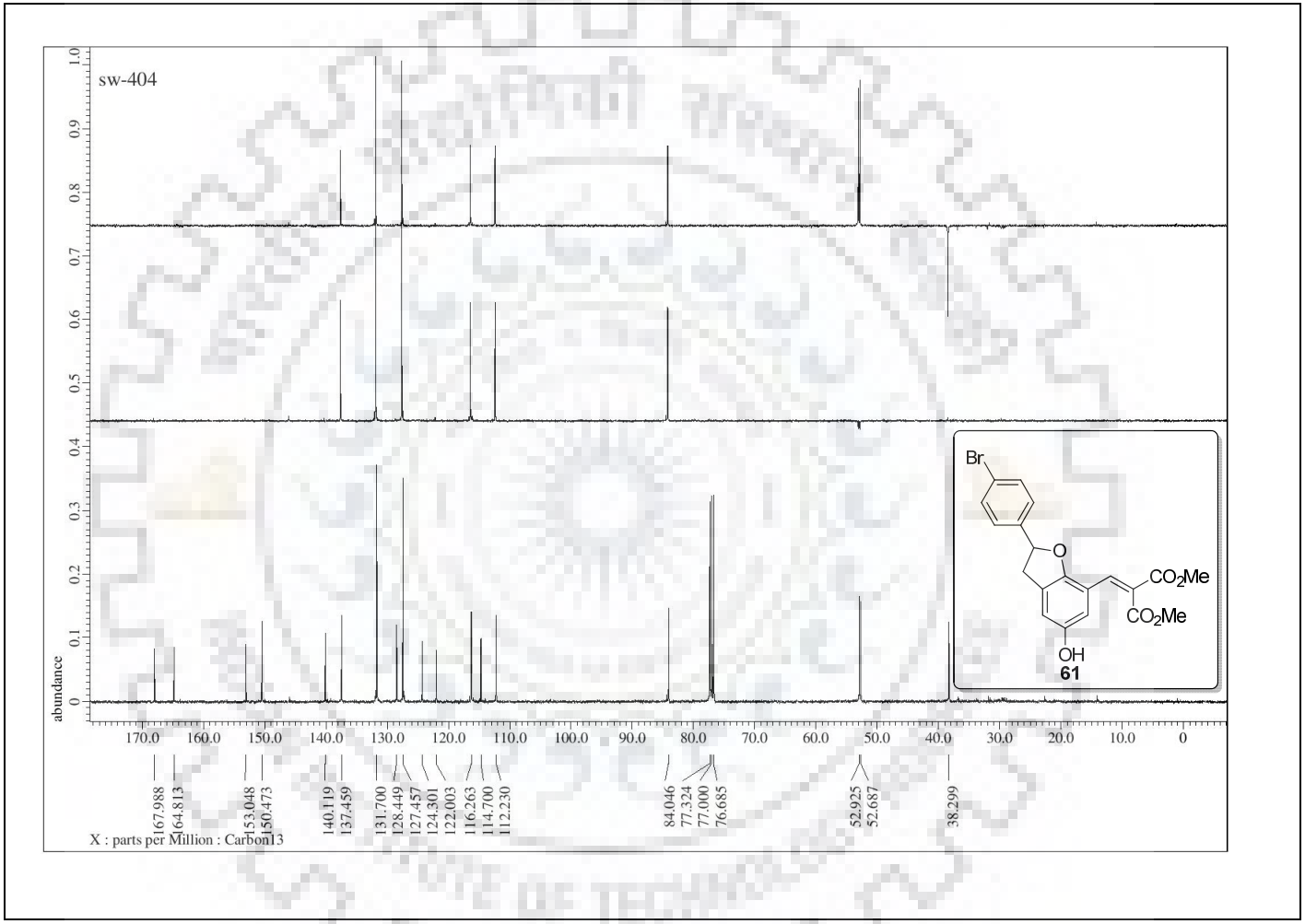


Figure S-34: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **61**.

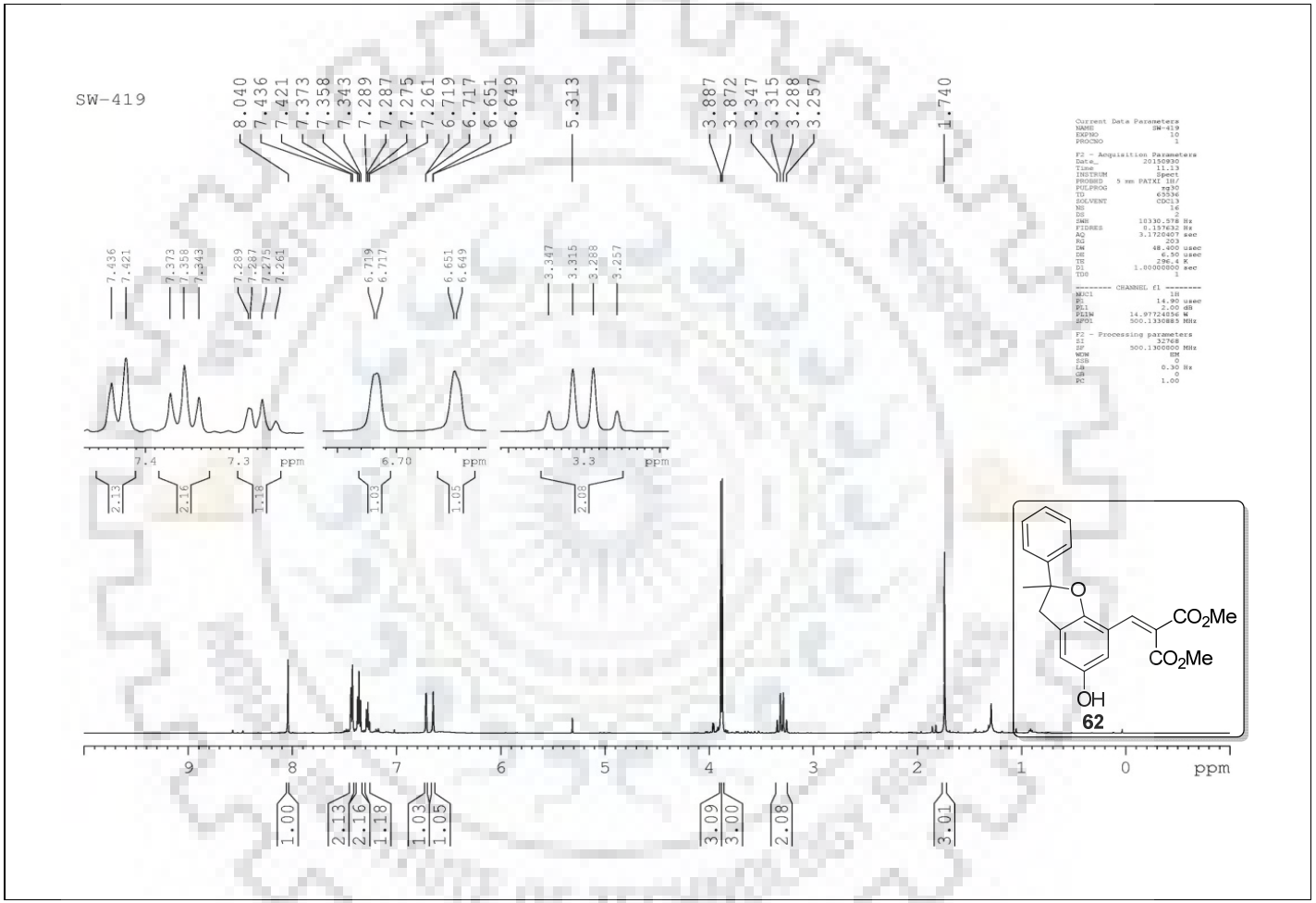


Figure S-35: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **62**.

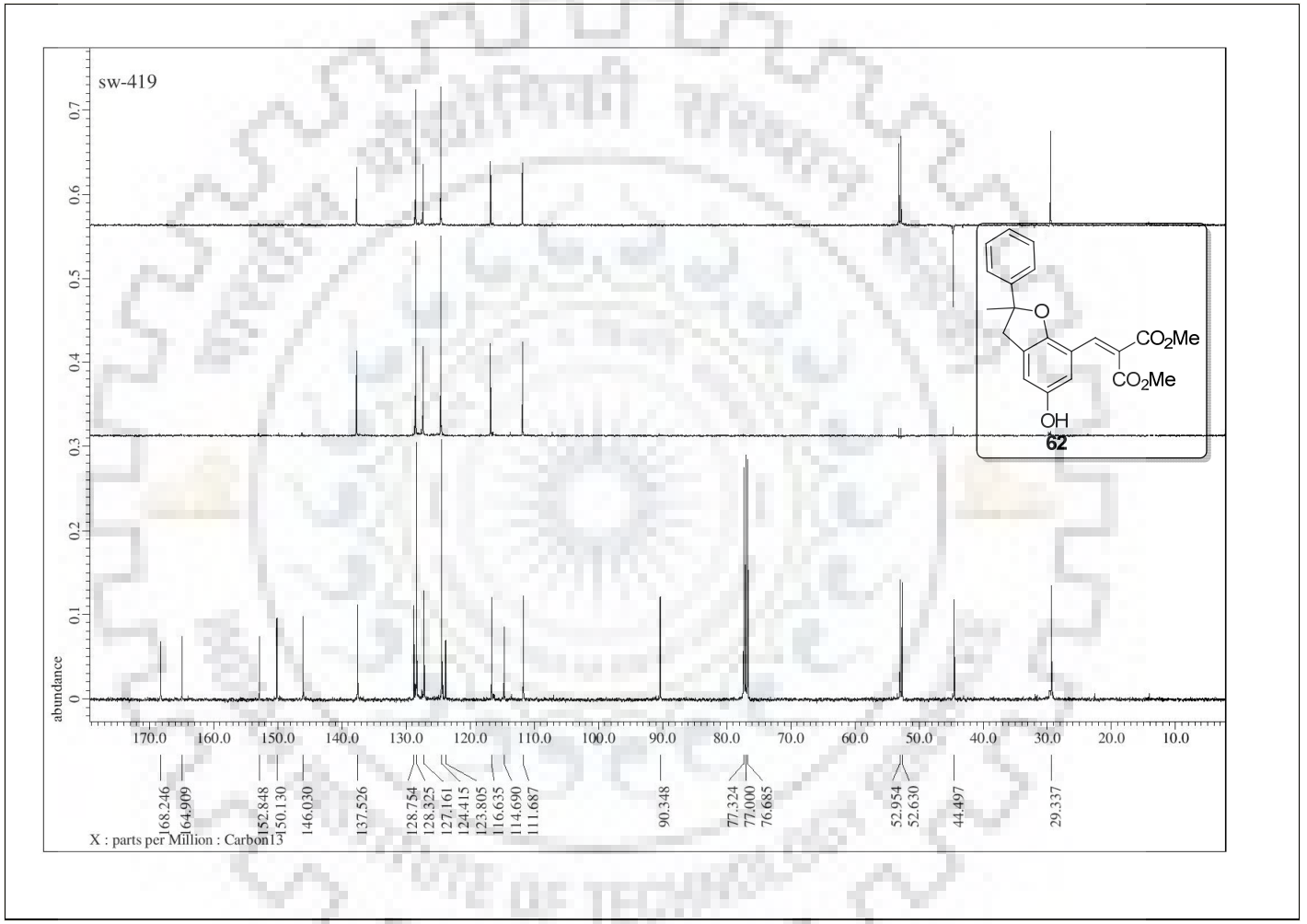


Figure S-36: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **62**.

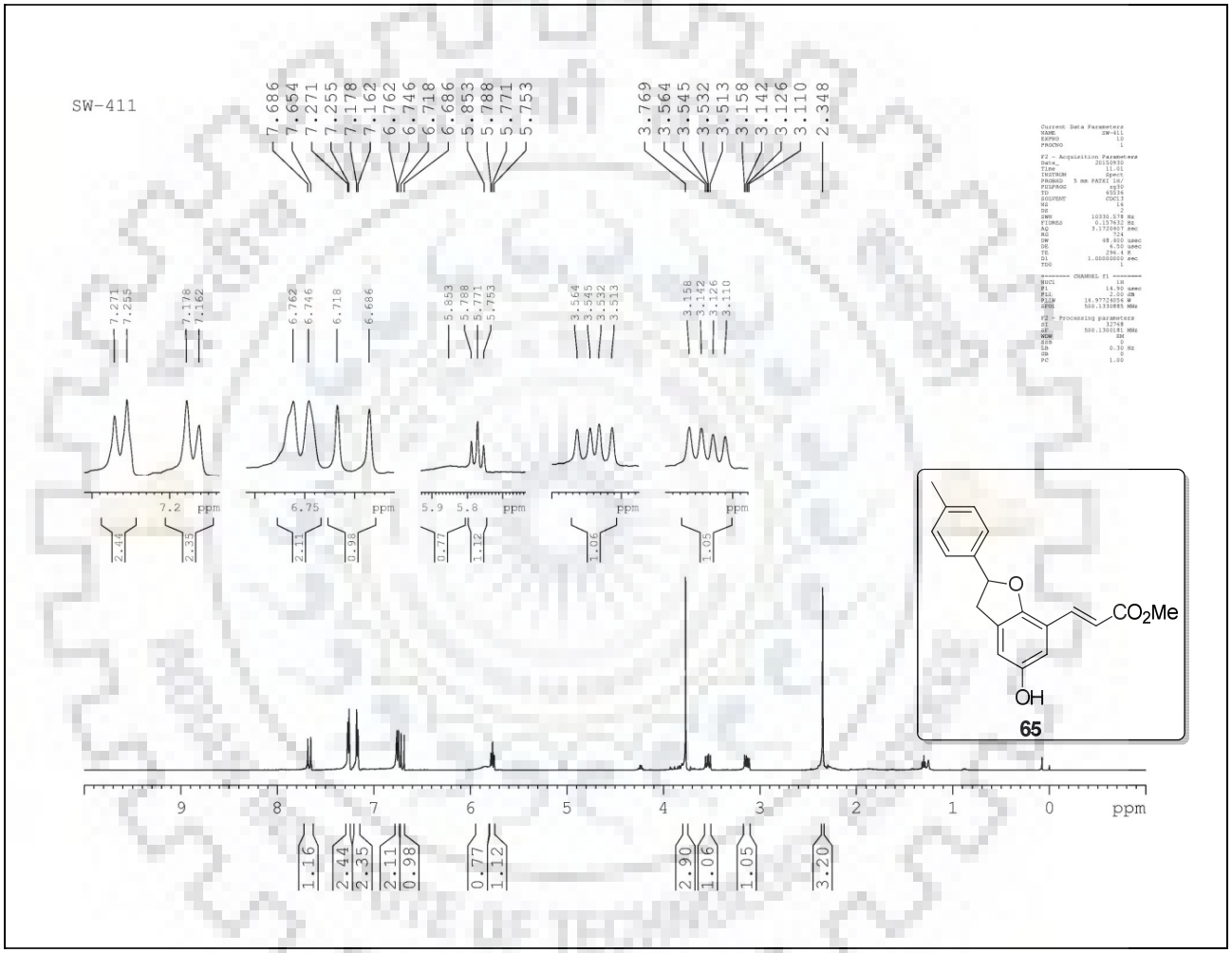


Figure S-37: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **65**.

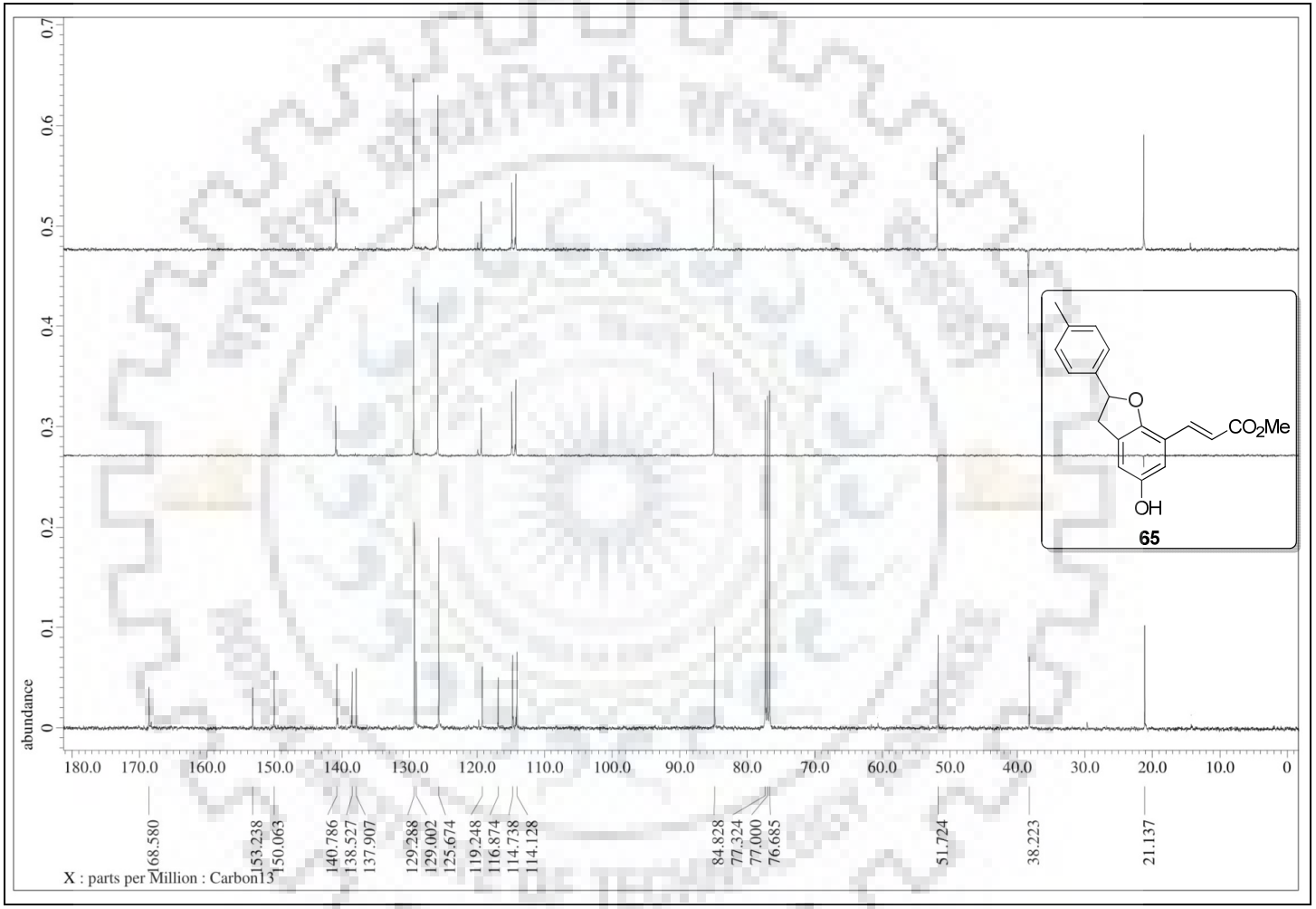


Figure S-38: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **65**.

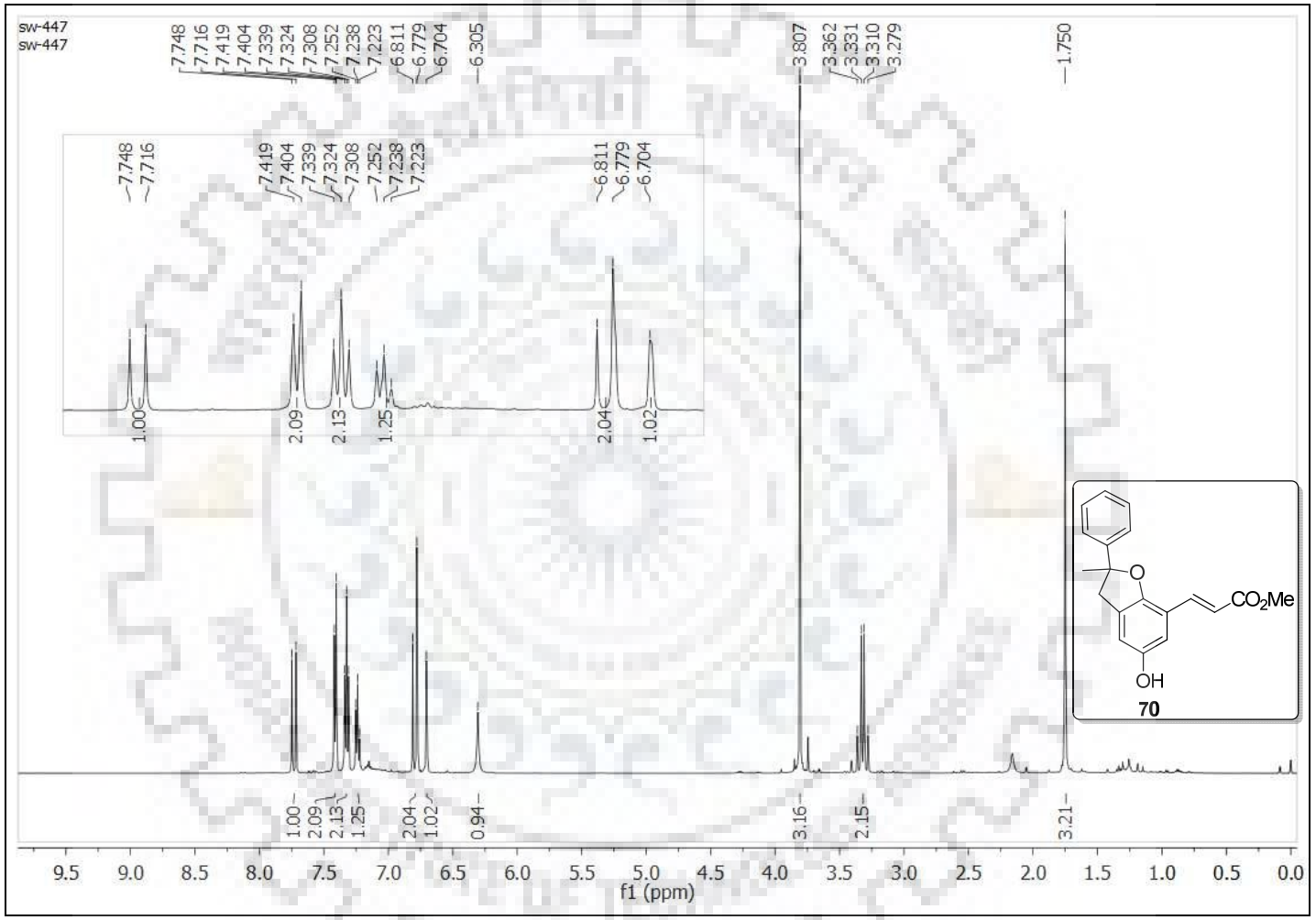


Figure S-39: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **70**.

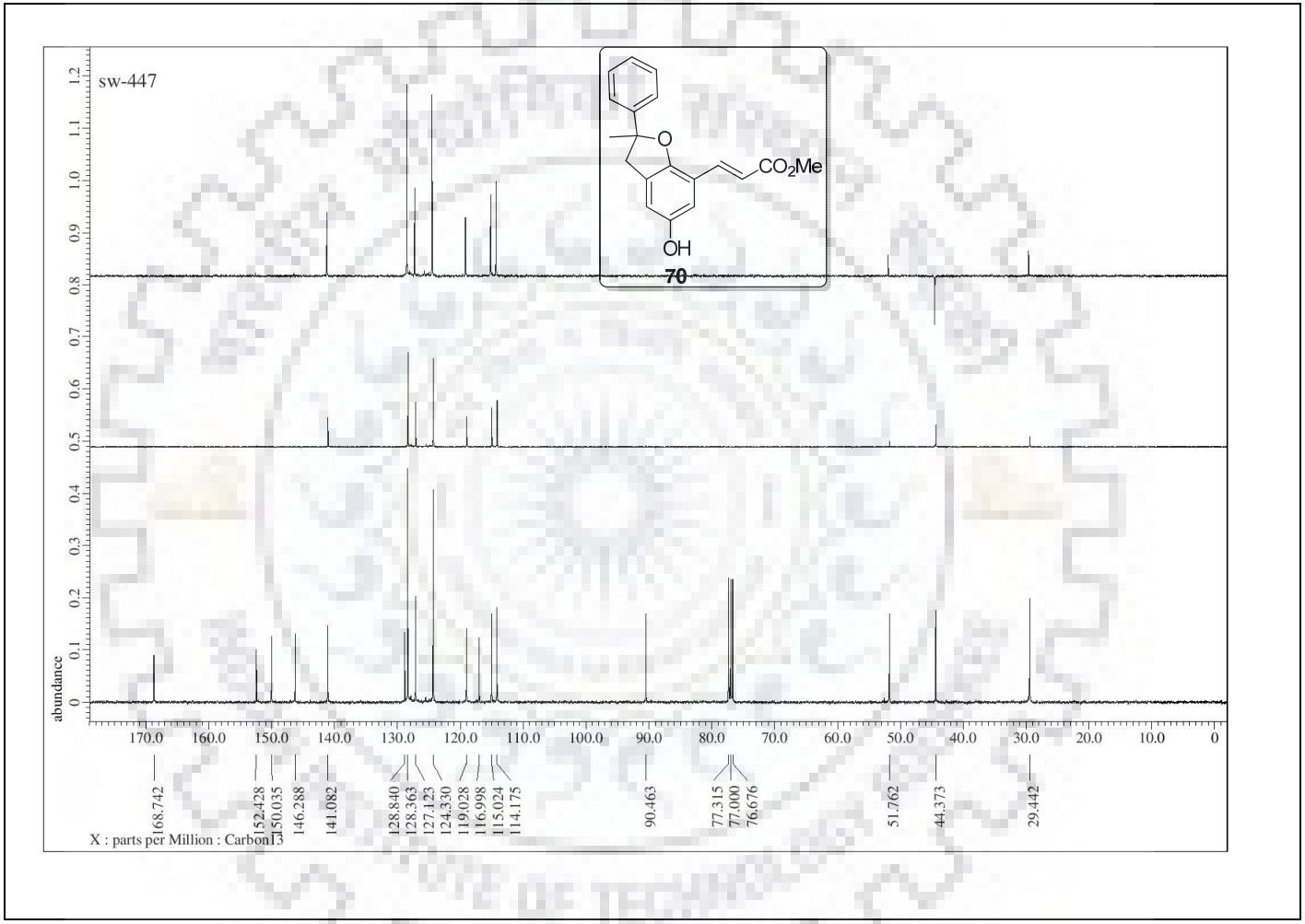


Figure S-40: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **70**.

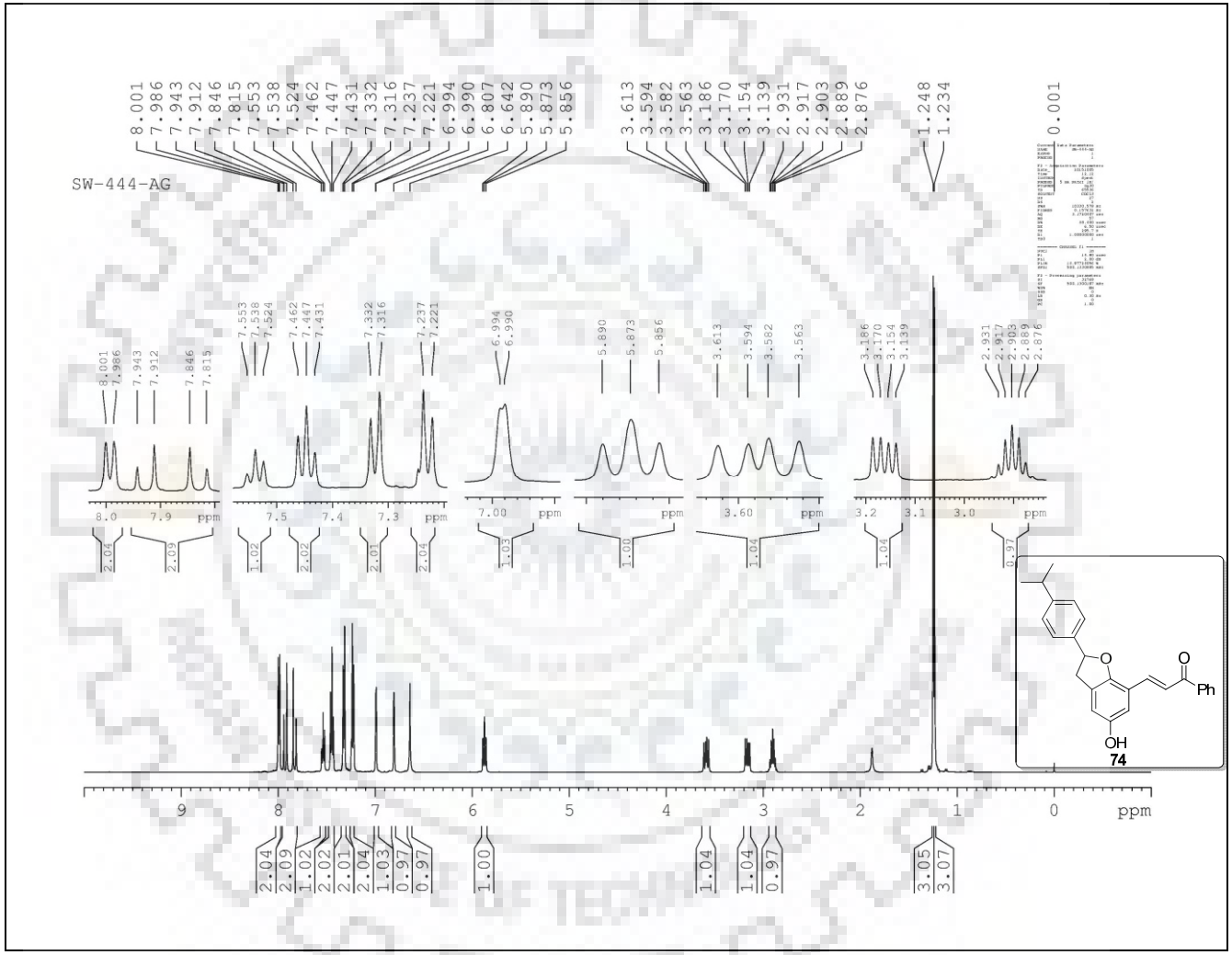


Figure S-41: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **74**.

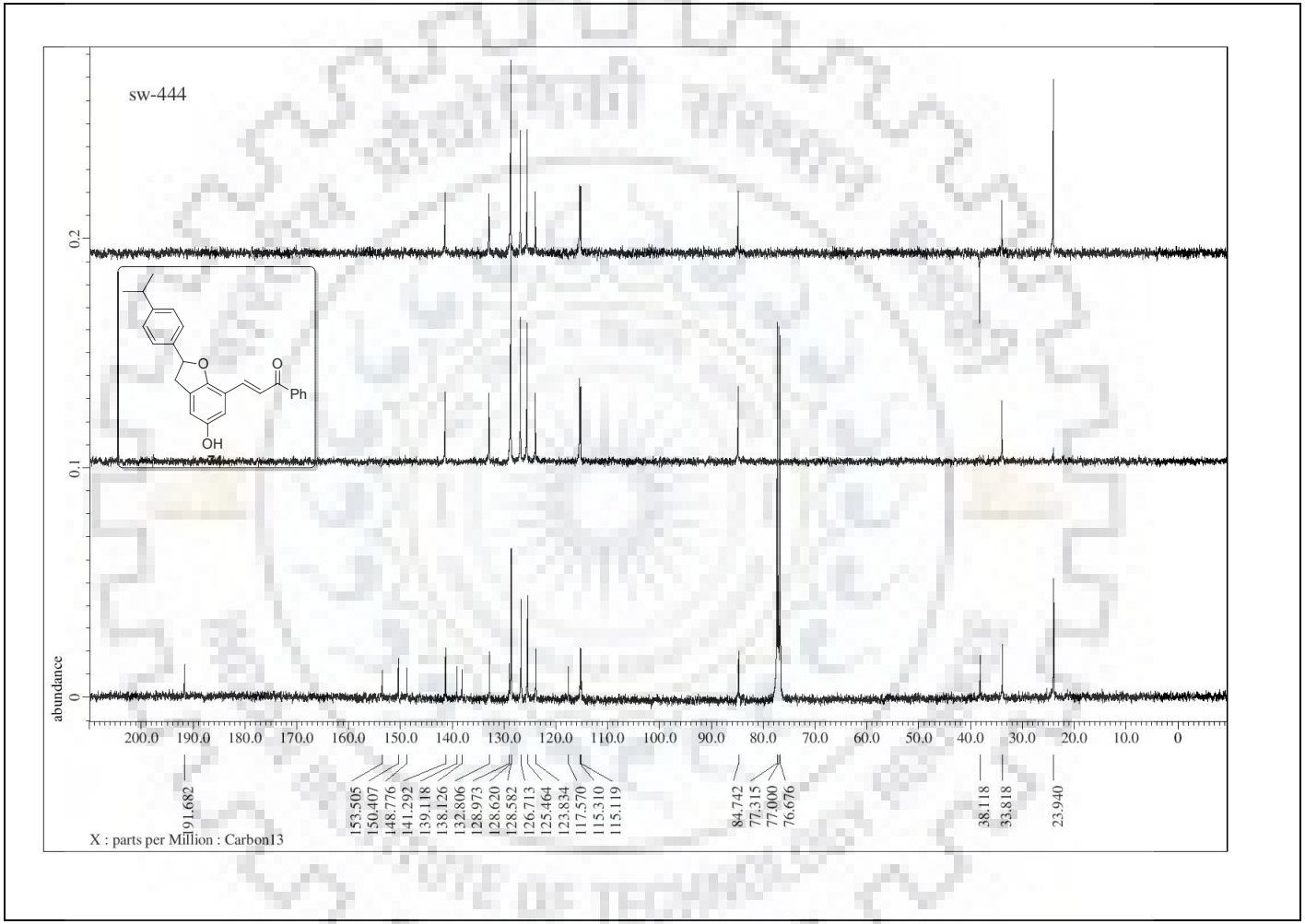


Figure S-42: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **74**.

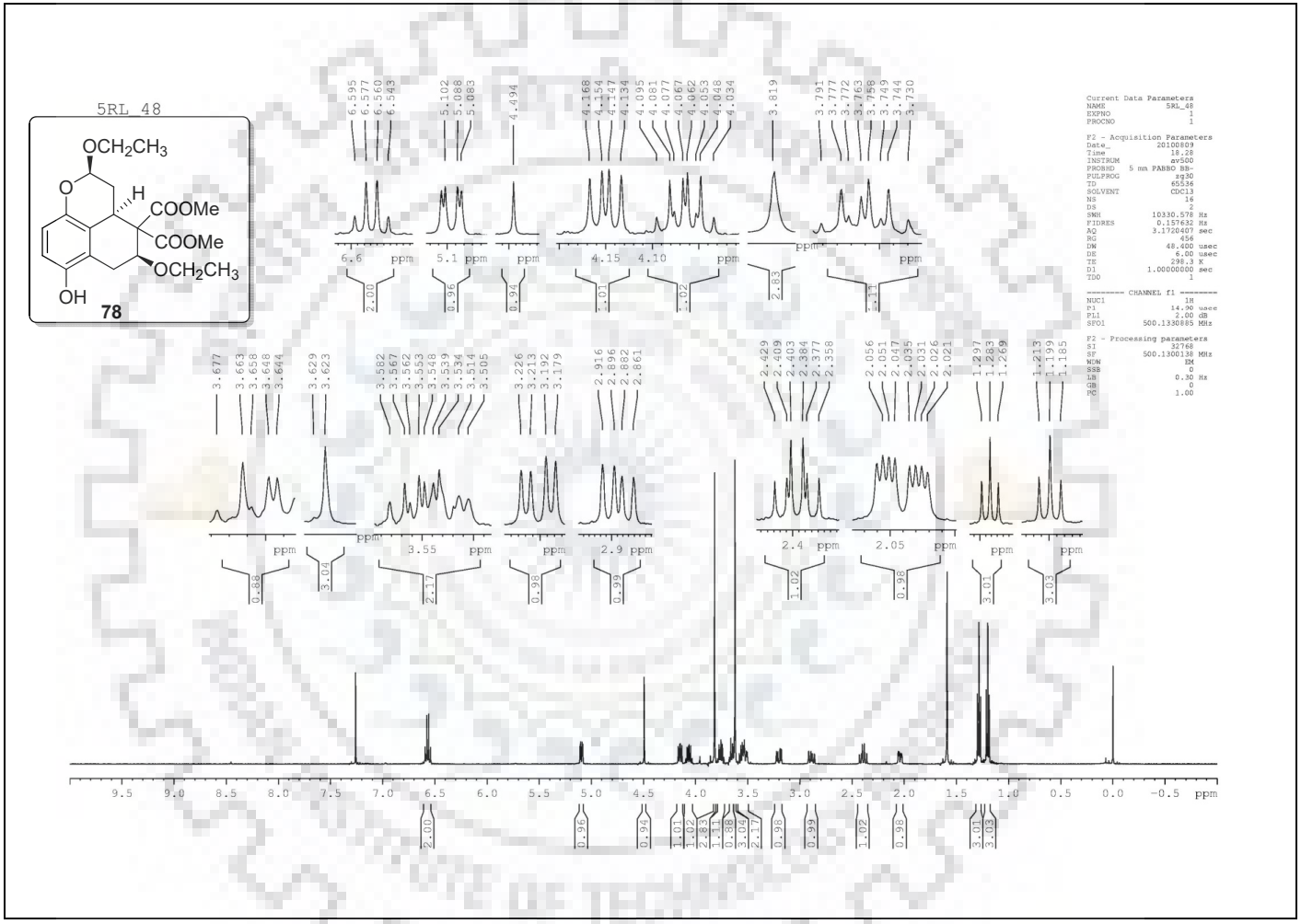


Figure S-43: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **78**.

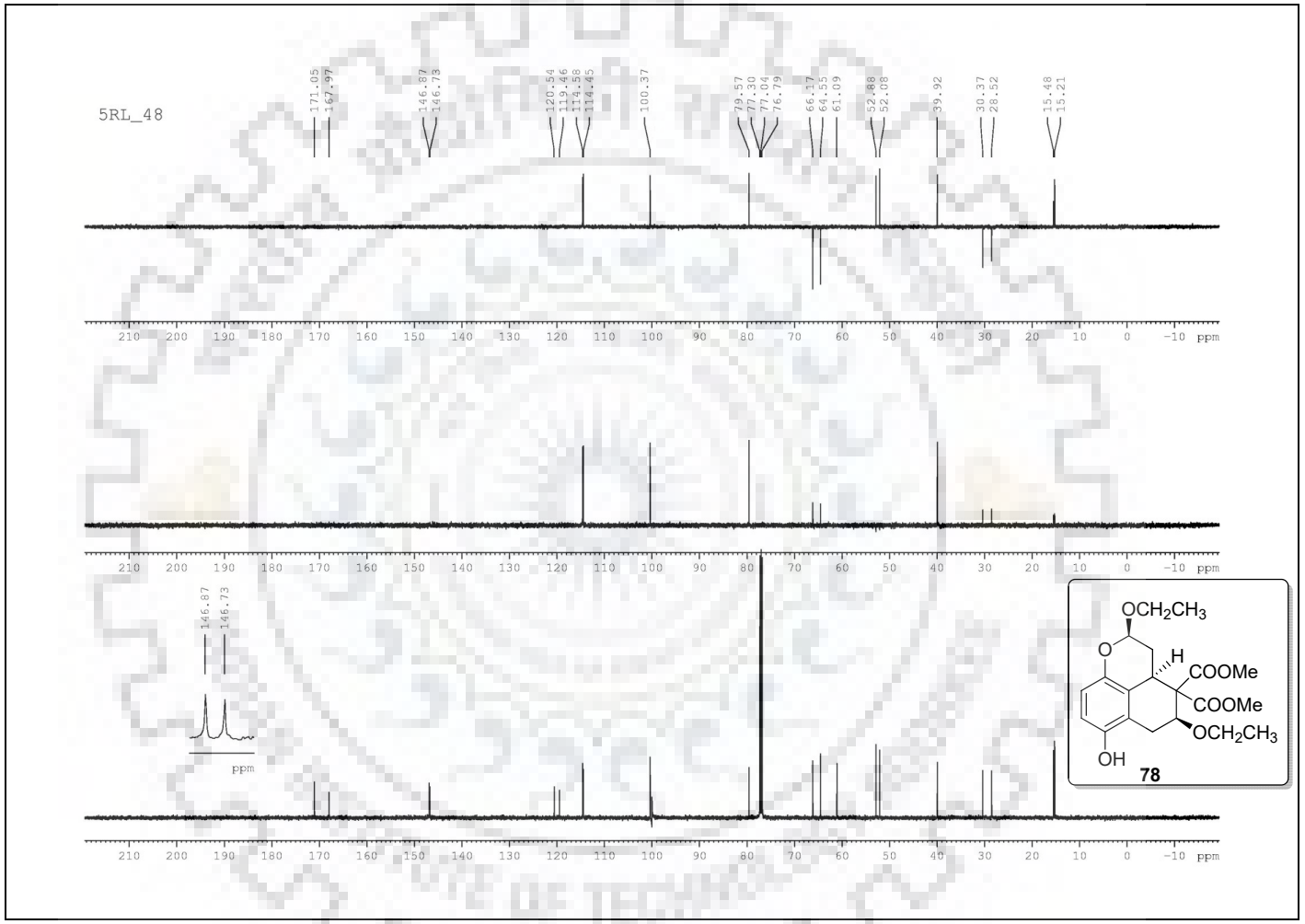


Figure S-44: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **78**.

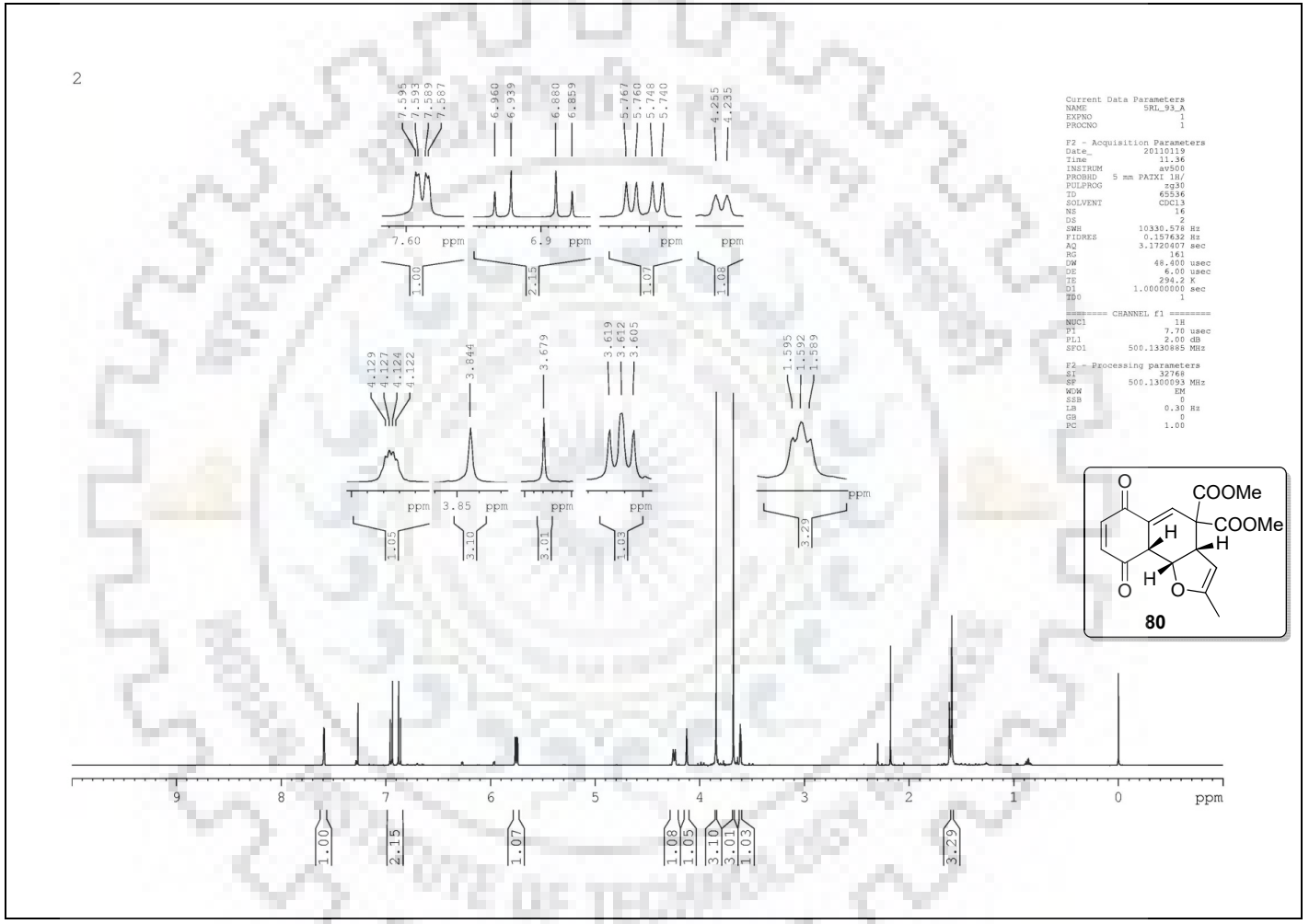


Figure S-45: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **80**.

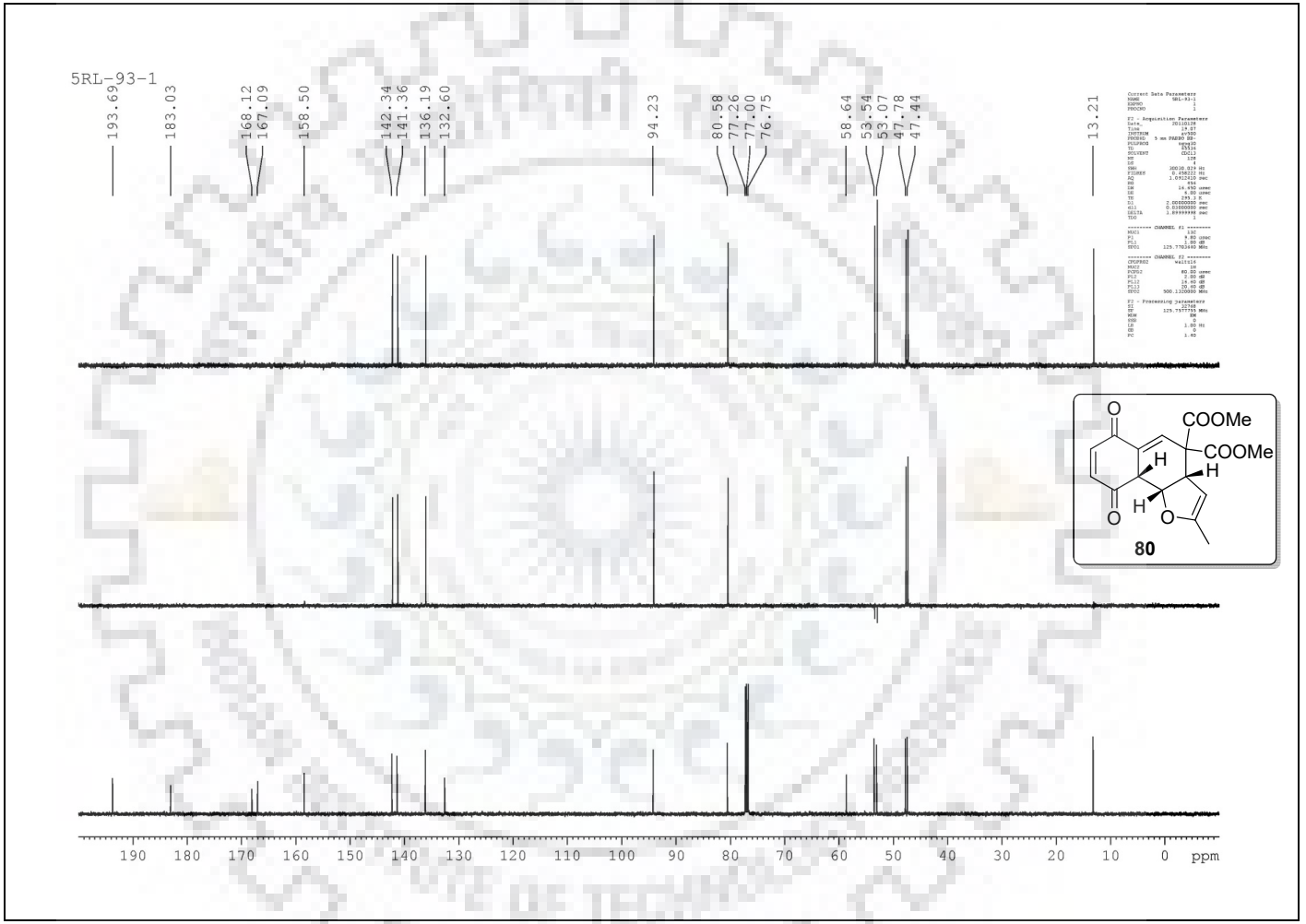


Figure S-46: ^{13}C and DEPT NMR (125 MHz, $CDCl_3$) Spectra of **80**.

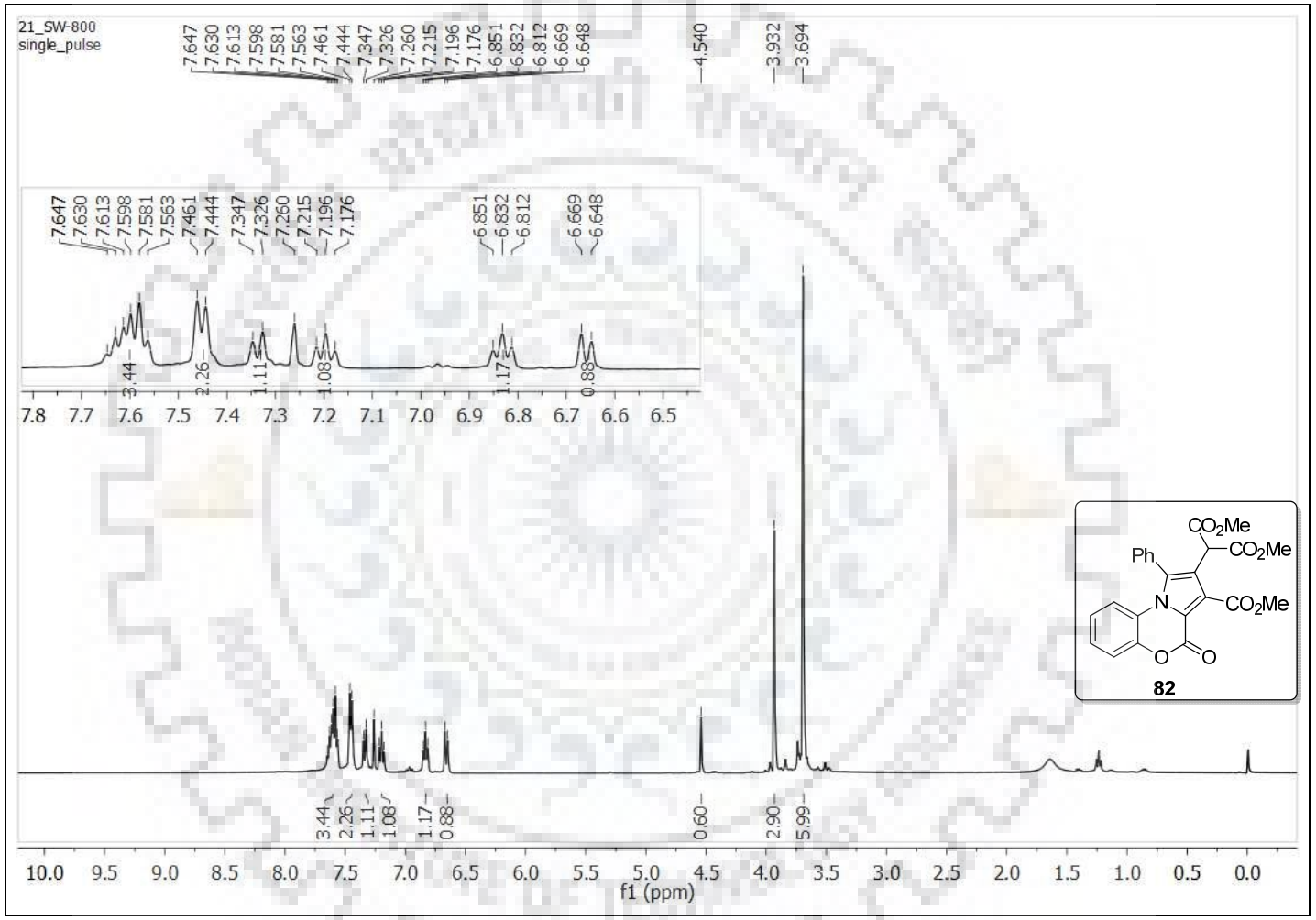


Figure S-47: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **82**.

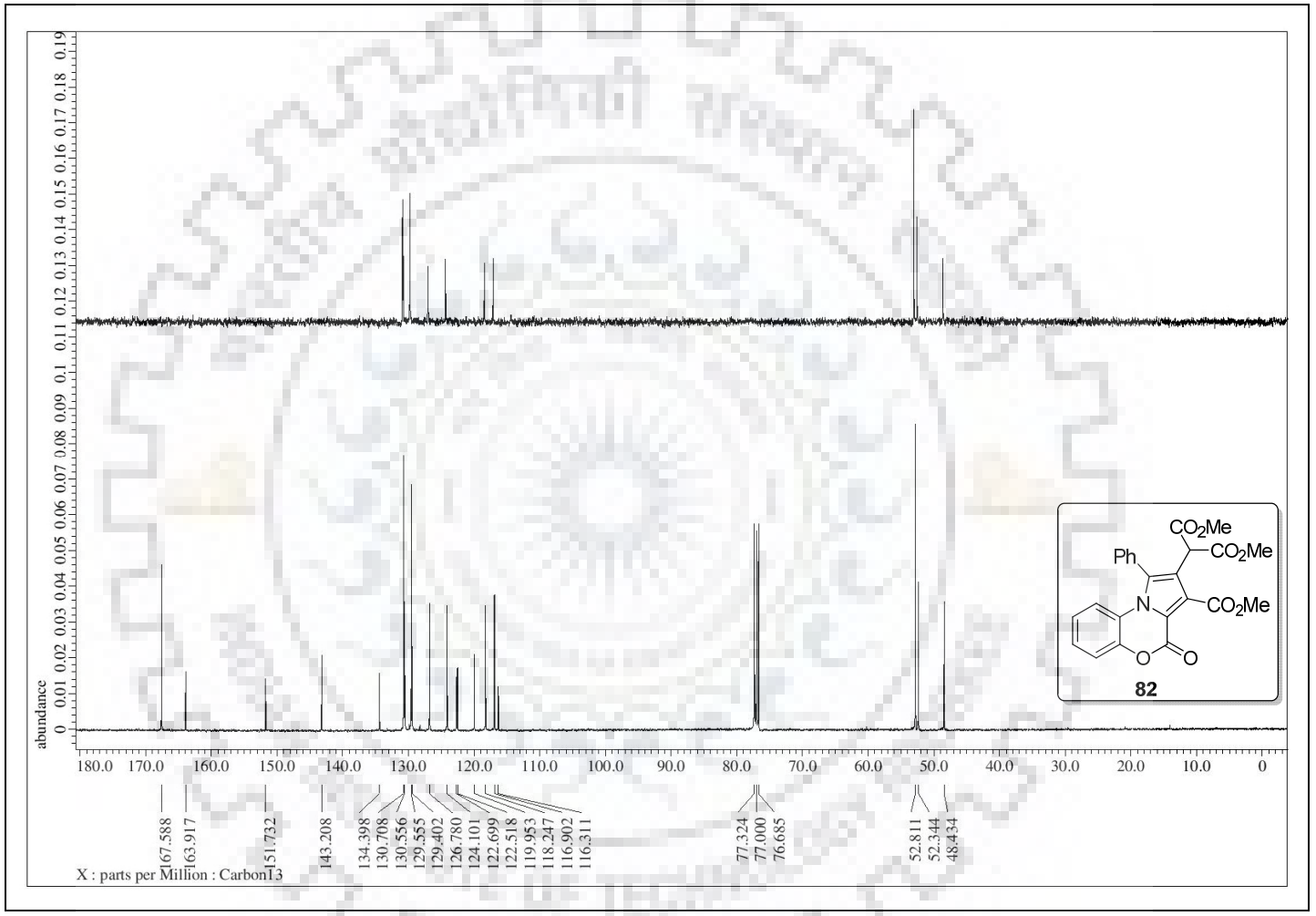


Figure S-48: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **82**.

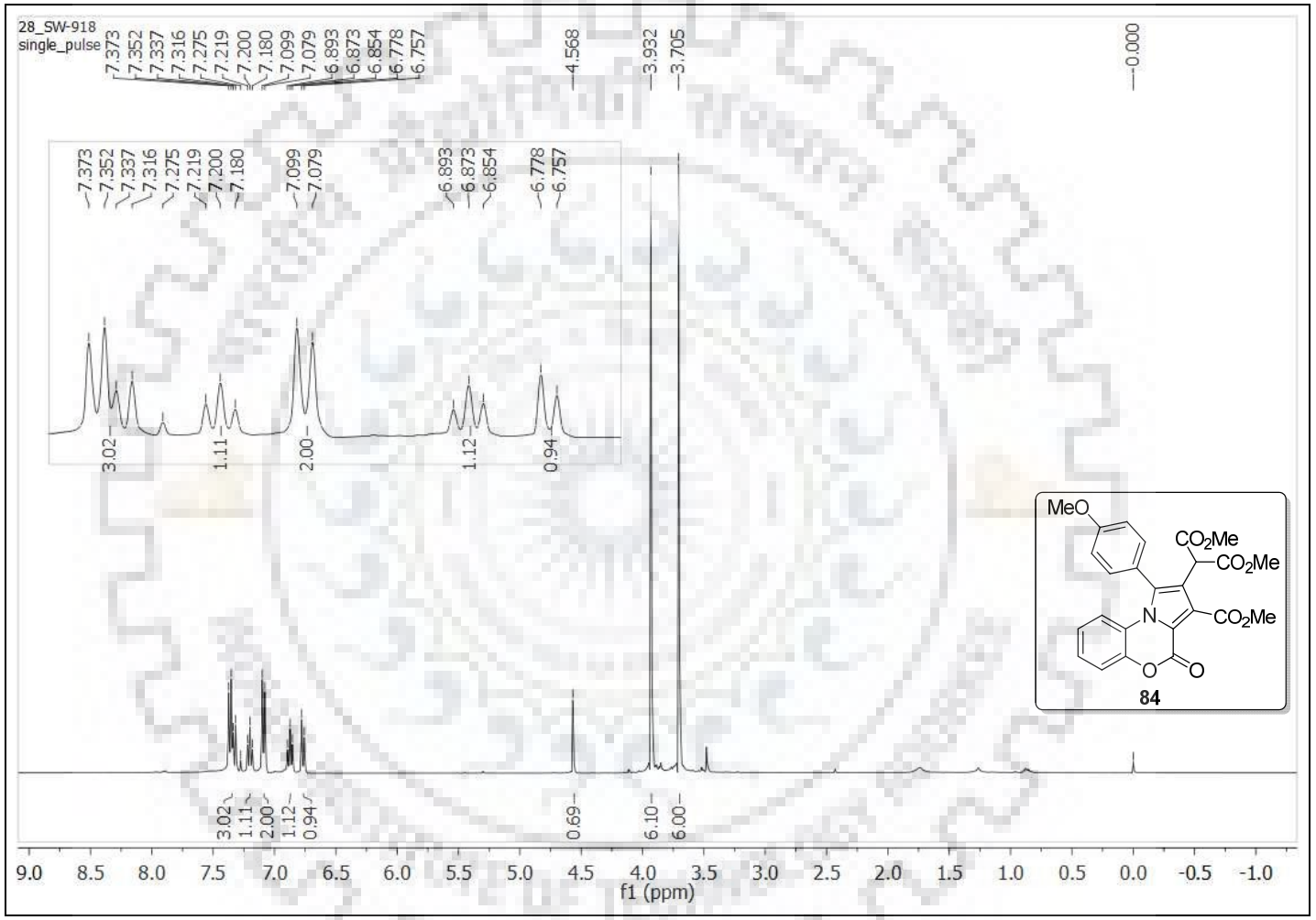


Figure S-49: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **84**.

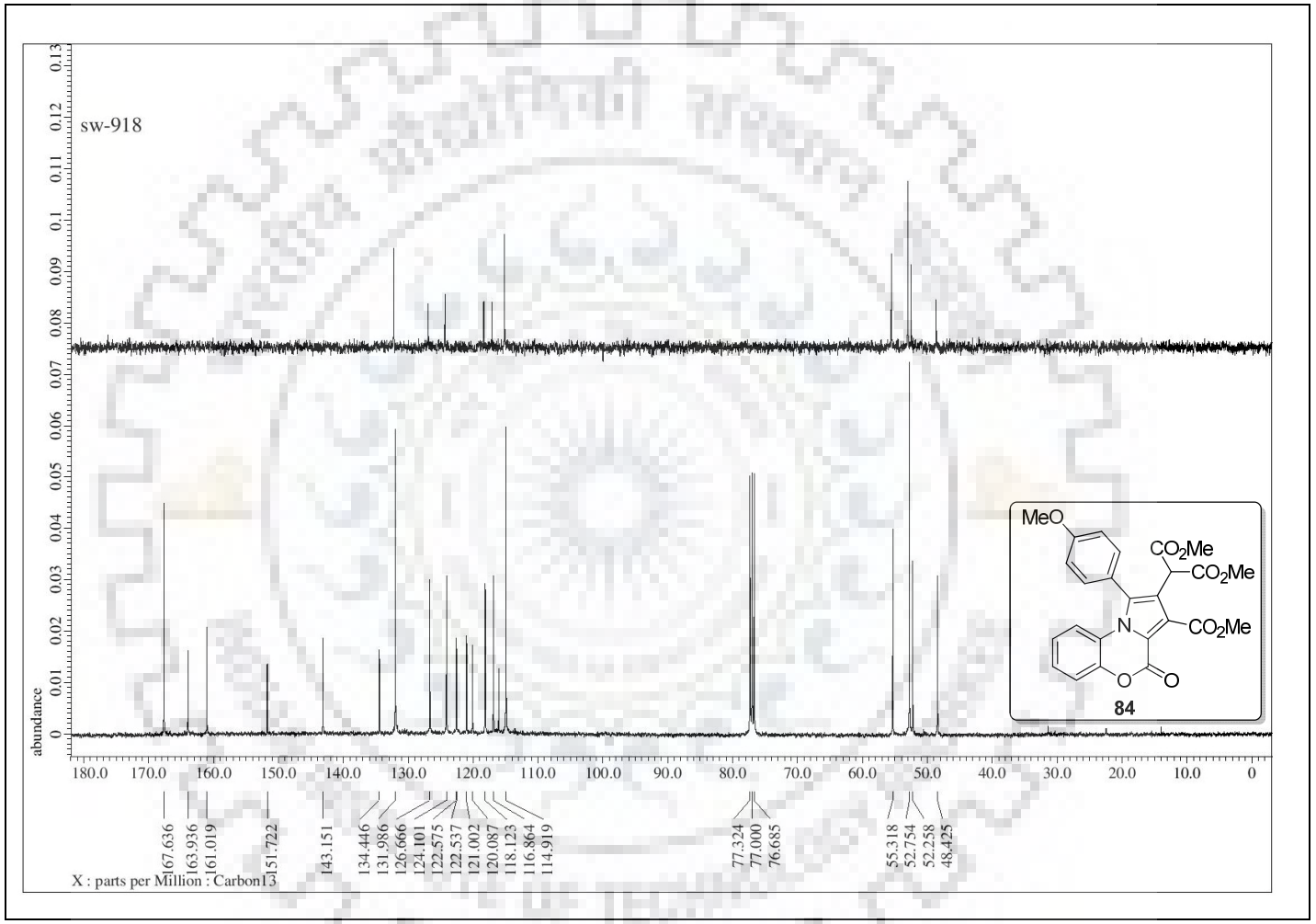


Figure S-50: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **84**.

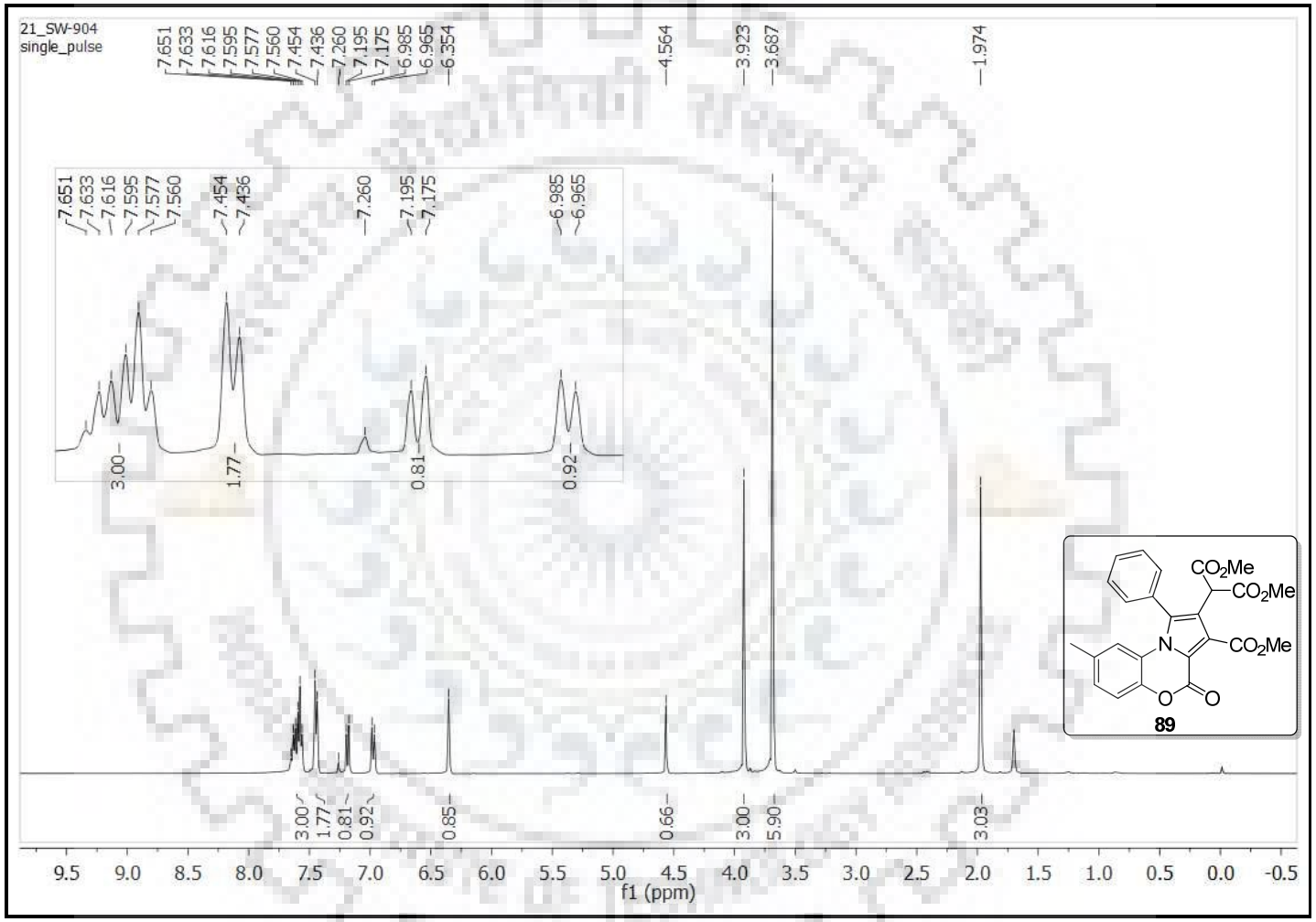


Figure S-51: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **89**.

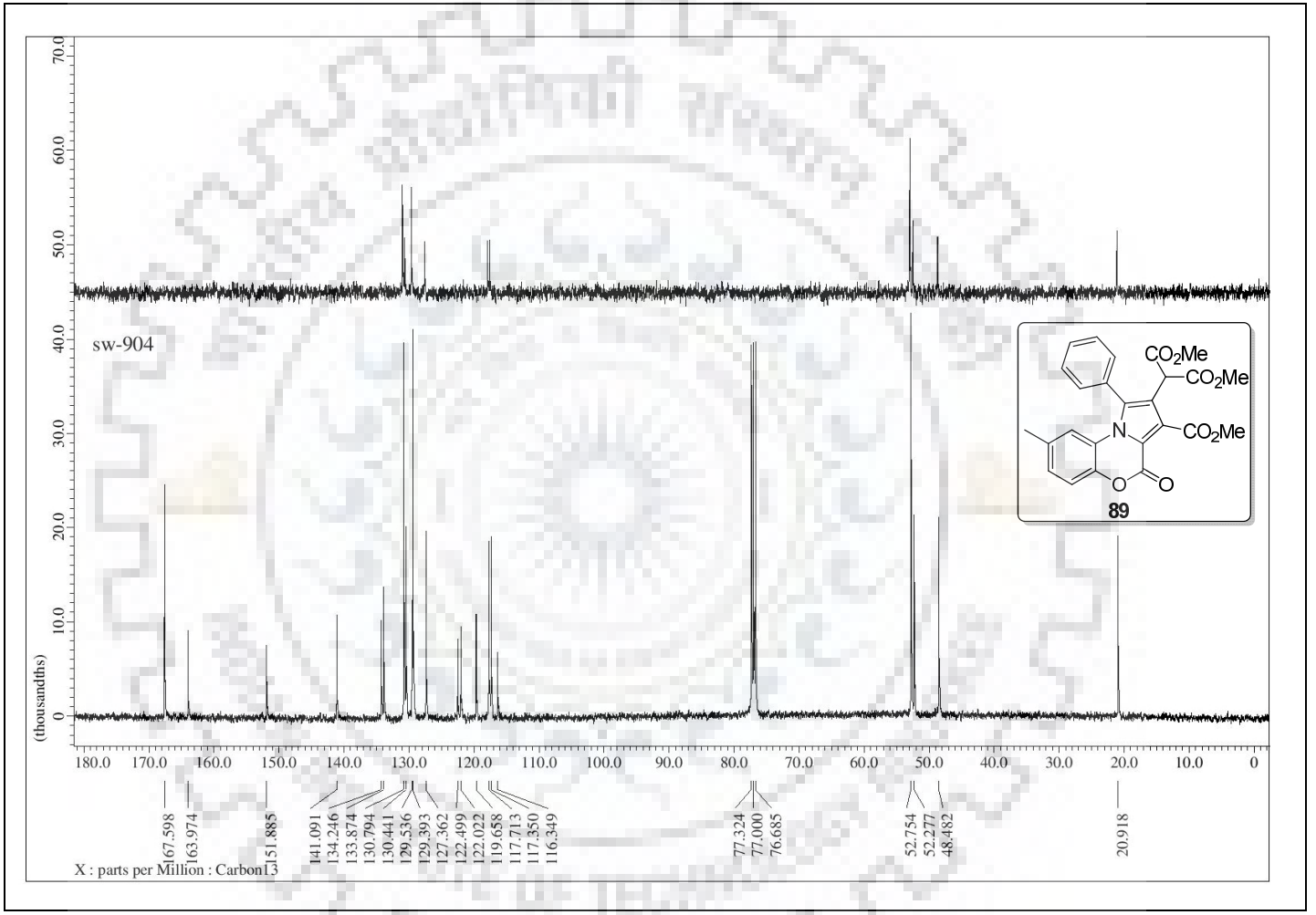


Figure S-52: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **89**.

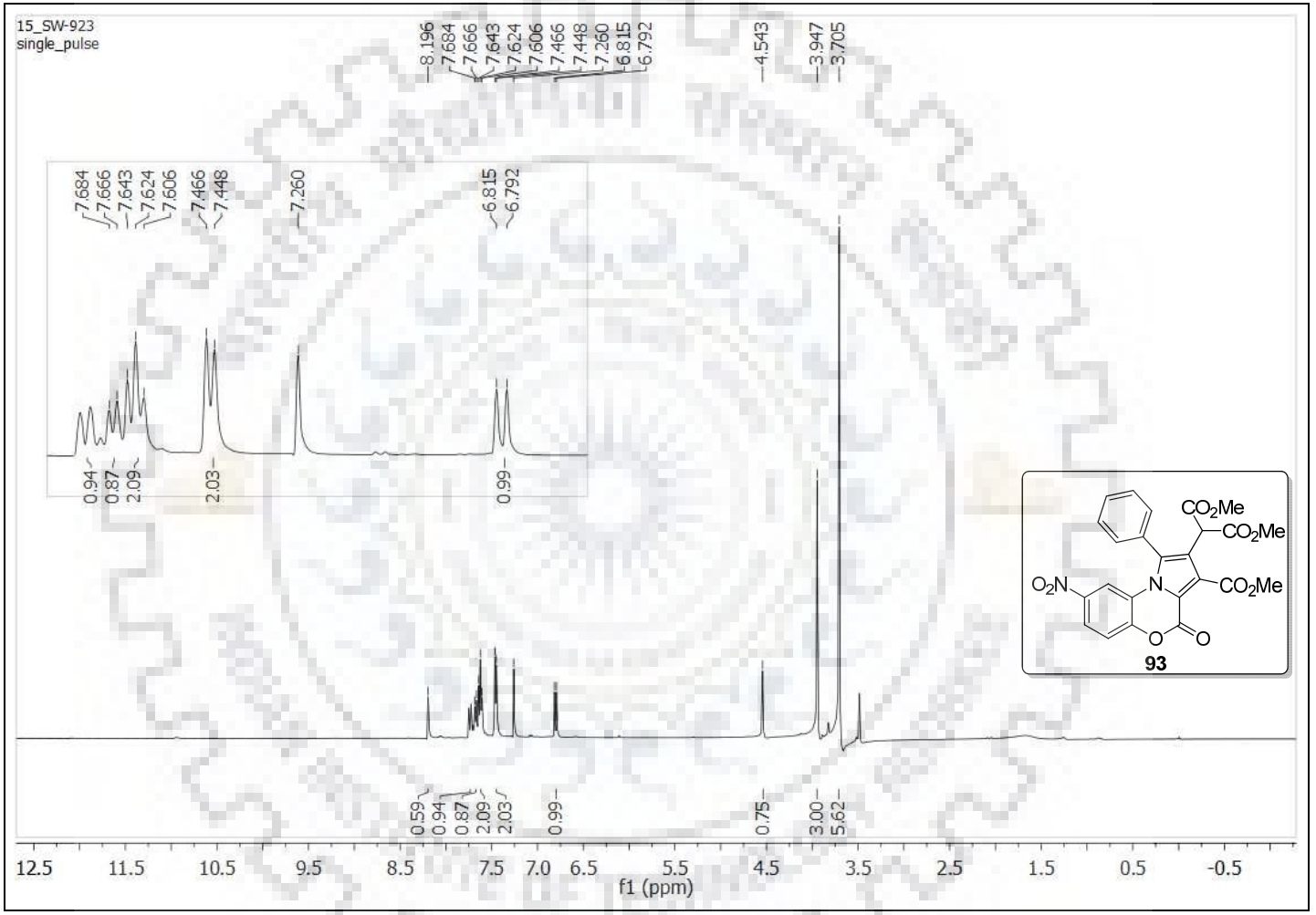


Figure S-53: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **93**.

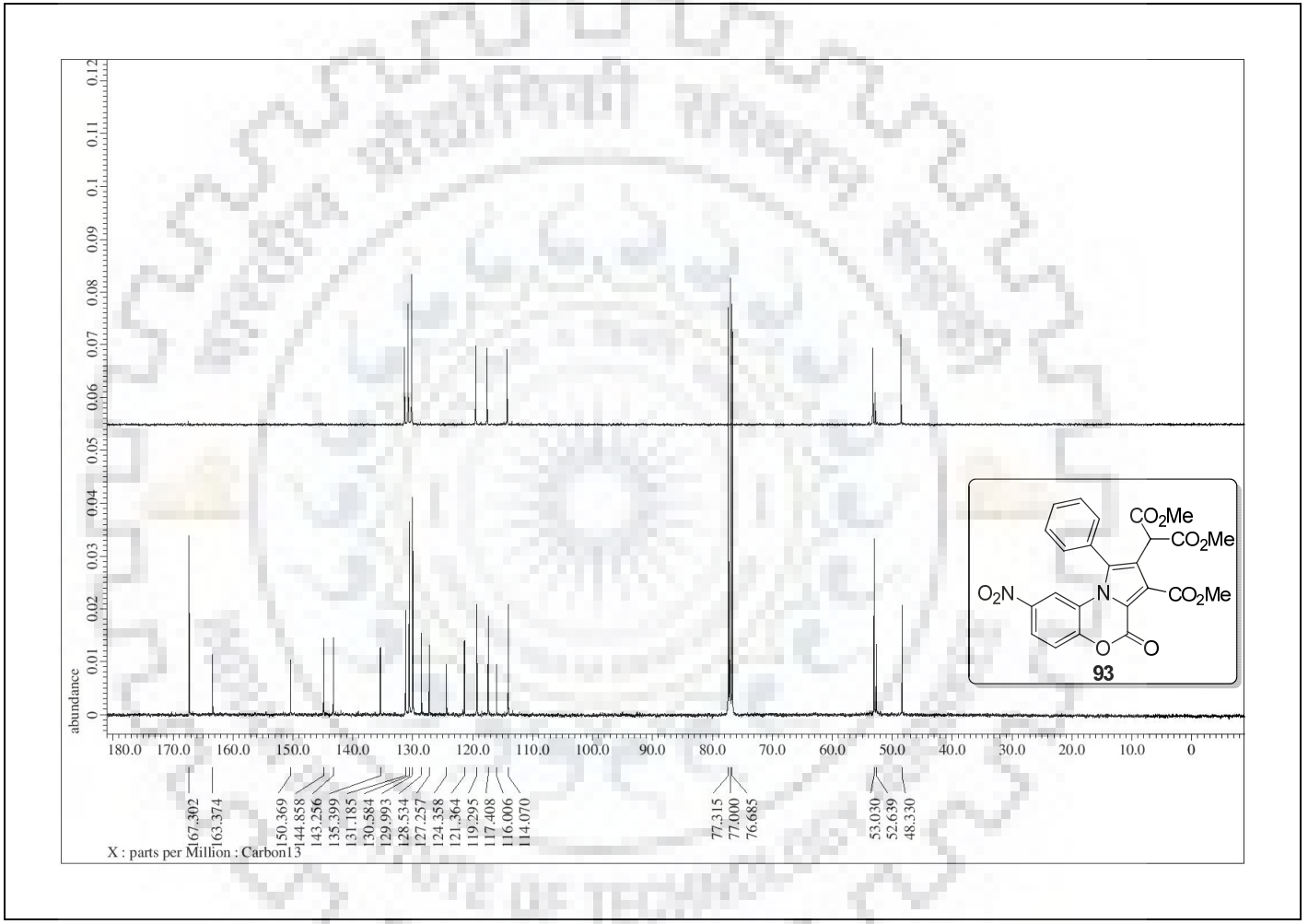


Figure S-54: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **93**.

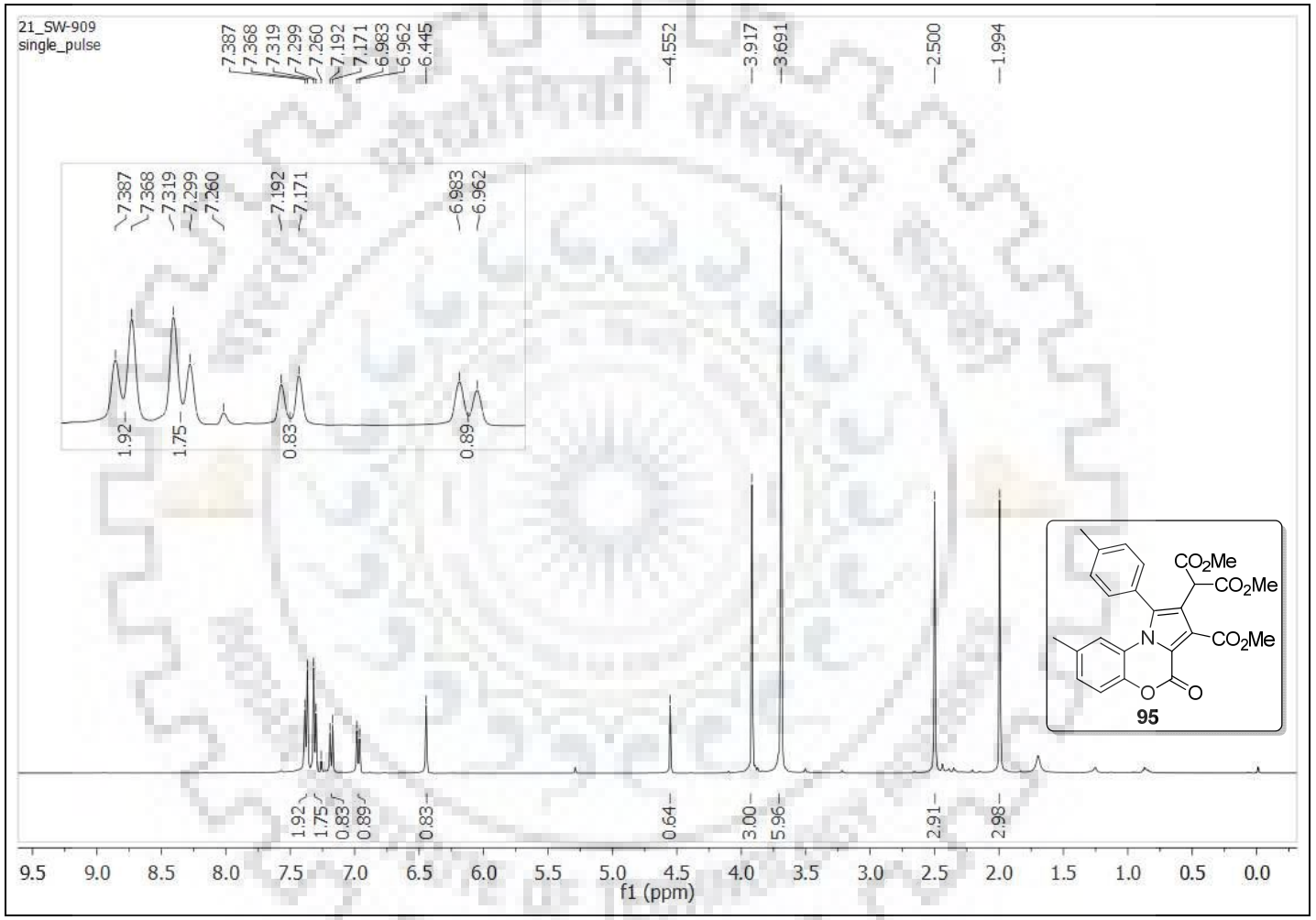


Figure S-55: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **95**.

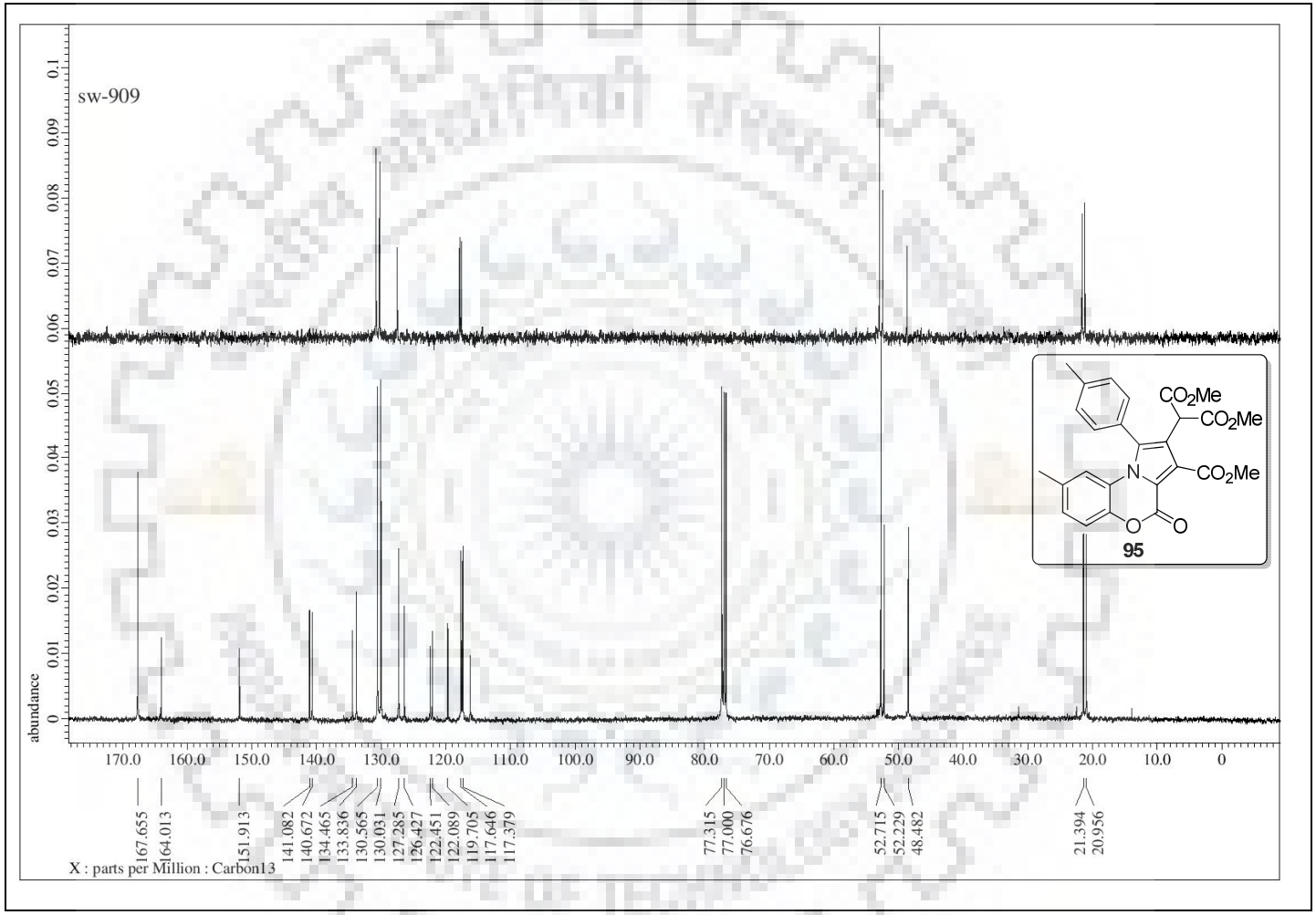


Figure S-56: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **95**.

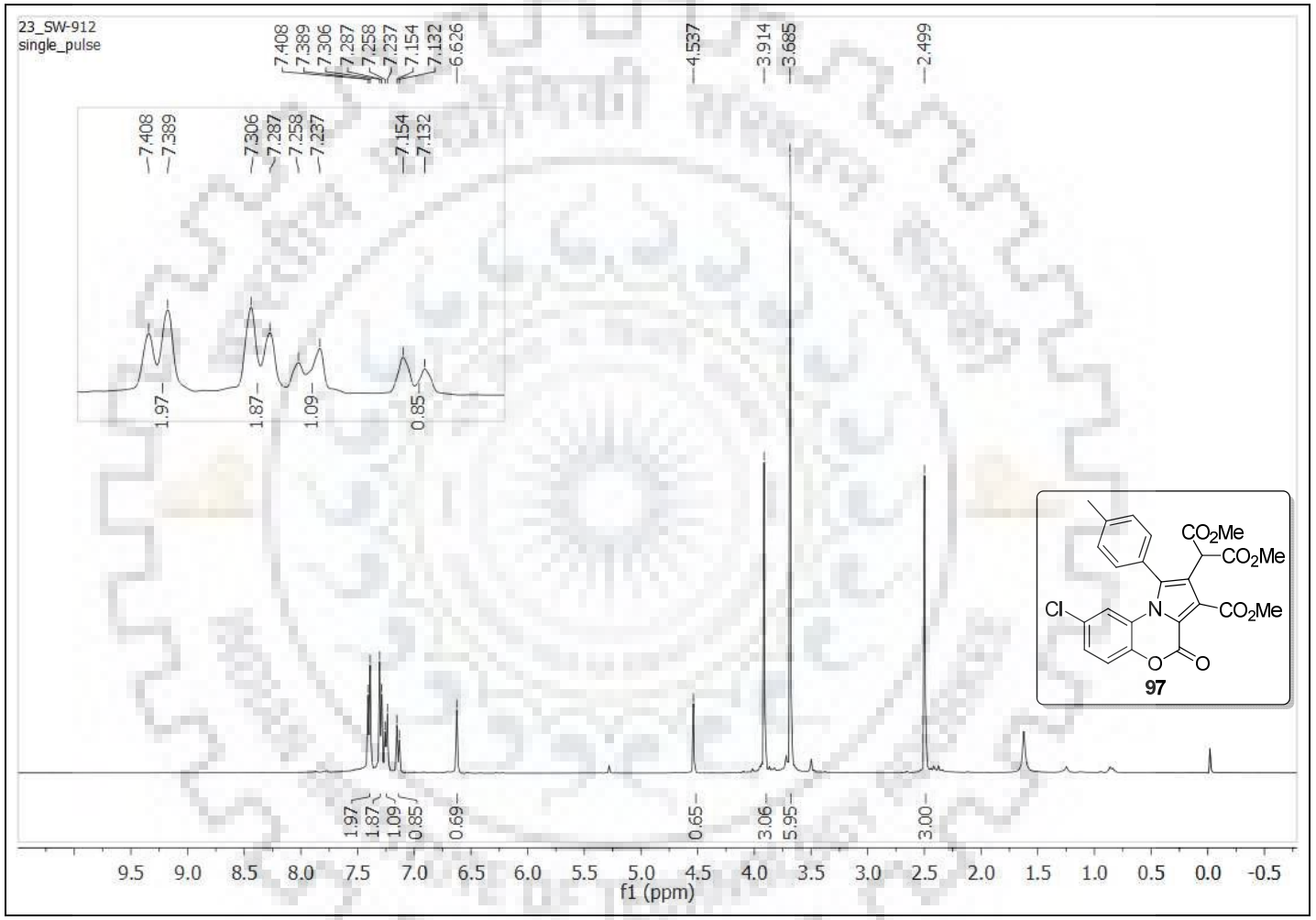


Figure S-57: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **97**.

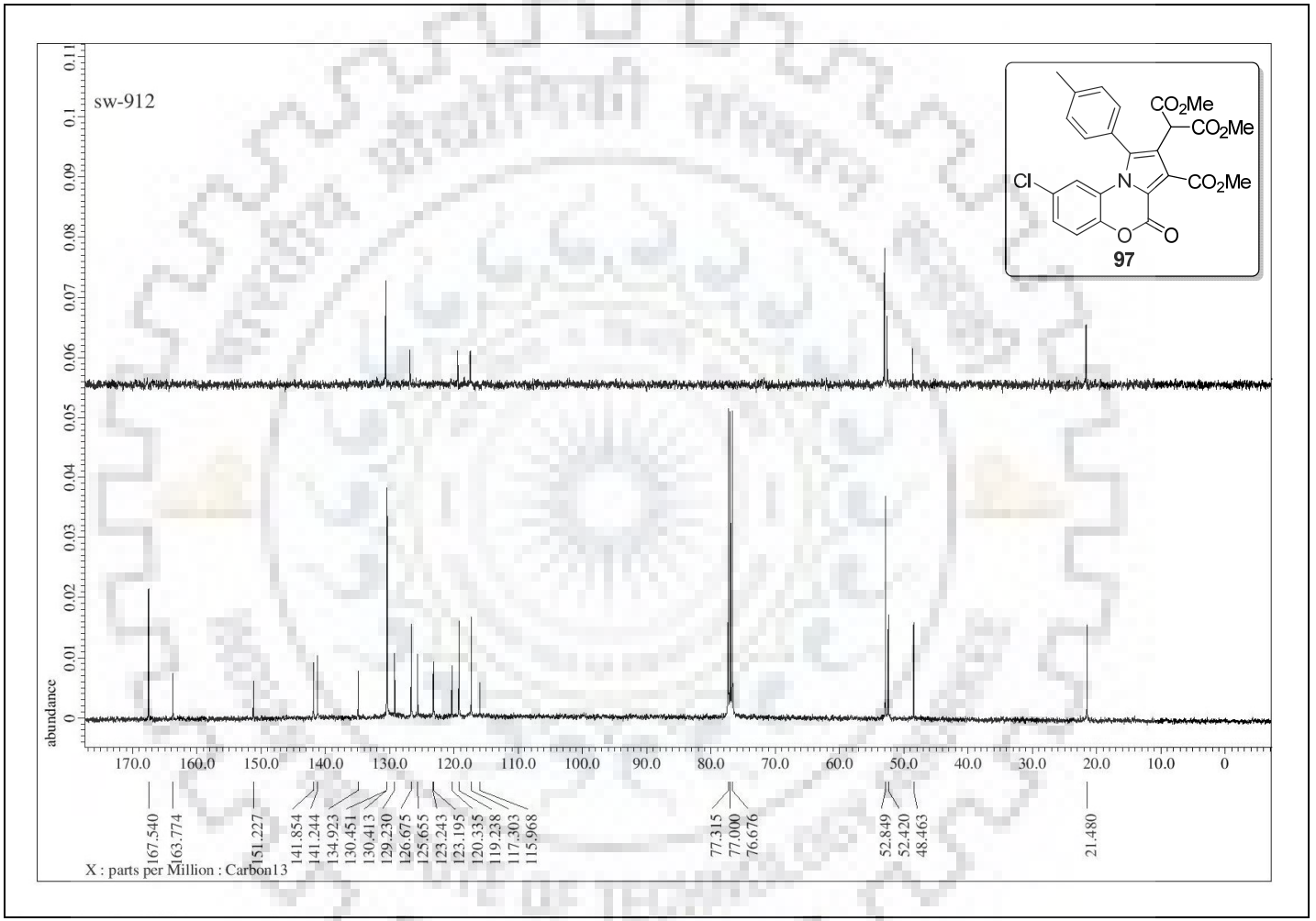


Figure S-58: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **97**.

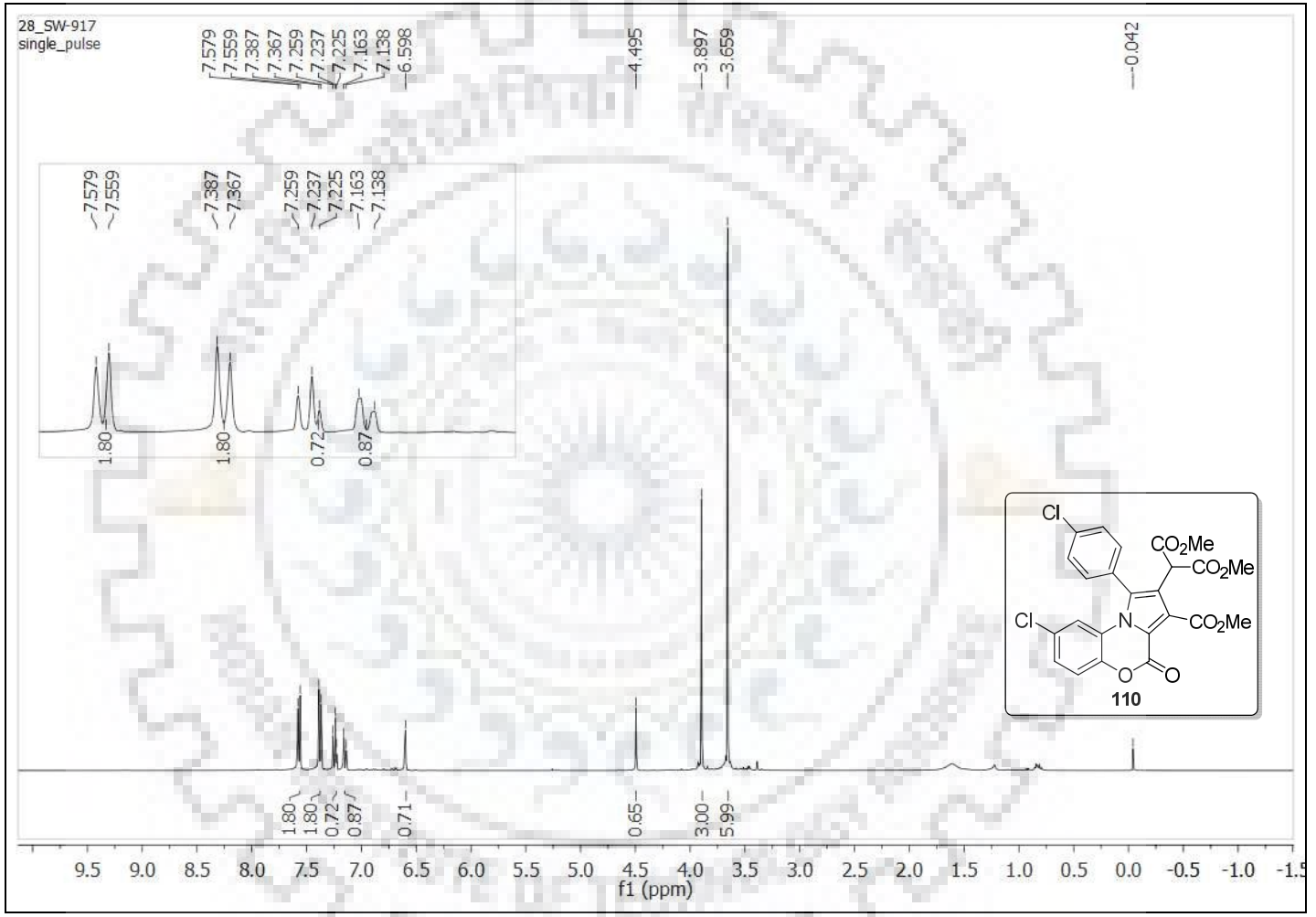


Figure S-59: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **110.**

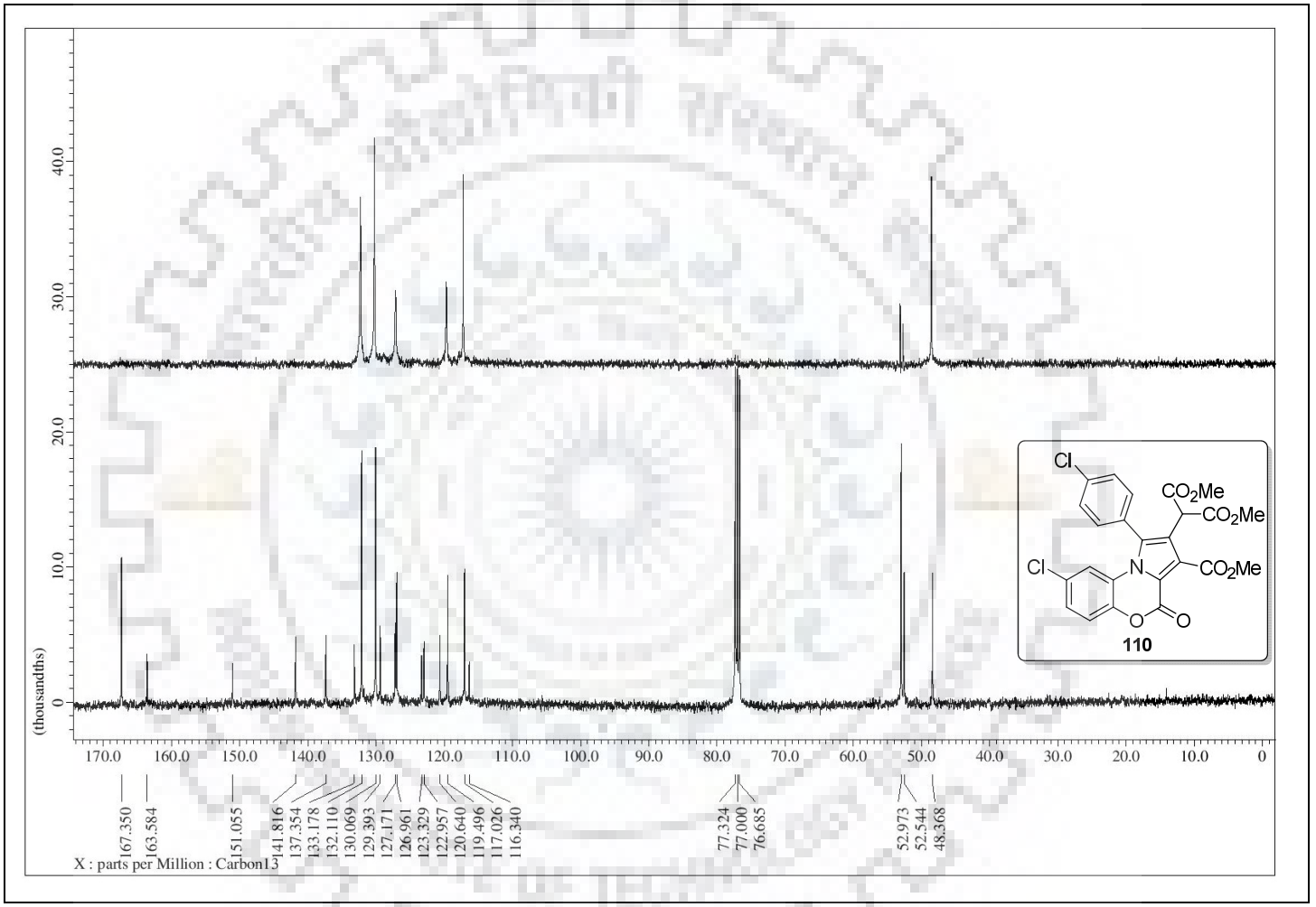


Figure S-60: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **110**.

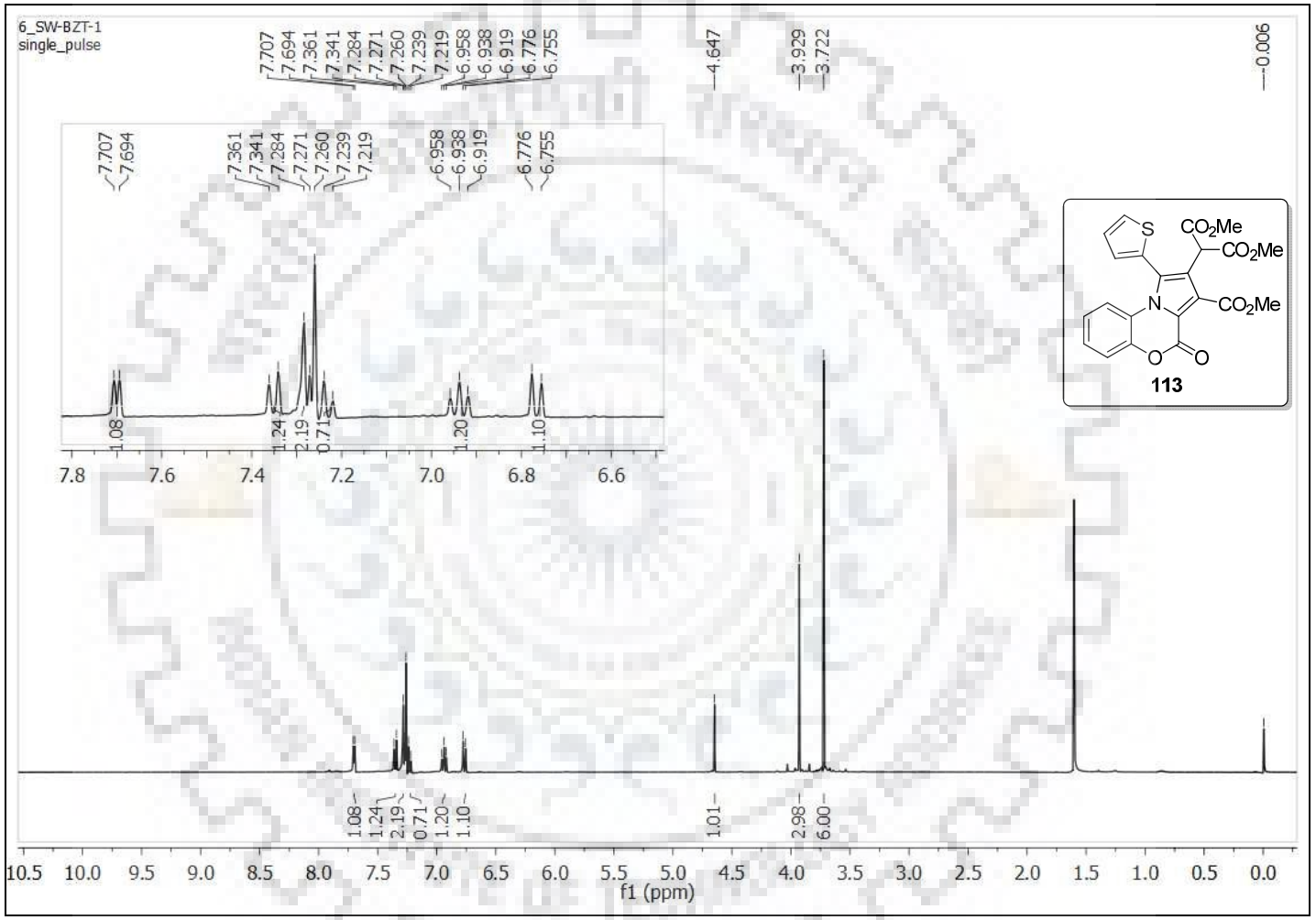


Figure S-61: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **113**.

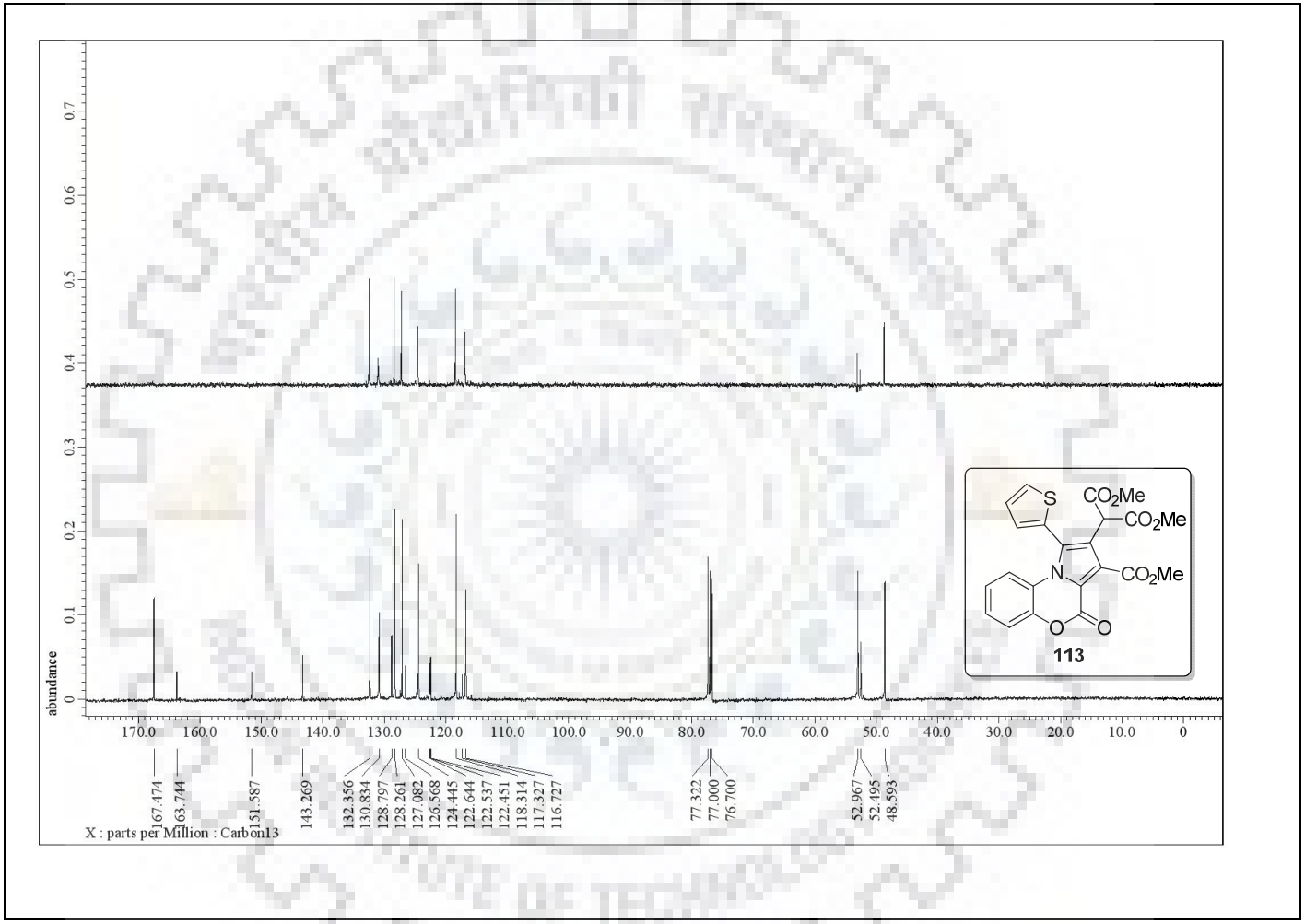


Figure S-62: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **113**.

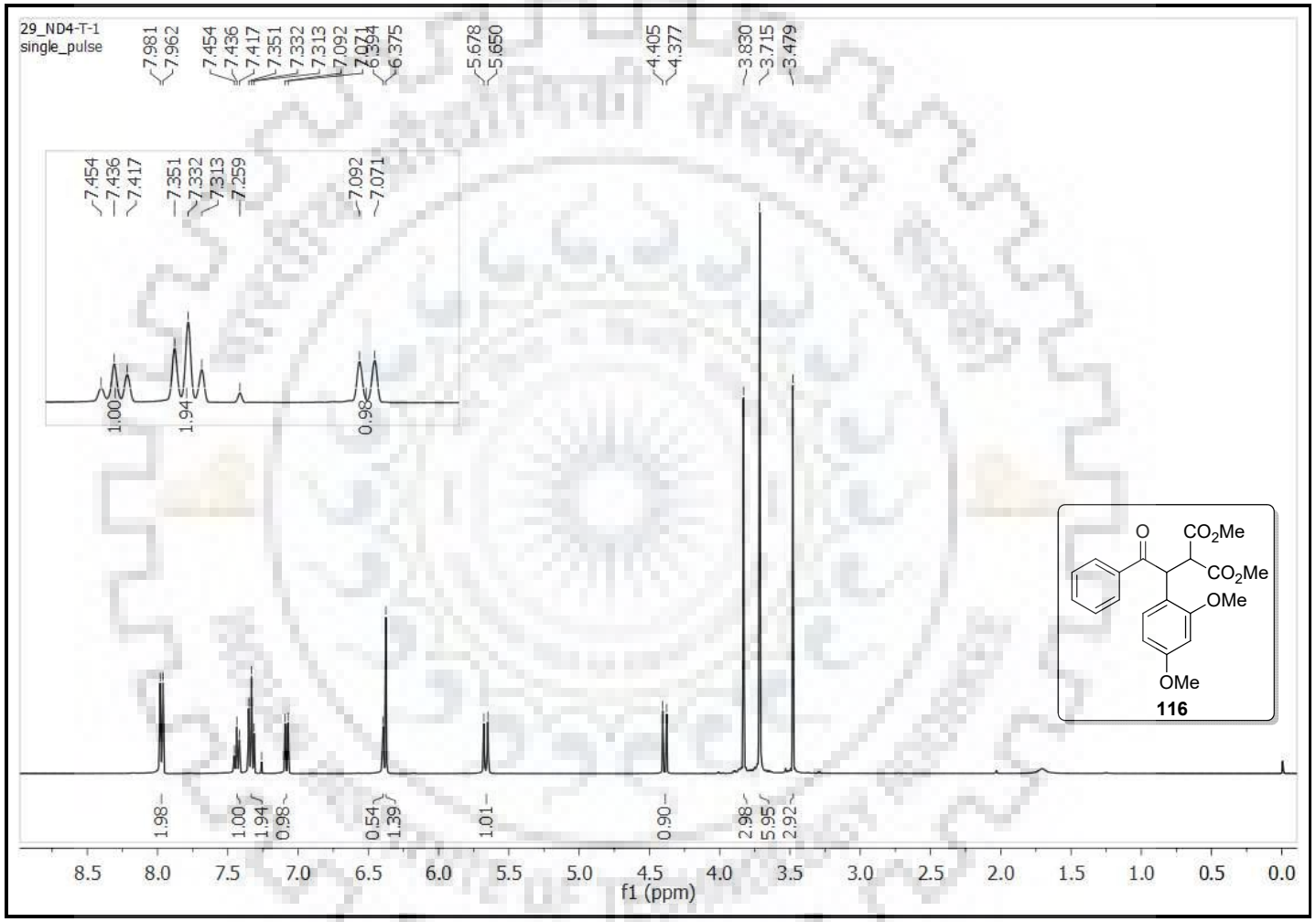


Figure S-63: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **116**.

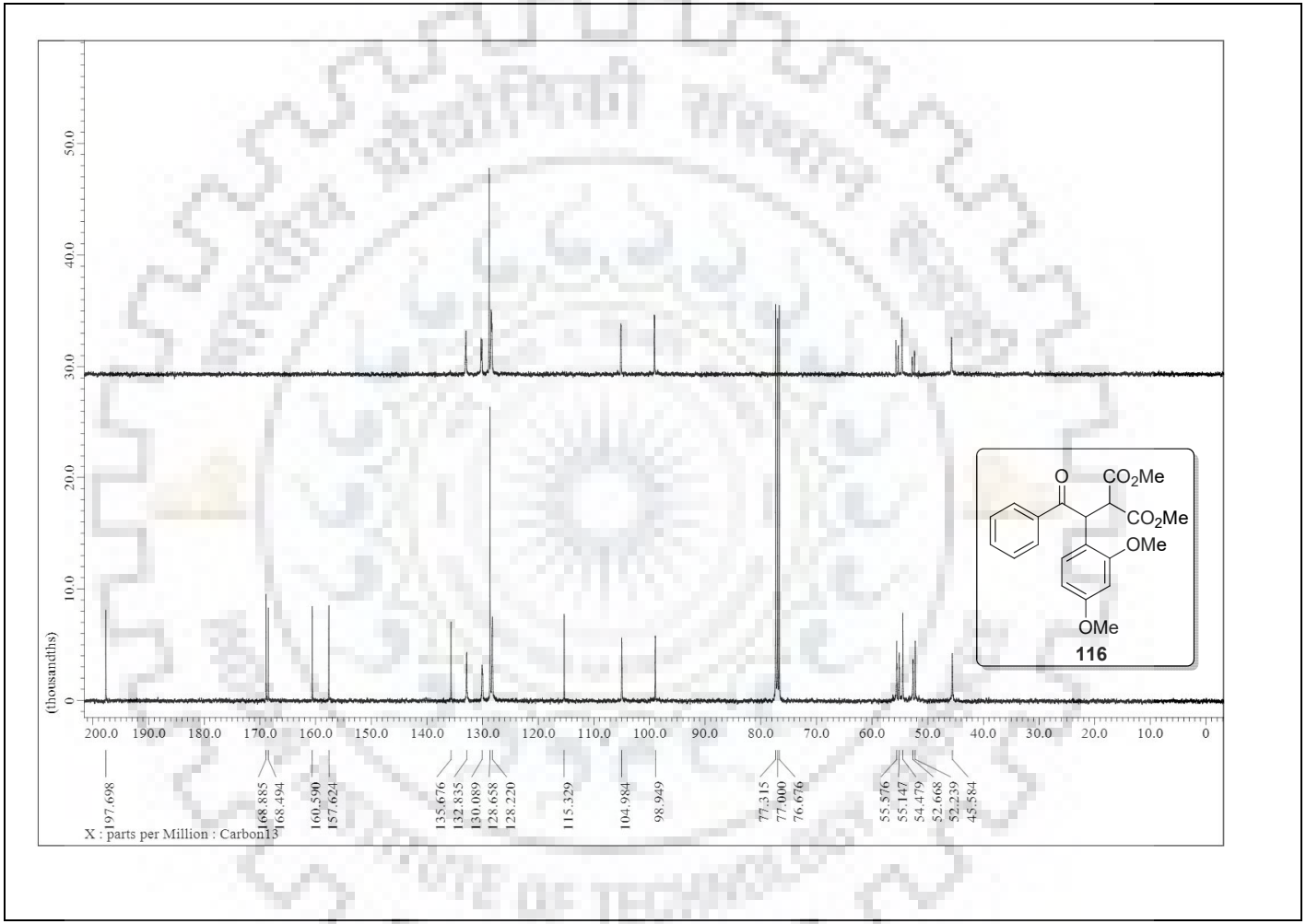


Figure S-64: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **116**.

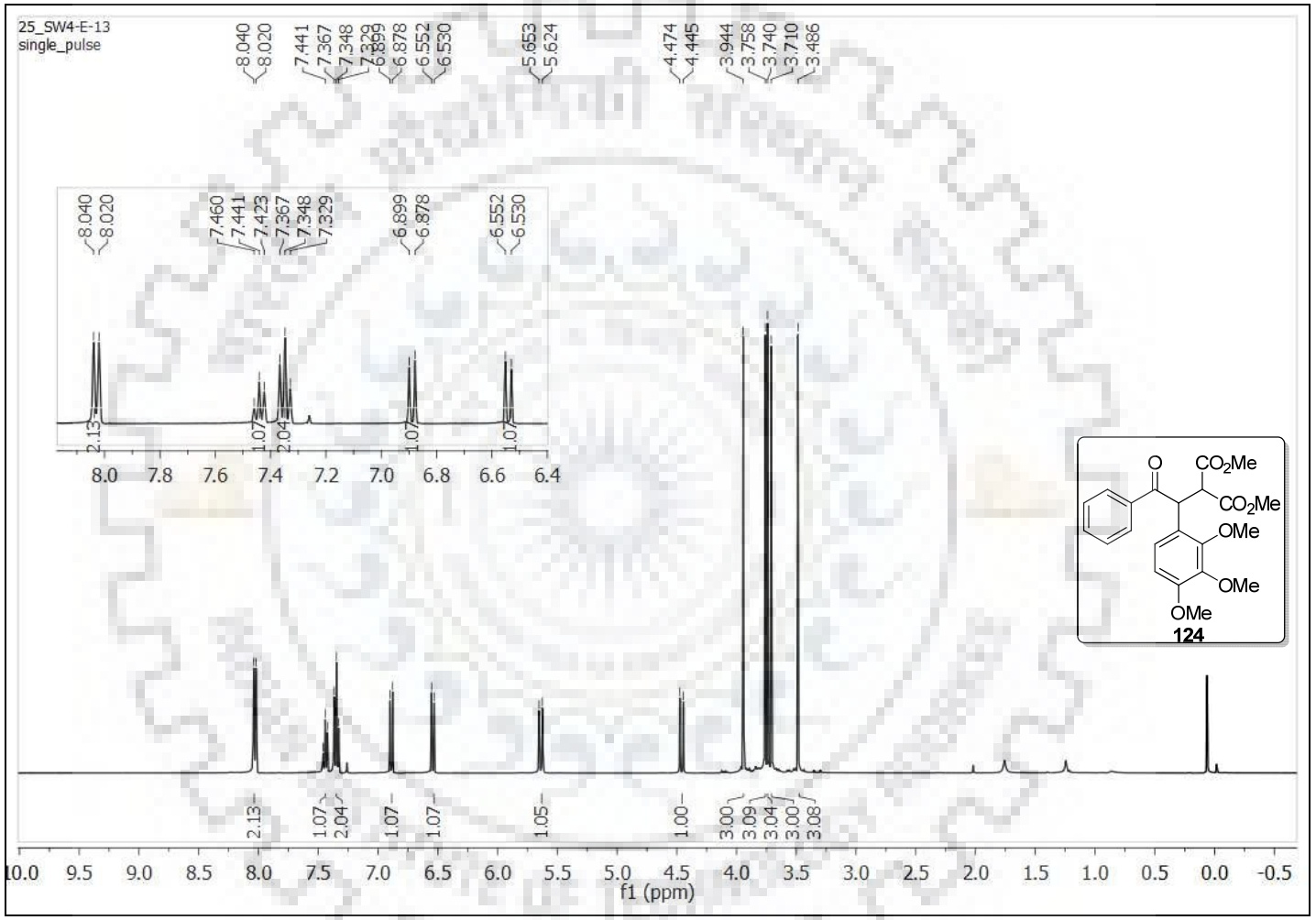


Figure S-65: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **124**.

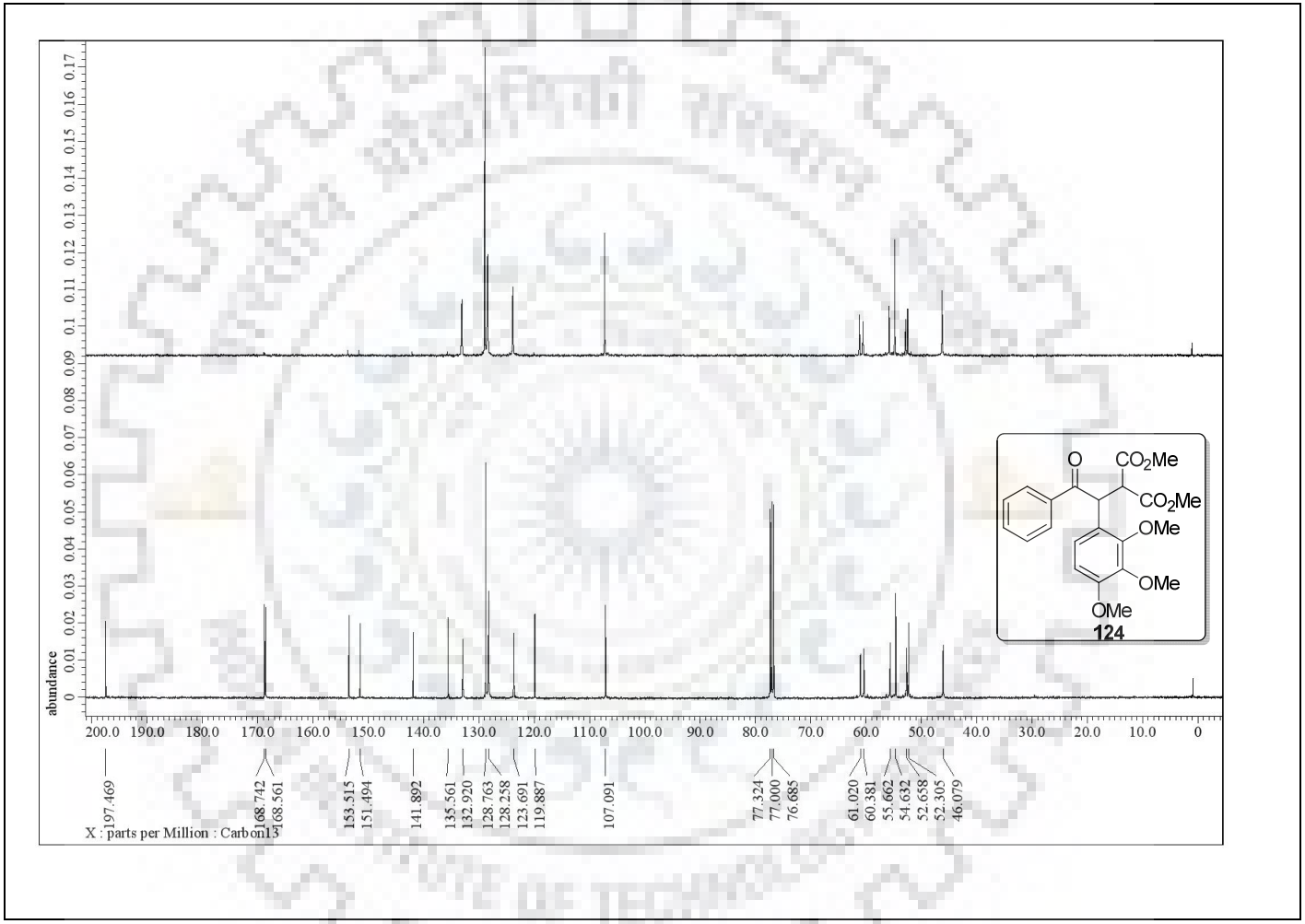


Figure S-66: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **124**.

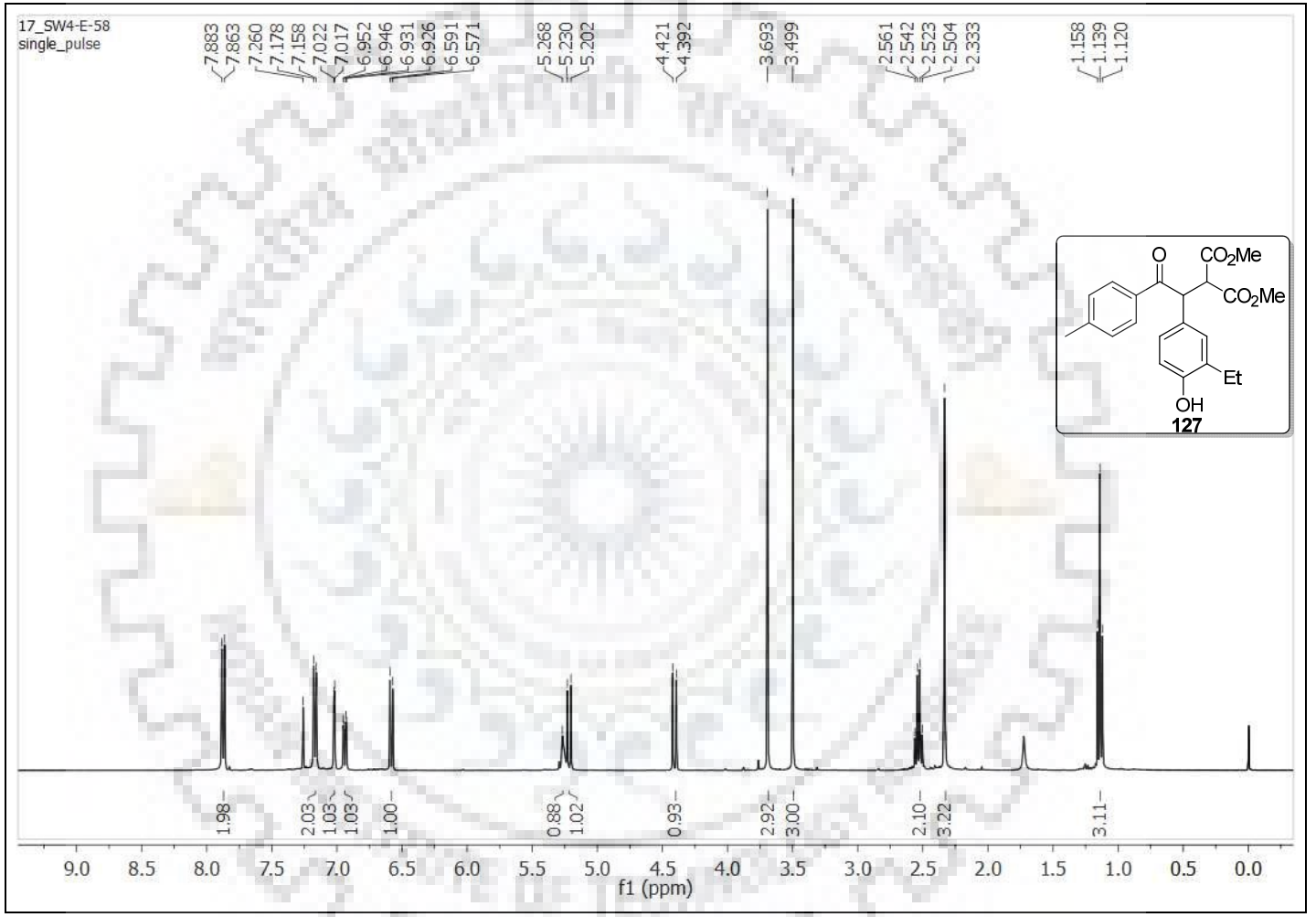


Figure S-67: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **127**.

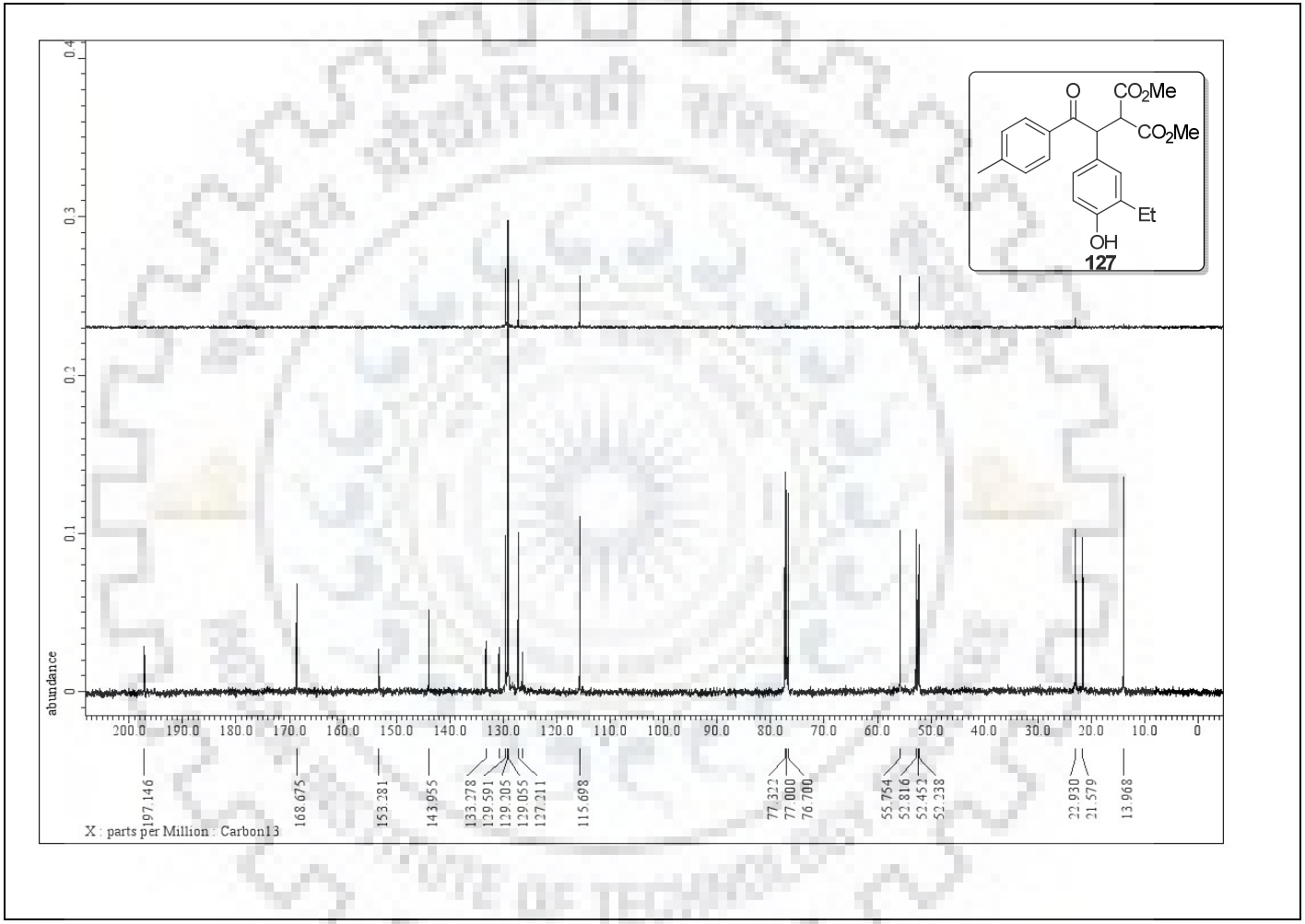


Figure S-68: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra **127**.

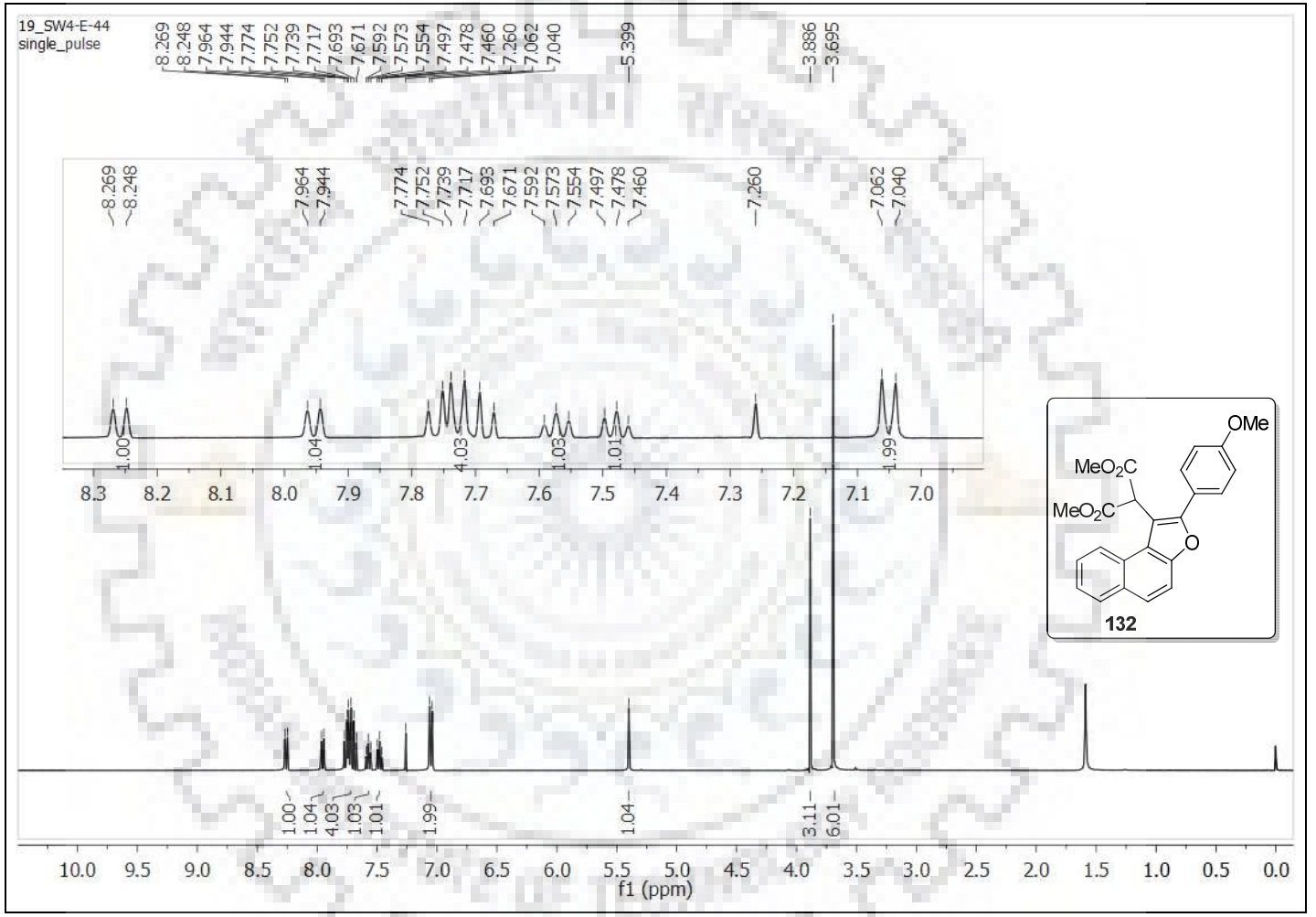


Figure S-69: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **132**.

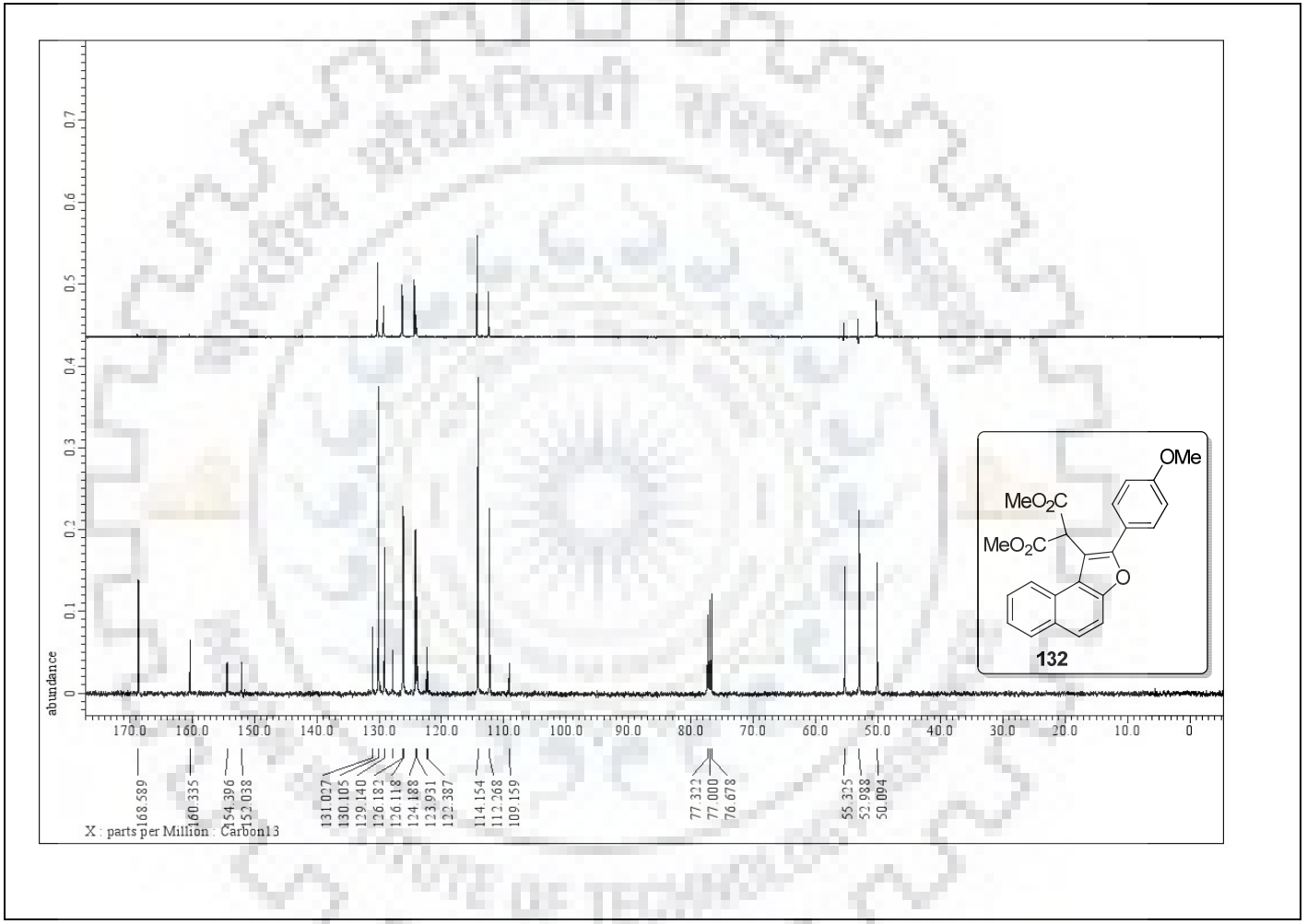


Figure S-70: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **132**.

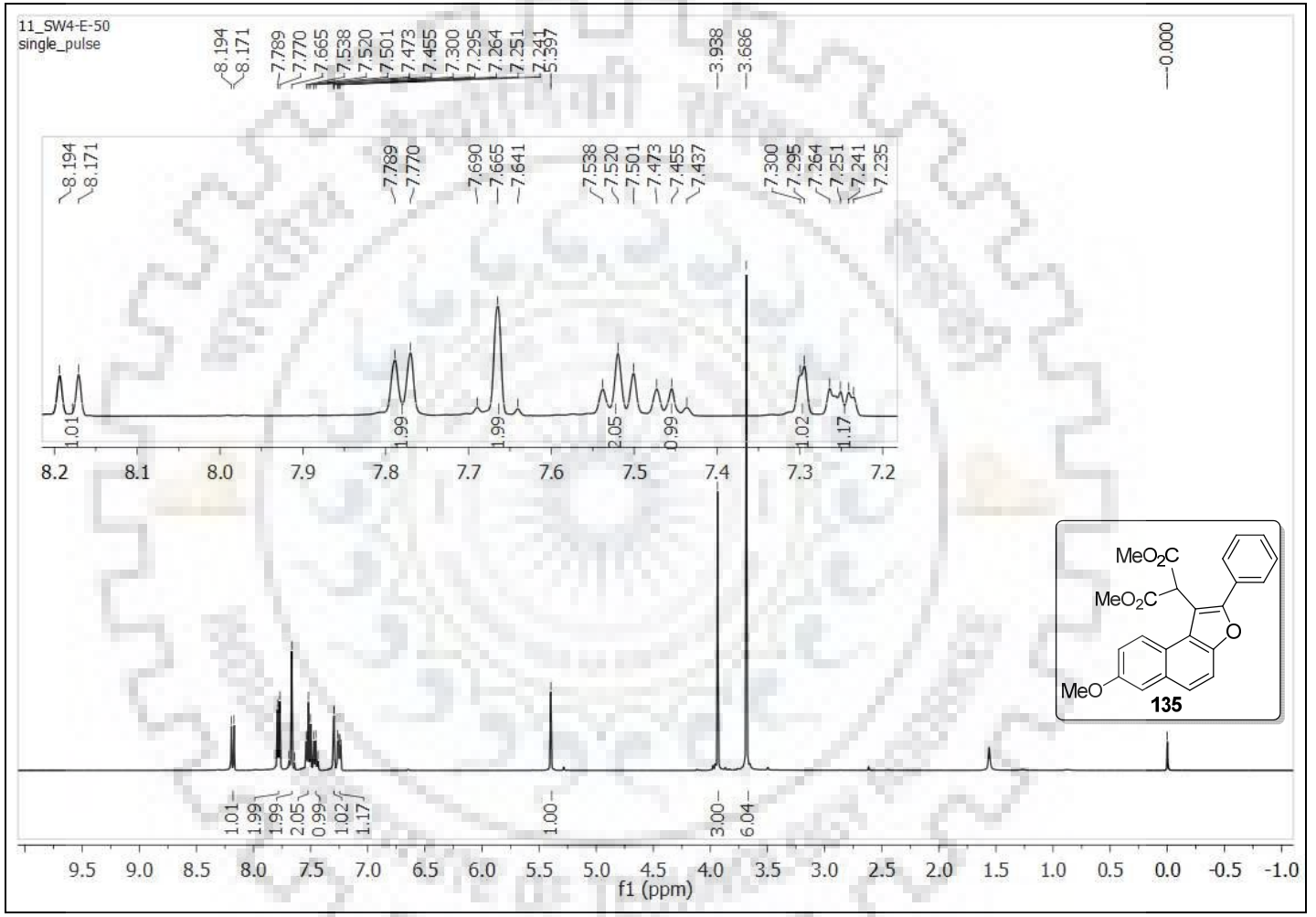


Figure S-71: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **135**.

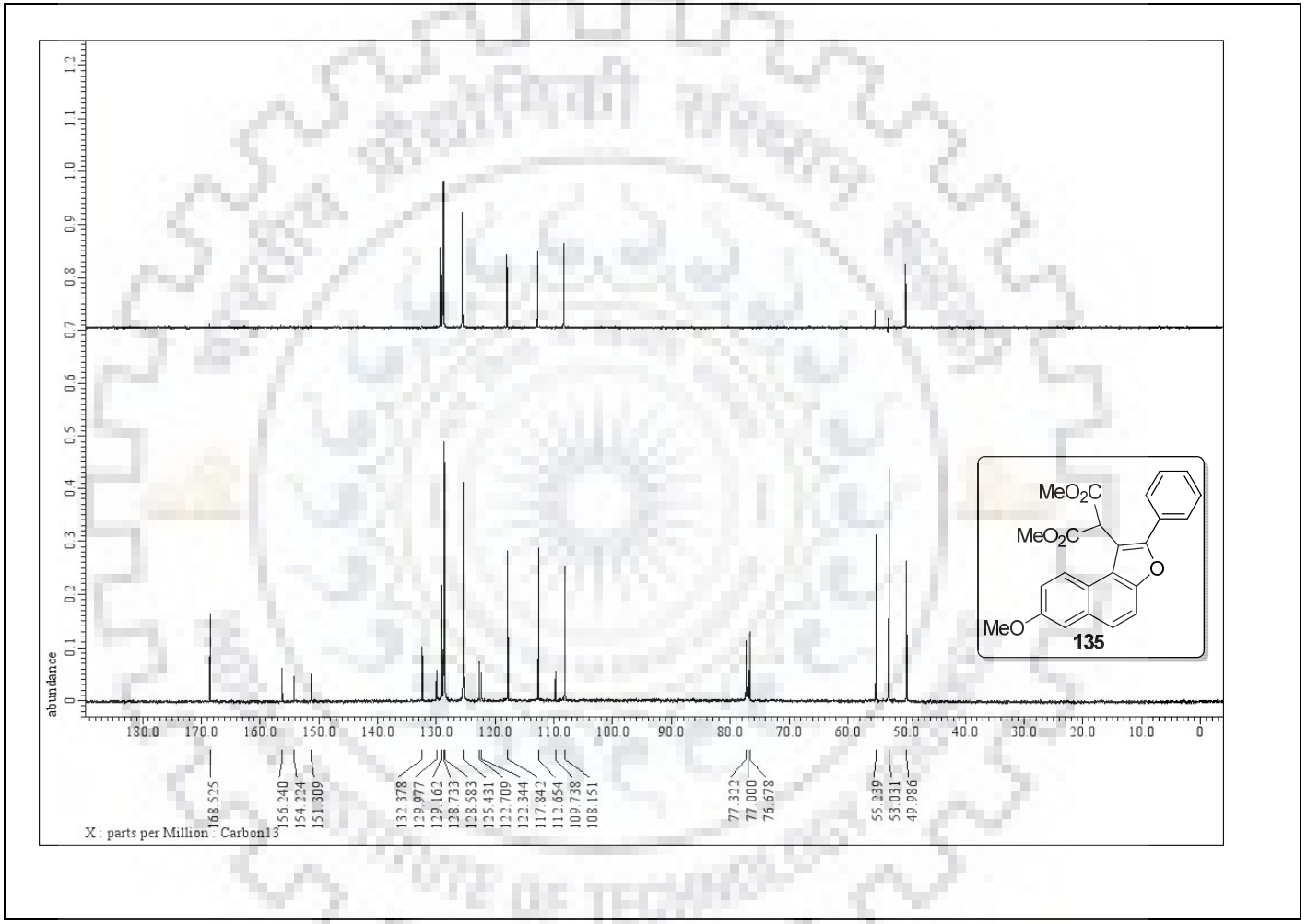


Figure S-72: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **135**.

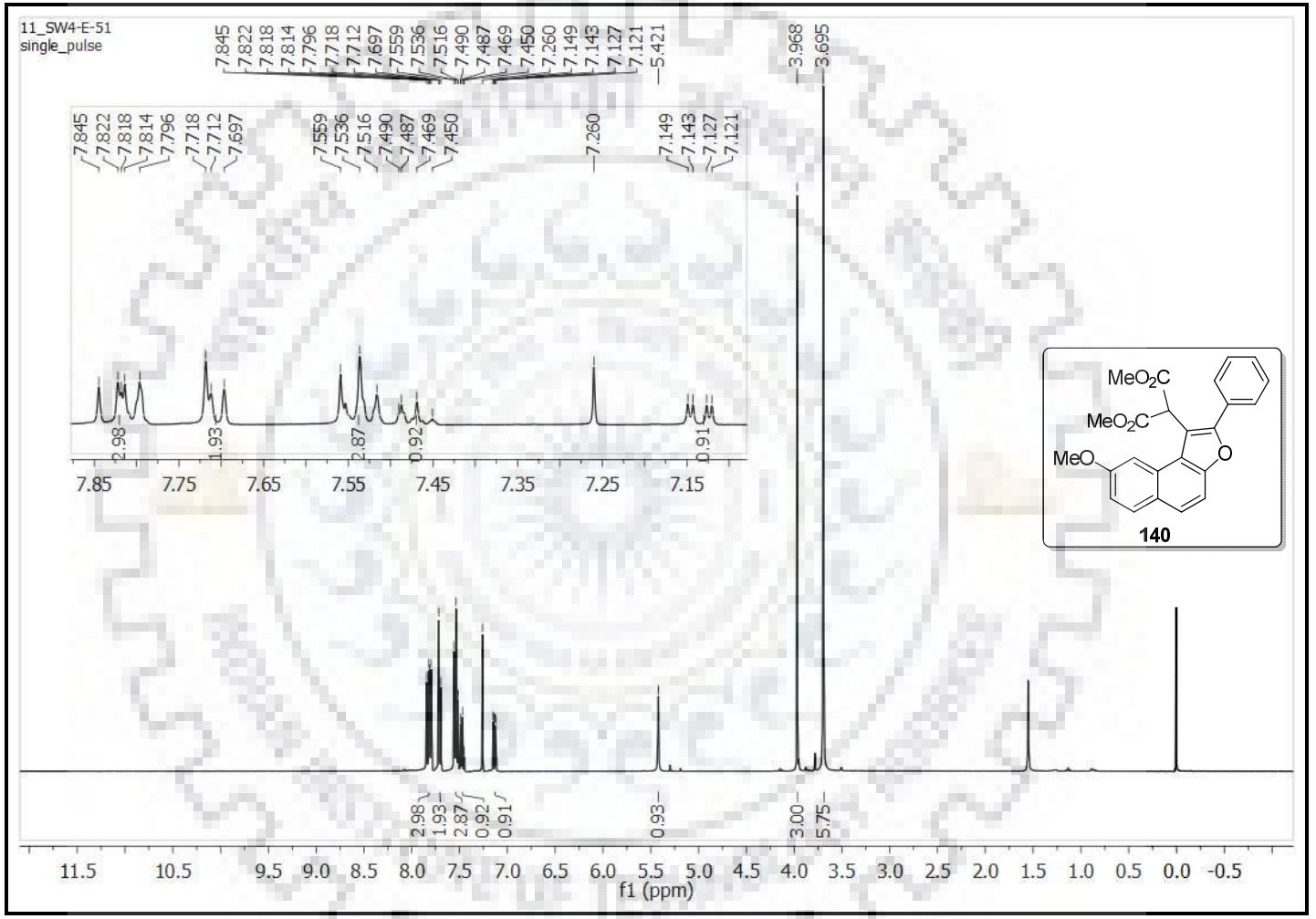


Figure S-73: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **140**.

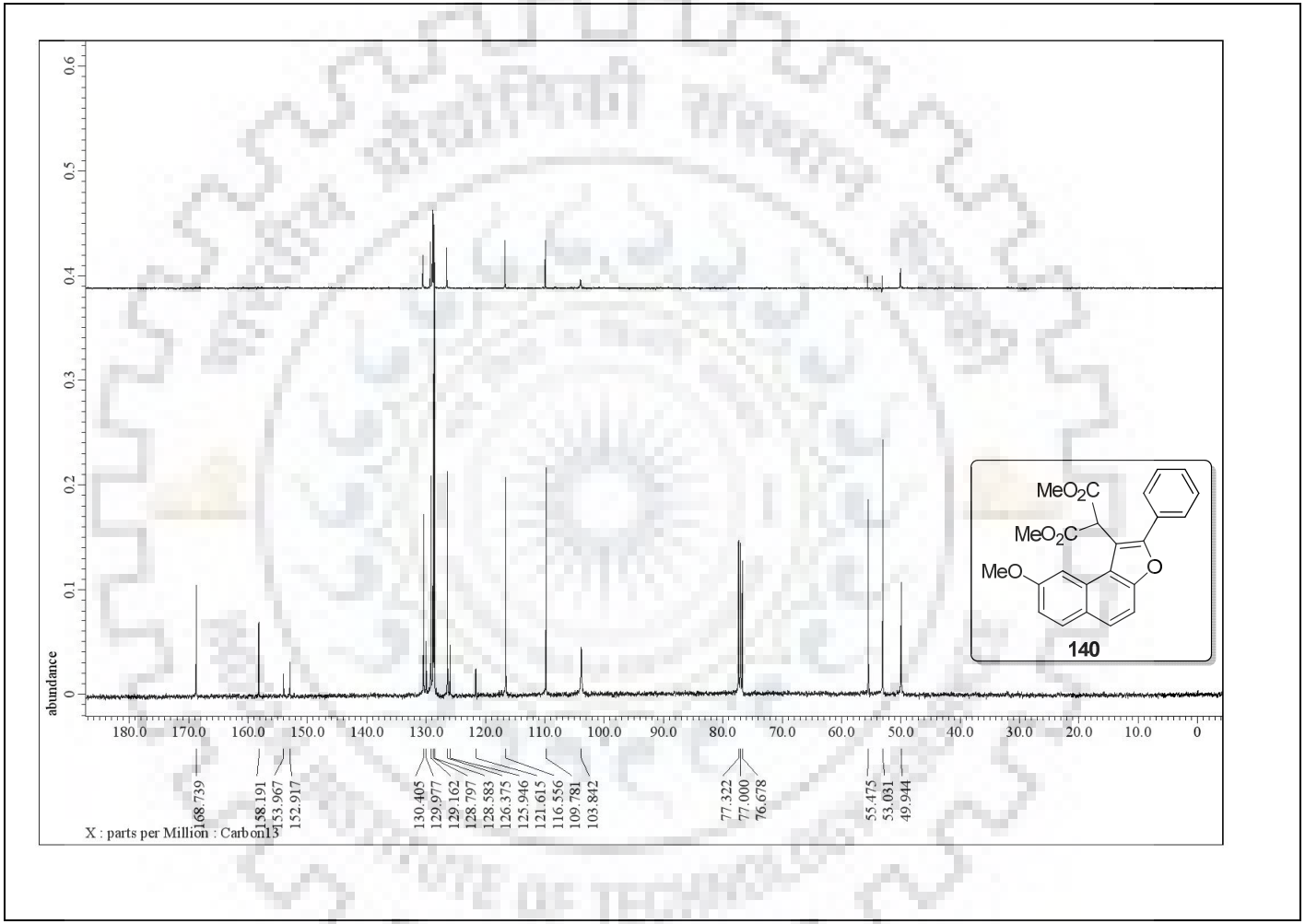
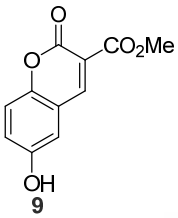


Figure S-74: ^{13}C and DEPT NMR (100 MHz, $CDCl_3$) Spectra of **140**.

STRUCTURES OF COMPOUNDS SYNTHESIZED



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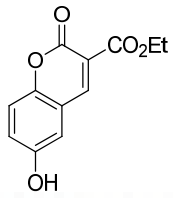

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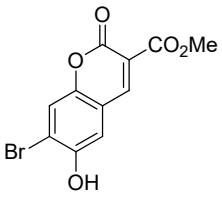

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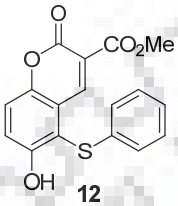

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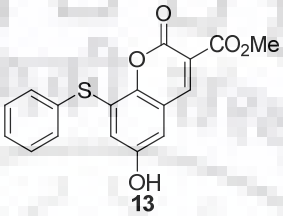

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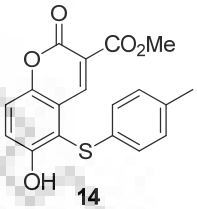

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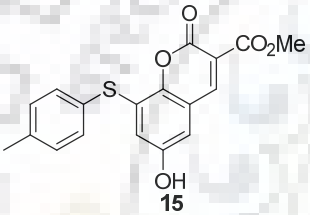

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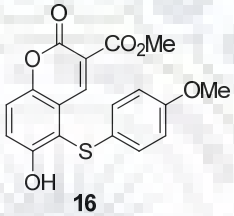

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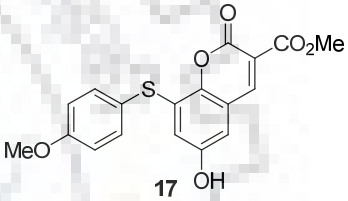

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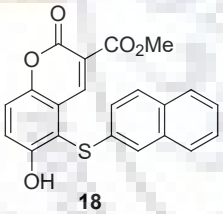

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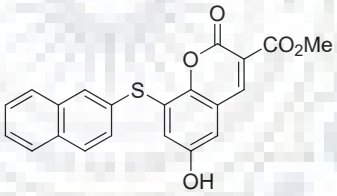

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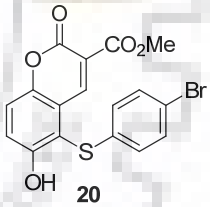

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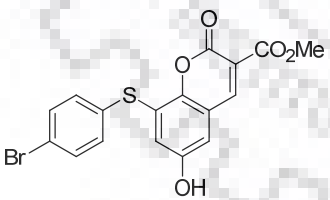

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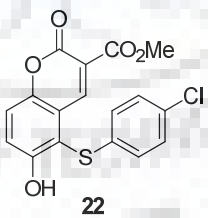

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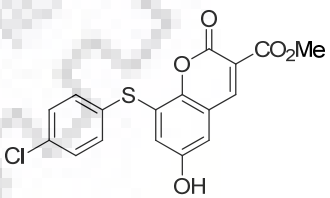

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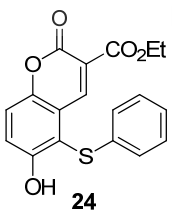

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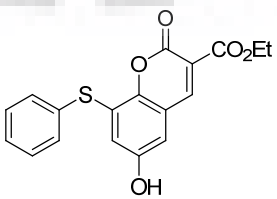

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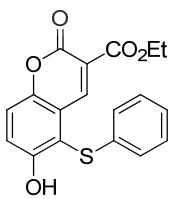

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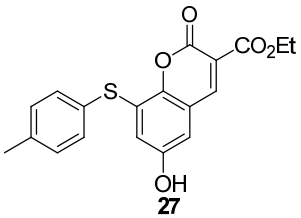

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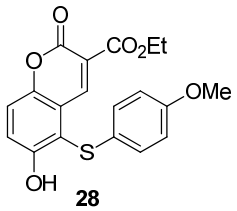

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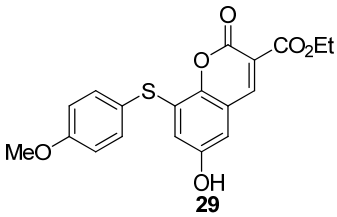

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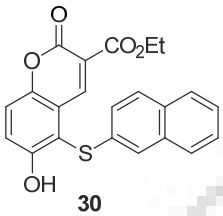

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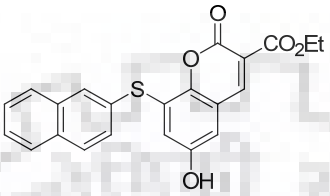

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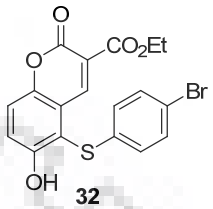

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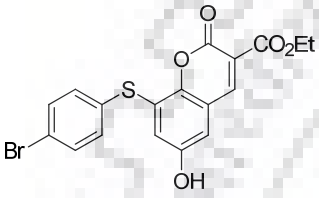

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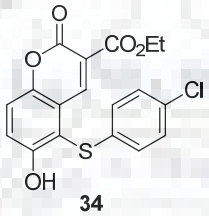

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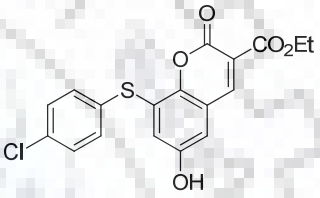

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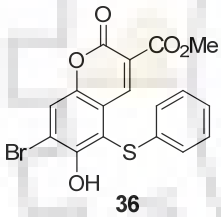

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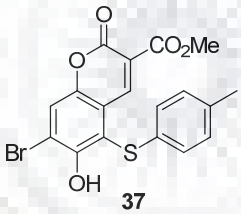

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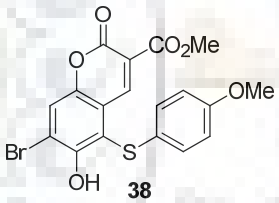

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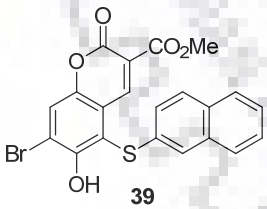

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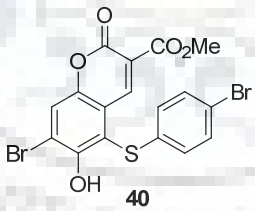

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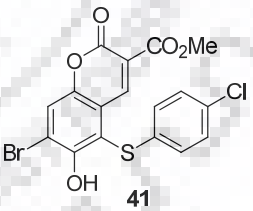

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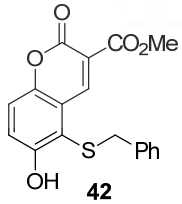

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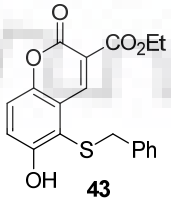

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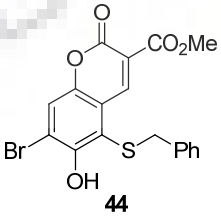

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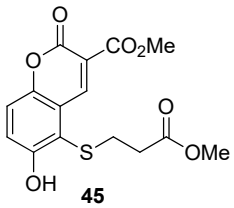

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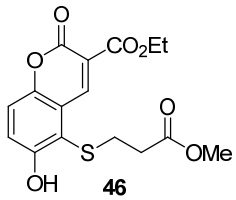

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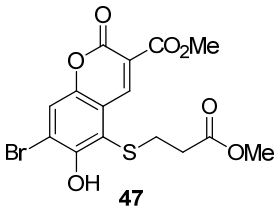

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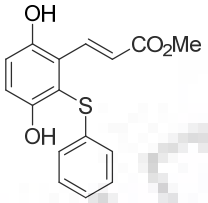

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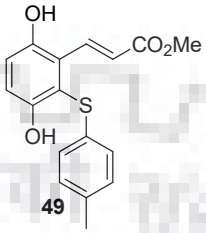

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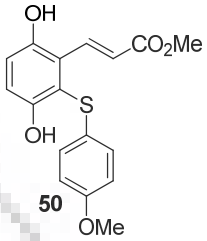

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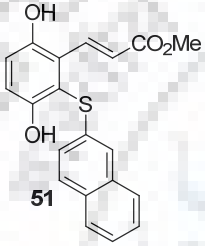

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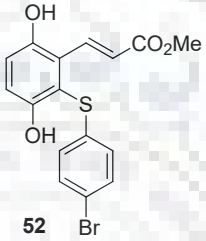

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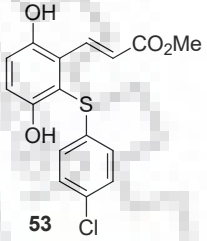

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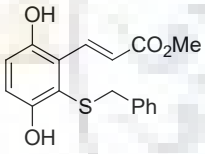

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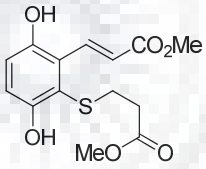

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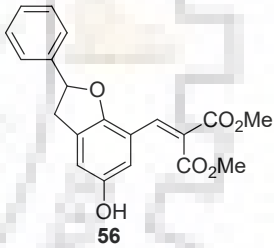

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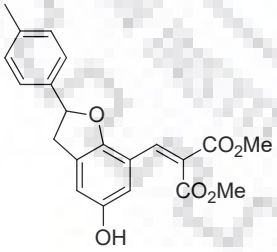

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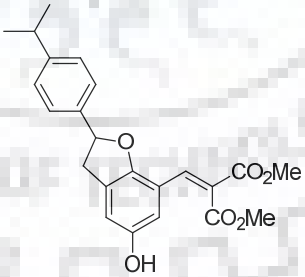

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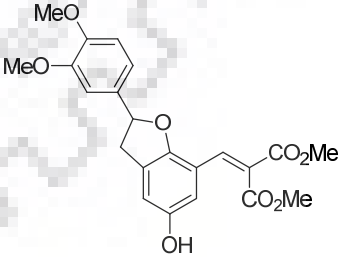

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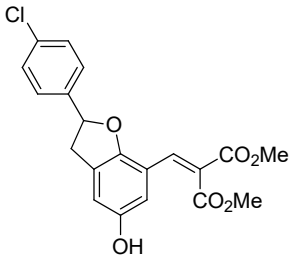

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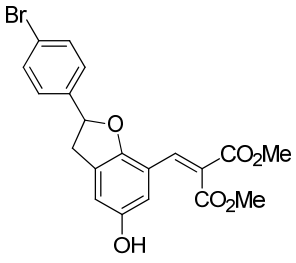

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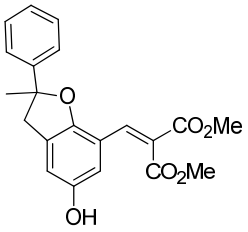

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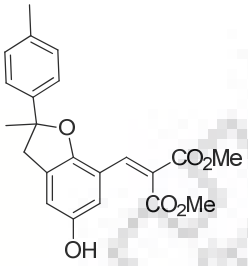

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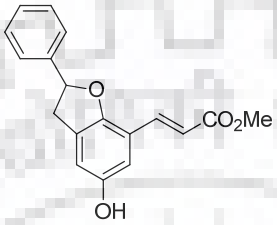

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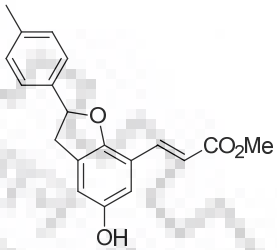

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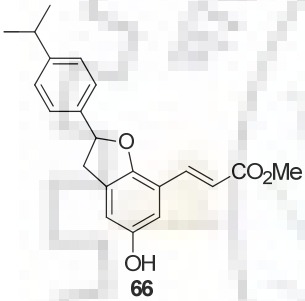

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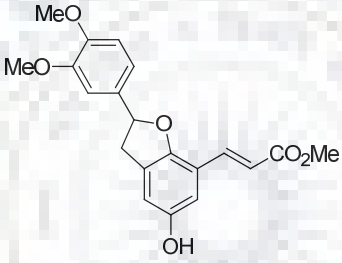

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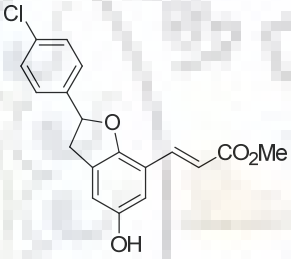

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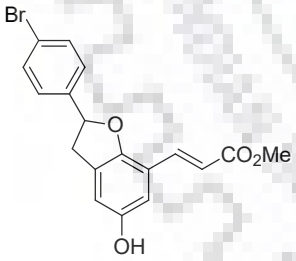

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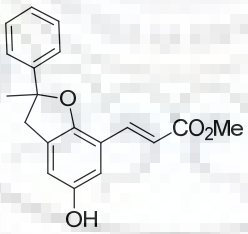

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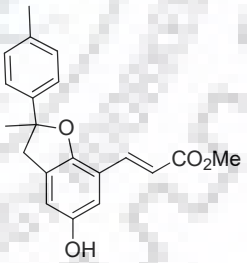

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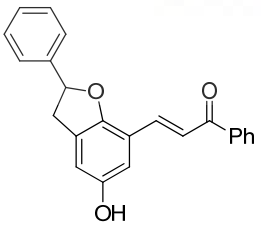

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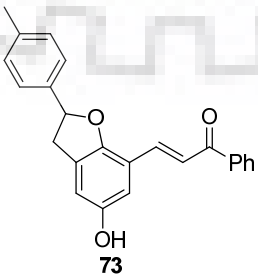

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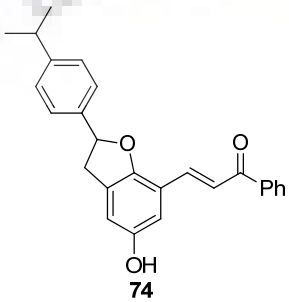

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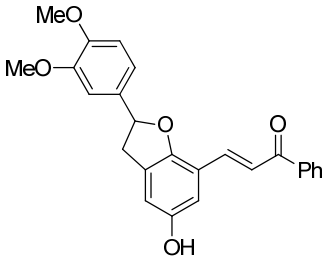

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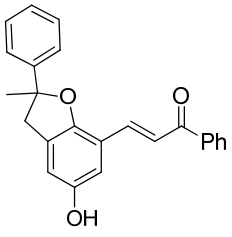

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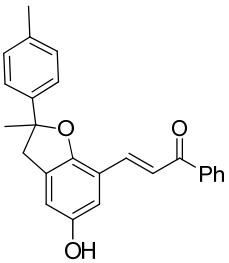

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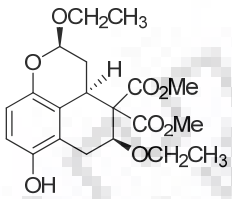

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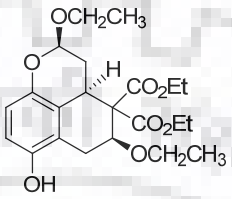

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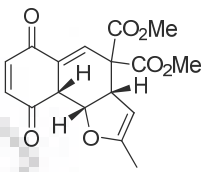

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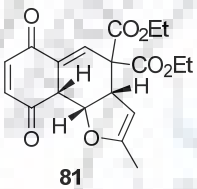

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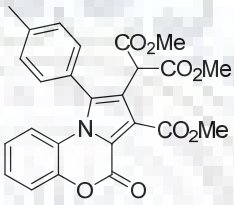

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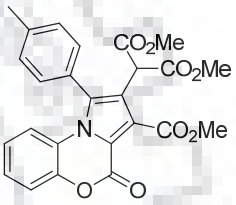

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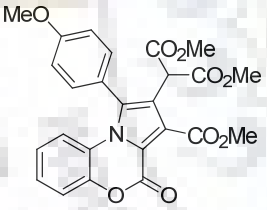

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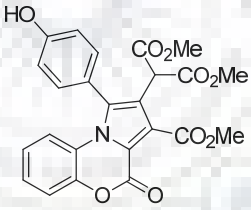

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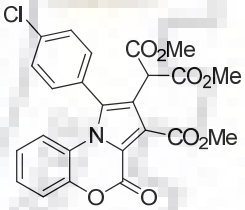

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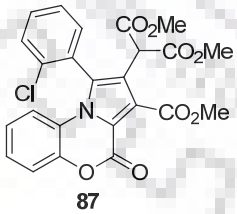

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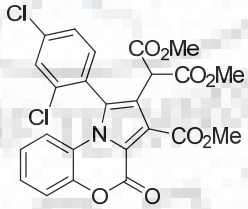

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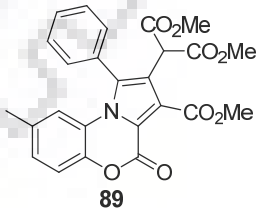

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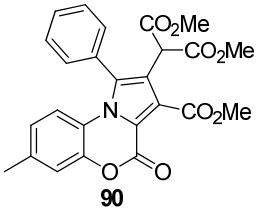

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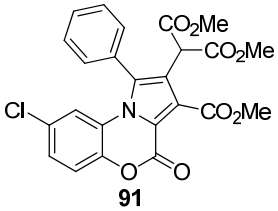

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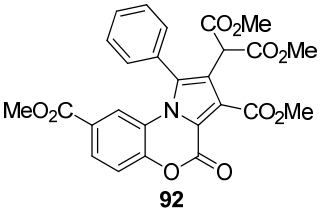

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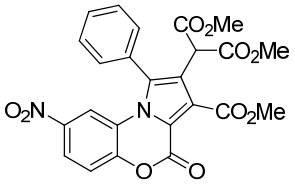

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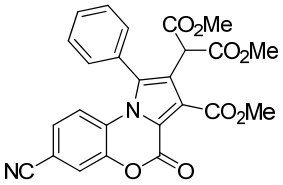

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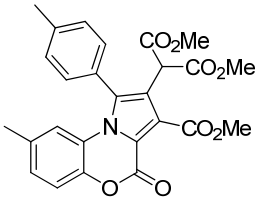

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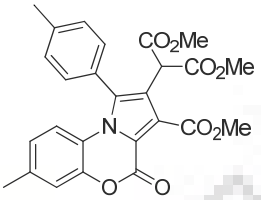

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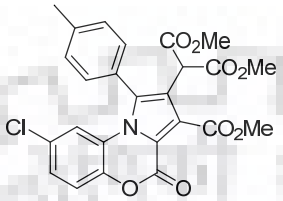

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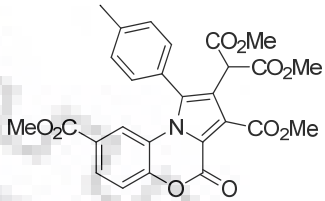

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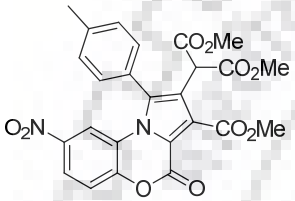

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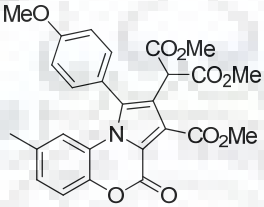

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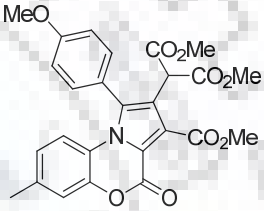

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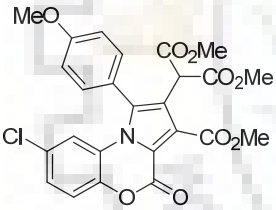

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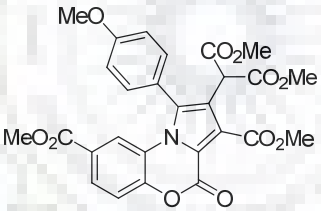

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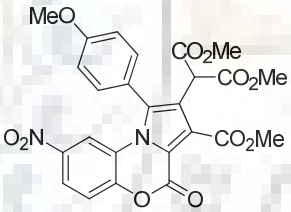

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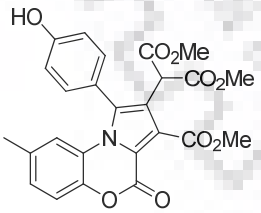

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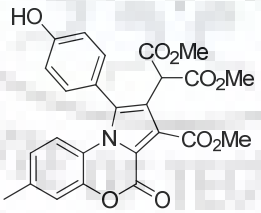

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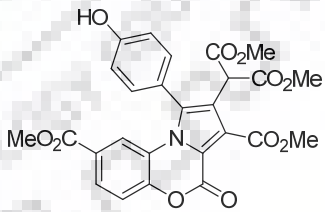

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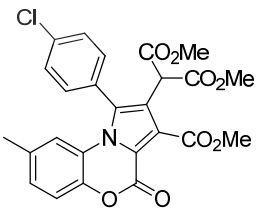

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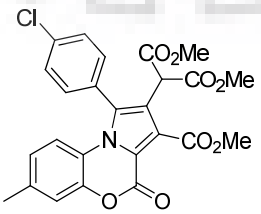

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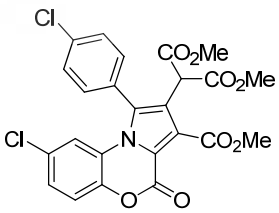

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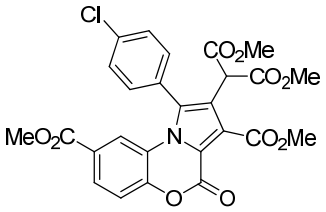

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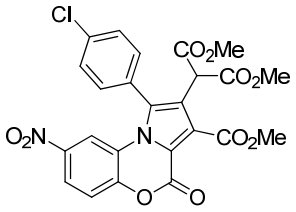

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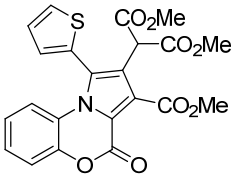

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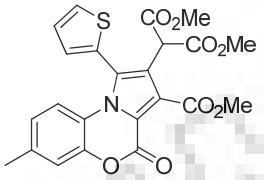

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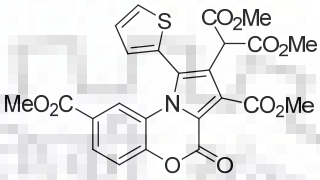

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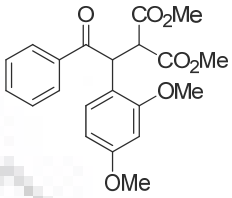

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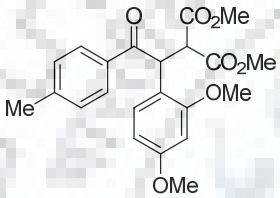

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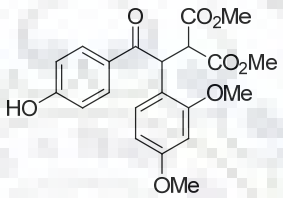

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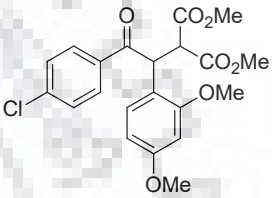

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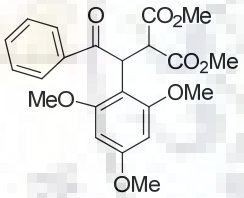

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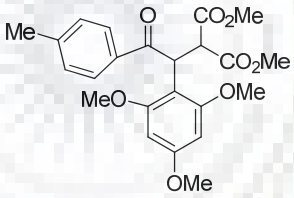

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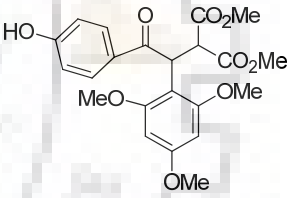

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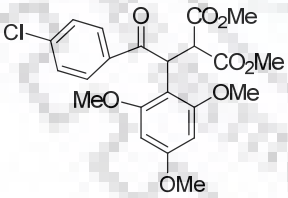

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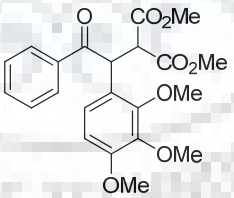

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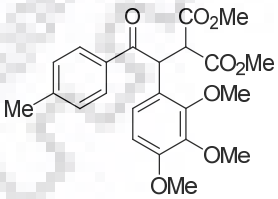

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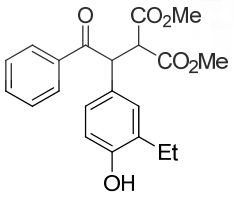

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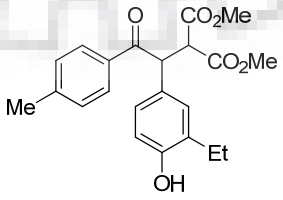

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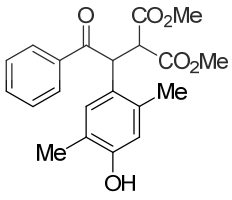

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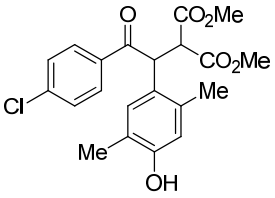

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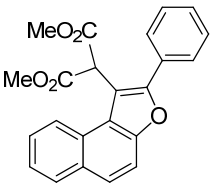

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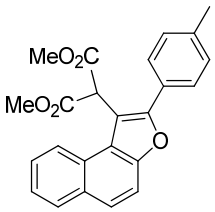

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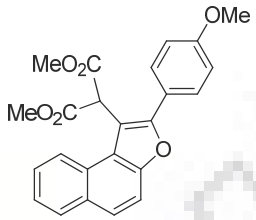

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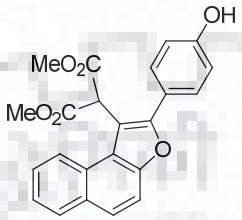

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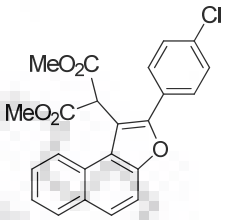

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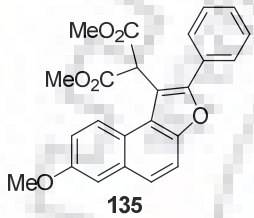

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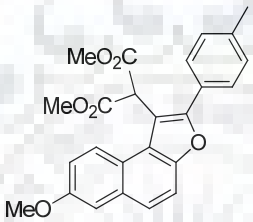

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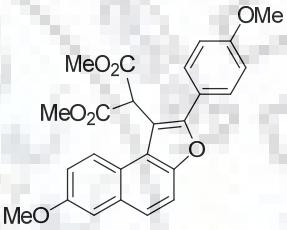

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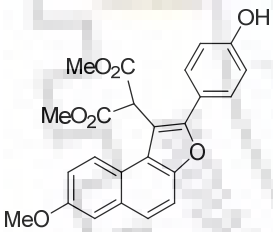

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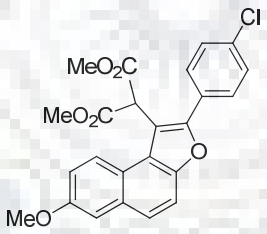

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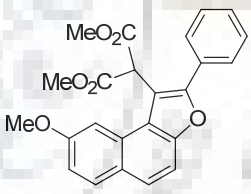

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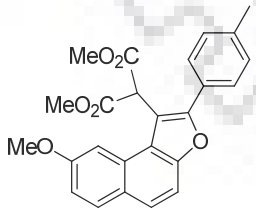

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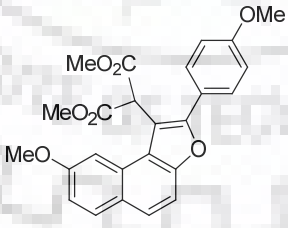

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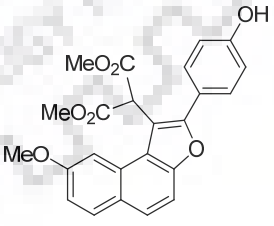

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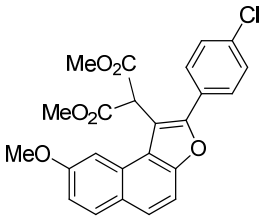

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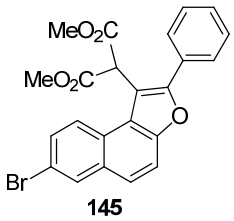

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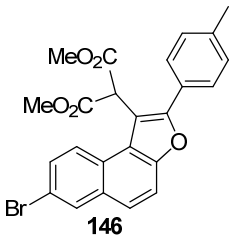

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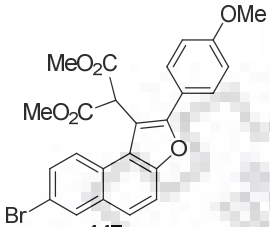

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VITAE

The author was born on 11th July 1989 at kota, Rajasthan. Following her early education she joined J. D. B. Girls College, Kota and received her B.Sc. and M.Sc. degree from University of Kota in 2009 and 2011. She was awarded CSIR NET-JRF (conducted by CSIR) and secured 31st rank in June 2012 and registered for Ph.D. in January 2013 at Indian Institute of Technology Roorkee. She was awarded JRF in January 2013-14 and SRF 2015-17 by CSIR, New Delhi. She Qualified her Graduate Aptitude Test in Engineering in January 2013 and January 2018.

LIST OF PUBLICATIONS

1. Domino reaction of alkenyl *p*-benzoquinones: Access to aryl sulfide derivatives of coumarins.
   Bisht, **S.**; Peddinti, R. K.
   Tetrahedron **2017**, *73,* 2591–2601.
2. $FeCl_3$-mediated domino reaction of benzoxazinones with aroylmethylidene malonates: Synthesis of functionalized pyrrolobenzoxazines.
   Bisht, **S.**; Peddinti, R. K.
   J. Org. Chem. **2017**, *82*, 13617–13625.
3. Regioselective synthesis of bicyclic and polycyclic systems by cycloaddition reactions of alkenyl *p*-benzoquinones.
   Bisht, **S.**; Rani, R.; Peddinti, R. K.
   J. Org. Chem. **2018**, *83*, 75–84.
4. Iodine catalyzed Friedel-Crafts/Michael addition reactions of electron-rich arenes, β-naphthol derivatives with aroylmethylidene malonates: An efficient access to α-substituted aryl ketones and functionalized naphthofuran derivatives.
   Bisht, **S.**; Peddinti, R. K.
   Manuscript under preparation.

CONFERENCES AND WORKSHOPS ATTENDED

- Presented poster on "Synthesis of pyrrolobenzoxazines *via* $FeCl_3$-mediated domino reaction of benzoxazinones with aroylmethylidene malonates" in ACS on campus held at Indian Institute of Roorkee, on 7th February 2018.
- Presented poster on "Synthesis of functionalized pyrroles *via* domino reaction of benzoxazinones with aroylmethylidene malonates" in CFOS-contemporary facets in organic synthesis held at IIT-Roorkee during December 22–24, 2017.
- Presented poster on "Regioselective synthesis of coumarin fused aryl sulfide derivatives *via* cascade Michael reaction of thiols to alkenyl *p*-benzoquinones" in International Conference on Advancing Green Chemistry: Building a Sustainable Tomorrow" held at University Conference Centre, University of Delhi during October 3–4, 2017
- Presented poster on "Domino reactions of alkenyl *p*-Benzoquinones: Access to aryl sulfide derivatives of coumarins" in 21st CRSI-ACS held at IICT-hyderabad during July 14–16, 2017.
- Attended CRSI-ACS Symposium on 13 July 2017 in Hyderabad, India.
- Participated in the National workshop entitled "Applications of high-field NMR spectrometers in drug discovery" held at the NMR centre, SAIF division, CSIR-Central Drug Research Institute, Lucknow during August 24–26, 2016.